

Breakthroughs in Diagnosing Prostate Cancer

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- Multidisciplinary approach to prostate cancer
- Epidemiology - incidence and risk factors
- PSA screening
- Elevated PSA, now what??
- Noninvasive testing before biopsy
 - MRI
 - Genomic markers
- Additional prostate evaluation if no prostate cancer
- Diagnosis - Gleason score, Grade, Stage
- Treatment Options



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**MULTIDISCIPLINARY
APPROACH**

- Urologists
- Radiation oncologists
- Medical oncologists
- Radiologists
- Genetic testing and counseling

- Significant Benefits
 - Improved outcomes
 - Shared decision making
 - More patient satisfaction with treatment decision
 - Offer multimodal therapies

- Multidisciplinary approach to prostate cancer
- [Epidemiology - incidence and risk factors](#)
- PSA screening
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Prostate Cancer


#1 cancer

#2 killer

Estimated New Cases

Males


Prostate	248,530	26%
Lung & bronchus	119,100	12%
Colon & rectum	79,520	8%
Urinary bladder	64,280	7%
Melanoma of the skin	62,260	6%
Kidney & renal pelvis	48,780	5%
Non-Hodgkin lymphoma	45,630	5%
Oral cavity & pharynx	38,800	4%
Leukemia	35,530	4%
Pancreas	31,950	3%
All Sites	970,250	100%



Estimated Deaths

Males

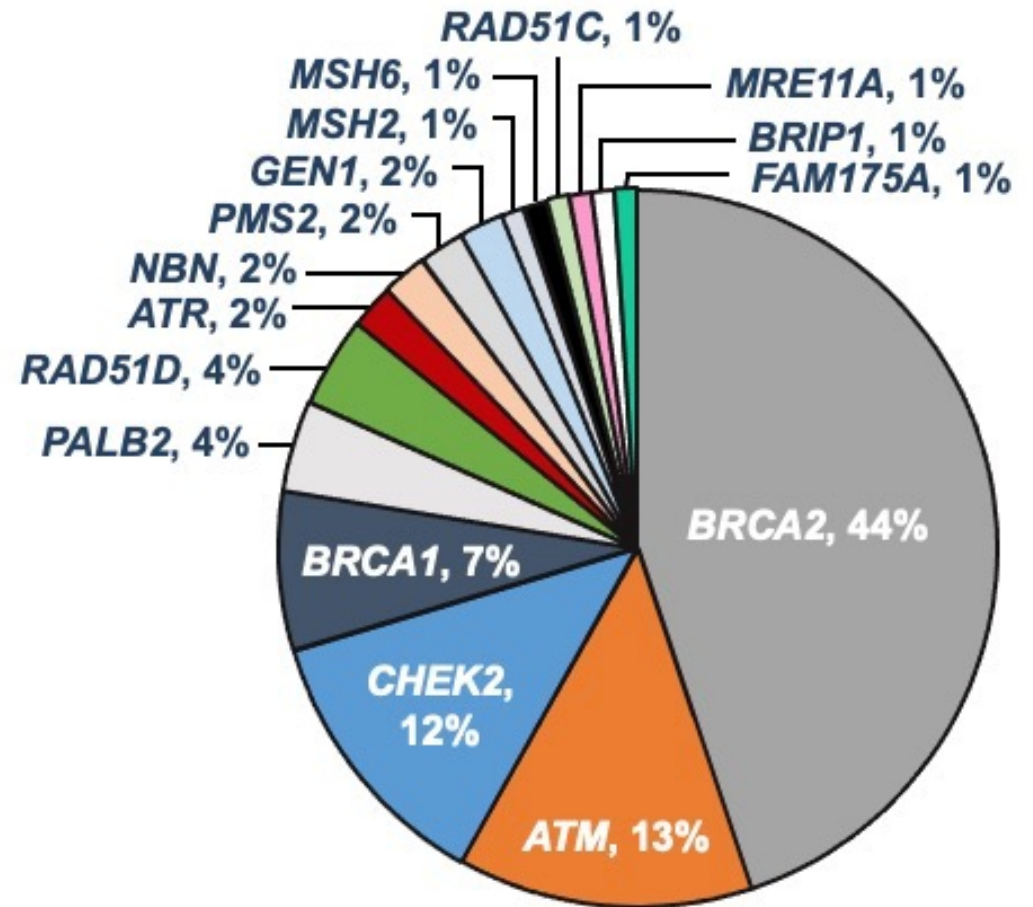
Lung & bronchus	69,410	22%
Prostate	34,130	11%
Colon & rectum	28,520	9%
Pancreas	25,270	8%
Liver & intrahepatic bile duct	20,300	6%
Leukemia	13,900	4%
Esophagus	12,410	4%
Urinary bladder	12,260	4%
Non-Hodgkin lymphoma	12,170	4%
Brain & other nervous system	10,500	3%
All Sites	319,420	100%



- Male gender and older age
- Family history
 - Father w prostate ca 2x more likely
 - Brother w prostate ca 4x more likely
 - Father and brother w prostate ca 8x more likely
- Ethnicity
 - African Americans 1.6 x more likely to have disease
 - Americans 2.2 x more likely to die of disease

- Family history
- Cancers
 - Metastatic prostate cancer
 - Ovarian cancer
 - Male or female breast cancer
 - Colorectal
 - Endometrial cancer
 - Pancreatic cancer
- Ashkenazi Jewish ancestry
- Multiple cancers in family

- Germline mutations
- BRACA2
- 11.8% metastatic prostate cancer
- 6% localized high-risk prostate cancer
- 2% low-to-intermediate-risk prostate cancer
- Future = targeted treatment using PARP inhibitors



