Carcinoma of Prostate

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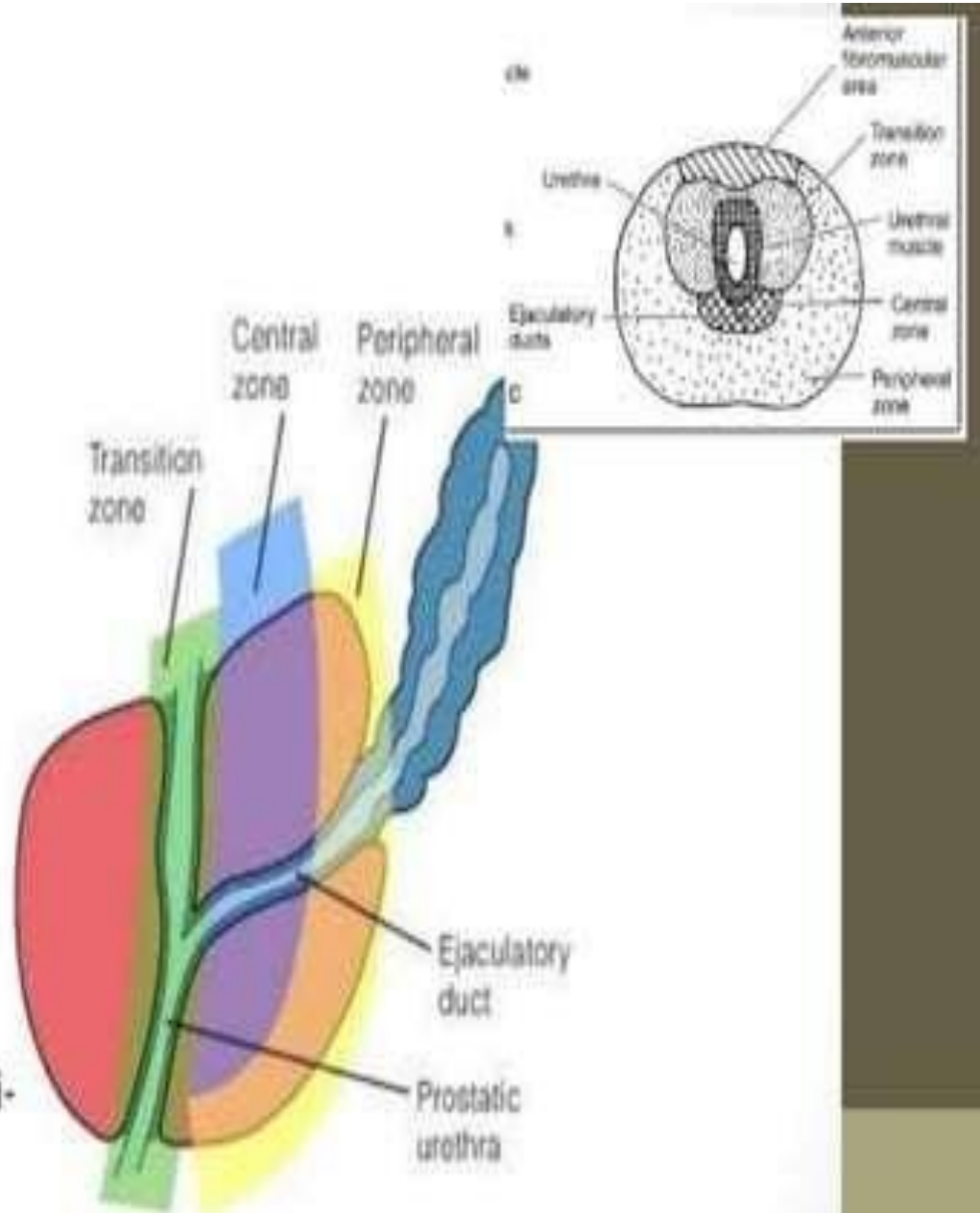
IOM

Introduction

- Peripheral zone (PZ)
  - 70% of cancers
- Transitional zone (TZ)
  - 20%
    - TZ prostate cancers are relatively nonaggressive
    - PZ cancers are more aggressive
      - Tend to invade the peri-prostatic tissues.



Epidemiology

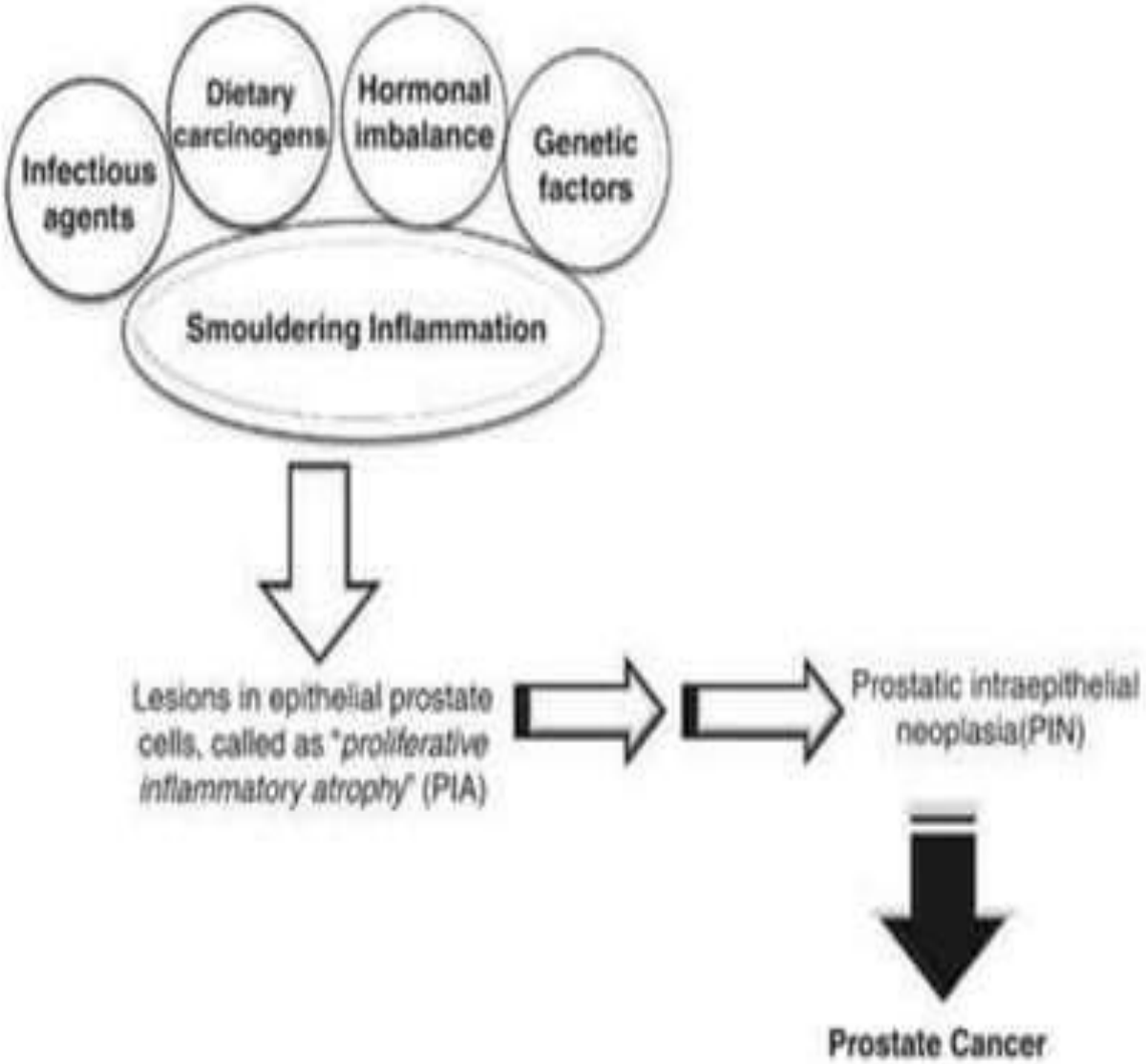
- Most commonly diagnosed cancer in men
- second leading cause of male cancer death
- Risk increases with age,
- In 80s, slow growing, lower grade, relatively harmless and have little impact on their survival.
- More common in Australia/Newzealand, in North Americans, African Americans ;less common in Asians and Hispanic descent than in Whites.
- The overall 5-year survival rate is 99% in the United States.

