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Anatomy of autonomic nerve component in the male pelvis: the new concept from a perspective for robotic nerve sparing radical prostatectomy

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Abstract The DaVinci Robot (Intuitive Surgical, Sunnyvale California) with its magnified 3-D vision and multi-jointed wristed instruments enabled us to perform radical prostatectomy with consideration for the pelvic anatomy. In the present paper, we review the pelvic autonomic neuroanatomy with respect to robotic prostatectomy and demonstrate the procedures and critical points of nerve-sparing robotic radical prostatectomy based on novel anatomic concepts. Microscopic and macroscopic data were acquired from 30 fresh and 25 fixed male cadavers. A video study of 205 surgeries was performed for establishing the anatomy relevant to robotic prostatectomy. From a practical standpoint, we could group the relevant neural tissue into three broad zones: (1) proximal neurovascular plate (PNP), (2) predominant neurovascular bundles (PNB), (3) accessory distal neural pathways (ANP). Autonomic ganglion cells existed widely not only in nerve components but also along the viscera. The critical areas of nerve sparing surgery were the distal end of PNP, the entire PNB, and the circumference of the apex. Interindividual differences of cell counts were evident in all sites. Based on these concepts, we established the Athermal Robotic Technique (ART) for nerve sparing prostatectomy. Surgical and oncological outcomes were not mature but feasible. These tri-zonal

and ganglion cell concepts may be of benefit to new surgeons undertaking nerve-sparing robotic radical prostatectomy.

Keywords Neural anatomy · Autonomic nerve · Robotic prostatectomy · Athermal technique · Nerve sparing

Introduction

Although the mapping for nerve-sparing during radical retropubic prostatectomy was laid down by pioneering contributions by Walsh et al. [20], there are some spaces for reemphasis of these anatomic principles in the robotic prostatectomy era. During open prostatectomy, all of the anatomic structures around the prostate could not be seen. Even though the anatomy around the pelvis was known, because of visual angles and magnification, e.g., the fine structure in the posterior aspect of the prostate remained elusive during surgery. Direct vision of anatomy is sometimes not possible during open radical prostatectomy, thus there has been a large gap between surgery and anatomy.

Robotic prostatectomy started in 2000 [11], and is estimated that 33,500 cases will be performed during 2006 in the World. It is increasing rapidly, and is growing to be an important option for the management of localized prostate cancer [5]. It is possible to view almost all of the pelvic anatomic structures during robotic prostatectomy. This enables the surgeon, in theory, to perform the operation with respect to the anatomic findings using the multi-jointed instruments, compared with the conventional laparoscopic radical prostatectomy.

We therefore felt the need to revisit the anatomic foundations in order to understand the macroscopic and microscopic findings and tailor them to the robotic approach. In the present paper, we focus on the anatomy of autonomic nerve component, illustrate the neuroanatomy around the prostate, and elucidate the proce-

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dures and critical points necessary for our nerve-sparing robotic radical prostatectomy.

Materials and methods

The data for this study were acquired from anatomic studies involving 30 fresh and 25 fixed male cadavers, which were more than 50 years of age, did not have any previous pelvic or urethral surgeries, and were known to have normal prostates and urinary bladders. Furthermore, we reviewed video studies from 205 nerve-sparing robotic radical prostatectomies performed by a single surgeon (AKT).

Cadaveric studies

Fixed cadaver dissections

Twenty-five male cadavers were collected at Department of Anatomy at Medical University of Innsbruck, Austria, and at Sapporo Medical University, Japan. The aim of these experiments were (1) to mimic robotic prostatectomy and provide visual clues to location of pelvic plexus in relationship to lateral aspect of bladder neck, seminal vesicles, and (2) to demonstrate the neural structures histologically including autonomic nerve fibers and ganglion cells. Using fixed cadavers, it was difficult to reproduce the surgical scenes completely and to dissect the precise structures of the thin fascias and nerve fibers, because of severe degeneration by the fixation.