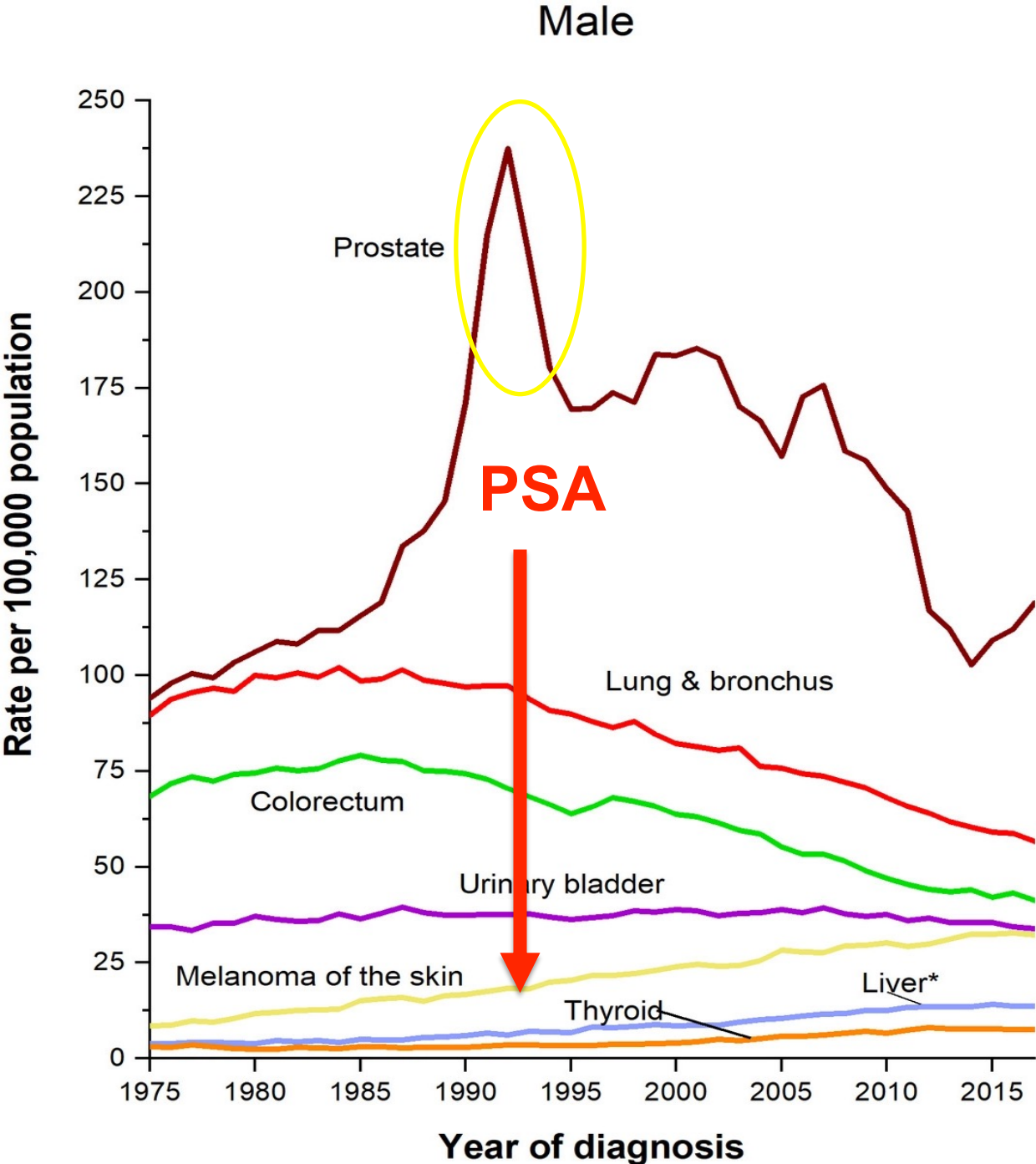
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What is the PSA?

- Prostate specific antigen (PSA)
- PSA is a blood test.
- Measures the amount of PSA in the blood stream.
- Secreted by normal and abnormal prostate cells.

- PSA can be higher in prostate cancer but also in:
 - Large prostates = Benign Prostate Hyperplasia (BPH)
 - Infections (prostatitis, urinary tract infections, epididymitis)
 - Recent ejaculation
 - Trauma
 - Recent urinary catheterization
 - Recent biking

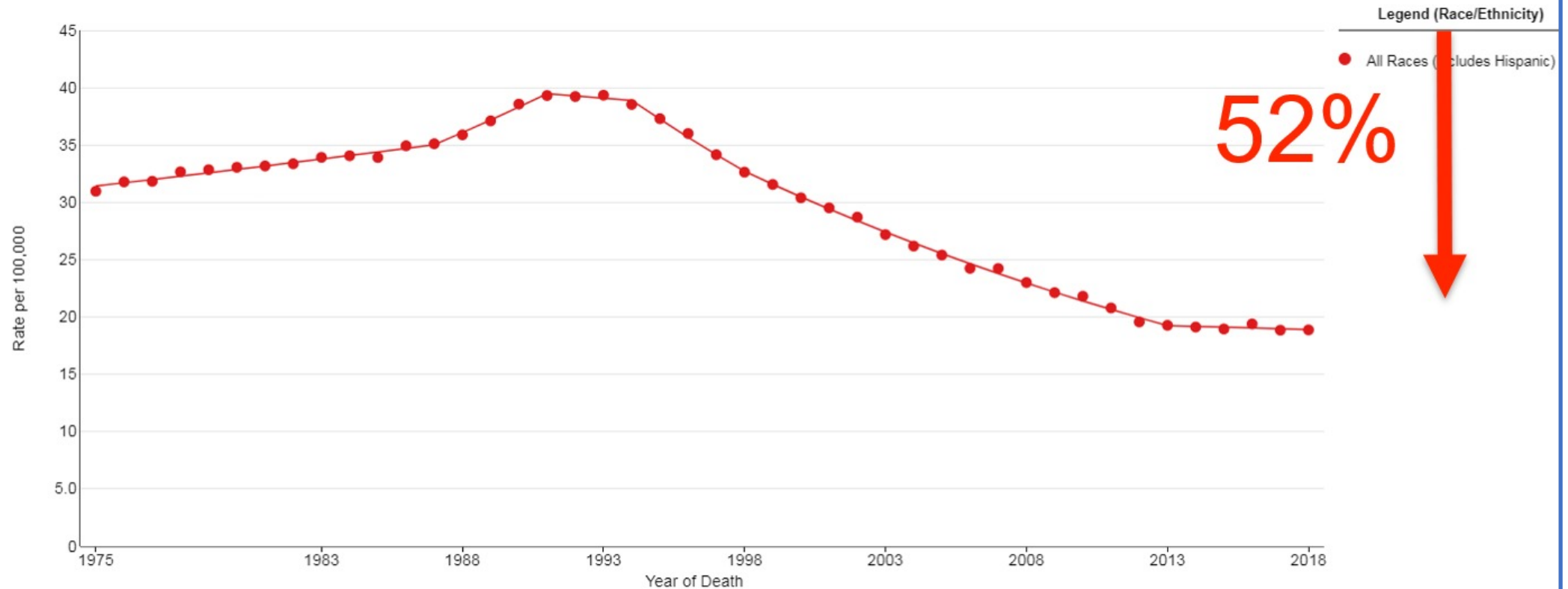
History of PSA and Prostate Cancer



Siegel RL, CA Cancer J Clin. 2021 Jan;71:7-33.