Risk factors

- older age
- positive family history,
- obesity,
- hypertension,
- lack of exercise,
- Alcohol, smoking
- persistently elevated testosterone levels,

Genetics

- One first degree relative (father or brother) : **twice** the risk of the general population.
- Two first-degree relatives affected have a **5-fold** greater risk.
- strong family history : present at a **younger age** (2.9 years) and with **more locally advanced disease.**
- Mutations in *BRCA1* and *BRCA2 implicated*
- *P53* mutations more frequently seen in metastatic disease


Infectious agents
Dietary carcinogens
Hormonal imbalance
Genetic factors
Smouldering Inflammation
Lesions in epithelial prostate cells, called as "proliferative inflammatory atrophy" (PIA)
Prostatic intraepithelial neoplasia(PIN)
Prostate Cancer

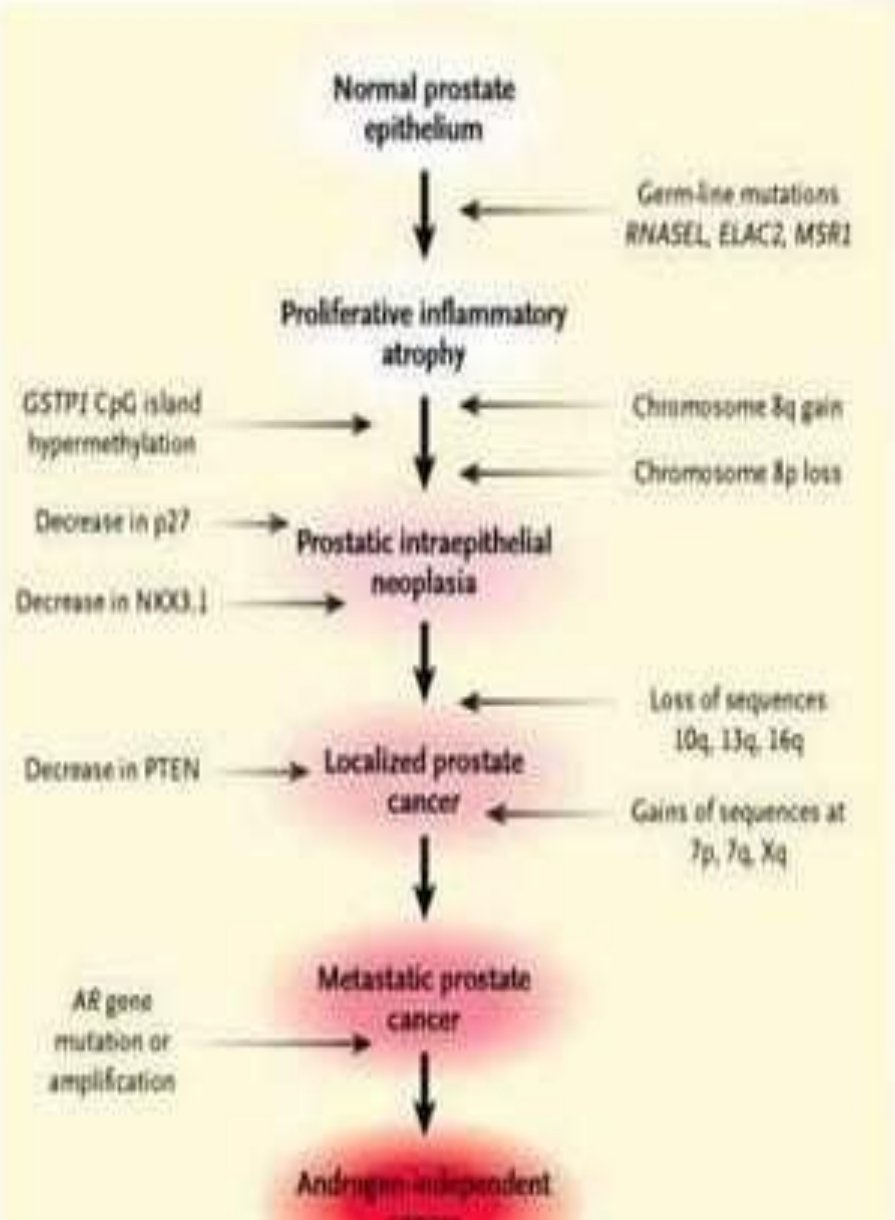
Pathophysiology

Pre-Malignant Lesions

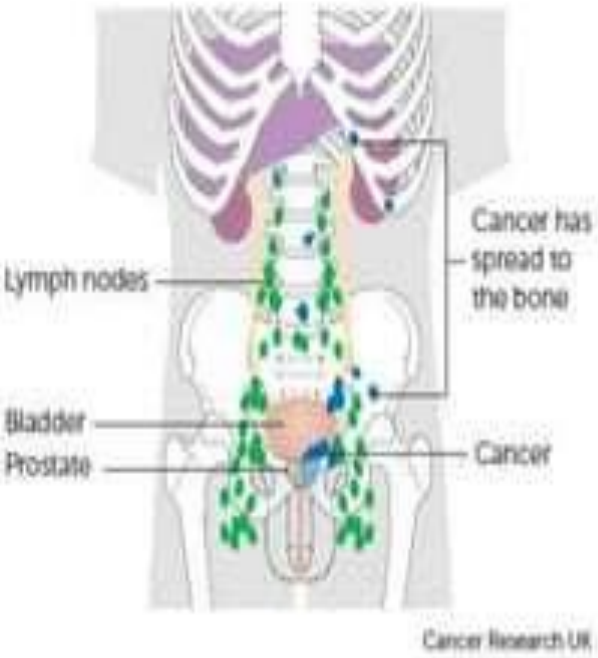
High-Grade Prostatic Intraepithelial Neoplasia (High-Grade PIN)

Atypical Small Acinar Proliferation (ASAP)

Atypical Adenomatous Hyperplasia (Adenosis)



- commonly metastasizes to the bones and lymph nodes.
- Metastases to the bone are thought to be at least partially a result of the **prostatic venous plexus draining into the vertebral veins.**



Presentation

EARLY STAGE

- Asymptomatic

LOCALLY ADVANCED DISEASE

- Obstructive or irritative voiding complaints :growth of the tumor into the urethra or bladder neck or from its direct extension into the trigone of the bladder

frequent urination, nocturia, difficulty starting and maintaining a steady stream, hematuria, and dysuria (like BEP)

- Retention of urine
- Hematuria
- Hematospermia, difficulty achieving an erection or painful ejaculation.

