

Current Diagnosis and Management of Prostate Cancer

Prostate Cancer

- Risk Factors
 - Age-median age of diagnosis is 72yo
 - Smoking
 - High Fat/ Western diet
 - Family History-8-9% of all cancers due to inherited gene higher for younger men

- Incidence of prostate cancer increases with age so that up to 70-80% of men in their 80-90's have autopsy evidence of prostate cancer

Prostate Cancer

- Most common non cutaneous malignancy in men
 - Second leading cancer killer of men

Prostate

180,400 cases/yr

36% of new ca cases

40,400 deaths

1/6 chance of dvlp.

Breast

182,000 cases/yr

32% of new ca cases

46,000 deaths

1/8 chance of dvlp.

Hormone dependence

hormone dependence

Prostate Cancer

- Prostate Cancer Development
 - Develops from the epithelium
- Possibly from the basal cell layer – Requires androgens to develop
- Patients castrated before puberty do not develop BPH or Prostate cancer
 - Increased cell proliferation and decreased apoptosis
 - BPH is not a risk factor

Prostate Cancer

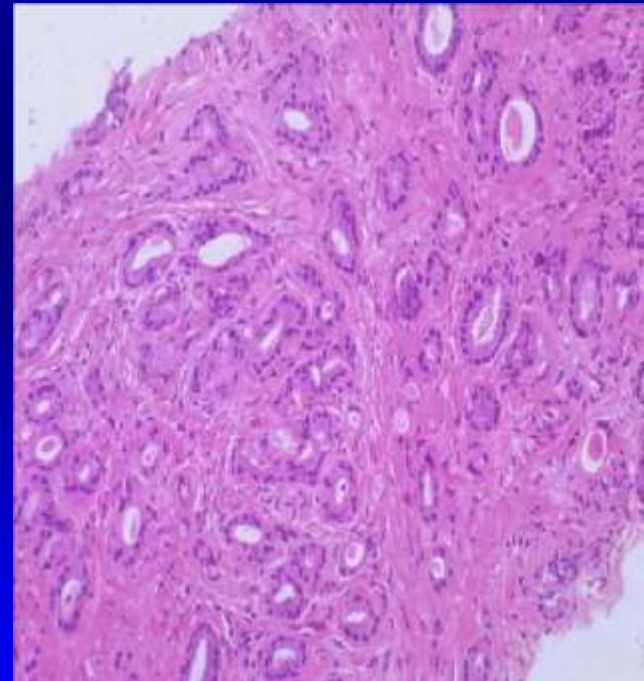
- What's in a name?
- PIN-prostatic intraepithelial neoplasia
 - May be a precursor lesion to prostate cancer
- Characterized by cytologically atypical cells with architecturally benign glands

- Approximately 20% of patients with PIN will go on to have a subsequently positive biopsy
- **ASAP-atypical small acinar proliferation**
 - Atypical glands and cells but can't quite call it cancer
 - Up to 50% will have a future positive biopsy



Prostate Cancer

Uniform round glands
Single cell layer (loss of basal cells)
Some prominent nucleoli
Perineural invasion

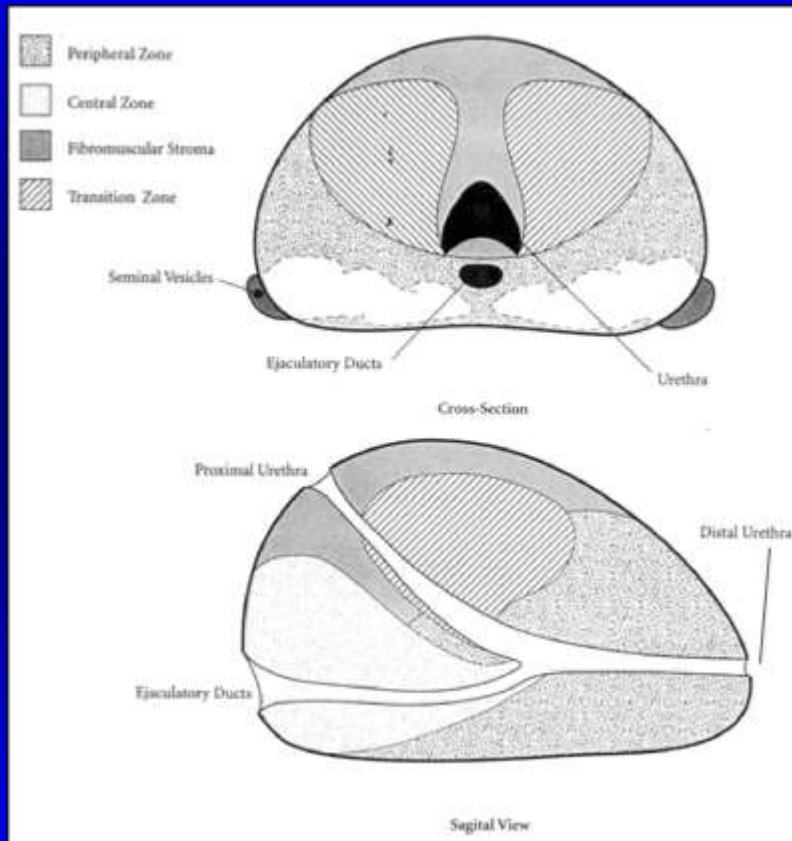


Prostate Cancer

- Grading
 - Gleason grade 1-5
 - 2 most predominant patterns combined to give Gleason score
 - 2-4 well differentiated
 - 5-7 intermediate
 - 8-10 poorly differentiated
 - Gleason scores very predictive of metastases and outcome
- Remember high grade PCa may not make much PSA



