Decision Memo for Cavernous Nerves Electrical Stimulation with Penile Plethysmography (CAG-00311N)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) has determined that electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography is not reasonable and necessary for Medicare beneficiaries undergoing nerve-sparing prostatic or colorectal surgical procedures. Therefore, we are issuing a national noncoverage determination on these uses of the test for the Medicare population.

Back to Top

Decision Memo

TO: Administrative File: CAG-00311N

FROM:

Steve E. Phurrough, MD, MPA
Director, Coverage and Analysis Group

Marcel Salive, MD, MPH
Director, Division of Medical and Surgical Services

William Larson
Lead Analyst, Division of Medical and Surgical Services

Lawrence Schott, MD, MS
Lead Medical Officer, Division of Medical and Surgical Services

SUBJECT:

Coverage Decision Memorandum for Cavernous Nerves Electrical Stimulation with Penile Plethysmography

DATE: August 24, 2006

I. Decision

The Centers for Medicare and Medicaid Services (CMS) has determined that electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography is not reasonable and necessary for Medicare beneficiaries undergoing nerve-sparing prostatic or colorectal surgical procedures. Therefore, we are issuing a national noncoverage determination on these uses of the test for the Medicare population.

II. Background

On December 9, 2005, CMS accepted a formal request for a national coverage analysis to evaluate the use of cavernosal nerve mapping during both open and post-radical prostatectomy in the Medicare population and the adequacy of evidence for improved sexual function resulting from assessment of integrity of the cavernous nerves by direct application of electrical stimulation with penile plethysmography.

The cavernous (or cavernosal) nerves and associated parasympathetic nerves that are part of the autonomic nervous system, an adequate vascular supply via the neurovascular bundles (NVBs), and psychological factors are all jointly responsible for male sexual function. In nerve-sparing prostatic and colorectal surgical procedures, nerve stimulator/locator devices utilizing cavernous nerve stimulation with penile plethysmography are intended to guide surgeons in mapping and preserving the NVBs in an attempt to maintain postoperative potency. To locate the nerves and test their excitability during removal of the prostate and/or suspect portion of the colon or rectum, a surgeon intermittently places the system's probe tip on the NVB to electrically stimulate the cavernosal and associated parasympathetic nerves. A tumescence sensor then measures any changes in penile circumference via plethysmography, and detected changes are compared to a baseline tumescence signal that could be stable within a specified range prior to the surgeon initiating a stimulation cycle. Tumescence changes can be visually and/or audibly monitored intraoperatively as either positive or negative 0.5%, 1%, 2% or 5% signal changes, which respectively reflect penile tumescence (increased circumference) or detumescence (decreased circumference). This testing can be performed either during the procedure to identify and potentially avoid nerve damage or at the completion of the procedure and prior to closure to determine if nerve damage occurred.

Anatomically, male pelvic autonomic nerves are comprised of sympathetic fibers (necessary for ejaculation) which are relatively easily surgically identified, as well as parasympathetic fibers (necessary for erection and orgasm) which can be more problematic to identify and preserve.[1] The parasympathetic nerves variably course within the pelvic fascia bordering the prostate and mesorectum (the rectum plus its surrounding layer of fatty tissue). While the risk of autonomic nerve damage and associated sexual dysfunction remain commonly reported complications of both prostatic and colorectal procedures, the dissection technique referred to as total mesorectal excision (TME) for rectal cancer has led to improvement in autonomic nerve preservation, and postoperative impotence has been reduced from 70-100% with conventional rectal cancer surgery to less than 30% with nerve-sparing TME.[2] Similarly, whereas post-prostatectomy erectile dysfunction was formerly almost universal, it has been estimated that after nerve-sparing radical prostatectomies performed by experienced surgeons at major academic centers as many as 60-85% of men will eventually recover erectile function satisfactory for sexual intercourse.[3]

Postoperative potency rates, however, are not uniformly high at all institutions or successful for all groups of patients. After surgery for rectal cancer, for example, the most important predictor of sexual dysfunction may be the patient's age.[4] Likewise, after radical prostatectomy, the most important predictors of erectile function are a patient's preoperative erectile function determined by his age and vascular risk factors (such as diabetes, heart disease and smoking), plus the nerve-sparing nature of the procedure determined by tumor stage and skill of the surgeon.[5] Nonetheless, even the patient's age, his preoperative sexual functioning and the surgeon's intraoperative visual documentation of the degree of unilateral or bilateral NVB sparing ("intact, possible damage but grossly intact, definite damage with partial resection, or complete resection") are not sufficient predictors for postoperative recovery of potency.[6]

III. History of Medicare Coverage

At present, there is no national coverage decision (NCD) or national Medicare coverage policy that has been issued by CMS on cavernous nerve stimulation devices. In the absence of an NCD or national coverage policy, local Medicare contractors have discretion to cover a diagnostic test or device whenever it is determined to be medically necessary for an individual patient.

Benefit Category

For an item or service to be covered by the Medicare program, it must meet one of the statutorily defined benefit categories outlined in the Social Security Act. Cavernous nerve stimulation devices may be considered a benefit under Social Security Act section 1861(s)(3), "other diagnostic tests." A reasonable and necessary diagnostic test must provide information that is used by the treating physician in management of the patient's specific medical problem.

IV. Timeline of Recent Activities

December 9, 2005	CMS accepts formal request from Blue Torch Medical Technologies, Inc. for a national coverage analysis of cavernous nerves electrical stimulation with penile plethysmography.
June 9, 2006	Proposed decision available for 30 days of public comment.
July 9, 2006	The 30 day public comment period ended.