Mortality from Prostate Cancer

Prostate
Long-Term Trends in U.S. Age-Adjusted Mortality Rates, 1975-2018
Male By Race/Ethnicity, All Ages



Created by <https://seer.cancer.gov/explorer> on Sun Jul 18 2021.
US Mortality Files, National Center for Health Statistics, CDC.
Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
The Annual Percent Change (APC) and Average Annual Percent Change (AAPC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software [<http://surveillance.cancer.gov/joinpoint/>], Version 4.9, March 2021, National Cancer Institute.
The APC's/AAPC's direction is "rising" when the entire 95% confidence interval (C.I.) is above 0, "falling" when the entire 95% C.I. is lower than 0, otherwise, the trend is considered stable.
For years prior to 1990, the Census Bureau has only provided county-level population estimates for White, Black, and Other races.
Cancer sites are defined using the SEER Cause of Death Recode 1969+ (04/16/2012) [https://seer.cancer.gov/codrecode/1969+_d04162012/index.html].

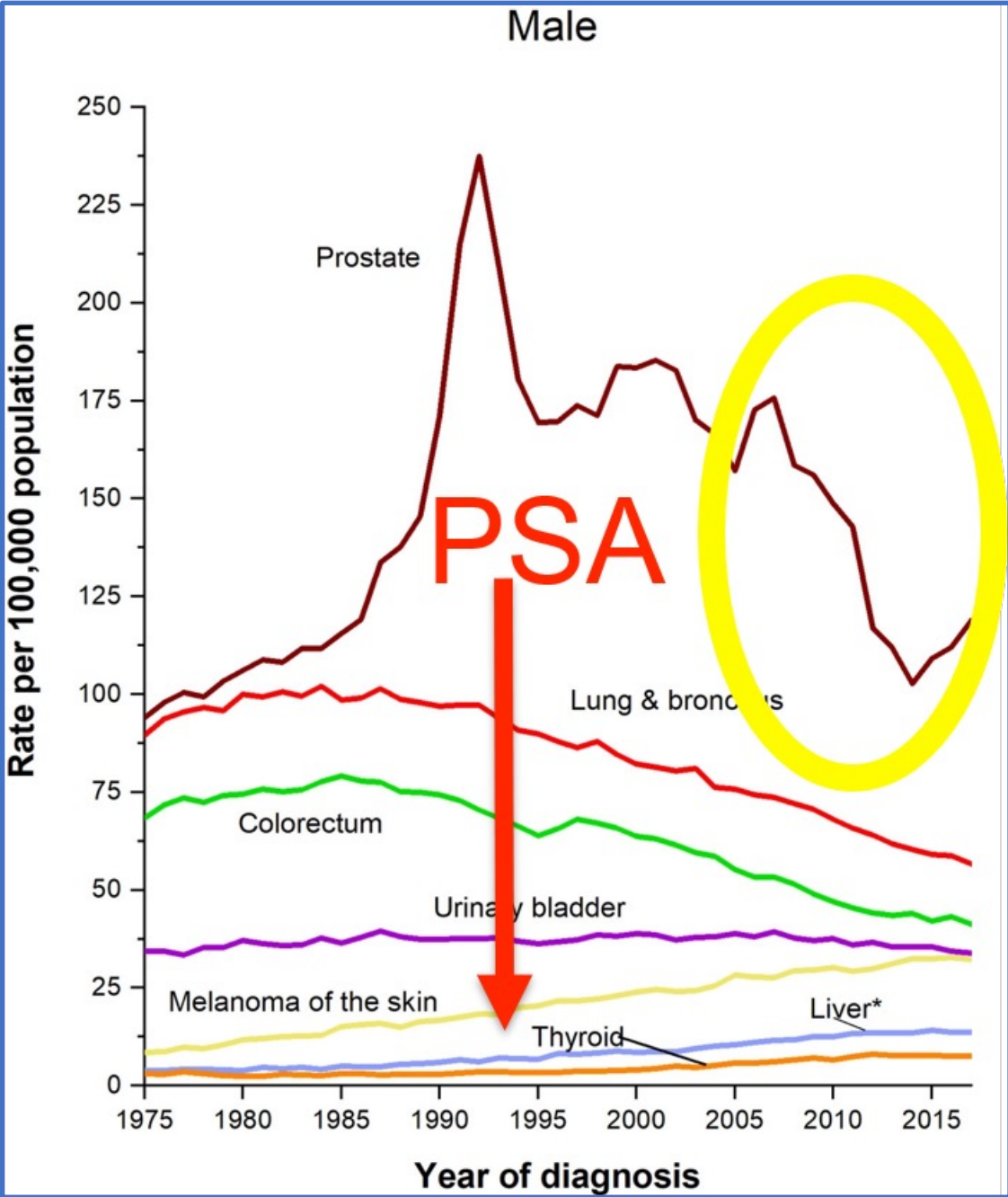
AUA Prostate cancer
updates 2021

US Preventative Task Force 2008-2012

- Discouraged use of PSA
- Task force
 - Panel of 16 experts:
 - family medicine, general internal medicine, nurses, obstetrician-gynecologists, occupational medicine physicians, and pediatricians.
 - **PANEL DID NOT INCLUDE UROLOGISTS OR CANCER SPECIALISTS**



Incidence of Prostate Cancer



MORE DEATHS FROM PROSTATE CANCER

Prostate cancer **DEATHS INCREASED** in 2018 for the first time in 2 decades from an estimated 26,730 in 2017 to 29,430 in 2018.

For 2022, the estimate is 34,500 deaths from prostate cancer.

- For men >70yrs
 - USPTF continues to recommend against PSA testing.
- **SHARED DECISION MAKING**

Prostate Cancer Screening Recommendation

2008 - 2016	2017
D/I	C
Discourage the use of this service	Offer or provide this service for selected patients (55 - 69), depending on individual circumstances

Join **ZERO** in the fight for every man to have access to early detection!

ZERO

Age < 40

- No reason to screen.

Ages 40 - 54

- No screening if at “average risk” but you should be screened if:
 - A family history of a first degree relative (sibling or parent) with prostate, breast, ovarian or pancreatic cancer
 - African-American

Ages 55 - 69

- This is the age group where screening is **most important**. This should be a **shared discussion** with your physician.

Ages > 70

- Continue screening if you are in excellent health with a 10 -15 year life expectancy, otherwise no screening is necessary.
- This should be a **shared discussion** with your physician.

- According to the American Cancer Society, if your PSA is:
 - less than 2.5, you can have your blood tested every four years
 - greater than 2.5, it should be done every two years

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- Maximize detection of **lethal** prostate cancer in a patient with life expectancy of greater than 10 -15yrs
- Accurately characterize the biology of the tumor
- Risk stratification of the cancer
 - Minimize immediate treatment (over-treatment) of indolent cancers.
 - Proceed with treatment of potentially lethal prostate cancers.