Prostate Cancer



Zonal Anatomy of the Prostate

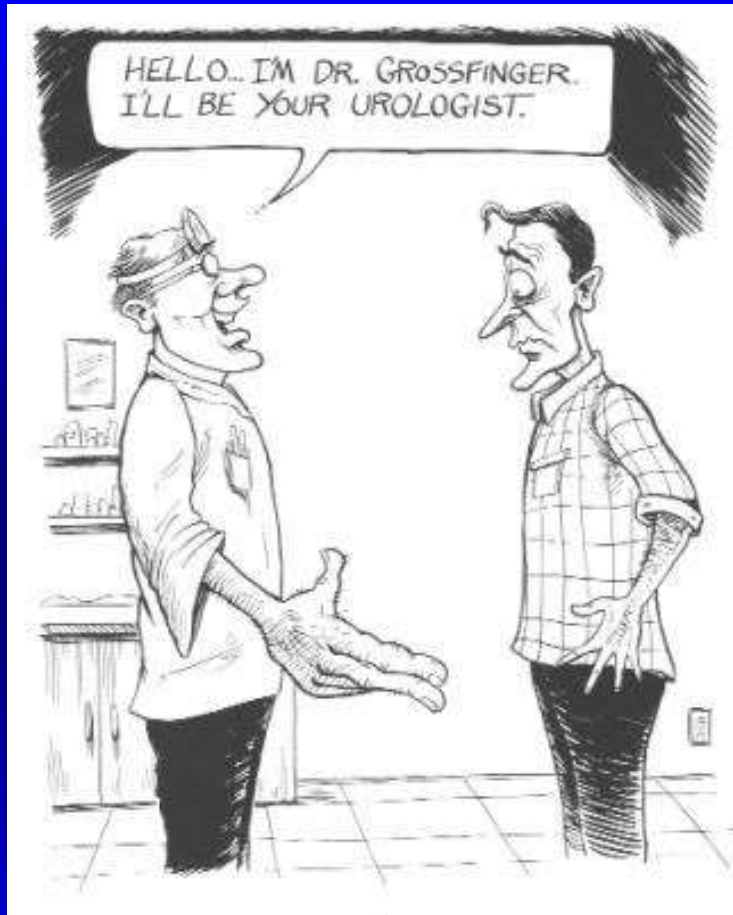
Prostate Cancer

- Develops in the peripheral zone of the prostate
 - 75% peripheral zone, 15-20% transition zone, 5% central zone, essentially none in AFMS
 - Biopsies directed toward the peripheral zone



Prostate Cancer

- Screening



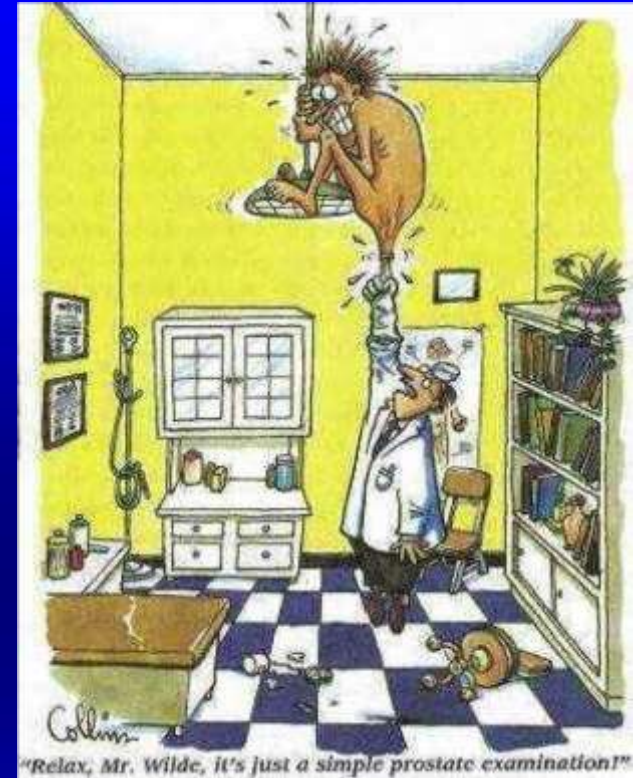
Prostate Cancer

- Diagnosis
 - Screening-Who should be screened?