The pelvic plexus, nerve bundles and periprostatic fascia were labeled with China ink (carbon particle suspension) to identify them during specimen trimming, embedding and sectioning. Specimens included all parts of the membranous urethra, the dorsal half of the prostate and small parts of the levator ani, bladder, seminal vesicle and rectum. After routine processing for paraffin embedding, semi-serial horizontal, but sometimes sagittal and frontal sections of 10 μ m were cut at 1-mm interval. Most sections were stained with hematoxylin and eosin, while others were stained with S-100 as a neural marker, tyrosine hydroxylase (TH) as a sympathetic nerve marker [4], and peptide histidine isoleucine (PHI) as a parasympathetic marker [14] to delineate the precise location and relationship of this neural tissue.

Fresh frozen cadaver dissections

Thirty male cadavers were collected at the Department of Anatomy at Sapporo Medical University, Japan, and at the Cornell Institute of Robotic Surgery, New York. The emphasis of fresh frozen cadaveric studies was to bring attention to the neural and fascial anatomy around the prostate according to the real proce-

dures of robotic prostatectomy. Especially, in 12 cadavers, the dissections were performed using a laparoscopic camera, light source, video monitor and hand equipment [17]. Then the course of the nerves was further traced by open dissection using 2.5 \times surgical loops.

Patient studies

Between January 2005 and December 2005, 205 patients underwent robotic nerve-sparing radical prostatectomy at Cornell Institute by a single surgeon (AKT). This technique is firmly based on the foundations of Menon's VIP (Vattikuti Institute Prostatectomy) technique for clinically localized prostate cancer [11, 12, 18]. Based on the above mentioned findings, we changed some procedures to achieve better nerve-sparing. We call this technique the Athermal Robotic Technique (ART) [19]. In terms of our anatomic study, we reevaluated each procedure of this technique in 205 video collections.

Fundamental principle of neuroanatomy

The autonomic nerves taken in this paper are the hypogastric nerve (HGN) and the pelvic splanchnic nerve (PSN). The roots of these nerves are usually out of the surgical field. However, the course of these nerves is important and should be understood because these nerves are responsible for erectile function, ejaculation, and urinary continence.

The HGN is thought to be the main pathway of sympathetic nerve fibers. The superior hypogastric plexus divided into bilateral HGNs below the bifurcation of the abdominal aorta. The HGN ran downward along the sacrum behind the ureter, it coursed a ventrally and laterally, and joined the nerve fibers from the PSN.

The PSN is thought to be the main pathway of parasympathetic nerve fibers and the origin of the cavernous nerve fibers. It emerged from the second, third, and fourth sacral spinal nerves. The PNS coursed almost vertically to the sacrum (Fig. 1).

The functional classification of these nerves was actually not very simple. Butler-Manuel et al. [2] reported the uterosacral ligament containing the HGN showed positive immunostaining of both TH as a sympathetic nerve marker and vasoactive intestinal polypeptide (VIP) as a parasympathetic nerve marker. We demonstrated that TH-positive and PHI (as a parasympathetic marker)-positive ganglion cells (GCs) were intermingled in one ganglion attaching to the posterolateral surface of the prostate, and TH-positive cells were seen in all ganglion cell clusters in the male pelvis, e.g., the mean TH-positive cell ratio in a ganglion cell cluster was 62% in HGN and 36% in PSN [15]. Simple classification of macroanatomic pelvic

