UCA

UROLOGY CENTERS OF ALABAMA

# Google Maps Isn't Going to Help with this: Navigating Prostate Cancer from Screening to Diagnosis

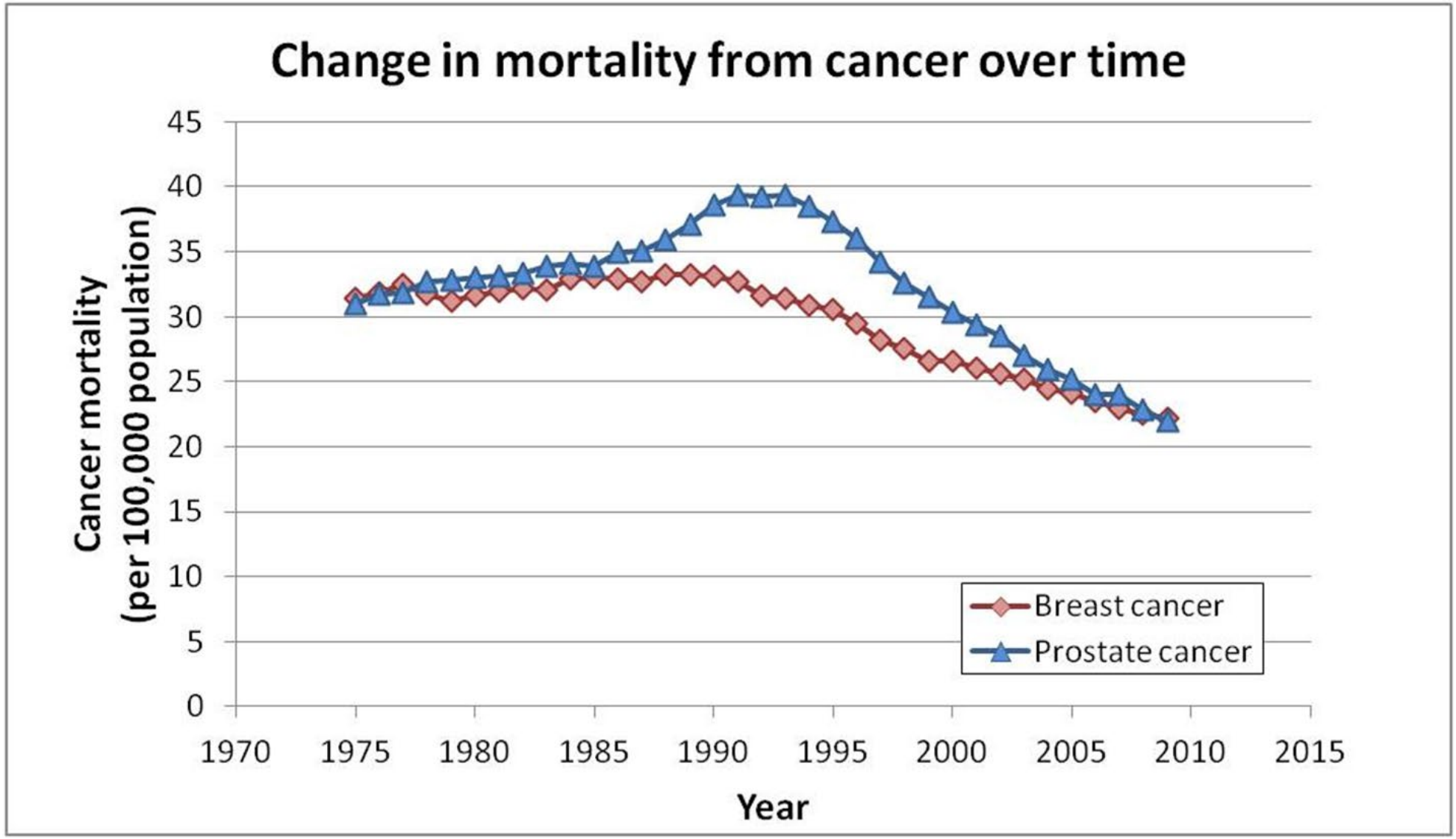
Dr. Eddie Bugg, *MD*

# History

- 1853: 1st case of prostate cancer; “a very rare disease”
- 1905: Radical perineal prostatectomy
- 1941: Androgen ablation for metastatic disease
- 1947: Radical retropubic prostatectomy
- 1987: PSA used to screen for prostate cancer
- 1992: Laparoscopic prostatectomy
- 2000: Robotic assisted lap prostatectomy
- 2003: Human Genome Project

