

# Jeffrey Thill, MD

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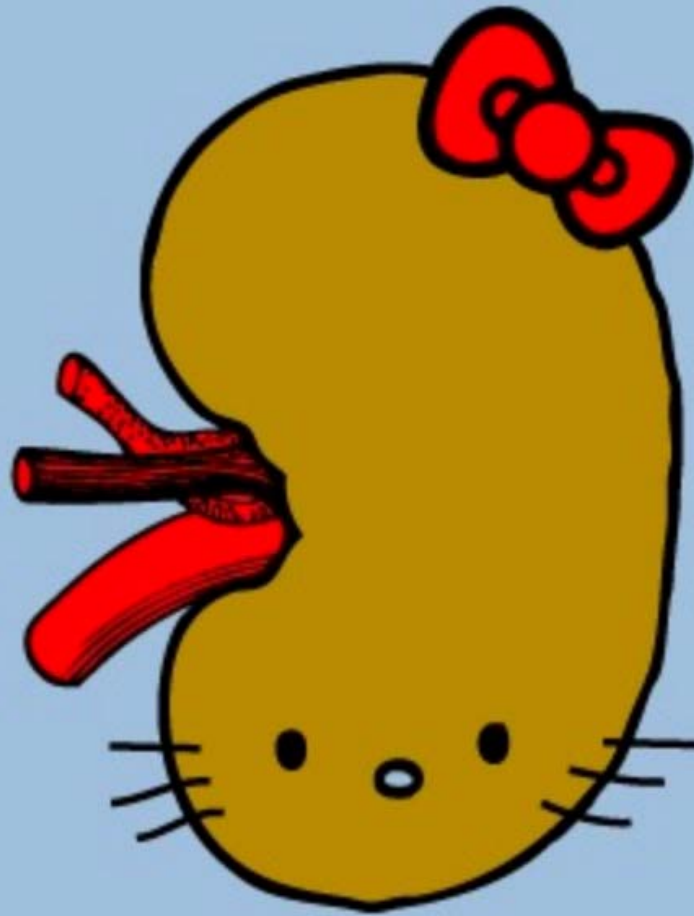
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# Overview of Urologic Cancer Care

First Annual Oncology Symposium  
May 19, 2018

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Hello Kidney

Standards are presented in green boxes; Recommendations are presented in yellow boxes; Options are presented in red boxes.

Key: AS, active surveillance; CKD, chronic kidney disease; CT, computed tomography; FNA, fine needle aspiration; MRI, magnetic resonance imaging; PN, partial nephrectomy; RFA, radiofrequency ablation; RN, radical nephrectomy; TA, thermal ablation