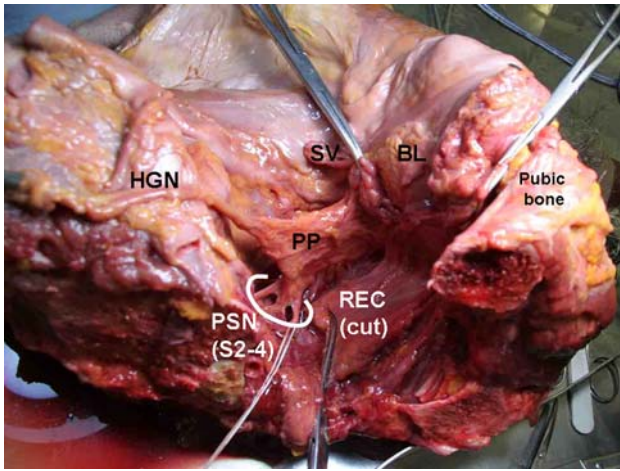


Fig. 1 Inside view of left autonomic nerves in the male pelvis. The rectum (*REC*) is cut and pushed down, and the seminal vesicle (*SV*) and bladder (*BL*) are lifted up. Pelvic splanchnic nerve (*PSN*) courses almost vertically to the sacrum. *PP* Pelvic plexus, *HGN* hypogastric nerve. Fresh cadaver, cut sagittally at 5 cm right from the midline

autonomic nerve components as sympathetic or parasympathetic would seem misleading.

Tri-zonal concept (Fig. 2)

In the classical concept, the neuroanatomy for nerve sparing radical prostatectomy and radical cystectomy has been described in the limited area, i.e., only posterolateral aspect of the prostate and the seminal vesicle [9]. Many urologists have imagined the preserved neural component to be a bundle-like structure. However, recent studies report the origin of the cavernous nerve is a distal branch of the PSN. Also these nerve fibers join the HGN with a spray-like arrangement

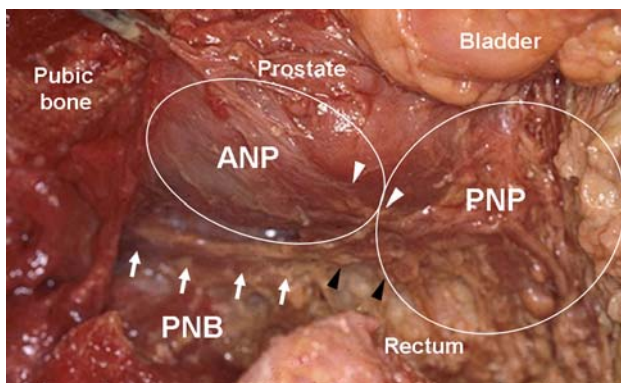


Fig. 2 The tri-zonal concept of proximal neurovascular plate (*PNP*), predominant neurovascular bundles (*PNB*, white arrows), and accessory distal neural pathways (*ANP*). White arrowheads indicate the continuity of *PNP* and *ANP*, and black arrowheads are *PNP* and *PNB*. Fresh cadaver

along the lateral wall of the rectum [3, 16]. We should understand the pelvic neuroanatomy in the wider area to perform the nerve-sparing surgery. Since we approach the prostate in an antegrade fashion during robotic prostatectomy, we need to understand the anatomy around the proximal and posterior aspect of the prostate. From a practical standpoint, the relevant neural tissue that we encounter during robotic prostatectomy can be grouped into three broad zones, the proximal neurovascular plate (*PNP*), the predominant neurovascular bundles (*PNB*), and the accessory distal neural pathways (*ANP*) (Fig. 2).

Proximal neurovascular plate

The *PNP* is an integrating center for the processing and relay of neural signals. This plate is located lateral to the bladder neck, the seminal vesicles and branches of the inferior vesical vessels. It is thick in the center near the seminal vesicles. Specifically, depending on variations in anatomy and prostate size, the *PNP* is located 5–10 mm (average 5 mm) lateral to the seminal vesicles, 2–7 mm (average 3 mm) thick, 5–25 mm (average 7 mm) wide and 4–30 mm (average 9 mm) in length. It is located within 4–15 mm (average 6 mm) of the bladder neck, within 2–7 mm (average 5 mm) of the endopelvic fascia and overlaps 0–7 mm (average 5 mm) of the proximal prostate.

The *PNP* extends posterolaterally to the base of the prostate and cavernous nerve candidates course in the most distal part. Distally the plate continues as the classical neurovascular bundle while a few branches travel through the fascial and capsular tissue of the prostate as accessory pathways.