# Top Deaths from Cancer (Men)

- 1st Lung
- 2nd Prostate (31,600 cases)
- 3rd Colorectal


Change in mortality from cancer over time
Cancer mortality (per 100,000 population)
45
40
35
30
25
20
15
10
5
0
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
Year
Breast cancer
Prostate cancer

# Prostate Cancer Screening Goals

- Initial Screening: simple, inexpensive, low morbidity, detect early stage
- Biopsy: only when necessary, minimal morbidity, improve accuracy
- Treatment: Increase life expectancy and decrease morbidity
- NOT all elevated PSA lead to biopsy and NOT all positive biopsies lead to treatment

# Initial Screening

# Screen for Prostate Cancer

- PSA (Prostate Specific Antigen) blood test
  - Protein released into blood by prostate cells
  - Increases with age, cancer, infection, etc.
  - Use age adjusted value and change in value
- Digital Rectal Exam
  - 5-10% prostate cancers have normal PSA
  - More aggressive prostate cancers release less PSA

# Prostate Cancer Screening

- Yearly PSA and DRE
- Elevated PSA
  - BPH, infection, inflammation, sexual activity
  - No antibiotics without infection
- DRE
  - May detect 10% cancers with normal PSA
  - Will not affect PSA
- Early detection = less mortality AND less morbidity

# Elevated PSA

- Repeat PSA
- Antibiotics
  - Anti-inflammatory properties

# AUA Statements About Screening

- 40-54 year old
  - Individualized (Evidence Strength Grade C)
- 55-69 year old
  - Shared decision (Evidence Strength Grade B)
- >69 year old
  - Not recommended but may benefit (Evidence Strength Grade C)

# PSA and AUA Guidelines

- Age adjusted PSA
  - Age 40-49= 2.5, 50-59= 3.5, 60-69=4.5, 70-79=6.5
- PSA density
  - PSA/prostate volume, >0.15 is indication for biopsy
- PSA velocity
  - PSA>4 ng/ml= 0.75 ng/ml/year
  - PSA<4 ng/ml= 0.35 ng/ml/year
- Free-Complexed PSA
  - PSA 4-10, Free PSA < 25% is abnormal

# Testosterone Replacement

- No definitive evidence that testosterone replacement will increase the incidence of PCA
  - Absence of large randomized trials to address issue
- Patients with no PCA or treated cancer (RRP or XRT)
  - safe
- Patients with untreated PCA or active surveillance
  - ???

# UCA Screening Recommendations

- Start screening age 40
- Continue screening if life expectancy >10 years
- Repeat elevated PSA in several weeks (no intercourse within 48 hours)
- Antibiotics only if evidence of infection
- Refer at any time

# Screening

- Screening ≠ Biopsy
- Screening ≠ Treatment

# Next Step Screening

## Improve Biopsy Yield

# Before Biopsy

- MRI
- Genetic Biomarkers

# Prostate MRI

- Biopsy-naïve patients
- Patients with previous negative biopsy
- Patients on active surveillance

# Prostate MRI

- Prostate Imaging Reporting and Data System (PIRADS)
  - PIRADS 1 or 2:  7-8% positive biopsy
  - PIRADS 3:  30% positive biopsy
  - PIRADS 4:  42% positive biopsy
  - PIRADS 5:  82% positive biopsy
- False negative up to 20%

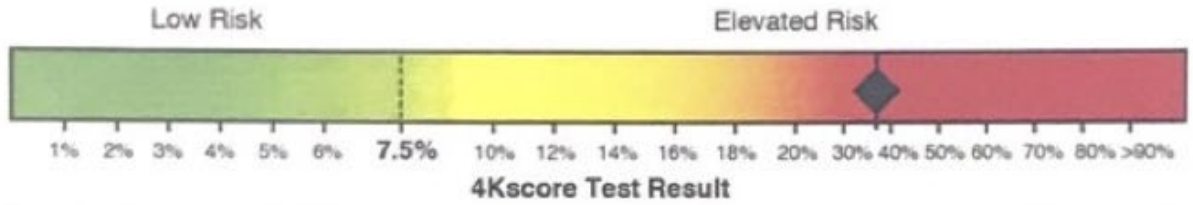
# Biomarkers

- 4K score:  4 kallikreins (total psa, free psa, intact psa and hK2)
- Select MDx:  urinary gene panel correlates with Pca
- ExoDx prostate (IntelliScore):  3 genomic biomarkers in urine
- >100 genetic variations of single base pair in DNA sequencing (SNPs) associated with developing prostate cancer