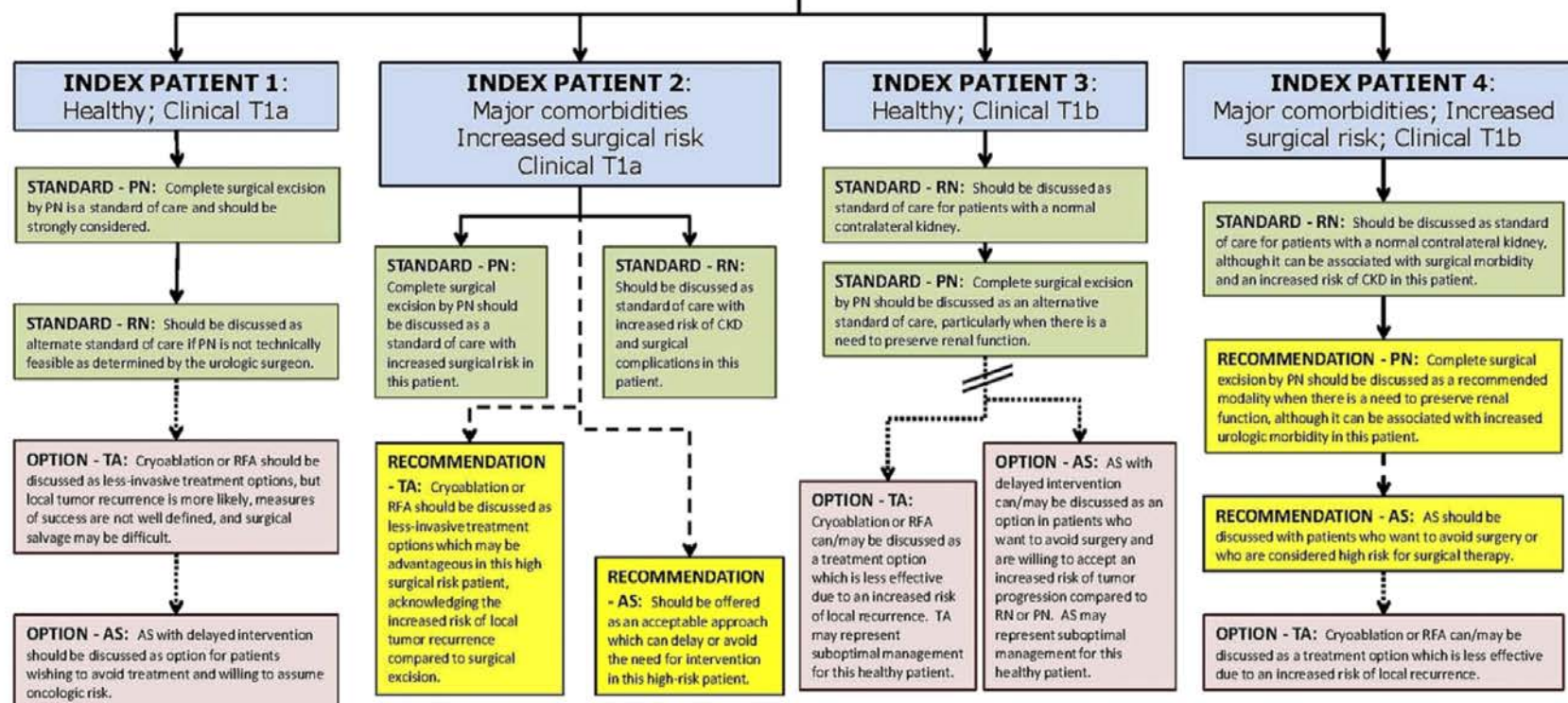
## Patient with clinical T1 renal mass

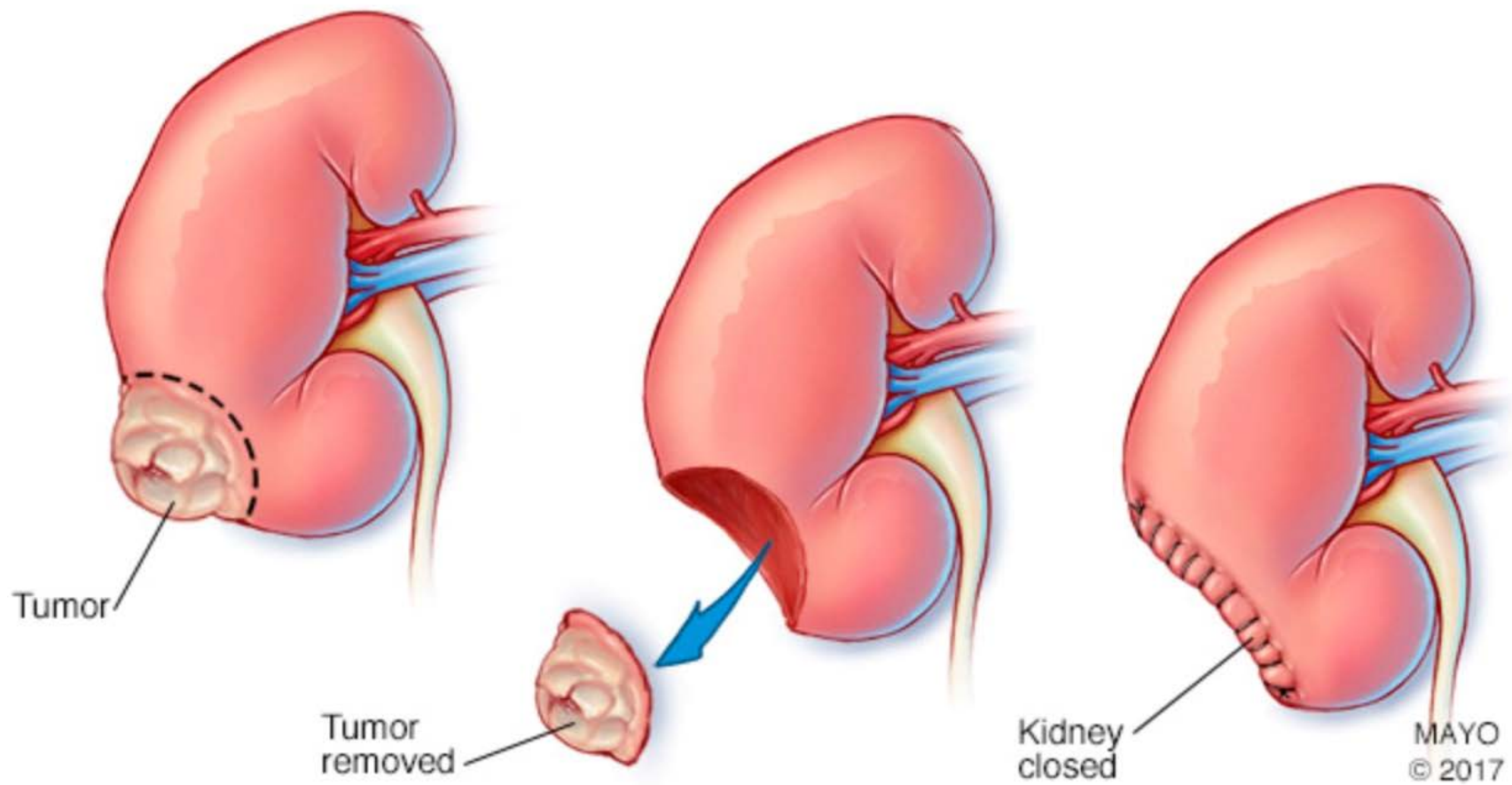
### EVALUATION

- High-quality cross-sectional imaging study (CT or MRI) with and without contrast (in the presence of adequate renal function) to assess contrast enhancement, exclude angiomyolipoma, assess for locally invasive features, define the relevant anatomy and evaluate the status of the contralateral kidney
- Percutaneous renal mass core biopsy with or without FNA for patients in whom it might impact management, particularly patients with clinical or radiographic findings suggestive of lymphoma, abscess or metastasis

### COUNSELING

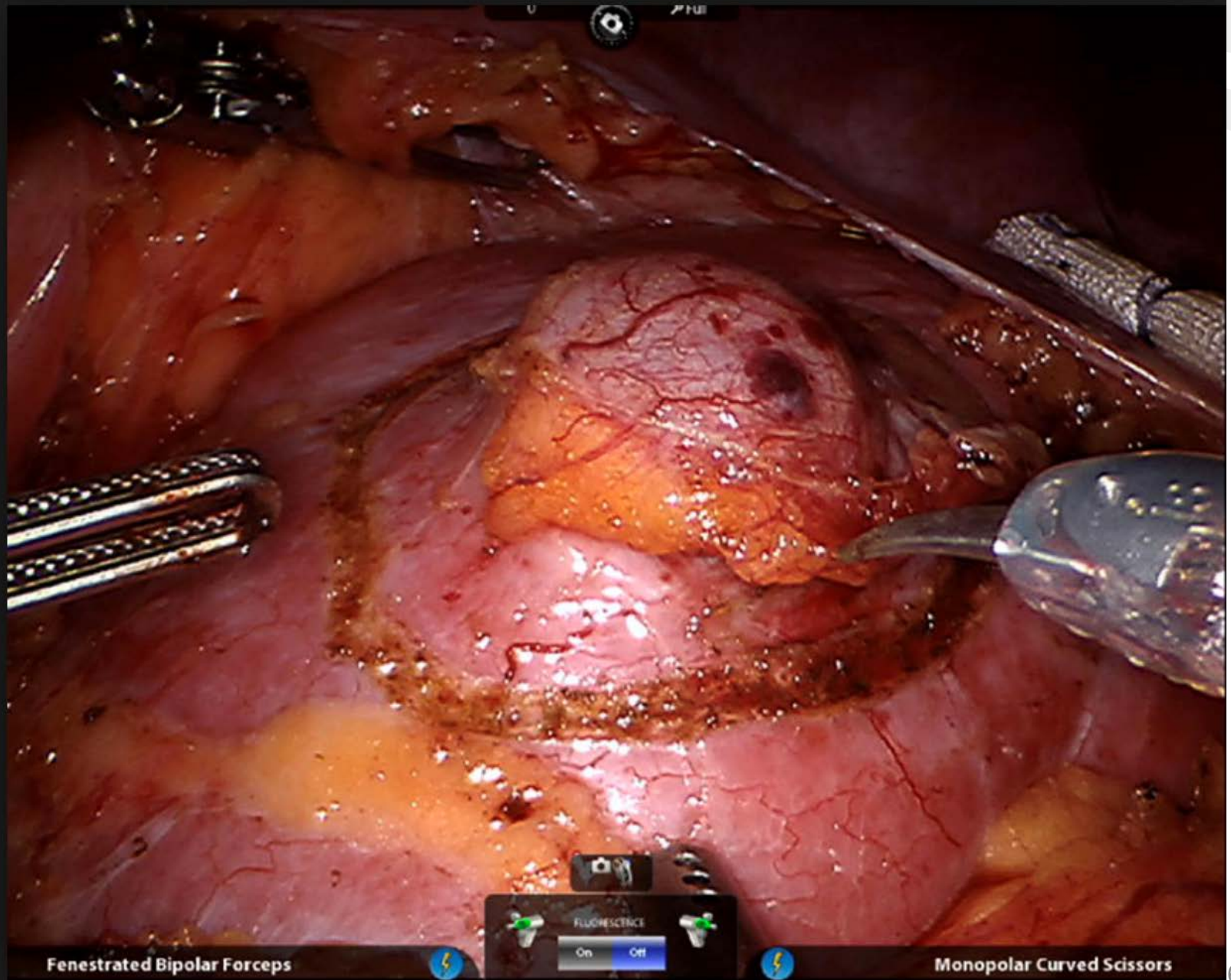
- Review the current understanding of the natural history of clinical T1 renal masses, the relative risks of benign vs. malignant pathology and the potential role of AS
- Review the available treatment options and the attendant benefits and risks, including oncologic considerations, renal functional considerations and potential morbidities
- Discuss the potential advantages of a nephron-sparing treatment approach in the imperative and elective settings, including the avoidance of dialysis and reduced risk of CKD with its attendant morbidity and mortality