- American Urological Association, American Cancer Society: recommend offering PSA and DRE to men at risk (ie, with a >10-year life expectancy)
- US Preventive Services Task Force: don't even offer DRE or PSA

– Arguments against screening

- Detection of clinically insignificant cancers
- Expensive-Initial estimates of screening men aged 50 to 70 years for prostate cancer \$25 billion during first year alone
- Not effective in decreasing mortality from the disease



Prostate Cancer

- Screening
 - Prostate, Lung, Colorectal, Ovarian (PLCO) screening study in the US (148,000 men and women randomized to screening or community standard of follow-up)
 - Europe: Rotterdam screening trial
 - Results of both: 10 years from now

Prostate Cancer

- Screening
 - Evidence that screening works
 - Fall in mortality now seen:
 - SEER*
 - Olmsted County, MN† – Canada/Quebec‡
 - US Department of Defense (DOD)
 - Tyrol, Austria
 - Mortality fall *not seen* (where PSA screening not performed) Mexico

SEER=Surveillance, Epidemiology and End Results

*Levy IG. *Cancer Prev Control*. 1998;2:159;

†Roberts RO, et al. *J Urol*. 1990;161:529-533;

‡Meyer F, et al. *J Urol*. 1999;161:1189-1191

Prostate Cancer

- PSA
 - 25% positive predictive value to detect disease
 - predictive of tumor stage
 - Most predictive factor for biochemical recurrence
 - Excellent tumor marker for detecting recurrent disease
- Free PSA
 - Portion of PSA which is not complexed to alpha-1 antichymotrypsin
 - Measured as ratio of Free/Total PSA
 - Decreased by 50% in patients on Proscar
- Therefore ratio still remains useful

Prostate Cancer

- Advantages and Disadvantages of Using Molecular forms of PSA
 - Advantage: eliminates about 10%–20% of negative prostate biopsies in men with PSA of 4.0–10.0 ng/mL
 - Disadvantage: misses some (about 5%–10%) of cancers that would be detected with PSA alone

Prostate Cancer

- PSA velocity
 - Defined as $>.75\text{ng/ml year}$
- Age specific PSA

Age (years)	Recommended Reference Range for Serum PSA (ng/mL)
40–49	0.0–2.5
50–59	0.0–3.5
60–69	0.0–4.5
70–79	0.0–6.5

Prostate Cancer

- Screening
 - Digital Rectal Exam
 - DRE abnormal in 6%–15% of men
 - About 25% of cancers found with DRE alone • Still plays a role

Prostate Cancer

- Digital Rectal Exam and Screening

Annals of Urology

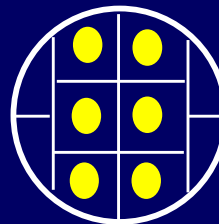
- “When Australian rugby player John Hopoate resigned in disgrace after receiving a 12-match suspension for jabbing his fingers into opposing players anuses, the New Zealand Cancer Society used his photo to promote prostate cancer checks. The ad, features a close-up photo showing Hopoate inserting his index finger into another player’s anus and states the exam “won’t hurt a bit-promise” AP 4/15/01



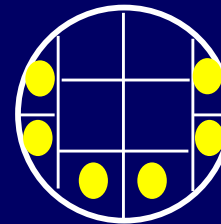
Prostate Cancer

- Diagnosis
 - Transrectal ultrasound and Biopsy
 - Traditionally Sextant Biopsy Used
 - More recently 10-12 core biopsy advocated
 - Cores may be sent separately to help identify margin at risk

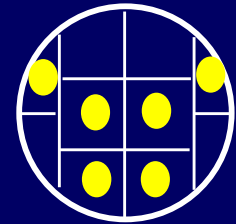
Detection Rates of Systematic Schemes



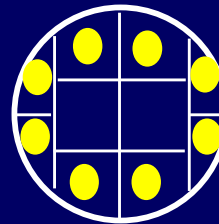
80%



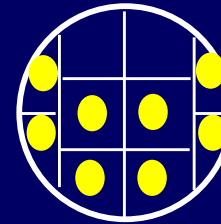
89%



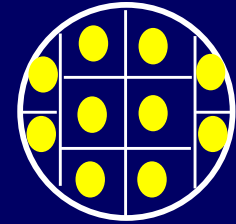
89%



91%



95%



96%

Chang JJ, et al *J Urol*. 1998;160:2111-2114.
Presti JC Jr, et al *J Urol*. 2000;163:1631-166.

