Best Practice for Localised Disease

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Prostate Cancer Masterclass
Prostate Cancer UK March 2013

Treatment for Localised Prostate Cancer in 2012

- Active Surveillance
- Radical Prostatectomy
- Brachytherapy
- External Beam Radiotherapy + hormones
- Brachytherapy + EBRT (no hormones)
- Alternatives:
  - HIFU?
  - Cryotherapy
  - Focal Therapy

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

### 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)

### Table 1: Risk stratification criteria for men with localised prostate cancer, men with clinical stage T2-M0 cancer have truly localised disease

<table>
<thead>
<tr>
<th>Risk</th>
<th>PSA (ng/ml)</th>
<th>Gleason score</th>
<th>Clinical stage</th>
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<td>Low risk</td>
<td>&lt; 10</td>
<td>≤ 6</td>
<td>T1-T2a</td>
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<td>10-20</td>
<td>7</td>
<td>T2b-T2c</td>
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<td>High risk</td>
<td>&gt; 20</td>
<td>8-10</td>
<td>T3-T4</td>
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### NICE 2008 Guidance

<table>
<thead>
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<th>Localised prostate cancer</th>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
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<td>✓</td>
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<td>Radical prostatectomy</td>
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<tr>
<td>Brachytherapy</td>
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<td></td>
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<td>Conformal radiotherapy</td>
<td>✓</td>
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<td>Cryotherapy</td>
<td>✓</td>
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<tr>
<td>High-intensity focused ultrasound</td>
<td>✓</td>
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</table>

* Offer if there is a realistic prospect of long-term disease control.

* Conformal radiotherapy should be given at a minimum dose of 74 Gy (set at a maximum of 2 Gy per fraction).

* Unless as part of a clinical trial comparing use with established interventions.
Active Surveillance:

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

**Disadvantages**
- Risks under treatment – Cancer may progress and become incurable before it is treated
- Later treatment may entail greater morbidity
- Increases anxiety of living with untreated cancer
- Requires frequent assessment, repeat biopsies with uncertain side effects
- Uncertain long-term (> 10 yrs) natural history of cancer

Active Surveillance Protocol
- Suitable low risk, low volume, T1c ≤2/12 cores
- Gleason 3+3, <50% core involvement, <75yrs?
- PSA & DRE 6 monthly
- Re biopsy 12-18/12
- 2nd Re-biopsy 3-5 years
- Stop AS if upgraded, Up-staged, up-volume, pt choice/anxiety

Guy’s Tran-perineal Sector Biopsy Format
- Cores placed on specimen template in order with medial end at basal end, placed in cassette and placed in labelled formalin pots

Guy’s AS Protocol
- Entry Biopsy usually TRUS
- Low Risk Disease identified
- All pts have multi parametric MRI
- Early Trans-perineal biopsy
- Repeat MRI and TP Bx 12-18 months

Trans-Perineal Biopsies
**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

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**Radical Prostatectomy Issues**

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

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**Randomized trial of RP v. WW**

- Single session can reduced the risk of metastases (HR 0.65) and death from prostate cancer (HR 0.65) significantly.

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**Dynamic Brachytherapy**

**Dynamic Inverse plan low dose brachytherapy: Guy’s**
Cancers with extraprostatic extension may be pathologically confined but are often "contained" within the surgical specimen, and are "clinically organ confined" and are often curable.

Probability of Cancer Control (PSA) & Cancer Specific Survival by pathologic stage
PSA Progression-Free Probability
Cancer Specific Survival

Survival after surgery for prostate cancer

Probability of dying after RP

Gold standard
Is it MORBID??
- Mortality <1%
- Blood transfusion 20-30%
- Complications 5-15%
- Hospital stay 6-8 days
- Incontinence <10%
- Erectile dysfunction 14-44%

Open radical prostatectomy

The solution?

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

da Vinci Surgical System U.S. Installed Base 1999 - 2010
**Downsides of RARP**

- Cost
- Availability
- Learning Curve
- Training
- Case Volume
- Team

**UK Da Vinci Robots**

- Addenbrooke's Hospital - Cambridge (2)
- Broomfield Hospital - Essex
- Christie's Hospital - Manchester
- East Kent Hospital - Canterbury
- Ealing Park NHS Foundation Trust - London
- Guy's Hospital London - London
- Lister Hospital - Hertfordshire
- Oxford Radcliffe Trust - Oxford
- Royal Marsden Hospital - London
- Royal Berkshire - Reading
- Royal Surrey County NHS Trust - Guildford
- Royal Hospital Liverpool

- St. George's Healthcare NHS Trust - London
- St. James's University Hospital - Leeds
- St. Mary's Hospital - School of Medicine - London
- South Devon Healthcare NHS Foundation Trust - Devon
- The London Clinic - London (2)
- The Princess Grace Hospital - London
- The Wellington Hospital
- Wexham Park Hospital - Berkshire
- Exeter
- Newcastle
### The evidence for...

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<th>Erectile dysfunction (%)</th>
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<th>Overall positive surgical margin (%)</th>
<th>Positive surgical margin (mm)</th>
<th>Mean follow-up (mo)</th>
<th>Mean (95% CI)</th>
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60 vs 60 pts Italy

- No difference in pathology: margins
- The continence rate was higher in the RARP group at every time point
  - 3 month: 80% RARP, 61.6% LRP (p=0.044)
  - 1 yr: 95.0% and 83.3%, respectively (p=0.042).
- Among preoperative potent patients treated with nerve-sparing techniques, the rate of erection recovery was 80.0% RARP and 54.2% LRP (p=0.020).

Has MIS merely raised the bar for surgery?

- Refining the anatomy
- Higher volume surgeons and centres
- Better reporting of data
- Removing less able surgeons from the field.

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

Randomised Controlled Trial Comparing Laparoscopic and Robot assisted Radical Prostatectomy, 2013

- Vickers and Scardino, 2008

Approach specific or surgeon specific?

MIS:
- Less blood loss/transfusion
- Less pain
- Earlier Discharge
- Faster return to work
- ? Better oncological and functional results
- Choose your surgeon wisely
External beam radiotherapy

- Outpatient procedure
- 20-30 minutes of treatment
- 5 days a week for 6-7 weeks, 74 Gy
- Neo-adjuvant hormones 3/12
- Intensity-modulated radiotherapy (IMRT), high doses of radiation precisely shaped to the individual patient's prostate
- Proton Beam

Complications of surgery and radiotherapy - what to expect

Locally advanced prostate cancer

- External Beam Radiotherapy
  - neoadjuvant and concurrent LHRHα therapy for 3-6 months
  - adjuvant LHRH 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 young, fit
  - As part of multimodal therapy

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
Treatment options

- Diverse
- Variable
- Challenging
- Exciting