ADVANCED DISEASE (spread to the regional pelvic lymph nodes)

- Edema of the lower extremities
- Pelvic and perineal discomfort

METASTATIC DISEASE

- Bone pain/pathological #
- Spinal cord compression symptoms (tingling, leg weakness, pain, paralysis, and urinary as well as fecal incontinence)
- Paraperesis
  - Para aortic LAP- edema of abdominal wall, genitalia or lower extremities/ mass abdomen

- Rectal involvement- • Hematochezia • Constipation • Intermittent diarrhoea • Abdomino-pelvic pain
- Renal impairment due to prolonged BOO.

Digital rectal examination (DRE)

- Cornerstone of the physical examination/ instrumental in staging
- detect prostate abnormalities, asymmetry, and suspiciously hard nodules
- not considered a definitive test for prostate cancer by itself.
- An abnormal DRE initially uncovers about 20% of all prostate cancers.

DRE

- Size: Craniocaudal and transverse dimension
- Consistency / Mobility
- Any firm/ elevated area and its size.
- Rectal mucosa: free/fixed
- Median sulcus: obliterated

Ca prostate- Hard, nodular, asymmetrical, may or may not be raised above the surface of gland, absent middle lobe and is surrounded by compressible prostatic tissue.

Prostatic induration - BHP nodule/ calculi/ infection/ granulomatous prostatitis

Prostate specific antigen(PSA)

- *A serine protease*
- PSA is organ specific but not proste cancer specific
- Also increases in BPH, prostatitis and other non-malignant conditions.
- only estimates the risk of prostate cancer.
- As an independent variable, PSA is a better predictor of cancer than either DRE or transrectal ultrasound (TRUS).
- Positive predictive value of a serum PSA between 4 and 10 ng/mL is approx 20–30%.
- For levels in excess of 10 ng/mL, the positive predictive value increases (40-70%)

- *PSA* levels greater than 4 ng/ml is seen in 80% of prostate cancers initial presentation.
- It is recommended at least 2 abnormal PSA levels or the presence of a palpable nodule on DRE to justify a biopsy and further investigation
- PCa can occur despite having low serum PS

PSA>10: suggestive of CaP
PSA>35: advanced CaP

Table 5.2.1: Risk of PCa in relation to low PSA values [137]

PSA level (ng/mL)	Risk of PCa (%)
0.0-0.5	6.6
0.6-1.0	10.1
1.1-2.0	17.0
2.1-3.0	23.9
3.1-4.0	26.9

:

- ***Free /Total PSA ratio***: .
- If the total PSA is between 4 and 10 ng/ml, a free PSA percentage is considered valid.
- If f/t PSA ratio> 25%, the cancer risk is less than 10%.
- If < 10%, the cancer risk is about 50%.

(Free/total PSA is of no clinical use if the total serum PSA is > 10 ng/mL or during follow up of known PCa.)

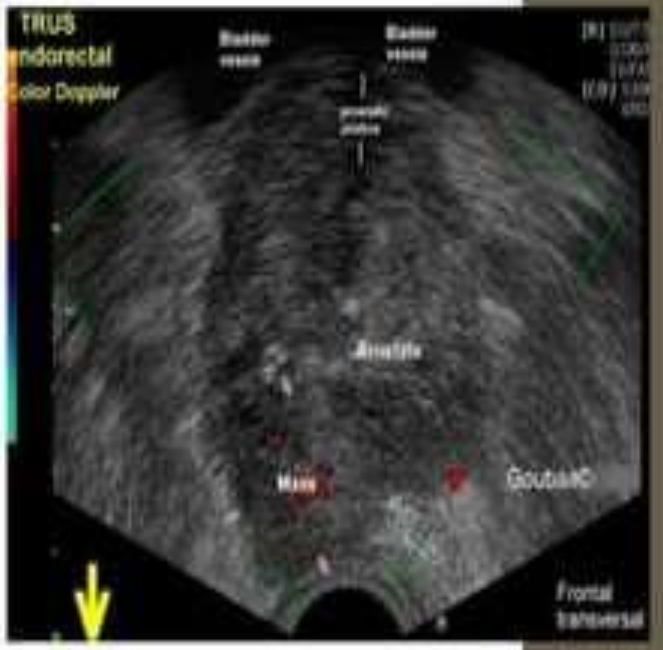
- ***PSA Density*** is the total PSA divided by the prostatic volume as determined by MRI or ultrasound (US). The PSA density is intended to minimize the effect of benign prostatic enlargement.

If > than 0.15, it is considered suggestive of malignancy.

- ***PSA Velocity*** compares serial, annual PSA serum levels.
  -An annual increase > 0.75 ng/ml or > 25% suggests a potential cancer (total PSA 4 to 10 ng/ml).
  - If the total PSA is 2.6 to 4 ng/ml, then an annual increase of 0.35 ng/ml would be considered suspicious.

- Prostate cancer is usually suspected on the basis of DRE and/or PSA levels. (DRE+PSA specificity **87%)**
- Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate biopsy cores.

Prostate Imaging



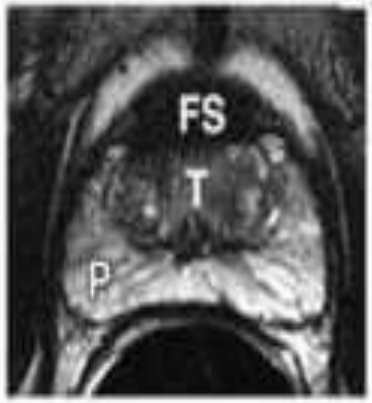
- Ultrasound and MRI are the main imaging modalities used for initial prostate cancer detection and diagnosis.

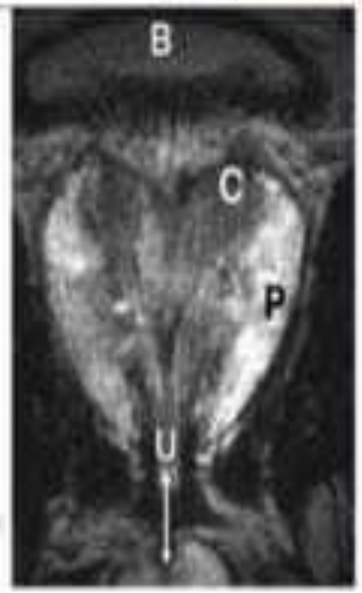
- **Transrectal ultrasound (TRUS)** "suspicious hypoechoic area seen," but ultrasound alone is not a reliable diagnostic test for prostatic malignancy.
- TRUS is best used for directing the needle for prostate biopsies.