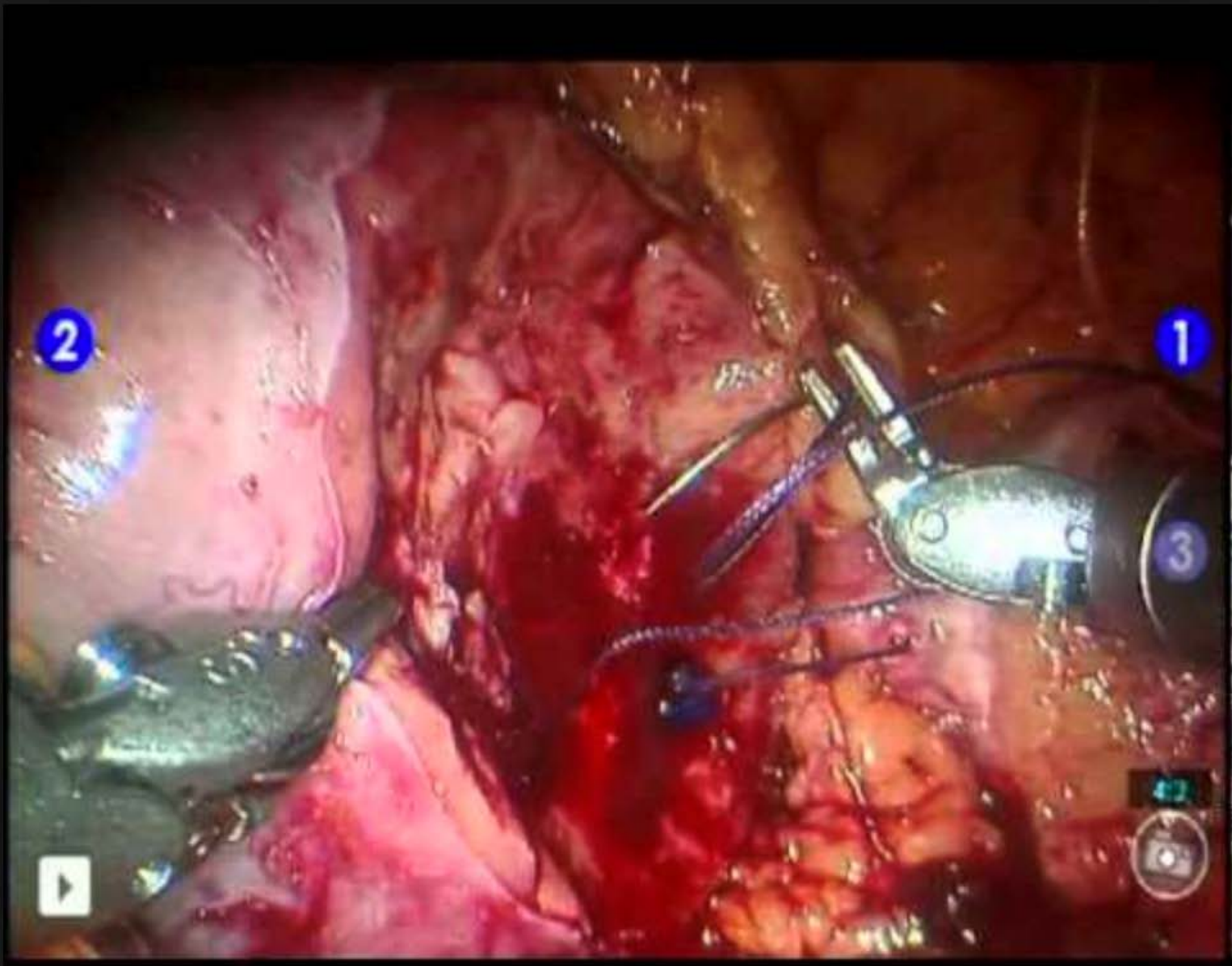




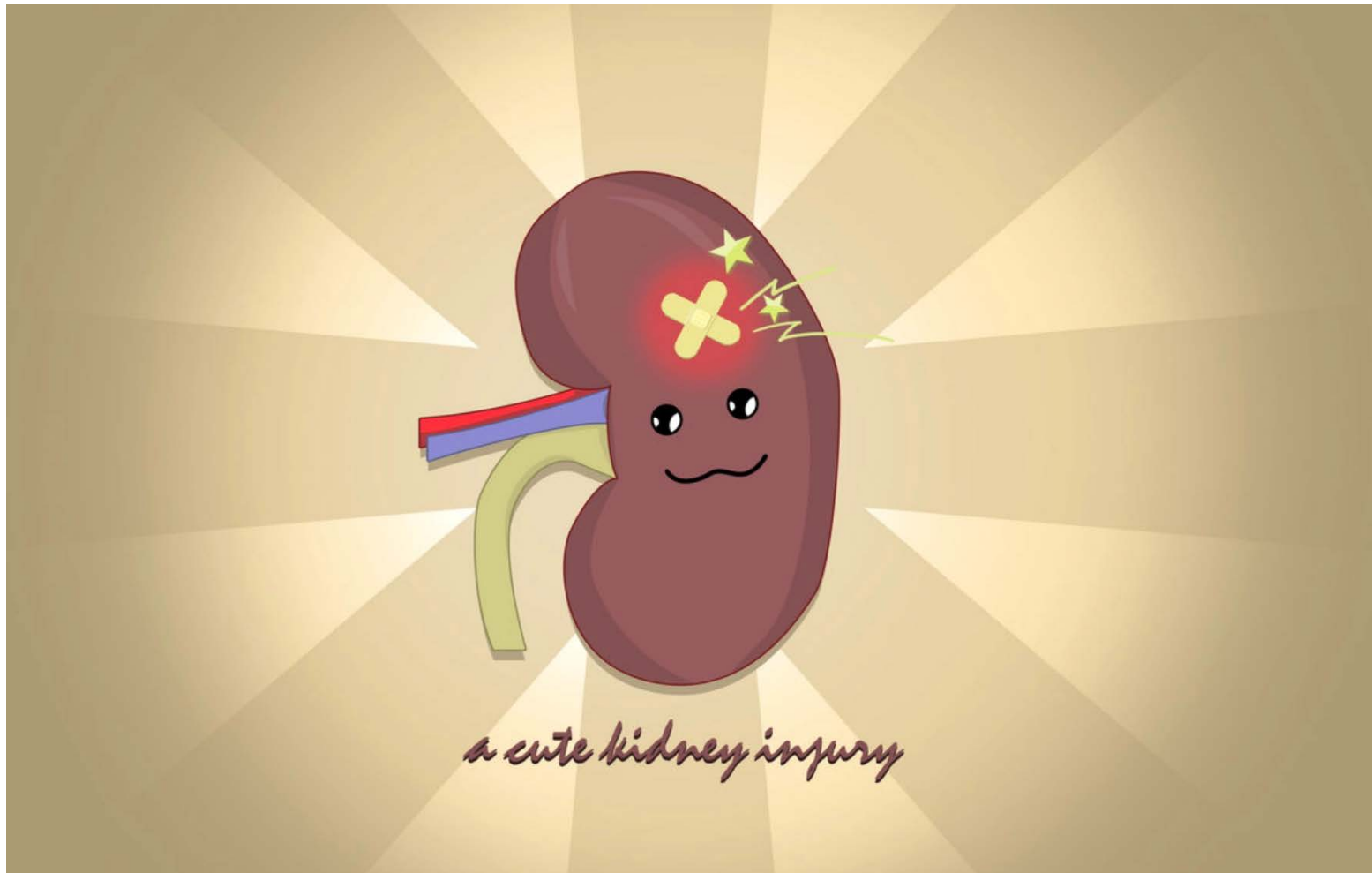






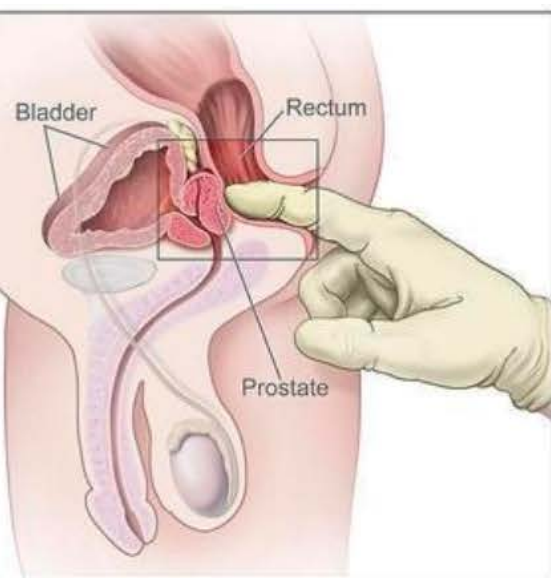














# Many Prostate Cancer Biomarkers!

## Genetic Markers

- Prolaris™
- Decipher™
- OncotypeDx™
- ConfirmMDx®
- ProstaVision™
- GWAS (genome-wide association study)
- SNIPS
- BRCA1&2
- HOX B13