## 4Kscore Test Results

**ELEVATED RISK** **4Kscore:** **37%**

There is a **37%** probability that this patient will have Gleason Score ≥ 7 prostate cancer if a biopsy were to be performed.




## Clinical Information

| Test | Result | Units | Reference | Reported | Previous | Prev. Date | DRE | Prior Biopsy |
|---|---|---|---|---|---|---|---|---|
| PSA Total | 7.01* | ng/mL | <4.00 | 08/17/2019 | | | No Nodule | No Prior Biopsy |

NOTE: For complete test results, performing laboratory and associated comments refer to the patient's clinical report.

# Biopsy

## Tissue Assessment is Still the Gold Standard

# Prostate Biopsy

- Blood in urine, semen and stool
- Difficulty voiding
- Infection 2-3%
  - Augmentin and Rocephin

# Prostate Cancer

## To Treat or Not to Treat?

### Biological and Clinical Heterogeneity



# Prostate Cancer

- PSA
- Clinical stage
- Gleason Score
- Volume of cancer
- Imaging
- Patient age
- Comorbidities

# Genomic Tests

- Oncotype Dx GPS
- Prolaris
- Decipher

# Oncotype Dx GPS

- 17 genes across 4 biological pathways
- GPS score 0-100 to estimate risk of adverse pathology at time of surgery (4+3, pT3)
- Estimate risk of metastasis and death within 10 years

# Genomic Prostate Score® (GPS™) Report

oncotype DX® Genomic Prostate Score

**PATIENT-LAST-NAME, FIRST-NAME I.**

Date of Birth: **19-Apr-1961** Gender: **Male** Report Number: **OR000123456-01** Report Date: **23-May-2019**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

## GPS + NCCN®[1] : Very Low Risk


| Clinical Interpretation | Clinical Endpoints | Individualized Risk (95% Confidence Interval [CI]) |
|---|---|---|
| The combination of GPS and clinical features predicts that this patient's risk is consistent with **NCCN Very Low Risk** disease.‡ | **Prostate Cancer Death Within 10 Years**† | <1% (95% CI: <1% - <1%) |
| In a clinical validation study including patients with NCCN Very Low, Low, and Intermediate Risk, **no patient with a GPS result <20 had metastasis or died** from prostate cancer within 10 years.† | **Metastasis Within 10 Years**†§ | 1% (95% CI: <1% - 4%) |
| | **Adverse Pathology**† (Gleason ≥ 4+3 and/or pT3+) | 16% (95% CI: 12% - 21%) |

**NCCN Risk Group**‖ **: Low**

**Physician-Provided Information**¶ **:**

| | |
|---|---|
| Gleason Score: **3+3** | Prostate Volume (cc): 23 |
| PSA (ng/mL): 5.0 | PSA Density (ng/mL/cc): 0.22 |
| Clinical Stage: T1c | Number of cores positive: **4** |
| Max. % of tumor involvement in any core: **≤ 50%** | Number of cores collected: **12** |

# Genomic Prostate Score® (GPS™) Report

oncotypeDX® Genomic Prostate Score

**PATIENT-LAST-NAME, FIRST-NAME I.**

Date of Birth: **18-Jan-1961** Gender: **Male** Report Number: **OR000123456-01** Report Date: **20-May-2019**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

## GPS + NCCN®[1] : Low Risk


| Clinical Interpretation | Clinical Endpoints | Individualized Risk (95% Confidence Interval [CI]) |
|---|---|---|
| The combination of GPS and clinical features predicts that this patient's risk is consistent with **NCCN Low Risk** disease.‡<br><br>In a clinical validation study including patients with NCCN Very Low, Low, and Intermediate Risk, **no patient with a GPS result <20 had metastasis or died** from prostate cancer within 10 years.† | **Prostate Cancer Death Within 10 Years**† | <1% (95% CI: <1% - 1%) |
| | **Metastasis Within 10 Years**†§ | 4% (95% CI: 1% - 9%) |
| | **Adverse Pathology**† (Gleason ≥ 4+3 and/or pT3+) | 31% (95% CI: 23% - 41%) |