- New sonographic modalities such as **sonoelastography, contrast-enhanced US or high-resolution micro-ultrasound**; either alone or combined used in the so-called 'multiparametric US'

Prostate MRI

- **Prostatic MRI is becoming a standard imaging modality for the diagnosis of prostate cancer.**
- Identifies and grade suspicious prostate nodules, extracapsular extension, evaluate the seminal vesicles for possible tumor involvement and lymph nodes that might indicate early metastatic disease
- Multiparametric MRI (mpMRI) has good sensitivity for the detection and localisation of ISUP grade ≥ 2 cancers
- for surgical planning (radical prostatectomy) and for improved biopsies, in strongly suspected despite a negative initial TRUS-guided biopsy.





- MRI of the prostate may also have a role in active surveillance as an alternative to periodic or repeated biopsies.

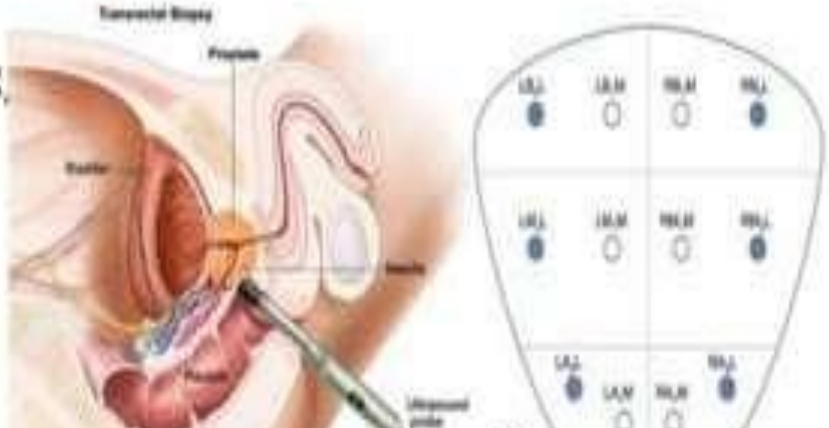
- **USG abd/pelvis**: obstructive features, HDN,large PVRU, LNs,Liver mets
- **Chest Xray**: pulmonary metastasis
- **Axial skeletal imaging**: xray/MRI: osteoblastic secondaries
- **CT scan**: size, extension, LN involvement, for planning RT, less sensitive, not prefered

Testing For Tumor Spread

- Bone scans can detect early metastases to the bones, but the PSA usually needs to be at least 20 before this is likely to be positive.
- MRI : evaluate extracapsular extension as well as the regional lymph nodes and seminal vesicles for possible tumor involvement.
- 68-gallium prostate-specific membrane antigen (PSMA) PET/CT scan is a new FDA-approved test for detecting metastatic prostate cancer

Biopsy

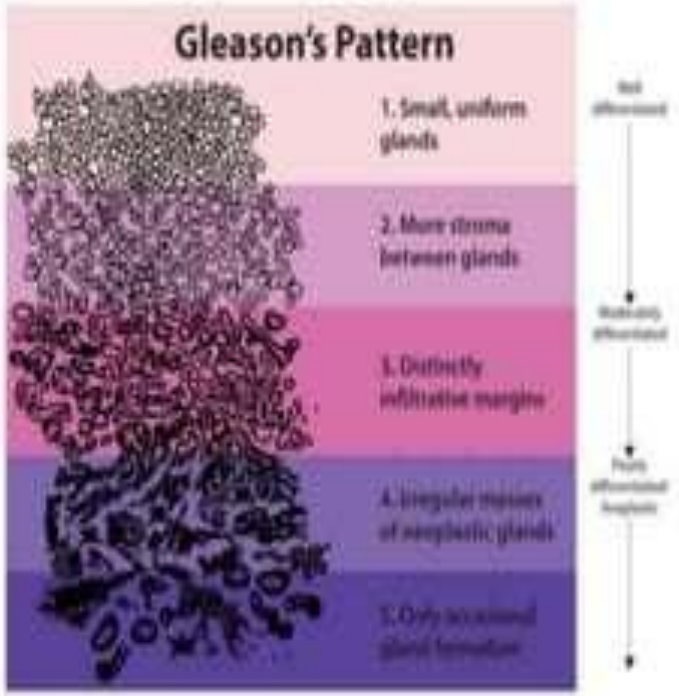
- In suspected case(DRE+PSA)
- Conclusive diagnosis
- TRUS guidance to make sure that all areas of the prostate are adequately sampled.
- The most commonly used pattern is to take **two specimens from each of three areas (base, mid-gland, and apex) on both sides**. This is called a 12 core sextant biopsy. The purpose is to better identify the extent and exact location of the tumor.
- Biopsy sites included the
  1. midlobe parasagittal plane at the apex,
  2. the midgland, and
  3. the base bilaterally.



Indication of repeat biopsy after previously negative biopsy

- Rising and/or persistently elevated PSA
- Suspicious DRE
- Atypical small acinar proliferation
- Extensive (multiple biopsy sites, i.e., > 3) high grade prostatic intraepithelial neoplasia (HGPIN)
- Intraductal carcinoma as a solitary finding, > 90% risk of associated high-grade prostate carcinoma
- Positive multiparametric MRI findings

Histopathology



The Gleason Scoring System

- Originally developed by pathologist **Dr. Donald Gleason in the 1960s**

- Based on the **microscopic arrangement, architecture or pattern of the glands** in the prostate
- Grade 1 to 5:
  - 1 representing an normal microscopic glandular pattern and appearance,
  - 5 where no glandular architecture remains, but sheets of abnormal cancer cells.

- The **predominant pattern(primary pattern)** is always the first number, 1 to 5, and the second number(second pattern) would be any secondary or minor pattern, also graded 1 to 5.
- lowest risk Gleason score : Gleason 1 + 1 = 2, and
- the worst high-grade pathology: Gleason 5 + 5 = 10.

- If only one Gleason grade or pattern is seen, then the Gleason score would consist of the same Gleason grade repeated and added together as in **Gleason 3 + 3 = 6;** which happens to be the most commonly found Gleason score.

1. Low-grade tumors: any Gleason score of 3 + 3 = **6 or less**.
2. Intermediate-grade Ca: Gleason score of 3 + 4 = 7.

(This would mean that most of the tumor was Gleason grade 3, but there was a smaller portion that was the more aggressive Gleason grade 4.)