V. FDA Status

In the most recent FDA 510(k) “Summary of Safety and Effectiveness” pertaining to electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography dated September 21, 2004, the “Indications for Use” section stated that:

“The system is indicated for use in the stimulation of the cavernosal and associated parasympathetic nerves during open or laproscopic [sic] prostatectomy, prostate brachytherapy placement, prostate cryotherapy, and open colorectal (surgical) procedures. The device aids the physician in locating these nerves. The device is designed as an adjunct to the current open or laproscopic [sic] prostatectomy, prostate brachytherapy placement, prostate cryotherapy, and open colorectal procedures in which a nerve sparing technique is used. The Surgical Aid is not designed to replace the surgeon’s expertise in mapping out the neurovascular bundles. Each physician’s skill determines whether these nerves are spared regardless of any aid.”[7]

VI. General Methodological Principles

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Comments from the public are welcomed at two stages of the NCD process: the initial posting of a tracking sheet and at the release of a proposed decision. Members of the public are encouraged to use the comments process to seek clarification of posted information, to provide additional information that may be useful in the decision making process, and to provide informed opinions on the subject under consideration. Researchers, physicians, and other others members of the health care community may have important insights that they wish to share, and professional societies may wish to impart their groups' positions. Public comments that cite the published clinical evidence are most helpful. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. No public comments were received in response to our initial posting of the tracking sheet for cavernous nerves electrical stimulation with penile plethysmography (CAG-00311N).

VII. Evidence

Introduction

This summary represents the body of evidence evaluating electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography for patients undergoing autonomic nerve-sparing prostatic or colorectal procedures. The health outcome of interest to CMS is a patient's improved sexual function, including measurements of potency, erectile function and health-related quality of life.

Reflecting the combined influence of neurologic, vascular and pyschologic factors, definitions of potency and impotency, as well as erectile function and dysfunction, vary according to the patient interview, questionnaire or scale utilized. Instruments discussed in the studies reviewed included measurement of erectile function utilizing the fifteen item International Index of Erectile Function (IIEF) questionnaire, which is a self-administered, multidimensional questionnaire addressing five domains of male sexual function (erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction).[8] The IIEF's reliability for evaluating sexual function has been questioned, and substantial recall or reporting bias may confound IIEF domain scores.[9,10] Study endpoints also incorporated a Sexual Function Inventory Questionnaire (SFIQ) included in one article's appendix but otherwise not referenced, as well as nocturnal penile tumescence and radial rigidity by rigiscan evaluation.[11] Interpretation of rigiscan testing and the influence of aging upon rigiscan device measurements have similarly been questioned.[12,13] Two other studies reviewed used nonvalidated questionnaires that were mailed to patients for self-reported assessments of erectile function and potency.[14,15]

CMS's proposed decision memorandum focuses on the following question: "What is the clinical evidence for improved sexual function resulting from assessment of integrity of the cavernous nerves by direct application of electrical stimulation with penile plethysmography to predict a patient's potency and guide choice of therapy after nerve-sparing prostatic or colorectal procedures?

1. Literature search

CMS searched the Cochrane Library, National Health Service Centre and International Network of Agencies for Health Technology Assessments databases for external technology assessments, systematic reviews or meta-analyses of cavernous nerve stimulation. CMS similarly searched PubMed (1995 to present) for randomized clinical trials (RCTs) and observational studies that evaluated assessment of the integrity of the cavernous nerves by direct application of electrical stimulation with penile plethysmography. Keywords included cavernous nerve stimulation, cavernous nerves, cavernosal nerve mapping and cavermap. Studies must have presented original data on nerve-sparing prostatic or colorectal procedures, included $\geq$ 10 patients, and been published in peer-reviewed English language journals. Eight relevant articles were identified.

2. External technology assessment

No external technology assessment, systematic review or meta-analysis was identified.

3. Internal technology assessment

Klotz and Herschorn (1998) reported a pilot study that enrolled 26 men (median age = 63 years; range 57 to 71 years) to determine if intraoperative stimulation of the cavernous nerves while monitoring changes in penile tumescence with plethysmography to map the course of these nerves resulted in improved postoperative erectile function. Eligible patients were those undergoing radical prostatectomy who were candidates for a nerve-sparing approach. Exclusion criteria included cardiac pacemakers or electromechanical prosthetic devices, prior pelvic radiation therapy, or neoadjuvant therapy more than 3 months before surgery. The primary endpoint was the intraoperative induction of penile tumescence by proximal cavernous nerve stimulation after removal of the prostate, and a minimum change of 0.5% was considered a response. Erectile function, the study's secondary endpoint, was assessed preoperatively by patient self-reporting and questionnaire (not described further) and by patient self-reporting "periodically 12 months postoperatively". Nerve stimulation and tumescence monitoring was performed in 23 of the 26 patients recruited. Results showed that 21 of the 23 patients stimulated demonstrated a tumescence response to intraoperative nerve stimulation. Nineteen of those 21 patients reported erectile function preoperatively. Seven of the 26 patients enrolled were not eligible for comparative evaluation of erectile function, including 2 preoperative erectile failures, 2 intraoperative technical device difficulties, 1 unavailable erectile function data postoperatively, 1 extracapsular disease making nerve sparing ill-advised, and 1 excluded from analysis due to androgen ablation for metastatic disease. Seventeen of the 19 patients evaluated demonstrated a tumescence response during surgery, and 16 of 17 patients who demonstrated a response and for whom surgery was guided by the response reported ability to have erections after surgery, including 5 (31%) with recovery of consistent full erectile function and 11 (58%) with inconsistent or partial function. Klotz and Herschorn (1998) concluded that intraoperative tumescence response to cavernous nerve stimulation may guide the surgeon in preserving the cavernous nerves and improving erectile function after radical prostatectomy.[16]

