The 12th Annual Advances in Urology

The Impact of Surgical Innovation on Reducing Death and Suffering from Prostate Cancer

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The James Buchanan Brady Urological Institute

Johns Hopkins Medical Institutions
Disclosures

• None
Radical Prostatectomy

- Historical Perspectives
- Anatomic Discoveries
- Perfecting the surgical technique
- Impact on:
  - Safety and quality of life
  - Mortality from prostate cancer
  - Research in the field
Radical Prostatectomy

- **Historical Perspectives**
- **Anatomic Discoveries**
- **Perfecting the surgical technique**
- **Impact on:**
  - Safety and quality of life
  - Mortality from prostate cancer
  - Research in the field
Historical Perspective

• 1904:
  – Radical **perineal** prostatectomy: H.H. Young at Johns Hopkins Hospital
Historical Perspective

• 1904:
  – Radical perineal prostatectomy: H.H. Young

• 1947:
  – Radical retropubic prostatectomy: Terrance Millin
Historical Perspective

• 1904:
  – Radical perineal prostatectomy: H.H. Young
• 1947:
  – Radical retropubic prostatectomy: Terrance Millin
• 1970’s
  – Radical prostatectomy rarely performed, despite excellent cancer control because of side effects:
    • **Major bleeding**: often life threatening
    • **Impotence**: 100%
    • **Total incontinence**: 10–25%
Historical Perspective

• 1904:
  – Radical perineal prostatectomy: H.H. Young

• 1947:
  – Radical retropubic prostatectomy: Terrance Millin

• 1974:
  • When I arrived at Johns Hopkins, radical prostatectomies were rarely performed, even at the institution where the operation was developed!
Historical Perspective

• 1904:
  – Radical perineal prostatectomy: H.H. Young

• 1947:
  – Radical retropubic prostatectomy: Terrance Millin

• 1974:
  • When I arrived at Johns Hopkins, radical prostatectomies were rarely performed, even at the institution where the operation was developed!
  • At this time I wondered why these side effects occurred and if it was possible to prevent them.
These Side-Effect Occurred Because We Did Not Understand the Anatomy *Around* the Prostate
These Side-Effect Occurred Because We Did Not Understand the Anatomy *Around* the Prostate

• Bleeding
  – Anatomy of the veins surrounding the prostate was not charted.
These Side-Effect Occurred Because We Did Not Understand the Anatomy Around the Prostate

• **Bleeding**
  - Anatomy of the veins surrounding the prostate was not charted.

• **Impotence**
  - Every one believed that the cavernous nerves ran *through the prostate*, but the actual location of the nerves responsible for erection was not known.
These Side-Effect Occurred Because We Did Not Understand the Anatomy *Around* the Prostate

• **Bleeding**
  – Anatomy of the veins surrounding the prostate was not charted.

• **Impotence**
  – Every one believed that the cavernous nerves ran *through the prostate*, but the actual location of the nerves responsible for erection was not known.

• **Incontinence**
  – Anatomical understanding of sphincteric complex was incorrect.
These Side-Effect Occurred Because We Did Not Understand the Anatomy Around the Prostate

• Why
  – The study of the anatomy around the prostate in cadavers was difficult because the abdominal viscera compress the pelvic organs into a thick pancake of tissue and formalin obliterates the soft tissue planes.
These Side-Effect Occurred Because We Did Not Understand the Anatomy *Around* the Prostate

• **Why**
  – The study of the anatomy around the prostate in cadavers was difficult because the abdominal viscera compress the pelvic organs into a thick pancake of tissue and formalin obliterates the soft tissue planes.

• **Solution**
  – *Using the operating room as an anatomy laboratory.*
These Side-Effect Occurred Because We Did Not Understand the Anatomy Around the Prostate

• Why
  – The study of the anatomy around the prostate in cadavers was difficult because the abdominal viscera compress the pelvic organs into a thick pancake of tissue and formalin obliterates the soft tissue planes.

• Solution
  – *Using the operating room as an anatomy laboratory.*
  – *Fetal dissections.*
Radical Prostatectomy

• Historical Perspectives
• Anatomic Discoveries
• Perfecting the surgical technique
• Impact on:
  – Safety and quality of life
  – Mortality from prostate cancer
  – Research in the field
Historical Article

The Discovery of the Cavernous Nerves and Development of Nerve Sparing Radical Retropubic Prostatectomy

Patrick Craig Walsh*

From the James Buchanan Brady Urological Institute, The Johns Hopkins Medical Institutions, Baltimore, Maryland

**Purpose:** This review is of the events that led up to the discovery of the cavernous nerves and the development of nerve sparing radical retropubic prostatectomy.

**Materials and Methods:** The correspondence between Pieter J. Donker and Patrick C. Walsh, along with the publication folders describing the anatomy of the dorsal vein complex, pelvic plexus and cavernous nerves, and pelvic fascia, are reviewed.

**Results:** Serendipity had a major role in the fateful meeting of Pieter J. Donker and Patrick C. Walsh on February 13, 1981 when they dissected out the cavernous nerves in a stillborn male infant. During the next year intraoperative observations identified the capsular arteries and veins of the prostate as the likely microscopic landmark that could be used in the adult male pelvis to identify the microscopic cavernous nerves. Twenty-five years ago, on April 26, 1982, the first purposeful nerve sparing radical prostatectomy was performed. One year following surgery patient sexual function was normal, and 25 years later he has retained his quality of life and an undetectable prostate specific antigen.

**Conclusions:** The events that led up to the first nerve sparing radical prostatectomy illustrate the influence of serendipity on discovery.

