The Role of the Pathologist
Active Surveillance for Prostate Cancer

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NO RELAVENT DISCLOSURES
## Active Surveillance vs Watchful Waiting

<table>
<thead>
<tr>
<th></th>
<th>Active surveillance</th>
<th>Watchful waiting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim</strong></td>
<td>To individualise treatment</td>
<td>To avoid treatment</td>
</tr>
</tbody>
</table>
| **Patient characteristics** | Fit for radical treatment  
                          | Age 50–80                                                | Age >70 or life expectancy <15 yrs                     |
| **Tumour characteristics** | T1–T2 GS ≤7 Initial PSA <15                     | Any T stage GS ≤7 Any PSA                              |
| **Monitoring**       | Frequent PSA testing  
                          | Repeat biopsies                                          | PSA testing unimportant  
                          |                                                         | No repeat biopsies                                      |
| **Indications for treatment** | Short PSADT  
                          | Upgrading on biopsy                                      | Symptomatic progression                                |
| **Treatment timing** | Early                                                    | Delayed                                                |
| **Treatment intent** | Radical                                                  | Palliative                                             |
Palpable and Visible Prostate Cancer
Nonpalpable but Visible Prostate Cancer
Prostate Cancer
Evaluation on MRI
Diagnosis of Prostate Cancer
Historical Perspective

• Early 1900s – open biopsy
• 1920s – fine needle aspiration biopsy (FNA)
• 1940s – 14 gauge cutting needle biopsy
• 1980s – convergence of three technologies:
  – transrectal ultrasound (TRUS)
  – 18 gauge spring-loaded biopsy gun
  – serum PSA screening

Leading to sextant (and more) biopsies
Anatomical Radical Prostatectomy
Patrick Walsh, M.D.
Figure 1.4: Age standardised (European) incidence and mortality rates, prostate cancer, males, GB, 1975-2008
Incidental Prostate Cancer Found at Autopsy
Detroit, MI

- African-Americans (n = 314)
- Caucasians (n = 211)

% of cases vs Age groups by decades

0 20-29 30-39 40-49 50-59 60-69 70-79
Prostate Cancer Clinical Risk Migration

1990–1994
- Low: 29.6%
- Intermediate: 26.5%
- Int/High: 16.5%
- High: 10.3%

2004–2007
- Low: 46.0%
- Intermediate: 30.0%
- Int/High: 13.7%
- High: 10.3%

Legend:
- Green: Low
- Yellow: Intermediate
- Orange: Int/High
- Red: High
Stage Migration at WRAMC 1988 - 1998

WRAMC = Walter Reed Army Medical Center.
Figure 1. Serum prostate-specific antigen concentration as a function of patient age.\textsuperscript{5}
Prostate Cancer is Frequently Multifocal, Even With Small Total Tumor Volume
Active Surveillance is not New
Tumor Volume Versus Percentage of Specimen Involved By Tumor Correlated With Progression in Stage A Prostatic Cancer

* Confirmed the cut point of 5% tumor involvement for separating T1a from T1b

* Probability of progression:

<table>
<thead>
<tr>
<th></th>
<th>4 years</th>
<th>8 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a:</td>
<td>2%</td>
<td>T1a: 16%</td>
</tr>
<tr>
<td>T1b:</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>
Limited Prostate Cancer on Biopsy

*small tumor or “tip of the iceberg” ?*
Nomogram to Predict Insignificant Cancer 3.0

Points

psa

stage

bxgg1c

bxgg2c

usvol

totalca

totalneg

Total Points

Predicted Value
"The Safest Prostate Cancer is in a Jar"
<table>
<thead>
<tr>
<th>Group</th>
<th>Tumor Volume (cm³)</th>
<th>Gleason Grade*</th>
<th>Extent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Unimportant</td>
<td>0.5 or less</td>
<td>1,2,3</td>
<td>Confined†</td>
</tr>
<tr>
<td>2. Curable</td>
<td>More than 0.5</td>
<td>1,2,3</td>
<td>Confined†</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>4 or 5</td>
<td>Confined†</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>Any</td>
<td>Extracapsular extension (Negative Surgical Margins)</td>
</tr>
<tr>
<td>3. Advanced</td>
<td>Any</td>
<td>Any</td>
<td>Extensive extracapsular extension,‡ seminal vesicle invasion, or lymph node metastasis</td>
</tr>
</tbody>
</table>

