

# Prostate Cancer

## An Update (2014)

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*UMassMemorial*



No Conflicts of Interest

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# Part 1

Natural History, Screening  
and Diagnosis

# Key Points

- Prostate cancer is **common**:
  - incidence in the United States (2014)
    - new cases: 233,000
    - deaths: 29,480



# Key Points

- Incidence in **Arizona** (2014; population 6.55M)
  - new cases: 4,390
  - deaths: 640
- **Massachusetts** (2014; population 6.64M)
  - new cases: ~5,600
  - deaths: ~630



# Risk Factors

- Probability increases with **age**:
  - <40 years: 1/13,000
  - 40-59 years: 1/44
  - 60-79 years: 1/7
- **Ethnicity** plays a role:
  - African American 1.5 > Caucasian
  - African American 2.7 > Asian

*-- more aggressive and later stage disease at diagnosis*

# Risk Factors

- **Family history** is important
  - Hereditary disease accounts for 5-10%
    - single relative: 2.2-fold
    - two relatives: 4-fold
  - higher with brother than with father*
- **Environmental factors**; key to development and cure
  - Obesity
  - Nutrition and exercise

# Prostate Cancer: Importance

- Extremely important health concern:
  - prostate cancer can be deadly
  - prostate cancer can cause considerable morbidity
  - early diagnosis is key
  - requires a rationale approach to treatment

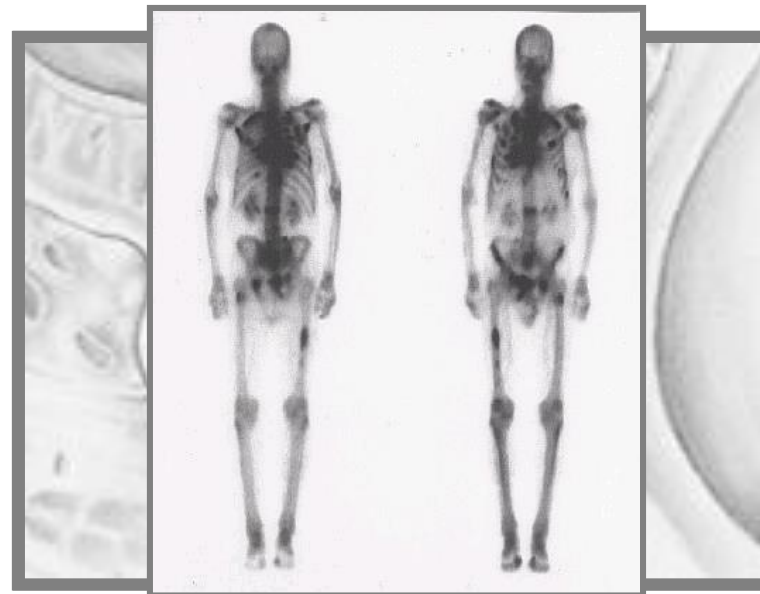
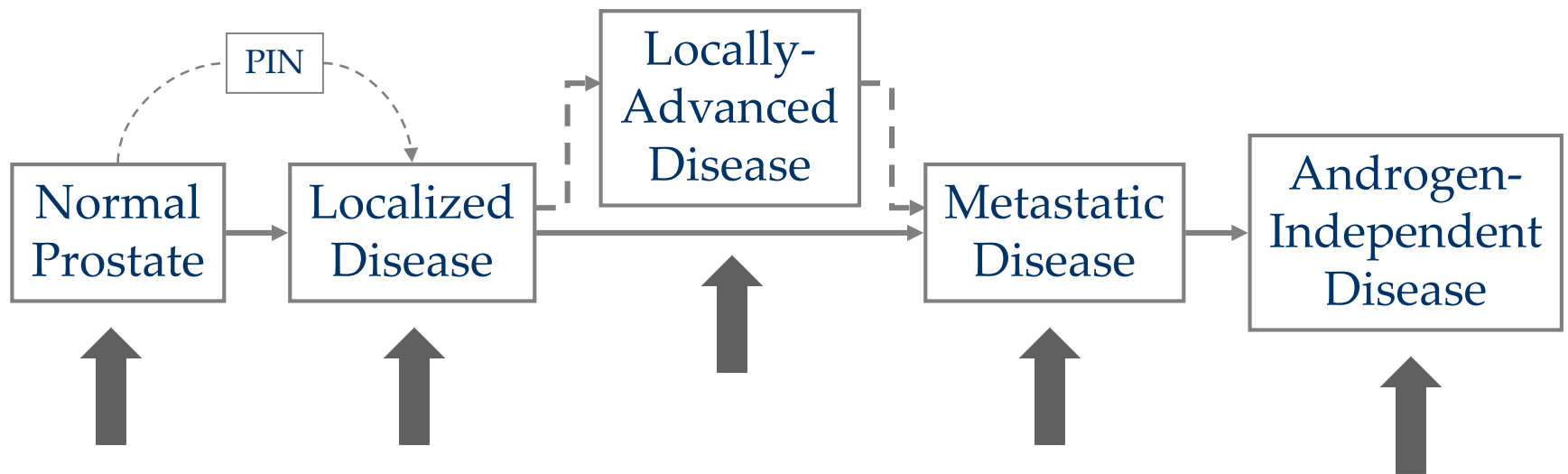
metastatic and recurrent disease is particularly worrisome



# Clinical Presentation

- Prostate cancer as a disease is not a single entity
- Prostate cancer represents a **range of clinical states** with differences in:
  - presentation
  - behavior
  - prognosis
  - outcomes





# Goals

- **Maximize Longevity** by eradicating cancer or conversion to a chronic disease
- **Minimize the Side Effects** that could compromise quality of life



# Screening

- Controversial Topic
  - **Is PSA screening is beneficial?**
  - advantage versus disadvantages
  - over versus under-treatment
  - effects on decision-making
  - still need improved tests and biomarkers



# Screening (continued)

- Controversial

- European and American Studies
- “stage migration”
- changes in survival
- still need improved tests and biomarkers

the key is a rational approach to treatment



# Screening (continued)

- Screening
  - **PSA** blood test; **digital exam (DRE)**
  - advantages and limitations to each
- Derivations of PSA test
  - total PSA
  - PSA velocity
  - free/total percent

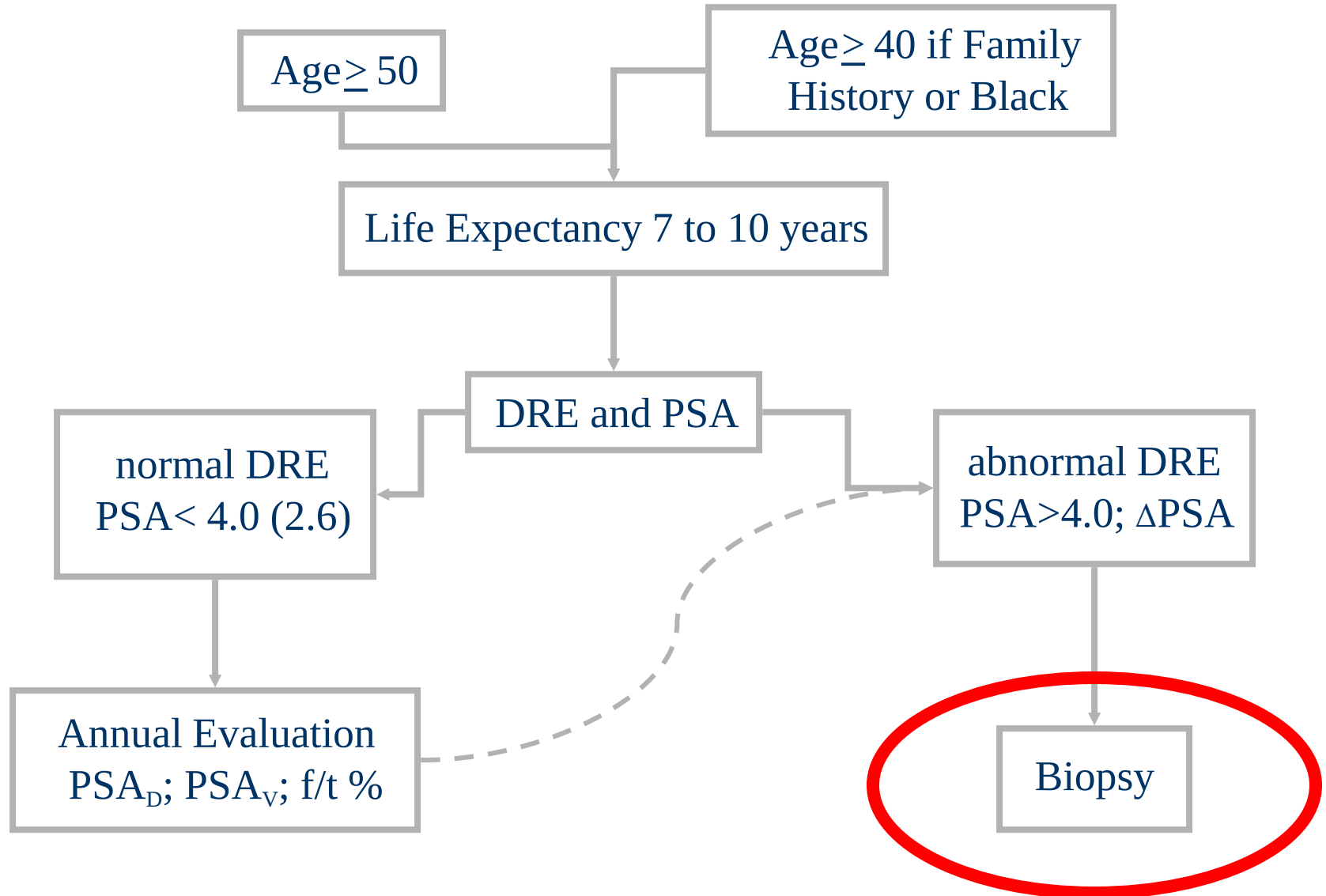


# Molecular Studies

- Who to biopsy: PCA-3<sup>TM</sup>, pro-PSA<sup>TM</sup>
- Who to re-biopsy (negative): Confirm MDx<sup>TM</sup>
- Who to treat (versus observation):  
Oncotype<sup>TM</sup>, Prolaris<sup>TM</sup>
- Predicting metastases: Decipher<sup>TM</sup>