**NCCN Risk Group**‖ **: Intermediate**

**Physician-Provided Information**¶ **:**

| | |
|---|---|
| Gleason Score: **3+3** | Prostate Volume (cc): **39** |
| PSA (ng/mL): **12.0** | PSA Density (ng/mL/cc): **0.31** |
| Clinical Stage: **T1c** | Number of cores positive: **2** |
| Max. % of tumor involvement in any core: **≤ 50%** | Number of cores collected: **14** |

# Genomic Prostate Score® (GPS™) Report

oncotypeDX® Genomic Prostate Score

**PATIENT-LAST-NAME, FIRST-NAME I.**

Date of Birth: **08-Jan-1960** Gender: **Male** Report Number: **OR000123456-01** Report Date: **21-May-2019**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

## GPS + NCCN®[1] : Favorable Intermediate Risk


| Clinical Interpretation | Clinical Endpoints | Individualized Risk (95% Confidence Interval [CI]) |
|---|---|---|
| The combination of GPS and clinical features predicts that this patient's risk is consistent with **NCCN Favorable Intermediate Risk** disease.‡ | **Prostate Cancer Death Within 10 Years**† | <1% (95% CI: <1% - <1%) |
| | **Metastasis Within 10 Years**†§ | 3% (95% CI: <1% - 21%) |
| | **Adverse Pathology**† (Gleason ≥ 4+3 and/or pT3+) | 35% (95% CI: 20% - 54%) |

**NCCN Risk Group**‖ **: Very Low**

**Physician-Provided Information**¶ **:**

| | |
|---|---|
| Gleason Score: **3+3** | Prostate Volume (cc): **55** |
| PSA (ng/mL): **4.1** | PSA Density (ng/mL/cc): **0.07** |
| Clinical Stage: **T1c** | Number of cores positive: **1** |
| Max. % of tumor involvement in any core: **> 50%** | Number of cores collected: **20** |

# Genomic Prostate Score® (GPS™) Report

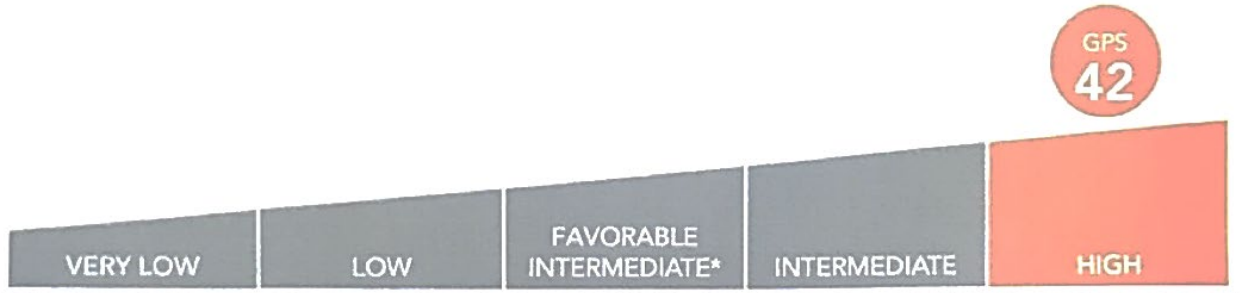
oncotype DX
Genomic Prostate Score

[redacted]

Date of Birth: [redacted] Gender: Male Report Number: OR001276789-01 Report Date: 09-Jul-2019

Ordering Physician: Dr. Charles Edward Bugg

## GPS + NCCN®[1] : High Risk




| Clinical Interpretation | Clinical Endpoints | Individualized Risk (95% Confidence Interval [CI]) |
|---|---|---|
| The combination of GPS and clinical features predicts that this patient's risk is consistent with **NCCN High Risk** disease.‡ | **Prostate Cancer Death Within 10 Years**† | 1% (0%–100%) |
| | **Metastasis Within 10 Years**†§ | 11% (0%–100%) |
| | **Adverse Pathology**† (Gleason ≥ 4+3 and/or pT3+) | 62% (0%–100%) |