After the transaction of the seminal vesicle in the mimic dissection of surgery, the *PNP* intermingles with the vessel pedicle of the prostate (Fig. 3). It is impossible to separate them clearly.

Predominant neurovascular bundles

This corresponds to the classical bundle, however, it carries the neural impulses not only to the cavernous tissue, but also urethral sphincter and to the end of the levator ani muscle. The *PNB* is enclosed within the layers of levator fascia and/or lateral pelvic fascia and is located at posterolateral aspect of the prostate. The course varies from base to the prostatic apex.

It occupies the groove between prostate and rectum, and is thickest at the base and has the most variable course and architecture near the apex. Our anatomic study [15] show the cavernous nerve candidate continued to the *PNB* through the distal part of the *PNP*. The fibers from *HGN* are more ventral and from *PSN* are more dorsal at the base of the prostate (Fig. 4).

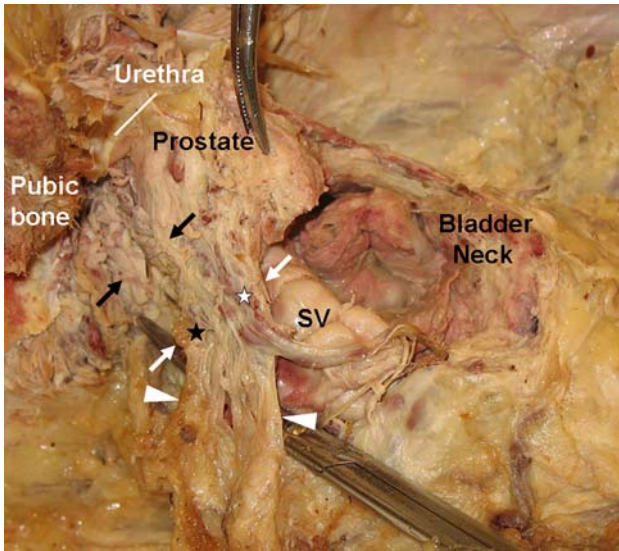


Fig. 3 The relationship between seminal vesicle (SV) and PNP according to the procedure of robotic prostatectomy. Bladder neck transection is performed, and the prostate is lifted up by the forceps. PNP (arrowheads) is intermingled with vascular pedicle of the prostate. Black arrow, PNB; White arrow, intermingled structure of vascular (white star) and neural (black star) component. Fixed cadaver

Accessory distal neural pathways

There have been discussions about putative accessory besides PNB around the prostate [8, 10, 13]. They were

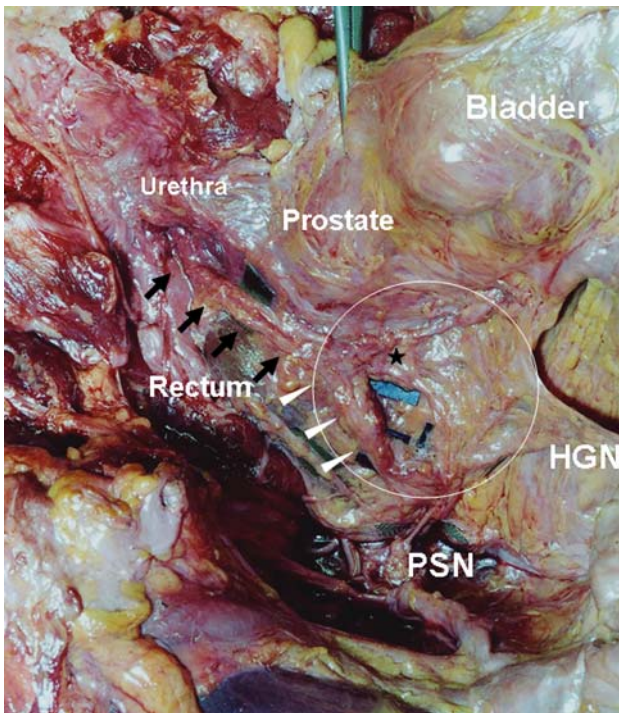


Fig. 4 Cavernous nerve candidates (arrowheads) from the root of pelvic splanchnic nerve (PSN). The fibers (star) from hypogastric nerve (HGN) is located more ventral than cavernous nerve candidates. White circle, PNP. Fresh cadaver

