PROSTATE CANCER – PAST, PRESENT and FUTURE

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WHO definition of "Health"(1948)

Health is not merely the absence of disease, but a state of complete physical, emotional and social well being

HRQOL Measurement in PCa

- General Domains

  Physical function

  Mental health

  Social interaction

  Role performance

- Disease-specific domains

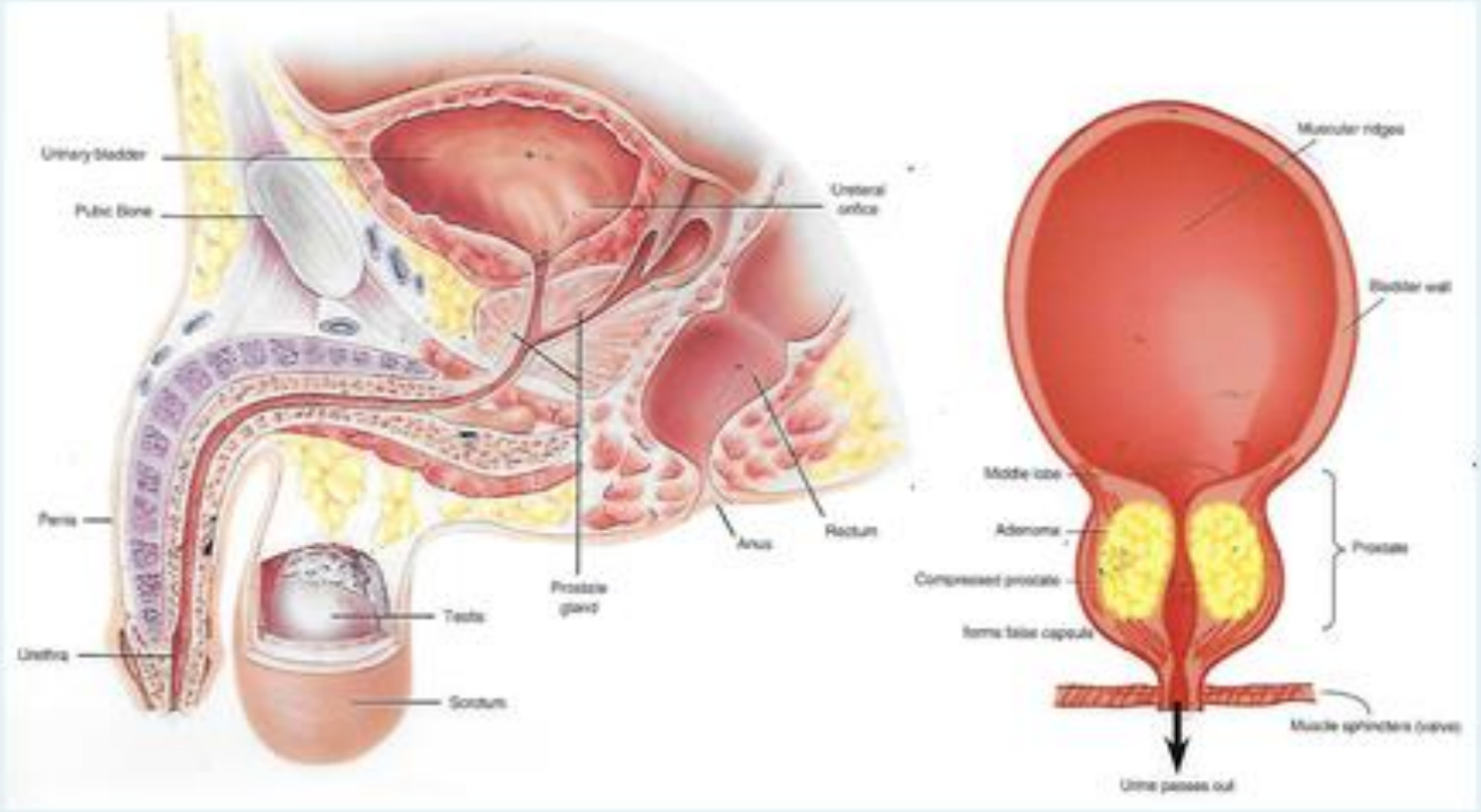
  Worry about recurrence

  Appetite, weight loss,etc

  Fatigue

  Urinary, sexual, bowel

Anatomy of the prostate gland



For practical purposes we use...

