Improving Outcomes from Surgery for Prostate Cancer

Prof A J Costello
Vancouver, April 2007

- Improved Understanding of Anatomy
- Technology Change: Laparoscopic / Robotic
- Surgery for High Risk Advanced Disease
Is Sir Astley Cooper’s 1823 Advice to Medical Students Still Relevant?
Importance of the study of anatomy

Factors leading to “adverse events”

The possible legal consequences of making errors

Anatomical Relations of the Neurovascular Bundle & Application to Radical Prostatectomy

Prof A J Costello
Now that most men achieve continence following RRP, the challenge for the urologist is preservation of potency by a meticulous nerve sparing approach.

“From everything you're describing, son, it sounds to me like you've just had your first boner.”
However even when nerve sparing surgery is meticulous in most hands some men still suffer erectile dysfunction – in spite of an anatomical approach – Why?

The major long term morbidity from RRP is erectile dysfunction
Range: 3% - 75%

What is the aetiology of erectile dysfunction post radical prostatectomy?
“If you ask me, Larry has the completely wrong attitude about prostate surgery.”

- Menon/Tewari suggest anterior prostatic fascial nerves are “important” and with “Veil Technique” – report 97% potency. Hypothesis only.

- Are there other autonomic pathways?
Potential Mechanisms of Nerve Injury

- Traction
- Thermal Injury Bipolar / Unipolar
- Division
- Excision
- Vasculogenic
- Other neural pathways – “anatomical redundancy”

Sound Anatomic/Pathologic Basis for Cancer Control

- The neurovascular bundle (NVB) is outside the fascia and capsule of the prostate. In men with organ confined cancer (80% of cases today) it is safe to preserve both NVB’s

- In the past, when all men were impotent postop, the NVB’s were not excised – they were unknowingly cut and left in place! Today, it is possible where necessary to obtain wide surgical margins by widely excising it

Walsh – AUA 2006
Pelvic Plexus

- Detailed microdissection (x 6 magnification) bilaterally in 12 fixed adult male cadavers
- To ascertain anatomy of the NVB and its relation to surrounding fascia and other structures
- Relationship of (L) + (R) NVBs to seminal vesicles + prostate
- Note large width of NVB, particularly neural constituents proximally, + large number neural structures descending with NVB

- Anterior wall of rectum deflected anteriorly
- Large rectal veins exit the NVB proximal to level of prostatic apex, coursing posteriorly to drain rectum
(L) Neurovascular Bundle

(R) Neurovascular Bundle
- Anterior wall of rectum deflected caudally
- Slit-like openings in lateral pelvic fascia through which nerves to LA musculature leave NVB

- Position of NVB and relationship to prostate, rectum and fascial layers revealed
- Widening Denonvilliers fascia fuses with lateral pelvic fascia and pararectal fascia
- Posterior and lateral divisions of NVB run within these fibrous leaves
The cavernous nerves from mid-prostate to apex are located in the anterior section of NVB, posterior to vessels and nerves of prostate and medial to vessels and nerves of the rectum and levator ani.
Anatomy of Cavernous Nerves Distal to Prostate

- Multiple communications between the Cavernous (CN) and Dorsal (DN) Nerves were noted
- Do CN use the Dorsal Nerve as a conduit or is the DN partly autonomic

Lue, Urology 1993

"Autonomic Redundancy"

The relationship between pelvic plexus and pudendal nerve with fibres seen communicating at level of A (noting the gap labelled B is where the pubic ramus would lie)
Techniques of Nerve Preservation

- Johns Hopkins Technique
- MSKCC Technique
- Heilbronn Technique – Retrograde
- Henry Ford Technique – “Veil”
- Cornell Technique
- UCI Technique
- Bordeaux Technique

WCE Cleveland August 2006

Cavernous Nerve Grafting

5 year “consistent” penetration rate post cavernous nerve interposition graft 11% (N:44)

Secin, Scardino: J.Urol 177 2007
Nerve Sparing & Prostatic Fascia

- NVB is outside prostatic fascia/capsule
- NVB is inside separate fascial compartment – Levator Ani / Denonvillers Fascia
- The prostatic fascia/capsule should be excised
- ECE – usually 1-2 mm – and is removed with the specimen
- Veil technique could lead to more +ve margins anteriorly
Wide excision of NVB on right side (extrafascial dissection) versus nerve-sparing excision on left side (interfascial dissection)
High Anterior Release of the Levator Fascia at the Apex

Recently it has been shown that branches of the nerves that innervate the striated sphincter and corpora cavernosa travel more anteriorly at the apex than previously appreciated (1,2,3).


