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·*Review*·

# Recent neuroanatomical studies on the neurovascular bundle of the prostate and cavernosal nerves: clinical reflections on radical prostatectomy

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**Abstract**

The neurovascular bundle of the prostate and cavernosal nerves have been used to describe the same structure ever since the publication of the first studies on the neuroanatomy of the lower urogenital tract of men, studies that were prompted by postoperative complications arising from radical prostatectomy. In urological surgery every effort is made to preserve or restore the neurovascular bundle of the prostate to avoid erectile dysfunction (ED). However, the postoperative potency rates are yet to be satisfactory despite all advancements in radical prostatectomy technique. As the technology associated with urological surgery develops and topographical studies on neuroanatomy are cultivated, new observations seriously challenge the classical teachings on the topography of the neurovascular bundle of the prostate and the cavernosal nerves. The present review revisits the classical and most recent data on the topographical anatomy of the neurovascular bundle of the prostate and cavernosal nerves and their implications on radical prostatectomy techniques. *(Asian J Androl 2005 Dec; 7: 339–349)*

**Keywords**: prostate cancer; cavernosal nerves; neurovascular bundle; neuroanatomy; prostatectomy; laparoscopy; robotics; nerve graft; penile erection

## 1 Introduction

Today, we are more eager than we were in the past to identify patients with more localized disease so that we can give them a chance of an almost curative treatment. Radical prostatectomy offers an effective curative treatment in selected patients [1–5] but is still associated with significant postoperative morbidities, including erectile dysfunction (ED) and urinary incontinence [6–10]. Nerve sparing techniques for anatomic radical prostatectomy developed by Walsh *et al.* [11–16] and others [17–21] have helped minimizing complications related to nerve injuries. However, the results regarding potency preservation from centers worldwide published in the urological literature are yet to be satisfactory.

Postoperative potency can be influenced by many factors, including preoperative erectile function, patient age, level of disease, surgeon's experience and interpersonal anatomic variations. The proper identification and preservation of the neurovascular bundle of the prostate and cavernosal nerves on both sides has a pivotal role in maintaining the preoperative erectile function. As the number of centers of excellence for radical prostatec-

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tomy have grown, more papers, chapters, excellent drawings and monographs on the topography of the neurovascular bundle have been published [11–13]. However, the potency preservation rates are far from being excellent. Recently, robotic/laparoscopic radical prostatectomy has emerged, claiming better rates as a result of the use of magnified imaging during surgery [22–37]. Despite this, some uncertainty remains on the topographical anatomy of the neurovascular bundle and the cavernosal nerves and this is hampering the outcome of robotic/laparoscopic radical prostatectomy.

Another promising technique that has emerged in recent years involves the nerve grafting of the distal and proximal ends of the neurovascular bundle [38–45] that have been severed because of disease-specific or technical reasons. Unfortunately, despite very delicate and surgically successful nerve anastomosis, nerve grafting also has not lived up to expectations regarding maintenance of potency [41, 43–45]. Unsuccessful nerve grafting outcomes have again shifted attentions to the topographical neuroanatomy of the neurovascular bundle of the prostate and the cavernosal nerves. Gross anatomic dissections [46–48] have developed into histological studies that aim to define the cavernosal nerves' origin and destination [49–56]. Different novel techniques including serial histological sections on adult and fetal tissues, immunohistochemical studies on histological sections to differentiate very fine nerves, and three-dimensional computerized reconstructions of images based on serial histological sections are also utilized to revalidate our classical knowledge of the cavernosal nerves and their interaction with surrounding structures [57–60]. In this study, recent advancements in neuroanatomical studies of the neurovascular bundle of the prostate and the cavernosal nerves was reviewed.

## 2 Pelvic plexus

The pelvic splanchnic nerves arise from the anterior sacral roots, with most originating from S4 and a few branches from S2 and S3. These parasympathetic fibers from the pelvic splanchnic nerves congregate with sympathetic fibers from the hypogastric nerve to form the pelvic plexus (Figure 1) [50].