# Screening Algorithm



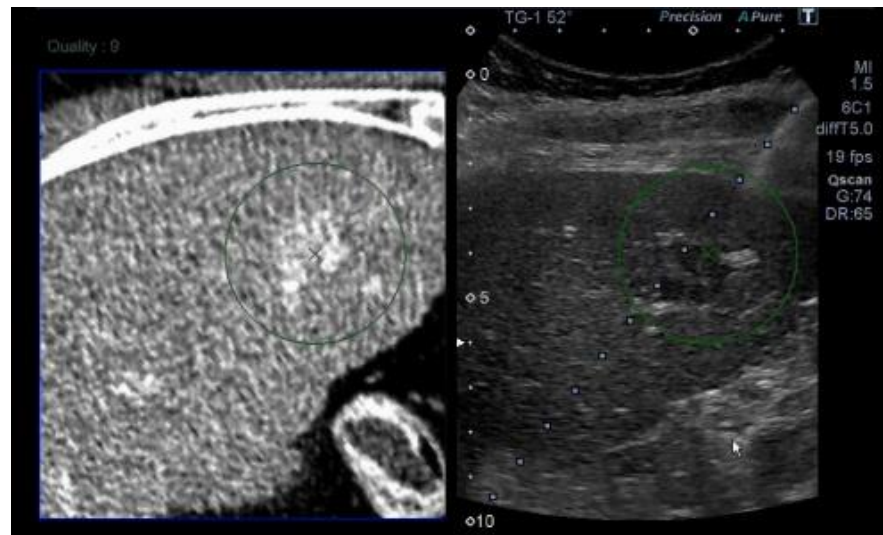
# TRUS/Biopsy

- The procedure
- **Diagnosis:** presence or absence of cancer
- **Volume and Histology (Pathology)**
  - number of cores; overall volume
  - high versus low grade:  
behavior and aggressiveness
- Other (pre-cancer): PIN and ASAP



# TRUS/Biopsy (continued)

- MRI and MRI/Ultrasound Fusion



# Key Points

- Importance of early diagnosis:
  - best chance of cure
  - greatest selection of treatments
- Choosing the optional treatment is difficult and challenging for many patients and their physicians



# Part 2

Risk Stratification

# Spectrum of Disease

Localized

Locally-advanced

Metastatic



- Prognosis and treatment options differ depending upon the extent and/or aggressiveness of your disease
- **Therapy is geared towards each patient**
  - there is no “one glove fits all” approach