*Key Words: prostatectomy, prostatic neoplasms, impotence*
Anatomical Observations: **Bleeding**

- Venous complex over the top of the prostate is *beneath dense fascia*. Because the anatomy was obscure, surgeons believed that excessive bleeding was inevitable.
Anatomical Observations: **Bleeding**

- Venous complex over the anterior surface of the prostate is beneath dense fascia. Because the anatomy was obscure, surgeons believed that excessive bleeding was inevitable.

- Using the operating room as an anatomy laboratory, it was possible to identify a common trunk over the urethra resulting in a surgical technique that reduced blood loss.

- This bloodless field made it possible to perform a safer more precise and thorough cancer operation.
AN ANATOMICAL APPROACH TO THE SURGICAL MANAGEMENT OF THE DORSAL VEIN AND SANTORINI'S PLEXUS DURING RADICAL RETROPUBIC SURGERY

WILLIAM G. REINER* AND PATRICK C. WALSH

Diagram:
- Deep dorsal v. of penis
- Symph.
- Puboprostatic lig.
- Superficial branch (deep dorsal v.)
- Blad.
- Prostate
- Lat. venous plexus
- Hypogastric vv.
- Urethra
- Urogenital diaph.
- Blad.
- Inf. vesical v.
- Middle hemorrhoidal v.
- Common trunk

*Note: The asterisk indicates a footnote or reference, which is not visible in the image.
Anatomical Observations: Impotence

• Shortly after developing the technique for controlling bleeding from the dorsal vein a 58 year old man returned 3 months following surgery and told me that he was potent!

• How could that be? At that time everyone believed that the nerves ran through the prostate because everyone who underwent surgery was impotent.

• From this one case I knew that this was not true, but where were the nerves? The answer was not in any anatomy book.
“Some things are just too coincidental to be a coincidence” Yogi Berra
Professor Pieter Donker – A Neurourologist - Professor and Chairman University of Leiden
Professor Pieter Donker – A Neuourologist - Professor and Chairman University of Leiden

- In 1977, I attended my first meeting of the American Association of Genitourinary Surgeons in Florida.

- Because there was no social event the night before the meeting, my wife and I went to dinner at a restaurant downtown.

- As we were walking to our table, I noticed an older man who was alone and impetuously asked him if he was attending the meeting, and if he would like to join us for dinner. His name was Pieter Donker.
In 1981, I was invited to be a visiting professor by Donker’s successor. On Friday February 13 Pieter volunteered to show me around Leiden. Instead, at my request, we went to his laboratory. There I learned that he was using a dissecting microscope to study the innervation of the bladder in a stillborn male infant.

When I asked to see the branches to the corpora cavernosa, he said that he had never looked. 3 hours later we identified them—outside the prostate!
Darker: **anatomy of autonomic nerves in pelvis**

![Diagram of pelvic anatomy with labels: bladder, rectum, nerves, and annotations]

Some of these fibers appear to go into the corpora cavernosa—
the bundle is lateral to the prostate or urethra.

2-13-81 Leiden
Cavernous nerves

Pelvic Plexus

February 13 1981
Anatomical Observations: Impotence

- Based on this observation, we knew where the cavernous nerves were located in a tiny fetus. But how could we identify these microscopic structures in the adult male pelvis? When I returned to Hopkins, once again I used the operating room as an anatomy laboratory.
Radical Mastectomy

10-21-81

There was a pedicle of vessels that ran from the most medial, parallel to the most lateral aspect of the U.S. diaphragm. Lateral to that medial pedicle was a frequent occurrence.

S.N. had a pocket around them as a result of surgery.
I realized that these were the capsular arteries and veins of the prostate and because they travelled in the exact same location as the nerves in the fetus I speculated that this neurovascular bundle could be used as the intraoperative landmark to identify the microscopic nerves.
First Purposeful Nerve-sparing Radical Prostatectomy

April 26, 1982 – the 25th anniversary
Anatomical Observations:  
**IMPOTENCE**

• Fetal dissections with Peter Donker (Leiden)  
  – schematic anatomy of the pelvic plexus and cavernous nerves.

• Intraoperative dissections  
  – neurovascular bundle (NVB)

• Step-section cadaveric reconstruction –  
  – precise localization of NVB – Herb Lepor.
• Shortly after death, an adult male was completely perfused with Bouin’s solution.

• The prostate, bladder, rectum, genitalia, and pelvic floor were completely excised.

• 10,000 whole mount step sections were prepared and this 3 dimensional drawing confirmed the constant association of the nerves to the vessels.
Anatomical Observations: IMPOTENCE

• Fetal dissections with Peter Donker (Leiden)
  – schematic anatomy of the pelvic plexus and cavernous nerves.

• Intraoperative dissections
  – neurovascular bundle (NVB)

• Fresh cadaveric dissection –
  – complete neuroanatomy of the male pelvis – Peter Schlegel.
Why Were All Men Impotent?

• Contrary to what you might believe, the neurovascular bundles were never excised with the specimen. Instead they were bluntly torn posterolaterally where they were firmly adherent to the rectum, left in place, and then cut.
Lateral view

- Bladder
- Prostate
- Rectum
- Divided dorsal v. penis
- Urogenital diaph.
- Urethra
- Rand L neurovascular bundles to corpora cavernosa
Why Were All Men Impotent?

• Contrary to what you might believe, the neurovascular bundles were never excised with the specimen. Instead they were bluntly torn posterolaterally where they were firmly adherent to the rectum, left in place, and then cut.