**NCCN Risk Group**‖ **: Intermediate**

**Physician-Provided Information**¶ **:**

- Gleason Score: **3+4**
- PSA (ng/mL): **4.0**
- Clinical Stage: **T1c**
- Max. % of tumor involvement in any core: **N/A**
- Prostate Volume (cc): **N/A**
- PSA Density (ng/mL/cc): **N/A**
- Number of cores positive: **1**
- Number of cores collected: **13**

# Prolaris

- 31 cell cycle proliferation genes
- Score 0-10
- Estimates 10 year risk of mortality on surveillance and 10 year risk of metastasis following treatment

## PROLARIS MOLECULAR SCORE

A measure of cell proliferation, independent of clinical variables.

**5.2**
**Considerably More Aggressive* than patients in the same risk category**

**This Prolaris Score is at percentile >99 for NCCN Very Low/Low patients**

**DSM Risk exceeds the threshold for active surveillance****

## VARIABLES USED FOR RISK ASSESSMENT

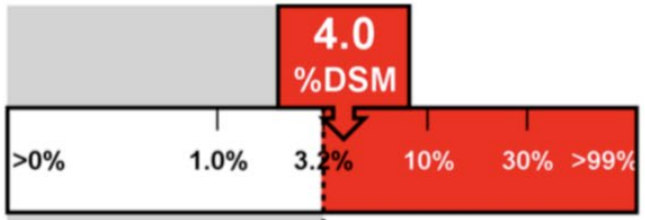
| | |
|---|---|
| Prolaris Molecular Score: | 5.2 |
| Patient Age at Biopsy: | 58 |
| PSA Prior to This Biopsy: | 3.3 |
| Clinical T Stage: | T1c |
| % Postive Cores: | < 34% |
| Gleason Score: | 3+3=6 (Group 1 ISUP[8]) |
| NCCN Risk[1]: | Very Low/Low |

## PATIENT'S RISK ASSESSMENT

Prolaris Score and clinical variables are combined in a clinically validated weighted algorithm

### When Considering Active Surveillance†

This patient's 10-Year prostate cancer Disease Specific Mortality (DSM) risk with conservative management is:

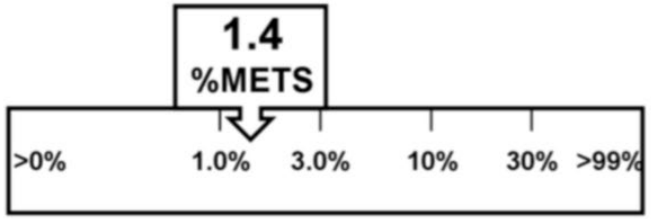



(95% CI:2.5-6.2%)

**Active Surveillance Threshold**:** DSM within the gray box may be considered appropriate for conservative management

### When Considering Primary Radiation Therapy or Radical Prostatectomy‡

This patient's 10-Year Metastasis (METS) risk with definitive treatment is:




(95% CI:0.7-2.9%)

Mortality risks could be altered by various therapeutic interventions.

## PROLARIS MOLECULAR SCORE

A measure of cell proliferation, independent of clinical variables.

| 2.2 | This Prolaris Score is at percentile 11 for NCCN Very Low/Low patients |
|---|---|
| Less Aggressive* than patients in the same risk category | |

**DSM Risk is within the threshold for active surveillance****

## VARIABLES USED FOR RISK ASSESSMENT

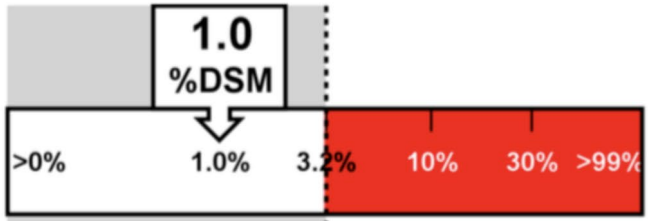
| | |
|---|---|
| Prolaris Molecular Score: | 2.2 |
| Patient Age at Biopsy: | 67 |
| PSA Prior to This Biopsy: | 4.2 |
| Clinical T Stage: | T1c |
| % Postive Cores: | < 34% |
| Gleason Score: | 3+3=6 (Group 1 ISUP[8]) |
| NCCN Risk[1]: | Very Low/Low |

