Pelvic Autonomic Nerve Mapping Around the Prostate by Intraoperative Electrical Stimulation With Simultaneous Measurement of Intracavernous and Intraurethral Pressure

Atsushi Takenaka,* Ashutosh Tewari, Rouei Hara, Robert A. Leung, Kohei Kurokawa, Gen Murakami and Masato Fujisawa

From the Departments of Urology, Weill Medical College of Cornell University (AT, AT, RAL), New York, New York, and Kawasaki Medical School (RH), Kurashiki and Takasaki National Hospital (KK), Takasaki, and Department of Anatomy, Sapporo Medical University (GM), Sapporo and Division of Urology, Department of Organ Therapeutics, Kobe University Graduate School of Medicine (AT, MF), Kobe, Japan

Purpose: In previous studies we noted that the neurovascular bundle was not identical to the bundle of the cavernous nerve fibers. In this study we sought to prove these anatomical findings electrophysiologically and map the autonomic nerve fibers by intraoperative simultaneous measurement of intracavernous pressure and intraurethral pressure.

Materials and Methods: Between January 2004 and May 2005 electrical stimulation was performed in 27 open pelvic surgeries, including 26 radical retropubic prostatectomies and 1 radical cystectomy, using an original bipolar electrode before prostate removal. Nerve stimulation was performed at the base of the so-called neurovascular bundle (point A) and the rectal wall about 1 cm posterolateral, apart from the neurovascular bundle (point B). Intracavernous pressure and intraurethral pressure were measured simultaneously.

Results: The mean ± SD increase in intracavernous pressure was 9.8 ± 6.3 cm H_2O at point A and 13.5 ± 7.3 cm H_2O at point B. Intracavernous pressure at point B was significantly higher than at point A ($p = 0.0240$). The mean increase in intraurethral pressure was 17.0 ± 9.4 cm H_2O at point A and 11.2 ± 8.1 cm H_2O at point B. Intraurethral pressure at point A was significantly higher than at point B ($p = 0.0353$).

Conclusions: The course of the cavernous nerves did not always agree with the surgically identified neurovascular bundle. The distribution of cavernous nerves was wider than our image of the neurovascular bundle and it existed on the rectal wall posterolateral, apart from the neurovascular bundle rather than the neurovascular bundle itself. The surgically identified neurovascular bundle contained the nerve fibers contributing to urinary continence.

Key Words: prostate, prostatectomy, urinary continence, electric stimulation, neuroanatomy

Sexual potency and stress incontinence are common comorbidities associated with radical prostatectomy. To improve postoperative quality of life we have studied the pelvic neuroanatomy, especially the NVB, using adult fresh and fixed cadavers.[1,2] We noted that the NVB is likely to differ from the actual course of the cavernous nerve fibers. The macroscopically identified NVB contains many nerve fibers to the cavernous tissue, urethral sphincter and bottom of the levator ani muscle (fig. 1, *A*). Microscopically we can detect the nerve fibers to the cavernous tissues and urethral sphincter between the membranous urethra and levator ani muscle fascia (fig. 1, *B*).

The most popular device for intraoperative NVB electrical stimulation is the CaverMap Surgical Aid (Uromed Corp., Boston, Massachusetts). Some groups reported that the potency rate in CaverMap positive cases after prostatectomy was significantly higher than in conventional nerve sparing cases.[3,4] However, others noted that the result of CaverMap did not correlate with the potency rate.[5,6] We also invented a simple and reliable monitoring system to confirm the cavernous nerves.[7] There is only 1 study describing IUP after stimulation.[8] We sought to prove these anatomical findings electrophysiologically and map the autonomic nerve fibers by intraoperative simultaneous measurement of ICP and IUP.

MATERIALS AND METHODS

Between January 2004 and May 2005, 26 patients who underwent open radical prostatectomy and 1 who underwent open radical cystectomy were approached to participate in this institutional review board approved study of male neuroanatomy. In these 27 patients age was 57 to 79 years (mean ± SD 70.0 ± 5.2). No patient had a history of pelvic surgery, pelvic irradiation, transurethral surgery or neurological disease. Only 1 patient with prostate cancer had received neoadjuvant androgen deprivation therapy for 6 months. Surgery was performed using general anesthesia with propofol for induction, N_2O plus sevoflurane for maintenance, vecuronium bromide as the muscle relaxant and

Submitted for publication February 13, 2006.
Study received institutional review board approval.
* Correspondence: Division of Urology, Department of Organ Therapeutics, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe, Japan (telephone: +81-78-382-6155; FAX: +81-78-382-6169; e-mail: atake@med.kobe-u.ac.jp).