# Spectrum of Disease

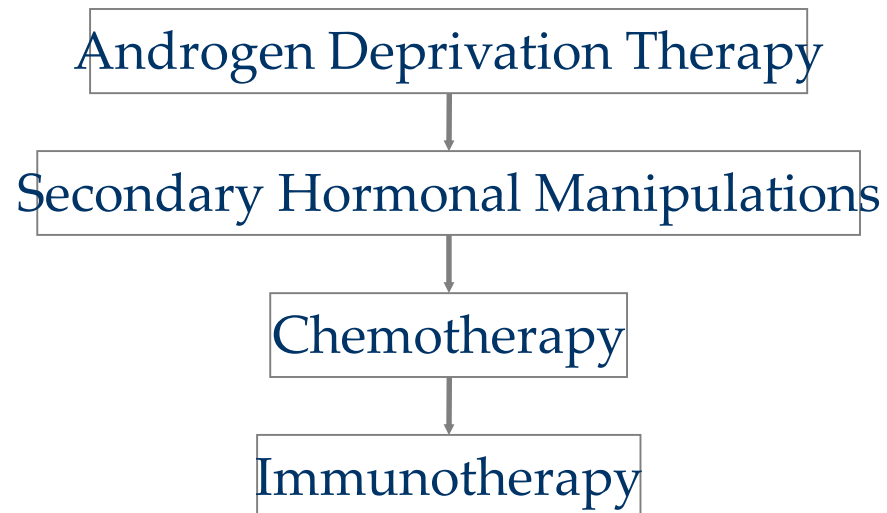
Localized

Locally-advanced

Metastatic



- Cancer has spread: “systemic” therapy



# Spectrum of Disease

Localized

Locally-advanced

Metastatic



- On exam, spread beyond the prostate but still in the pelvis

# Spectrum of Disease

Localized

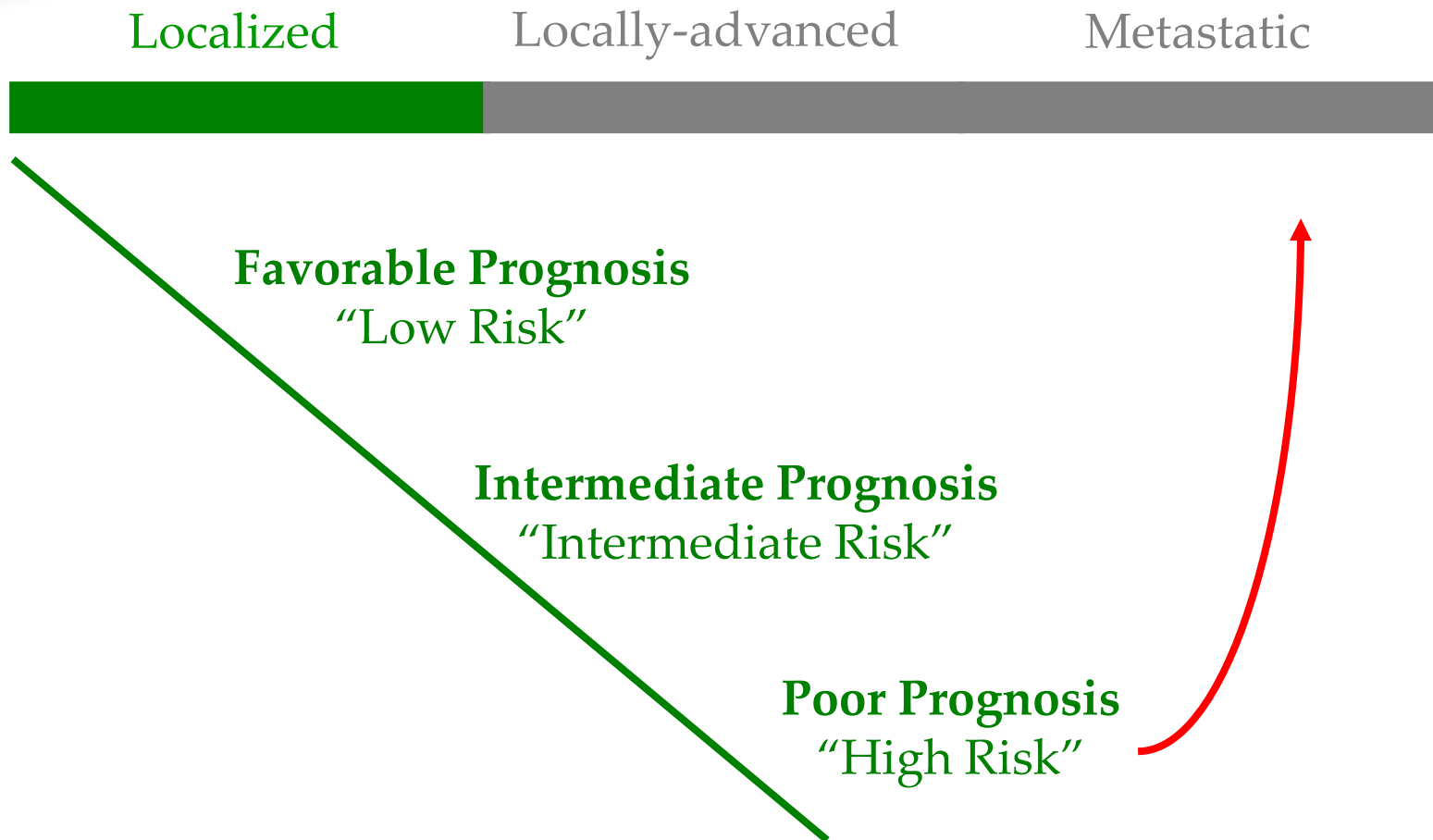
Locally-advanced

Metastatic



- On exam, cancer is within the prostate

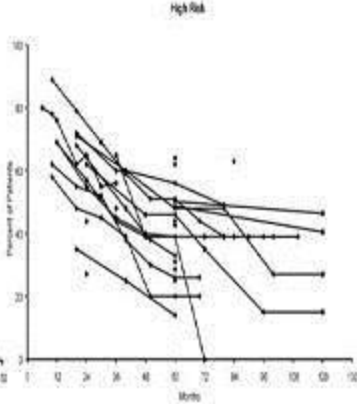
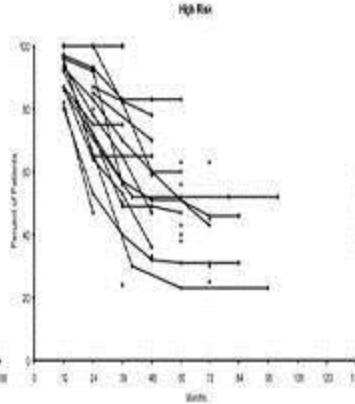
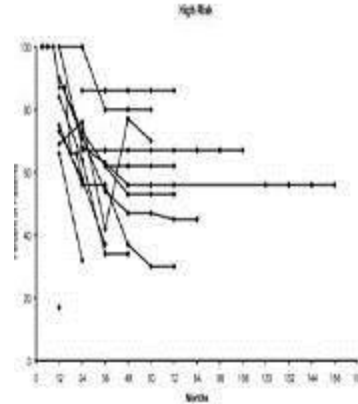
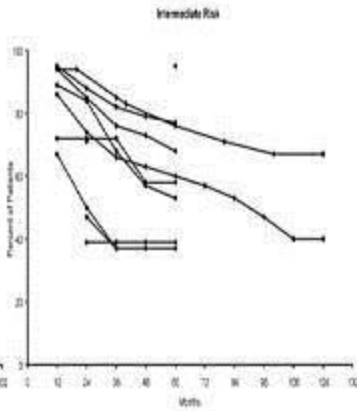
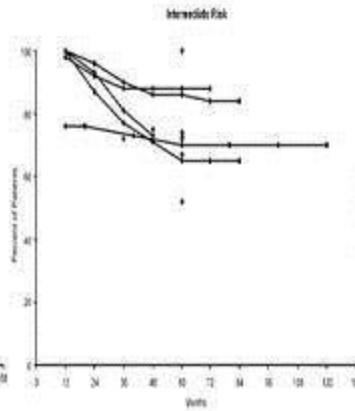
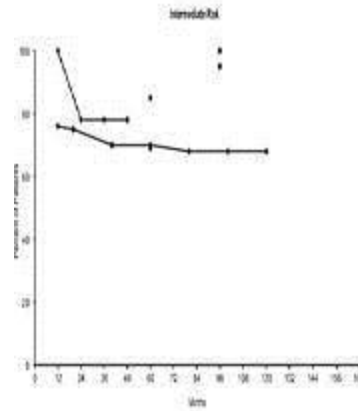
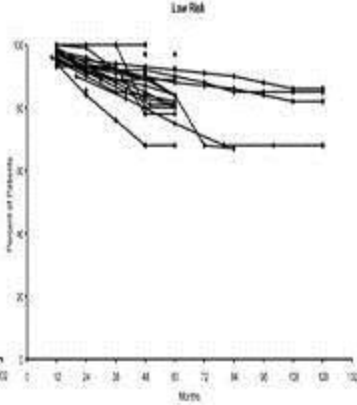
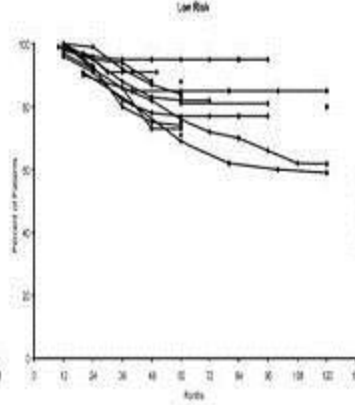
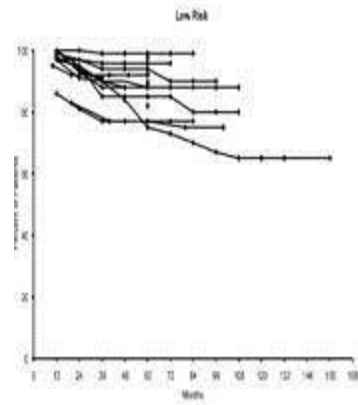
# Risk Stratification



# Interstitial Prostate Brachytherapy

# External Beam Radiotherapy

# Radical Prostatectomy



# Estimating Prognosis

Localized

Locally-advanced

Metastatic



Favorable Prognosis  
"Low Risk"

Intermediate Prognosis  
"Intermediate Risk"

Poor Prognosis  
"High Risk"

- We have three tools to stratify each patient's risk
  - **PSA** (blood test)
  - **Grade** (biopsy results)
  - **Stage** (results from exam and X-ray studies)

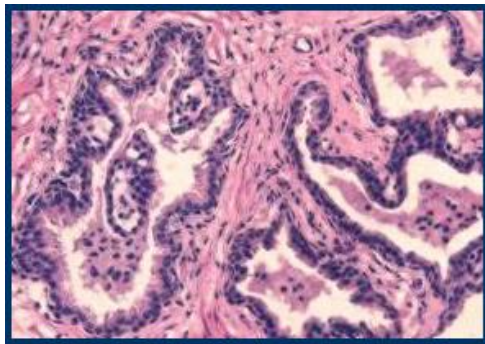
# PSA

- It has three applications/uses:
  - screen for cancer ( $>4\text{ng/ml}$ ; rapid increase)
  - monitor after therapy ( $\rightarrow$  undetectable)
  - **estimate risk of spread or metastasis;**  
increased for the following:
    - $>10\text{ng/ml}$ ;  $>20\text{ng/ml}$
    - doubles  $<6\text{-}9$  months

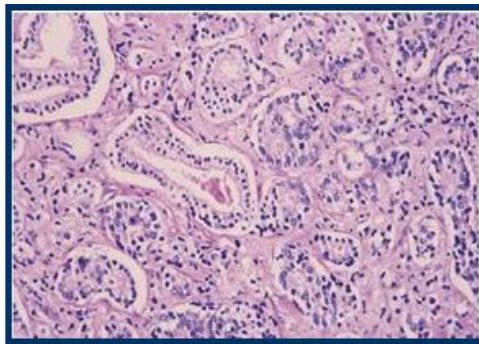


# Grade

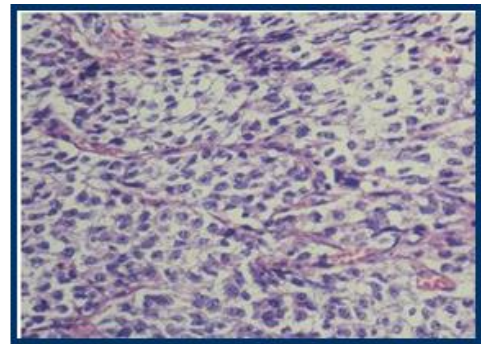
- Gleason grade – describes aggressiveness
  - a scale of 1 to 5: **prognostic** indicator
  - cellular and glandular architecture (appearance under microscope)



Normal



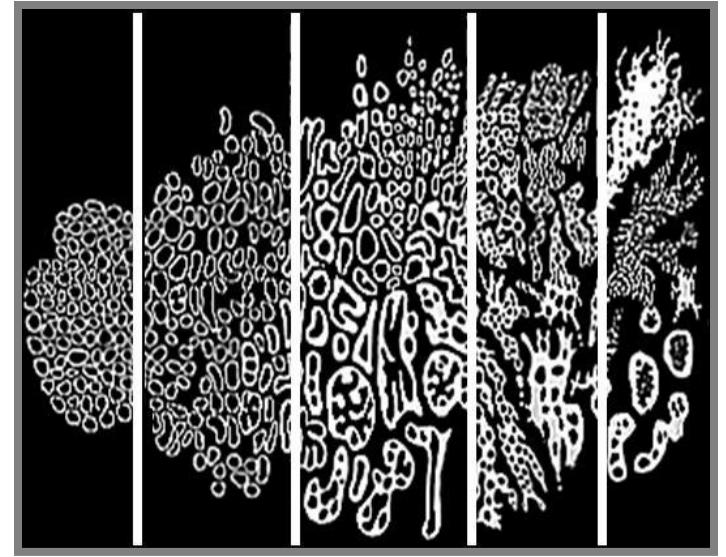
Grade 3



Grade 4/5

# Gleason Score

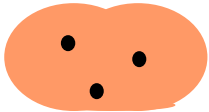
- Individual cancers can have a single or multiple grade(s)
- Assign a “score”



Score = most prevalent + second most prevalent grade

*\* indicate presence of grade 4 or 5*

# Stage

|                                                                                     |                      | <b>T · N · M</b>                                                                          |
|-------------------------------------------------------------------------------------|----------------------|-------------------------------------------------------------------------------------------|
|    | Incidental (TUR/PSA) | T1 <sub>A</sub> , T1 <sub>B</sub> , T1 <sub>C</sub>                                       |
|    | Localized            | T2 <sub>A</sub> , T2 <sub>B</sub> , T2 <sub>C</sub>                                       |
|    | Locally-advanced     | T3 <sub>A</sub> , T3 <sub>B</sub> , T3 <sub>C</sub><br>and T4                             |
|  | Metastatic           | $\left\{ \begin{array}{l} \text{N(0) vs N(+)} \\ \text{M(0) vs M(+)} \end{array} \right.$ |