3. high-grade cancer: A Gleason score of 4 + 3 = 7 or higher

International Society of Urological Pathology (ISUP) grade

The 2014 ISUP endorsed grading system limits the number of PCa grades, ranging them from 1 to 5

Table 4.2: International Society of Urological Pathology 2014 grades

Gleason score	ISUP grade
2-6	1
7 (3+4)	2
7 (4+3)	3
8 (4+4 or 3+5 or 5+3)	4
9-10	5

Table 4.3 EAU risk groups for biochemical recurrence of localised and locally advanced prostate cancer

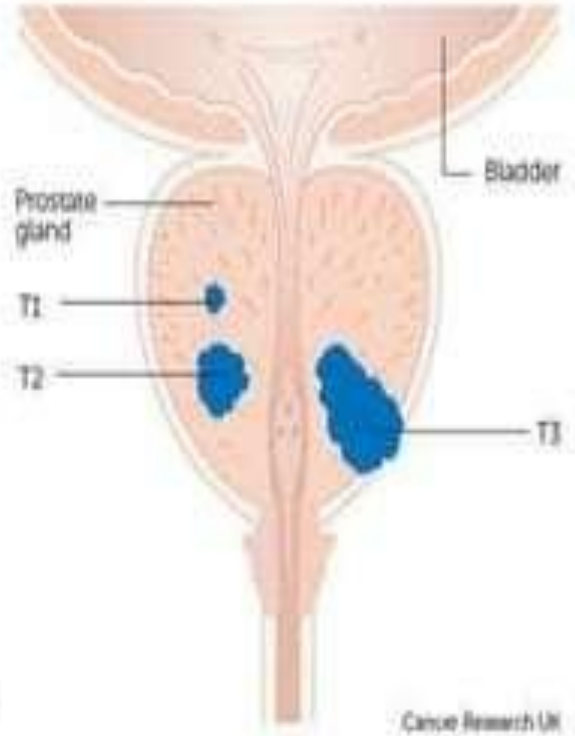
Definition	Clinical risk group		
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL	PSA 10-20 ng/mL	PSA > 20 ng/mL	any PSA
and GS < 7 (ISUP grade 1)	or GS 7 (ISUP grade 2/3)	or GS > 7 (ISUP grade 4/5)	any GS (any ISUP grade)
and cT1-2a	or cT2b	or cT2c	cT3-4 or cN+
Localised			**Locally**

Staging

- TNM staging
- T1 and T2 cancers are limited to just the prostate and are considered "**localized.**"
- T3 cancer has spread outside the prostatic capsule but has not reached the rectum or bladder. Cancer may also have spread to the seminal vesicles (stage T3c), and this tends to be an ominous sign.
- T4 cancers have spread outside the prostate to adjacent regional structures such as the bladder. They may also metastasize to the lungs, lymph nodes or liver which would be identified by their N (nodes) or M (metastasis) scores.
- Stage T4 prostate cancers with distant metastases have an overall 5-year survival rate of only 29%.

Clinical Tumor Staging

TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
T1	Clinically inapparent tumour that is not palpable	
	T1a	Tumour incidental histological finding in 5% or less of tissue resected
	T1b	Tumour incidental histological finding in more than 5% of tissue resected
	T1c	Tumour identified by needle biopsy (e.g. because of elevated prostate-specific antigen [PSA])
T2	Tumour that is palpable and confined within the prostate	
	T2a	Tumour involves one half of one lobe or less
	T2b	Tumour involves more than half of one lobe, but not both lobes
	T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule	
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
N - Regional (pelvic) Lymph Nodes[1]		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	



Cancer Research UK

M - Distant Metast	
M0	No distant metastasis
M1	Distant metastasis
	M1a Non-regional lymph node(s)
	M1b Bone(s)
	M1c Other site(s)

[1] *Metastasis no larger than 0.2 cm can be designated pN0.*

[2] *When more than one site of metastasis is present, the most advanced category is used. pM1c is the most advanced category.*

Clinical T stage only refers to DRE findings; imaging findings are not considered in the TNM classification. Pathological staging (pTNM) is based on histopathological tissue assessment

Prostate Imaging, Reporting and Data System (PIRADS)

- Various MRI tissue characteristics ultimately determine the relative cancer risk which is documented as PIRADS score.

- A PIRADS score of **1 or 2** is highly unlikely to be cancer.
- A PIRADS score of **4 or 5** is highly suspicious for clinically significant disease (Gleason 3 + 4 = 7 and higher).
- **PIRADS 3** is equivocal. Histological confirmation with a biopsy is recommended for all PIRADS 3, 4 and 5 lesions.

Biomarker

Prostate Cancer Antigen 3 (PCA3)

is an RNA based genetic test performed from a urine sample obtained immediately after a prostatic massage.

- PCA3 is a long, non-coding RNA molecule that is overexpressed exclusively in prostatic malignancies.
-
- If PCA3 is elevated, it suggests the presence of prostate cancer.
- It is more reliable than PSA as it is independent of prostate volume.
- Serial PCA3 testing may also be helpful in monitoring patients with low-grade prostate cancers on active surveillance

5.2.2.6. Guidelines for risk-assessment of asymptomatic men

Recommendation	Strength rating
To avoid unnecessary biopsies, offer further risk-assessment to asymptomatic men with a normal digital rectal examination and a prostate-specific antigen level between 2-10 ng/mL prior to performing a prostate biopsy. Use one of the following tools: • risk-calculator; • imaging;	Strong
• an additional serum or urine-based test.	Weak

Treatment

- Treatment options depend on stage of disease, life expectancy of the patient and patient preference.
- Prostate cancer, **especially low-grade tumors**, often grow so slowly that frequently **no treatment** is required; particularly in elderly patients and those with comorbidities that would reasonably limit life expectancy to 10 additional years or less.
- **Localised cancer** can be treated by radical prostatectomy, radiation therapy and active monitoring.
- Treatment of **advanced disease** is palliative, and hormone ablation remains the first-line therapy.

Active Surveillance

- Many low-risk cases can now be followed with active surveillance.
- Appropriate for low-grade prostate cancer (Gleason 3+3=6 or less with a PSA<20) and limited sized cancers.

- It aims to avoid unnecessary treatment in men with clinically localised PCa who do not require immediate treatment, but at the same time achieve the correct timing for curative treatment in those who eventually do.
- In active surveillance, patients are usually required to have regular, periodic PSA testing and at least one additional biopsy 12 to 18 months after the original diagnosis.

	Active surveillance	Watchful waiting
Treatment intent	Curative	Palliative
Follow-up	Predefined schedule	Patient-specific
Assessment/markers used	DRE, PSA, re-biopsy, mpMRI	Not predefined
Life expectancy	> 10 years	< 10 years
Aim	Minimise treatment-related toxicity without compromising survival	Minimise treatment-related toxicity
Comments	Mainly low-risk patients	Can apply to patients with all stages

DRE = digital rectal examination; PSA = prostate-specific antigen; mpMRI = multiparametric magnetic resonance imaging.

- Use of active surveillance for selected, lower risk, intermediate-grade prostate cancers (Gleason 3 + 4 = 7 with a PSA less than 10) is controversial but seems reasonable in selected cases.
- MRI of the prostate can also be used to follow these patients and avoids the discomfort of repeated biopsies.
- The best option depends **on the cancer stage, Gleason score, and the PSA level** as well as individual patient preferences, health, comorbidities, quality of life, and age.