For another article on a related topic see page 390.

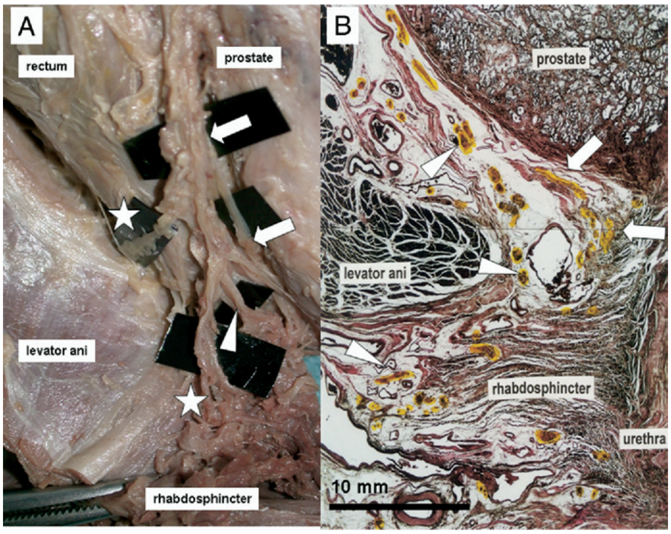

FIG. 1. *A*, macroscopic dissection of so-called right NVB in fixed cadaver. NVB contains many nerve fibers to cavernous tissue (arrowhead), urethral sphincter (arrow) and bottom of levator ani muscle (star). *B*, frontal histological section around so-called right NVB stained with hematoxylin and eosin. Some nerve fibers go to cavernous tissues and urethral sphincter between membranous urethra and levator ani muscle fascia. H & E stain.

epidural anesthesia with fentanyl citrate plus ropivacaine hydrochloride hydrate.

After we incised the endopelvic fascia the posterolateral aspect of the prostate and lateral rectal wall were exposed, where the cavernous nerves and autonomic continence nerves should run toward the membranous urethra.[1,2] Electrical stimulation was performed using a Neuropack nerve stimulator device (Nippon Kohden, Tokyo, Japan) and a bipolar electrode before prostate removal (fig. 2). The interval between the 2 electrodes was 7 mm long. As described previously,[7] stimulation was administered for 30 seconds using certain conditions, including a monophasic rectangular pulse, 50 mA, 10Hz and 0.2-millisecond duration.

We measured ICP with a 23 gauge needle inserted into the corpus cavernosum of the penis at the penile root, connected to a Menuet compact urodynamic device (Dantec Medical, Skovlunde, Denmark) through an SCKD-5006 disposable pressure transducer set (Nippon Kohden). IUP was measured with an intraurethral balloon catheter, which was especially ordered, and a 7.5Fr catheter with a 5 cm A4219 balloon (Fuji System, Tokyo, Japan) (outer diameter 2.5 mm). After we examined catheter insertion by transrectal ultrasound we positioned the balloon filled with sterile saline at the urethral sphincter. It was connected to the same urodynamic device through the same transducer set. Nerve stimulation was performed at the base of the so-called NVB (point A) and the rectal wall about 1 cm posterolateral, apart from the NVB (point B) (fig. 3). We then simultaneously measured ICP and IUP. Pressure at the 2 points was compared using the Mann-Whitney U test with statistical significance considered at $p < 0.05$.

RESULTS

With intraoperative electrical stimulation we measured ICP and IUP in 27 and 22 patients, respectively. In all cases we caused a significant increase.

The mean increase in ICP with stimulation was 9.8 ± 6.3 cm H_2O (range 2 to 22) at point A and 13.5 ± 7.3 cm H_2O (range 4 to 32) at point B. ICP at point B was significantly higher than at point A, ie the NVB ($p = 0.0240$). Of the 27 patients 20 (74.1%) had a higher measured ICP at point B than at point A. ICP began to increase gradually within 10 to 30 seconds after the initiation of stimulation. It attained a peak at the conclusion of stimulation and finally decreased gradually (fig. 4).