## Others

- PCA3
- TMPRSS ERG
- VPAC1
- CTC
- Prostate Core Mitomic Test (PCMT)
- RNA: micro/exosomal / mitochondrial
- Urinary sarcosine
- Promark (tissue staining)
- Circulating DNA
- 4K
- PTEN

J.Urol 2013; 189(2): 422

# PROSTATE CANCER MARKERS

## WHO TO BIOPSY

TEST	INDICATION	SCIENCE	RESULTS	COST
<b>Prostate Health Index</b> Beckman Coulter	Blood based test for patients with a PSA between 2-10ng/ml (4-10ng/ml FDA) • Reduces negative biopsies • Calculates risk of finding prostate cancer on biopsy	FDA approved index of proteins in the blood that combines the concentrations of PSA, freePSA and pro2PSA in a formula that produces the PHI Score, which has three times the specificity for prostate cancer compared to PSA alone.	• PHI results fall into four categories of risk that prostate cancer may be found on biopsy.	• \$499 • Medicare: Currently not covered • Financial assistance: Available by PCLS • 866-725-7522 (PCLS)/855-420-7140 (IDL) • Prostatehealthindex.us
<b>4Kscore®</b> OPKO	Indicated for men with an abnormal PSA or DRE as a reflex blood test combined with clinical information to determine an individual patient's risk for high-grade prostate cancer on biopsy • For patients who are considering a first biopsy or who have had a prior negative biopsy	Laboratory test measuring 4 kallikreins in the blood (Total PSA, Free PSA, Intact PSA and hK2) and combined with the patient's clinical information in an algorithm to predict the individual patient's risk of having high-grade prostate cancer versus indolent or no cancer.	• 4K results provide percent probability (positive predictive value) of an individual patient's risk of having high-grade prostate cancer on biopsy.	• \$1,185 • Medicare: Currently not covered • Financial assistance: Contact billing office for issues • 800-883-7999 • Clinical.opko.com
<b>ConfirmMDx™</b> MDxHealth	Biopsy tissue based test for patients who are repeat biopsy candidates • Provides risk stratification on decision for repeat biopsy • Eligibility: Patients with a prior negative or HGPIN biopsy result in past 24 months	Three-gene methylation assay to detect an epigenetic field effect associated with the cancerization process at the DNA level.	• Negative ConfirmMDx result: Avoid repeat biopsy and monitor with routine screening. • Positive ConfirmMDx result: Suspicious areas marked as positive providing repeat biopsy guidance on a prostate map.	• \$3,300 • Medicare: Covered (LCD#35368) • Financial assistance: Available for out of pocket expenses • 866-259-5644 • Mdxhealth.com
<b>ProgenSA® PCA3 Assay</b> Hologic Inc.	Urine-based test, post DRE, which adds useful info when PSA or DRE is inconclusive • For patients who are considering first or repeat biopsy • FDA approved for use in conjunction with other patient info to aid in the decision for repeat biopsy in men ≥ 50 years	Test detects PCA3 gene that is highly specific for prostate cancer. Measures concentration of prostate cancer gene3(PCA3) and prostate specific antigen (PSA) RNA in post-DRE urine and calculates ratio of PCA3 molecules to PSA molecules to produce the PCA3 score.	• As the PCA3 score increases, the likelihood for positive biopsy increases. As the PCA3 score decreases, the likelihood for a positive biopsy decreases • The greatest diagnostic utility occurs at a cutoff score of 25	• \$300-500 • Medicare: Covered (CPT Code: 81313) • 800-523-5001 • Pca3.org
<b>Oncotype DX®</b> Genomic Health	Biopsy tissue based test to help determine how aggressive cancer is by providing a likelihood of favorable pathology. • For patients that are NCCN Very Low, Low & Intermediate Risk • Provides personalized Risk Assessment, aids in the decision for active surveillance or immediate treatment	Assay looks at 17 genes within 4 pathways (androgen signaling, stromal response, cellular organization, proliferation) to assess tumor aggressiveness.	• Genomic Prostate Score (GPS) from 0 to 100. • Likelihood of freedom from high grade and/or non-organ-confined disease. • GPS is reflective of the biology of the tumor at the time of biopsy.	• \$4,180 • Medicare: Covered • Financial assistance: Available for out of pocket expenses • 866-662-6897 • Oncotypedx.com
<b>ProMark™</b> Metamark Genetics	Biopsy tissue based prognostic assay for patients with biopsy Gleason Scores 3+3 and 3+4 • For patients who are deciding between active surveillance and treatment • Provides a personalized risk score • Can be used as stand-alone risk score or combined with NCCN risk categories	Eight-protein signature predicts cancer aggressiveness (>4+3 and/or non-organ confined). Selected markers eliminate sampling variability, provides a direct analysis of cancerous regions of interest. Test requires 4 tissue sections.	• ProMark Score gives a personalized % probability of aggressive cancer. • Interpretation as stand-alone result and in combination with NCCN risk categories. • Results delivered within an easy-to-interpret, personalized report.	• Cost: \$3,900 • Medicare: Not currently covered • Financial assistance: Available if out-of-pocket cost are greater than \$350 • 877-743-3338 • Metamarkgenetics.com
<b>Prolaris®</b> Myriad Genetics	Biopsy tissue based test for patients who are Active Surveillance candidates. • Available post-prostatectomy available to determine relative risk of BCR	46-gene expression signature includes cell cycle progression genes selected based upon correlation with prostate tumor cell proliferation	• Prolaris score • Biopsy is < or = or > than AUA risk group and estimates 10year mortality risk. • Post-surgical results are similar but provide 10 year risk for BCR.	• \$3,400 • Medicare: Covered • Financial assistance: Available if estimated out-of-pocket costs are greater than \$375 • 800-469-7423 • Prolaris.com
<b>Decipher®</b> GenomeDx Biosciences	Tissue based test for patients with adverse pathology post-surgery (radical prostatectomy) • Provides metastatic risk stratification that can help guide post-operative treatment decisions • For patients with pT3 or positive surgical margin or rising PSA • Helps determine the need & optimal timing of radiation	22 RNA biomarkers across multiple biological pathways associated with metastatic progression including cell cycle progression, immune system modulation and androgen signaling. Measures each patient tumor's metastatic risk. Based on the whole transcriptome analysis platform.	• Decipher provides probability of metastasis at 5 years after surgery, and 3 years after detectable PSA • Decipher high risk men may benefit from adjuvant radiation • Decipher low risk men can be safely observed with PSA monitoring	• Cost: \$3,400 cash pay price • Medicare: Covered • Financial assistance: Available and patients pay no more than \$295 out-of-pocket • Contact phone number for doctor: 1-888-972-1601 • Genomedx.com
<b>Know Error®</b> Strand Diagnostics	Oral swab and biopsy tissue based test provides DNA confirmation of specimen provenance • Rules out undetected transposition or contamination of specimen among patients which could lead to misinterpretation of pathology or biomarker. • Increases diagnostic accuracy	Buccal swab in the clinic sent for DNA match to pathology specimen; may be used with all tissues. STR profiles assessed from multiplex panel of 16 genetic markers.	Results Confirm: • DNA Match • DNA Non-match • Contamination	• \$1,780 • Medicare: Currently not covered • Financial assistance: Available and patients pay no more than \$295 out-of-pocket • 888-924-6779 Ext. 2 • Knowerror.com