• Once the neurovascular bundles were identified, it became possible to excise them widely where necessary thus providing a wider margin of excision.
Anatomical Observations: Fascia

- The fascia surrounding the pelvic organs was poorly understood. We understood Denonvelliers’ fascia but the lateral fascia was unknown.
What is this???
Fig. 839.—Low-power magnification of a horizontal section of the prostate and seminal vesicle, from a normal individual. The urethra is circular in form owing to the fact that the specimen was hardened with a catheter in situ. The fascial investments of the prostate and vesicles are well shown. Also the relations between the prostate and the prostatic venous plexus which must be avoided in the radical operation for removal of the prostate. From Mr. Henry Wade.

Fig. 840.—Transverse section of prostate and surroundings at level of verumontanum, the anterior surface of the prostate being shown uppermost. Arrows indicate the point at which the anterolateral fascia should be reflected from the prostate.
Hugh Young recommended using the plane beneath the fascia to avoid bleeding.
Anatomical Observations: Fascia

Fig. 3. Periprostatic fascia illustrating location of neurovascular bundle between levator fascia and prostatic fascia. Reprinted with permission, Brady Urological Institute.
Principles of Nerve-Sparing

- The neurovascular bundle (NVB) is outside the prostate between 2 layers of lateral pelvic fascia (levator & prostatic fascia). If nerve-sparing is performed correctly, the prostatic fascia must remain on the prostate.
Anatomical Observations: Fascia

• The fascia surrounding the pelvic organs was poorly understood.

• In performing a radical perineal prostatectomy, to avoid bleeding from the dorsal vein complex, the dissection was performed inside the levator fascia leaving little soft tissue on the prostate leading to positive surgical margins in cases where the tumor penetrated the prostatic fascia (capsule).
Plane of Dissection in Radical Perineal Prostatectomy
Radical Perineal Specimen with no surrounding soft tissue
Anatomical Observations: Fascia

• The fascia surrounding the pelvic organs was poorly understood.

• In performing a radical retropubic prostatectomy, the dissection is performed *outside* the levator fascia with the exception of the area near the neurovascular bundle – providing more soft tissue on the prostate than the perineal approach.
Prostatic fascia = Capsule of prostate. They are the same structure.
Anatomical Observations: \textbf{INCONTINENCE}

- The external sphincter was not where we thought it was!
Anatomic Illustration Depicting the Prostate Like An Apple Sitting On a Shelf - Incorrect
We thought that the sphincter was here.

Based on this incorrect concept, when we divided the urethra at the pelvic floor the striated sphincter was excised.
Striated urethral sphincter
Immediately after developing the technique for ligation of the dorsal vein, continence rates improved markedly. Why?

In dividing the dorsal vein, the dissection was beneath the ligature and not out at the pelvic floor.

This resulted in better preservation of the striated sphincter.
Radical Prostatectomy

• Historical Perspectives
• Anatomic Discoveries
• Perfecting the surgical technique
• Impact on:
  – Safety and quality of life
  – Mortality from prostate cancer
  – Research in the field
Perfecting the Technique:
Perfecting the Technique: Using the Operating Room As An Anatomy Laboratory
Perfecting the Technique:
Using the Operating Room As An Anatomy Laboratory

• Database day 1: anatomical observations, changes in technique, cancer control and quality of life.
Perfecting the Technique:

Using the Operating Room As An Anatomy Laboratory

• Database day 1: anatomical observations, changes in technique, cancer control and quality of life.

• Telephone appointments every 3 months evaluating outcomes and coaching the patient to recovery
Perfecting the Technique: Using the Operating Room As An Anatomy Laboratory

• Database day 1: anatomical observations, changes in technique, cancer control and quality of life.

• Telephone appointments every 3 months evaluating outcomes and coaching the patient to recovery

• I told myself the truth by dictating exactly what the patient said when asked “are you wearing a pad” and “have you been able to have intercourse more than 50% of the attempts”. The correlation between the database and an independent 3rd party questionnaire was 95% ¹

Perfecting the Technique:
Using the Operating Room As An Anatomy Laboratory

• Colleagues:
  – Pathologist: Joseph Eggleston and Jonathan Epstein - to “protect the patient from the surgeon”.
RADICAL PROSTATECTOMY WITH PRESERVATION OF SEXUAL FUNCTION: PATHOLOGICAL FINDINGS IN THE FIRST 100 CASES

JOSEPH C. EGGLESTON* AND PATRICK C. WALSH

From the Departments of Pathology and Urology, and the James Buchanan Brady Urological Institute, The Johns Hopkins Medical Institutions, Baltimore, Maryland

ABSTRACT

In an effort to preserve sexual function, a nerve-sparing technique for radical retropubic prostatectomy has been used in 100 consecutive men with clinically localized prostatic cancer. Each gland was submitted for total histological examination in a way that permitted determination of the extent of the tumor and adequacy of surgical margins. Although 41 patients had established tumor in periprostatic tissue only 7 had positive surgical margins; all 7 had extensive extraprostatic involvement by tumor, while 5 had involvement of the seminal vesicles and none had surgical margins positive only at the site of the nerve-sparing modification. Sexual function was evaluated in 60 of the patients who were potent preoperatively and who have been followed for a minimum of 1 year: 84 per cent of the patients with an intact prostatic capsule were potent compared to 43 per cent with extensive involvement of periprostatic tissue and 33 per cent with involvement of the seminal vesicles or pelvic lymph nodes. Based upon our findings there is no indication that the nerve-sparing modification compromises the adequacy of the removal of the cancer, which is determined primarily by the extent of the tumor rather than the operative technique. Thus, it appears possible to preserve sexual function in a majority of patients undergoing radical prostatectomy without compromising the adequacy of the cancer operation.
Perfecting the Technique:
Using the Operating Room As An Anatomy Laboratory