# Definitions

- Risk Stratification

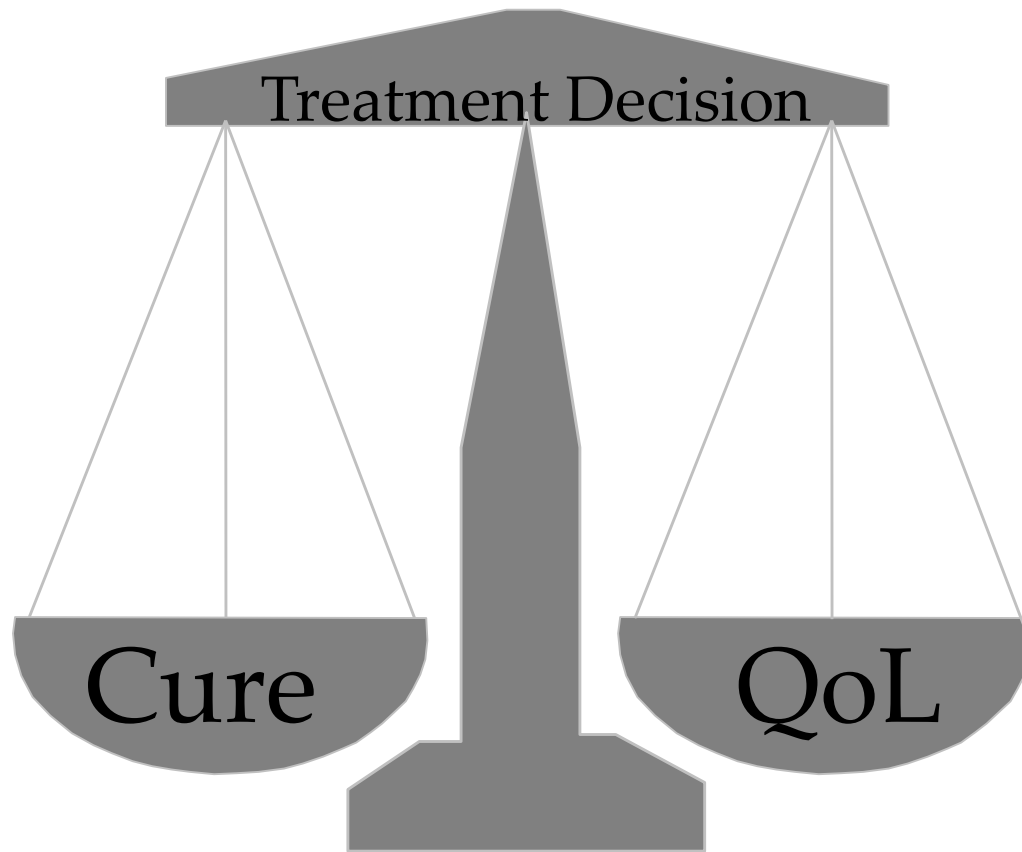
| Risk         | Clinical Stage | PSA          | Gleason Score |
|--------------|----------------|--------------|---------------|
| Low          | T1-T2A         | ≤10ng/ml     | ≤6            |
| Intermediate | T2B            | 10.1-20ng/ml | 7             |
| High         | T2C            | >20ng/ml     | ≥8            |

— D'Amico, et al; *Journal of Clinical Oncology* (2003) 21:2163

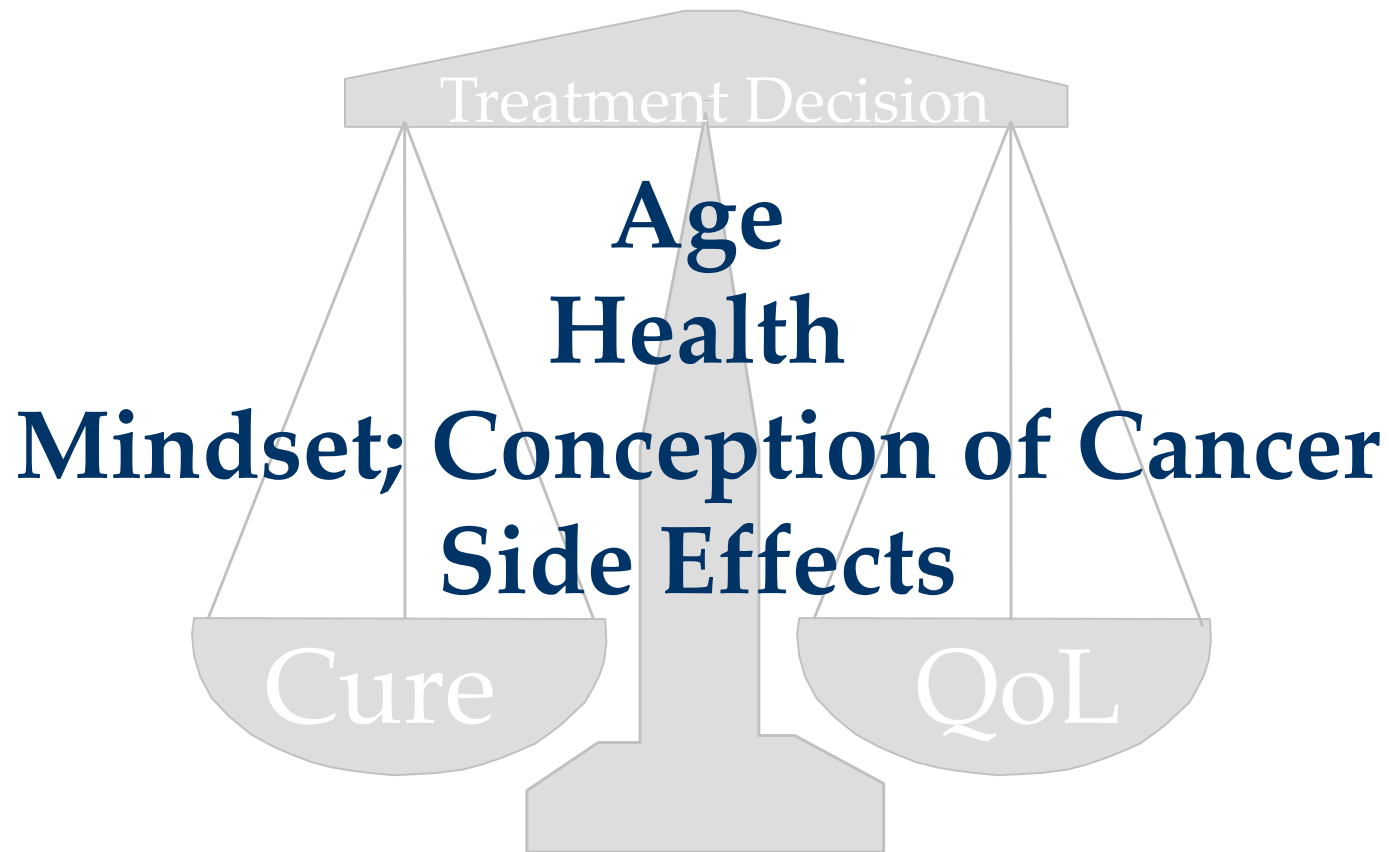
# Part 3

Management

# Decision-Making



# Decision-Making



# Treatment Options

- Potentially Curative
  - surgery
  - radiation
  - energy ablation
  - active surveillance with delayed intervention (not watchful waiting)
- Palliation
  - androgen-deprivation

# Outcomes

- Optimal Treatments

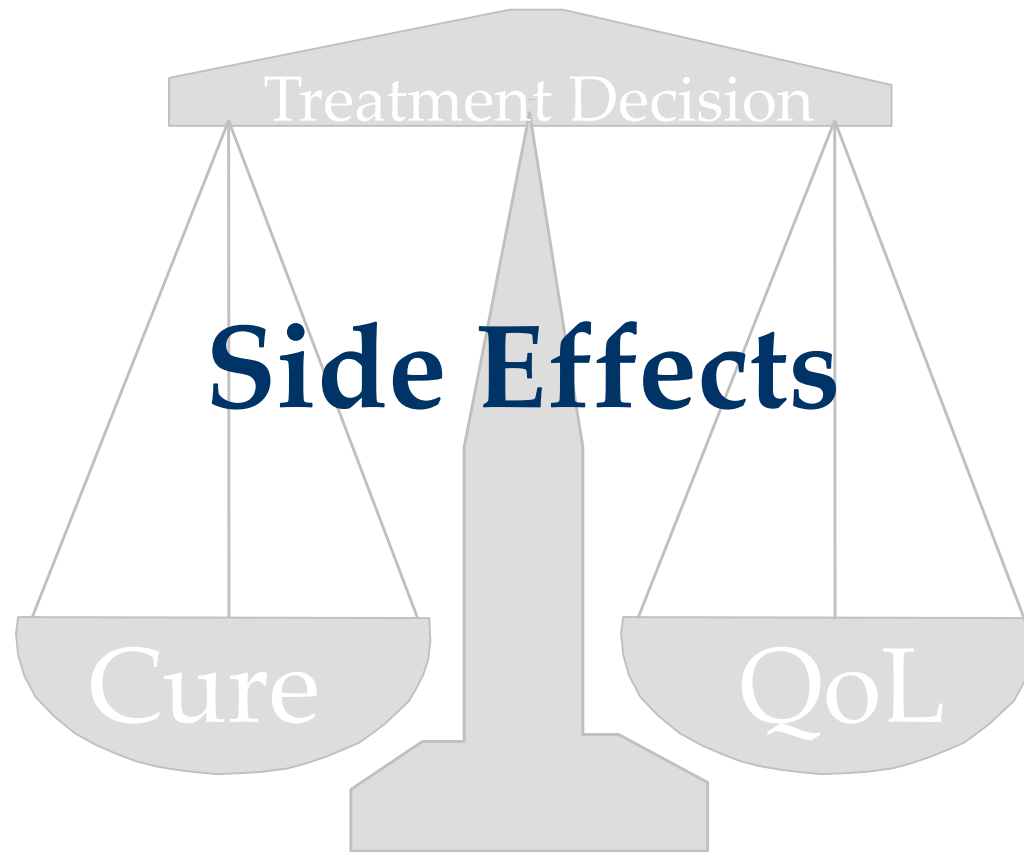
| Risk         | Treatments                                        | 5-yr DFS |
|--------------|---------------------------------------------------|----------|
| Low          | RALP+PLND<br>Brachytherapy<br>Active Surveillance | 90-95%   |
| Intermediate |                                                   | 80-85%   |

# Outcomes

- High Risk Localized Disease

| Risk | Treatments                 | 5-yr DFS |
|------|----------------------------|----------|
| High | Surgery<br>Radiation + ADT | <75%     |