Kim, *et al.* (2000) reported on a cohort of 60 men (mean age = 58 ± 6.8 years) who underwent radical retropubic prostatectomy by a single surgeon (May 1998 to April 1999) to determine whether unilateral or bilateral preservation of the NVBs defined by response to cavernous nerve stimulation with plethysmography correlated with postoperative recovery of potency. Patients who preoperatively reported reduced or absent erectile function (no scale or questionnaire referenced) were excluded, and postoperative potency was assessed by a mailed questionnaire and telephone interview administered independently of the treating surgeon. During follow-up, men were considered potent if they reported erections sufficient for vaginal penetration at least 50% of the time intercourse was attempted. Nerve stimulation was used intraoperatively after removal of the prostate to assess integrity of the NVBs, and a positive response was defined by tumescence or detumescence that registered a change in penile circumference of 1%. Results showed that of 25 patients who underwent attempted unilateral preservation of the NVBs, 20 (80%) had a positive response. Of 35 patients who underwent attempted bilateral preservation of the NVBs, 9 (26%) had a positive response on one side and 22 (63%) had a positive response on both sides. With attempted unilateral NVB preservation, 3 (15%) of the 20 patients with a positive response were potent. With attempted bilateral NVB preservation, 2 (22%) of 9 with a unilateral response and 6 (27%) of 22 with a bilateral response were potent. When patients with any positive nerve stimulation response (unilateral or bilateral) were compared to patients with a negative nerve stimulation response, differences in potency did not reach statistical significance. While a positive response (suggesting a successful nerve-sparing prostatectomy) was obtained in 73 (77%) of the 95 NVBs tested, after 1 year median follow-up only 11 (18%) of the total 60 patients studied regained potency. The authors noted that recovery of erectile function did not correlate with intraoperative nerve stimulation response; and that although preservation of the NVBs appeared necessary, it did not guarantee recovery of erectile function. Kim and colleagues (2000) concluded that other factors remain critical to recovery of sexual function after radical prostatectomy.[17]

Klotz, *et al.* (2000) reported a single-blinded RCT (patients blinded to their allocation cohort) that initially enrolled 61 patients (mean age = 60.5 years; range 39 to 70 years) at 6 Canadian centers. The study's objective was to determine if cavernous nerve mapping during radical prostatectomy using intraoperative nerve stimulation with tumescence monitoring resulted in improved erectile potency compared to conventional nerve-sparing surgery. Patients had elected to undergo nerve-sparing surgery and had normal preoperative erectile function as determined by a Sexual Function Inventory Questionnaire (SFIQ) and rigiscan testing. Neural continuity was assessed intraoperatively after prostate removal by proximal cavernous nerve stimulation, and a minimally detectable change in tumescence of 0.5% was considered a response. Study endpoints were change in the SFIQ and rigiscan evaluation. Five patients were not evaluable due to lack of post-prostatectomy nerve stimulation data, and 3 patients were not evaluable due to device failure. Of the remaining 53 patients receiving either conventional nerve-sparing surgery alone (N = 36 controls) or nerve-sparing surgery assisted by cavernous nerve stimulation (N = 27 study group), 8 additional patients were excluded from evaluation at 12 months due to postoperative radiation therapy (7 patients) and hormonal therapy (1 patient), leaving 45 potentially evaluable patients. Of those 45 patients, 10 patients declined to have rigiscan testing at 1 year postoperatively "for unknown reasons", leaving only 35 evaluable patients (17 controls, 18 study group) with 1-year rigiscan data. Compared to a mean of 2.1 minutes (median 1.0) in the control group who received nerve-sparing surgery alone, results showed improvement in erectile function with a mean of 15.9 minutes (median 3.0) of greater than 60% nocturnal tumescence measured by rigiscan testing in the 18 remaining patients in the study group who underwent nerve-sparing surgery assisted by cavernous nerve stimulation ($p < 0.024$). There was, however, no significant difference in postoperative erectile function as measured by the SFIQ, for which there were 45 evaluable patients (21 controls, 24 study group). Of patients who had bilateral, unilateral and no response to stimulation after resection, erectile function assessed by the SFIQ recovered in respectively 68%, 27% and 0% ($p = 0.016$, for bilateral versus unilateral plus none). Mean duration of surgery for the control and study groups was respectively 160 and 183 minutes. Klotz and colleagues (2000) concluded by noting that "further studies of this approach are warranted to confirm the benefit of this technique with respect to preservation of erectile function."[18]

Holzbeierlein, Peterson and Smith (2001) reported on a cohort of 61 patients (mean age = 59.8 years; range 43 to 72), whose cavernous nerve function was assessed during radical retropubic prostatectomy using an electrical nerve stimulator with penile plethysmography to assess reliability of NVB stimulation for producing an erectile response. In 44 patients a nerve -sparing dissection was performed; in 4 patients a unilateral NVB excision was performed because of a palpable nodule near the bundle; and in 13 patients both NVBs were excised due to a large volume or high grade of tumor. Intraoperatively, before and after prostatic removal, the stimulator probe (coarse mode) was first placed directly on the left NVB, next on the right NVB, and then as each patient's own control on the anterior bladder wall distant from the NVB stimulations. Any positive change in penile circumference measured (i.e., 0.5%, 1%, 2% or greater) was considered to be a tumescence response, and any negative change was considered detumescence. Prior to apical dissection, stimulation (reported as percentage of all 61 patients for respectively the right NVB versus the anterior bladder wall control) showed that 41% versus 46% had tumescence, 31% versus 21% had detumescence, and 28% versus 33% had no response. After prostate removal, 42% versus 25% had tumescence, 16% versus 18% had detumescence, and 42% versus 57% had no response. A table listed composite responses (but no statistical analysis or additional data stratification) for NVB and control stimulation on both the right and left. Holzbeierlein, Peterson and Smith (2001) concluded that response to NVB stimulation did not necessarily correlate with precise anatomic location of the cavernous nerves and that there was considerable background variability that may cause minor but measurable changes in penile circumference.[19]

