ORIGINAL ARTICLE

Neuromodulation of Pelvic Visceral Pain: Review of the Literature and Case Series of Potential Novel Targets for Treatment

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■ **Abstract**

Chronic pelvic pain (CPP) is complex and often resistant to treatment. While the exact pathophysiology is unknown, the pain states resultant from conditions such as interstitial cystitis and the like yield patients with a presentation that bears a striking similarity to neuropathic syndromes that are known to respond to neuromodulation. While there has been past success using the sacral region as a target for spinal cord stimulation (SCS) to treat these patients, there remains to be a consensus on the optimal location for lead placement. In this article, the authors discuss the potential etiology of CPP, examine the current literature on lead placement for SCS as a method of treatment, as well as present several cases where novel lead placement was successfully employed. ■

Key Words: pelvic pain, spinal cord stimulation, pain, intractable, complex regional pain syndromes, dorsal root ganglion, neuralgia

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INTRODUCTION

Spinal cord stimulation (SCS) has been utilized as a method of controlling complex, intractable pain syndromes for over 40 years and has continued to expand its indications at every turn. Although the modality's precise mechanism of analgesia (ie, ''gate theory''[1]) is still a topic of debate, its success in improving outcomes is well known and has prompted physicians to attempt to expand its applicability to other wayward pain patterns. Many studies over the last 15 years have documented the ability of SCS to effectively treat neuropathic pain states. In 1997, Kumar[2] reported that peripheral neuropathy and complex regional pain

syndrome (CRPS) were among the top 5 most common etiologies for treatment with SCS and also the most successfully treated. Other studies have gone on to describe success with SCS in neuropathic or ''sympathetically-driven'' pain states.[3,4] With the ability to now offer improvement in such difficult conditions as those mentioned above, physicians began to search for other patient populations with neuropathic or ''CRPS-like'' pain states that could potentially benefit from SCS neuromodulation—one such entity being pelvic pain.

The pelvis is a complex region of the body. It is comprised of both visceral and somatic structures, including the sexual organs, all of which receive innervation from the sympathetic, parasympathetic, and somatic nervous system either in combination or in singularly. The complex innervation of the pelvis makes diagnosis of pain in the region extremely difficult. The geography and complicated neuroanatomy of the pelvis makes identifying noxious catalysts in the area troublesome. Delay in diagnosis could arguably delay treatment, which could subsequently convert an acute, noxious stimulus into the entity termed chronic pelvic pain (CPP).

CPP has been defined as a ''non-malignant pain perceived in the pelvis in either men or women. In the case of documented nociceptive pain that becomes chronic, the pain must have been chronic or continuous for at least 6 months.''[5] Studies from the United States and United Kingdom have reported a prevalence of 14.7% and 24%, respectively, in women of reproductive age.[6,7] The direct costs of CPP have been estimated at over $2.8 billion.[6,7] Previously identified by various names such as pelvalgia, and inclusive to a variety of diagnoses ranging from abacterial prostatitis to pelvic floor dysfunction, the entity was subsequently renamed ''chronic pelvic pain syndrome'' in an effort to better define the presence of ongoing pelvic pain in the absence of clearly identified, nociceptive input.[8,9]

CPP occurs more often in the female population (affecting over 9 million women in the U.S.[10]) and has often initially been labeled as interstitial cystitis/painful bladder syndrome (IC/PBS). In men, CPP is frequently referred to as chronic prostatitis (CP). The exact cause of CPP is unknown, but may be related to a number of inciting pathologies that render one susceptible to the signs and symptoms characteristic of CPP. Predisposing (or associated) factors in the female population include a history of multiple laparoscopies,[11] endometriosis, sexual or physical abuse,[9,12] vulvar vestibulitis, fibromyalgia, and irritable bowel syndrome.[13–15] In men, the most common etiology of CPP is thought to be either an inflammatory or noninflammatory insult to the prostate, with the syndrome accounting for up to 90% to 95% of all cases of prostatitis.[8,16] There is no known, direct cause for CPP, and it remains a diagnosis of exclusion.