Localized Disease

- In **localized disease,(T1c/T2)** definitive therapy if expected to live >10yrs based on age and co-morbidities.
- Definitive treatment includes

1. radical prostatectomy
2. radiation therapy (external beam and/or brachytherapy radioactive seed placement)
3. cryotherapy (usually reserved for radiation therapy failures).

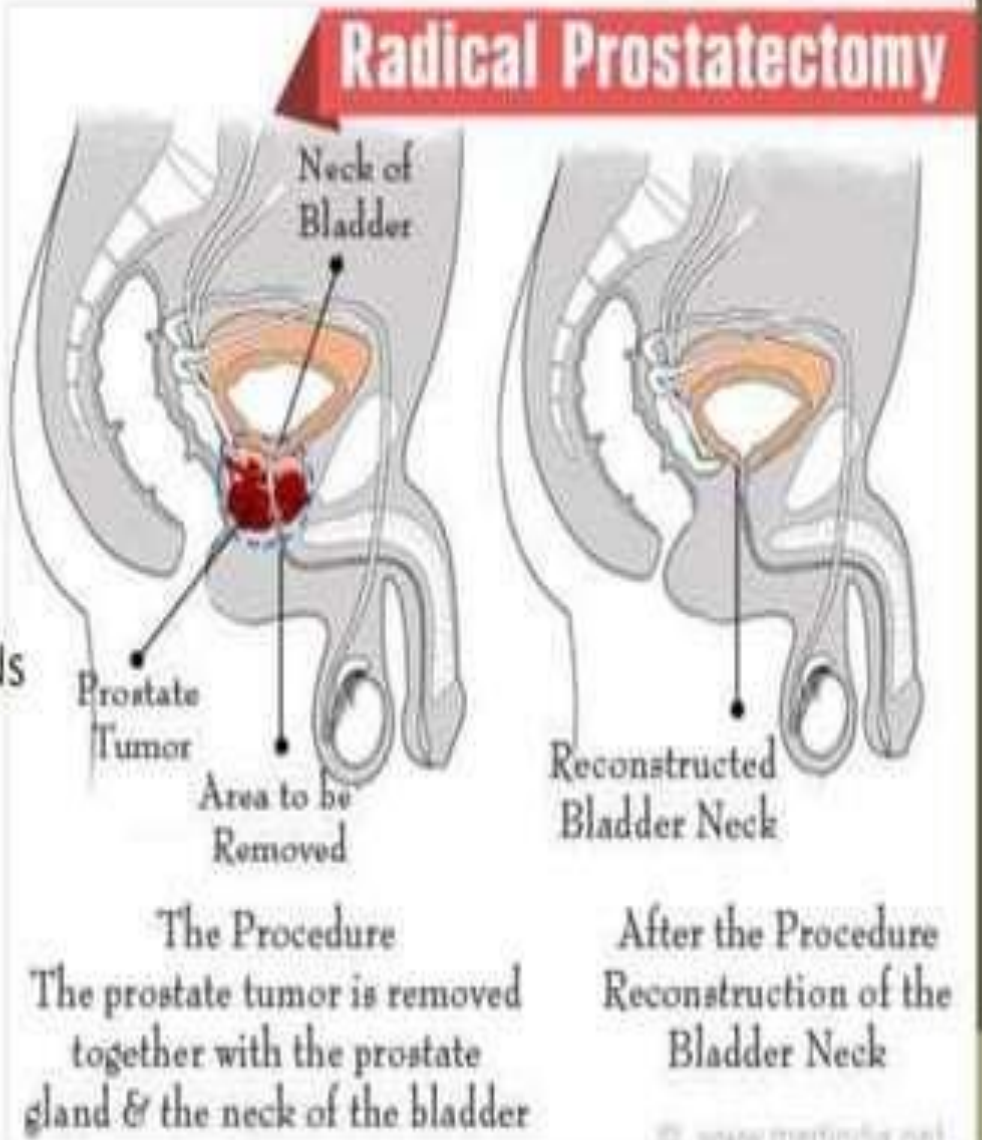
- **For most patients with potentially curable, localized disease, good performance status, reasonably good QOL and >10-year life expectancy, the choice of treatment should be an informed patient decision made after discussions including both urology (surgery) and radiation therapy.**
- Discuss side effects such as erectile dysfunction and urinary incontinence, complications, cost, possible lack of ultimate survival benefit and questionable quality of life improvement over doing nothing.

Surgery

Radical Prostatectomy

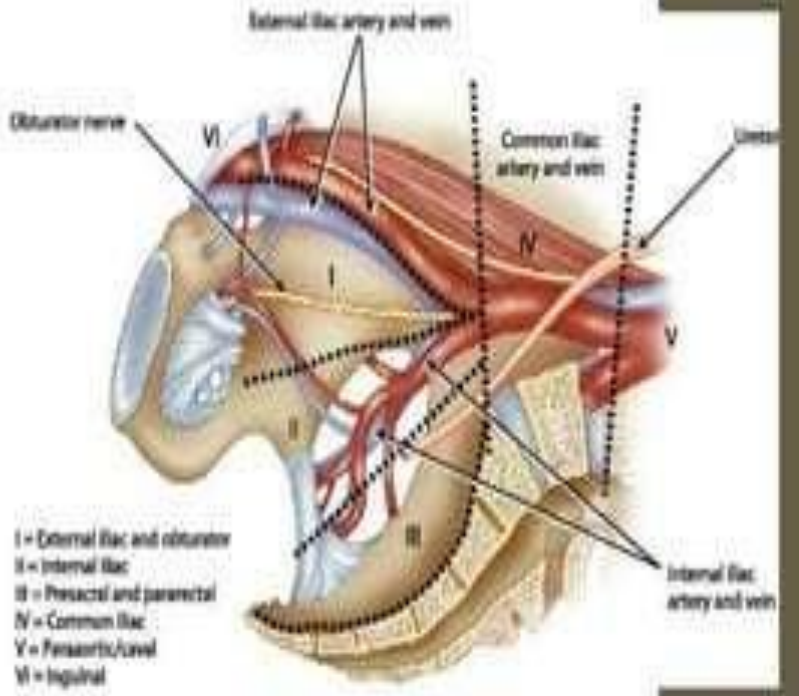
- definitive cure for localized prostate cancer
- a significant improvement in overall survival
- suitable for localised disease and with a life expectancy of>10 years
- These benefits over other definitive, curative therapies are not evident before 10 years after treatment for localized disease and are most pronounced in men younger than 65 years at the time of diagnosis.
- Not appropriate if the tumor is fixed to surrounding structures or there are distant metastases.
- Nerve sparing RP

- open-, laparoscopic- or robot-assisted (RARP).
- entire prostate gland between the urethra and bladder, and resection of both seminal vesicles, along with b/l Pelvic LNs



Lymph Node Dissections (PLND)

- Not done in low-risk patient
- may remove undetectable micrometastases and therefore potentially improve survival.
- In the past, **a pelvic lymph node dissection** was sufficient, but it is now known that metastases will often go directly to the **common iliac, paraaortic, perirectal or presacral nodes,** so a more extended dissection is recommended; particularly in higher risk disease



- limited PLND : confined to the external iliac and obturator fossa areas
- extended PLND: external iliac, hypogastric and obturator nodes and other including the pre sacral and pre sciatic nodes.