- **AGE SPECIFIC PSA**

40 TO 49 YEARS = < 2.5

50 TO 59 YEARS = < 3.5

60 TO 69 YEARS = < 4.5

70 TO 79 YEARS = < 5.5

Causes of Raised PSA

A very large prostate Gland

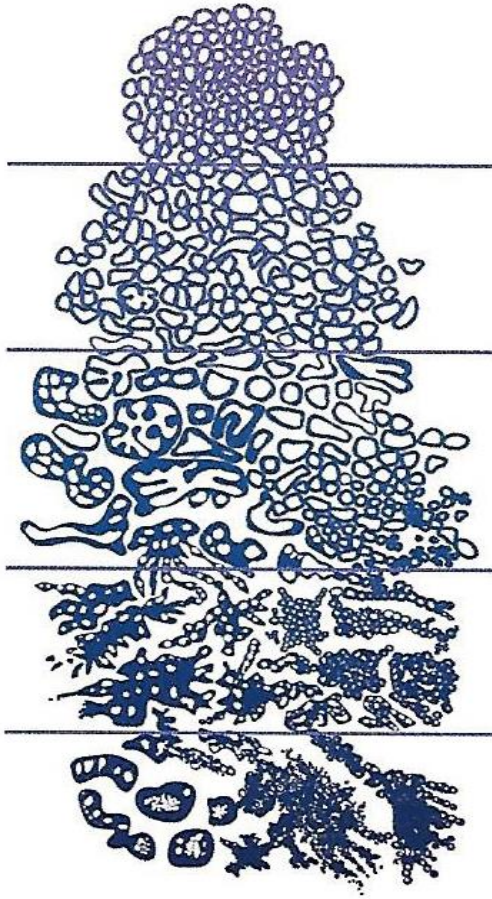
Infection of urine or Prostate Gland

Possibility of prostate Cancer

Gleason score

Gleason Grading System[25]*

A scoring system based on identifying the two most prevalent glandular patterns of the tumour cells. Each pattern is assigned a grade from 1 to 5 and the grades are added together. A Gleason score ≤6, with a PSA <10ng/mL, is considered low-risk prostate cancer and may be most amenable to curative, localised therapy.[26,27]



1 Simple round glands, closely packed in rounded masses with well-defined edges.

2 Simple round glands, loosely packed in vague, rounded masses with loosely defined edges.

3A Medium-sized single glands or irregular spacing with ill-defined infiltrating edges.

3B Very similar to 3A, but small to very small glands, which must not form significant chains or cords.

3C Papillary and cribriform epithelium in smooth, rounded cylinders and masses; no necrosis.

4A Small, medium or large glands fused into cords, chains, or ragged infiltrating masses.

4B Very similar to 4A, but with many large clear cells, sometimes resembling 'hypernephroma'.

5A Papillary and cribriform epithelium in smooth, rounded masses. More solid than 3C with central necrosis.

5B Anaplastic adenocarcinoma in ragged sheets.

*Reprinted from Human Pathology, V23, Gleason DF, Histologic grading of prostate cancer: a perspective, p273-279, copyright (1992), with permission from Elsevier.

Gleason score

- 2-4: well differentiated (seldom reported now): Low risk
- 5-7: moderately well differentiated (usually 3+4 but 4+3 is high risk): Intermediate risk
- 8-10: poorly differentiated (4+4=8 Or 4+5=9 Or 5+4=9 Or 5+5=10) ; High risk
- PIN/ASAP

Risk factors for prostate cancer

Family History

- There is a two fold or greater risk with one first degree relative[2]
- There is a nine fold risk with one first degree relative and one second degree relative[2]

Race

- Scandinavians[3,4] and African-Americans[4,5] have an increased risk
- Asians[4] have a decreased risk

Hormones

- There may be an increased risk with circulating male hormone levels[4,6-8]

Vasectomy

- Men undergoing vasectomy are more likely to be screened for prostate cancer therefore there is no definitive correlation[9]

Smoking

- Smoking has shown no definitive correlation[4]

