PROSTATE CANCER

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Maidstone Masterclass November 2013

The diagnostic pathway, e.g. TRUS and biopsy, bone scan, MRI etc.
- Gleason scoring and clinical staging
- Treatment options in early prostate cancer
- Treatment options in advanced prostate cancer
- Complications of surgery and radiotherapy – what to expect

Presentation
- Screening
- Case Finding:
  - Family History
  - Racial Risk Groups
  - Well man check/pt choice
- LUTS
- Bleeding
- Systemic/Metastatic

DRE: “If you don’t put your finger in it, you might put your foot in it!”
- Size ➞ risk stratification aid
- Soft/Firm/Nodular
- Other diagnoses:
  - Most prostate cancer in peripheral zone
  - 50% abnormal DREs associated with CAP
  - Only 40% cancers diagnosed by DRE are T1-2
  - “Normal” PSA + abnormal DRE ➞ 30% chance cancer

Chance of Cancer

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<tr>
<th>PSA</th>
<th>4-10</th>
<th>&gt;10</th>
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<tr>
<td>DRE normal</td>
<td>27%</td>
<td>&gt;50%</td>
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<tr>
<td>DRE abnormal</td>
<td>45%</td>
<td>&gt;75%</td>
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TRUS and biopsy
- 12 cores
- Antibiotics, local anaesthetic
- Bleeding, sepsis 2-5%, retention
- Trans-perineal template/sector biopsy
- 24-32 cores, can be 60-80
- General anaesthetic

Bone scan
- Intermediate and high risk

MRI
- TRUS and biopsy
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- Bleeding, sepsis 2-5%, retention
- Trans-perineal template/sector biopsy
- 24-32 cores, can be 60-80
- General anaesthetic
- Bone scan
- Intermediate and high risk

Trans-perineal template/sector biopsy
- 32 cores, GA

Active Surveillance
- Discordance of parameters
- Previous negative biopsies
- High risk of sepsis
- ? Everyone?
Goals:

1. To optimize treatment selection
   - Active surveillance
   - Focal therapy
   - Radical prostatectomy
   - Radiation or systemic therapy
2. To optimize both cancer control (negative surgical margins) and recovery of sexual function (tailored approach to nerve sparing) in men undergoing open and robotic prostatectomy
3. Prevent unnecessary biopsies?

MRI has become much better

- Multiparametric approaches
  - Diffusion Weighted MRI
  - T1: greater than 1.5T
  - Needle core biopsies
- T2 weighted image
- Irregular capsule

Bone Scan

- Gleason Primary Pattern 2:4
- PSA >20
- Clinical T1 disease
- Bone symptoms
- Clarify with:
  - MRI/CT/plain x-ray or biopsy

Gleason grading and clinical staging

- Dr. Donald Gleason, pathologist from 1960s.
- Grade most common tumour pattern, and a second grade to next most common pattern.
- The two grades are added together to get a Gleason Score (3+3, 4+5)
- ASAP
- HG PIN

- HG PIN
  - Prostatic intraepithelial neoplasia
  - Scanning normal area and dark bled with cytologically abnormal cells
  - Prevalent for intermediate/high grade cancer
  - 25-30% cancer on re-biopsy

- ASAP
  - Atypical small acinar proliferation
  - Suspicious for cancer
  - Acini small with cytologically abnormal cells
  - Basement membrane intact
  - 40-46% cancer on re-biopsy

Table 2. CBT Risk Group Classification.

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<tr>
<th>Risk Group</th>
<th>T Stage</th>
<th>PSA</th>
<th>Gleason Grade</th>
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<td>T1a</td>
<td>≤ 10</td>
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<td>T1b</td>
<td>&gt;10 ≤ 20</td>
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<td>T3</td>
<td>&gt;20</td>
<td>8-10</td>
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Evaluation of the primary tumour

- T1: tumour present, but not detectable clinically or with imaging
  - PSA ≤4, PSA >4
  - PSA >4, PSA ≤10
  - PSA >10
- T2, the tumour can be palpated, but has not spread outside the prostate
  - PSA <4, PSA ≤10
  - PSA >10
  - PSA >10
- T3, the tumour has spread through the prostatic capsule
  - PSA >10
- T4, the tumour has invaded other nearby structures
  - PSA >10

Path: T3a Gleason 4+3

- 53 year old male
- PSA 9.5
- 3 biopsies
- Gleason Score 4+3 in 75% of Sample on the right

Deferred therapy recommended pending MRI and repeat biopsy.

MRI: large anterior TZ cancer.

Treatment: RP.

Pathology

Gleason 4
Gleason 3

Gleason Primary Pattern ≥ 4
PSA >20
Clinical T3 disease
Bone symptoms
Clarify with
MRI/CT/plain x-ray or biopsy

Dr. Donald Gleason, pathologist from 1960s.

Grade most common tumour pattern, and a second grade to next most common pattern.
The two grades are added together to get a Gleason Score (3+3, 4+5)

Tertiary patterns added
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Why is a staging MRI useful?

MRI staging of low risk prostate cancer

- 55 year old man with PSA 7.4 ng/ml.
- T2c (Gleason 4+3) in 5% of 1/6 cores.
- Dr. Donald Gleason recommended avoiding MRI and biopsy.
- MRI large anterior TZ cancer.