High Anterior Release of the Levator Fascia at the Apex

To preserve these nerves and to avoid excessive traction on the neurovascular bundles during the apical dissection, the levator fascia should be more anteriorly in cases where it is felt it would not lead to a positive apical margin (1).

Takenaka A, et al. BJU Int. 95:766, 2005
High Anterior Release of the Levator Fascia at the Apex
Johns Hopkins

- Less Traction

Neurovascular Bundle Anatomy
The Veil of Aphrodite
Detroit Technique

- 35 patients SHIM > 21 pre-op
- Veil of Aphrodite Technique
- 12 mo 97% potency 86% normal erection

Menon – Urology 106, 2005
Neurovascular Bundle Anatomy
The Veil of Aphrodite

➢ The cavernous nerves seen posterolateral to the prostate in a separate fascial sheath not anterolateral.

➢ There are no nerves to cavernous tissue in the anterolateral region of the Veil of Aphrodite.

➢ Maybe early anterior fascial release as described by Menon protects the cavernous nerves.

Cornell Technique
What We Do in Melbourne – Modified UCI Technique

Dissection of Right Pedicle & Hemaloc to NVB
Conclusion

- We need further neuroanatomical clarification of the course and distribution of the cavernosal nerves
- Detroit theory is hypothesis driven not anatomically driven
- There may be autonomic redundancy via communication between pudendal nerve and NVB

Technology Change
Laparo-Robotic Radical Prostatectomy

Improved:
- Visualization
- Dexterity
- Operative Field
  (Pneumo peritoneum reduces bleeding)
- Minimally invasive
History of Laparo-Robotic Prostatectomy

- 1992: Scheussler’s first report – too difficult
- 1997: Gaston, Guillonneau, Montsouris technique
- 2001: Menon – robotic-laparoscopic prostatectomy
ROBOTIC PROSTATECTOMY
Evidence for Change

- “Meta-analysis” 2007, Ficarra, *Eur Urol*
- 35 manuscripts clinical, pathologic follow-up data

Systematic Review Outcome
RALP

- Short learning curve
- Earlier return to continence
- Early data only – potency
- Surgical margin +ve rate: 5 – 7% T2
Epworth Hospital, Melbourne
Robotic Experience
2003 - 2007

RARP DATABASE
Pre Op Data

- Age
- BMI
- PSA
- Sexual function: status, aids used, SHIM
- Continence: pad use
- Biopsy Gleason Grade
- T Stage
- Pre op hormone therapy
RARP DATABASE

- Prospective
- Commenced by NP
- Secretarial support required after 6 months (questionnaires posted out, returns checked)
- Data manager assistance with Tissue Bank database
- Huge task: >500 patients
- Nursing study: clinical outcomes compared with open RRP: funding applications submitted
- Data management remains problematic

RARP DATABASE
Operative Data

- OR time
- Robot time per stage
- Tissue banking status
- Nerve-sparing status
- Change in technique: Haem-o-lok Vascular Clamp use (February 2006)
RARP DATABASE
Pathological Data

- Prostate volume / weight
- Prostate Gleason Grade
- P stage
- Surgical margin status: site of +ve margin
- Seminal vesicle status
- Capsule status

RARP DATABASE
Inpatient Data

- Length of stay
- Catheter time
- Drain tube time
- Immediate complications
- Blood transfusion requirements
RARP DATABASE
Post Operative Data

- PSA follow-up (at 3 months then annually)
- Any adjuvant Rx: hormone therapy / DXRT
- Long-term complications
- At 12 months: Satisfaction with Rx choice

RARP DATABASE
Continence & Sexual Function Data

Self-administered, postal questionnaires

- Preoperative
- 3 months post-operative
- 6 months post-operative
- 12 months post-operative
- Then annually
RARP DATABASE
Continence Data

- Frequency of urinary leakage when straining
  (never, almost never, sometimes, always)
- Need for pad use
  (never, almost never, sometimes, always)
- # of pads worn
- How long pads worn after catheter removal