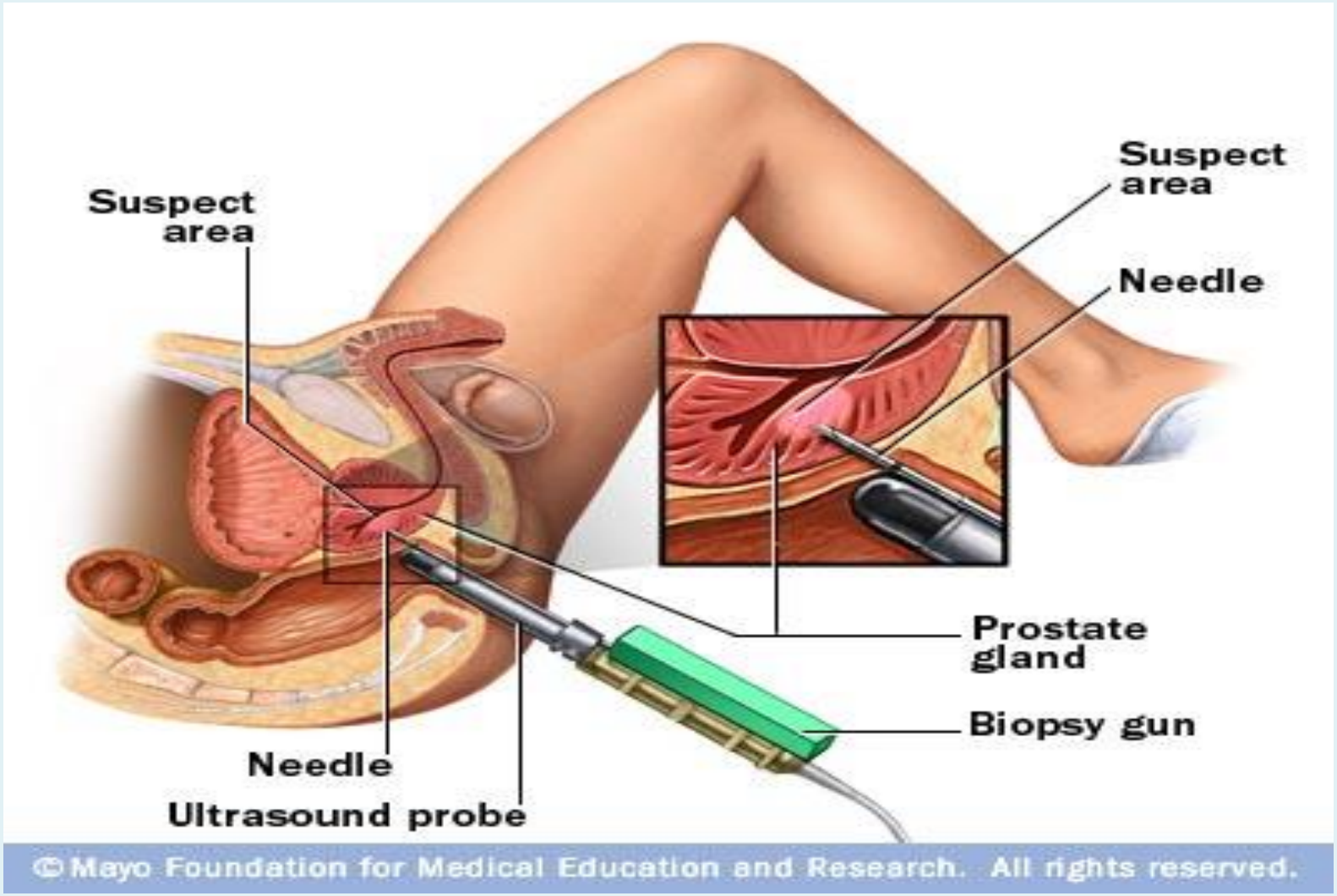
Occupation

- There is a weak association with the cadmium industry (eg newspaper printing, mining)[10]

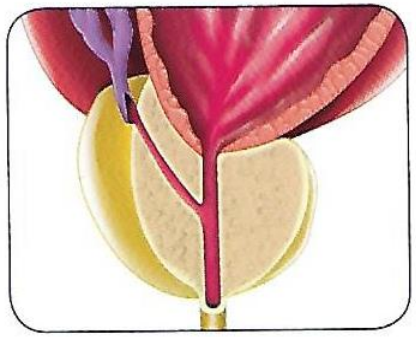
Diet

- Some studies have shown that a diet high in fat[11,12] (fatty meats, dairy foods)* and vitamin A from animal sources[13] can potentially increase the risk
- Some studies have shown that there is potentially a decreased risk with a diet high in:
  - vitamin A from plant sources[13]
  - dark green vegetables, eg green beans, broccoli, brussel sprouts, cabbage, kale, peas and spinach)*[14]
  - isoflavonoids[11,15] (plant based weak oestrogens found in soy products)*
  - lycopenes[16] (carotenoid antioxidant found in tomatoes)*
  - selenium[17] (seafood, meats, grains)*
  - vitamin E (in smokers)[18]

TRUS BIOPSY Prostate Gland

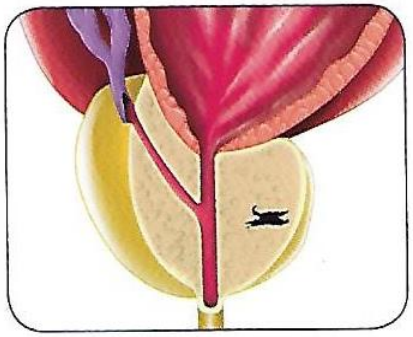


Clinical stages



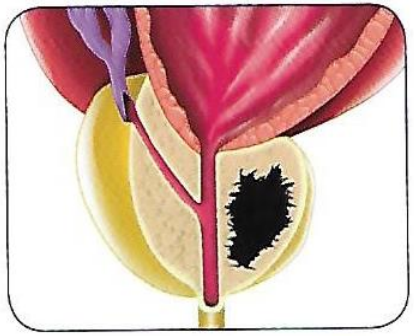
TX, T0, T1, T1a, T1b, T1c

Tumour not palpable or otherwise clinically evident.



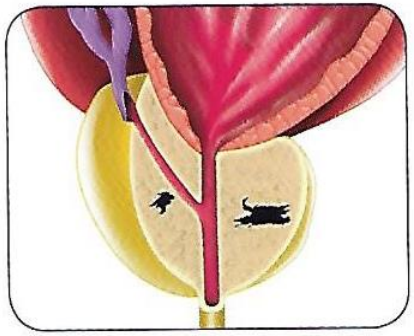
T2, T2a

Tumour palpable, confined to one half of the lobe or less, remains within prostate capsule.



T2b

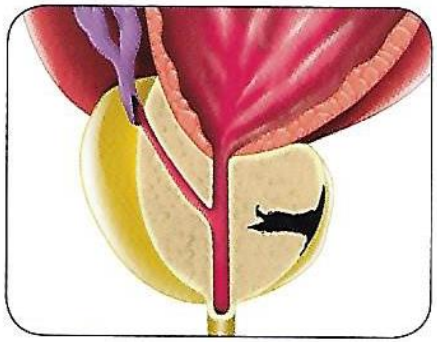
Tumour involves more than one half of lobe, but not both lobes, remains within prostate capsule.



T2c

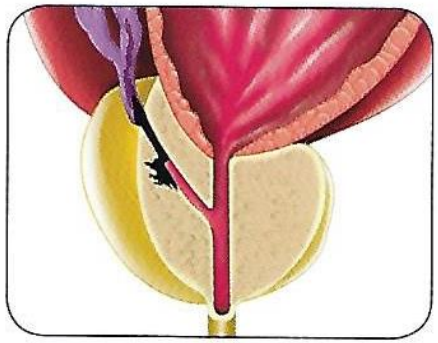
Tumour involves both lobes, remains within prostate capsule.