The pelvic plexus is located retroperitoneally on both lateral sides of the rectum. The pararectal fascia and perirectal adipose tissue separates the lateral surfaces of the rectum from the pelvic plexus. The pelvic plexus pat-

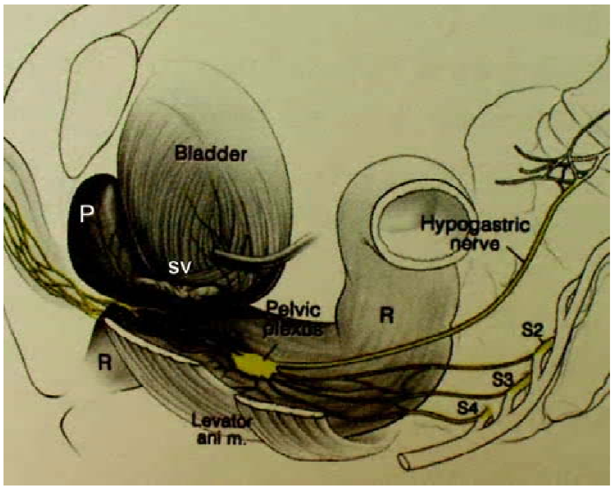


Figure 1. Schematic presentation of the lower urogenital tract neuroanatomy of the male. Parasympathetic nerves arise form S2 to S4. Hypogastric nerves and parasympathetic nerves merge to form the pelvic plexus on each side of rectum (R). Note the distribution of nerves around the seminal vesicle (SV) and prostate (P). The neurovascular bundle is shown to extend inferiorly to innervate corpus cavernosum. Reprinted with permission from Costello *et al*. [50].

tern shows a high interpersonal anatomical variation. Each ganglion at the pelvic plexus contains about 20 nerve cell bodies. The superior part is arbitrarily called the vesical plexus and the inferior part, the prostatic plexus. The pelvic plexus can extend as far as 1.5 cm–2.0 cm posterior to the dorsal edge of the rectum and 1.0 cm–1.5 cm superior to the rectovesical pouch (pouch of Douglas). Only histologic sections allow us to define the projections of pelvic plexus since it is very hard to identify the neural tissue amount and mass in the projections in macroscopic adult male anatomic dissections.

The pelvic plexus is intimately associated with the branches of the inferior vesical vein and artery. These vessels are particularly close to the lateral surfaces of the pelvic plexus (Figure 2). Nevertheless, adipose and connective tissue dissections show distinct separable layers of nerves and vessels posteriorly.

However, there are three surgically sound major projections from the pelvic plexus: 1) anterior, extending across the lateral surfaces of the seminal vesicles and infero-lateral surface of the bladder; 2) antero-inferior, extending to the prostatovesical junction and obliquely along the lateral surfaces of the prostate; 3) inferior, running between the rectum and posterolateral surface of the prostate. It is the inferior that is known as the neu-

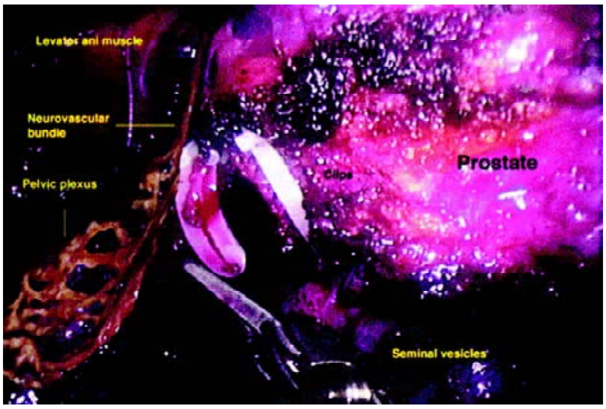


Figure 2. Note the location of the pelvic plexus, neurovascular bundle and left prostatic pedicle, which is clipped and divided. Reprinted with permission from Tewari *et al*. [65].

rovascular bundle of the prostate [49, 50, 55, 61–64] (Figure 1).

There are many cross-communications between these major projections and the pelvic plexus on both sides of the rectum. These connections mostly run within the fascial layer and their physiologic significance has not been clarified yet [49, 50, 57, 59, 60, 62–65]. For urological purposes, the inferior projection from the pelvic plexus and its connections to the pelvic plexus are especially important. Particular caution is needed when an incision of the posterior bladder neck is made. Because the pelvic plexus is very close, overzealous dissection of the posterior bladder neck may put some pelvic, vesical or prostatic plexus fibers at risk [65].

The control of the lateral pedicles of the prostate is a precarious step because the pelvic plexus lies posterolaterally (Figure 2). When performing this step, staying very close to the prostate surface may help to avoid neural damage [66]. Vattikuti Institute (Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA) claims that robotic/laparoscopic radical prostatectomy may be associated with a lower risk to the pelvic plexus because this is the only technique that allows for an antegrade approach (dissection beginning from the prostate base) to the dissection of the prostate surface [65].

## 3 Neurovascular bundle of the prostate and cavernosal nerves

Before the studies done by Walsh and Donker [46] on fetal specimens, the cause of ED after radical prostatectomies was not well understood. By tracing the autonomic innervation of the corpora cavernosa, Lepor *et al*. [47] showed that ED can occur secondary to injury to the cavernosal nerves. Classically, it was thought that these nerves branched from the pelvic plexus and ran as a plexus of small nerves within a prominent neurovascular bundle on the posterolateral border of the prostate, before piercing the urogenital diaphragm and descending along the lateral aspect of the urethra. They are intimately associated with capsular vessels of the prostate and they course outside the prostatic capsule [11–15, 47, 48, 67, 68]. These initial findings have since been supported by additional anatomic studies, which have further characterized the anatomy of the neurovascular bundle of the prostate. Detailed histological studies have revealed the cross-sectional profile of the neurovascular supply of the prostate and have shown that it runs through leaves of the lateral pelvic fascia. Eventually, the cavernosal nerves and the neurovascular bundle of the prostate have been used to describe the same neural structures.

New advancements in surgery, including the use of laparoscopic/robotic modalities and magnifying visual devices in open surgery, have enabled very precise nerve dissection. Nerve grafting and interposition to realign the neurovascular bundle after neurovascular bundle resections are now offered to patients to restate their potency [38–45]. However, despite all these advancements in nerve preservation or restoration, potency rates have remained unsatisfactory [41, 43–45]. Therefore, the classical knowledge of the neurovascular bundle of the prostate and the cavernosal nerves was challenged and revisited. It has been suggested that the neurovascular bundle of the prostate may not cover all of the cavernosal nerves and these unidentified nerves may be severed inadvertently during surgery [49, 50, 62].

To assist with our understanding of the neuroanatomy of the prostate area, we should be familiar with the fascias and their locations. Generally, the neural structures are covered with the fasciae around the prostate. Simply, the inferior extension of the pelvic plexus unites with several vessels to form a prominent neurovascular bundle of the prostate. The neurovascular bundle of the prostate descends along the postero-lateral border of the prostate. It extends laterally to the junction of the lateral pelvic fascia and pararectal fascia, and posteriorly to the dorsal layer of Denonvilliers' fascia, which forms a thick fibrous sheath separating the prostatic capsule from the rectum. Laterally and posteriorly, it is continuous with the pararectal fascia, and anteriorly with lateral pelvic fascia. The pararectal fascia extends along the lateral surface of the rectum, while the lateral pelvic fascia separates the levator ani musculature from the lateral surface of the prostate. At the prostatic midline, Denonvilliers' fascia exists as a single sheet, and widens laterally. At the junction of these three fasciae there are many fibrous tissue layers. The posterior and lateral aspects of the neurovascular bundle run through these layers. Denonvilliers' fasciae and the pararectal fasciae are separated from the anterior and lateral surfaces of the rectum by perirectal adipose tissue that shows a high degree of anatomic variation in amount [18, 30, 37, 49, 50, 59, 62, 69] (Figures 3 and 4).

More recently, there have been observations that refute the dogma that the cavernosal nerve is always within the neurovascular bundle of the prostate [49, 50, 62, 64, 65] (Figure 5). Proximally, the pelvic splanchnic nerve has a nice spray-like arrangement instead of appearing as a prominent thick bundle. Cavernosal nerves originate from the pelvic splanchnic nerve and course along the most caudal margin of the pelvic plexus not contained within the neurovascular bundle. At the level of the prostatovesical junction, thick identifiable branches originating from the pelvic splanchnic nerves do not reach the dorso-lateral margin of the bladder and prostate to form the prominent neurovascular bundle. Rather, they originate from the hypogastric nerves from the dorso-superior direction and course along the lateral aspect of the seminal vesicles.

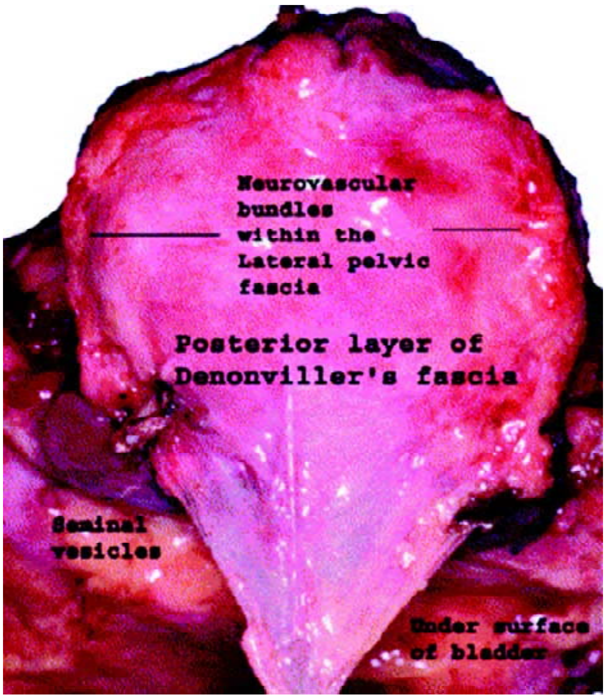


Figure 3. An anatomical undersurface view of the prostate to show Denonvilliers' fascia and neurovascular bundles. Reprinted with permission from Tewari *et al*.[65].

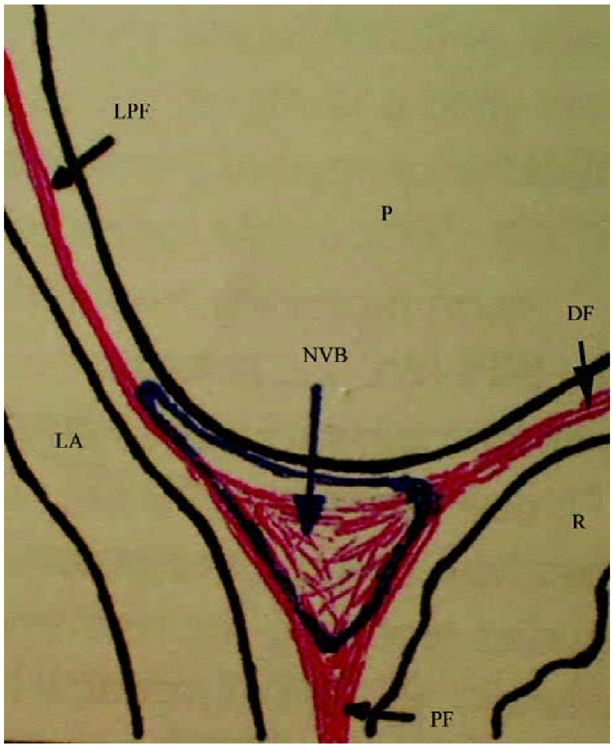


Figure 4. The fascial relationship of the neurovascular bundle (NVB) of prostate (P) showing the position of NVB and its relation to the prostate and rectum (R) and fascial layers. The widening Denonvilliers' fascia (DF) laterally fuses with the lateral pelvic fascia (LPF) and pararectal fascia (PF). The posterior and lateral divisions of the NVB run within these layers. Reprinted with permission from Costello *et al*.[50]. LA: levator ani muscle.

At the level or just below the prostatovesical junction some nerves run around and along the dorsal aspect of the prostate but they do not form a fascicle. Although the hypogastric nerve is a part of the sympathetic nervous system, hypogastric nerve branches contain ganglion cell clusters comprising autonomic ganglia at superior levels, for example, around the ureter [70]. Below this area, there is no surgically identifiable thick nerves to reach the dorso-lateral area of the prostate. This obvious gap in nerve supply extends almost 1 cm along the


Figure 5. An anatomical view of the nerves and the prostate after the urethra has been transected. Reprinted with permission from Tewari *et al*. [65].

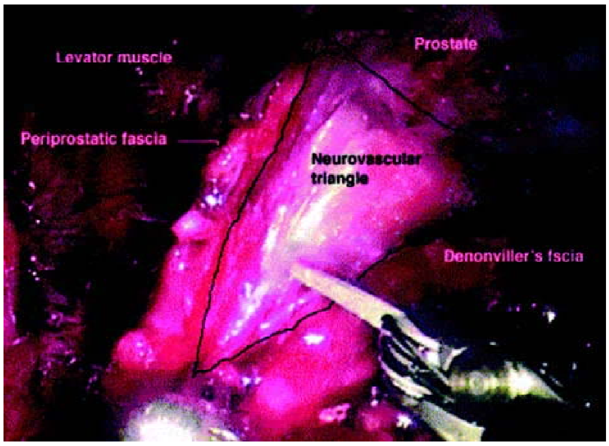


Figure 6. Computer enhanced figure showing the intraoperative relationship between the lateral pelvic fascia, Denonvilliers' fascia and the prostate and neurovascular bundles. Note the triangle of lateral pelvic fascia, prostate and Denonvilliers' fascia and their relation with the nerves. Reprinted with permission from Tewari *et al*. [65].

cranio-caudal axis except for several thin nerves that run from the dorso-lateral aspect of the prostate.

Right below this level, vascular structures appear at the dorso-lateral margin of the prostate. The lateral pelvic fascia covers these vascular structures. However, nerve components along these vessels are far fewer than those running dorsal and lateral to the vascular bundle. Thus, the neurovascular bundle does not appear to contain terminal components at this level. Instead, it is accompanied dorso-laterally by extra nerves.

In other words, the plexus of nerves running within the neurovascular bundle branch from the postero-inferior aspect of the pelvic plexus are inferior to the level of the tip of the seminal vesicles (Figure 2). On branching from the pelvic plexus these nerves are spread significantly, with up to 3 cm separating the most anterior and most posterior nerves. The nerves located most anteriorly are intimately associated with the seminal vesicle, coursing along the posterolateral surface, while the nerves located posteriorly run dorsal to the postero-lateral verge of the seminal vesicle. Generally, most of the neurovascular bundle descends posteriorly to the seminal vesicle. The nerves converge en route to the mid-prostatic level, forming a more condense neurovascular bundle, only to diverge once again when approaching the prostatic apex [49, 50, 62, 64] (Figure 6).

Therefore seminal vesicles are an important step in radical prostatectomy. The posterior surface of the seminal vesicle is not vascularized and a surgical plane between the posterior layer of the Denonvilliers' fascia, and the seminal vesicle could be easily developed. Vessels often approach the seminal vesicle laterally and there is often one artery traveling on the anterior surface of the seminal vesicle between the superficial layers of Denonvilliers' fascia. In dissection, the key is to get to the surface of the seminal vesicles and avoid dissecting outer layers. Sharp dissection instead of coagulation should be preferred in this area [71]. The bulk of the pelvic plexus and its main branches are located laterally and posteriorly to the seminal vesicles. Therefore, the seminal vesicles should be used as an intraoperative landmark to avoid injuring the pelvic plexus. Some believe that because the neurovascular bundle is very close to the tip of the seminal vesicle, an initial dissection behind the bladder leaves a bloodless area to ease the neurovascular bundle dissection [25, 27, 34, 72]. However, Tewari *et al.* [65] claim that laparoscopic or robotic surgery enables very delicate dissection of the seminal vesicle without prior retrovesical dissection. Another point to note relates to the traction of the seminal vesicle during surgery. Excessive traction of the seminal vesicle may tether the branches from the pelvic plexus medially. Thus, vessels should be controlled on the seminal vesicle to avoid the risk of injuring nerves [65].

The nerves running in the neurovascular bundle innervate the corpora cavernosa, rectum, prostate, and levator ani musculature. The last three also receive a vascular supply from vessels coursing in the neurovascular bundle. Artery and nerve branches supply the anterolateral wall of the rectum from the prostatic apex to the mid-prostate level. Nerves running in the neurovascular bundle pass through slit-like openings in the lateral pelvic fascia to innervate the superior and middle sections of the levator ani. Many nerve and vascular branches pierce the lateral pelvic fascia distally to supply the inferior portion. The nerves innervating the posterior aspect of the prostate are intimately associated with the capsular arteries and veins of the prostate. These structures penetrate the prostatic capsule along its base, mid-portion and apex [49, 50, 62, 64].

The constituents of the neurovascular bundle of the prostate are organized into three functional compartments. The neurovascular supply to the rectum is generally in the posterior and postero-lateral sections of the neurovascular bundle, running within the leaves of Denonvilliers' fasciae and the pararectal fasciae. The levator ani neurovascular supply is in the lateral section of the neurovascular bundle, descending along and within the lateral pelvic fascia. The cavernosal nerves and the prostatic neurovascular supply descend along the posterolateral surface of the prostate, with the prostatic neurovascular supply most anterior. Part of this anterior compartment runs ventral to Denonvilliers' fascia. The functional organization of the neurovascular is not absolute, and is less pronounced proximally at the levels of the seminal vesicles and the prostatic base. In addition to the nerves descending within the neurovascular bundle, a scattering of nerves extends from the medial margin of the neurovascular bundle to the prostatic midline. The deepest nerves innervate the anterior surface of the rectum at the level of the prostatic apex. The more superficial nerves descend posterior to the prostatic apex and merge laterally with the neurovascular bundle [49, 50, 62, 64] (Figure 7).

Nerve graft interposition from the sural nerve after neurovascular bundle removal has recently been offered by Kim *et al.* [38]. However, the report they compiled after a 1-year-long follow-up revealed that successful vaginal penetration had occurred in only 33 % of patients [41, 43]. Takenaka *et al.* [49] developed the nerve graft interposition technique by adding intraoperative electrical stimulation to clearly identify the cavernosal nerve. Unfortunately, they also admit that their success rate is no higher than that of Kim *et al.* [38]. These recent elegant neuroanatomical studies may enlighten these disappointing results. Takenaka *et al.* [49, 62] observed that they did the cranial end anastomosis to the hypogastric nerve branches rather than the pelvic splanchnic nerve branches in human fresh cadavers. But how can then be a 30 % success rate if anastomosis is performed to hypogastric nerve branches? They thought that the hypogastric nerve in men contained sympathetic and parasympathetic elements. Finally, they recommended intraoperative electrical stimulation in the dorsal, lateral, and caudal areas (including the surgically created neurovascular bundle) for the best cranial anastomosis.

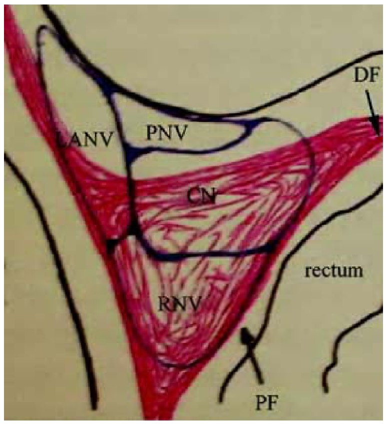


Figure 7. The functional organization of the neurovascular bundle, neurovascular supply to the rectum (RNV), Denonvilliers' fascia (DF), pararectal fascia (PF), neurovascular supply to the levator ani (LANV), neurovascular supply to the prostate (PNV) and the cavernosal nerves (CN). Reprinted with permission from Costello *et al.* [65].