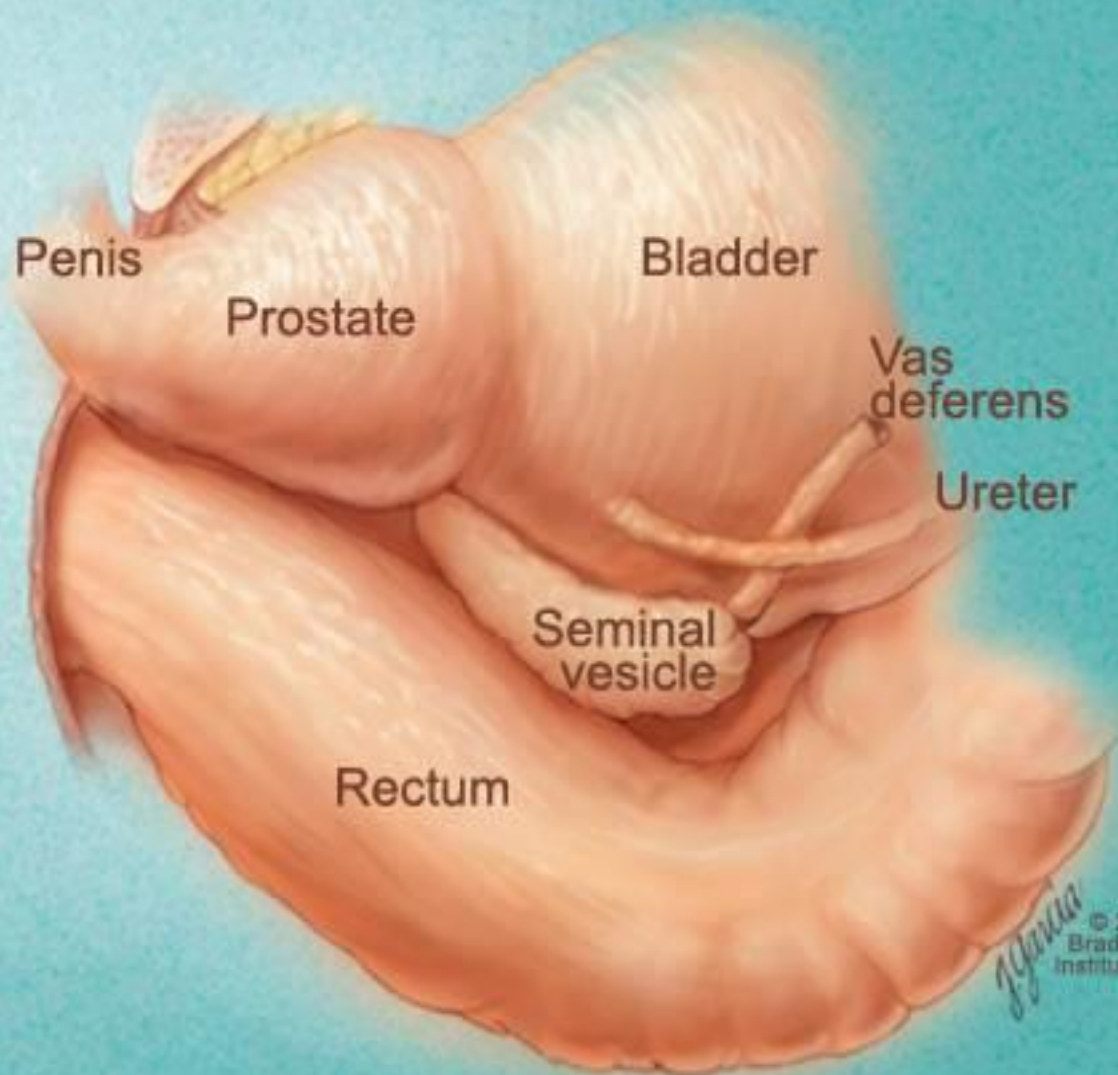
# Decision-Making



# Side Effects of Treatment

- Not due to physical absence of prostate
  - prostate function is for reproduction
  - absence of prostate = infertility
- Side effects from prostate cancer treatment are due to **“injury” to surrounding tissue** by surgery, radiation, or energy or due to the effects of drugs (if used)





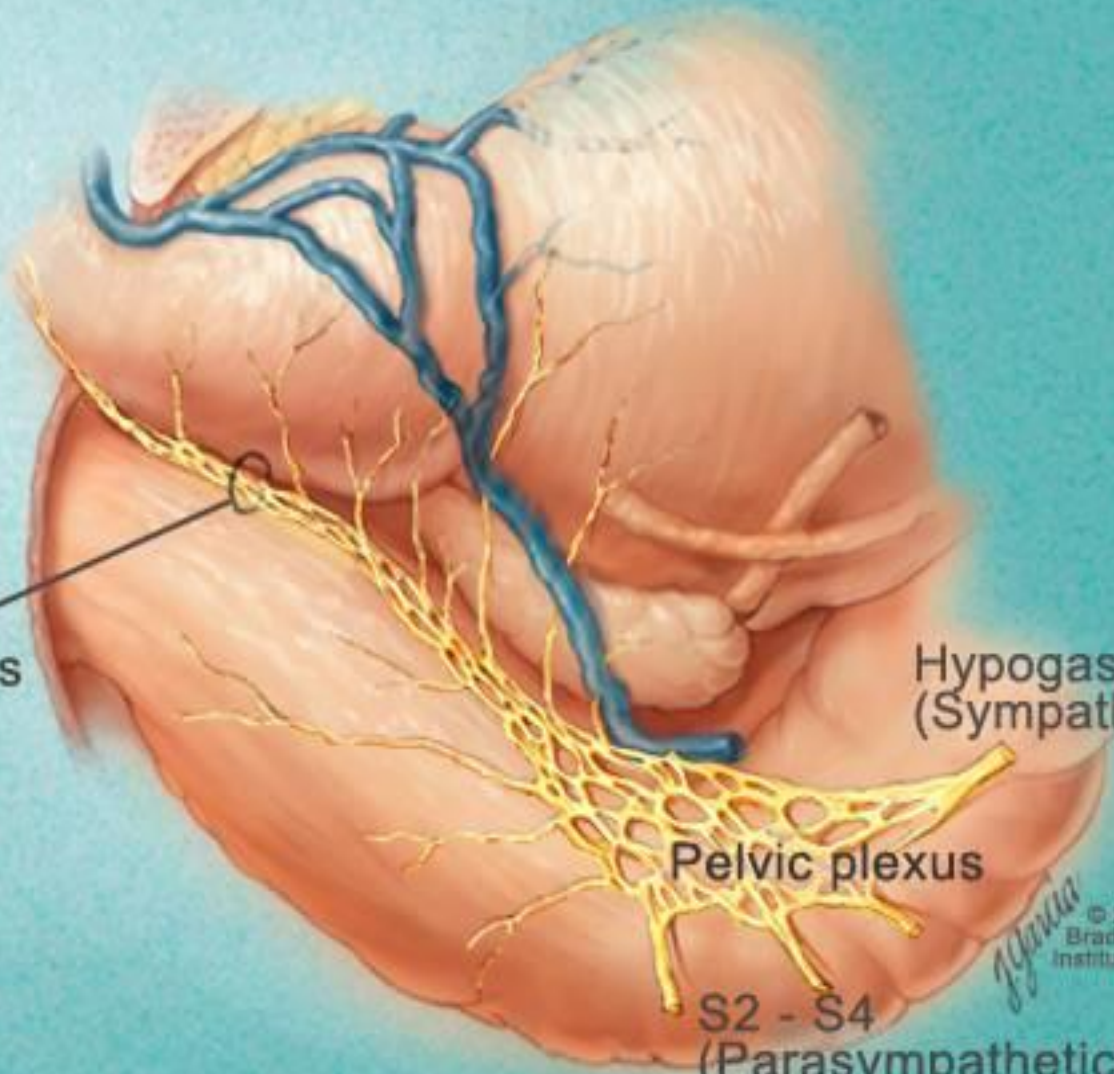
Cavernous  
nerve

Hypogastric n.  
(Sympathetic)