In a second publication from the same urology department, Chang, Peterson and Smith (2001) reported on a nearly identical cohort to determine whether intraoperative electrical nerve stimulation with penile plethysmography response after prostate removal predicted postoperative potency. Like Holzbeierlein's study, any measured sustained change on the monitor screen of the device (graded to ±1 to ±4) was considered a positive response, and the greatest observed change was recorded. Chang, *et al.'s* results section reported that their study included 63 patients with a mean age = 59.8 years and range 43 to 72 years (identical to the mean and range for Holzbeierlein's cohort of 61 patients), but Chang, *et al.'s* Table 1 describing patient characteristics discordantly stated a mean age = 59.6 years and range 48 to 72 years. Among the study's 63 consecutive patients undergoing radical prostatectomy, 41 were said to have had a bilateral nerve-sparing procedure and 22 underwent bilateral wide resection of the NVBs. Potency was determined by patient interview both preoperatively and postoperatively by the physician, and potency was defined as ability to have erections sufficient for vaginal penetration more than 50% of the time intercourse was attempted. Results showed that of the 22 patients with wide resection, 16 (73%) had no observed stimulated response, 4 (18%) had a measurable tumescence response, and 2 (9%) had detumescence. All 22 of these patients with wide resection were impotent postoperatively. At a minimum follow-up of 1 year, 27 (66%) of the 41 patients who underwent nerve-sparing radical prostatectomy had postoperative erections sufficient for penetration. Of the 30 patients with an intraoperative stimulated tumescence response, 24 (80%) were potent. Of the 6 with a detumescence response, 2 (33%) were potent. Of the 5 with no stimulated nerve response, 1 (20%) was potent. A tumescence response was reported to be significantly more predictive of postoperative potency than no response ($p = 0.017$), and Chang, *et al.* (2001) concluded that a tumescence response to stimulation of the NVBs after prostate specimen removal was more likely to correspond to successful postoperative sexual function than was no tumescence response to stimulation.[20]

Walsh, *et al.* (2001) reported on a cohort of 50 patients (mean age = 52.5 years; range 43 to 59 years) to evaluate the ability of first-generation electrical nerve stimulation with penile plethysmography to intraoperatively identify the cavernous nerves and predict recovery of sexual function. Enrolled patients had localized prostate cancer, underwent nerve-sparing radical prostatectomy (90% bilateral), and had a sexual partner. Erectile function was evaluated preoperatively by patient self-report using the IIEF, and at 3, 6 and 12 months postoperatively by measures including the IIEF administered to both the subject and his partner. Men were considered potent if they were able to achieve unassisted intercourse in ≥ 50% of their attempts, and preoperatively eligible enrollees had to be highly or very highly satisfied with their sexual relationship with their partner. Exclusion criteria included but were not limited to cardiopacing or electromechanical prosthetic devices, prior surgery within 6 months such as transurethral resection of the prostate that could affect sexual function, neoadjuvant hormonal therapy, change of antihypertensive medication within 6 months, diabetes or significant neurologic disease. Nerve stimulation with penile plethysmography was used intraoperatively to test for presence of the cavernous nerves once the NVB was visually identified, as well as to determine whether the nerves were intact after the prostate was removed. That is, nerve stimulation "was used as previously described" to evaluate the visually identified regions of the NVB before the NVB was mobilized, and "stimulation and monitoring were also performed after removal of the surgical specimen to ascertain whether the nerves had been preserved and were functional." Of the 56 patients recruited, 50 patients were available for evaluation (2 incomplete operative data, 1 marked scarring, 1 adjuvant radiotherapy, 1 failure to return study information, and 1 withdrawn consent). Results showed that prior to prostatic removal, response to stimulation was 87.8% (295 of 336 sites identified as the NVB), which represented the device's sensitivity. When tissue said by investigators not to contain the NVB was stimulated, no tumescence response occurred in 54% (29 of 54 anatomic sites), which represented the device's specificity. Intraoperatively after prostatectomy (i.e., after removal of the surgical specimen), bilateral response to stimulation occurred in 90%, unilateral response in 5%, and no response in 5%. In patients demonstrating bilateral stimulation after removal of the prostate, 78% were potent at 12 months. Walsh and colleagues concluded that lack of specificity of the first-generation cavernous nerve stimulation device limited its use for deciding which structures could be safely preserved or excised, and that because most patients demonstrated a positive response after removal of the prostate, the value of cavernous nerve stimulation to predict recovery of sexual function could not be determined.[21]