## PATIENT'S RISK ASSESSMENT

Prolaris Score and clinical variables are combined in a clinically validated weighted algorithm

### When Considering Active Surveillance†

This patient's 10-Year prostate cancer Disease Specific Mortality (DSM) risk with conservative management is:

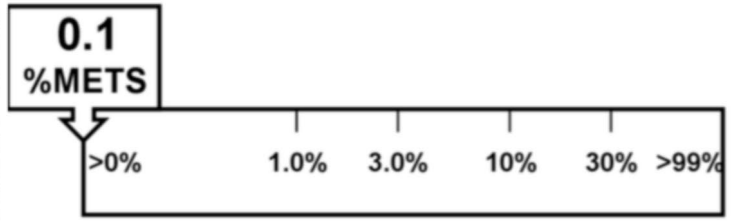



**Active Surveillance Threshold****: DSM within the gray box may be considered appropriate for conservative management

Mortality risks could be altered by various therapeutic interventions.

### When Considering Primary Radiation Therapy or Radical Prostatectomy‡

This patient's 10-Year Metastasis (METS) risk with definitive treatment is:



## PROLARIS MOLECULAR SCORE

A measure of cell proliferation, independent of clinical variables.

**1.9**
**Less Aggressive* than patients in the same risk category**

**This Prolaris Score is at percentile 3 for NCCN Favorable Intermediate patients**

**DSM Risk is within the threshold for active surveillance****

## VARIABLES USED FOR RISK ASSESSMENT

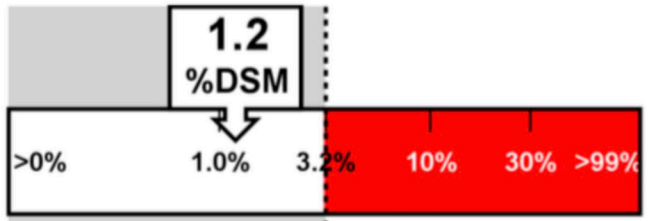
| | |
|---|---|
| Prolaris Molecular Score: | 1.9 |
| Patient Age at Biopsy: | 67 |
| PSA Prior to This Biopsy: | 5.4 |
| Clinical T Stage: | T1c |
| % Postive Cores: | < 34% |
| Gleason Score: | 3+4=7 (Group 2 ISUP[8]) |
| NCCN Risk[1]: | Favorable Intermediate |

## PATIENT'S RISK ASSESSMENT

Prolaris Score and clinical variables are combined in a clinically validated weighted algorithm

### When Considering Active Surveillance†

This patient's 10-Year prostate cancer Disease Specific Mortality (DSM) risk with conservative management is:



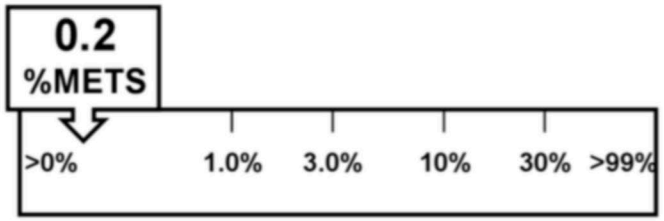

(95% CI:0.6-2.3%)

**Active Surveillance Threshold****: DSM within the gray box may be considered appropriate for conservative management

Mortality risks could be altered by various therapeutic interventions.

### When Considering Primary Radiation Therapy or Radical Prostatectomy‡

This patient's 10-Year Metastasis (METS) risk with definitive treatment is:




(95% CI:0.1-0.5%)

## PROLARIS MOLECULAR SCORE

A measure of cell proliferation, independent of clinical variables.