RARP DATABASE
Pre Operative Sexual Function Data

- ? sexually active
- ? any difficulty with erections
- ? any erectile aids used
- Sexual Health Inventory for Males Score
  (SHIM / IIEF-6)
RARP DATABASE
Post Operative Sexual Function Data

- ? Spontaneous erections
  (no, partial, sometimes, yes)
- ? any erectile aids tried
  (yes/no: which one/s?)
- If yes, still using any? which one/s?
- Unassisted SHIM Score
- SHIM Score if using erectile aids

RARP
Epworth Hospital
Melbourne, Australia

- First case: 8th Dec 2003
- To date: 507
- 2004: 134 cases
- 2005: 166 cases
- 2006: 153 cases
- 2007 (to end March): 51 cases
## RARP Pre Op Demographics

- **Age (years):** 41 – 75 (60.1)
- **Pre op PSA(µg/mL):** 0.3 – 42.0 (8.2)
- **Prostate weight (cc):** 10.4 – 121.21 (39.41)
- **BMI:** 27.2 (20.2 – 40.1)

### P Stage

<table>
<thead>
<tr>
<th>P Stage</th>
<th>n</th>
<th>+ve margins</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT2a</td>
<td>54</td>
<td>4</td>
<td>7.40%</td>
</tr>
<tr>
<td>pT2b</td>
<td>88</td>
<td>17</td>
<td>9.3%</td>
</tr>
<tr>
<td>pT2c</td>
<td>191</td>
<td>33</td>
<td>17.2%</td>
</tr>
<tr>
<td>pT3a</td>
<td>116</td>
<td>60</td>
<td>51.7%</td>
</tr>
<tr>
<td>pT3b</td>
<td>23</td>
<td>13</td>
<td>56.52%</td>
</tr>
<tr>
<td>pT3c</td>
<td>2</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td><strong>52.48%</strong></td>
</tr>
</tbody>
</table>

- **pT2:** 333, 54, 16.22%
- **pT3:** 141, 74, 52.48%
RARP

- Length of Stay: 1 – 11 days (mean 3)
- IDC time: 3 – 43 days (mean 8, median 7)

RARP Complications

- Transfusion: 12 (2.4%)
- UTI: 7 (1.3%)
- Acute retention 4 (0.78%)
- Clot retention: 5 (0.98%)
- Bladder neck stenosis: 7 (1.38%)
- Pulmonary embolus: 2 (0.39%)
- Anastomotic breakdown: 1 (0.19%)
- Port site bleed: 2 (0.39%)
- Long-term infected lymphocoele: 2 (0.39%)
- Rectal injury oversewn: 3 (0.59%)
- Rectal injury, delayed presentation: colostomy: 1 (0.19%)
- Perirectal abscess: colostomy: 1 (0.19%)
- Paralytic ileus: 4 (0.78%)
- Acute renal failure: 1 (0.19%)
- Unrelated death (Day 7): 1 (0.19%)
The introduction of an athermal nerve sparing technique in 2005 has dramatically altered post-operative potency outcomes

Studies of Effect of Thermal Injury on NVB

- Ong J.Urol 2004 (canine)
- Ahlering Urol 2005
- Gill Urol 2005
### POTENCY OUTCOMES

**Thermal vs Athermal Technique**

<table>
<thead>
<tr>
<th></th>
<th>Cautery Free Technique</th>
<th>Bipolar Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># patients</strong></td>
<td>55</td>
<td>36</td>
</tr>
<tr>
<td><strong>Nerve-sparing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bilateral</strong></td>
<td>42 (76%)</td>
<td>28 (78%)</td>
</tr>
<tr>
<td><strong>Unilateral</strong></td>
<td>13 (24%)</td>
<td>8 (22%)</td>
</tr>
<tr>
<td><strong>Potency @ 3/12</strong></td>
<td>23/55 (42%)</td>
<td>3/36 (8.3%)</td>
</tr>
<tr>
<td><strong>Potency @ 9/12</strong></td>
<td>26/34 (77%)</td>
<td>6/30 (20%)</td>
</tr>
<tr>
<td><strong>Mean SHIM</strong></td>
<td>18.9</td>
<td>14.4</td>
</tr>
</tbody>
</table>

Eichel, Skarecky, Costello, Ahlering

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### Outcomes of Athermal Dissection