Hanna, *et al.* (2002) reported on a cohort of 21 consecutive men (mean age = 48.1 years; range 28 to 67 years) with normal preoperative erectile function whose cavernous nerves were assessed during TME both visually by an experienced surgeon and by intraoperative electrical nerve stimulation with penile plethysmography. The study's objectives were to determine ability to demonstrate penile tumescence in response to intraoperative parasympathetic nerve stimulation after rectal cancer resection, as well as to correlate the nerve stimulation responses with sexual function outcomes (erection and orgasm) at 6 months after surgery. After completion of pelvic dissection, the surgeon visually estimated the likelihood of the nerves remaining intact on a scale of 1 to 5, where 1 meant the nerves were intentionally or inadvertently completely divided, and 5 meant the nerves were completely intact. Nerve integrity was assessed intraoperatively with the electrical stimulator device, and the minimal effective current necessary to produce a 2% increase in penile tumescence was recorded. Two patients were not included in the final outcomes analysis due to equipment failure in one patient and postoperative death of the other patient. Results showed that the surgeon's visual assessment of nerve integrity after pelvic dissection was deemed intact in 20 (95.2%) of 21 patients. Of the 20 patients who were intraoperatively evaluated with the nerve stimulator after completion of TME, 17 patients (85%) had a tumescence response with sequential bilateral nerve stimulation, and 3 patients (15%) had unilateral response only. Of the 19 patients evaluated for sexual function outcomes 6 months after surgery, 18 patients (94.7%) had normal function, including the 3 patients with only unilateral nerve stimulation tumescence response. Intraoperative control stimulation of contiguous pelvic sidewall structures (piriformis muscle) in multiple patients failed to produce tumescence. Hanna and colleagues (2002) concluded that intraoperative mapping of the parasympathetic nerve trunks by electrical nerve stimulation with plethysmography may aid less experienced pelvic surgeons and may help in autonomic nerve preservation during TME.[22]

Da Silva, *et al.* partially reported (2004) and then fully detailed (2005) results on a cohort of 29 sexually active men (median age = 58 years, range 40 to 67 years) who underwent TME. Study objectives were to assess the efficacy of electrical nerve stimulation with penile plethysmography to assist in intraoperative identification of the autonomic nerves and to confirm nerve preservation after rectal resection and removal of the surgical specimen. During pelvic dissection, the surgeon attempted to visually localize the hypogastric nerves in 26 patients who chose to participate in the study protocol. Attempts to visualize the cavernous nerves during dissection, however, were made in only 13 patients "according to the surgeons preference". Intraoperatively after proctectomy (i.e., after completion of pelvic dissection and removal of the specimen), all 29 patients had their hypogastric nerves tested, and 27 patients had their cavernous nerves tested. Results showed visual identification of the hypogastric nerves during dissection in 19 (73%; 17 bilaterally, 2 unilaterally) of 26 patients participating. The stimulator device identified the nerves in 6 (85%; 3 bilaterally, 3 unilaterally) of the 7 remaining patients, and failed to identify the hypogastric nerves in 1 patient. Attempted visual localization of the cavernous nerves during dissection was successful in 8 (61.5%; 7 bilaterally, 1 unilaterally) of 13 patients. The stimulator device facilitated nerve identification in 4 (80%; 3 bilaterally, 1 unilaterally) of the remaining 5 patients, and failed to identify the cavernous nerves in the same patient where identification of the hypogastric nerves was not possible. Intraoperatively after proctectomy, the stimulator device confirmed nerve preservation in 28 (27 bilaterally, 1 unilaterally) of 29 patients whose hypogastric nerves were tested, and confirmed parasympathetic function in 26 (23 bilaterally, 3 unilaterally) of 27 patients whose cavernous nerves were tested. History of prior surgery correlated with inability to visually identify the hypogastric nerves ($p = 0.005$), but no other risk factor analyzed (rectal cancer versus benign disease, prior radiation therapy, abdominoperineal versus low anterior resection, or body mass index) affected identification or confirmation of the autonomic nerves. No adverse events or complications were related to device use. Da Silva and colleagues concluded that intraoperative electrical nerve stimulation with penile plethysmography may be a useful tool to facilitate identification of pelvic autonomic nerves during TME and to objectively confirm nerve preservation.[23,24]

4. Medicare Coverage Advisory Committee (MCAC)

This issue was not referred to the MCAC.

5. Evidence-based guidelines

No relevant evidence-based guidelines were identified.

6. Professional Society Position Statements

No professional society position statements were identified.

7. Expert Opinions

No expert opinions were received.

8. Public Comments

During the initial comment period, CMS received no comments on our consideration of this request.

Comments on the Proposed Decision Memorandum

CMS received a total of 3 comments during the public comment period for the proposed decision memorandum. Of the 3 comments, one was received from the requestor, and a second was received from a consulting company, Medical Technology Partners, Inc., which has been representing the requestor in many of its contacts with CMS, and a third was received from a retired individual who had a radical prostatectomy performed a number of years ago.

The requestor appreciated CMS's review of this technology which the company believes is important for patients undergoing a radical prostatectomy of a colorectal cancer surgery. The requestor did not submit any additional evidence or dispute CMS's proposed decision. The consultant commended CMS for taking the time to review the issue of coverage of electrical nerves stimulation with penile plethysmography. While acknowledging that CMS found insufficient evidence to support national coverage at this time, the consultant expressed the hope that this clarification of Medicare policy might eventually result in further research being done that might demonstrate the value of their technology.

The retired individual who commented suggested that coverage of the cavernous nerves stimulation procedure might help him decide whether he should have a penile implant to correct the problems he has had since his surgery a number of years ago. Our review of the available evidence on this test did not include an evaluation of that issue.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act § 1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." § 1862(a)(1)(A).

This decision memorandum focuses upon the following question: “What is the clinical evidence for improved sexual function resulting from assessment of integrity of the cavernous nerves by direct application of electrical stimulation with penile plethysmography to predict a patient’s potency and guide choice of therapy after nerve-sparing prostatic or colorectal procedures?” To answer that question required that we examine the evidence regarding the device’s accuracy, as well as any evidence of its effect upon patient outcomes.