Clinical stages



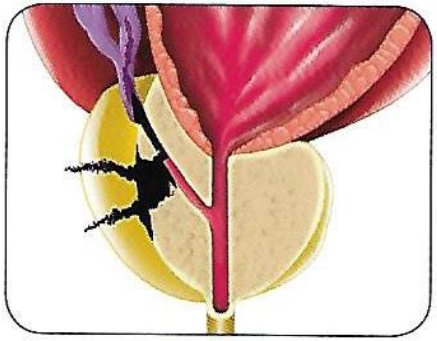
T3, T3a

Tumour extends through prostate capsule.



T3b

Tumour extends through prostate capsule and invades seminal vesicle(s).



T4

Tumour is fixed or invades adjacent structures other than the seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, or pelvic wall.

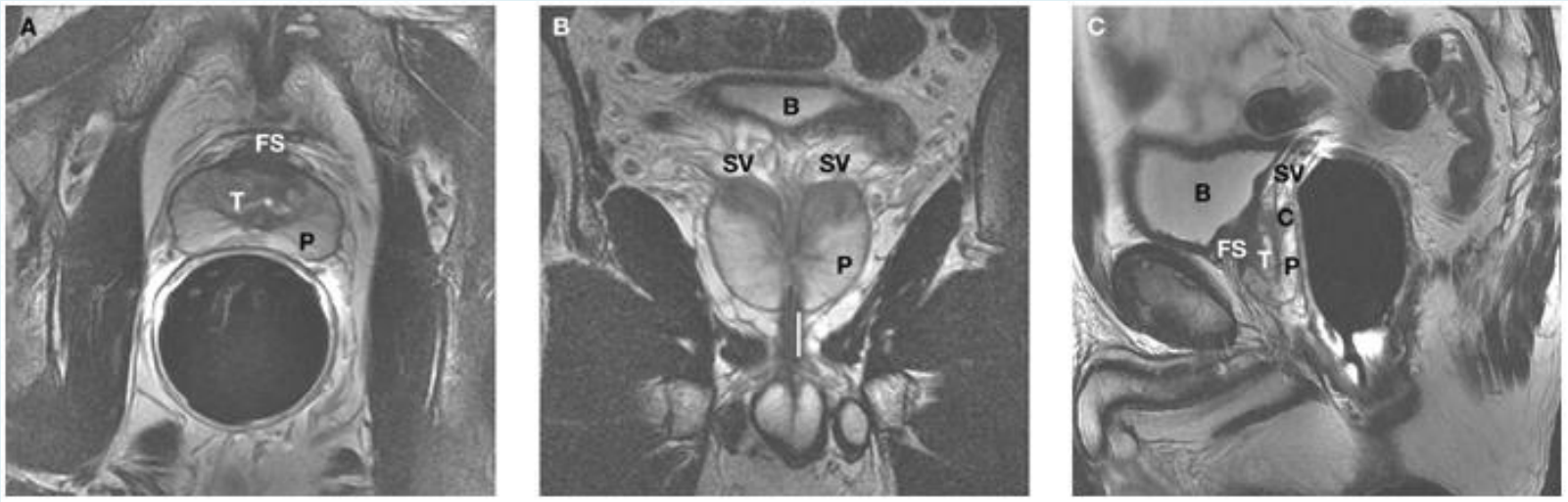
Imaging tools to improve staging

- Multiparametric MRI prostate
  (excellent for local staging)