* Primary or secondary grade, not score.
† Confined to the prostate gland.
‡ Extracapsular extension of cancer to the surgical margins of resection.
Kaplan-Meier Life Table Analysis of Progression-Free Rate (Determined by Serum PSA Levels) of Each Prognostic Group in Radical Prostatectomy Series

- **Unimportant** (n=37)
- **Curable** (n=206)
- **Advanced** (n=99)

<table>
<thead>
<tr>
<th>Group</th>
<th>Five years (percent)</th>
<th>Logrank test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>100</td>
<td>1 vs. 2 p = 0.0610</td>
</tr>
<tr>
<td>Group 2</td>
<td>86±7</td>
<td>1 vs. 3 p &lt; 0.00005</td>
</tr>
<tr>
<td>Group 3</td>
<td>45±14</td>
<td>2 vs. 3 p &lt; 0.00005</td>
</tr>
</tbody>
</table>

(n=342)
The Critical Role of the Pathologist in Determining Eligibility for Active Surveillance as a Management Option in Patients With Prostate Cancer

Consensus Statement With Recommendations Supported by the College of American Pathologists, International Society of Urological Pathology, Association of Directors of Anatomic and Surgical Pathology, the New Zealand Society of Pathologists and the Prostate Cancer Foundation

Mahul B. Amin, MD; Daniel W. Lin, MD; John L. Gore, MD, MS; John R. Srigley, MD, FRCPC, FRCPA; Hema Samaratunga, MBBS, FRCPA; Lars Egevad, MD; Mark Rubin, MD; John Nacey, MD; H. Ballentine Carter, MD; Laurence Klotz, MD; Howard Sandler, MD; Anthony L. Zietman, MD; Stuart Holden, MD; Rodolfo Montironi, MD, FRCPATH, IFCAP; Peter A. Humphrey, MD, PhD; Andrew J. Evans, MD; Brett Delahunt, MD; Jesse K. McKenney, MD; Dan Berney, MD; Thomas M. Wheeler, MD; Arul M. Chinnaian, MD, PhD; Lawrence True, MD; Beatrice Knudsen, MD, PhD; Elizabeth Hammond, MD

Archives of Pathology and Lab Medicine, 2014
The Critical Role of the Pathologist in Determining Eligibility for Active Surveillance as a Management Option in Patients With Prostate Cancer

**Table 2. Surveillance Schedules for Several Large Active Surveillance Cohorts**

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Patients, No.</th>
<th>PSA and DRE</th>
<th>Repeat Prostate Biopsy, mo After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newcomb et al, 2010</td>
<td>351</td>
<td>PSA, every 3 mo; DRE, every 6 mo</td>
<td>6–12 then 24 then every 2 y</td>
</tr>
<tr>
<td>Dall’Era et al, 2008</td>
<td>640</td>
<td>Every 3 mo</td>
<td>Every 12–24</td>
</tr>
<tr>
<td>Tosoian et al, 2011</td>
<td>870</td>
<td>Every 6 mo</td>
<td>Every 12</td>
</tr>
<tr>
<td>Klotz et al, 2010</td>
<td>453</td>
<td>Every 3 mo for 2 y then every 6 mo</td>
<td>6–12, then every 3–4 y</td>
</tr>
<tr>
<td>Royal Marsden, London, UK</td>
<td>471</td>
<td>Every month for a year, then every 3 mo for a year, then every 6 mo</td>
<td>18–24, then every 2 y</td>
</tr>
<tr>
<td>Memorial Sloan-Kettering Cancer Center, New York, NY</td>
<td>238</td>
<td>Every 6 mo</td>
<td>12–18, then every 2–3 y</td>
</tr>
<tr>
<td>PRIAS</td>
<td>2494</td>
<td>Every 3 mo for 2 y, then every 6 mo</td>
<td>1, 4, 7, and 10 y</td>
</tr>
</tbody>
</table>
Hopkin’s Criteria for Active Surveillance