Klotz, *et al.* (2000) published the only RCT of electrical nerve stimulation with plethysmography but reported “lack of standardization” of the nerve-sparing technique among the 9 surgeons at 6 participating Canadian sites and only a “small number of patients at some of the sites”. The study was supported by a grant from the device manufacturer, and 4 authors acknowledged potential financial and/or intellectual conflicts of interest. While the mean age of the 61 initially enrolled patients was 60.5 years, ages and clinical characteristics of the remaining evaluable 45 patients with 1-year SFIQ data and 35 patients with 1-year rigiscan data (upon whom the results were predicated) were not reported. The final statistical analysis in “Table 4. Return of erectile function measured at 12 months postoperatively according to tumescence response to nerve stimulation at the end of surgery” also appears to have been reported for only 30 of 35 patients said to have 1-year rigiscan data. That is, results were potentially biased because they were only based upon approximately 50% of the patients initially enrolled. Despite some statistically significant results reported for the small number of remaining evaluable patients with available measurements, both the study group (nerve-sparing surgery assisted by intraoperative nerve stimulation) and control group (nerve-sparing surgery alone) reported substantial degrees of erectile dysfunction measured by the 1-year SFIQ data. There was, however, no significant difference between the study and control groups in the proportion of patients with no or minimal erectile dysfunction, and there was no significant difference between the study and control groups in the likelihood of patients who postoperatively reported erections adequate for intercourse.[25]

Critical review of the 7 small case series of predominantly middle-aged patients showed serious methodological deficiencies, non-standardized outcome measurements, plus inconsistent results regarding the accuracy and clinical impact of electrical nerve stimulation with plethysmography. Study conclusions were limited by information bias due to self-reporting by both patients and investigators, and there were large amounts of missing data secondary to patient dropout, loss to follow-up, and lack of intention-to-treat analysis. Additionally, selection bias is likely when there are different characteristics between those patients participating and those theoretically eligible for study but not participating. Thus, based upon the overall younger age of enrolled subjects, smaller less advanced tumors, and better preoperative sexual function of patients choosing nerve-sparing procedures, study results likely further exaggerated the degree of postoperative sexual function. Finally, for those studies without matched or historical controls, it was not possible to ascertain whether the use of electrical nerve stimulation contributed to any improved health outcomes, or if the device's reported results influenced selection of more appropriate therapy than would have been used if nerve stimulation with penile plethysmography had not been available.

In Klotz and Herschorn's (1998) study, 4 of 5 patients who recovered full erectile function showed a positive tumescence response to electrical nerve stimulation, whereas 1 experienced a detumescence response to stimulation. In 2001, Walsh, *et al.* detailed similar difficulties with nerve stimulation not consistently resulting in tumescence. Equally concerning was Klotz and Herschorn's identification of heterogeneous response to nerve stimulation. That is, as noted in "Table II. Results of intraoperative stimulation in 23 cases", the only 2 patients who reported no preoperative erectile function both had positive intraoperative tumescence responses; and 2 of the patients with normal preoperative erectile function failed to demonstrate an intraoperative tumescence response. Noting the multifactorial nature of erectile impotence in many patients, Klotz and Herschorn posited that patients with vasculogenic impotence might still respond with minimal increase in tumescence after nerve stimulation, and that failure to demonstrate a response could be due to variable course of the nerve, diffusion of current by blood at the stimulation site, or misplacement of the stimulator probe tip. Additional methodological shortcomings of the study noted in an accompanying editorial comment included that it suffered from "the usual problems of pilot studies (small numbers, use of nonvalidated questionnaires, failure to document previous success of nerve-sparing prostatectomy by the same surgeons, and failure to report unilateral versus bilateral cavernous nerve salvage)."[26]

Kim, *et al.* (2000) reported positive nerve stimulation defined by plethysmography as tumescence or detumescence responses that registered change in penile circumference of 1%. This definition of a positive response to stimulation differed from other studies, including Klotz and Herschorn's (1998) pilot study and Klotz, *et al.'s* (2000) RCT, in which a minimum change in tumescence of 0.5% was considered a tumescence response. Kim and colleagues (2000) also delivered current to areas away from the NVBs "as a negative control" in order to confirm the absence of an erectile response, and using 1% change to define a positive response, obtained no false positive responses when areas away from the NVBs were stimulated. Only 11 (18%) of the total 60 patients in this study, however, regained potency at a median follow-up of 1 year. The authors thus concluded that postoperative recovery of erectile function did not correlate with response to intraoperative electrical nerve stimulation with plethysmography, and that erectile dysfunction is probably multifactorial.[27]

Holzbeierlein, Peterson and Smith (2001) reported that the nerve stimulation device was capable of detecting as little as a 0.5% change in penile circumference, "a difference so small that it may be of no relevance." Their article provided no statistical analysis, and there was no stratification of results according to gradation of measured responses said to vary from ±1 to ±4. Rather, any measured change was considered a tumescence or detumescence response, and only the greatest observed change was recorded. There was no stratification of responses according to age, extent of disease or surgical technique; and the multifactorial nature of potency and heterogeneous selection criteria biased reported composite results. Also noted was that even in patients with normal preoperative erectile function "nerve stimulation did not consistently produce a measurable response" prior to NVB dissection, which raises concern regarding the lack of a true reference standard for nondiseased and diseased, or potent and impotent patients. Holzbeierlein, *et al.* (2001) consequently stated that they were unable to draw any conclusions about the ability of electrical nerve stimulation with plethysmography to predict outcome after nerve-sparing radical prostatectomy, and that variability in responses made interpretation of observed tumescence or detumescence changes difficult.[28]