Some patients with CPP are successfully treated with conservative measures and medication, while many others require more aggressive treatment. Interventional options range from injection therapy (hypogastric plexus block, ganglion impar block, pudendal nerve block) to even more invasive options such as surgery (eg, hysterectomy). Currently, no consistently effective treatments are available. One reason that a definitive treatment for CPP remains elusive is that its exact etiology remains unknown. Although unclear, the pathophysiology of CPP seems to parallel many common, centralized, neuropathic, and sympathetically driven pain models. Some have proposed that the disease process would likely have been labeled CRPS had it occurred in an extremity. For instance, just as patients with CRPS often complain of hyperesthesia and allodynia in the affected extremity, patients with CPP often experience similar, painful sensations with normally non-noxious activities such as urination, sexual contact, or ovulation. In 2003, Janicki[11] proposed the idea that CPP was a form of CRPS and postulated that a ''wind-up'' phenomenon served to hypersensitize neurons in a manner similar to CRPS such that normally non-noxious stimuli (ie, the sensation of a full bladder) become perceived as painful. Recognizing the similarities to a pathology known to respond to SCS, neuromodulation has been utilized as a treatment modality for CPP.

The most significant challenge in successfully utilizing neuromodulation for the treatment of chronic pain lies in correctly identifying proper SCS lead position, which provides adequate and appropriate coverage of the affected area. Despite various alternatives proposed in the past, there has yet to be a true consensus on optimal lead positioning for the treatment of CPP. This article will attempt to outline the pathophysiology and some of the differential diagnoses of CPP, outline the current treatments modalities for the syndrome as it pertains to SCS, and describe several cases of novel SCS lead placement for the treatment of CPP.

CASE SERIES

We present a technical report in the form of a case series of 5 patients with CPP treated with neuromodula-

Table 1. Patient Demographics

Patient	Sex/Age (years)	Location of Pain	Cause	Duration of Pain (years)	Final Placement of Lead	Proceeded to Permanent
CB	F/59	Vaginal pain	Yeast infection	17	T7	No
LC	F/39	Pelvic/lower abdominal (visceral)	Endometriosis	3	T7	Yes
NL	M/74	Rectal/low back and bilateral lower extremities	Rectal fistula and spinal stenosis	3.5	T6	Yes
CN	F/73	Rectal pain	Unknown	3	T6	Yes
DF	F/71	Sacral/rectal neuritis and vulvodynia	Hemorrhoidectomy	16	T12-L1	Yes

tion via SCS after having failed treatment with conventional medications and interventional techniques (Table 1). The etiology of each of the patient's CPP varied as well as the overall distribution of the pain. In each case, the patient was given in-depth counseling regarding the possibility of utilizing SCS for his or her condition and provided literature as well as time for review. Prior to the trial phase, each patient was required to obtain psychiatric clearance. Pertinent potential risks and benefits were reviewed, and informed written consent was obtained.

Patient #1

CB: 59-year-old female with a several-year history of vaginal pain caused by treatment of a yeast infection that resulted in an outbreak of sores to the external vagina. Carrying a diagnosis of vulvodynia, the patient described a constant pain, sharp and burning in character, that was located in both labia majora (Right > - Left). Interventions to alleviate her pelvic pain prior to SCS included multiple ganglion impar blocks, caudal epidural steroid injections, right L5/S1 transforaminal epidural steroid injections, and a Simplicity III radiofrequency lesioning of right S1-S4 primary dorsal rami in conjunction with radiofrequency lesioning of right primary dorsal ramus L5.

The trial was performed with fluoroscopy, utilizing the standard, percutaneous technique to insert the leads. The patient was positioned prone, with the lumbar spine prepared in a typical sterile fashion and sterilely draped. A 14-gauge Touhy needle was then advanced at T12/L1 with intermittent fluoroscopic guidance into the epidural space. Position of the needle tip in the epidural space was confirmed both with fluoroscopy and using the loss-of-resistance-to-air technique. Thereafter, a Medtronic SCS, single octrode lead was advanced under live-fluoroscopic guidance with final lead position at T7 (Figure 1). An intraoperative stimulation trial was then conducted to ensure appropriate coverage of the affected pelvic regions. Leads were then secured with an anchoring device and attached to external pulse generators. The patient was discharged home the same day and told to return in 1 week to evaluate the efficacy of the trial.