- Gleason score $\leq 6$
- PSA Density $\leq 0.15$
- $< 3$ biopsy cores containing cancer
- No core showing more than 50% cancer
Active Surveillance
PRIAS STUDY
Actuarial Estimate of Remaining on Active Surveillance – Multi Institutional Trial
Figure 3. Probability of remaining progression free stratified by the results of the first repeat biopsy.

Rebiopsy negative (n=43)

Rebiopsy positive (n=27)

Log Rank Test p=0.004
Are the Biopsy Findings Representative?
Gleason Score

Biopsy vs Radical Prostatectomy

- * indicates significant difference

- Bar graph comparing Biopsy and Radical Prostatectomy for Gleason Score:
  - 3+3: Biopsy > Radical Prostatectomy
  - 3+4: Biopsy = Radical Prostatectomy
  - 4+3: Biopsy > Radical Prostatectomy
  - ≥4+4: Biopsy = Radical Prostatectomy
## Reasons for Abandoning Active Surveillance

A Multi-Institutional Study

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleason 7 or greater on surveillance biopsy</td>
<td>15 (35)</td>
</tr>
<tr>
<td>Surveillance biopsy with more than 3 cores or more than 50% in single core</td>
<td>7 (16)</td>
</tr>
<tr>
<td>Change in pt preference</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Increasing PSA without worsening biopsy features</td>
<td>2 (5)</td>
</tr>
<tr>
<td>MRI findings</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Voiding symptoms</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Up staging via digital rectal examination</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (28)</td>
</tr>
</tbody>
</table>

Overall greater than 100% as some patients had multiple reasons.
### Table 2. Radical prostatectomy findings

<table>
<thead>
<tr>
<th>Description</th>
<th>No./total</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean gm RP (range)</td>
<td>75.5</td>
<td>(34.3–152.8)</td>
</tr>
<tr>
<td>No./total No. GS (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>19/48</td>
<td>(39.6)</td>
</tr>
<tr>
<td>6 With tertiary pattern 4</td>
<td>6/48</td>
<td>(12.5)</td>
</tr>
<tr>
<td>3 + 4 = 7</td>
<td>15/48</td>
<td>(31.3)</td>
</tr>
<tr>
<td>4 + 3 = 7</td>
<td>6/48</td>
<td>(12.5)</td>
</tr>
<tr>
<td>Greater than 7</td>
<td>2/48</td>
<td>(4.2)</td>
</tr>
<tr>
<td>No./total No. organ confined (%)</td>
<td>31/48</td>
<td>(65)</td>
</tr>
<tr>
<td>No./total No. EPE (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal</td>
<td>7/48</td>
<td>(14.6)</td>
</tr>
<tr>
<td>Nonfocal</td>
<td>10/48</td>
<td>(20.8)</td>
</tr>
<tr>
<td>No./total No. seminal vesicle involvement (%)</td>
<td>1/48</td>
<td>(2.1)</td>
</tr>
<tr>
<td>No./total No. lymph node involvement (%)</td>
<td>2/48</td>
<td>(4.2)</td>
</tr>
<tr>
<td>No./total No. pos margins (%)</td>
<td>7/48</td>
<td>(15)</td>
</tr>
<tr>
<td>Mean cm(^3) total tumor vol (range)</td>
<td>1.3</td>
<td>(0.02–10.8)</td>
</tr>
<tr>
<td>No./total No. total tumor vol less than 1 cm(^3) (%)</td>
<td>33/48</td>
<td>(68)</td>
</tr>
<tr>
<td>Mean cm(^3) dominant tumor nodule vol (range)</td>
<td>1.03</td>
<td>(0.01–10.57)</td>
</tr>
<tr>
<td>No./total No. dominant tumor nodule vol greater than 1 cm(^3) (%)</td>
<td>10/48</td>
<td>(20.8)</td>
</tr>
</tbody>
</table>
### Table 3. Radical prostatectomy predominant tumor location