Prostate Cancer

Staging

T1a-<5% on TURP

T1b>>5% on TURP

T1c-non palpable diagnosed by PSA

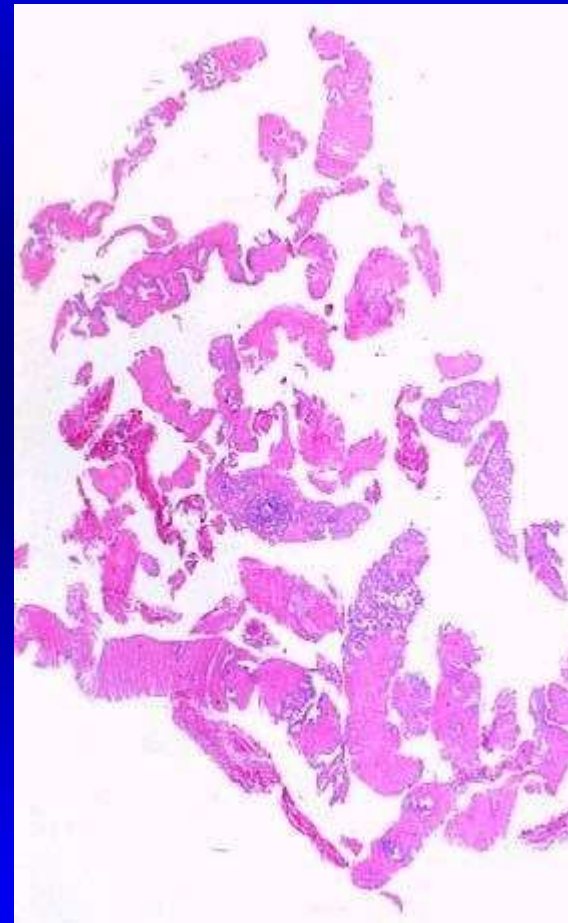
T2a-palpable one lobe

T2b-both lobes

T3a-extraprostatic

T3b-seminal vesicle involvement

T4 adjacent structures



Prostate Cancer

- Diagnosis
 - Transrectal ultrasound and biopsy



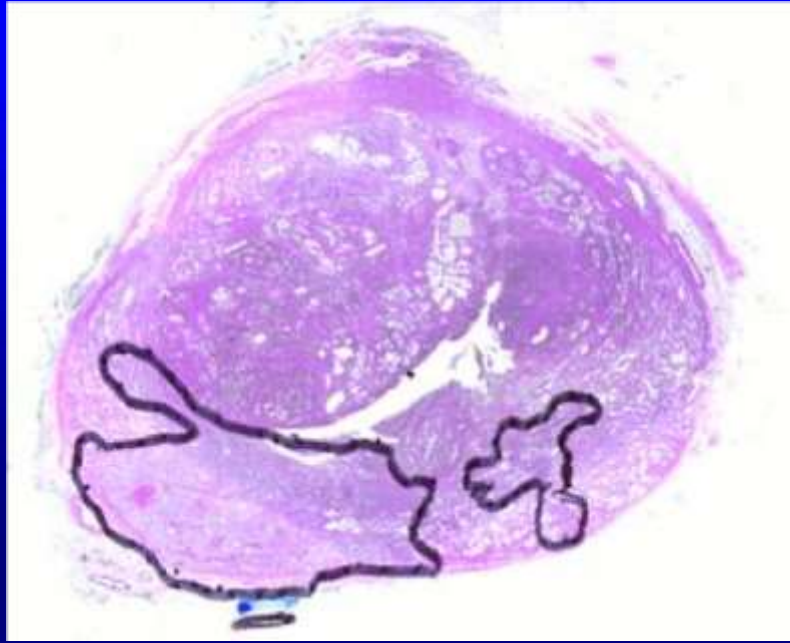
Prostate Cancer

- Diagnosis-Other tools
 - _ Endorectal coil MRI



NVB

Tumor



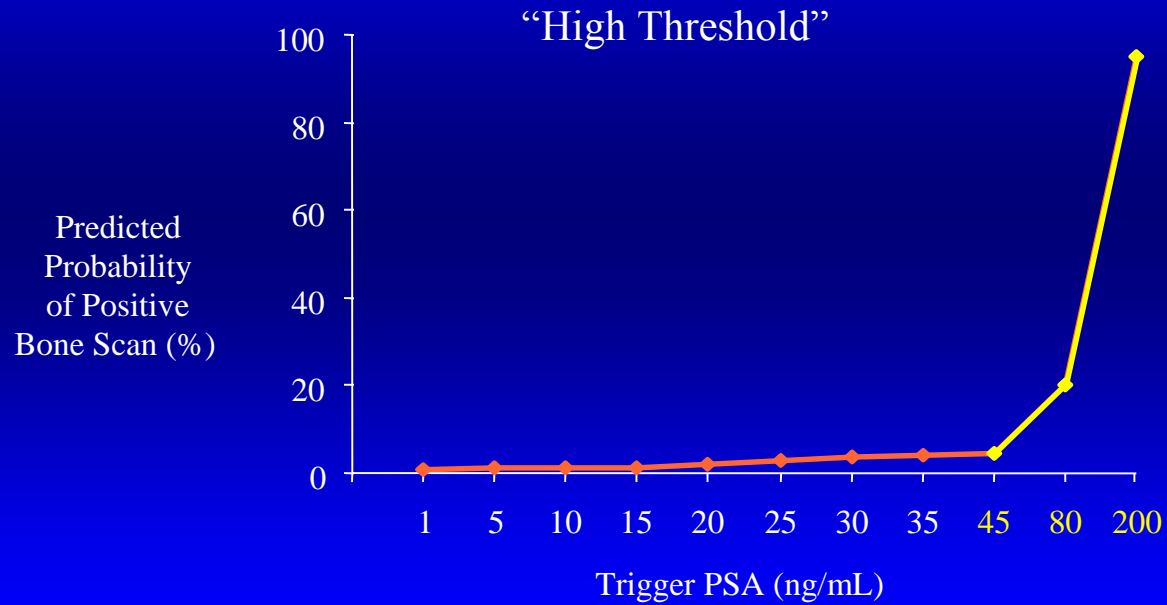
Prostate Cancer



Prostate Cancer

- Diagnosis-Other diagnostic tools

– Bone Scans-limited usefulness with PSA<20



Cher, et al. *J Urol.* 1998;160:1387 .