## WHO TO RE-BIOPSY

## WHO TO TREAT Postive Biospy

## WHO TO TREAT Post Sugery

## Specimen Provenance



<b>Oncotype DX</b>	<ul style="list-style-type: none"> <li>Measures expression of 17 genes across multiple pathways to determine disease aggressiveness</li> <li>Assigns a genomic prostate score that is considered in the context of clinical pathologic features (eg, Gleason score, PSA) to determine management</li> <li>NCCN guidelines recommend for treatment-naïve patients with very low and low-risk disease who are candidates for active surveillance</li> </ul>
<b>ProMark</b>	<ul style="list-style-type: none"> <li>Measures 8 proteins linked to aggressiveness and lethal outcome of prostate cancer</li> <li>Risk predictor of whether aggressive therapy is appropriate</li> <li>NCCN guidelines recommend test for patients with very low and low-risk prostate cancer who have not received treatment and are candidates for active surveillance or definitive therapy</li> </ul>
<b>Prolaris Test</b>	<ul style="list-style-type: none"> <li>Determines how fast cancer cells are dividing to predict aggressiveness</li> <li>Can be used for postprostatectomy patients to better estimate risk of biochemical recurrence</li> <li>Reports include 10-year risk of metastatic disease following definitive treatment</li> <li>NCCN guidelines recommend for treatment-naïve patients with very low and low-risk disease post-biopsy who are candidates for active surveillance</li> </ul>
<b>Decipher</b>	<ul style="list-style-type: none"> <li>Measures expression of 22 RNA biomarkers involved associated with prostate cancer aggressiveness</li> <li>Calculates probability of clinical metastasis within 5 years of radical prostatectomy</li> <li>NCCN guidelines recommend for patients after radical prostatectomy to assess if additional treatment is needed</li> </ul>
<b>ConfirmMDx</b>	<ul style="list-style-type: none"> <li>Epigenetic assay tests for signs of DNA methylation as a signal of cancer aggressiveness</li> <li>Tests for methylation of the <i>APC</i>, <i>GSTP1</i>, and <i>RASSF1</i> genes</li> <li>NCCN guidelines recommend test for higher-risk patients who have had at least 1 prior negative biopsy</li> </ul>
<b>4Kscore Test</b>	<ul style="list-style-type: none"> <li>Measures the plasma levels of 4 prostate-derived kallikrein proteins: total PSA, free PSA, intact PSA, and human kallikrein 2</li> <li>Combines biomarkers with a patient's age, DRE status (nodule/no nodule), and prior biopsy status</li> <li>Calculates the risk of a finding of prostate cancer with Gleason score <math>\geq 7</math> if a biopsy were conducted</li> <li>NCCN guidelines recommend test for higher-risk patients who have had at least 1 prior negative biopsy</li> </ul>

DRE indicates digital rectal examination; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen.



## ORDERING PHYSICIAN

John Jones MD  
320 Wakara Way  
Salt Lake City, UT 84108

## SPECIMEN

Specimen Type: Tissue Block  
Tissue: Prostate  
Biopsy Date: Mar 13, 2011  
Accession Date: Jul 20, 2012  
Report Date: Aug 16, 2012

## PATIENT

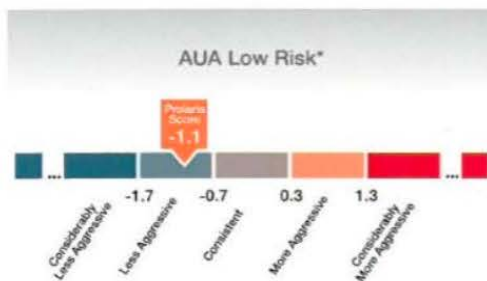
Name: James C.  
Date of Birth: Feb 2, 1940  
Patient ID: 7602  
Gender: Male  
Accession #: 00987602-BLD  
Requisition #: 00987602

Block(s) Analyzed: 2067a

## Polaris Score: -1.1

► **Less Aggressive Than Average AUA Low Risk**

**Interpretation:** The Polaris Score of -1.1 indicates that this cancer is less aggressive than the average cancer in the American Urology Association (AUA)<sup>1</sup> Low Risk category.



The above chart illustrates the AUA Low Risk category, which is composed of patients with varying degrees of cancer aggressiveness. Cancer aggressiveness can be stratified within this category based upon Polaris Scores, which are indicated below the graph.<sup>2</sup>

► **US Distribution Percentile: 7%**

(For AUA Low Risk)

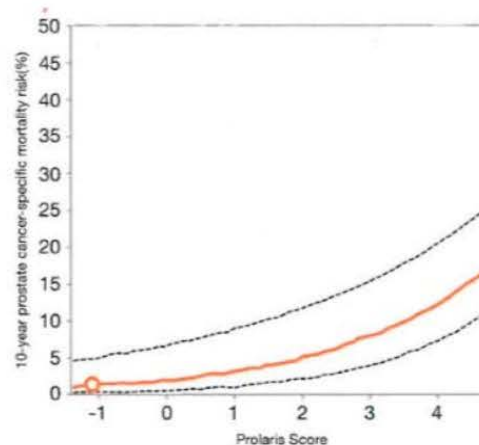
**Interpretation:** 7% of patients in the AUA Low Risk category have a lower Polaris Score.

## CLINICO-PATHOLOGIC FEATURES USED FOR ANALYSIS

PSA Prior to This Biopsy: 4.2  
Gleason Score: 3+3=6  
Clinical T Stage: T1c

► **10-Year Prostate Cancer-Specific Mortality Risk: 1% (95% CI:0-5%)**

**Interpretation:** The patient has a 10-year mortality risk of 1% if managed conservatively. Mortality risks could be altered by various therapeutic interventions.



Patients with similar clinico-pathologic features, as defined by their CAPRA score, have the same *a priori* 10-year prostate cancer-specific mortality risk. The addition of the Polaris Score further differentiates this risk, as illustrated in the above graph, which is specific to this patient's CAPRA score.<sup>3,4</sup> The orange line depicts the relationship between the Polaris Score and the mortality risk with the 95% confidence interval indicated by dashed lines and the patient's Polaris Score indicated by the orange dot.

## CLINICO-PATHOLOGIC FEATURES USED FOR ANALYSIS

PSA Prior to This Biopsy: 4.2    % Positive Cores: 25% (3/12)  
Gleason Score: 3+3=6    Patient Age: 72  
Clinical T Stage: T1c

**Note:** Clinico-pathologic parameters are provided by the healthcare provider and have not been verified by Myriad.

Physician and patient names have been changed to ensure confidentiality, but data presented is from actual cases.