- Digital rectal exam (DRE) + PSA
- A DRE should be done in all men with an abnormal PSA.
- If abnormal DRE and elevated PSA —
 - Positive predictive value for prostate cancer is 48.6% vs 22.4% for men elevated PSA and a normal DRE.
- Only 25% of men with PSA 4-10 ng/mL have a subsequent positive biopsy.
- If a new high PSA is observed, then repeat the test.
 - 5 days pelvic rest prior to test and at least 1 month from last PSA

- Some prostate cancers do not make PSA.
- Positive predicative value of an abnormal DRE in men with normal PSA only 4%– 21%.
- BUT an abnormal DRE should be evaluated!!

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- Men (and their urologist) want to avoid a biopsy if possible.
- A prostate biopsy is still considered “gold standard”.
- BUT noninvasive options to determine if a biopsy is needed are always discussed.

Goal - NOT just find prostate cancer, but find potentially lethal prostate cancer.

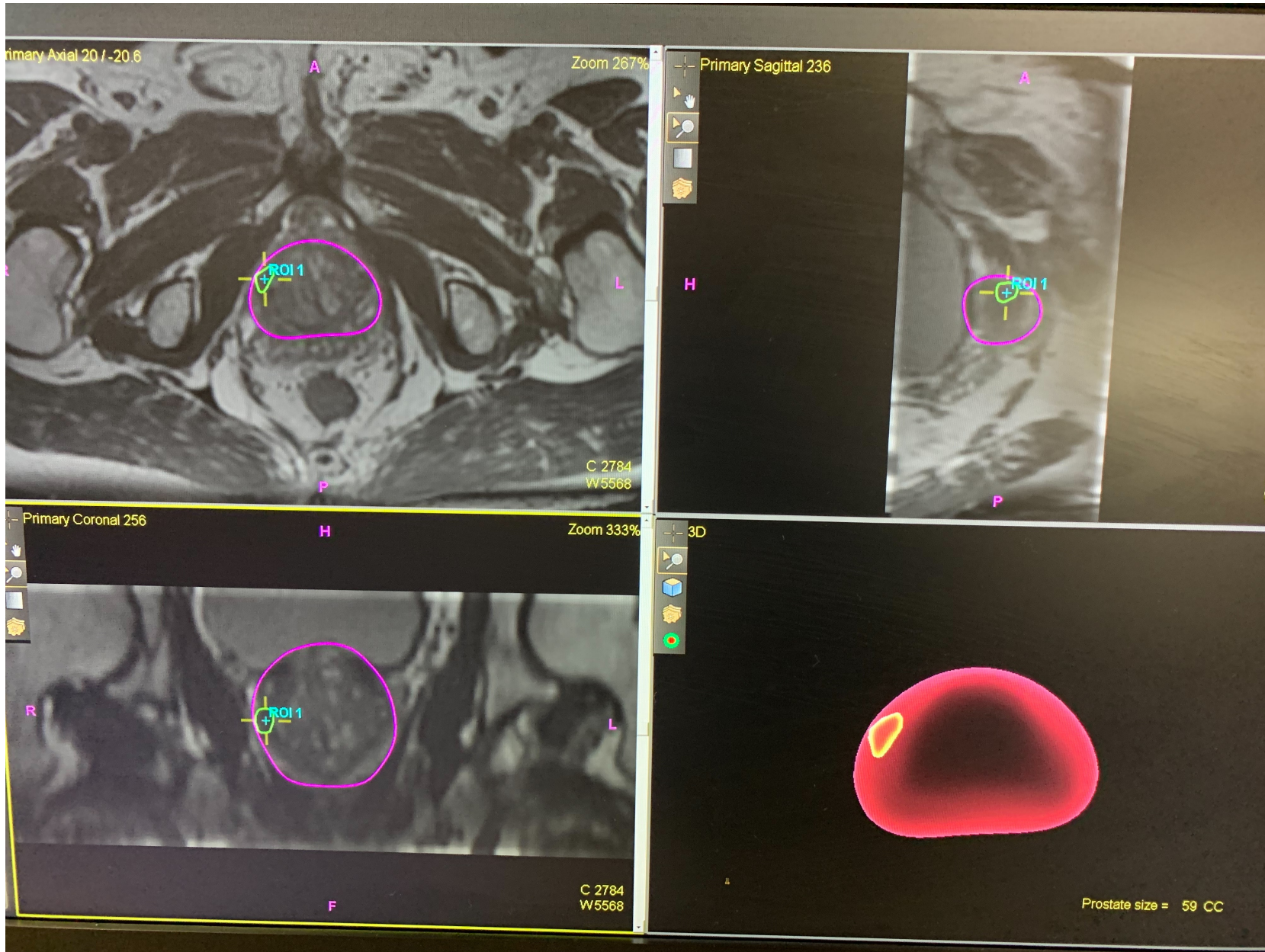
- Multiparametric (mp) MRI of the prostate
 - Anatomic evaluation - a “window” into the prostate
- Benefits
 - Characterize suspicious lesions felt on DRE
 - Evaluate elevated PSA to help decide on the need for biopsy
 - Perform **targeted biopsy** of a suspicious lesion
 - Reduced biopsy rate of benign tissue (PIRAD1 and PIRAD2 tissue)
 - Reduce the identification of low-risk prostate cancer by 87%
 - Increase finding intermediate/high-risk tumors by 18%
 - Active surveillance to follow lesions