- CT scan (Computerised Tomography) if PSA is >20 to exclude lymph nodal spread

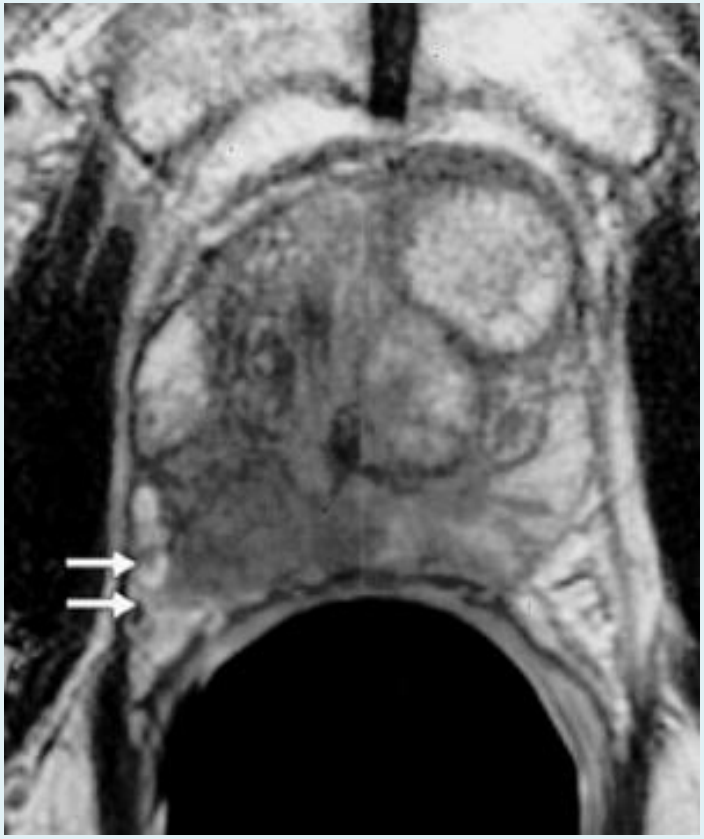
- Isotope bone scan when PSA is > 15

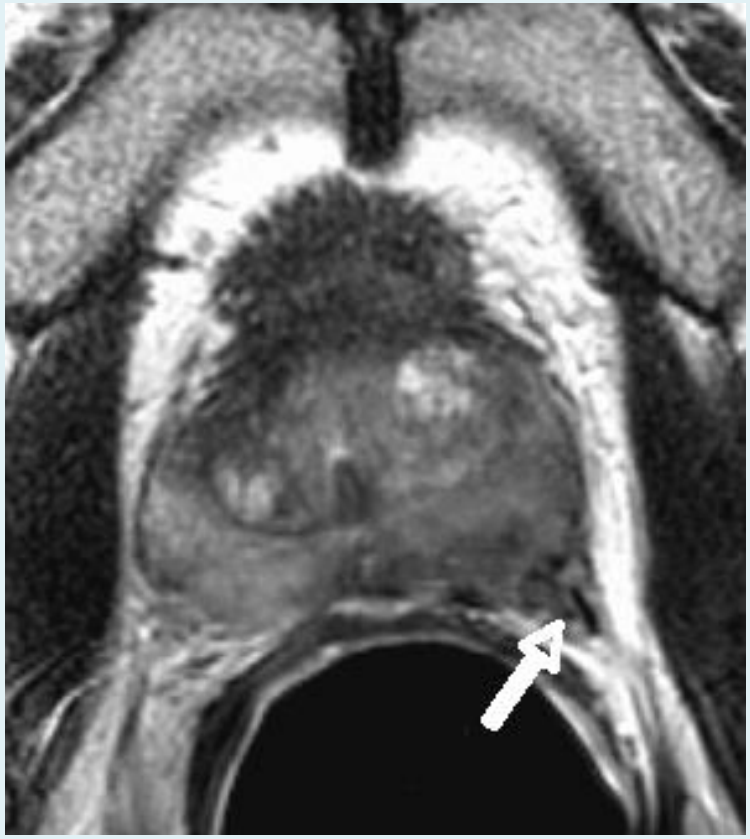
Figure 1 A 57-year-old male with Gleason score 6, pT2b prostate cancer



Huzjan R *et al*. (2005) Magnetic resonance imaging and magnetic resonance spectroscopic imaging of prostate cancer *Nat Clin Pract Urol* **2:** 434–442 doi:10.1038/ncpuro0296

MRI: Stage T3 prostate cancer (extracapsular extension)





Active Surveillance

- Low risk prostate cancer - Gleason 3+3 <5% of +ve cores, one or both lobes
- Intermediate risk prostate cancer – Gleason 3+4 <5 % of +ve cores, one or both lobes
- Low PSA within age -pecific range or just above that.

  MRI very useful tool
- Men with significant co-morbidity
- Patient’s choice

NICE Guidelines – Treatment and Management of Localised Prostate Cancer

Treatment and management options for men with localised prostate cancer[30]

Option	Risk category		
	Low	Intermediate	High
Management approaches			
Watchful waiting	T	T	T
Active surveillance	✓	T	✗
Radical treatments			
Prostatectomy	T	✓	✓*
Brachytherapy	T	T	✗
Conformal radiotherapy**	T	✓	✓*
Cryotherapy***	✗	✗	✗
High-intensity focused ultrasound***	✗	✗	✗

NICE Guidelines – Treatment of Locally Advanced Prostate Cancer

Treatment options for men with locally advanced prostate cancer*[30]

In men receiving radiotherapy	
Offer neoadjuvant and concurrent luteinising hormone-releasing hormone agonist (LHRHa) therapy for 3–6 months	Offer adjuvant hormonal therapy for a minimum of 2 years if Gleason score ≥8
In men with >15% risk of pelvic lymph node involvement who will receive neoadjuvant hormonal therapy and radiotherapy†	
Consider pelvic radiotherapy	

†Risk is estimated using the Roach formula: 2/3 PSA + (10 x [Gleason score –6])

✗ Do not offer:

- Bisphosphonates to prevent bone metastases
- Adjuvant hormonal therapy in addition to prostatectomy, even to men with margin-positive disease‡
- Immediate post-operative radiotherapy after prostatectomy, even to men with margin-positive disease‡
- High-intensity focused ultrasound (HIFU) or cryotherapy‡

Radical treatment of prostate cancer with an intent to CURE

- Radical surgery
  - Open
  - Laparoscopic
  - Robotic
- Radiotherapy
- Brachytherapy
- All expected survival 10 – 15 years prior to radical treatment

Factors influencing radical surgery

- Younger age
- Motivated patient
- Ability to carry out nerve sparing surgery
- Larger volume of prostate gland
- High IPSS/Gleason score/PSA
- Extended lymphadenectomy
- You get the BEST staging information

Factors influencing non-surgical radical treatment

- Co-morbidity
- Patient choice
- Low IPSS Score
- PSA >20
- TRUS/MRI/CT suggesting capsular penetration

Complications: What do we say ?