usually described within the layers of the levator fascia and/or lateral pelvic fascia, on the anterolateral and posterior aspect of the prostate, which may serve as additional conduits for neural impulses. As mentioned in the previous section, many cadavers (75%) had the proximal third of prostate covered by the PNP where these nerve fibers were most prominent.

Additional pathways were noted posteriorly. In 25% of specimens, a posterior pathway arose from medial aspect of the PNP near the base of the seminal vesicles. Other accessory branches occasionally formed an apical plexus on the posterolateral aspect of the prostatic apex and urethra incorporating fibers from both the PNB. This distal plexus was observed in 35% of cases, penetrating the recto-urethral muscle (Fig. 5). This could potentially act as a neural pathway for not only cavernous tissue but also the urethral sphincter. It could also serve as a safety mechanism for providing backup neural crosstalk between two sides. In 10% of cases the fibers were circumferential at the apex.

Distribution of autonomic ganglion cells

In nerve-sparing prostatectomy, major components for preservation included nerve bundles. However, GC have received little consideration in this strategy, although surgical damage to GCs can result in a much worse outcome than injury to nerve fibers, since GCs cannot repair themselves [7]. To our knowledge, we first reported the distribution of the autonomic GCs in the male pelvis [15]. As shown in Table 1, autonomic CG existed not only in the macroanatomic nerve components but also along viscera.

We could detect many GCs in the PNP and the PNB. In the ANP, some GCs exist in bladder/prostate junction, dorsal aspect of seminal vesicle, dorsal aspect and near apex of the prostate. On the other hand, there were almost no GCs in ventral aspect of the prostate and

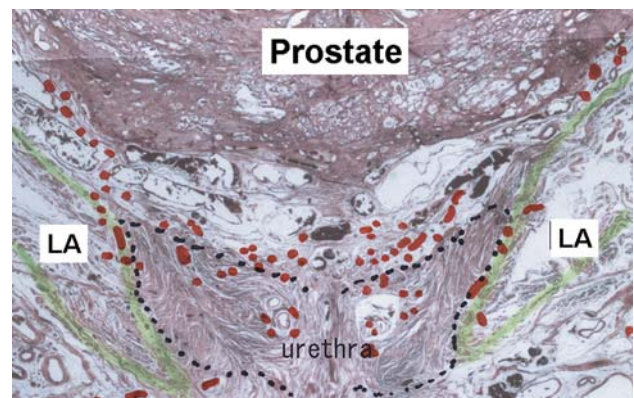


Fig. 5 Frontal section through the posterior aspect of membranous urethra. Many nerve fibers (red ink) which course along or in the rectourethral muscle (enclosed by dots), form the posterior plexus behind the apex and urethra. LA lavator ani. Hematoxylin and eosin stain

Table 1 Pelvic ganglion cell numbers and distribution in male hemi-pelvis

Specimen	M1	M2	M3	M4	M5	M6	M7	Average no.
PNP	1,113	332	250	–	534	411	575	535.8 ± 307.7
PNB	698	230	448	66	908	96	500	420.9 ± 313.3
ANP								
Bladder, dorsal aspect	172	48	44	0	10	162	567	143.3 ± 199.1
B/P junction	78	280	135	53	50	232	211	148.4 ± 93.2
SV, dorsal aspect	163	25	78	–	212	45	273	132.7 ± 99.2
Prostate, dorsal aspect	155	101	0	65	230	15	535	157.3 ± 184.7
Prostate, ventral aspect	0	0	10	–	3	0	0	2.2 ± 4.0
Prostate, near the apex	15	0	10	109	177	104	387	114.6 ± 136.8
Other site								
HGN	604	945	276	–	248	–	825	579.6 ± 314.8
PSN	1,262	396	223	84	853	285	765	552.6 ± 420.9
Sacral sym.ganglion	1,566	687	–	249	1,092	849	1,884	1054.5 ± 596.2
Levator ani	0	0	–	16	0	3	0	3.2 ± 6.4

levator ani muscle. The critical areas for cutting plane where many GCs exist close or attaching, were the distal end of the PNP intermingling with vascular pedicle, the entire PNB along posterolateral aspect of the prostate (Fig. 6), and the circumference of the apex. The anterolateral ANP seems to be merely accessory fibers. The interindividual differences which were evident in all sites are shown in Table 1. This might lead to varying post-operative outcomes with respect to patient quality of life (QOL).

Surgical procedure

Based on the aforementioned findings, we explain the anatomically critical points during surgery according to each procedure. The procedure below is the ART of nerve-sparing radical prostatectomy.

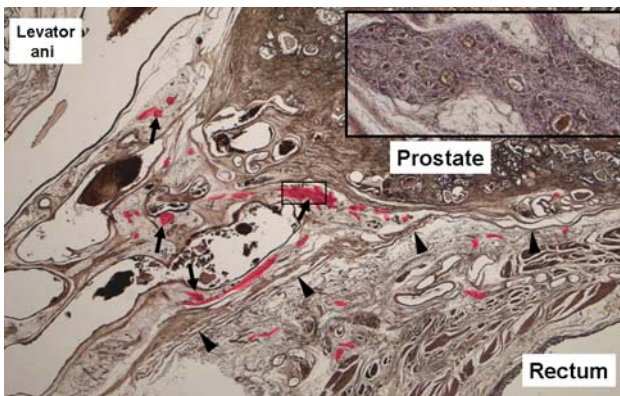


Fig. 6 Ganglion cells in PNB along or attaching to the posterolateral aspect of the prostate. The square at upper right corner is the magnification of the small one in the center. Red, neural component; arrows, ganglion cell cluster; arrowheads, Denonviller's fascia. Hematoxylin and eosin stain

Dissection of the endopelvic fascia

Holding the lateral aspect of the prostate medially, we cut the endopelvic fascia athermally inside of the fascial tendinous arch of the pelvis using the tip of the scissors. The incision should not be too proximate, not too deep, and not to anterior. If the thermal dissection is extended too far, PNP, PNB and ANP may be damaged. Because we separate the apex in the final step, it is acceptable if we can ligate the dorsal vein complex at the middle of the prostate.

Dorsal vein stitch and bladder neck stitch

The dorsal vein stitch is placed only at the middle of the prostate using 0-Vicryl on CT-1. At this time we don't suture any stitch above the apex. This stitch is placed on the anterior surface of the prostate between bilateral cutting edges of the endopelvic fascia. If the stitch is too deep, the ANP can get damaged, and the neural component might be lifted ventrally by the stitch.

We place the stitch about 1 cm proximally to the imagined cutting line of the bladder neck and more in the midline strip. If stitch is too proximally, and too deep, the PNP and the ANP can get damaged, respectively.

Bladder neck transaction

First, the assistant holds the aforementioned bladder neck stitch proximally. We use a bimanual pinching technique to define the bladder-prostate junction. However, the fatty tissue of the bladder may hang over in this area because the dorsal vein stitch and bladder neck stitch is minimal as not to injure the nerve components. Although some surgeon report starting the bladder neck dissection laterally, we start electrocautery dissection adjacent to the midline, because of the presence of many vessels and neural structures at the lateral

aspect of the bladder neck. After the Foley catheter is seen, the balloon is deflated and the tip of catheter is pulled out ventrally by the assistant. The mucosa of bladder neck is cut along its fold except for the cases with a large median lobe. Then we gradually divide the posterior bladder neck with electrocautery adjacent to the midline, confirming it laterally occasionally using bimanual pinching. Electrocautery dissection is not used laterally. The lateral pedicle, where it is very close to the distal end of PNP, is preserved at this time.