<table>
<thead>
<tr>
<th>Location</th>
<th>No./Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominant nodule:</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>20/48 (41.7)</td>
</tr>
<tr>
<td>Posterior/posterolat</td>
<td>23/48 (47.9)</td>
</tr>
<tr>
<td>Lateral</td>
<td>4/48 (8.3)</td>
</tr>
<tr>
<td>Scattered foci</td>
<td>1/48 (2.1)</td>
</tr>
<tr>
<td>Dominant nodule greater than 1 cm³:</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>10/10 (100)</td>
</tr>
<tr>
<td>Dominant nodule less than 1 cm³:</td>
<td></td>
</tr>
<tr>
<td>Posterior/posterolat</td>
<td>23/38 (60.5)</td>
</tr>
</tbody>
</table>
Table 7. Problems Associated With Tumor Quantification in Needle Biopsy

- Measuring discontinuous foci of cancer
- Tissue core and tumor fragmentation
- Inadequate sectioning
- Inadequate core length
- Whether total core length should include extraprostatic tissues
Quantifying the Extent of Cancer in Needle Biopsies

100% or 100%

100%
Needle Biopsy with Discontinuous Cancer
Radical Prostatectomy Specimen
Needle Biopsy Reporting

Adenocarcinoma, Gleason 3+3=6, 2mm focus (15% of core)
An Update With Discussion on Practical Issue to Implement The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma

Jonathan I. Epstein, MD,* Mahul B. Amin, MD, Victor E. Reuter, MD, and Peter A. Humphrey, MD, PhD

Vote at the 2014 Consensus Conference: “Should we provide a grade for”:

- Each positive core: 28 (45.2%)
- Each positive specimen jar: 11 (17.7%)
- Whole case overall (global grade): 2 (3.2%)
- 1+2: 4 (6.5%)
- 1+3: 8 (12.9%)
- 2+3: 8 (12.9%)
- 1+2+3: 1 (1.6%)
Prostate Cancer
Biopsy Reporting

Prostate, left base, needle biopsy:
- Adenocarcinoma, Gleason 3+3=6, 5% of submitted tissue, one core involved.

Prostate, left base, needle biopsy x 2
- Adenocarcinoma, Gleason 3+3=6, 1.5 mm focus (10% of one core)
Prostate Cancer

Biopsy Reporting

Prostate, right side, needle biopsies:
   Adenocarcinoma, Gleason 3+4=7, 7% of submitted tissue, 3 cores involved

Prostate, right side, needle biopsy x 6:
   Adenocarcinoma, Gleason 3+4=7, 3 mm focus (20% of first core)
   Adenocarcinoma, Gleason 3+3=6, 1.5 mm focus (10% of second core)
   Adenocarcinoma, Gleason 3+3=6, 0.5 mm focus (5% of third core)
   Few small glands suspicious for adenocarcinoma (fourth core)
Update:
Needle Biopsy Reporting

Prostate, right medial base, needle biopsy:

- Adenocarcinoma, Gleason 3+4=7, 3mm focus (20% of core), 5% Gleason pattern 4; Prognostic Grade Group II.
Prostate Cancer Biopsy Embedding

**No more than two cores per block**: 

Example:
Eight cores per container, right and left:

Right: A1-A4
Left: B1-B4
The Critical Role of the Pathologist in Determining Eligibility for Active Surveillance as a Management Option in Patients With Prostate Cancer
Table 6. Recommendations for Reporting Carcinoma Extent in Prostate Needle Biopsy Tissue