- General

Thrombo-embolic

Respiratory

Infection (UTI, MRSA etc)

- Specific

Impotence

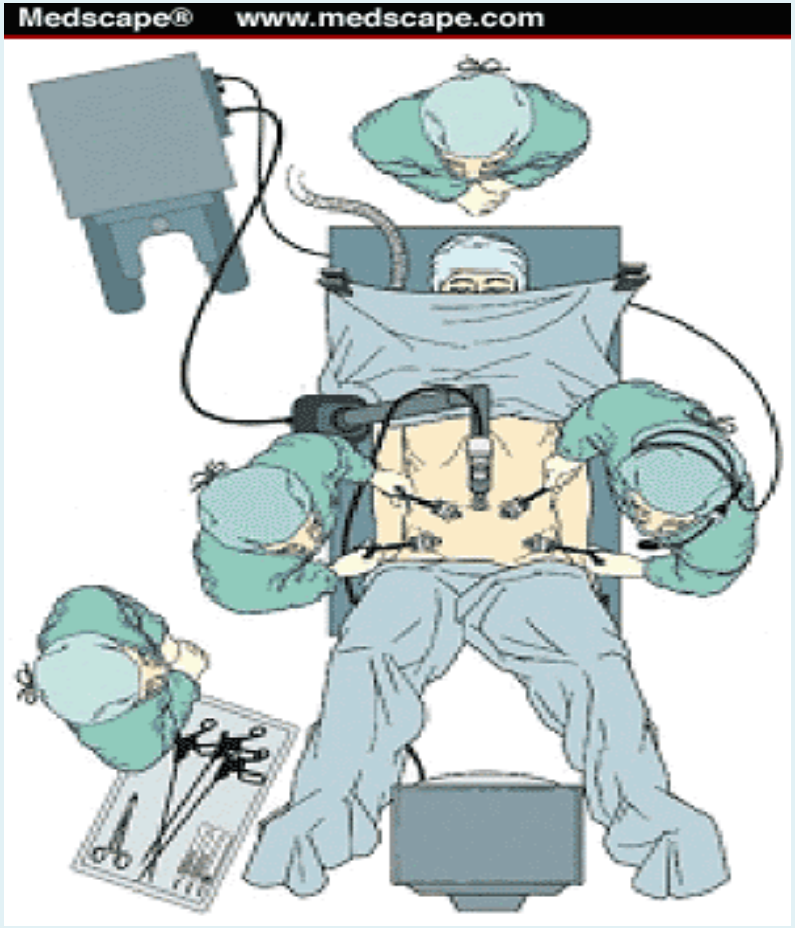
Permanent Dry Orgasm

Bladder Neck stenosis (10%)

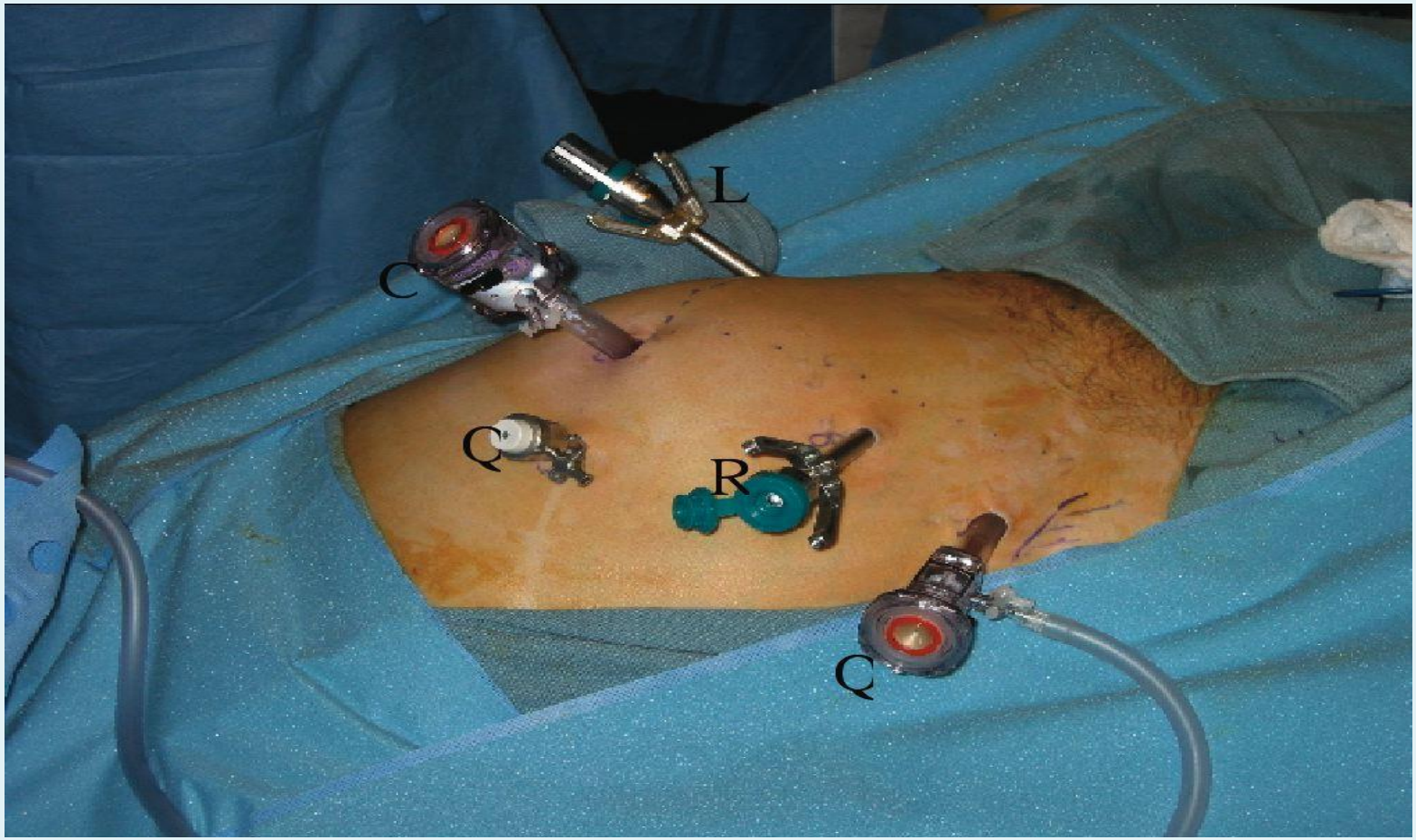
Severe incontinence (2%)