• Colleagues:
  – Pathologist: Joseph Eggleston and Jonathan Epstein - to “protect the patient from the surgeon”.
  – Medical Illustrator: Leon Schlossberg - an artist and anatomist
Leon Schlossberg, PhD (Hon)
Perfecting the Technique: Using the Operating Room As An Anatomy Laboratory

• Collegues:
  – Pathologist: Joseph Eggleston and Jonathan Epstein - to “protect the patient from the surgeon”.
  – Medical Illustrator: Leon Schlossberg - an artist and anatomist
  – Residents:
Perfecting the Technique:
*Using the Operating Room As An Anatomy Laboratory*

• Colleagues:
  – Pathologist: Joseph Eggleston and Jonathan Epstein - to “protect the patient from the surgeon”.
  – Medical Illustrator: Leon Schlossberg - an artist and anatomist
  – Residents:
  – Patients: my partners in discovery
Perfecting the Technique: Using the Operating Room As An Anatomy Laboratory

• Change one thing at a time: 28 major changes over 29 years in 4569 patients.

• Constant re-evaluation

• Video documentation
  – To teach others
  – To teach myself

• Goal – to have every patient continent and potent at 3 months.
LEGENDS IN UROLOGY

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Baltimore, Maryland USA

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Perfecting Nerve-sparing Radical Prostatectomy: Sailing in Uncharted Waters
<table>
<thead>
<tr>
<th>Date</th>
<th>Patient number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 1984</td>
<td>#110</td>
<td>Wide excision of the neurovascular bundle</td>
</tr>
<tr>
<td>March 1985</td>
<td>#160</td>
<td>Fine ligation of the branches of the NVB</td>
</tr>
<tr>
<td>April 1985</td>
<td>#166</td>
<td>Mucosal eversion at the bladder neck</td>
</tr>
<tr>
<td>September 1987</td>
<td>#474</td>
<td>Vicryl instead of chromic for anastomotic sutures</td>
</tr>
<tr>
<td>October 1987</td>
<td>#485</td>
<td>Bulldog clamps on hypogastric arteries</td>
</tr>
<tr>
<td>April 1988</td>
<td>#567</td>
<td>Accessory / Aberrant pudendal artery recognized</td>
</tr>
<tr>
<td>January 1989</td>
<td>#672</td>
<td>Direct division of the posterior striated sphincter</td>
</tr>
<tr>
<td>January 1989</td>
<td>#678</td>
<td>Lateral pedicle divided but not ligated</td>
</tr>
<tr>
<td>October 1989</td>
<td>#785</td>
<td>Intermittent compression devices on lower extremities</td>
</tr>
<tr>
<td>June 1990</td>
<td>#883</td>
<td>Preservation of aberrant anterior pudendal artery</td>
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<tr>
<td>February 1991</td>
<td>#989</td>
<td>Nerve graft series initiated</td>
</tr>
<tr>
<td>March 1995</td>
<td>#1680</td>
<td>Six urethral sutures</td>
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<tr>
<td>March 1995</td>
<td>#1688</td>
<td>Vicryl replaced by Monocryl</td>
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<tr>
<td>June 1996</td>
<td>#1497</td>
<td>McDougal clamp discontinued</td>
</tr>
<tr>
<td>July 1996</td>
<td>#1963</td>
<td>Refined division of the dorsal vein</td>
</tr>
<tr>
<td>March 1997</td>
<td>#2087</td>
<td>Video documentation; Viagra</td>
</tr>
<tr>
<td>September 1997</td>
<td>#2202</td>
<td>Pubic stitch</td>
</tr>
<tr>
<td>November 1998</td>
<td>#2425</td>
<td>Release of peritoneum</td>
</tr>
<tr>
<td>May 1999</td>
<td>#2545</td>
<td>Closure bladder neck/new stoma on anterior bladder</td>
</tr>
<tr>
<td>June 1999</td>
<td>#2553</td>
<td>2.5 power loupes</td>
</tr>
<tr>
<td>August 1999</td>
<td>#2587</td>
<td>Division umbilical ligament</td>
</tr>
<tr>
<td>August 2000</td>
<td>#2766</td>
<td>Stopped traction on bladder with malleable blade</td>
</tr>
<tr>
<td>October 2000</td>
<td>#2801</td>
<td>Babcock clamp to stabilize the anastomosis while tying the sutures</td>
</tr>
<tr>
<td>May 2003</td>
<td>#3275</td>
<td>High anterior release of the neurovascular bundle</td>
</tr>
<tr>
<td>December 2004</td>
<td>#3558</td>
<td>4.5 power loupes</td>
</tr>
<tr>
<td>January 2005</td>
<td>#3581</td>
<td>8 cm incision</td>
</tr>
<tr>
<td>June 2005</td>
<td>#3649</td>
<td>High anterior release of the neurovascular bundle</td>
</tr>
</tbody>
</table>
Perfecting the Technique: Sequential Modifications of Radical Prostatectomy 1982 - Present

- March 1997 #2087: Video documentation. I videotaped 61 consecutive cases, followed their outcome with validated questionnaires sent to an independent third party, and after 18 months reviewed the tapes frame by frame to identify factors that correlated with the early return of potency and continence. Four steps correlated with early recovery of potency. One was injury to the neurovascular bundles when dividing the striated sphincter too close to the apex.
• At the apex the neurovascular bundles often do not run in a straight line.
• Instead, they are attached to the apex by apical vessels.
• If you do not know this, when you attempt to preserve the sphincter you can injure them.
October 2000 #2801: Bladder neck intussusception. In reviewing the videos I was unable to identify any anatomic or technical details at the apex that correlated with early continence. For this reason, I focused on the bladder neck and developed bladder neck intussusception, which improved continence at 3 months.
Recent Results: Continence