Bone scan

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Pre-malignant or perimalignant

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Risk of death from prostate cancer or other causes after RP

By Gleason grade in the RP specimen for men age 60-69

From Eggener S et al. Cancer-specific mortality after RP: a collaborative study (n=23,910)

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D’Amico Risk Stratification

- Low Risk
  - PSA <10, clinical stage T1c, Gleason ≤6
- Intermediate Risk
  - PSA 10-20, clinical stage T2a-c, Gleason ≥7 (3+4, 4+3)
- High Risk
  - PSA >20, clinical stage T3, Gleason ≥ 8 (4+4, 4+5, 3+5)

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Active Surveillance: NICE Guidance

- Avoids (or postpones) side effects of therapy
- Retains quality of life
- Maintains normal activities and work schedule
- Minimizes overtreatment of indolent cancers

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Active Surveillance Protocol

- Suitable low risk, low volume, T1c, ≤2/12 cores
- Gleason 3+3 ≤50%
- Close involvement.
- PSA & DRE monthly
- Re biopsy 12/18/24 + TPBx
- 2nd Re-biopsy 3-5 years
- Stop AS if upgraded, Lp-staged, vu-volume, pt choice/anxiety
Brachytherapy
- Low/Intermediate risk
- IPSS <15
- FR/RV
- Small gland <60mls
- No prev pelvic DXT

Dynamic Inverse plan low dose brachytherapy:
- Single session
- No catheter
- Day case
- Safe with minimal side effect profile
- Bad for basal disease, high risk?, significant LUTS, very large prostates, caution in younger patients.
- Difficult to do after TURP

Dynamic Inverse plan low dose brachytherapy: Outcomes

Radical Prostatectomy Issues
- Cancer control: Margins and PSA
- Continence
- Potency
- Complications
- Return to normal activity/ general wellbeing: quality of life

Probability of Cancer Control (PSA) & Cancer Specific Survival:
- PSA Progression Free Probability
- Cancer Specific Survival

Survival after surgery for prostate cancer
- 12,677 men treated at 4 institutions (MSKCC, Baylor, Cleveland Clinic and U. Michigan, with RP in the PSA era (1987-2005)
- Neither PSA velocity nor BMI added to the accuracy of the prediction model.
- Only 17% had a predicted 15-year PCSM rate >5% and 4% had a probability >30%.
**Open radical prostatectomy**

- Gold standard
- 1-2 months post op
- Mortality <1%
- Blood transfusion 20-30%
- Complications 9-30%
- Hospital stay 6-4 days
- Incontinence <10%
- Erectile dysfunction 14-44%

**The solution?**

A robot cut out my prostate— and I was back to work in days

**Dual Console Da Vinci SI**

**The evidence for...**

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<td>Author</td>
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<td>Mean PSA (ng/mL)</td>
<td>Mean operative time (m)</td>
<td>Mean blood transfusion (%)</td>
<td>Mean hospital stay (d)</td>
<td>Overall positive surgical margins (pT2 margins) (%)</td>
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Vickers and Scardino, 2008

- Case volume is Key
- The robot is here to stay
- MIS:
  - Less blood loss/transfusion
  - Less pain
  - Earlier Discharge
  - Faster return to work
  - Better oncological and functional results
- Choose your surgeon wisely

- Treatment options in advanced prostate cancer
**Locally advanced prostate cancer**
- External Beam Radiotherapy
  - Neoadjuvant and concurrent LHRHa therapy for 3–6 months
  - Adjuvant LHRHa therapy for a minimum of 2 years if Gleason > 8
  - Pelvic radiotherapy for men with > 15% risk of pelvic lymph node involvement
- Radical Prostatectomy if very young.
  - As part of multimodal therapy

**Metastatic prostate cancer**
- LHRHa therapy
- Options
  - Bilateral orchidectomy as an alternative
  - Monotherapy with bicalutamide (150 mg) if the man hopes to retain sexual function and is willing to accept gynaecomastia and reduced survival
  - LHRHa antagonist
  - Intermittent androgen withdrawal
  - Maximum androgen blockade if fails

**Castrate resistant prostate cancer**
- Docetaxel chemotherapy
  - If Karnofsky score is ≥ 60%. PS 0/1
  - If planned cycles
  - A corticosteroid as a third-line therapy after androgen withdrawal and MAB
- Bisphosphonates to prevent or reduce the complications of bone metastases
- New agents: abiraterone and enzalutamide
- Immunotherapy: sipuleucel-T, Provenge
  - Vaccine is made by isolating dendritic cells
  - Reinjected into the patient three times, at intervals of two weeks.

**Complications of surgery**
- Immediate:
  - Bleeding
  - Infection
  - Rectal/Bowel injury
  - Anastomotic stricture
- Recurrence
  - Salvage DXT, Radicals, WW
- Incontinence
  - PFE, Advance sling, AUS
  - Erectile dysfunction
    - PDE5, vacuum pump, MUSE, Caverject

**Complications of radiotherapy**
- Urinary Symptoms
  - Dysuria, bladder irritation, frequency, urgency
  - Bowel symptoms
  - Rectal irritation or discomfort
  - Diarrhoea and bleeding
  - Erectile dysfunction: gradually over 6–12/12
  - Second tumours
    - Slightly higher risk of developing rectal or bladder cancer
  - Difficult salvage options

**Side effects of ADT**
- Decreased libido and erectile dysfunction
- Hot flashes
- Gynaecomastia
- Loss of muscle and an increase in body fat
- Osteoporosis
- An increased risk of developing type 2 diabetes
- An increased risk of developing or worsening coronary heart disease

**Screening ERSPC Update**
- NNT 1:48 at 9 yrs, likely to rise
- 20% reduction in 5% death rate actually screened
- Adjuvant 10% reduction in death screened
- Metastasis at 5%: 35% reduction, NNT 69, NNT 27
- Larger effect with larger (≥ 10%)
- Goteborg: 21% at 14 yr, NNS 293, NNT 12, 56% RR
- Effect of statins

**Friday**
- UK Perspective: fence sitting
- HGPIN/ASAP
  - HGPIN 27% CaP on subsequent biopsies
  - ASAP 46% CaP on 2nd biopsy