Both Holzbeierlein, Peterson and Smith (2001) and Chang, Peterson and Smith (2001) reported on virtually the same heterogeneously diseased group of patients with localized to high grade prostatic cancer (N = 61 versus N = 63). These two articles may represent duplicate publication, and therefore our analysis takes this into account. Patient characteristics in each article's Table 1 matched precisely except for 2 additional patients in Chang's cohort exhibiting clinical stage T1c localized prostate cancer with Gleason scores of 5-6. Despite these nearly identical study populations, it was difficult to reconcile the published differences between types of procedures, e.g., 13 versus 22 bilateral wide NVB resections. Variable responses to cavernous nerve stimulation reflected the heterogeneity of patients and procedures, and precluded comparison and synthesis of these and other studies. While Chang and colleagues concluded that a positive tumescence response after prostate removal more likely corresponded to successful postoperative sexual function than no response to NVB stimulation, the authors definition of "any" measured sustained positive change on the device's monitor screen differed from Kim, *et al.'s* (2000) definition of a 1% or greater change. Chang's group further described an overall false positive rate of 29% in their patients with a tumescence response, and noted that "patients who were impotent may in fact have been affected by poorer function preoperatively or may had a more extensive dissection or may be older." Notably, the determination of potency pre- and postoperatively in Chang's (2001) article appeared to have been obtained unblinded by physician-patient interviews without mention of a standardized or validated instrument; whereas Kim's (2000) article had stated that their patients' potency was assessed with a questionnaire administered independently of the treating surgeon. Chang, *et al.'s* (2001) discussion importantly described that "Even though we were able to identify some correlation with the postdissection response and postoperative erectile function, in our opinion, the association is not sufficiently strong to predict results for every patient. As a result, we do not currently use the responses to determine or alter postoperative management."[29]

Walsh, *et al.'s* (2001) study of 50 men younger than 60 years old evaluated the efficacy of first-generation electrical nerve stimulation with penile plethysmography, but the study was explicitly not designed to determine whether the device improved surgeons' ability to preserve the nerves or improved postoperative sexual outcomes. The nerve stimulation device was said to have been used as previously described (i.e., by Klotz), but the minimum change in monitored tumescence considered by Walsh and colleagues to be a positive response was not definitively stated. Based upon the expertise of urologists at high-volume centers of excellence for prostate cancer, positive nerve stimulation was recorded in 87.8% of sites where the NVB was visualized; but responses to nerve stimulation were variable and inconsistent. Where positive stimulation was recorded, the nature of the positive response was increased tumescence in 6.4%, decreased tumescence in 32.2%, and decreased tumescence preceded or followed by increased tumescence in 60.4%. But where investigators stated the NVB was not present, the device's lack of specificity (only 54%) suggested that surgeons could not reliably depend upon nerve stimulation results to make intraoperative decisions concerning whether a structure can be safely preserved or excised.[30]

Hanna, *et al.* (2002) reported a small uncontrolled pilot study of middle-aged men (only one ≥ 65 years) with intact preoperative sexual function before diagnosis of rectal cancer who subsequently underwent TME. Walsh, *et al.'s* problems with lack of specificity in use of the nerve stimulation device by experienced urologists performing nerve-sparing radical retropubic prostatectomies seemingly did not apply to Hanna, *et al.'s* experience performing nerve-sparing low anterior colonic resection using a technique of sharp pelvic dissection and TME. Suggesting that technical differences likely explained the discrepancy, Hanna's group noted that in their hands extensive exposure of the pelvic sidewall and putative nerve trunks allowed clear definition of the area to be stimulated and resulted in 100% specificity, i.e., no false positive responses observed. Reflecting, however, lack of a standardized definition of a positive response, the 100% specificity reported might be partially or wholly explained by the assessment of nerve integrity using the minimal current required to produce a 2% increase in tumescence, rather than any change or a minimum change in tumescence of 0.5%. Alternatively, some of the favorable postoperative sexual functioning reported might also have been secondary to or confounded by careful patient selection, more extensive exposure of the pelvic sidewalls and nerve trunks in these colorectal procedures, and/or differing skill levels of the operating surgeons rather than utilization of electrical nerve stimulation with plethysmography.[31]

Da Silva, *et al.* (2004) reported on 29 patients whose median age was 58 years and noted that advanced disease, a narrow pelvis, intraoperative bleeding and prior pelvic surgical dissection all placed autonomic nerves at risk for damage during rectal dissection. Highlighting the study's selection bias, visual identification with nerve stimulator confirmation during dissection was attempted in only 13 of the 29 patients enrolled "according to the surgeon's preference"; but electrical nerve stimulation with plethysmography was reported to have confirmed preservation of the autonomic nerves "at least unilaterally" in 27 of 29 patients at the end of the procedure. The authors stated that while the nerve stimulator/locator is approved by the FDA for use during rectal surgery and "may potentially" increase identification of autonomic nerves during TME, its role required further evaluation.[32, 33]

In summary, the body of evidence is overall of poor quality. Published results are undermined by selection bias and lack of generalizability, and review of the literature does not support Medicare coverage of electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography to accurately inform intraoperative decision-making or improve postoperative health outcomes for patients undergoing nerve-sparing prostatic or colorectal surgical procedures. Therefore, the evidence is not adequate to conclude that electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography is reasonable and necessary for Medicare beneficiaries undergoing nerve-sparing prostatic or colorectal surgical procedures.

IX. Decision

CMS has determined that the evidence is not adequate to conclude that electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography is reasonable and necessary for Medicare beneficiaries undergoing nerve-sparing prostatic or colorectal surgical procedures. Therefore, we are issuing a national noncoverage determination on these uses of the test for the Medicare population.