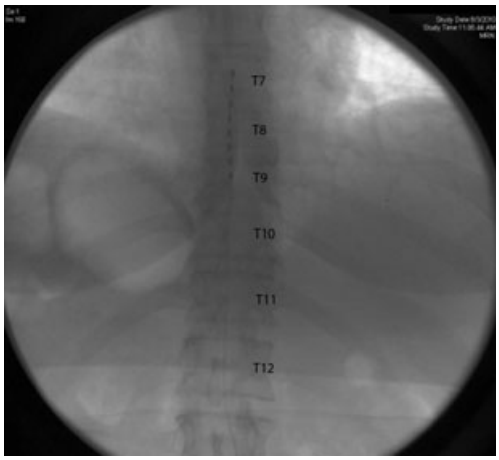

Figure 1. Patient—CB, diagnosis—vulvodynia, final lead placement—T7 (image from trial).

The patient had appropriate coverage over the entire affected area; however, the patient found the sensation created by the SCS intolerable—she, therefore, chose not progress to the implant phase. The patient is still returning to the Pain clinic for regular follow-up with no overall improvement in her pain. There were no complications during the trial or implant phase of the procedures.

Patient #2

LC: 39-year-old female with a long-standing history of endometriosis who originally presented with chronic abdominal, visceral, and pelvic pain. The patient described a left-sided, lower abdominal pain involving the perineum that was aggravated by walking and

described as ''intermittent contraction.'' Prior to SCS, the patient was treated with a hypogastric block that was unsuccessful in relieving her pain.

The trial was performed with fluoroscopy, utilizing the standard, percutaneous technique to insert the leads. The patient was positioned prone, with the lumbar spine prepared in a typical sterile fashion and sterilely draped. A 14-gauge Touhy needle was then advanced at L2/3 with intermittent fluoroscopic guidance into the epidural space. Position of the needle tip in the epidural space was confirmed both with fluoroscopy and using the loss-of-resistance-to-air technique. Thereafter, a Medtronic SCS, single octrode lead was advanced under live-fluoroscopic guidance with final lead position at T7. An intra-operative stimulation trial was then conducted to ensure appropriate coverage of the affected pelvic regions. Leads were then secured with an anchoring device and attached to external pulse generators. The patient was discharged home the same day and told to return in 1 week to evaluate the efficacy of the trial. The trial was deemed a success at week's end by the patient and practitioner (decreased pain and/or increased functional status); she was scheduled for permanent implantation.

LC subsequently underwent permanent implant of 2 Medtronic SCS octrode leads. The epidural space was accessed at L2/3 and L3/4 for the dual-lead, permanent implant. Final lead placement of the permanent implant was as follows: left lead at the inferior portion of the T7 vertebral body, midline, and the right at the middle of the T8 vertebral body (Figure 2). LC reports her pain is greatly improved and that stimulation continues to cover the affected area at 3-month follow-up.

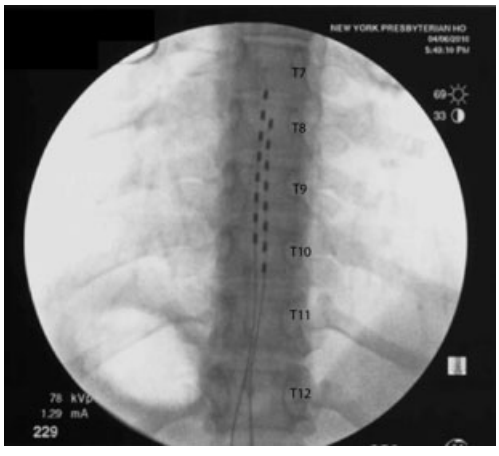

Figure 2. Patient—LC, diagnosis—visceral pain secondary to complications of endometriosis, final Lead placement—T7.

She also reports that her chronic headaches have decreased in frequency since the implant. There were no complications during the trial or implant phase of the procedures.

Patient #3

NL: 74-year-old male with a 10-year history of chronic rectal and perianal pain secondary to a rectal fistula. The patient described a rectal discomfort he described as a gnawing and burning sensation that not only prevented him from walking, but also interfered with his ability to perform many activities of daily life. Interventions prior to SCS for this patient included multiple epidural steroid injections, trigger point injections, and a ganglion impar block.

The trial was performed with fluoroscopy, utilizing the standard, percutaneous technique to insert the leads. The patient was positioned prone, with the lumbar spine prepared in a typical sterile fashion and sterilely draped. A 14-gauge Touhy needle was then advanced at L4/5 with intermittent fluoroscopic guidance into the epidural space. Position of the needle tip in the epidural space was confirmed both with fluoroscopy and using the loss-of-resistance-to-air technique. