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

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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

A pril 26, 2007 marks the 25th anniversary of the first purposeful nerve sparing radical retropubic prostatectomy. In 1982 virtually all men who underwent surgical treatment for prostate cancer were impotent after surgery. However, in contrast, this patient had complete recovery of sexual function within 1 year following surgery, and 25 years later has retained his quality of life and an undetectable PSA. This account of the events that led up to that operation illustrates the influence of serendipity on discovery.

BACKGROUND

Radical perineal prostatectomy was first developed in 1904 at the Johns Hopkins Hospital by Hugh Hampton Young and in 1947 the retropubic approach was introduced by Terence Millin.1,2 Although radical prostatectomy provided excellent cancer control it never gained widespread popularity because of major side effects. Virtually all men who underwent surgery were impotent, many had significant urinary incontinence and when performed via the retropubic approach excessive bleeding was common. With the introduction of external beam radiotherapy for the treatment of prostate cancer it was possible to avoid many side effects. The agents used for tissue fixation dissolve adipose tissue, thus obscuring normal tissue planes, and the abdominal viscera compress the pelvic organs into a thick pancake of tissue making anatomical dissection difficult. These problems were overcome by using the operating room as an anatomy laboratory and by using infant cadavers for anatomical study.

THE DISCOVERY

In 1974, shortly after I arrived as the new director of the Brady Urological Institute, I embarked upon a series of anatomical studies to understand the source of morbidity from radical prostatectomy with the hope that it might be avoided. Soon it became clear that excessive bleeding occurred because the anatomy of the dorsal vein complex and Santorini’s plexus was not charted, impotence was universal because the location of the autonomic innervation to the pelvic organs and the corpora cavernosa was not known, and incontinence was common because the anatomical understanding of the sphincteric complex was incorrect. This deficit in the understanding of the periprostatic anatomy can be traced to the use of adult cadavers, which were not ideal for these investigations. The agents used for tissue fixation dissolve adipose tissue, thus obscuring normal tissue planes, and the abdominal viscera compress the pelvic organs into a thick pancake of tissue making anatomical dissection difficult. These problems were overcome by using the operating room as an anatomy laboratory and by using infant cadavers for anatomical study.
1977, shortly after I had worked out the technique for controlling blood loss from the dorsal vein, a 58-year-old patient from Philadelphia told me that he was fully potent within a year following radical prostatectomy. From this single observation I knew that the commonly held belief of urologists that the cavernous nerves ran through the prostate was incorrect. That same year I attended my first meeting of the American Association of Genitourinary Surgeons. The night before the meeting my wife and I went to a restaurant and there, standing in the shadows behind the maitre d’, I spotted an older man. Impetuously I asked if he was also attending the meeting and whether he would like to join us for dinner. That night was the first time I met Pieter Donker, the Professor and Chairman of Urology at the University of Leiden. At dinner I learned a lot about his career and he learned about the training program at Hopkins. As a result, the following year one of his residents, Jaab Zwartendijk, joined us for a 1-year fellowship, further cementing my relationship with Donker.

For the next several years I took every opportunity to learn more about the anatomy of the pelvic plexus and the location of the branches to the corpora cavernosa. Unfortunately the anatomy texts in that era were not very helpful and contained no information on the exact anatomical location of the autonomic innervation to the corpora cavernosa. However, long after the discovery was made 2 articles published many years earlier were called to my attention that did provide some of this information.

In February 1981 I was invited to attend a meeting in Leiden, the Netherlands. Although I had expected to do some sightseeing it did not work out that way, and instead I spent a week in operating rooms, laboratories and lecturing. On the final day before we returned to the United States, Friday, February 13, 1981, my 43rd birthday, my host Professor Udo Jonas offered a tour of Leiden, and because of my friendship with Pieter Donker he asked Pieter to be my guide. Had it not been for that dinner 4 years earlier we would have never met and this opportunity would have been missed.

Pieter offered to show me the windmill museums, the canals and other local sights. However, I was interested in what he was doing now that he had retired, and when he told me that he was working in the anatomy laboratory I said that I would like to see what he was doing, without any idea of the connection between his work and my interest. In the basement of the anatomy building Pieter took out an infant cadaver, a dissecting microscope and his drawings. When I asked why he was dissecting out the nerves to the bladder, he stated that this had never been done successfully before, and when I asked why he was using the infant cadaver, he said that this was the best model, avoiding the previously described complications with the use of adult cadavers. In studying his drawings I asked about the location of the branches to the corpora cavernosa. He stated that he had never looked. Three hours later both of us could see that the cavernous nerves were located outside the capsule and fascia of the prostate. Figure 1 is my illustration from that day showing how important discoveries can have humble beginnings.

During the next year Pieter continued to perform dissections and I once again used the operating room as an anatomy laboratory. Based upon the findings in the infant cadaver we had a schematic diagram of where the nerves were located, but no landmarks to identify their location in the adult male pelvis (fig. 2). In the operating room I noticed that there was a cluster of vessels, the capsular arteries and veins of the prostate, that traveled in this exact location. In March 1982 I met with Pieter to review our results, and he agreed with my suggestion that these vessels provided the scaffolding for the nerves and that the neurovascular bundle could be used as the macroscopic landmark to identify them during surgery.