**5.7**
**Considerably More Aggressive* than patients in the same risk category**

**This Prolaris Score is at percentile >99 for NCCN Very Low/Low patients**

**DSM Risk exceeds the threshold for active surveillance****

## VARIABLES USED FOR RISK ASSESSMENT

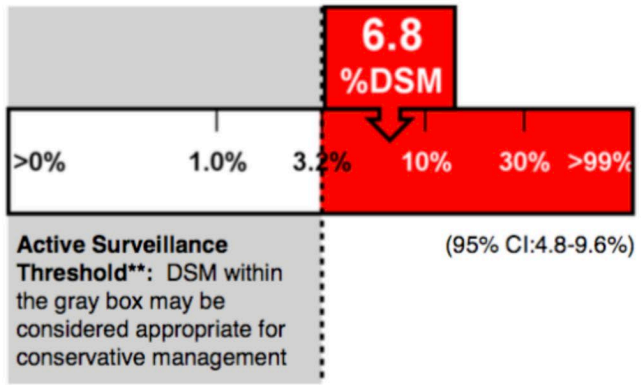
| | |
|---|---|
| Prolaris Molecular Score: | 5.7 |
| Patient Age at Biopsy: | 74 |
| PSA Prior to This Biopsy: | 6.79 |
| Clinical T Stage: | T1c |
| % Postive Cores: | < 34% |
| Gleason Score: | 3+3=6 (Group 1 ISUP[8]) |
| NCCN Risk[1]: | Very Low/Low |

## PATIENT'S RISK ASSESSMENT

Prolaris Score and clinical variables are combined in a clinically validated weighted algorithm

### When Considering Active Surveillance†

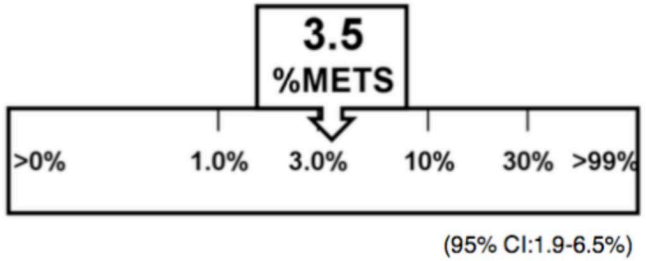
This patient's 10-Year prostate cancer Disease Specific Mortality (DSM) risk with conservative management is:




Mortality risks could be altered by various therapeutic interventions.

### When Considering Primary Radiation Therapy or Radical Prostatectomy‡

This patient's 10-Year Metastasis (METS) risk with definitive treatment is:



# Active Surveillance

# AUA Guidelines for Active Surveillance

- Very low risk localized prostate cancer
- Life expectancy <5 years with low and intermediate risk cancer
- For low risk localized cancer, tissue based genomic biomarkers have not shown a clear role in patient selection

# Active Surveillance Monitoring

- PSA and DRE every 6 months
- Prostate MRI 6 months after diagnosis
- Repeat prostate biopsy
- Testosterone replacement and AUA annual meeting:  does not increase progression rate

# Untreated Prostate Cancer Morbidity

- Obstruction/Retention
- Hematuria/clot retention
- Hydronephrosis/stents
- Fractures

# Treatment Options

- Surgery
- Radiation
- Cryotherapy
- HIFU
- Hormones
- Chemotherapy

# XRT After Surgery

- Prolaris
- Decipher genomic testing
  - 22 genes across multiple pathways
  - Score 0-1
  - 5 year metastasis rate
  - 10 year mortality rate

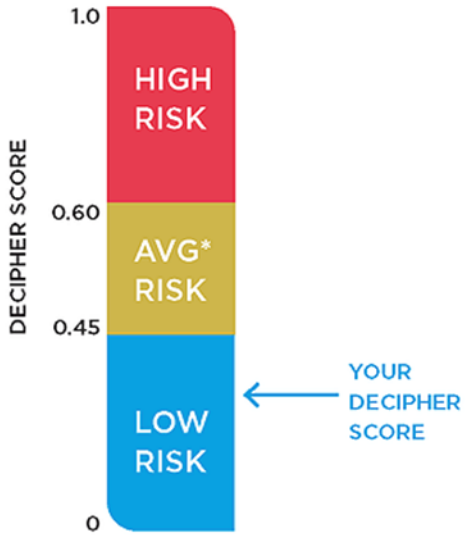
## CLINICAL DETAILS

PSA, most recent (ng/mL): **4.9**

Gleason Score: **4+3**

Specimen Type:

☐ SM+ ☒ EPE ☐ SVI ☐ LNI ☐ BCR ☐ Tertiary Gleason 5




## YOUR DECIPHER RESULT – GENOMIC LOW RISK

| DECIPHER SCORE 0.3 | |
|---|---|
| Risk - Percent Likelihood | |
| 5-Year Metastasis | **1.6%** |
| 10-Year Prostate Cancer Specific Mortality | **2.5%** |