The mean increase in IUP with stimulation was 17.0 ± 9.4 cm H_2O (range 6 to 38) at point A and 11.2 ± 8.1 cm H_2O (range 0 to 35) at point B. IUP at point A was significantly higher than at point B ($p = 0.0353$). Of the 22 patients in whom we measured IUP 15 (68.2%) had higher IUP at point A than at point B. The IUP waveform was greatly different from that of ICP. IUP increased rapidly just after the initiation of stimulation and it decreased rapidly as soon as stimulation ended (fig. 4).

DISCUSSION

To our knowledge this is the first report of intraoperative simultaneous measurement of ICP and IUP in pelvic surgery. Our study suggests that the course of the cavernous nerves does not always agree with the surgically identified NVB. It exists on the rectal wall posterolateral, apart from the NVB rather than at the NVB. These results support our recent anatomical findings of the cavernous nerve course.[1,2] In addition, the surgically identified NVB contained the nerve fibers contributing to urinary continence.

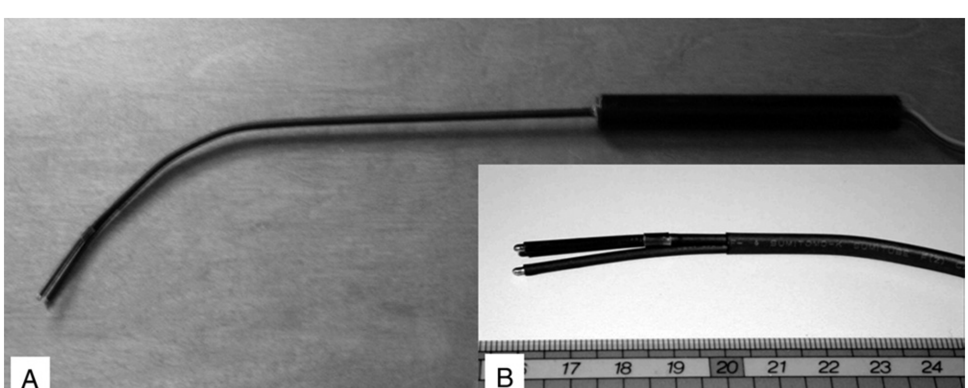

FIG. 2. *A*, original bipolar electrode used for intraoperative electrical stimulation. *B*, magnification shows 7 mm interval of 2 electrodes

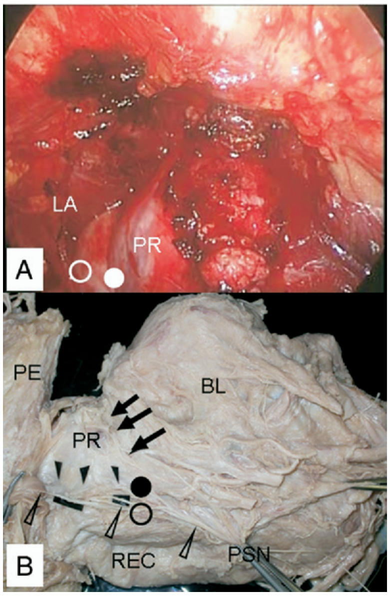

FIG. 3. Nerve stimulation positions. *A*, living subject. *LA*, levator ani muscle. *PR*, prostate. *B*, cadaveric subject. *REC*, rectum. *BL*, bladder. *PE*, penis. *PSN*, pelvic splanchnic nerve. Black arrowheads indicate so-called NVB. Open arrowheads indicate main trunk of cavernous nerve. Black arrows indicate bladder-prostate junction. Closed circles indicate point A on so-called NVB at prostate base. Open circles indicate point B about 1 cm posterolateral, apart from point A.

