Minimising the consequences of urological cancer treatment

Dr Justin Vale, Chair - LCA UrologyPathway Group
Prostate Cancer – Clinical Outcomes

“The Big 3”

1. Cancer Control – Margins
2. Urinary Control – Continence
3. Sexual Function – Potency
Computer Technology - Used everywhere
RAP

- 3 dimensional vision
- 10 x magnification
- 7 degrees of freedom
- Motion scaling
- Tremor elimination
- Ergonomic working position for the operating surgeon
SUTURE A HAIR TO A TICK'S ASS

OK, you wouldn't, but you could.
With the amazing power and precision of da Vinci robotics.

da Vinci
Surgical System
Surgical Approaches

“Evidence”

Minimally invasive versus open RP
• Shorter hospital stay, shorter recovery period and reduced risk of intraoperative blood Tx with minimally invasive techniques

Robotic versus laparoscopic RP*
• Reduced risk of major intraoperative harm, lower risk of positive margins (17.6% vs 23.6%) which may translate into reduced risk of recurrence
• There was no difference in continence rates at 12 months
• There was insufficient evidence on erectile function to draw conclusions

*[Robertson et al, BJU Int, 2013, 112, p798-812]
Prostate Cancer – Clinical Outcomes

“The Big 3”

1. Cancer Control – Margins
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3. Sexual Function – Potency
## Positive Margins (T2)

<table>
<thead>
<tr>
<th>Radical Prostatectomy Series</th>
<th>% Positive margins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guillonneau&lt;sup&gt;1&lt;/sup&gt; (Lap.)</td>
<td>7.7%</td>
</tr>
<tr>
<td>Scardino&lt;sup&gt;2&lt;/sup&gt; (Open)</td>
<td>5.9%</td>
</tr>
<tr>
<td>Tewari&lt;sup&gt;3&lt;/sup&gt; (Robotic)</td>
<td>4.3%</td>
</tr>
<tr>
<td>Lee&lt;sup&gt;4&lt;/sup&gt; (Robotic)</td>
<td>6.0%</td>
</tr>
<tr>
<td>Locke&lt;sup&gt;5&lt;/sup&gt; (Robotic)</td>
<td>6.2%</td>
</tr>
<tr>
<td>Menon&lt;sup&gt;6&lt;/sup&gt; (Robotic)</td>
<td>6%</td>
</tr>
<tr>
<td>Ahlering&lt;sup&gt;7&lt;/sup&gt; (Robotic)</td>
<td>4.5%</td>
</tr>
<tr>
<td>Patel&lt;sup&gt;8&lt;/sup&gt; (Robotic)</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

## Urinary Continence Outcomes

<table>
<thead>
<tr>
<th>Surgeon</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walsh¹ (Open)</td>
<td>54 %</td>
<td>80%</td>
<td>93%</td>
</tr>
<tr>
<td>Guillonneau (Lap.)</td>
<td>N/A</td>
<td>N/A</td>
<td>89.2 %²</td>
</tr>
<tr>
<td>Rassweiler³ (Lap.)</td>
<td>N/A</td>
<td>74%</td>
<td>97%</td>
</tr>
<tr>
<td>Menon⁴ (Robotic)</td>
<td>N/A</td>
<td>96%</td>
<td>N/A</td>
</tr>
<tr>
<td>Locke⁵ (Robotic)</td>
<td>92.9%</td>
<td>94.9%</td>
<td>97.4%</td>
</tr>
<tr>
<td>Ahlering⁶ (Robotic)</td>
<td>75%</td>
<td>N/A%</td>
<td>95%</td>
</tr>
<tr>
<td>Patel⁷ (Robotic)</td>
<td>82%</td>
<td>89%</td>
<td>98%</td>
</tr>
</tbody>
</table>

# Sexual Potency Outcomes

<table>
<thead>
<tr>
<th>Best Potency Outcomes</th>
<th>Walsh (2004)(^1) N=25</th>
<th>UCI (2005)(^2) N=27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op IIEF-5 &gt;21</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>Average Age</td>
<td>50.1</td>
<td>55.7</td>
</tr>
<tr>
<td>Follow-up</td>
<td>12 mos.</td>
<td>9 mos.</td>
</tr>
<tr>
<td>Coitus</td>
<td>71 %</td>
<td>74 %</td>
</tr>
<tr>
<td>BNS</td>
<td>100%</td>
<td>(78%) (^{\text{a}})</td>
</tr>
<tr>
<td>UNS</td>
<td>NA</td>
<td>(67%) (^{\text{a}})</td>
</tr>
<tr>
<td>Post RP Average IIEF-5 Potent men score</td>
<td>15.7</td>
<td>19.3</td>
</tr>
</tbody>
</table>


\(^{\text{a}}\) Approximation based on available data.
Randomised controlled trial (RCT) of Laparoscopic, OPEN and Robot-Assisted prostatectomy as treatment for organ-confined prostate cancer. LopeRA feasibility study (CI – Ara Darzi)

Prostate cancer patient who had chosen radical prostatectomy as treatment, after discussion at MDT

Eligible patients required all of the following:
- Clinical stage T1, T2a, T2b or T2c
- Gleason score ≤7,
- PSA ≤20
- Written Informed Consent