- Self reported confidential validated survey sent to a third party:

<table>
<thead>
<tr>
<th></th>
<th>Dry (no pad)</th>
<th>Little/ No Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>79% *</td>
<td>94%</td>
</tr>
<tr>
<td>12 months</td>
<td>98%</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Previously, 55% dry at 3 months

Parsons, K et al Urology:64: 987-990, 2004
Perfecting the Technique: Sequential Modifications of Radical Prostatectomy 1982 - Present

- **December 2004 #3558**: 4.5 power loupes.
- **January 2005 #3581**: 8 cm incision
INCISION

• Length - no longer from the umbilicus to the pubis. The incision now is only 3 inches above the pubis. But it's more than cosmetic:
INCISION

• Length - no longer from the umbilicus to the pubis. The incision now is only 3 inches above the pubis. But it’s more than cosmetic:
  – Optimal exposure with less traction on the nerves when using the malleable blade and sponge stick.
INCISION

• Length - no longer from the umbilicus to the pubis. The incision now is only 3 inches above the pubis. But it’s more than cosmetic:
  – Optimal exposure with much less traction on the nerves when using the malleable blade and sponge stick.
  – No thromboembolic events in the last 988 consecutive cases. In the prior 988 there were 11 (p=0.0009).
Perfecting the Technique: Sequential Modifications of Radical Prostatectomy 1982 - Present

- **June 2005 #3649:** High anterior release of the neurovascular bundle at the apex.

*High Anterior Release of the Levator Fascia Improves Sexual Function Following Open Radical Retropubic Prostatectomy*

Matthew E. Nielsen,* Edward M. Schaeffer, Penny Marschke and Patrick C. Walsh

* J Urol 2008; 180:2557
Release of levator fascia
Ligation of proximal and distal deep dorsal vein
Dissection planes - *Inter*fascial

- Prostatic fascia
- Levator fascia
- NVB

Denonvilliers’ fascia

Rectum

*J. Garcia*  
© 2003  
Brady Urological Institute
Ligation and division of levator fascia and associated vessels
Division of dorsal vein complex
Levator fascia

Neurovascular bundle
Results HAR at 12 months

• HAR on one or both sides improved sexual function in men who were fully potent preoperatively and had bilateral nerve sparing..

<table>
<thead>
<tr>
<th></th>
<th>NO HIGH RELEASE</th>
<th>HIGH RELEASE</th>
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<tbody>
<tr>
<td>Potent</td>
<td>77% versus 93%</td>
<td></td>
</tr>
<tr>
<td>SHIM &gt; 21</td>
<td>52% versus 70%</td>
<td></td>
</tr>
<tr>
<td>+SM pT2</td>
<td>1.5% versus 1.3%</td>
<td></td>
</tr>
</tbody>
</table>

• We believe that reduced traction on the NVB is major factor responsible for the improved results.
Perfecting the Technique: Sequential Modifications of Radical Prostatectomy 1982 - Present

- October 2009 #4262  Use of the Babcock Clamp During Release of the NVB
Use of the Babcock Clamp During Release of the NVB

• I had always used a sponge stick to displace the prostate when exposing the NVB
Clamp introduced from midline to lateral position

Apical branch is clipped and divided
Use of the Babcock Clamp During Release of the NVB

• I had always used a sponge stick to displace the prostate when exposing the NVB

• However I adopted a different approach using a Babcock clamp instead. Why?
Use of the Babcock Clamp During Release of the NVB

• I had always used a sponge stick to displace the prostate when exposing the NVB

• However I adopted a different approach using a Babcock clamp instead. Why?
  – Exposure is better because you lift the prostate **anteriorly** and have better exposure of the posterolateral edge of the prostate
Use of the Babcock Clamp During Release of the NVB

• I had always used a sponge stick to displace the prostate when exposing the NVB

• Recently I adopted a different approach using a Babcock clamp instead. Why?
  – Exposure is better because you lift the prostate anteriorly and have better exposure of the posterolateral edge of the prostate
  – This enables you to dissect the prostate from the NVB rather than the NVB from the prostate thus reducing traction on the NVB
Levator fascia is dissected...

...as NVB branches are released to just above the seminal vesicle
CONCLUSIONS

• The operating room can be used effectively as an anatomy laboratory.
CONCLUSIONS

• The operating room can be used effectively as an anatomy laboratory.

• Minor variations in surgical technique can have a major impact on outcomes.
CONCLUSIONS

• The operating room can be used effectively as an anatomy laboratory.
• Minor variations in surgical technique can have a major impact on outcomes.
• Intraoperative videos provide objective documentation of surgical technique.
CONCLUSIONS

• The operating room can be used effectively as an anatomy laboratory.
• Minor variations in surgical technique can have a major impact on outcomes.
• Intraoperative videos provide objective documentation of surgical technique.
• Repeated re-evaluation of outcomes correlated with changes in surgical approach is the best way to reduce morbidity and improve cancer control.
Goal

• I stopped operating in June 2011 after performing 4569 operations. I did not reach my goal of having every patient potent and continent at 3 months, but over the last 2 years using all of these modification I had the best results I ever had
Goal

- In the patients who underwent surgery during the last 18 months that I was operating.