Mortality: thromboembolism, MI

Laparoscopic radical prostatectomy



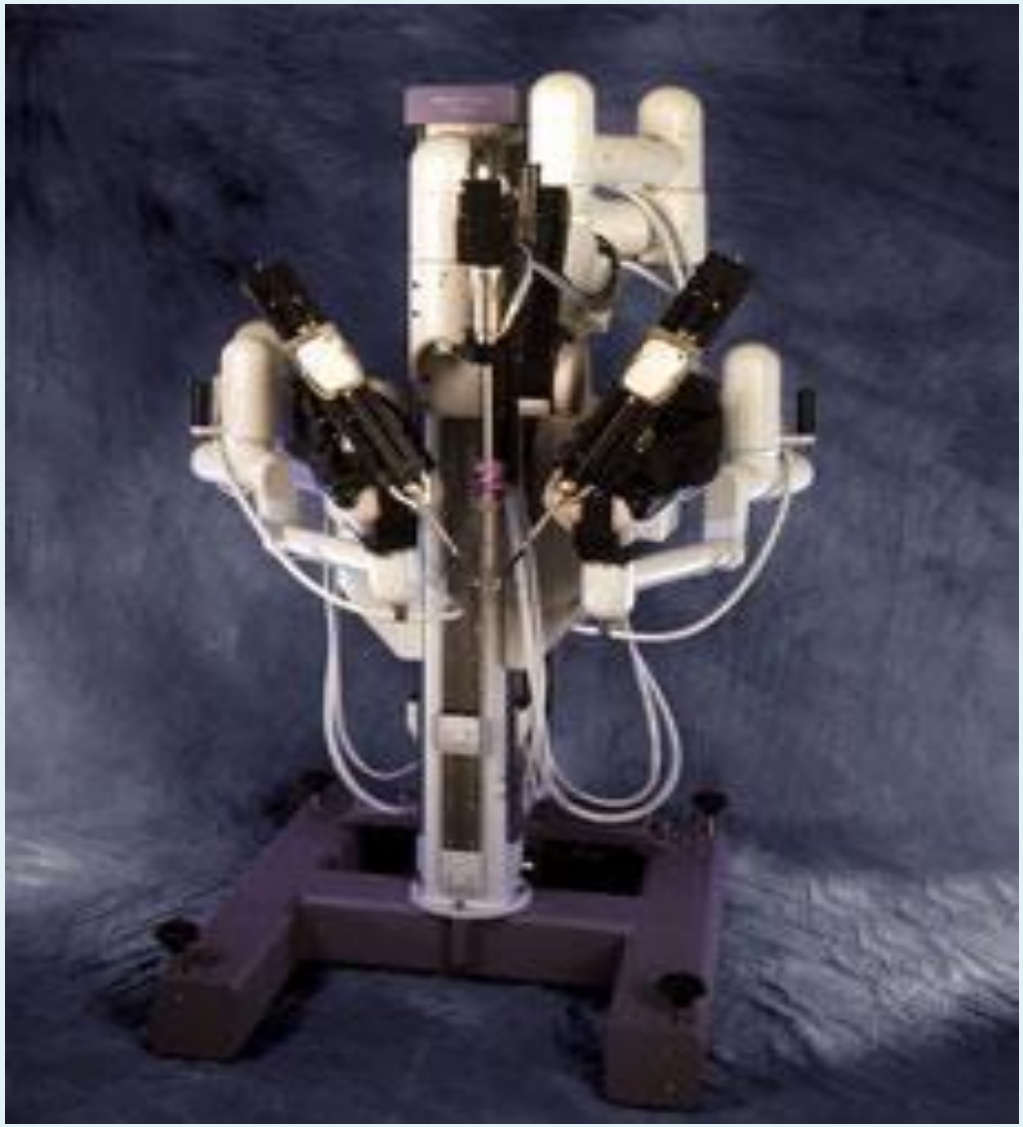
Usually 5 ports - Lap. radical prostatectomy