<table>
<thead>
<tr>
<th>College of American Pathologists&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Number of cores positive/total number of cores,</td>
</tr>
<tr>
<td>• Proportion (linear percentage) of prostatic tissue involved by tumor, and/or</td>
</tr>
<tr>
<td>• Total linear millimeters of carcinoma/length of core(s)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Association of Directors of Anatomic and Surgical Pathology&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Absolute number of involved cores out of total number of cores and</td>
</tr>
<tr>
<td>• Linear extent of tumor (in millimeters) per core or total or</td>
</tr>
<tr>
<td>• Percentage of cancer in each involved core</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>World Health Organization&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Number of cores involved (if possible, include percentage of cores involved)</td>
</tr>
<tr>
<td>• Amount of carcinoma in biopsy specimen (either of the 2 methods listed can be used)</td>
</tr>
</tbody>
</table>

Optional
1. Composite (global) percentage of carcinoma in all needle biopsy tissue
2. Percentage of carcinoma in most extensively involved core

<sup>a</sup> Data derived from Meng et al<sup>36</sup> and Srigley et al.<sup>72</sup>
<sup>b</sup> Data derived from Epstein et al.<sup>73</sup>
<sup>c</sup> Data derived from Amin et al.<sup>74</sup>
GLEASON GRADING SYSTEM
Veterans Administration (VACURG)

- Employs extent of glandular differentiation and pattern of growth
- Nuclear atypia, mitoses not used

Developed from 1960-1975 and based on follow-up of 5,000 prostate cancer patients

1968 GLEASON DRAWING
Gleason Grading Evolution

Original Gleason

PROSTATIC ADENOCARCINOMA (Histologic Patterns)

1

2

3

4

5

Hum Pathol 23;273-79, 1992

ISUP 2005 Gleason

Am J Surg Pathol 29;1228-42, 2005

Gleason with proposed refinements and modifications to ISUP 2005

J Urol 183;433-40, 2010
Problems with Gleason Score

• Gleason 6 is the lowest grade reported although the scale goes from 2-10
• Gleason 7 is not homogeneous: 4+3=7 has a much worse prognosis than 3+4=7
• Gleason 8-10 is often considered as one group - high grade disease
Modified Gleason Scores on Biopsy are *Higher* than Classical Gleason

- Basically excludes less than pattern 3 on needle biopsy
- Inclusion of any amount of higher tertiary grades in the final modified Gleason score (most common plus highest pattern)
- Ignoring low volume (< 5%) low grade tumor from the final score calculation (96% pattern 4 and 4% pattern 3: 4+4=8)
- Shift of some morphologic Gleason pattern 3 (classical) to Gleason pattern 4 (modified)
Figure 1 – Differences between the traditional Gleason score (G) and the modified Gleason score in five hypothetical prostatic needle biopsies with prostate cancer.

A) $G = 3 + 3 = 6$, modified $G = 3 + 3 = 6$
B) $G = 3 + 4 = 7$, modified $G = 3 + 4 = 7$
C) $G = 3 + 4 = 7$, modified $G = 3 + 5 = 8$
D) $G = 4 + 3 = 7$, modified $G = 4 + 5 = 9$
E) $G = 4 + 3 = 7$, modified $G = 4 + 3 = 7$

The three shades of grey correspond to prostate cancer in Gleason patterns 3, 4 and 5, from lighter to darker respectively.
Reporting of Gleason Score
Prognostic Grade Groups

- Gleason score ≤ 6:
  - Prognostic Grade Group I
- Gleason score 3 + 4
  - Prognostic Grade Group II
- Gleason score 4 + 3
  - Prognostic Grade Group III
- Gleason score 8
  - Prognostic Grade Group IV
- Gleason score 9-10
  - Prognostic Grade Group V

INCORPORATION OF PROGNOSTIC GROUPS
ENDORSED BY THE ISUP (2105) & WHO (2016)
Probability of recurrence-free progression for different prognostic grade groups

Approx. 20,000 pts treated at 4 institutions

5 yr Biochem Risk free Surv.