Prostate Cancer

- Predictive Models

- Preoperative Nomograms

- Available at Nomograms.org
- Available for pre treatment, post RRP, and radiation
- PSA continues to be a driving variable

- Partin tables

- Recently updated, also useful for prediction of outcomes

Pre Tx Prostromogram 			
PreTx	PostOp	DT	?
Pre Tx PSA:		(+)
Primary Gleason:		▼ NA	
Secondary Gleason:		▼ NA	
Gleason Sum:		▼ NA	
1992 Clinical Stage:		(?) ▼ NA	
1997 Clinical Stage:		(?) ▼ NA	
Rad Tx Dose (Gy):		(+)
Neo-Adj.Hormones:		<input type="checkbox"/>	
Click (i) for References			<input type="button" value="Compute"/>

Partin et al. *Urology* 2001

Extra Credit





Prostate Cancer

- Treatments
 - Watchful Waiting
 - Hormone Therapy
 - Surgery

- Radiation
- Cryotherapy

Prostate Cancer

- Watchful Waiting
- Waiting for what?
 - 70-80% of men in 80's have prostate cancer not all men need to be treated
 - Look at PSA doubling times
 - Look at comorbid conditions
 - May rebiopsy in one year and follow PSA

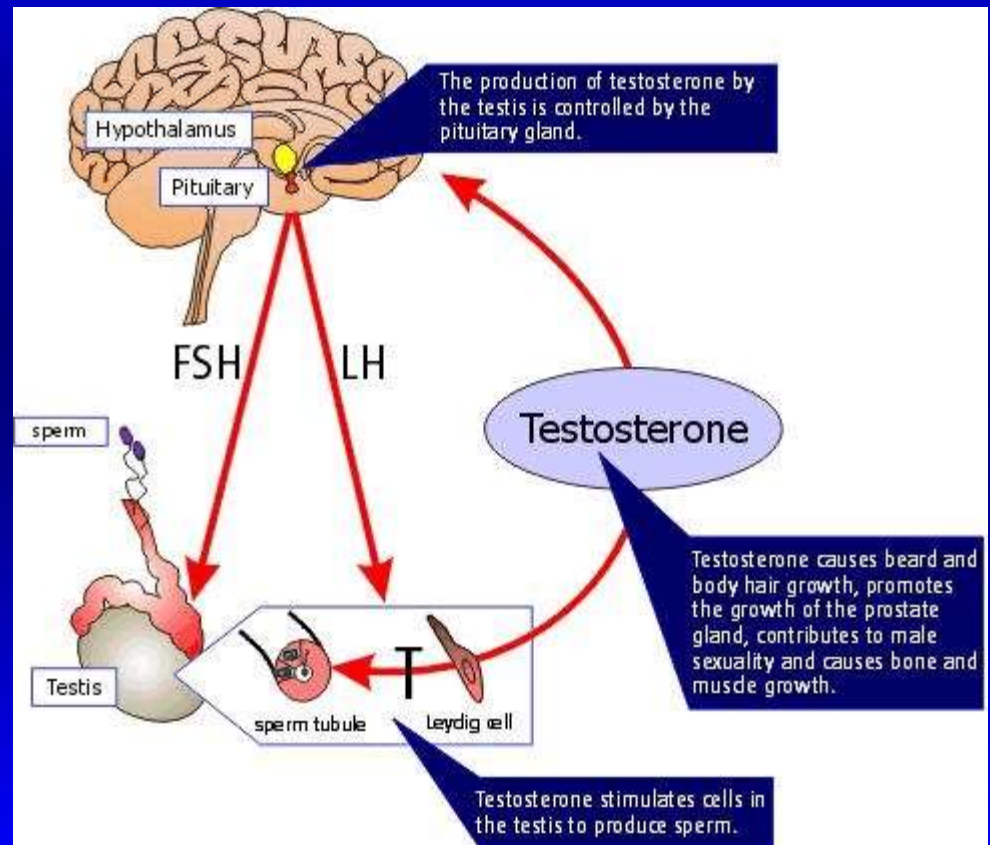
Prostate Cancer

- Hormonal Therapy

- LHRH agonists and antagonists
- Block production of testosterone
- Anti-androgens block the androgen receptor

Prostate Cancer

- Hormonal Therapy



- Casodex Monotherapy-150mg per day
 - Initial results seem to show equal efficacy to LHRH agonists (US data still pending)
 - Side effects
 - Gynecomastia and nipple tenderness a significant problem causing high withdrawal from studies
 - Improvement in side effects of osteoporosis, hot flashes seen with LHRH agonists.