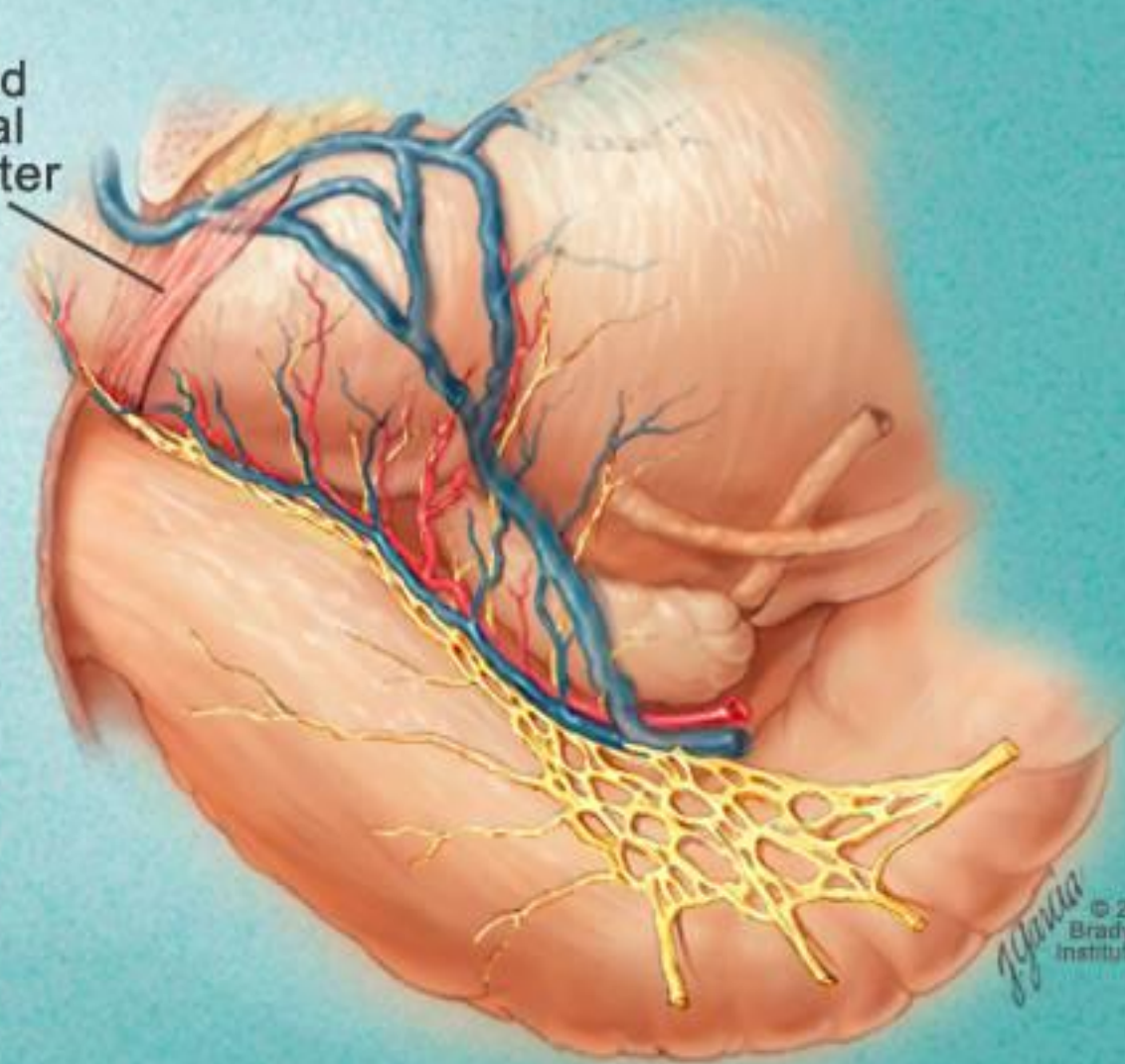
Pelvic plexus

S2 - S4  
(Parasympathetic)

*Brady*  
© 2003  
Brady Urological  
Institute



Striated  
urethral  
sphincter



# Side Effects of Treatment

- Bladder Function
  - Sexual Function
  - Bowel Function
- 
- Time course (sudden versus delayed)
  - Type of side effect



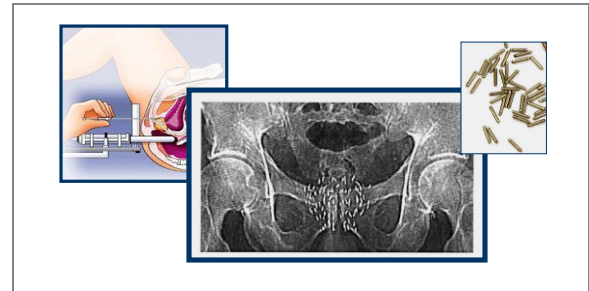
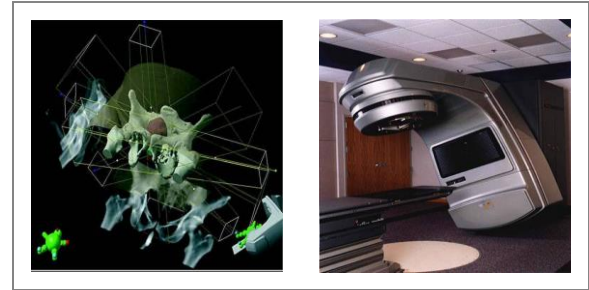
# Side Effects of Treatment

- Bladder Function (both surgery and radiation)
  - incontinence (1° surgery)
  - irritability/instability (1° radiation)
- Sexual Function (both surgery and radiation)
  - erectile dysfunction
  - ejaculation (impact on reproduction)
- Bowel Function (1° radiation)
  - irritability

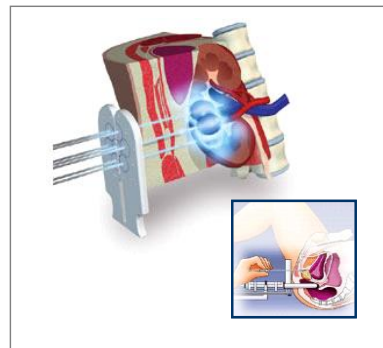
# Treatment Choices



Surgery



Radiation



Cryoablation

# Radical Prostatectomy

- Approaches at University of Arizona:
  - open retropubic (traditional)
  - robotic-assisted laparoscopic
- **Anatomic, nerve-sparing prostatectomy**
- Incisions and retraction are difference:
  - hasten recovery

# Radical Prostatectomy

- **Objectives (Open and Robotic):**
  - remove the regional lymph nodes
  - remove the prostate and seminal vesicles
  - reconnect the bladder to the urethra

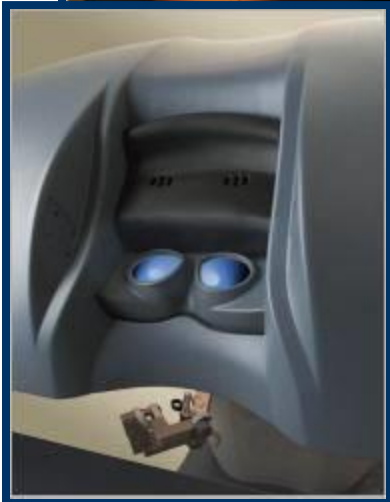


# DaVinci Surgical Platform



# DaVinci Robot

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# Robotic Prostatectomy

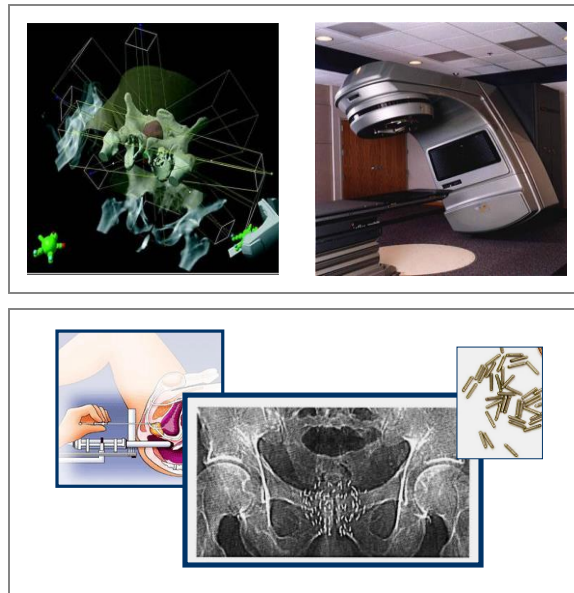
- Advantages of Robotic Approach:
  - similar cancer control
  - less trauma to tissue
    - smaller incision
  - improved magnification
  - less retraction of muscle
  - stronger reconnection (anastomosis)
  - **quicker recovery**

# Prostatectomy: Take Home

- Excellent Cancer Control
- Most Definitive Treatment
- Most Extensive Treatment
- Pathologic Staging
- Quickest Measure of Response



# Treatment Choices



Radiation

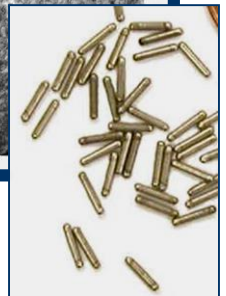
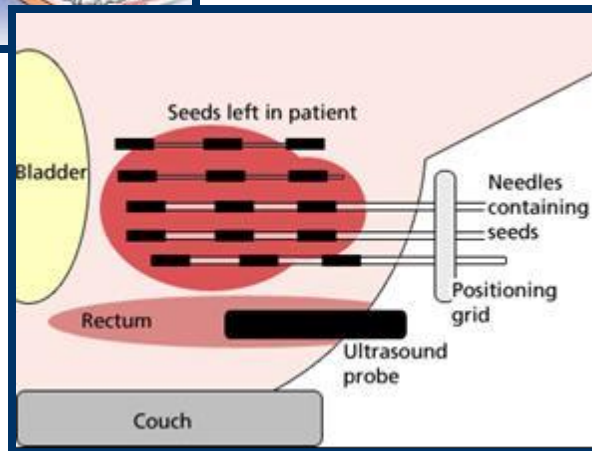
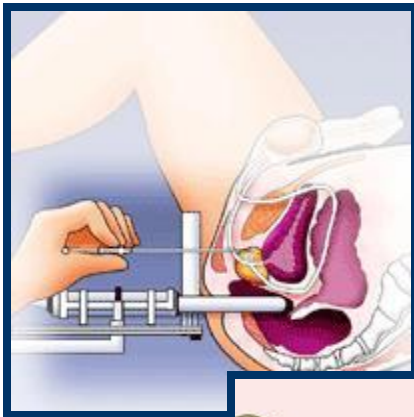
# Types of Radiation Therapy

- External Beam
  - IMRT
  - proton-beam
- Brachytherapy (seeds)



# Types of Radiation Therapy

- Brachytherapy



# Radiotherapy: Take Home

- Excellent Cancer Control
  - **may take 12-18 months to assess**
- Limited Complications
- Less Invasive then Surgery
- Complications Increase Over Time
- Salvage for Local Recurrence is Morbid