The most popular device for intraoperative cavernous nerve electrical stimulation is the CaverMap Surgical Aid. It consists of a control unit, a nerve stimulating probe with 8 electrodes in a 1.2 cm linear array and a tumescence sensor placed around the penis to measure changes in circumference. There are at least 3 aims in using this device, including to 1) determine accurate dissection planning for nerve sparing surgery, 2) examine the electrical continuity of the surgically preserved NVB and 3) identify the cavernous nerve ends for interposition nerve graft anastomosis. On the usefulness of this device Klotz et al reported that the postoperative potency rate was 94% (16 of 17 patients) in early experience with CaverMap assisted prostatectomy.[3] In another prospective, randomized, multicenter study there was substantial improvement in RigiScan (Dacomed, Minneapolis, Minnesota) performance in the CaverMap group over that in the conventional nerve sparing group at 1 year of followup ($p = 0.024$).[4] However, Kim et al reported that the potency rate after CaverMap assisted prostatectomy was 0% in those with a bilateral negative CaverMap response, 22% in those with a unilateral response and 27% in those with a bilateral response.[5] Furthermore, there were no statistical differences in the potency rate for a negative vs unilateral response and negative vs bilateral response ($p = 0.46$ and 0.32, respectively). Walsh et al indicated that the lack of specificity (54%) of this device limited its application for deciding which structures could be safely preserved or excised.[6] In contrast with CaverMap, we reported that sensitivity was 64.3% (postoperative potency in 9 of 14 nerve sparing cases) and specificity was 100% (postoperative impotence in 11 of 11 nonnerve sparing cases) using our original device by not measuring the circumference of the penis but by monitoring ICP.[7] An increase of more than 4 cm H_2O was considered a positive response and erectile status was examined using the International Index of Erectile Function-5 and nocturnal penile tumescence testing in that study. In addition to this device, the bipolar stimulating electrode enabled us to meticulously map the distribution of the nerve fibers. We consider that the large CaverMap electrode led to high sensitivity and low specificity.

Using dissection of male and newborn cadavers Walsh and Donker first reported the course of the cavernous nerve.[9] This milestone study was confirmed by Lepor et al, who postulated the macroscopic concept that the NVB was expected to contain the cavernous nerve.[10] However, in adult fresh and fixed cadavers we recently observed that the cavernous nerves appear to be located beyond the NVB at the base and middle of the prostate, and we should not regard the NVBs as cavernous nerves themselves.[1] The result that ICP at the rectal wall about 1 cm posterolateral, apart from the NVB, was significantly higher than at the NVB supports our anatomical findings and indicates that cavernous nerve distribution is wider than our image of the NVB. Also, within a wide distribution the density of the cavernous nerves was higher at a point apart from the NVB than at the NVB itself.

Based on the traditional concept of the NVB we cannot hope for a satisfactory outcome after interposition nerve graft surgery. Indeed, Kim et al reported that 1 year after surgery vaginal penetration was possible in only 33% of patients, suggesting a need for refinement.[11] We anticipate better outcomes in the near future using tissue engineered conduits[12] or some gel attaching method.[13] This is because we cannot interpose a bundle-like material, but rather a wide and universal shape material. On the other hand, we may not need to take excessive care to prevent injury to the cavernous nerves at the base of the prostate, although interindividual variation exists.

To confirm nerve sparing we also performed nerve stimulation after prostate removal. Negative ICP changes were observed in a few macroanatomically nerve sparing cases (unpublished data). Based on our anatomical[2] and electrophysiological study the most critical point for nerve sparing surgery must be near the apex of the prostate, where the real nerve courses are quite different from the so-called NVB. Recently Chuang et al indicated that early release of the NVB from the apex of the prostate led to improved postoperative potency rates and decreased time to potency in men undergoing radical retropubic prostatectomy.[14]

Similar to the report by Nelson et al,[8] our data support that the nerve fibers contributing to urinary continence exist near the macroanatomically identified NVB and

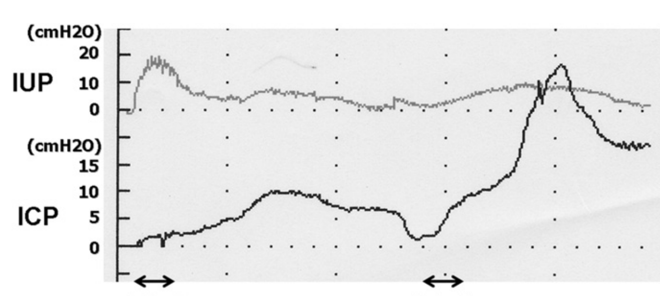

FIG. 4. Typical monitoring picture of simultaneous measurement of ICP and IUP. Arrows indicate stimulation duration.