Complications of radical prostatectomy

- Bleeding.
- Urinary tract infection.
- Urinary incontinence.
- Erectile dysfunction (impotence)
- Narrowing (stricture) of the urethra or bladder neck.
- Formation of cysts containing lymph (lymphocele)
- Injury to the rectum (rare)

Salvage Radiation Therapy After Radical Prostatectomy

- The serum PSA should become and remain undetectable after successful radical prostatectomy surgery.
- If not or if there are positive margins after surgery, salvage radiation therapy should be considered
- Typically, salvage radiation therapy is 60 to 70 Gy, which is substantially less than for primary definitive radiation therapy.
- Salvage radiation therapy may also be recommended if the PSA becomes detectable at a later date, indicating **possible residual disease** that was present but previously undetectable could now be growing in the immediate area of the prostatic bed

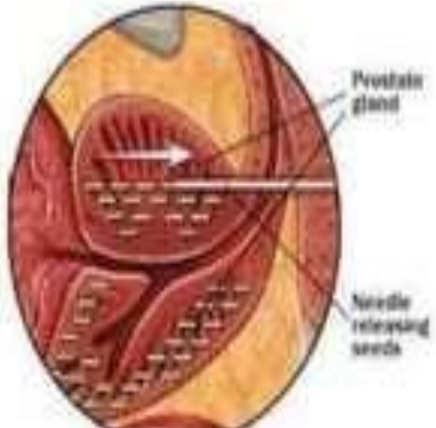
Radiation therapy

- The goal of radiation therapy is to provide a lethal dose of radiation to the tumor without harming the surrounding normal tissue of the bladder and rectum.
- As Adjuvant (margin positive after RP) or Primary therapy in Locally advanced
- After radiation therapy, the PSA is expected to decrease for about 18 months.
- Treatment failure is usually noted by a rise in PSA level of 2 ng/ml or more above the baseline level before initiation of radiation therapy

- **External Beam Radiation Therapy(XRT)**
- Dose of 75-80 Gy results in lower recurrence and higher local cancer control

- **Brachytherapy (Radioactive Implants):**
- temporary-high dose Iridium 192
- Permanent-lose dose, seed implants- I125,Cs131

- Radiation therapy tends to have much fewer side effects (about 50% less) than radical prostatectomy surgery with very similar overall survival.



Treatment Selection: Radiation Therapy versus Radical Prostatectomy

- The best available data suggest **no significant difference in overall survival in most cases of potentially curable, localized, prostate cancer treated with either external beam radiation therapy, stereotactic radiotherapy, brachytherapy (radioactive seed implants), or radical prostatectomy surgery.**

- (Wang Z et al. The efficacy and safety of radical prostatectomy and radiotherapy in high-risk prostate cancer: a systematic review and meta-analysis. World J Surg Oncol. 2020;18(1):42. Published 2020 Feb 24)

Focal Ablation Therapy for Localized Prostate Cancer

- for selected patients with localized disease.

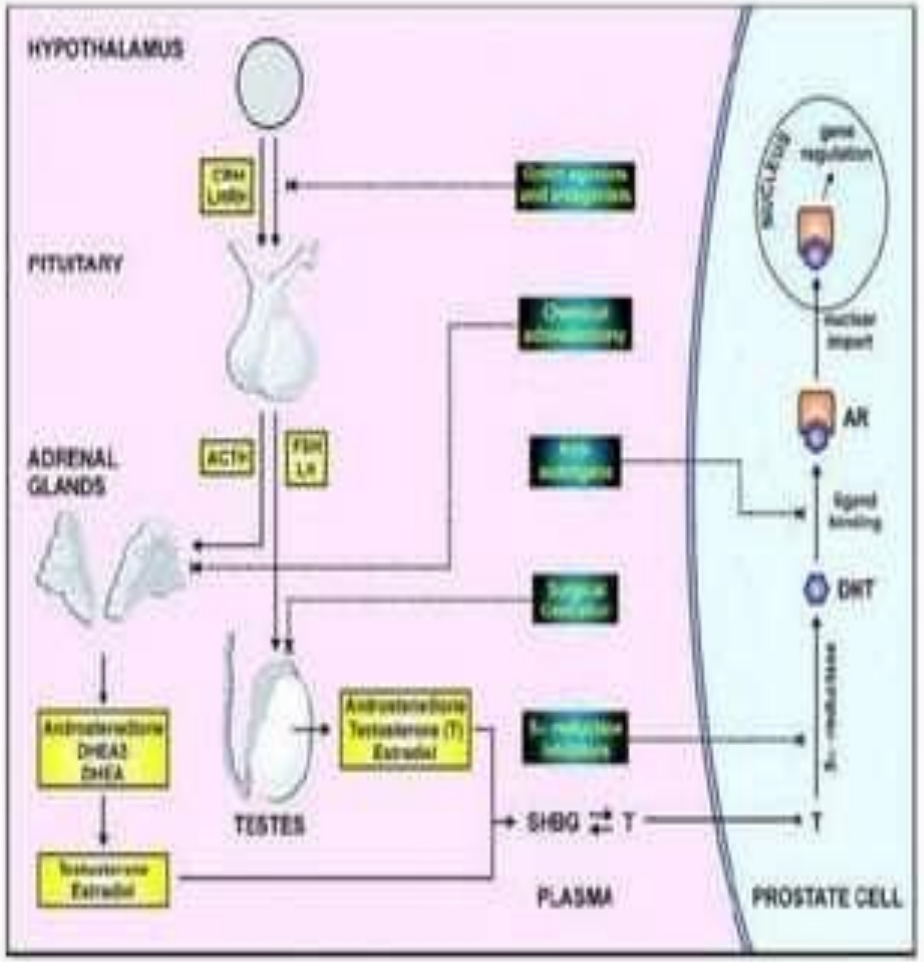
- Focal ablative therapy can use microwave, cryotherapy, laser, high intensity focused ultrasound, etc., to precisely treat a localized malignant prostatic lesion.
- Optimal patients :a single, isolated Gleason 7 (3 + 4 or 4 + 3) lesion and no evidence of extraprostatic or more widespread disease on MRI or prostatic biopsies.
- *Focal Laser Ablation* uses laser fibers to heat and destroys prostatic cancer nodules based on MRI imaging using MRI-Fusion guided targeting
- Cryotherapy

Cryotherapy

- Cryotherapy can be the primary surgical therapy for prostate cancer,
- But most useful as a salvage surgical treatment after radiation therapy has failed
- Control tumors resistant to all other therapies which will still be susceptible to ablation by alternating freeze-thaw cycles that disrupt cell membranes resulting in tissue destruction.
- Freezing...Coagulative necrosis
- T1-2N0M0, GS<7, who have not undergone TURP
- Since cryotherapy cannot treat nodal involvement, lymph node dissections may be needed.[

Hormone Therapy

- In 1941, Urologist Charles Huggins MD from the University of Chicago discovered that androgen deprivation (castration) would cause prostate glands to atrophy and prostate cancer to regress.
- Prostate cells (normal and malignant) are physiologically dependent on androgens to grow, function and proliferate
- Dihydrotestosterone (DHT) is a metabolite of testosterone,is more potent androgen
- Testosterone doesn't 'cause' prostate cancer but promotes and encourages growth.