Prostate Cancer

- Hormone Therapy
 - Typically hormone deprivation will cause PSA to go very low and stay low for 18 months

- May add anti-androgen which may work for another 3-6 months
- Antiandrogen Withdrawal

Prostate Cancer

- Disadvantages of Hormone Therapy
- Side effects
 - Hot flushes – Helped with soy, depo-provera, megace
 - Osteoporosis-leading to pathologic fractures
 - Start patients on Vit D 400IU and Calcium(Citracal) 500mg per day when initiating treatment
 - Bisphosphonate is DEXA scan shows osteoporosis
 - » Fosamax oral

» Zolendronic Acid-IV

- Other side effects: fatigue, impotence, anemia, etc..

Prostate Cancer

- Treatment-Surgical

– Radical Retropubic Prostatectomy

- Complications associated with RRP continue to decline

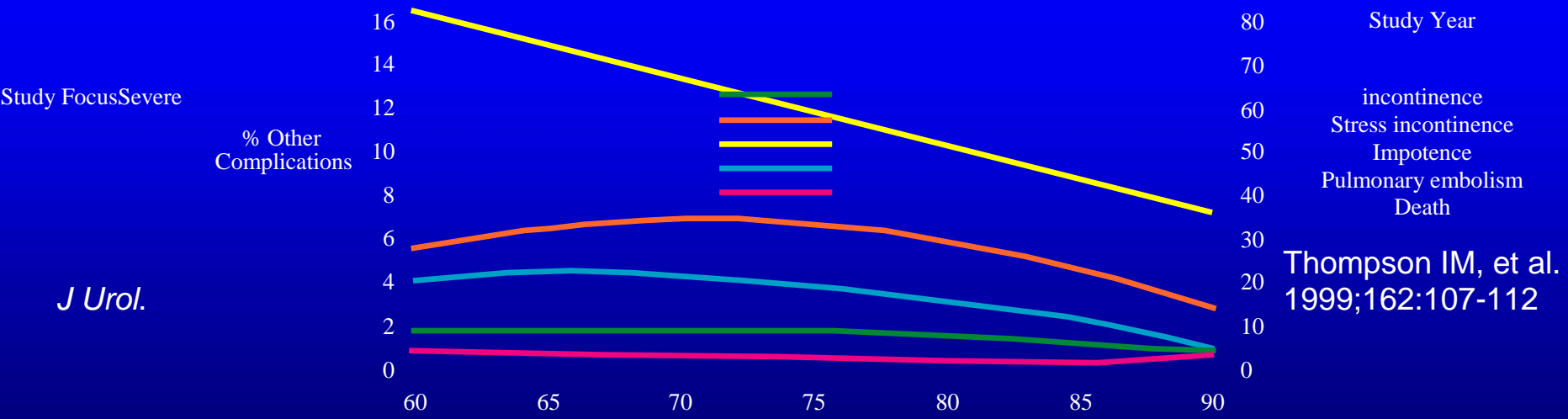
20

18

100

90

%
Impotence

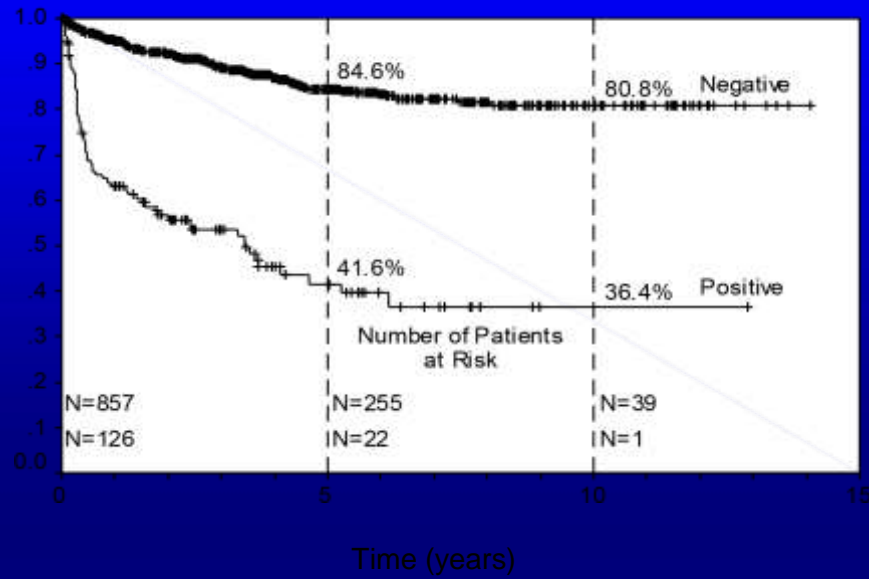


Prostate Cancer

- Treatment Surgical
 - Radical Prostatectomy
- Have come to realize the importance of surgical margins