Recently, there has been much ongoing research into how to define cavernosal nerve mapping by intraoperative electrical stimulation [39, 44, 73–82]. This is particularly important in understanding the interpersonal cavernosal nerve topographical variations. Surgical dissection of the cavernosal nerve can be even more troublesome at the prostate apex than at the cranial end. Takenaka *et al.* [49, 62] observed that the surgically defined neurovascular bundle is often likely to differ from the actual axial course of the cavernosal nerve passing through the pararectal space and the rectourethral muscle. They identified a statistically significant interindividual variation of the topography of the cavernosal nerve at the apex of the prostate (three of eight cadavers). They stated that if we approach the apex of the prostate histologically in three different axes, namely frontal, sagittal and axial, we would observe interindividual variations. For example, a frontal course shows a relatively stable path at the 9–10 o'clock positions. However, sagittal and axial sections showed a shift from the 7–8 o'clock to the 10–11 o'clock position of the cavernosal nerves at the apex of the prostate.

Another critical finding in the recent neuroanatomical studies is the rectourethralis muscle and its close association with cavernosal nerves [59, 60, 62] (Figure 8). In the retropubic radical prostatectomy, rectourethral muscle should be incised near the apex to protect the nerves passing through the muscle mass (Figure 9). While managing the rectourethralis muscle, every effort should be taken to not put excessive traction on the muscle through the urethral catheter or use forceps to preserve the nerves. Some studies indicated that nerve-sparing approaches could obtain a better continence rate [83–85].

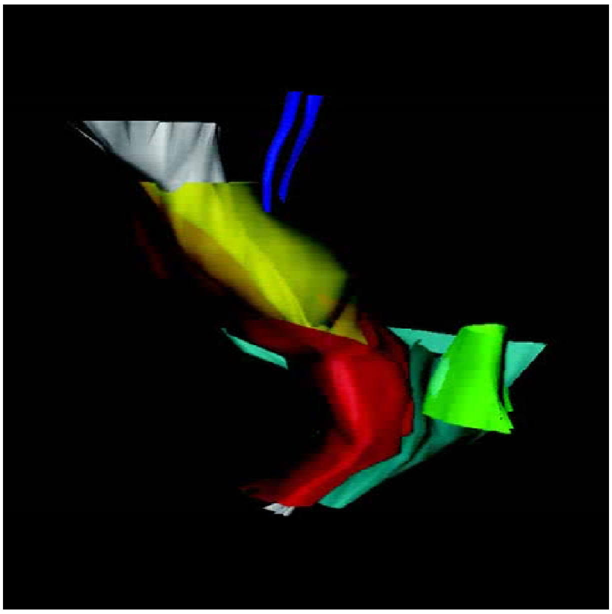

Figure 8. A 3-dimensional computerized image of the fetal male lower urogenital tract based on serial histological sections. Note the relationship between the levator ani muscle (turquoise color), external urethral sphincter (red), rectourethralis muscle (green), prostate (yellow), urethra (white) and vas deferense (blue).

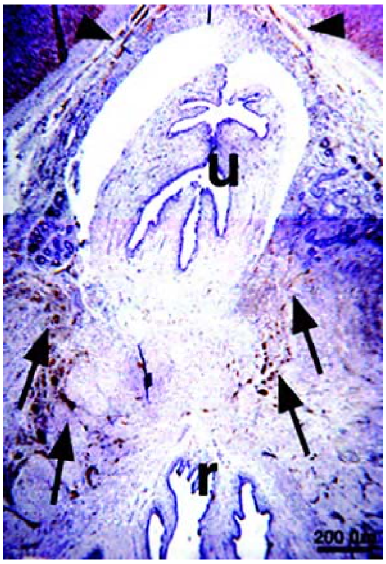


Figure 9. A cross-sectional histologic image of the posterior urethra in a male human fetus immunostained with nerve specific S-100 antibody. Arrowheads (▲) point the nerves (brown color) anterior to the urethra (u) and beneath the pubic bone. These branches of neurovascular bundle of prostate eventually innervate the corpus cavernosum. Arrows (↑) note the neurovascular bundle of prostate on both sides of the rectum (r). Scale bar = 200 µm.

Therefore, Strasser *et al.* [53] proposed that the neurovascular bundle could contain motor and/or autonomic nerves to the rhabdosphincter. However, recent detailed neuroanatomical studies concluded that these two nerves follow separate courses and that the somatic nerve is a different intra-pelvic nerve while the autonomic nerve is in the neurovascular bundle [18, 59, 60].