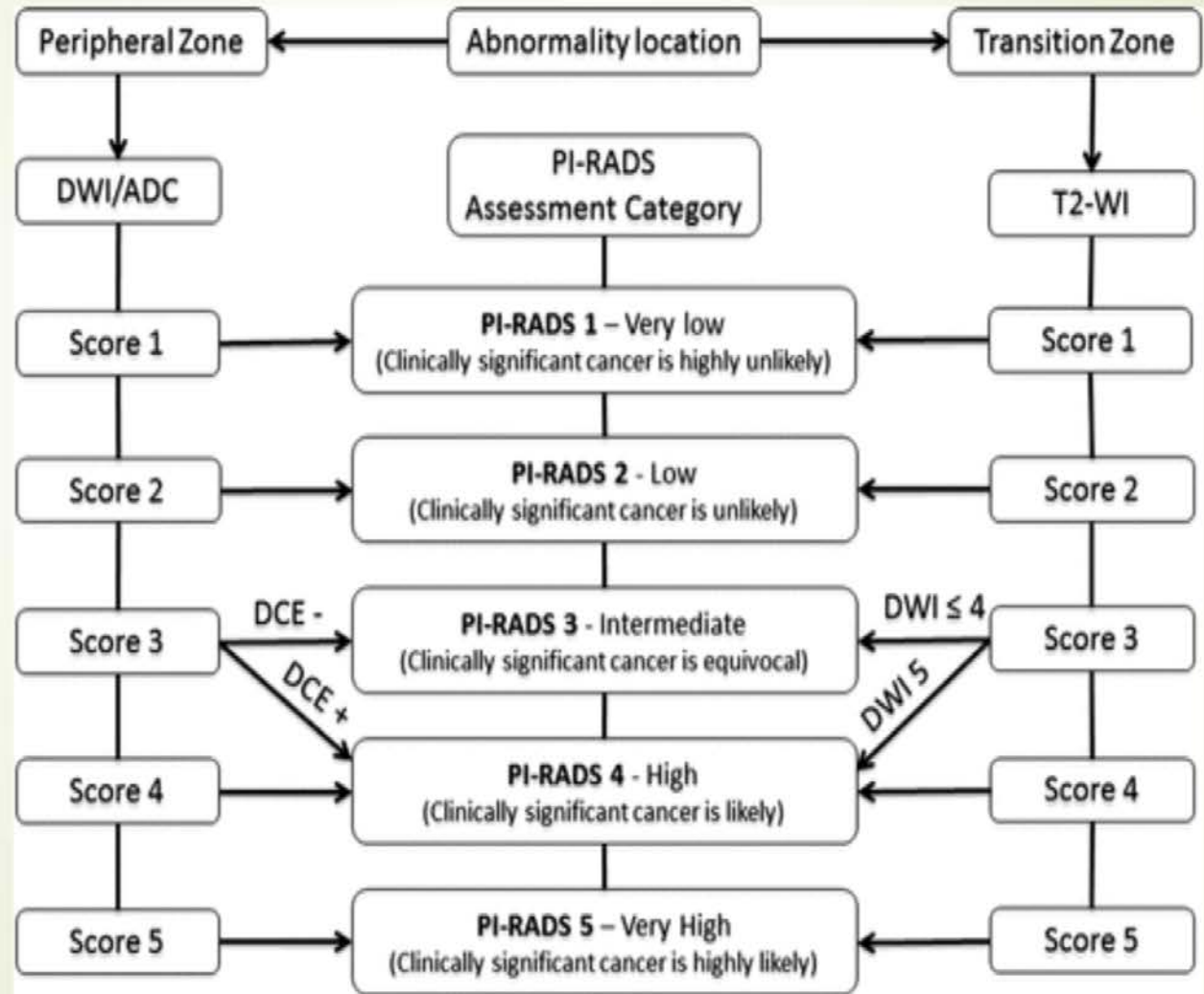


# Why Perform Prostate MRI

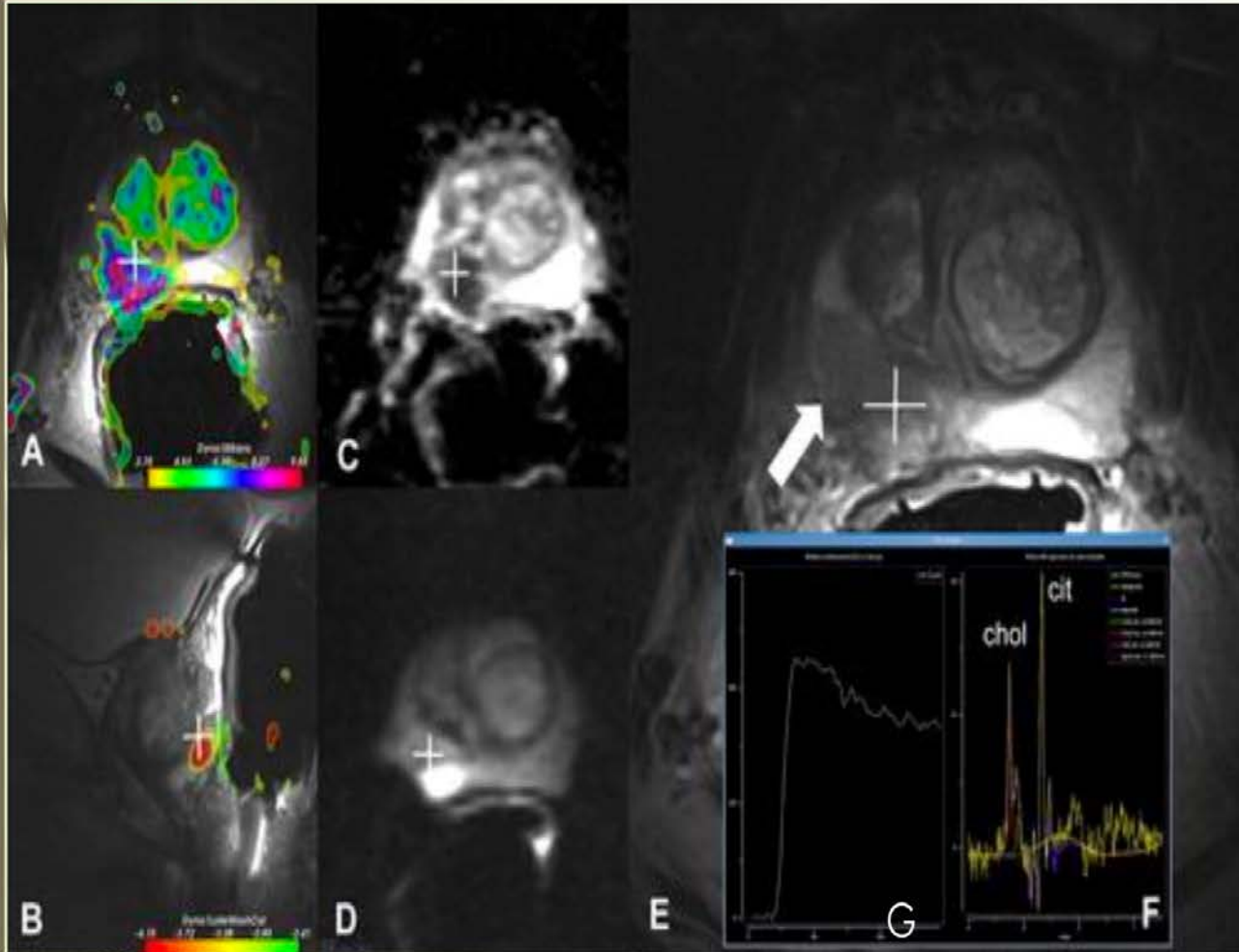
- Elevated PSA values inevitably lead to random prostate biopsies, which, in turn, lead to the discovery of incidental, often inconsequential, tumors.
- Random biopsies may miss significant disease.
- MRI may play a role in conjunction with PSA for localizing biopsy sites and identifying those tumors more likely to cause death if left untreated.

<http://www.ajronline.org/doi/full/10.2214/AJR.12.8510>

# PIRADS Version 2



# PI-RADS Example



T2 Score is 4 (B and E)

DWI/ADC Score is  
5 (C and D)

DCE-MRI Score is 3  
(A and G)

Total Score is 12  
(not including  
MRS)