nerve sparing radical retropubic prostatectomy may result in improved continence postoperatively. The distribution of autonomic nerves responsible for maintaining urinary continence is also wide, and within this wide distribution the density of these nerves was higher near the NVB than away from the NVB. Controversy exists as to whether the surgically defined NVB contains these fibers in addition to the cavernous nerves, and whether nerve sparing radical retropubic prostatectomy can achieve a better postoperative continence rate than the usual procedure. Catalona et al noted that the recovery of urinary continence was independent of nerve sparing surgery in 1,325 prostatectomies performed by a single surgeon ($p = 0.3$).[15] Gralnek et al also reported that using the UCLA Prostate Cancer Index nerve sparing status did not affect urinary function and urinary bother ($p = 0.70$ and 0.06, respectively).[16] On the other hand, to our knowledge there are sparse data on the effect of nerve sparing technique on post-prostatectomy continence.[17] It may be difficult to prove statistically that the nerve sparing technique contributes to the recovery of urinary continence because patients cannot be randomly assigned to nerve sparing or nonnerve sparing surgery. Also, the accurate assessment of nerve sparing is complicated. However, nerve sparing should be useful for the recovery of continence according to the current data and our recent anatomical study. Kaiho et al reported interesting data that the electrophysiologically classified bilateral nerve sparing group had significantly better urinary function than the unilateral sparing or nonnerve sparing group, especially 3 months after prostatectomy ($p < 0.05$), although no differences between the groups were seen when patients were classified based on macroanatomical assessment.[18] We are not sure how these nerve contribute to urinary continence. However, they may contribute to the early recovery of urinary continence.[18]

A question arises, that is if the NVB contains the autonomic nerve fibers responsible for urinary continence, why do nonnerve sparing cases have better urinary outcome than expected? The answer to this question is multifactorial. Several factors are associated with the complicated continence mechanism. Limited to the innervation to the sphincter, there are many nerve fibers. These autonomic fibers for the smooth muscle sphincter are accompanied by the cavernous nerves, and the somatic fibers from the pudendal nerve[19] and perineal nerve[20] innervate the external sphincter. These autonomic nerves are only 1 factor.

CONCLUSIONS

To our knowledge this is the first report of intraoperative simultaneous measurement of ICP and IUP during pelvic surgery. The course of the cavernous nerves did not always correspond with the surgically identified NVB. The distribution of cavernous nerves was wider than our image of the NVB and it existed on the rectal wall posterolateral, apart from the NVB. The surgically identified NVB contained the nerve fibers contributing to urinary continence. The current study should prove useful during nerve sparing pelvic surgery to preserve urinary continence.

Abbreviations and Acronyms

ICP = intracavernous pressure
IUP = intraurethral pressure
NVB = neurovascular bundle