<table>
<thead>
<tr>
<th>Months Post-op</th>
<th>Potent*</th>
<th>No Pad</th>
<th>&gt; 1 pad</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>60%</td>
<td>94%</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>92%</td>
<td>95%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

* Preoperative SHIM > 21 and at least a portion of both NVBs preserved
Campbell-Walsh Urology 10th Edition

Complete up-to-date description of the latest surgical technique with videos
Radical Prostatectomy

• Historical Perspectives
• Anatomic Discoveries
• Nerve-sparing surgical technique
• Impact on:
  – Safety and quality of life
  – Mortality from prostate cancer
  – Research in the field
1983 - 1993

• **Increased popularity:** radical prostatectomy became the most common in-patient operation at Johns Hopkins and one of the most common operations performed by urologists.
Figure: Proportion of men in the USA with prostate cancer treated by radical prostatectomy

Merrill, Lancet 348:963, 1996
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  - Fewer side-effects
  - PSA testing:
    - More men with localized disease.
Radical Prostatectomy

• Historical Perspectives
• Anatomic Discoveries
• Nerve-sparing surgical technique

• Impact on:
  – Safety and quality of life
  – Mortality from prostate cancer
  – Research in the field
Accomplishments

• Cancer control: Over the last 2 decades, more men were subjected to potential curative therapy and over the last decade deaths from prostate cancer in the U.S. have fallen 40%. Why?
• Deaths from Cancer in US Men

Deaths from Cancer in US
Men

- Lung
- Colon
- Nerve-sparing radical prostatectomy
- PSA Testing
Radical Prostatectomy Reduces Prostate Cancer Deaths and Improves Overall Survival*
Radical Prostatectomy Reduces Prostate Cancer Deaths and Improves Overall Survival*

- **SPCG-4**: Scandinavian Prostate Cancer Group 4
- **Sweden, Finland, Iceland**
- **Randomized trial of watchful waiting vs. radical prostatectomy**
- **Pre-PSA era.**
- **695 T2 (75%); mean age 65**
- **Follow-up 18 years following randomization.**
# Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

**NEJM 2014;370:932**

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D.,

<table>
<thead>
<tr>
<th>%</th>
<th>Metastases</th>
<th>Deaths From Any Cause</th>
<th>Deaths From Cancer</th>
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<td>All</td>
<td>43%</td>
<td>39%</td>
<td>44%</td>
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<td>&lt; 65 years of age</td>
<td>49%</td>
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<tr>
<td>Low risk</td>
<td>57%</td>
<td>43%</td>
<td>46%</td>
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Relative Reduction at 18 years
Results in Men < 65 years at Randomization

= Watchful waiting men < 65 yo
Age-adjusted death rate in US Men

Lung
Nerve-sparing radical prostatectomy
PSA Testing
Colon
Stomach
Colon and Rectum
Pancreas
Leukemia
Liver

In 1983, only 7% of men with prostate cancer underwent surgery and radiotherapy was too underpowered to cure. Essentially no one was being treated with curative intent.
• In 1983, only 7% of men with prostate cancer underwent surgery and radiotherapy was too underpowered to cure. Essentially no one was being treated with curative intent.

• By 1993 70% of men in their 50s and 55% of men in their 60s underwent surgery.
How can we be certain that surgery is responsible for this decline in mortality 1994-2003?
• What about improvement in the management of metastatic disease?
• What about improvement in the management of metastatic disease?

• Conclusion: improvements in survival of men with metastatic disease have not contributed to the observed drop in mortality in the PSA era.
How can we be certain that surgery is responsible for this decline in mortality 1994-2003?

• Surgery was the most common form of treatment for men with localized prostate cancer during this era.
How can we be certain that surgery is responsible for this decline in mortality 1994-2003?

- Radiation was too underpowered to cure
  - 1970-1990’s: limited dose (65-70 GY) 2 D
  - Dose escalation: better targeting
    - Late 1990s: 3D: (70-75 Gy)
    - 2004-07: IMRT (≥ 75 Gy)
    - 2005-09: IGRT (image guided)
  - 2000: neoadjuvant and adjuvant hormonal therapy for higher risk patients
After 15 years of follow-up, there were 568 deaths, including 104 from PC. RP was associated with statistically significant advantages for overall (hazard ratio [HR] = 0.60, 95% confidence interval [CI] = 0.53 to 0.70, \( P < .0001 \)) and disease-specific mortality (HR = 0.35, 95% CI = 0.26 to 0.49, \( P < .0001 \)). Mortality benefits for RP were also observed within treatment propensity quintiles, when subjects were pair-matched on propensity scores, and in subgroup analyses based on age, tumor characteristics, and comorbidity.
Comparative effectiveness of radical prostatectomy and radiotherapy in prostate cancer: observational study of mortality outcomes 1996-2009; Sweden

Cancer-specific survival

BMJ 2014; 348
Sooriakummaran et al
Radical Prostatectomy

• Historical Perspectives
• Anatomic Discoveries
• Nerve-sparing surgical technique
• Impact on:
  – Safety and quality of life
  – Mortality from prostate cancer
  – Research in the field
Impact on Research

• In breast and colon cancer, tissue was always available for pathologic correlation and biochemical/molecular study. This accelerated discovery in these fields.

• However, prior to the development of anatomic radical prostatectomy only 7% of men with localized disease underwent surgery. Thus, only small needle biopsy material was available for research.

• Today, tissue harvested from surgical specimens has galvanized research. Indeed, this contribution of surgery in the long run may have the greatest impact in reducing death from prostate cancer.
Clinical Discoveries From Surgical Specimens

• In the past, without information on pathologic stage it took many years to identify prognostic factors because of the protracted natural history of the disease.
Clinical Discoveries From Surgical Specimens

• In the past, without information on pathologic stage it took many years to identify prognostic factors because of the protracted natural history of the disease.