Laparoscopic radical prostatectomy

Operating surgeon at the console

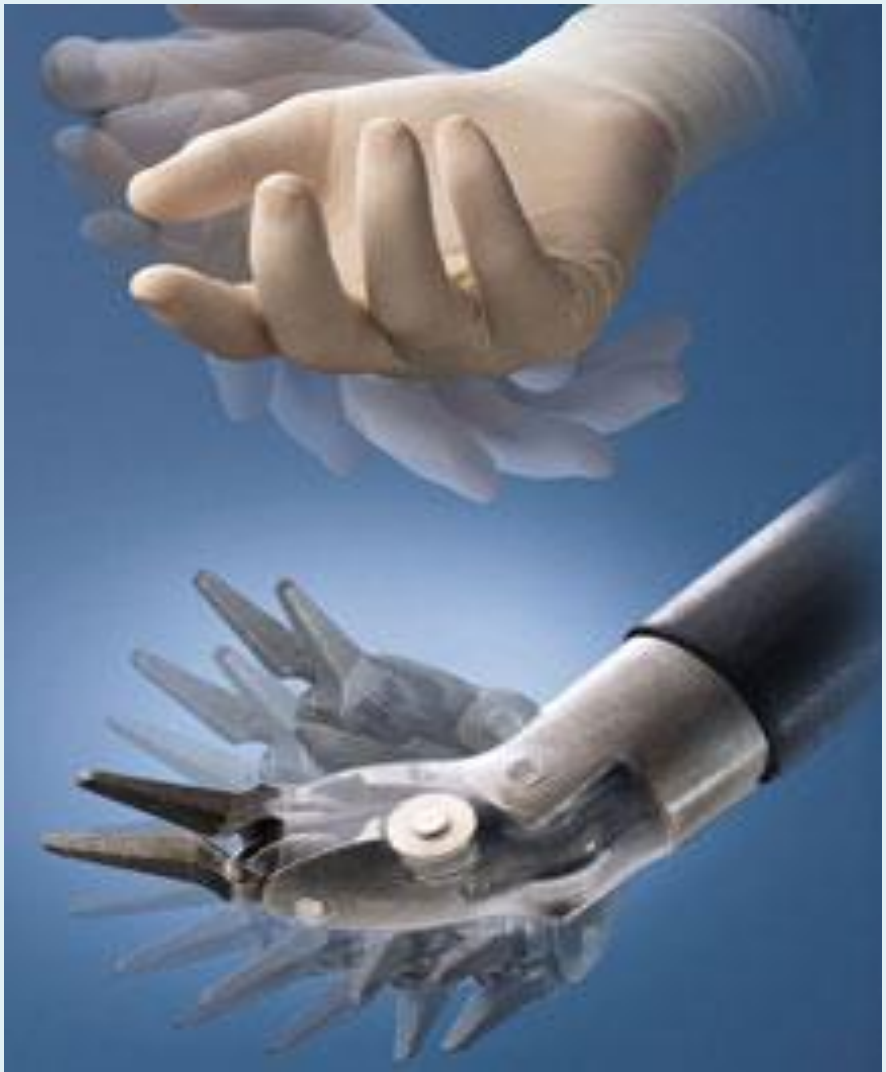
Robot with four arms



Working console for the surgeon

Surgeon’s hand tools

Robotic arms utilize endowrist instruments: more degrees of freedom than human hand



Facts about robotic technology

- In 2007 – there were 5 units in the UK.
- In 2015 – there are 62 units in the UK
- Cost of a robot - £1.2 - £1.4 million
- Maintenance cost = £130,000/year
- Disposable Cost per patient £1500-£1700
- National Tariff for radical prostatectomy=£3900
- Not all CCG's are paying increased tariff for robotic-assisted radical prostatectomies

Facts about robotic technology

- NHS England has committed to support Trusts doing >150 cases per year
- HEFT figures are currently >200 cases/year
- Robots around HEFT

  Wolverhampton 2011

  QEH 2014

  UHCW (Coventry) 2015

  UHNS (Stoke-on-Trent) 2015

Which surgical approach is better?

- Open radical
  - Hospital stay 2 - 3 days
  - Operating time 2.5–3 hours
  - Can do nerve sparing procedure
  - Palpation can clear T3 disease
  - Practically no learning curve
  - Much better lymph node dissection
  - Catheter time 4-7 days
  - LONGER RECOVERY TIME POST OP
  - MOST COST EFFECTIVE

Which surgical approach is better?

- Laparoscopic radical
  - Long learning curve
    - 80-120 Non-lap Surgeons
    - 40-60 Lap surgeons
  - Longer theatre time
  - Better nerve sparing
  - Hospital stay 2 days
  - MUCH QUICKER RECOVERY
  - Catheter time 7-10 days
  - More expensive than open radical

Which surgical approach is better?

- Robotic-assisted
  - MOST EXPENSIVE
  - Much shorter learning curve for open surgeons
  - Shorter for experienced open surgeons then for experienced lap surgeons
  - Hospital stay 1-2 days
  - Catheter time 5-14 days
  - MUCH QUICKER RECOVERY (as for lap rad)
  - PATIENTS PREFER THIS (more BUZZ!)

Surgical outcomes

- Longest survival figures to date
- Minimum morbidity
- Minimal post-operative mortality
- Minimise positive margins
- Good lymphadenectomy
- Maintain potency
- Maintain continence
- Inpatient stay of 2 days

Radical radiotherapy

- Used to give 55 Gray in 20 fractions
- We were giving 74 Gray in 37 Fractions
- For the past 2 months- we are giving 60 Gray in 20 fractions (based on the CHIPP Trial)
- IMRT (Intensity Modulated RadioTherapy)
- IGRT (Image Guided RadioTherapy)
- Stereotactic (Cyber Knife) radiotherapy

Adjuvant hormones

- Everybody having radiotherapy will have 3-6 months of neo-adjuvant hormonal treatment
- High risk patients will have 2–3 years of adjuvant hormones to reduce the chance of relapse.
- Hormonal treatment is NOT without side effects

Brachytherapy

- Strict selection criteria
- Radioactive iodine seeds offer interstitial radiation thereby minimising local side effects
- The number of seeds are calculated based on the prostate size (volume in cc's)
- This is a General Anaesthetic procedure lasting about an hour
- These seeds are permanent

What's new? (FUTURE)

- Chemotherapy for metastatic Prostate Cancer
- Numerous Trials are in place
- CRPC(Castrate Resistant Prostate Cancer)
- ADT(Androgen Deprivation Therapy)
- Abiraterone
- Enzulotamide
- Vaccines
- Radiofrequency

THANK YOU FOR LISTENING !

AND NOW THIS IS THE TIME FOR QUESTIONS FROM THE FLOOR