**PI-RADS 4**  
**Probably**  
**Malignant**



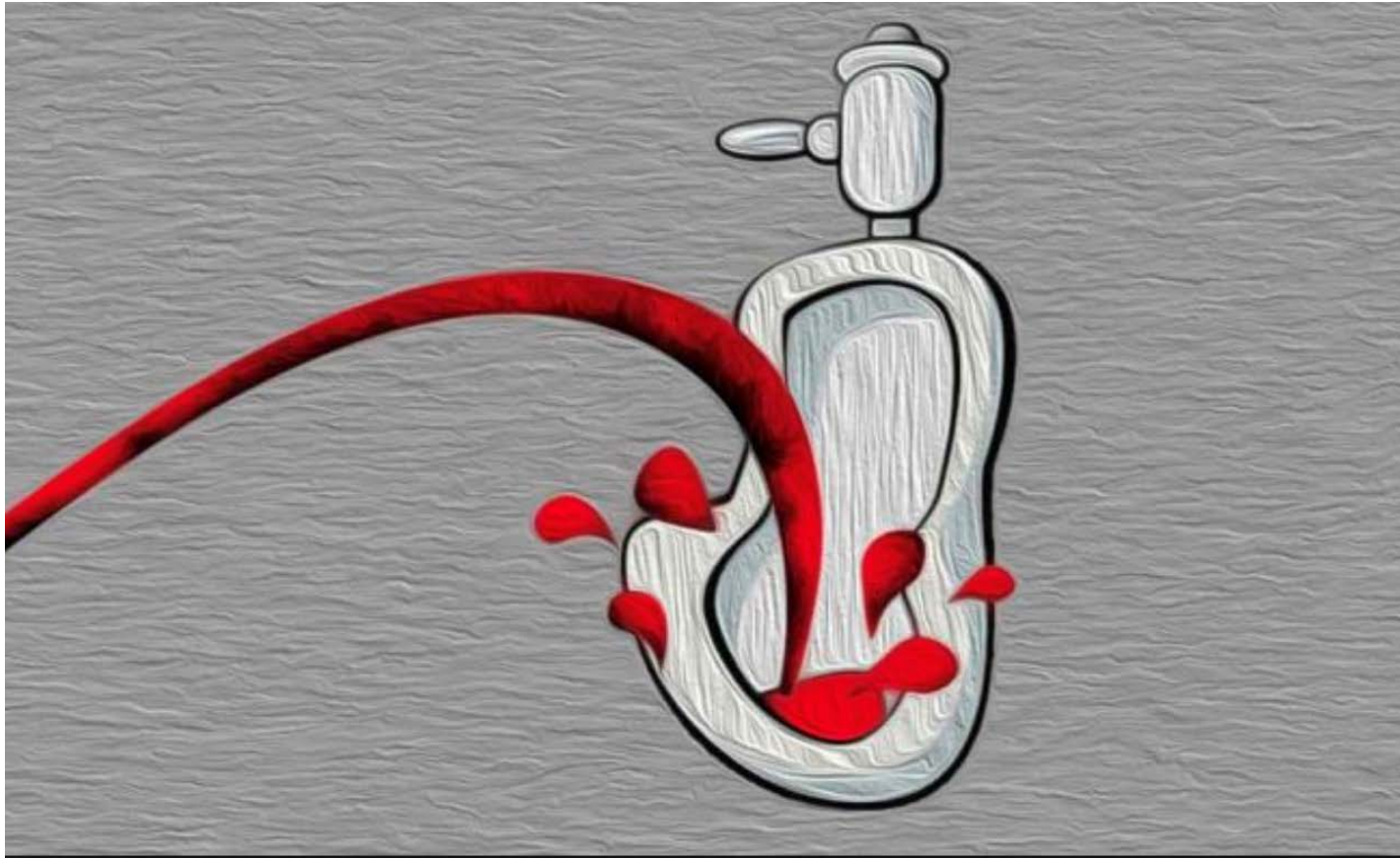




# The Argument for Carboplatin for Stage I Seminoma

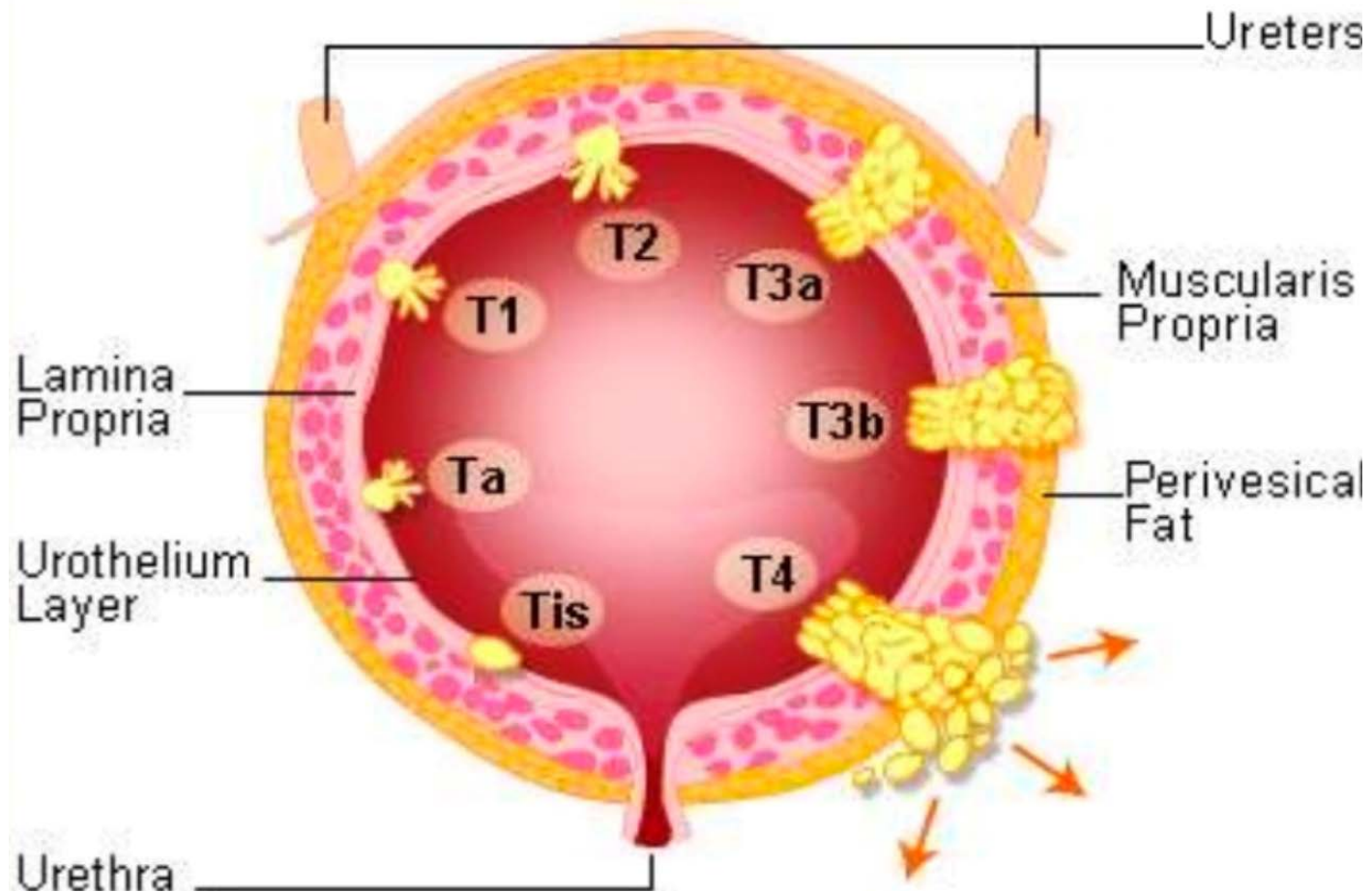
- Carboplatin is the most effective way to prevent relapse
- Carboplatin is associated with minimal acute toxicity
- Radiation therapy is associated with unacceptable late toxicity
- The risk of late complications from single agent carboplatin is hypothetical whereas the risk of late complications from radiation therapy is well documented
- Carboplatin appears to reduce the risk of second primary germ cell tumors