• However once we had pathologic information on surgically removed specimens we were able to predict who was cured.
Probability of Cure (undetectable PSA) Following Radical Prostatectomy Based on Pathologic Findings

- Organ Confined
- Extraprostatic extension
- Seminal vesicle invasion
- Positive Lymph Nodes

Years Postoperative

Likelihood of undetectable PSA

0.00 0.25 0.50 0.75 1.00

0 5 10 15 20
Clinical Discoveries From Surgical Specimens

• In the past, without information on pathologic stage it took many years to identify prognostic factors because of the protracted natural history of the disease.

• However once we had pathologic information on surgically removed specimens we were able to predict who was cured.

• Next, we went on to develop tables that could be used **preoperatively** to predict who was curable, e.g. the Partin Tables.
Partin Tables: To Predict Pathologic Stage Preoperatively

- PSA – excellent in predicting recurrence.
Kaplan-Meier actuarial likelihood of PSA recurrence by preoperative serum PSA levels
Partin Tables: To Predict Pathologic Stage Preoperatively

- PSA – prostate specific antigen is prostate specific but not cancer specific. It is excellent in detecting recurrence
- Clinical stage – TNM
Kaplan-Meier actuarial likelihood of PSA recurrence by clinical stage (1992 AJCC)
Partin Tables: To Predict Pathologic Stage Preoperatively

• PSA – prostate specific antigen is prostate specific but not cancer specific. It is excellent in detecting recurrence; less helpful in predicting extent of disease.

• Clinical stage – TNM

• Gleason score –
Kaplan-Meier actuarial likelihood of PSA recurrence by Gleason score

Gleason Score
2-4
5
6
7
8-10

Likelihood of undetectable PSA

Years Postoperative
0
5
10
15
20

analysis time
But Which of the 3 Parameters Was Most Important??
But Which of the 3 Parameters Was Most Important??

- In 1991 Pope John Paul II requested that I evaluate a special patient—
- He was 53 years old, PSA 2.4 ng/ml, Gleason 8, T2b disease.
- What was more important – his low PSA or high Gleason score?
- Unfortunately for him it was the Gleason score – but this case revealed a new effective approach to predicting curability.
Impact of Gleason Score on Tumor Volume and PSA/cc of Tumor

The Use of PSA, Clinical Stage, and Gleason Score
To Predict Pathologic Stage Preoperatively

THE USE OF PROSTATE SPECIFIC ANTIGEN, CLINICAL STAGE
AND GLEASON SCORE TO PREDICT PATHOLOGICAL STAGE IN
MEN WITH LOCALIZED PROSTATE CANCER

ALAN W. PARTIN,* JOHN YOO, H. BALLENTINE CARTER, JAY D. PEARSON, DANIEL W. CHAN,
JONATHAN I. EPSTEIN AND PATRICK C. WALSH

From the Departments of Urology, Pathology and Laboratory Medicine, The Johns Hopkins University School of Medicine and the James
Buchanan Brady Urological Institute, The Johns Hopkins Hospital and The Longitudinal Studies Branch of the Gerontology Research Center,
National Institute on Aging, Baltimore, Maryland
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<td>46 (53-39)</td>
<td>18 (24-13)</td>
<td>11 (15-7)</td>
<td>12 (18-7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>41 (50-34)</td>
<td>40 (51-31)</td>
<td>40 (52-30)</td>
<td>33 (46-22)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>7 (12-4)</td>
<td>23 (33-15)</td>
<td>19 (29-10)</td>
<td>28 (42-16)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>5 (8-2)</td>
<td>18 (30-9)</td>
<td>29 (44-15)</td>
<td>26 (44-12)</td>
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</table>
### CLINICAL STAGE T2B (PALPABLE ≥ ½ OF ONE LOBE) OR T2C (PALPABLE ON BOTH LOBES)

<table>
<thead>
<tr>
<th>PSA Range (ng/ml)</th>
<th>Pathologic Stage</th>
<th>5 - 6</th>
<th>3 + 4 = 7</th>
<th>4 + 3 = 7</th>
<th>8 - 10</th>
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<tbody>
<tr>
<td>0–2.5</td>
<td>Organ confined</td>
<td>84 (89–78)</td>
<td>59 (70–47)</td>
<td>44 (58–31)</td>
<td>49 (65–32)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>14 (19–9 )</td>
<td>24 (33–16)</td>
<td>29 (42–19)</td>
<td>24 (36–14)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>1 (3–0)</td>
<td>6 (14–0)</td>
<td>6 (14–0)</td>
<td>8 (21–0)</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>1 (3–0)</td>
<td>10 (25–2)</td>
<td>19 (40–4)</td>
<td>17 (42–3)</td>
</tr>
<tr>
<td>2.6–4.0</td>
<td>Organ confined</td>
<td>74 (80–68)</td>
<td>47 (56–39)</td>
<td>36 (45–27)</td>
<td>39 (50–28)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>23 (29–18)</td>
<td>37 (45–28)</td>
<td>46 (55–36)</td>
<td>37 (48–27)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>3 (5–1)</td>
<td>13 (21–7)</td>
<td>13 (22–7)</td>
<td>19 (32–9)</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>0 (1–0)</td>
<td>3 (7–0)</td>
<td>5 (14–0)</td>
<td>4 (13–0)</td>
</tr>
<tr>
<td>4.1–6.0</td>
<td>Organ confined</td>
<td>66 (72–59)</td>
<td>36 (43–29)</td>
<td>25 (32–19)</td>
<td>27 (37–19)</td>
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<td>Extraprostatic extension</td>
<td>30 (36–24)</td>
<td>41 (47–33)</td>
<td>47 (55–38)</td>
<td>38 (48–28)</td>
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<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>4 (6–2)</td>
<td>16 (23–10)</td>
<td>15 (23–9)</td>
<td>22 (33–13)</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>1 (2–0)</td>
<td>7 (12–3)</td>
<td>13 (21–6)</td>
<td>11 (23–4)</td>
</tr>
<tr>
<td>6.1–10.0</td>
<td>Organ confined</td>
<td>62 (68–56)</td>
<td>32 (38–26)</td>
<td>22 (29–17)</td>
<td>24 (33–17)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>30 (38–26)</td>
<td>41 (49–33)</td>
<td>47 (56–38)</td>
<td>38 (48–29)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>4 (6–2)</td>
<td>20 (28–13)</td>
<td>19 (28–11)</td>
<td>27 (39–16)</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>1 (2–0)</td>
<td>6 (11–3)</td>
<td>11 (19–5)</td>
<td>10 (20–3)</td>
</tr>
<tr>
<td>&gt;10.0</td>
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<td>26 (44–12)</td>
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</tbody>
</table>
Basic Science Discoveries