Seminal vesicle and vas dissection

We encounter the translucent tissue, i.e., anterior layer of Denonvillier's fascia, adjacent to the midline, and can see the ampulla of vas deferens and seminal vesicles through it, that is called "the window sign" [6]. After the left assistant pulls up the base of the prostate by the atraumatic forceps, the bilateral vas deferens are dissected and cut. The right assistant pulls the proximal end of the vas deferens proximally. We start to dissect the seminal vesicles from the medial aspect without electrocautery because of the presence of small vessels. Some seminal vesicle arteries can be seen in the middle and lateral aspect. Small clips are preferred to cut the vessels. We dissect the lateral aspect of the seminal vesicles athermally not to injure the PNP.

Separation of the prostate and rectum

The assistant pulls the prostate and the seminal vesicle ventrally. To avoid the neural injury of the PNP, PNB, and posterior ANP, it was very important to cut Denonvilliers' fascia at the middle line. After that, we shave off the fascial structures which might contain posterior ANP at midline from the posterior wall of the prostate until a little short of the apex. We must not go to the apex at this time to avoid rectal injury and posterior nerve plexus injury. Then, we extend the space laterally without electrocautery. The relationship between the lifted prostate and nerve plate looks like "the train on the railroad".

Control of pedicle

This is one of the most critical procedures during surgery, because the distal end of the PNP and the PNB intermingle with the vascular pedicle (Fig. 3). Furthermore the issue gets even more complex when we have to save the ANP, which is present in the anterolateral aspect of the prostate. We avoid electrocautery and bulldog clamp [1] during this phase of operation. The first key is to stay close to the prostate, where the pedicle and neural component are gradually apart resembling a "Y-shape". The next step is to dissect the vessels in smaller packets using the EndoWrist (Intuitive Surgical, Sunnyvale, CA, USA) forceps, to identify them entering into

the prostate and to control them athermally using small clips. This meticulous separation is necessary, because no clear border between pedicles and neural component exist. Since orientation, size and extent of the pedicle varies significantly based on the prostate size, individual variations in anatomy and cancer induced neo-vascularization, appropriate time should be invested to gently freeing the prostate base. Dissection gets further complicated due to competing goals for staying away from the cancer containing prostatic capsule. It is crucial to stay right on the surface of prostatic fascia to avoid inadvertent entry in the deeper plane, which may compromise cancer control, especially if there is pathological capsular penetration.

Release of predominant neurovascular bundles

Once prostate is freed from the vascular pedicle, it becomes more mobile by the support of the assistant. It can be rotated to expose a potentially avascular triangle which is bounded posteriorly by Denonvilliers' fascia, laterally by levator fascia/lateral pelvic fascia, and medially by prostatic capsule (Fig. 7). Once this triangle leaves the prostate, the dissection appears very elegant and usually can be done by gentle pushing of the prostate.

We avoid traction injury to the PNB by excessive pull and blunt dissection. If patients have a small (5%) focus of less than Gleason 7 prostate cancer, we might preserve the anterior ANP, i.e., Veil technique by Menon's group [13].

Apical transaction

This is also one of the most critical procedures, because almost all the nerve fibers and GCs converge to the apex circumferentially. The assistant pulls the prostate ventrally again. We perform sharp meticulous dissections not only at the PNB but also the posterior aspect of the

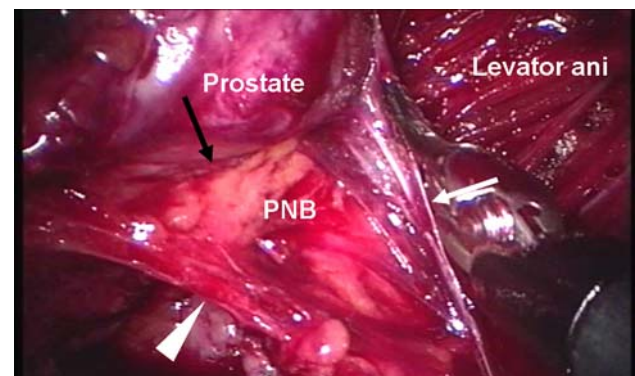


Fig. 7 Release of PNB. We should imagine PNB as a triangle. Arrowhead, Denonvilliers' fascia; white arrow, levator fascia/lateral pelvic fascia; black arrow, prostatic capsule

apex, i.e., posterior plexus (Fig. 8). It is very important to dissect the neural component together with rectourethral muscle from the various aspects slightly.