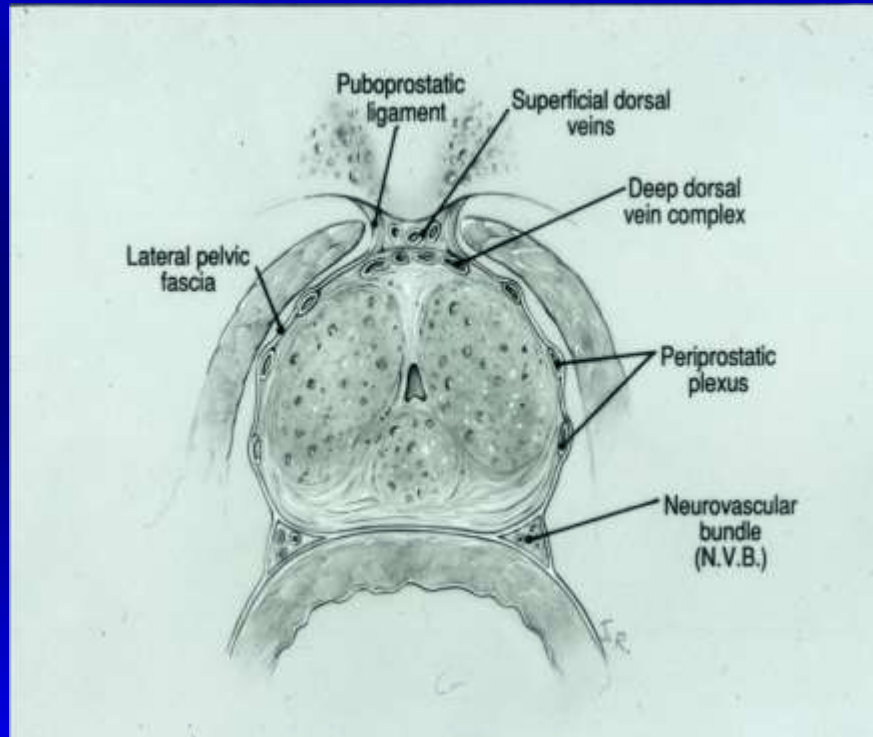
Progression-free Probability

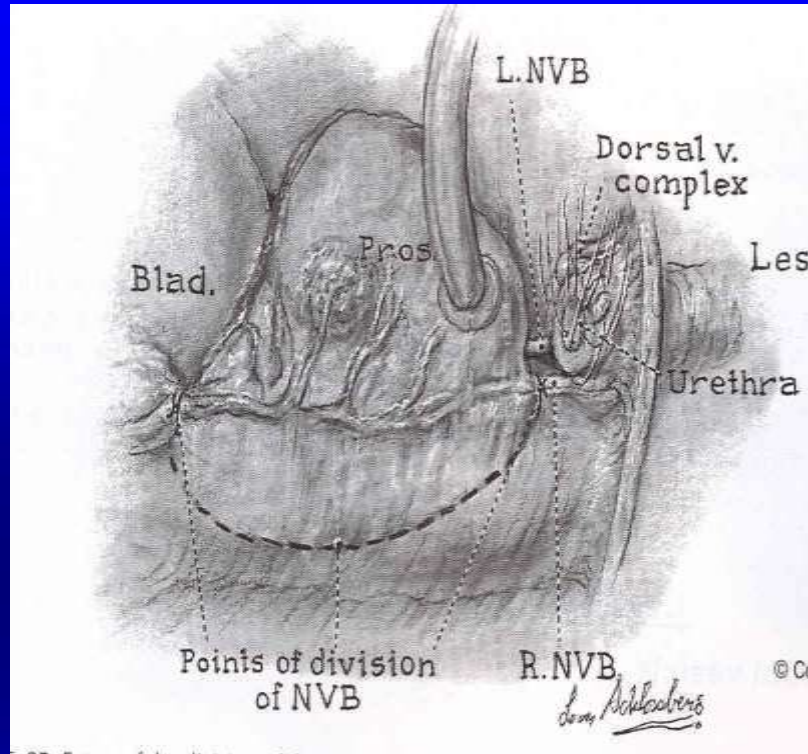
(Surgical Margin Status)