Terada *et al.* [86] reported that the neurovascular bundle was macroscopically severed on 16 sides, and that a positive intracavernous pressure increase after intraoperative electrical stimulation was detected in five cases. This can be explained by the recent neuroanatomical finding that showed that the cavernous nerve is not contained in the neurovascular bundle. In fact, it is located in the fascia, so deep that some non-nerve-sparing surgeries may result with inadvertent nerve-sparing surgery [87]. On the other hand, a very delicate nerve-sparing procedure could end with ED, because the proximal or distal ends could be damaged. Bhandar *et al.* [61] proposed a different approach for robotic/laparoscopic radical prostatectomy that did not involve opening the periprostatic fascia, thus leaving all small cavernosal nerves intact within the fascia. They called the neurovascular bundle and cavernosal nerves the "veil of

Aphrodite" and developed a technical modification to the nerve sparing procedure that spared the main neurovascular trunk, but dissected a wide band of periprostatic fascia extending from the reflection from the pelvic fascia proximally, puboprostatic ligaments distally, Denonvilliers' fascia posteriorly and free edge anteriorly.

The cavernosal nerves and several small vessels pierce the urogenital diaphragm posterolateral aspect of the membranous urethra, before penetrating the posterior aspect of the corpora cavernosa. Right around the penile hilum, there are some intercommunicating branches between the dorsal nerve of the penis and the cavernosal nerves. It is hypothesized that there is a redundant neural system to maintain the erectile function when cavernosal nerves are severed (Figure 10). However, the functional significance of these intercommunicating branches has not been studied and this hypothesis has yet to be confirmed [55, 57, 62].

Although neurovascular bundle dissection techniques have been developed in recent years along with advancements in laparoscopic/robotic assisted radical prostatectomy, the ideal energy source for dissection is still lacking. Open surgery advocates the avoidance of electrosurgical or ultrasonic energy sources but laparoscopic/robotic assisted surgical techniques are very much dependent on them. In a recent study by Ong *et al.* [71], electrosurgical or ultrasonic hemostasis energy source related thermal injury to cavernosal nerves has been reported to jeopardize erectile function in a canine model. They have also developed an alternate method for the use of ultrasonic shears in conjunction with a fine-angled clamp, which keeps the active element away from the critical structures. Therefore, apart from advancements in surgical neuroanatomy, refinements in the making of surgical instruments also appear to have contributed to the improved success rates of radical prostatectomies.

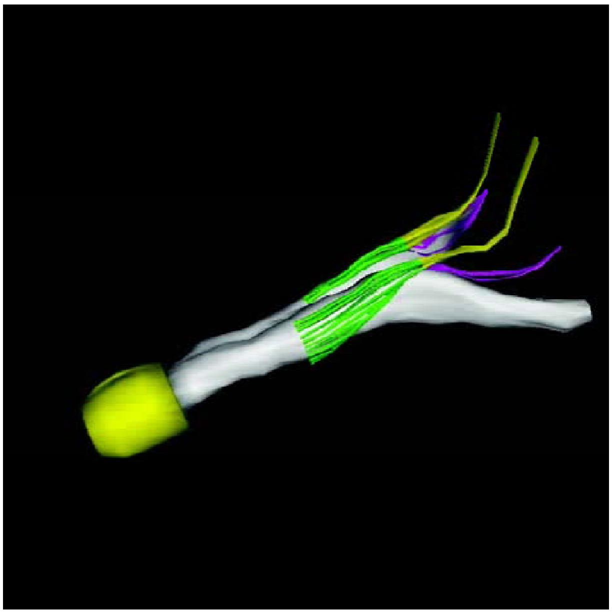

Figure 10. A 3-dimensional computerized image of a fetal penis, cavernosal nerves and dorsal nerve of the penis based on serial histological sections. Note the relationship between the dorsal nerve of the penis and cavernosal nerves (magenta color). The dorsal nerve of the penis (which is not immunostained with neuronal nitric oxide synthase (nNOS [yellow color]) turns into an nNOS positive nerve (green color) right at the level of the corporal hilum. The white color shows the corpus cavernosums and the yellow color represents the glans penis. The cavernosal nerve sends some branches to the dorsal nerve of the penis to change its immunostaining character into nNOS positive.

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