Prostate Imaging – Reporting and Data System version 2

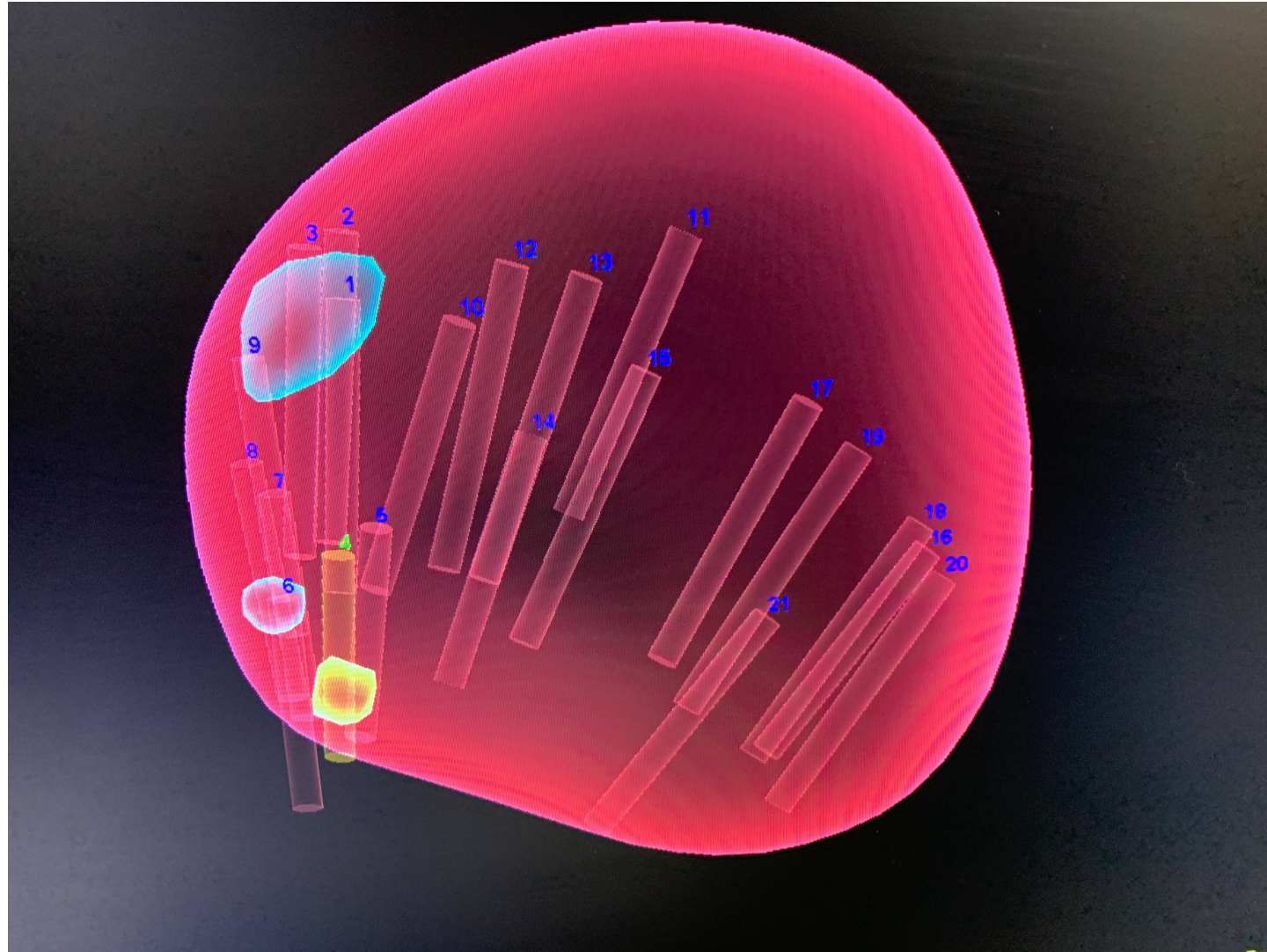
PI-RADS classification	Definition	Total T2 + DWI + DCE score	Total T2 + DWI + DCE + MRS score
I	Most probably benign	3 - 4	4 - 5
II	Probably benign	5 - 6	6 - 8
III	Indeterminate	7 - 9	9 - 12
IV	Probably malignant	10 - 12	13 - 15
V	Most probably malignant	13 - 15	17 - 20

PI-RAD IV and V should have targeted biopsy

MRI Fusion Biopsy Set Up

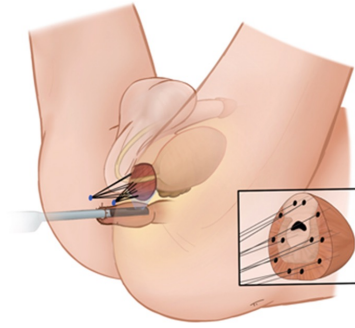
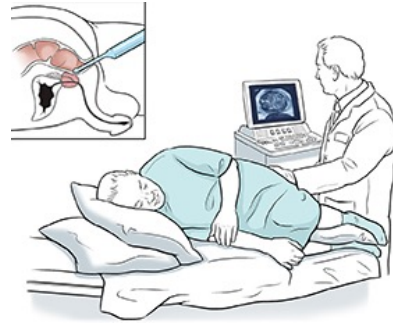


MRI Fusion Biopsy Completed



- Not perfect (no test is)
- MRI before biopsy approach could miss 24% of potentially lethal prostate cancers.
- Interobserver variability
 - One radiologist scores prostate lesions one way and another radiologist scores the lesion another way.
 - Boulder Community Health radiologists read all our scans
 - Two Boulder Community Health radiologists often read each MRI