Appendix A: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS normally divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)
- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Improved health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

---

[1] Hanna, *et al.* 2002

[2] Maurer 2005

[3] Burnett 2005

[4] Keating 2004

[5] Meuleman and Mulders 2003

[6] Rabbani, *et al*. 2000

[7] http://www.fda.gov/cdrh/pdf4/k041732.pdf

[8] Rosen, *et al.* 1997

[9] Briganti, *et al.* 2005

[10] Karakiewicz, *et al.* 2005

[11] Klotz, *et al.* 2000

[12] Allen, *et al.* 1993

[13] Yaman, *et al.* 2004

[14] Klotz and Herschorn 1998

[15] Kim, *et al.* 2000

[16] Klotz and Herschorn 1998

[17] Kim, *et al.* 2000

[18] Klotz, *et al*. 2000

[19] Holzbeierlein, *et al.* 2001

[20] Chang, *et al.* 2001

[21] Walsh, *et al.* 2001

[22] Hanna, *et al.* 2002

[23] da Silva, *et al.* 2004

[24] da Silva, *et al.* 2005

[25] Klotz, *et al.* 2000

[26] Klotz and Herschorn 1998

[27] Kim, *et al.* 2000

[28] Holzbeierlein, *et al.* 2001

[29] Chang, *et al.* 2001

[30] Walsh, *et al.* 2001

[31] Hanna, *et al.* 2002

[32] da Silva, *et al.* 2004

[33] da Silva, *et al.* 2005

Back to Top

Bibliography

FDA 510(k) for electrical stimulation of the cavernous and associated parasympathetic nerves with penile plethysmography. Last accessed August 2006 at: http://www.fda.gov/cdrh/pdf4/k041732.pdf

NCA tracking sheet for cavernous nerves electrical stimulation with penile plethysmography. Last accessed May 2006 at: http://www.cms.hhs.gov/mcd/viewtrackingsheet.asp?id=174

Allen R, Smolev J, Engel R, *et al.* Comparison of rigiscan and formal nocturnal penile tumescence testing in the evaluation of erectile rigidity. *Journal of Urology* 1993;149(5 Pt 2):1265-1268.

Briganti A, Gallina A, Salonia A, *et al.* Reliability of classification of erectile function domain of the international index of erectile function in patients affected by localized prostate cancer who are candidates for radical prostatectomy. *Urology* 2005;66(5):1140; author (Karakiewicz 2005) reply 1140-1141.

Burnett A. Erectile dysfunction following radical prostatectomy. *Journal of the American Medical Association* 2005;293(21):2648-2653.

Chang S, Peterson M and Smith J. Intraoperative nerve stimulation predicts postoperative potency. *Urology* 2001;58(4):594-597.

da Silva G, Zmora O, Borjesson L, *et al.* The efficacy of a nerve stimulator (cavermap) to enhance autonomic nerve identification and confirm nerve preservation during total mesorectal excision. *Diseases of the Colon & Rectum* 2004;47(12):2032-2038. Corrected and republished in: *Diseases of the Colon & Rectum* 2005;48(12):2354-2361.

da Silva G, Zmora O, Borjesson L, *et al.* The efficacy of a nerve stimulator (cavermap) to enhance autonomic nerve identification and confirm nerve preservation during total mesorectal excision. *Diseases of the Colon & Rectum* 2005;48(12):2354-2361.

Hanna N, Guillem J, Dosoretz A, *et al.* Intraoperative parasympathetic nerve stimulation with tumescence monitoring during total mesorectal excision for rectal cancer. *Journal of the American College of Surgeons* 2002;195(4):506-512.

Holzbeierlein J, Peterson M and Smith J. Variability of results of cavernous nerve stimulation during radical prostatectomy. *Journal of Urology* 2001;165(1):108-110.

Karakiewicz P, Shariat S, Naderi A, *et al.* Reliability of remembered international index of erectile function domain scores in men with localized prostate cancer. *Urology* 2005;65(1):131-135.

Keating J. Sexual function after rectal excision. *Australian and New Zealand Journal of Surgery* 2004;74:248-259.

Kim H, Stoffel D, Mhoon D, *et al.* A positive cavermap response poorly predicts recovery of potency after radical prostatectomy. *Urology* 2000;56(4):561-564.

Klotz L, Heaton J, Jewett M, *et al.* A randomized phase 3 study of intraoperative cavernous nerve stimulation with penile tumescence monitoring to improve nerve sparing during radical prostatectomy. *Journal of Urology* 2000;164(5):1573-1578.

Klotz L and Hershorn S. Early experience with intraoperative cavernous nerve stimulation with penile tumescence monitoring to improve nerve sparing during radical prostatectomy. *Urology* 1998;52(4):537-542.

Maurer C. Urinary and sexual function after total mesorectal excision. *Recent Results in Cancer Research* 2005;165:196-204.

Meuleman E and Mulders P. Erectile function after radical prostatectomy: a review. *European Urology* 2003;43:95-102.

Rabbani F, Stapleton A, Kattan M, *et al.* Factors predicting recovery of erections after radical prostatectomy. *Journal of Urology* 2000;164:1929-1934.

Rosen R, Riley A, Wagner G, *et al.* The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49:822-830.

Walsh P, Marschke P, Catalona W, *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(3):491-494.

Yaman O, Tokatli Z, Oxdiler E, *et al.* Effect of aging on quality of nocturnal erections: evaluation with NPTR testing. *International Journal of Impotence Research* 2004 Apr;16(2):150-153.

Back to Top