- the first line treatment for advanced/metastatic prostate Ca.
- For asymptomatic men, immediate ADT will delay progression to the symptomatic stage and avoid/decrease the risk of cancer related complications such as a spinal cord compression or pathological fracture.

Androgen deprivation therapy (ADT)

- Androgen deprivation can help to induce apoptosis (cell death) or at the very least prevent further growth.

1. Surgical or medical 'castration'- stops the production of testosterone
2. Anti-androgen therapy- inhibits the action of testosterone preventing its interaction with the receptors on the prostate cancer cells

❑ **Testosterone-lowering therapy**

- LHRH agonists (first line): Depot Inj;busereline, gosereline, leuproreline, triptoreline
- LHRH antagonists e.g. abarelix, degarelix
- Estrogen-DES
- Surgical castration-B/L orchidectomy;

❑ **Anti-androgens**

- steroidal, e.g. cyproterone acetate (CPA), megestrol acetate and medroxyprogesterone acetate;
- non-steroidal e.g. nilutamide, flutamide and bicalutamide.

- Initial therapy with **leuprolide, goserelin (LHRH) agonists** should be preceded by **anti-androgen therapy, such as bicalutamide** when the PSA >10 ng/ml to prevent any clinical response to the temporary testosterone surge (flare phenomnon) that typically accompanies initiation of hormonal therapy with these agents.
- Hormonal therapy has been found to improve survival when **combined with radiation therapy** but not with radical prostatectomy for intermediate (Gleason 3 + 4 = 7) and higher grade disease.

- The hormonal therapy is usually **continued for at least one year and optimally for at least two years after radiation**.
- Side effects : **hot flashes, reduced libido, and loss of bone density resulting in osteopenia or osteoporosis.**
- Intermittent hormone therapy is another option in selected cases to minimize the side effects of sustained, very low testosterone levels.

Castrate Resistant Tumor (CRPC)

- CRPC is present when PSA rises after medical castration (LHRH suppressor) or surgical castration (orchiectomy), despite having a serum testosterone< 50 ng/dl (i.e the cancer grows despite castration).
- "hormone refractory" or "androgen independent"; however, the preferred term is castration resistant

Medical Oncology

Aggressive Prostate Cancer

- defined as either locally advanced(T3/T4), higher Gleason score (Gleason 4 + 5 = 9 or higher) or rapid PSA doubling time of two years or less.

- **Early use of chemotherapy** has been shown to be helpful in many patients presenting with aggressive or advanced, localized disease.

Chemotherapy

- typically consists of docetaxel in addition to modified hormonal therapy.
- **Docetaxel** is the standard initial chemotherapy agent used to treat CRPC with a median survival benefit of 2 to 3 months.
- Docetaxel plus prednisone now the first line standard (delivered every 3 weeks for up to 10 cycles)
- The early use of docetaxel in hormone naive patients with high volume or high grade localized disease appears to be beneficial based on increased survival noted in several studies (STAMPEDE, CHAARTED, RTOG 0521 and GETUG 12).
- Second-Line chemotherapy treatment is **cabazitaxel**.
- Other: Mitoxantrone

- **Enzalutamide, abiraterone, and apalutamide** are newer, hormonally based drug treatments that often work even when initial hormonal therapy has failed.

Prostate cancer vaccine

Sipuleucel-T

- Is an autologous, dendritic cell-based vaccine that targets prostatic acid phosphatase.
- survival benefit for men with metastatic, castrate-resistant prostate cancer (CRPC)
- quite expensive and provides only a relatively limited improvement in life expectancy.

Summary of treatment for Ca prostate

Low-risk	Intermediate-risk	High-risk	
PSA < 10 ng/mL	PSA 10-20 ng/mL	PSA > 20 ng/mL	any PSA
and GS < 7 (ISUP grade 1)	or GS 7 (ISUP grade 2/3)	or GS > 7 (ISUP grade 4/5)	any GS (any ISUP grade)
and cT1-2a	or cT2b	or cT2c	cT3-4 or cN+
Localised			**Locally advanced**

1) Low risk disease

- For men in their 70s, conservative treatment
- Radical surgical treatment considered in younger (<70years) man , although even in this group, some men will elect to pursue a conservative course when counselled about risks versus benefits.

2) Intermediate risk disease

- In younger, fitter men (<70years), this may be treated by **radical prostatectomy or radiotherapy.**
- Active monitoring remains an option, particularly for more elderly patients towards the lower end of the risk spectrum.
- In the elderly patient with out-flow obstruction, transurethral resection with or without hormone therapy is indicated.

Summary .....

3) High risk disease.

- Early androgen ablation is favoured if close follow-up is not possible.
- For the sexually active,a careful conservative approach with the adoption of androgen ablation when symptoms arise is reasonable.
- Androgen ablation coupled with radiotherapy, perhaps with surgery as part of a multimodal approach, is standard treatment for younger men with T3 disease.

4) Metastatic disease

- Once metastases have developed, the outlook is poor.
- For patients with symptoms: androgen ablation will provide symptomatic relief in over two-thirds of patients.
- For patients with asymptomatic metastases, the timing of treatment is less clear. Systemic chemotherapy with **docetaxel** should be considered in younger, fitter men

Follow up *after treatment with curative intent*

Recommendations	Strength rating
Routinely follow up asymptomatic patients by obtaining at least a disease-specific history and serum prostate-specific antigen (PSA) measurement. These should be performed at 3, 6 and 12 months after treatment, then every 6 months until 3 years, and then annually.	Strong
At recurrence, only perform imaging to detect local recurrence if the outcome will affect treatment planning.	Strong
Only offer bone scans and other imaging modalities to men with biochemical recurrence or symptoms suggestive of progression without signs of biochemical relapse.	Strong

Screening

- the 'systematic examination of asymptomatic men (at risk)' and is usually initiated by health authorities
- reduction in mortality due to PCa

- disadvantage- overdiagnosis, overtreatment

Recommendations
Do not subject men to prostate-specific antigen (PSA) testing without counselling them on the potential risks and benefits.
Offer an individualised risk-adapted strategy for early detection to a well-informed man and a life-expectancy of at least 10 to 15 years.
Offer early PSA testing to well-informed men at elevated risk of having PCa: • men > 50 years of age; • men > 45 years of age and a family history of PCa; • men of African descent > 45 years of age; • men carrying *BRCA2* mutations > 40 years of age.
Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of 2 years for those initially at risk: • men with a PSA level of > 1 ng/mL at 40 years of age; • men with a PSA level of > 2 ng/mL at 60 years of age; Postpone follow-up to 8 years in those not at risk.
Stop early diagnosis of PCa based on life expectancy and performance

References

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THANK YOU