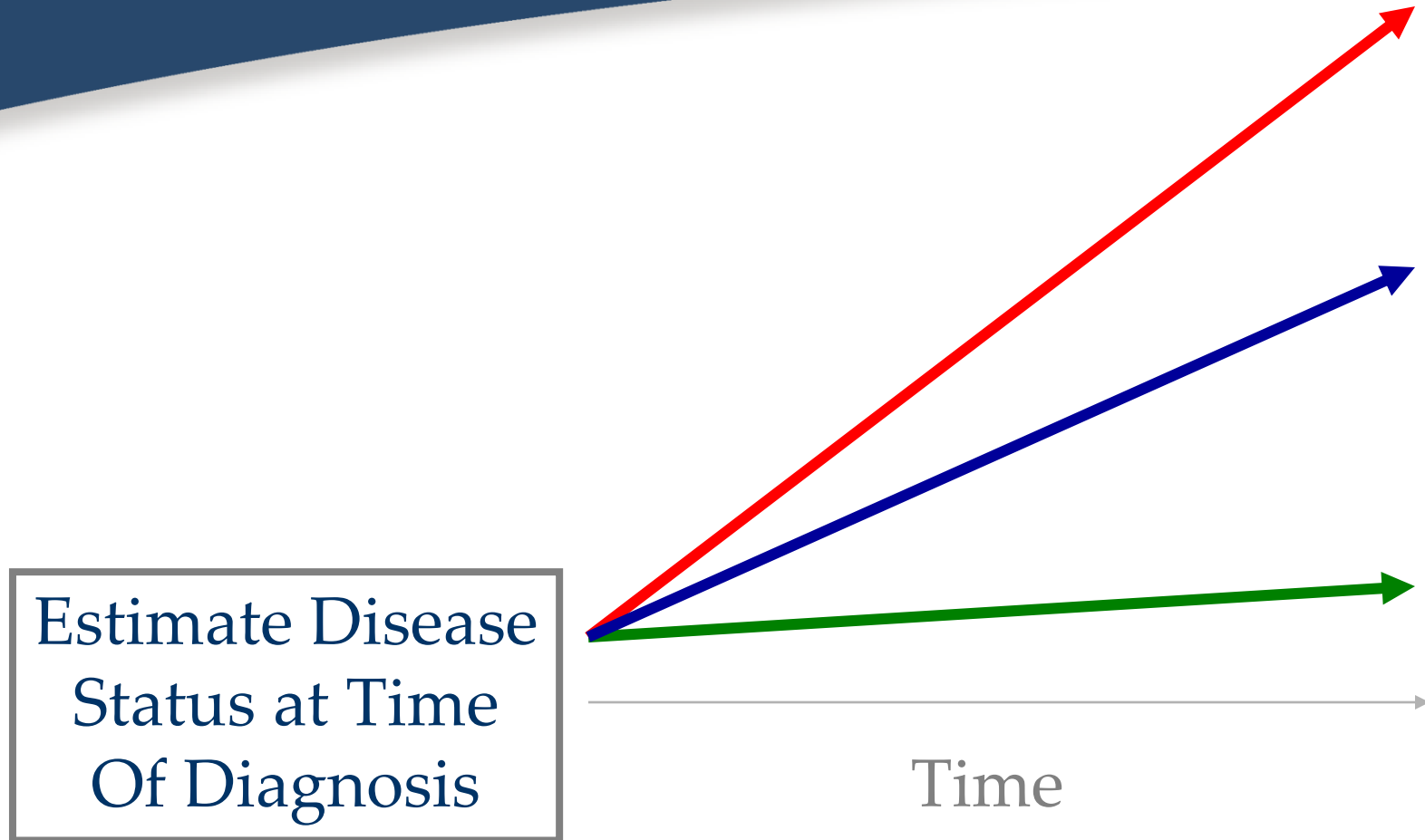


# Treatment Choices

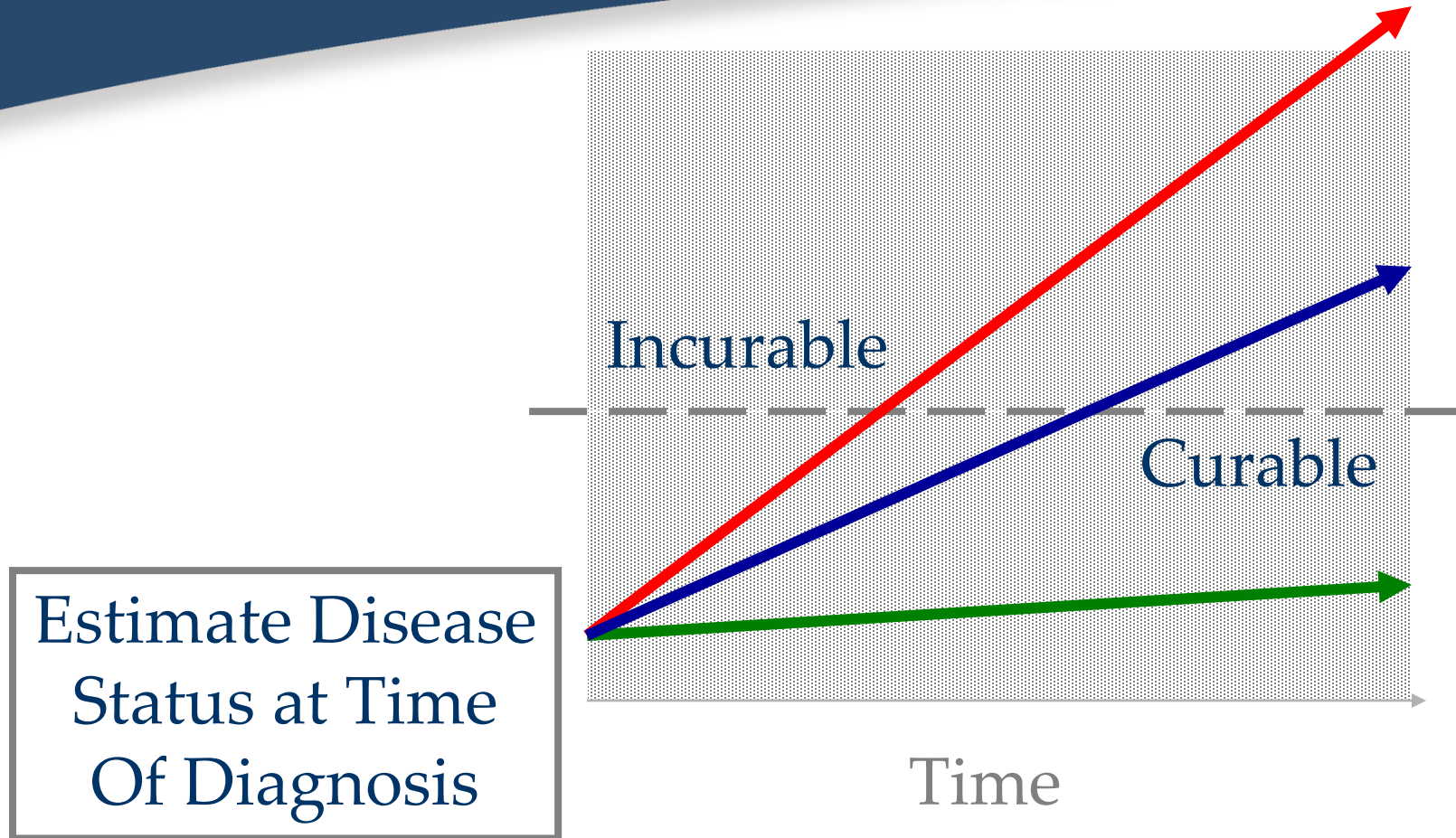


Active Surveillance

# Active Surveillance



# Active Surveillance (continued)



# Active Surveillance (continued)

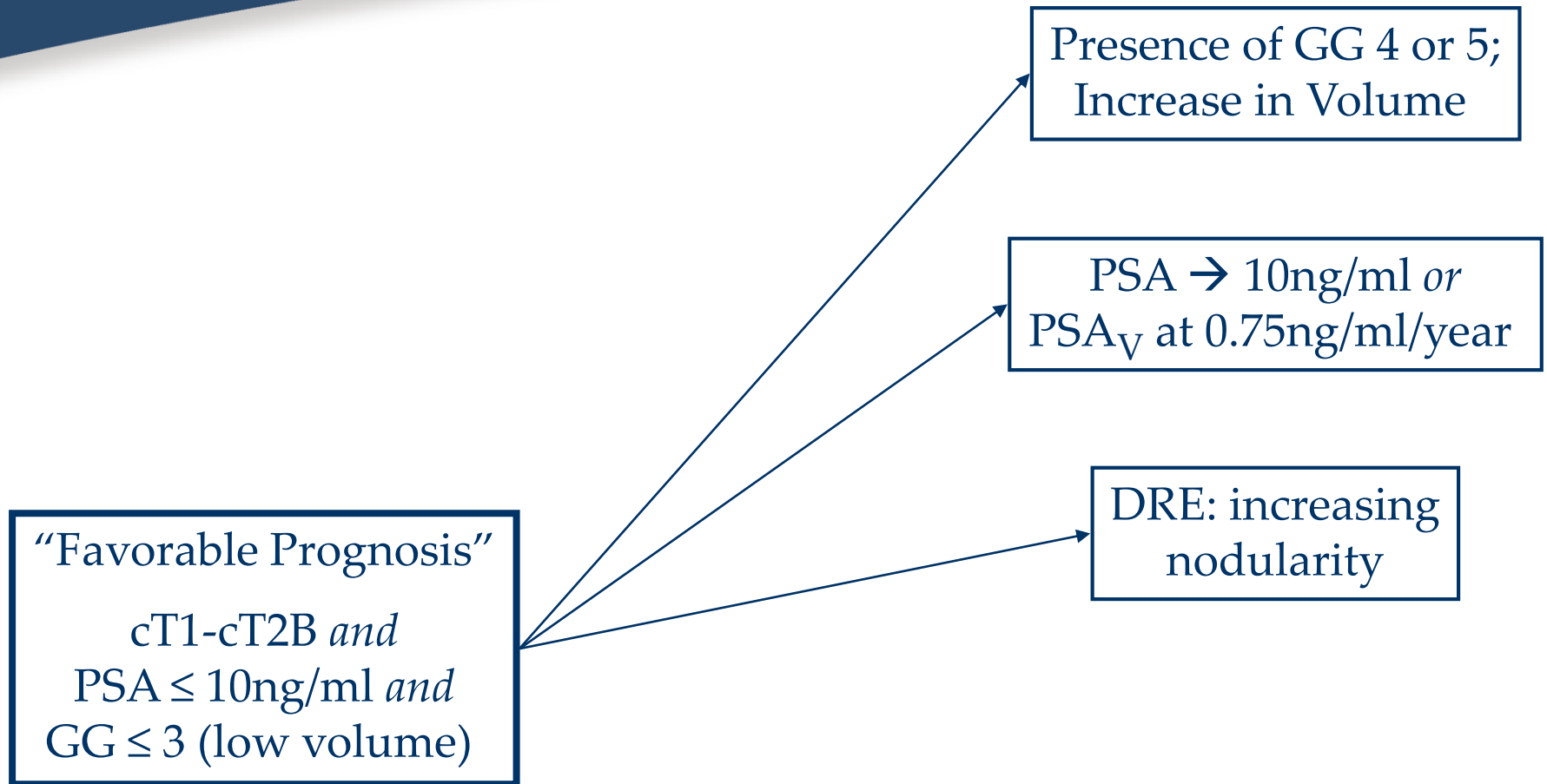
“Favorable Prognosis”