After the complete apical separation from the PNB and posterior plexus, we stitch the dorsal vein complex at the apex with a small needle. We should assume that the neural components exist almost circumferentially except for the dorsal vein complex.

Viewing the apex from various aspects and imaging the shape of the apex, we cut the dorsal vein complex and anterior wall of the urethra. Finally, the posterior wall of the urethra is sharply cut in order to avoid injury to the PNB and posterior plexus.

Urethral anastomosis

The running suture is done using a slight modification of the Menon's group [11]. The tails of a 9 inch dyed and 9 inch undyed 3-0 Biosin on a small needle are tied each other ten times, making a bulky knot in the center. The anastomosis starts from the outside-in fashion at the 4-o'clock of the bladder neck and inside-out of the urethra. The first urethral stitch is carefully performed as not to catch the preserved neural structures.

Results

The mean age in 205 cases of robotic radical prostatectomies using ART is 60.4 years old. The operating time ranged 2-3 h and blood loss was less than 150 ml. Post operative blood transfusion was 3%, and hemoglobin concentration and hematocrit at discharge was 13 g/dl and 38%, respectively. Pain score (Face scaled) [21] at day 1 was 2-3. Urinary catheter was placed during 4-14 days (median, 7 days). Ninety-eight percent of patients were discharged within 24 hours. Continence rate with 0-1 security pad was 48% at 6 weeks and 58% at

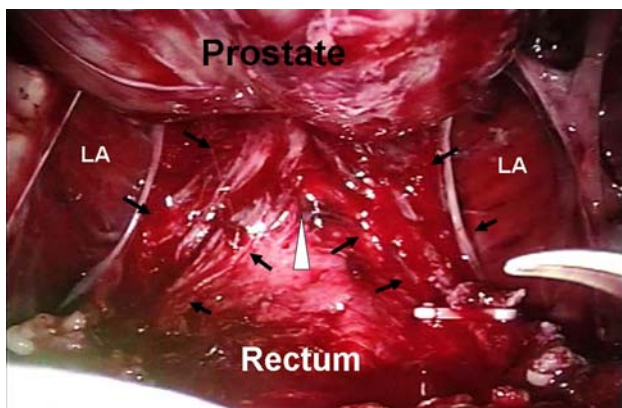


Fig. 8 Dissection of posterior plexus from the apex. Bilateral PNB overlap behind the apex, and formed posterior plexus. *Arrows*, PNB; *arrowhead*, posterior plexus; *LA*, lavator ani

3 months. Return to intercourse or masturbation was seen in 43% at 6 weeks and 54% at 3 months.

Margin positive rate is as follows; 5.8% in all cases, 3.0% in the last 100 cases, 3.8% in cases with Gleason 6 or less than 6, 7.2% in Gleason 7 (3+4), 9.0% with Gleason 7 (4+3) or more than 7, 4.8% with T2, and 11.0% with T3.

Conclusions

This manuscript summarizes the surgical neuroanatomy of the male pelvis as relevant to robotic prostatectomy. While most surgical techniques have focused on release of the neurovascular bundles during robotic prostatectomy, we introduce the tri-zonal concept of the PNB, PNB, and ANP, and the distribution of autonomic GCs. Based on these concepts, we established the ART for nerve-sparing prostatectomy. The surgical and oncological outcomes, although not mature, are feasible. This presentation may be of benefit to new surgeons undertaking nerve-sparing robotic radical prostatectomy.

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