Grade Group 1: 97.5%
Grade Group 2: 93.1%
Grade Group 3: 78.1%
Grade Group 4: 63.3%
Grade Group 5: 48.9%
Do not **Overdiagnose** Gleason Pattern 4

**FIGURE 1.** Adenocarcinoma, Gleason score $3 + 3 = 6$ with rare poorly formed glands probably representing tangential sectioning of well formed glands and are only identified at high magnification (original magnification $\times 40$).
Intraductal Carcinoma
Contraindication for Active Surveillance
Lymph/vascular Invasion
Contraindication for Active Surveillance
Perineural Invasion
Possible contraindication for Active Surveillance
Molecular Testing: Myriad

More Aggressive
Than Average AUA\textsuperscript{1} Low Risk

PROLARIS SCORE 4.3

US Distribution Percentile: 93%
(For AUA Low Risk)

Interpretation: 93% of patients in the AUA Low Risk\textsuperscript{*} category have a lower Prolaris Score

Mortality Risk

Mortality Risk: 3% 10-Year Prostate Cancer-Specific

3% DSM
Molecular Testing: Genomic Health
Oncotype DX - Prostate

Clinical Information

- Calculated NCCN® Risk Group: Low
- PSA (ng/mL): 6.0
- PSA Density (ng/mL/cc): 0.30
- Prostate Volume (cc): 20
- Gleason Score: 3+3
- Number of cores positive/collected: 2/12
- Max. % of tumor involvement in any core: ≤ 50%
- Clinical Stage: T2a

GPS + NCCN Predicted Individualized Risk: Refined from Low to Very Low

NCCN ALONE

- VERY LOW
- LOW
- INTERMEDIATE

GPS + NCCN

- VERY LOW
- LOW
- INTERMEDIATE

Likelihood of Favorable Pathology (LFP)

100%  More Favorable

What does a GPS + NCCN Very Low Risk classification mean?

This patient’s result predicts that his tumor is less aggressive than indicated by clinical features alone, and is more consistent with that of an NCCN Very Low Risk patient.
Molecular Testing: GenomeDX

Sample Patient Test Result

Decipher
prostate cancer classifier

Patient Details
Patient Name: John13 Doe
Medical Record Number: 123456789
Date of Birth: 01/01/1940
Date of Prostatectomy: 09/01/2014

Order Information
Order Date: 09/15/2014
Specimen Received Date: 09/30/2014
GenomeDX Accession ID: DEC14068
Specimen ID: Lab0993783

Ordering Physician: x
Clinic/Hospital: y

Clinical Details
Pathology Report Date: 01/29/2013
Referring Pathologist Laboratory: x

Pre-operative PSA (ng/mL): n/a
Gleason Score (Surgical Pathology): 4+5
P E E P S V T B L N T L R B C R

Decipher Result: Genomic low risk

Summary of Decipher genomic risk results

Decipher 5 year risk of metastasis: 2.9%

Genomic risk of developing metastasis within five years of radical prostatectomy is 2.9x the average clinical risk for a patient with adverse pathology.

Comments: Decipher indicates a patient’s probability of developing metastasis within 5 years of a radical prostatectomy. The average risk* for metastasis by 5 years after surgery for clinically high-risk men is 6.0%. The Decipher risk reported here has a 95% confidence interval of 1.6% to 4.2%, which is significantly lower than average clinical risk and therefore the patient is considered to have a lower than average risk of clinical recurrence within 5 years.

5 Year Probability of Metastasis
100% High risk (>99%)
6% Average clinical risk
6% Low risk (<4%)

Note: Average clinical risk refers to the average cohort risk of clinically high-risk men post surgery, established in a cohort of 1,129 clinically high-risk patients that underwent radical prostatectomy as a first-line treatment at the Mayo Clinic between 2000 and 2006. The average incidence of metastases was 6.0% at 5 years post-radical prostatectomy. Risk score categories are determined using a Cox proportional hazards model risk model based on a cohort of 1,129 clinically high-risk patients, with 856 patients of follow-up data at 5 years. Decipher risk categories are determined using a Cox proportional hazards model, accounting significantly clinical risk parameters of African-American race, PSA, Gleason score, and initial tumor stage.

GenomeDX Medical Director (Name & Signature)
Medical Directors: Timothy L. Tchek ME, PhD, Doug Deggens, MD

Date: [Redacted]

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Thank You

BAYLOR COLLEGE OF MEDICINE
Houston, Texas