TI-T2NxM0 tumors

Anatomy of NVB



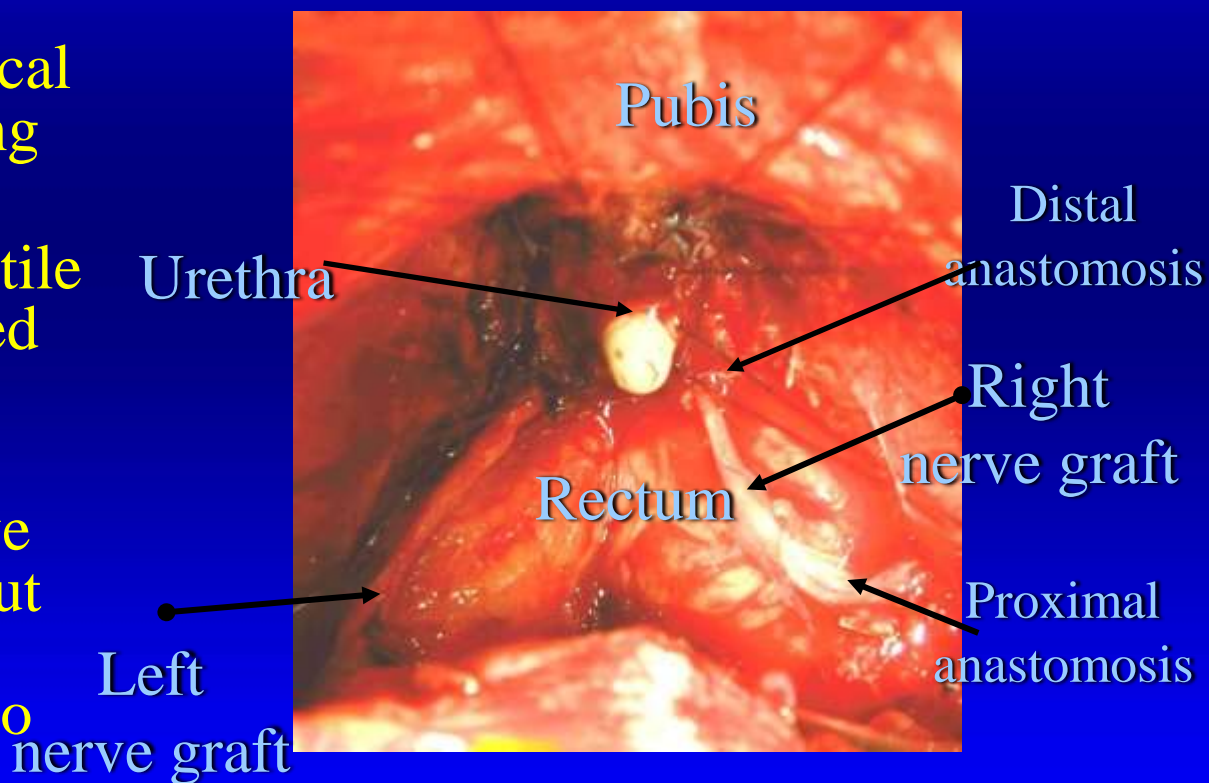


Prostate Cancer

Radical Prostatectomy

- Used to hopefully help improve surgical margins by allowing wider dissection
- Restoration of erectile function in damaged nerves or resected nerves
- Uses the sural nerve most commonly, but genitofemoral or ilioinguinal can also be used

– Sural Nerve Grafts



Prostate Cancer

- Surgical Treatment
 - Laparoscopic Prostatectomy
- Initial results from high volume centers look good
 - High learning curve
 - » Results in up to 50% positive margins initially
 - Need longer follow-up
 - Erectile function and continence still need validation and longer follow-up
 - Sural nerve grafts can be done laparoscopically
 - » Typically use fibrin glue for anastomoses
- Probably will be reserved for a few centers

Prostate Cancer

- Surgical Treatment
 - Perineal Prostatectomy
 - Renewed interest with decreased morbidity shown by laparoscopy
 - Good data to support oncologic efficacy
 - Nerve sparing possible, although no reports of sural nerve grafts
 - Decreased morbidity over RRP, mainly in blood loss and transfusion requirements

Prostate Cancer

- Cryotherapy
 - New generation of cryotherapy units uses a template similar to brachytherapy
 - Allows for more accurate probe placement



Prostate Cancer

- Radiation Therapy
 - External beam radiotherapy

- Dose escalation studies now pushing doses up into the 80-90Gy range
- IMRT allows better targeting
- Side Effects
 - Incontinence-rare
 - Impotence-common
 - Rectal irritation
 - Hematuria, bladder/urethral irritation



Prostate Cancer

- Radiation
 - Brachytherapy-

- Outpatient, low morbidity
 - Incontinence rare
 - Impotence occurs over 2 year period
 - Urethral irritation, worsening of BPH symptom
- Best for low grade, low stage tumors in older patients



Prostate Cancer

- Biochemical Recurrence

- Approximately 30-40% of patients will experience a rising PSA after local therapy[#]
- 180,400 patients diagnosed with prostate cancer in 2000
- 2/3 (119,064) of these patients receive definitive local therapy
- 30-40% (35,719-47,6259) recur
 - Definition of biochemical recurrence varies
 - Best data from Amling paper >0.4ng/ml*

#Based on SEER statistics. 1998

**Amling CL, et al. J Urol 2001;165: 1146*

Prostate Cancer

- Hormone Refractory Prostate Cancer

- Typically patients will remain hormone responsive for median of 18 months
 - Hormone deprivation options include
 - LHRH agonists
 - Antiandrogens
 - Orchiectomy
 - Estrogens
 - On average from time of HRPC to death is median of 2 years