cT1-cT2B *and*  
PSA  $\leq$  10ng/ml *and*  
GG  $\leq$  3 (low volume)

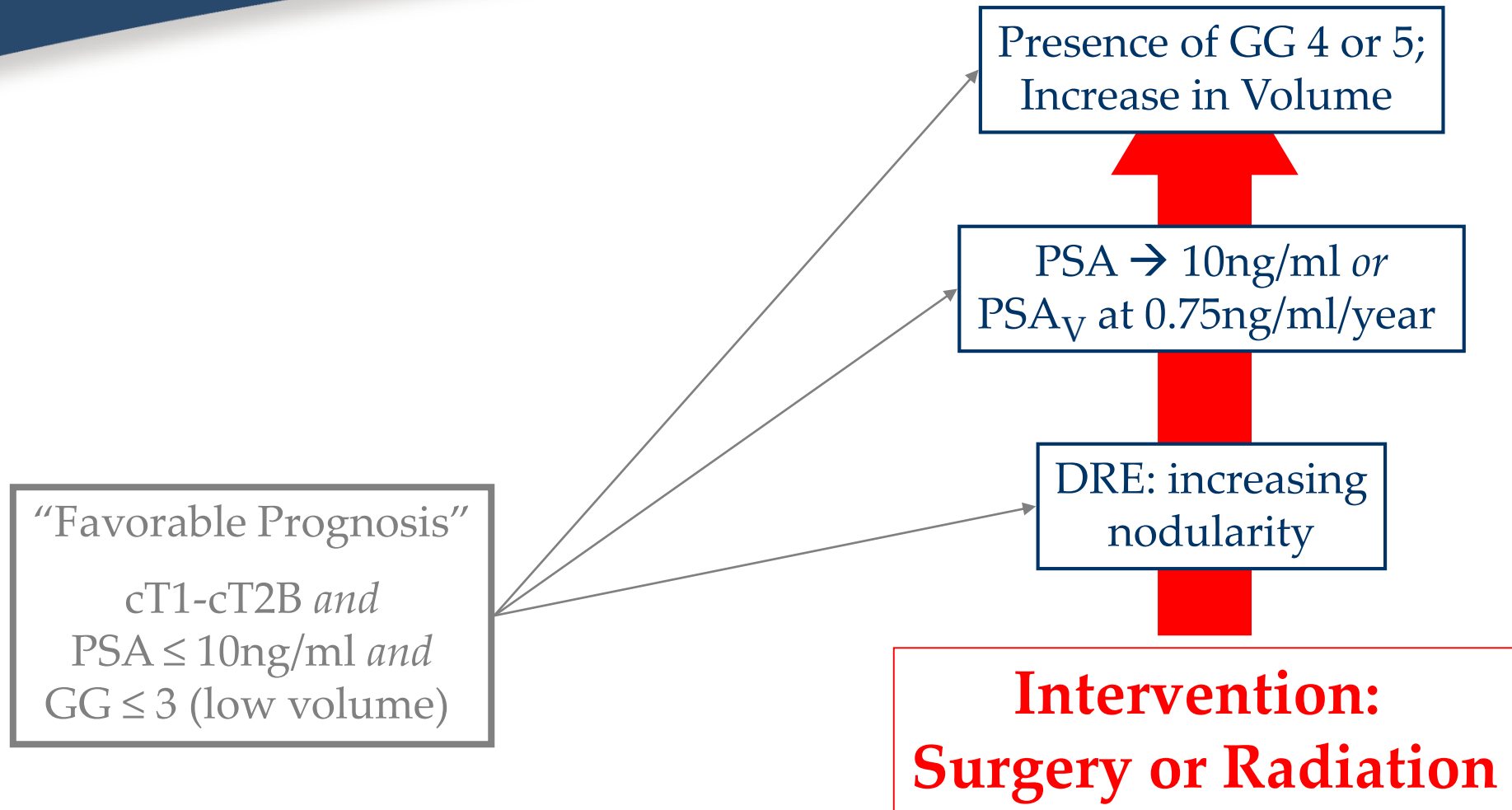


Every 4-6 months: PSA and DRE  
Every 6-12 months: biopsy

# Active Surveillance (continued)



# Active Surveillance (continued)



# Salvage Therapies

# Salvage Therapy

- Recurrence after Primary Treatment
- Surgery or cryotherapy after radiation
- Radiation after surgery
- Can be effective in selected patients
- Increase in side effects



# Palliation and Systemic Disease

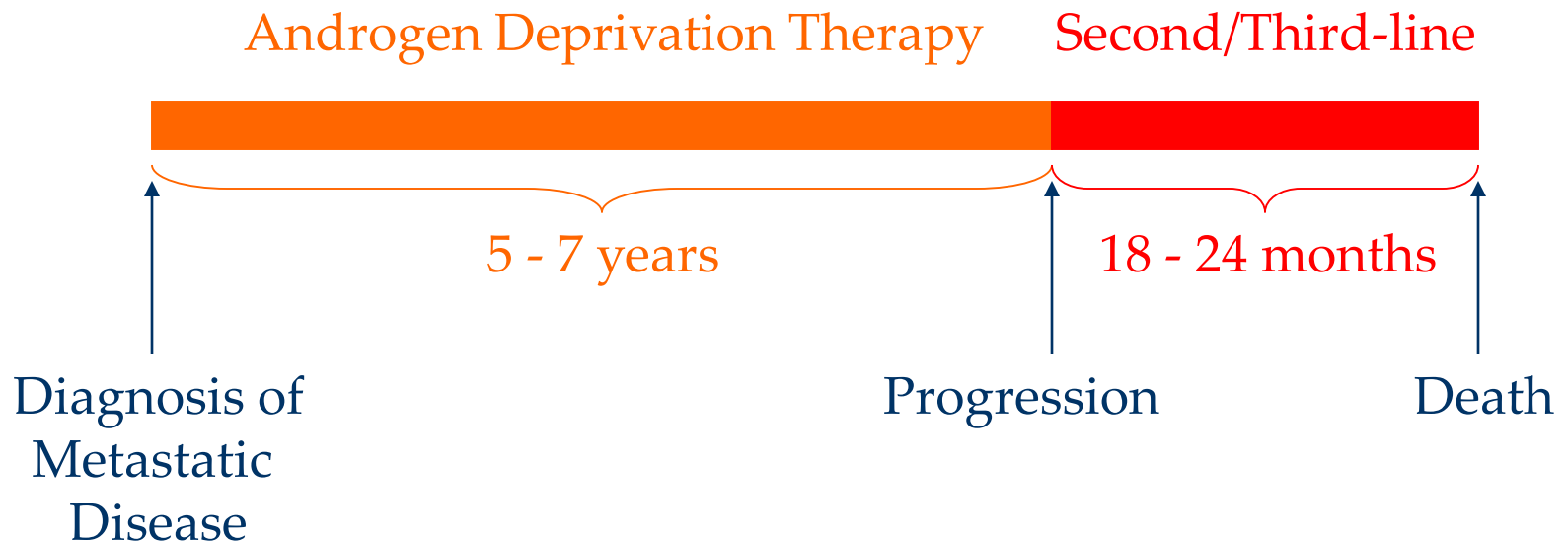
# Palliation - ADT

- Androgen Ablation or Hormonal Therapy
  - **castration**
  - depletes testosterone and slows prostate cancer growth and spread
  - can be surgery, shots, or pills
  - limited durability (3-7 years)
  - used primarily for metastatic disease
    - sometimes with radiation



# Advanced Prostate Cancer

- Metastatic Disease



# Systemic Therapy

- Androgen Deprivation Therapy
- Chemotherapy
- Targeted Therapies
- Immunotherapy





Take Home Messages

# Take-home Message

- **Many choices** in treatment; decision upon:
  - definitiveness of treatment
  - extent of treatment
  - complications from treatment
  - aggressiveness of the cancer



# Take-home Message (continued)

- The patient (and his family) must be comfortable with his decision
- Research and education is key
- Seek care at high volume center with a surgeon who specializes in prostate cancer treatment and has access to a multi-disciplinary team