I returned to Baltimore and in March 1982 performed a radical cystectomy on a 60-year-old man. I had never seen a patient who was potent after radical cystectomy, but the patient awoke with a normal erection on postoperative day 10. On April 26, 1982 I performed the first purposeful nerve sparing radical prostatectomy on a 52-year-old professor of psychology from Cleveland, Ohio and within 1 year he was fully potent. Today he is cancer-free with an excellent quality of life.

The final 2 pieces of the puzzle came together shortly thereafter. Although everyone who performed prostatectomies was familiar with Denonvilliers’ fascia, little or nothing had been written about the layers of the lateral pelvic fascia. However, based upon a whole mount step sectioned prostate that was harvested by Herb Lepor when he was a resident, it became clear that the lateral pelvic fascia was divided into 2 layers—the prostatic fascia and the levator fascia—and that when nerve sparing is properly performed the prostatic fascia must remain on the prostate (fig. 3). Subsequently, Herb Lepor and Peter Schlegel provided documentation of the precise location of the cavernous nerves. The role of Leon Schlossberg, the noted Hopkins medical illustrator, in translating these discoveries into anatomically accurate drawings cannot be overstated. His knowledge of anatomy and his ability to translate what he saw in the operating room to paper made it possible to share these discoveries with surgeons around the world.

Development of the technique for ligation of the dorsal vein not only reduced blood loss but was also associated with improvement in urinary control. The reason became evident from a review of Olerich’s 1980 publication which demonstrated that the sphincteric complex responsible for passive urinary control was a vertically oriented tubular sheath that

![Figure 1](image.png)

**Figure 1.** Original schematic drawing of pelvic autonomic nerves in male stillborn infant. Dissection performed February 13, 1981.
embraced the apex of the prostate. This anatomy had important implications in transection of the dorsal vein complex, which is intimately associated with the striated sphincter. Before the anatomical approach was developed, surgeons cut through the dorsal vein complex immediately adjacent to the pelvic floor. In these cases the dorsal vein retracted out of sight and could not be controlled, and the anterior major portion of the striated sphincter was excised. However, with improved approaches to control of hemostasis more of the anterior striated sphincter was preserved, thus resulting in improved urinary control (fig. 4).

THE IMPACT

This discovery came at a critical time in the field of urology. In 1980 only 7% of men with localized prostate cancer underwent surgery. However, armed with the ability to cure prostate cancer more safely with surgery and with fewer side effects, radical prostatectomy was rapidly adopted. As a result of the marked reduction in blood loss the 30-day mortality from radical prostatectomy decreased 10-fold, from 2% to 0.2%, and by the mid 1990s 35% of men with localized prostate cancer underwent surgery nationwide. Had this operation not come along who knows how men would have been treated when PSA made it possible to identify so many men with curable disease?

The improved popularity of radical prostatectomy is also closely linked to the dramatic decrease in prostate cancer deaths during the last decade. Based on the findings of the Scandinavian Prostate Cancer Group randomized trial of radical prostatectomy vs watchful waiting, at 10 years 15% of men in the watchful waiting group died of prostate cancer vs only 10% in the radical prostatectomy group. In 1992, 104,000 men underwent radical prostatectomy in the United States. If surgery reduced prostate cancer deaths by 5%, 10 years later this should explain much of the observed decrease (35,000 prostate cancer deaths in 1995 vs 27,350 in 2006).

However, one could argue that the most important impact has been on research in prostate cancer. Up until the early 1980s investigation in the field of prostate cancer was stalled because there was little or no tissue for scientific investigation other than small needle biopsy specimens. Furthermore, because most men were treated with radiotherapy it was impossible to know the true extent of disease at diagnosis and to determine whether the disease had been controlled. Instead, we had to wait for 15 years to see whether the patient died of prostate cancer. However, once radical prostatectomy became more widely available we were able to determine the pathological stage of disease and use this as a surrogate for predicting the probability of cure. Once PSA became available we were able to use these data to establish the Partin Tables to predict the probability of cure. At last, with the widespread availability of tissue it
was possible to perform biochemical and genetic studies into the molecular pathogenesis of the disease.

I share these thoughts not to take credit, but to describe how important discoveries can be made—a simple act of kindness to a lonely older man followed 4 years later by trying to understand what he was doing now that he had retired. Never underestimate what you can learn from others. It puzzles me why it took so long for someone to solve this problem, and who knows how much longer it would have taken without these serendipitous events.

### Abbreviations and Acronyms

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<td>PSA</td>
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### REFERENCES

1. Young HH: The early diagnosis and radical cure of carcinoma of the prostate: being a study of 40 cases and presentations of a radical operation which was carried out in 4 cases. Bull Johns Hopkins Hosp 1905; 16: 315.