### INTERPRETATION

References on reverse

Clinical studies concluded that Decipher low risk results in men with adverse pathology have good prognosis overall and may be optimally managed with observation after surgery.[1-3,12] Upon PSA rise, these patients may be treated with delayed radiotherapy without concurrent hormone therapy.[4,11]

Relevant findings from published clinical studies: Patients with Decipher low risk had >97% 5-year metastasis free survival and >94.7% 10-year cause specific survival.[1,2,3] For these patients there were no significant differences in metastasis free survival with adjuvant, early or late salvage postoperative radiotherapy treatment.[5,6,11]

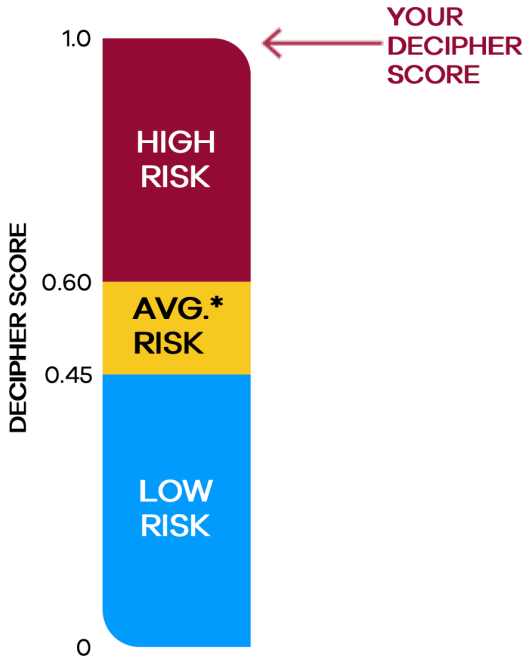
In patients with PSA rise or biochemical recurrence after surgery that received salvage radiotherapy, >97% 5-year metastasis free survival was observed with or without concurrent hormone therapy.[4]

## CLINICAL DETAILS

PSA, Most Recent (ng/mL): **4.1**
Specimen Type: **Needle Biopsy**

NCCN Risk Category: **Low Risk**
# of Positive Cores: **8 (8 of 32 Cores)**

Gleason Score: **3+3**
Clinical Stage: **T2a**




## YOUR DECIPHER RESULT: GENOMIC HIGH RISK

### DECIPHER SCORE: 0.99

| Risk at RP - Percent Likelihood | |
|---|---|
| High Grade Disease (primary Gleason grade 4 or 5) | **33.7%** |
| 5-Year Metastasis | **11.6%** |
| 10-Year Prostate Cancer Specific Mortality | **9.1%** |

### INTERPRETATION

References on reverse

Clinical studies have shown that men with a Decipher high risk have an unfavorable prognosis. These men may not be suitable candidates for active surveillance and may benefit from intensification with multi-modal therapy.[1-3]

# Rising PSA After Localized Treatment

- CT scan and bone scan
- Axumin PET scan (fluciclovine)
- PSMA PET scan (gallium)

# Rising PSA After Localized Treatment

- No radiographical lesions
- Oligometastasis (1-5 metastatic lesions)
  - Surgery, radiation, radiofrequency ablation
- More diffuse metastasis

# Metastatic Prostate Cancer

- LHRH agonists: Lupron, degarelix, etc
- Hormone resistant: zytiga, xtandi, etc
- Immunotherapy: Provenge
- Chemotherapy

# Sample Patient

- 46 year old, father died from prostate cancer
- Initial PSA 2.1 at age 41
- Next PSA age 46 was 11
- Repeat PSA 2 weeks later 10.8

# Sample Patient

- Prostate MRI: PR3 left anterior apex
- Fusion biopsy: Gleason 3+4 PR3 area, 3+3 in 2 separate cores
- Oncotype test: high risk

# Sample Patient

- Robotic RRP: Gleason 4+4 (tertiary grade 5), T3b with left seminal vesicle invasion, 0/5 lymph node involvement, margins clear
- Decipher test: high risk
- Adjuvant XRT

# Sample Patient

- PSA nadir 0.01
- 2 years later PSA 2.3
- CT and bone scan negative
- PSA followed Q3 months

# Sample Patient

- PSA increased to 5.1
- Axumin PET: left iliac wing lesion
- Referred for XRT of oligometastasis and medical oncology

# THANK YOU

UCA | Urology Centers Of Alabama

UCA | Women's Center