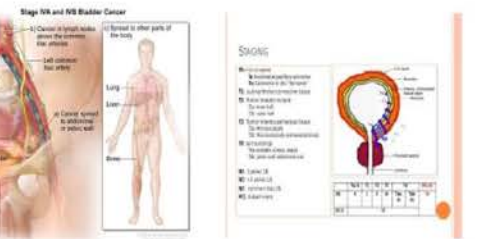
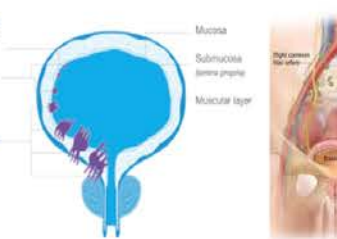
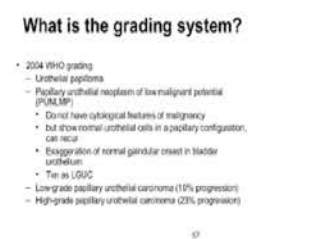
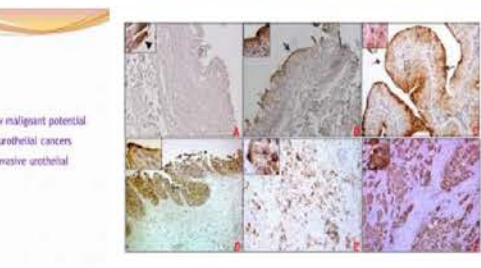
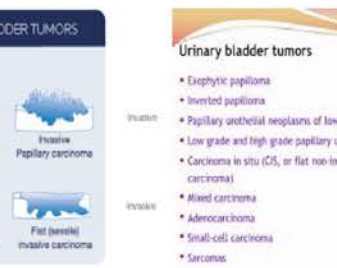
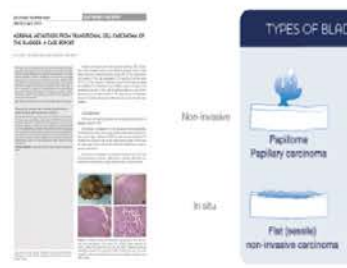
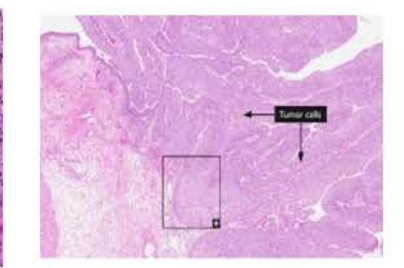
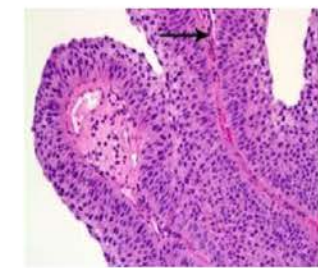
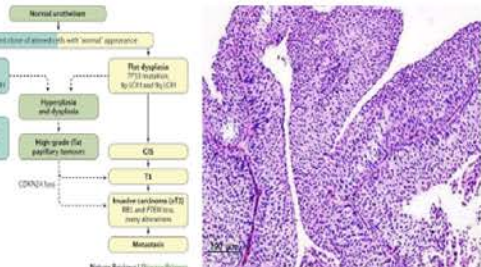
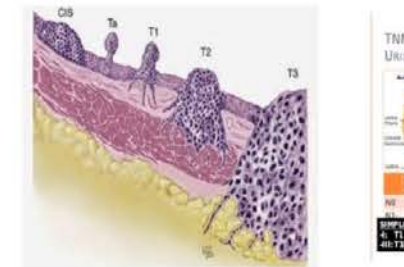
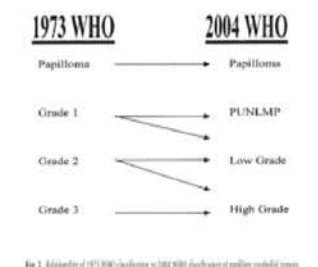
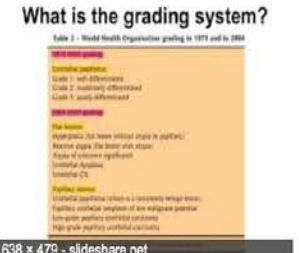
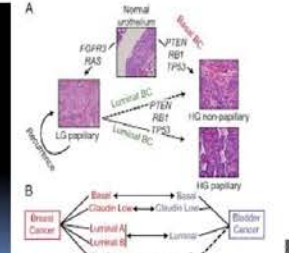
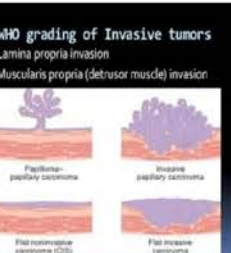
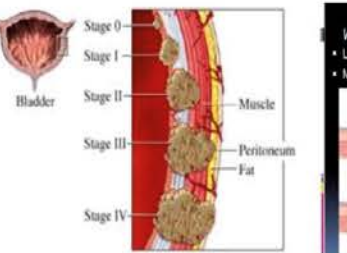
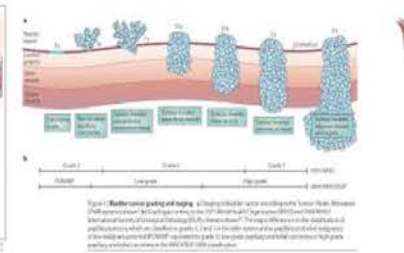
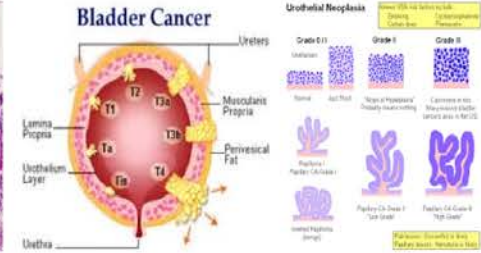
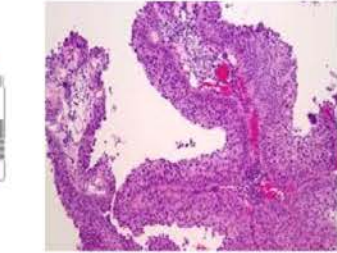
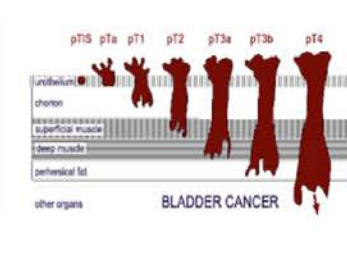
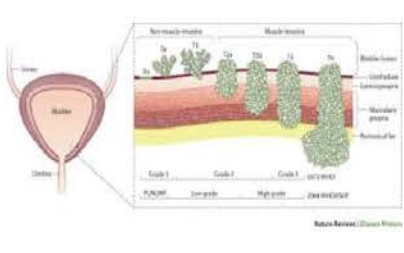




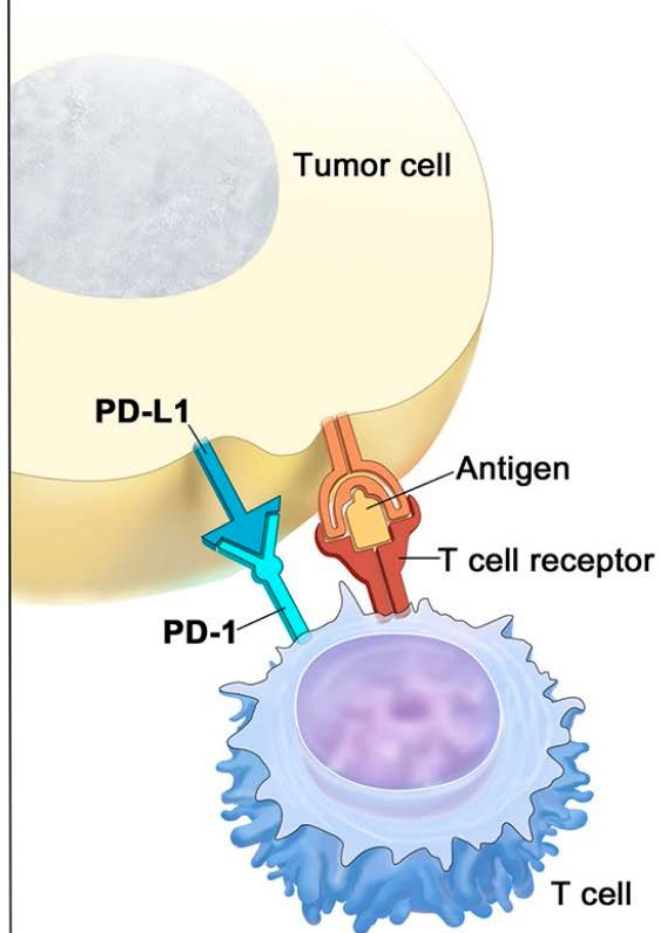
# Bladder Cancer







**PD-L1/PD-1 binding inhibits T cell killing of tumor cell**



**Blocking PD-L1 or PD-1 allows T cell killing of tumor cell**