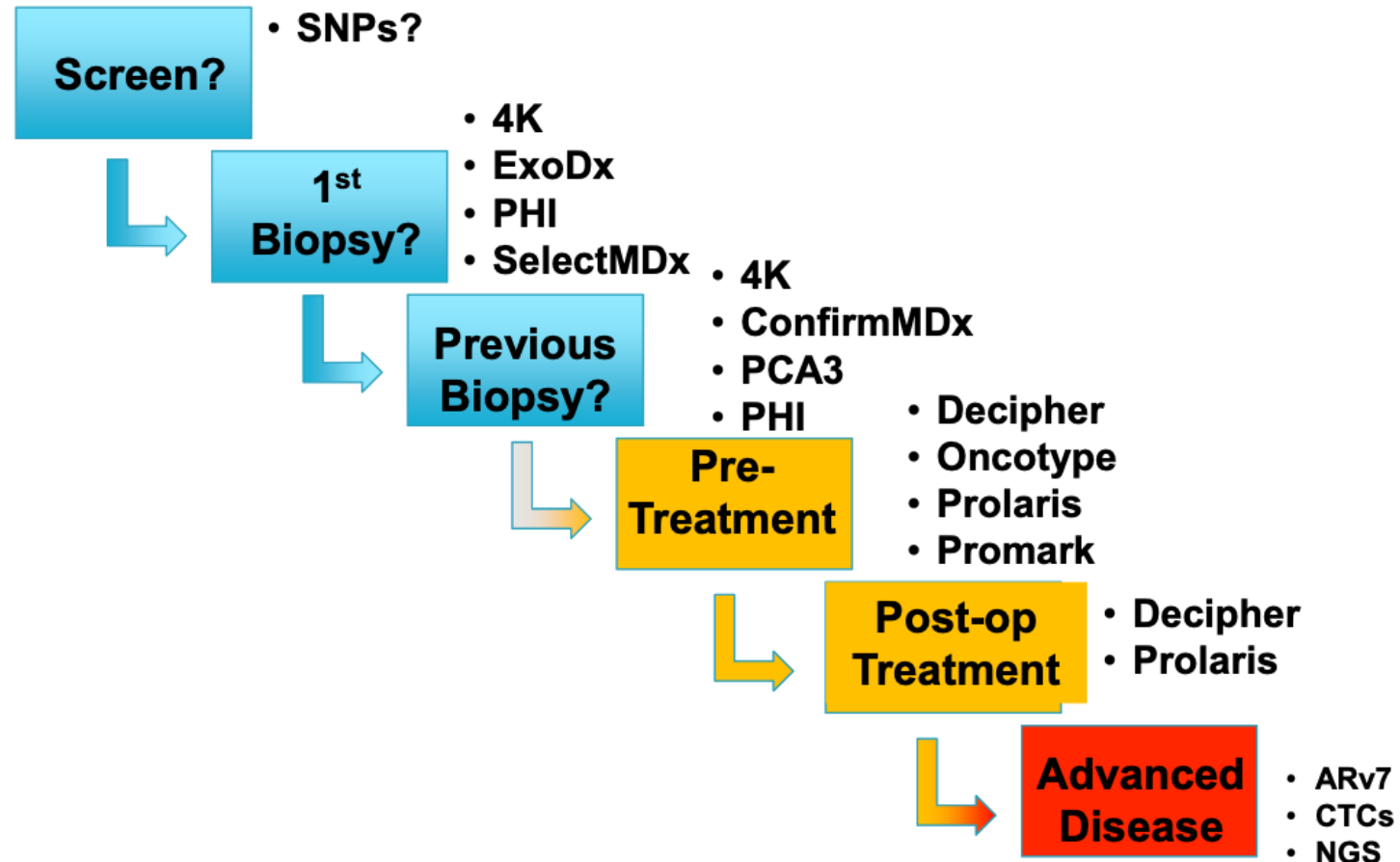
Prostate Biopsy Technique



Comparison	Transrectal	Transperineal
Infection	0.38-4.2%	0.6-1.03%
Urinary obstruction (need for foley)	0-0.8%	0.5-7.9%
Need for anxiolytic (valium)	NO	YES
Need for general or spinal anesthesia	NO	YES
Accuracy of detecting prostate cancer	Same	Same
Cost	Less expensive	More expensive

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Disease State Biomarkers (partial list)



- Algorithm patient's age, family history, race, digital rectal exam, and previous biopsy status
- Panel of 4 known markers
 - total PSA
 - free PSA
 - intact PSA
 - hK2
- Gives percent likelihood of finding potentially lethal cancer on biopsy
- Biopsies can be avoided, high grade cancer detected, but 5-10% cancers are missed in reported trials

- Urine assay for RNA
- Urine collected after digital rectal exam
- *DLX1* and *HOXC6* mRNA
- Has a 95% negative predictive value and 93% sensitivity for the detection of clinically significant prostate cancer
 - Translation - if low risk result, then highly likely there is no cancer, and the test has good accuracy for determining if there is cancer.
- Reduces the number of unnecessary biopsies
 - 53% prostate biopsies can be avoided

- Urinary exosomal RNA
- No DRE required
- For high-grade disease:
 - Excellent negative predictive value of 97.5% (if low risk, then 97.5% chance there is no cancer)

- If prostate biopsy comes back benign, can do additional genetic testing with ConfirmDx.
- Hypermethylation of the promoter regions of *GSTP1*, *APC*, and *RASSF1* is assessed in core biopsy tissue samples.
- Improve the stratification of men with prior negative biopsy being considered for repeat prostate biopsy.
 - Who needs to be followed more aggressively?

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- If no cancer found or low grade prostate cancer found and the man has bothersome urinary symptoms.

Bothersome Urinary Symptoms

- Evaluate urinary retention
- Evaluate bladder health



- Discuss medical vs surgical intervention
- Discuss minimally invasive treatment options

International Prostate Symptom Score (I-PSS)

Patient Name: _____ Date of birth: _____ Date completed: _____

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	1 Time	2 Times	3 Times	4 Times	5 Times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							27