REFERENCES

1. Takenaka A, Murakami G, Soga H, Han SH, Arai Y and Fujisawa M: Anatomic analysis of the neurovascular bundle supplying cavernous tissue to ensure a reliable nerve graft after radical prostatectomy. J Urol 2004; **172:** 1032.
2. Takenaka A, Murakami G, Matsubara A, Han SH and Fujisawa M: Variation in course of cavernous nerve with special reference to details of topographic relationships near prostatic apex: histologic study using male cadavers. Urology 2005; **65:** 136.
3. Klotz L and Herschorn S: Early experience with intraoperative cavernous nerve stimulation with penile tumescence monitoring to improve nerve sparing during radical prostatectomy. Urology 1998; **52:** 537.
4. Klotz L, Heaton J, Jewett M, Chin J, Fleshner N, Golgenberg L et al: A randomized phase 3 study of intraoperative cavernous nerve stimulation with penile tumescence monitoring to improve nerve sparing during radical prostatectomy. J Urol 2000; **164:** 1573.
5. Kim HL, Stoffel DS, Mhoon DA and Brendler CB: A positive CaverMap response poorly predicts recovery of potency after radical prostatectomy. Urology 2000; **56:** 561.
6. Walsh PC, Marschke P, Catalona WJ, Lepor H, Martin S, Myers RP et al: Efficacy of first-generation CaverMap to verify location and function of cavernous nerves during radical prostatectomy: A multi-institutional evaluation by experienced surgeons. Urology 2001; **57:** 491.
7. Kurokawa K, Suzuki T, Suzuki K, Terada N, Ito K, Yoshikawa D et al: Preliminary results of a monitoring system to confirm the preservation of cavernous nerves. Int J Urol 2003; **10:** 136.
8. Nelson CP, Montie JE, McGuire EJ, Wedemeyer G and Wei JT: Intraoperative nerve stimulation with measurement of urethral sphincter pressure changes during radical retropubic prostatectomy: a feasibility study. J Urol 2003; **169:** 2225.
9. Walsh PC and Donker PJ: Impotence following radical prostatectomy: insight into etiology and prevention. J Urol 1982; **128:** 492.
10. Lepor H, Gregerman M, Crosby R, Mostofi FK and Walsh PC: Precise localization of the autonomic nerves from the pelvic plexus to the corpora cavernosa: a detailed anatomical study of the adult male pelvis. J Urol 1985; **133:** 207.
11. Kim ED, Nath R, Kadmon D, Lipshultz LI, Miles BJ, Slawin KM et al: Bilateral nerve graft during radical retropubic prostatectomy: 1-year followup. J Urol 2001; **165:** 1950.
12. Hisasue S, Kato R, Sato Y, Suetomi T, Tabata Y and Tsukamoto T: Cavernous nerve reconstruction with a biodegradable conduit graft and collagen sponge in the rat. J Urol 2005; **173:** 286.
13. Matsuura S, Obara T, Horikawa Y, Kakinuma H, Togashi H, Tsuchiya N et al: Regeneration of excised pelvic plexus using alginate or chitosan gel: "simply-attaching" method without sutures. J Urol, suppl., 2005; **173:** 333, abstract 1228.
14. Chuang MS, O'Connor C, Laven BA, Orvieto MA and Brendler CB: Early release of the neurovascular bundles and optical loupe magnification lead to improved and earlier return of potency following radical retropubic prostatectomy. J Urol 2005; **173:** 537.

15. Catalona WJ, Carvalhal GF, Mager DE and Smith DS: Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies. J Urol 1999; **162:** 433.
16. Gralnek D, Wessella H, Cui H and Dalkin BL: Differences in sexual function and quality of life after nerve sparing and nonnerve sparing radical retropubic prostatectomy. J Urol 2000; **163:** 1166.
17. Wei JT, Dunn RL, Marcovich R, Montie JE and Sanda MG: Prospective assessment of patient reported urinary continence after radical prostatectomy. J Urol 2000; **164:** 744.
18. Kaiho Y, Nakagawa H, Ikeda Y, Namiki S, Numahata K, Satoh M et al: Intraoperative electrophysiological confirmation of urinary continence after radical prostatectomy. J Urol 2005; **173:** 1139.
19. Takenaka A, Hara R, Soga H, Murakami G and Fujisawa M: A novel technique for approaching the endopelvic fascia in retropubic radical prostatectomy, based on an anatomical study of fixed and fresh cadavers. BJU Int 2005; **95:** 766.
20. Shafik A and Doss S: Surgical anatomy of the somatic terminal innervation to the anal and urethral sphincters: role in anal and urethral surgery. J Urol 1999; **161:** 85.

EDITORIAL COMMENT

These authors report the functional relevance of portions of the periprostatic NVB, that is the posterolateral extent at the prostate base and rectum for regulating penile erection, and the more anterior extent contributing to urinary continence. One may reconcile the portion responsible for penile erection as representing the distribution of parasympathetic nerves, which coalesce with nerve fibers of sympathetic origin in forming the cavernous nerves (reference 1 in article). The study does not directly establish what portion of nerves at the prostate apex precisely represent functional cavernous nerves. Presumably maximal nerve sparing during radical prostatectomy would heighten the recovery of erection and possibly such for continence, given the topographical variability and diffuseness of the neurovascular bundle.[1] Despite these efforts, erection recovery currently often remains delayed and incomplete.[2] This insight suggests that innovative perioperative interventions, such as pharmacological rehabilitation and neuromodulation, lend therapeutic adjuncts to improve functional outcomes.

Arthur L. Burnett
Department of Urology
The Johns Hopkins Hospital
Baltimore, Maryland

1. Costello AJ, Brooks M and Cole OJ: Anatomical studies of the neurovascular bundle and cavernosal nerves. BJU Int 2005; **94:** 1071.
2. Burnett, A.L: Erectile dysfunction following radical prostatectomy. JAMA 2005; **293:** 2648.