• Cell lines
• Molecular insight into the role of known genes in initiation and promotion.
  – Methylation of GST\(\pi\)
  – Loss of heterozygosity
  – Hereditary genes
  – Androgen receptor mutations
• Identification of new genes
  – cDNA microarrays
  – Proteomics
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  – Proteomics
Prostate Cancer: Mechanism of Disease

- W. Nelson: identified inactivation of the major defense mechanism against oxidative damage (GSTP1) as the earliest and most universal genetic defect leading to prostate cancer.

Insight Into the Pathogenesis of Prostate Cancer

normal prostate epithelium

prostatic intraepithelial neoplasia

localized prostate cancer

exposure to dietary oxidants and electrophiles

metastatic prostate cancer

androgen independent cancer

GSTP1
# GSTP1 CpG Island Hypermethylation in Laser Dissected Archival Prostate Specimens

<table>
<thead>
<tr>
<th>Condition</th>
<th>n (patients)</th>
<th>Any GSTP1 Methylation* (n, areas)</th>
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<tr>
<td>Normal</td>
<td>27</td>
<td>0/48 (0.0%)</td>
</tr>
<tr>
<td>BPH</td>
<td>20</td>
<td>0/22 (0.0%)</td>
</tr>
<tr>
<td>PIA</td>
<td>27</td>
<td>4/64 (6.3%)†</td>
</tr>
<tr>
<td>HGPIN</td>
<td>23</td>
<td>22/32 (68.8%)††</td>
</tr>
<tr>
<td>CaP</td>
<td>27</td>
<td>30/33 (90.9%)†††</td>
</tr>
</tbody>
</table>
Insight Into the Pathogenesis of Prostate Cancer

normal prostate epithelium

prostatic intraepithelial neoplasia

GSTP1 CpG island hypermethylation

exposure to dietary oxidants and electrophiles

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androgen independent cancer
Conclusion
An Anatomical Approach Has Improved

- Surgical exposure
- Blood loss
- Surgical margins
- Potency
- Continence
- Cancer control
- Deaths from prostate cancer
- Galvanized research in prostate cancer
Lessons for Discovery
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• If you want to make an important discovery, pick an important problem
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• Who teaches the professors – their patients. Listen to them.
Lessons for Discovery

• If you want to make an important discovery, pick an important problem

• Who teaches the professors – their patients. Listen to them.
  – If they tell you something everyone believes is wrong, this may point to a new discovery – that was the secret to the success I just described.
Lessons for Discovery

- If you want to make an important discovery, pick an important problem.
- Who teaches the professors – their patients. Listen to them.
- Do one thing well before doing the next - less is more – you do not have to do everything.
Lessons for Discovery

• If you want to make an important discovery, pick an important problem
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• Do one thing well before doing the next - less is more – you do not have to do everything
• Never underestimate what you may learn from an older person.
Lessons for Discovery

• **Timing** – the wild card in the equation. Follow Wayne Gretzky’s advice and “skate to where the puck is going to be”. Ask where your field is headed or what new research tools are available. You will win out.
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• Find a partner in life who inspires and shares your dreams and who will be willing to make the sacrifices that will be necessary.
UCLA Chief Resident: Graduation Celebration – June 1971
Acknowledgments

- To all residents, faculty, and support staff, past and present, at Johns Hopkins
- To my patients - who have been my partners in discovery.
- Special thanks to valued collaborators:
<table>
<thead>
<tr>
<th>Valued Collaborators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donald Coffey</td>
</tr>
<tr>
<td>William Isaacs</td>
</tr>
<tr>
<td>H.B. Carter</td>
</tr>
<tr>
<td>Alan Partin</td>
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<tr>
<td>Herb Lepor</td>
</tr>
<tr>
<td>Peter Schlegel</td>
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<tr>
<td><strong>Matthew Nielsen</strong></td>
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<tr>
<td>Jonathan Epstein</td>
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<tr>
<td>Elizabeth Platz</td>
</tr>
<tr>
<td>William Nelson</td>
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<td>Stacy Loeb</td>
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<tr>
<td>Daniel Chan</td>
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<tr>
<td>Edward Schaeffer</td>
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<td>Mario Eisenberger</td>
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<tr>
<td>Bruce Trock</td>
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<tr>
<td>Jianfeng Xu</td>
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<td>Angelo DeMarzo</td>
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