Score: 1-7: Mild 8-19: Moderate 20-35: Severe

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

Urolift Center of Excellence



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Dr. Carolyn Fronczak

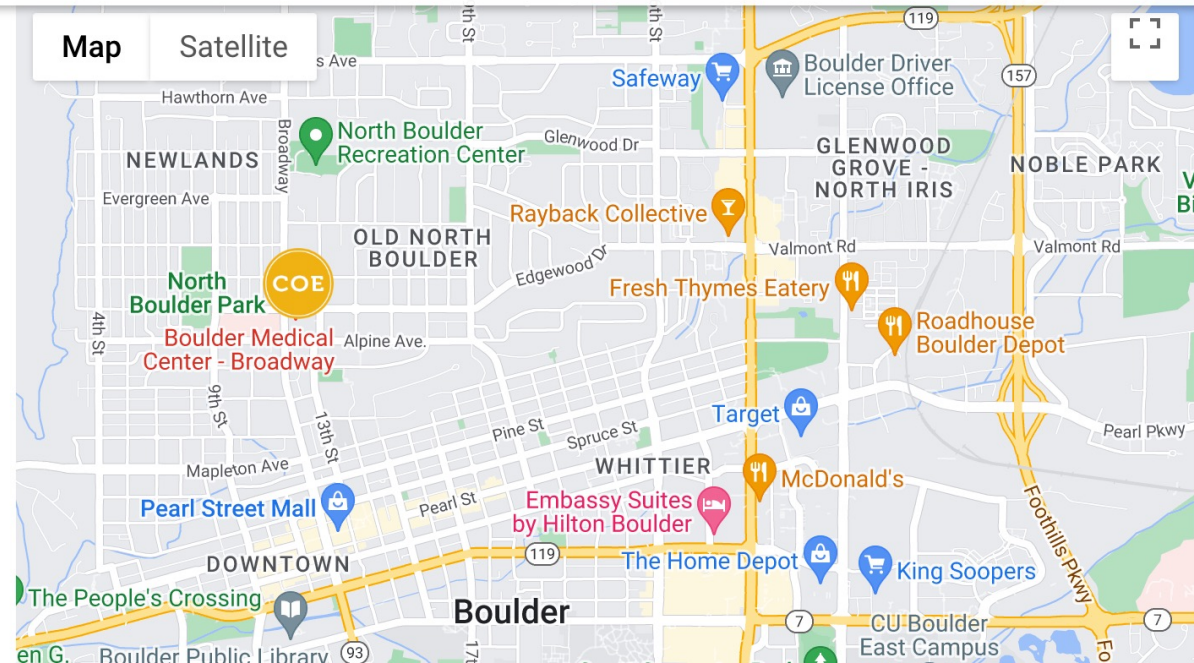
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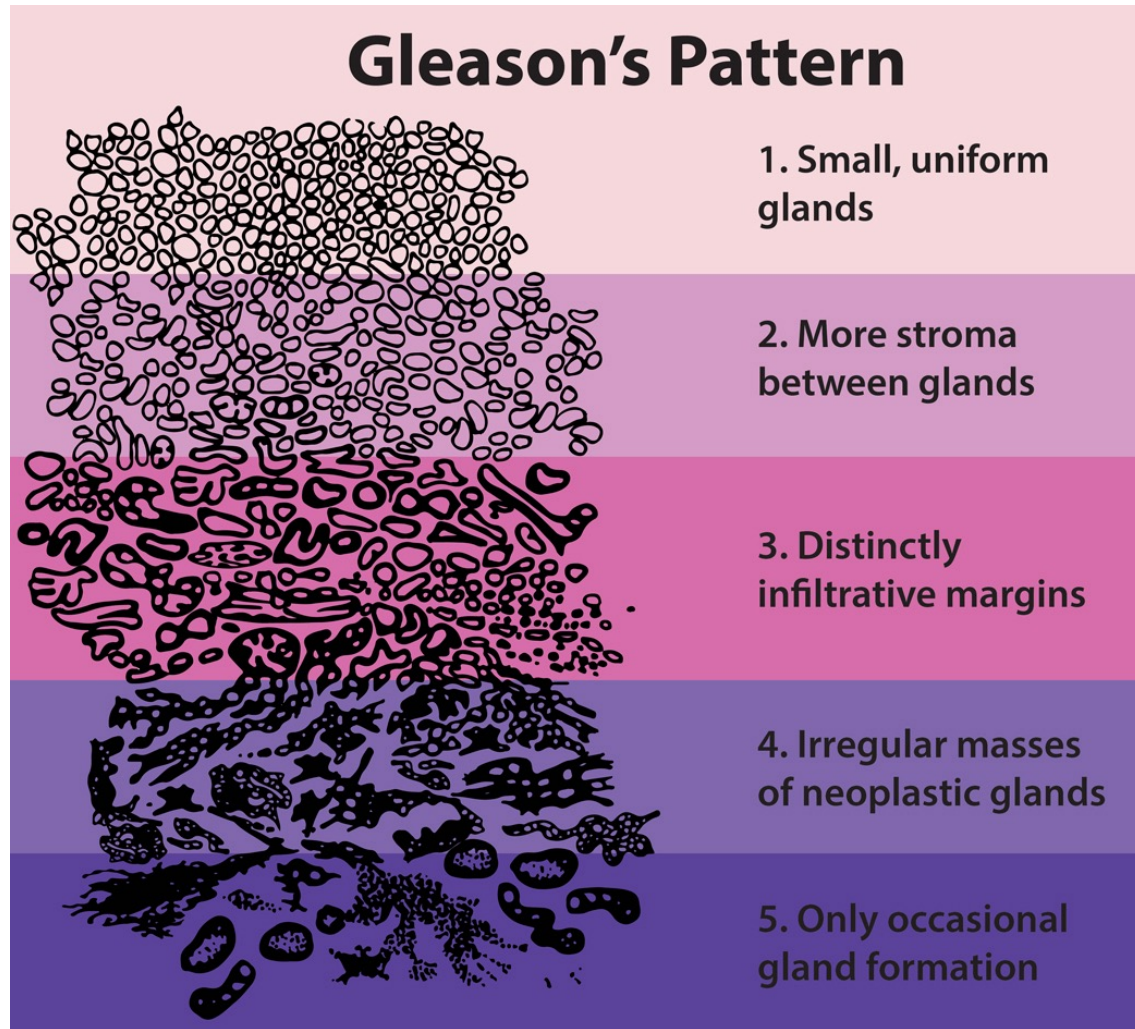
Distance: 4.28 miles
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Gleason score

- $3+3=6$
- $3+4=7$
- $4+3=7$
- $4+4=8$
- $4+5=9$
- $5+4=9$
- $5+5=10$



Grade group

Well differentiated

Moderately differentiated

Poorly differentiated/
Anaplastic

- 1
- 2
- 3
- 4
- 5
- 5

Prostate Cancer Risk Stratification

	AUA Risk Category	NCCN Risk Category
Very Low	—	PSA \leq 10 ng/mL, Gleason score \leq 6, clinical stage T1c, $<$ 3 positive biopsy cores, \leq 50% in each core, and PSA density $<$ 0.15 ng/mL/g
Low	PSA \leq 10 ng/mL, Gleason score \leq 6, and clinical stage T1c or T2a	PSA $<$ 10 ng/mL, Gleason score \leq 6, and clinical stage T1-T2a
Intermediate	PSA $>$ 10-20ng/mL or Gleason score 7, or clinical stage T2b	PSA 10-20 ng/mL, Gleason score 7, or clinical stage T2b-T2c
High	PSA $>$ 20ng/mL or Gleason score 8-10, or clinical stage \geq T2c	PSA $>$ 20ng/mL or Gleason score 8-10, or clinical stage T3a
Very High	—	Clinical stage T3b-T4

Prostate Cancer Risk Stratification

	AUA Risk Category	NCCN Risk Category
Very Low	—	PSA ≤ 10 ng/mL, Gleason score ≤ 6, clinical stage T1c, < 3 positive biopsy cores, ≤ 50% in each core, and PSA density < 0.15 ng/mL/g
Low	PSA ≤ 10 ng/mL, Gleason score ≤ 6, and clinical stage T1c or T2a	PSA < 10 ng/mL, Gleason score ≤ 6, and clinical stage T1-T2a
Intermediate	PSA > 10-20ng/mL or Gleason score 7, or clinical stage T2b	PSA 10-20 ng/mL, Gleason score 7, or clinical stage T2b-T2c
High	PSA > 20ng/mL or Gleason score 8-10, or clinical stage ≥T2c	PSA > 20ng/mL or Gleason score 8-10, or clinical stage T3a
Very High	—	Clinical stage T3b-T4

- **Genomics adds helpful information**
- Each tumor is unique
- What is the REAL RISK of harm by not doing treatment?
- Can you wait and follow the tumor and decide later to do treatment?
- Tumors can get upstaged or downstaged
- Overall survival is “gold standard”BUT...

- **Metastasis free survival** is the STRONGEST surrogate for OVERALL survival in localized prostate cancer.