Exclusion Criteria:
- Patient unfit for surgery
- Prior Pelvic radiotherapy or rectal excisional surgery
- Evidence of metastasis
- Neoadjuvant hormone therapy

Randomised (n=30)

Laparoscopic Radical Prostatectomy N=11
Open Radical Prostatectomy N=11
Robot-assisted Radical Prostatectomy N=8

All patients followed up in the LopeRA trial at the following intervals:
- PSA Blood test: Six weeks, six months and at one year (and 18 months if recruited within first six months)
- Quality of life questionnaires: two weeks, six weeks & three, six, nine and 12 months.
Randomised controlled trial (RCT) of Laparoscopic, OPEN and Robot-Assisted prostatectomy as treatment for organ-confined prostate cancer. LopeRA feasibility study (CI – Ara Darzi)

- Over 16 month period, 30 patients were randomised into LopeRA

- Recruitment rates were below target (average: 2 patients per month), with only 2 centres demonstrating any consistent ability to recruit patients

- This represented 25% of eligible patients who were approached

- 64 (73%) patients declining randomisation expressed a preference for laparoscopic and/or robotic prostatectomy

- Centre feedback indicated that preferences were influenced by patient research on the internet and unwillingness to travel to different centre.
Randomised controlled trial (RCT) of Laparoscopic, OPEN and Robot-Assisted prostatectomy as treatment for organ-confined prostate cancer.

LopeRA feasibility study (CI – Ara Darzi)

- Targeting via letter and trial summary to clinicians at peripheral sites who refer to participating centres to emphasise clinical equipoise had little impact.

- Based largely on evidence acquired through qualitative study process (run in parallel), TSC supported closure to recruitment 2013

- The need for a phase III randomised controlled trial to inform future delivery of radical prostatectomy services remains, but patient choice and perceived benefits of minimally invasive prostatectomy limited recruitment to this feasibility study.

- Further work integrating qualitative research methods to understand consent consultations and patients’ preferences in surgical trials such as this is needed.
High Resolution Display – Multiple Inputs
Dr Eddie Edwards, Imperial College London
Cyberknife
High Intensity Focused Ultrasound

Cryotherapy
Challenges for focal therapy 1

“Prostate cancer is typically a multifocal disease”

- Of 1274 patients undergoing RP, 176 (14%) fulfilled criteria for unifocal tumours of whom 28% had ECE, 11% SVI, 6% were N+ve and 60% had Gleason 4 or 5 in the specimen [Masterson et al, BJU Int, 2011, 107, p1587-91]
- Of 1458 men undergoing RP, 590 of 880 evaluable men had unilateral disease on their pre-operative Bx. On final histology, 163 (27.6%) had unilateral disease overall. On further stratification, of men with low risk disease (GI3+3, clinical T1c, PSA<10) on biopsy, only 28.4% had unilateral disease [Tareen et al, BJU Int 2009, 104, p195-9]
- Of 321 with low risk prostate cancer on biopsy, only 29.3% had unilateral disease on final RP histology [Gallina et al, BJU Int, 2012, 110, E64-8]
“The concept of the primary tumour focus (index tumour) and significant cancer”

• In 100 consecutive RP specimens, there were 374 tumour foci with a median number per patient of 3.5. The median volume of the largest tumour was 0.95ml and the median volume of the largest secondary tumour 0.2ml. In no patient was the index lesion insignificant and secondary tumours significant [Bott et al, BJU Int, 2010, 106, 1607-11]
Challenges for focal therapy 2

So, if we accept the theory of the index tumour, can we target it?


- Extended core (saturation) Bx also unreliable: of 203 men undergoing 24 core biopsy, 115 had unilateral +ve biopsies of whom 26 (22.6%) had unilateral disease in their RP specimen [Abdollah et al, BJU Int, 2011, 108, p366-71]
The solution 2

Seq: SE
Slice: 3 mm
Pos: 39.6
TR: 5773.99
TE: 120
AC: 4

Seq: RM
Slice: 6 mm

Prostate mapping
Template Mapping Biopsies

Needle to take samples from the prostate

FFS
FoV: 180 mm
Image no: 13
Image 13 of 24
29/10/2013, 17:18:42

29/10/2013, 17:23:46
The status of focal therapy in 2014

• Currently unproven, but may have a place in low/intermediate risk prostate cancer
• Therefore should men who are candidates for active surveillance be offered focal therapy?
• Or are we creating a niche for an unnecessary treatment?

Recent meta-analysis from Valerio et al

Eur Urol, 2013, Epub 2013/06/19
A Multi-centre Prospective Single Arm Intervention Trial
Evaluating Focal Therapy using High Intensity Focused Ultrasound (Sonablate 500) for Localised Prostate Cancer

Topic
Cancer

Portfolio Eligibility
Adopted non-commercial study

Research Summary
To evaluate medium term cancer control, genitourinary, rectal and overall health-related quality of life outcomes, and to model potential cost effectiveness of focal therapy for localised prostate cancer using HIFU.
Summary

- There are lots of new and exciting things happening for patients with organ confined prostate cancer.
- The fundamental issue remains that for high risk disease, which typically occurs peripherally, radical therapy inevitably carries risk in terms of recovery/quality of life.
- Focal therapy may have a role in selected cases, especially if advances in diagnostics mean we pick up prostate cancer earlier and can more reliably target it.