- 55% < 65 yrs pre-op SHIM 22+
- 3 month potency 42%
- 9 month potency 80%

IEEF at 18.9

Eichel, Skarecky, Costello, Ahlering

Nerve Sparing Robotic Prostatectomy – 107
Smith Textbook Endourology 2007
RARP CONTINENCE
n = 123 (continent pre-op)

<table>
<thead>
<tr>
<th>LEAK WHEN STRAINING</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>19 (15.8%)</td>
<td>25 (21.4%)</td>
<td>39 (31.7%)</td>
</tr>
<tr>
<td>Almost never</td>
<td>27 (21.8%)</td>
<td>43 (34.7%)</td>
<td>46 (37.1%)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>56 (45.2%)</td>
<td>41 (33.1%)</td>
<td>30 (24.2%)</td>
</tr>
<tr>
<td>Always</td>
<td>18 (14.5%)</td>
<td>8 (6.5%)</td>
<td>8 (6.5%)</td>
</tr>
</tbody>
</table>

PAD USE / 24 hours

<table>
<thead>
<tr>
<th>PADS</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 1 pads</td>
<td>94 (78.3%)</td>
<td>102 (87.1%)</td>
<td>116 (94.3%)</td>
</tr>
</tbody>
</table>
Now, this is going to feel like I’m sticking my finger up your ass.
“These stem cells taste funny.”

Surgery as an Option in
Advanced Localized Prostate Cancer
& Neoadjuvant Protocol
Historically urologists have been reluctant to offer attempt at curative surgical treatment in locally advanced prostate cancer.

Radiation is usually preferred now with neoadjuvant hormone therapy 6 months vs. 24 months.

Improvement in surgical technique has reduced the likelihood of urinary incontinence to 1-2%.

Radiation and hormones produces sexual dysfunction + bladder and bowel problems.

Some patients are overstaged and will not need hormonal therapy.
How do we define High Risk Prostate Cancer

- PSA > 20
- Gleason 8 +
- T2 C / T3

AUA Guidelines 2006

Radical Prostatectomy for Clinically Advanced (cT3) Prostate Cancer – 13 yr outcome

- 27% overstaged → pT2
- Cancer control rates approached those Of pT2 disease
- Complication rates comparable to pT2 disease

Ward – BJU 95, 2005
Stage migration has shifted to mean cT3 disease is an unusual presentation – 3% at Mayo in 2001 vs. 25% in 1987. Majority T1C.

Surgery Rates for cT1 – T3 Disease

- 30% for newly diagnosed cT1 – T2
- 6% for cT3 disease
- Young men with T1-2 = 67% T3 = 19%
- Most T3 disease receives WW or XRT +/- hormones

Ward 2005

Meltzer – Am J. Pub Health 2001
Surgery in cT3 Disease
Mayo Clinic

Number  841
Age  66
PSA  10.2 (4-24)
Grade > 7 (54)
15 yr Freedom from Disease 67%
Cancer Sp. Survival 15 yr 79%
Adjuvant Hormone or RT 58% 27%

Ward – BJU 95, 2005

Cleveland cT3 Study

- N 281
- T2B or worse, Gleason 8+, PSA 15+
- Organ confined 11%, ECE 56%, SV +ve 23%, N+ 9%
- PSA < 0.1 at 34 mo = 70%

Berglund – Urology 2006
How Effective is Combined RT & Hormone Therapy in cT3 Disease?

- Biopsy after XRT shows persistent prostate cancer in men with advanced disease
- Postulate that RT causes a biologic alteration resulting in a late wave of metastatic seeding

Coen, Zietman 2002

Node Dissection in Advanced Local Disease

- Node +ve in this cohort (10-25%)
- May or may not impact on survival
- Controversy whether therapeutic or staging procedure

Studer; Meticulous Node Dissection – J.Urol 169, 2003
Neoadjuvant Chemo / Hormonal Therapy and RRP

- Surgery as single agent for PT3 disease usually not curative
- 2 Neoadjuvant RRP studies for pathological proof of principle also suggestive of efficacy
  
  Gleave 2003, Dreicer 2004
- Necessity for Taxotere based neoadjuvant / adjuvant protocols with surgery

RMH Studies

1. Adjuvant Tax
2. Adjuvant Tax + Zometa
3. Neoadjuvant Z + T + H
“So, how long have you been working at the plutonium plant?”