J Clin Oncol 35, 3097-3104, doi:10.1200/JCO.2017.73.9987 (2017)

- Genomic test.
- Predicts metastasis in a prostate biopsy.
- Use RNA, 22 genes across 7 cancer pathways.
- Divides the results into high, intermediate, and low risk category.
- DECIPHER outperforms all other clinical risk factors for predicting metastasis
 - Better than PSA, stage, Gleason score, NCCN risk categories

Decipher Result

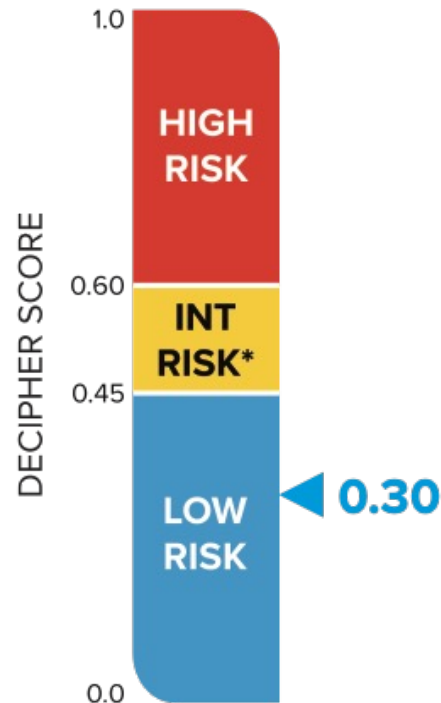
CLINICAL AND PATHOLOGY DETAILS For reference only, not used in calculation of genomic risk

Specimen: **Needle Biopsy**
Clinical Stage: **T1c**

Most Recent PSA: **4.9 ng/mL**
Gleason Score: **3+4**

NCCN Risk Category: **Intermediate**

DECIPHER GENOMIC RISK RESULTS



GENOMIC RISK IS: **LOW**

0.5%	1.2%	2.4%	14.6%
<i>5-year</i>	<i>10-year</i>	<i>15-year</i>	<i>At RP</i>
Risk of Metastasis with RT[†] or RP[‡]	Risk of Prostate Cancer Mortality with RT or RP	Risk of Adverse Pathology	
Clinical studies have shown that Decipher low-risk patients have a favorable prognosis. <ul style="list-style-type: none">• These patients may be ideal candidates for active surveillance.^{1-3,6}• Patients considering definitive treatment may have excellent oncologic outcomes when treated with local therapy alone.^{2-5,9}			

The Decipher score is determined solely by genomic characteristics of the tumor, independent of the NCCN risk category. No other clinical or pathologic parameters factor into the score.

Decipher Result

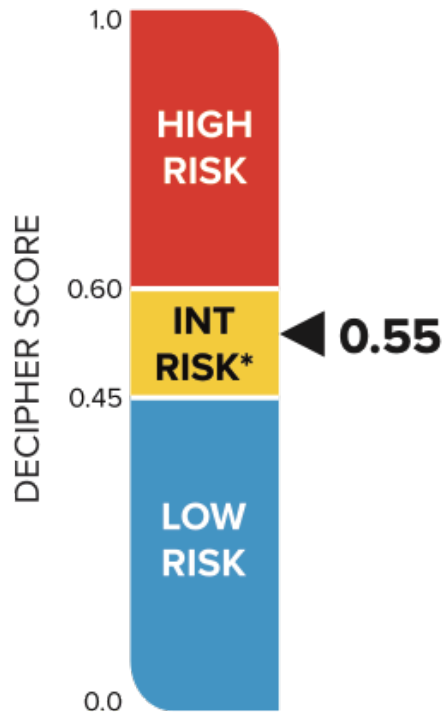
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Clinical Stage: **T1c**

Most Recent PSA: **4.9 ng/mL**
Gleason Score: **3+4**

NCCN Risk Category: **Intermediate**

DECIPHER GENOMIC RISK RESULTS



GENOMIC RISK IS: INTERMEDIATE			
1.1%	2.7%	4.6%	28.4%
<i>5-year</i> Risk of Metastasis with RT [†] or RP [‡]	<i>10-year</i>	<i>15-year</i> Risk of Prostate Cancer Mortality with RT or RP	<i>At RP</i> Risk of Adverse Pathology
Clinical studies have shown that Decipher intermediate-risk patients have an average clinical risk and prognosis. Depending on life expectancy and overall health status: <ul style="list-style-type: none">• These patients may not be ideal candidates for active surveillance.^{1-3,6}• These patients may benefit from definitive therapy.^{2-5,9}			

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Decipher Result

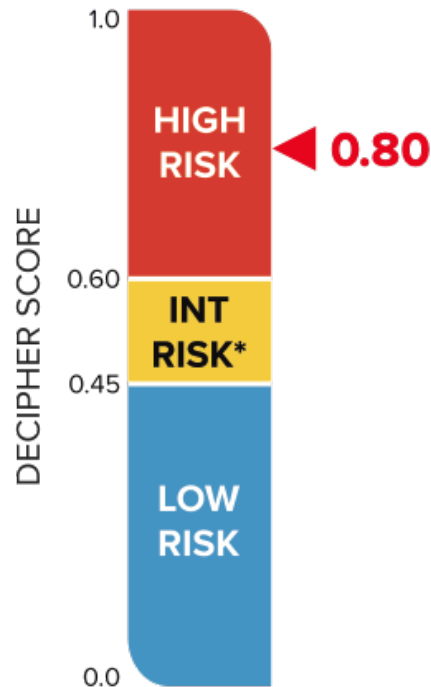
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Specimen: **Needle Biopsy**
Clinical Stage: **T1c**

Most Recent PSA: **4.9 ng/mL**
Gleason Score: **3+4**

NCCN Risk Category: **Intermediate**

DECIPHER GENOMIC RISK RESULTS



GENOMIC RISK IS: **HIGH**

2.6%	6.5%	8.8%	48.1%
<i>5-year</i> Risk of Metastasis with RT [†] or RP [‡]	<i>10-year</i> Risk of Prostate Cancer Mortality with RT or RP	<i>15-year</i> Risk of Prostate Cancer Mortality with RT or RP	<i>At RP</i> Risk of Adverse Pathology
<p>Clinical studies have shown that Decipher high-risk patients have an unfavorable prognosis.</p> <ul style="list-style-type: none"> • These patients may benefit from treatment intensification with multimodal therapy.^{2-5,9,10} • These patients may not be ideal candidates for active surveillance.^{1-3,8} 			

The Decipher score is determined solely by genomic characteristics of the tumor, independent of the NCCN risk category. No other clinical or pathologic parameters factor into the score.

- Decipher can also help guide:
 - If treatment with radiation, does patient need radiation treatment along with hormone therapy?
 - And what is the duration of hormone therapy?

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Which Treatment Option is Right for Me?

Attend the BCH lecture on Tuesday, June 28, 2022

- Dr. Patrick Richard (radiation oncologist)
- Dr. Dario Pasalic (radiation oncologist)
- Dr. Stephen Siegel (urologic surgeon)



Boulder
Medical Center



MULTIDISCIPLINARY APPROACH

Bolder Boulder 2022



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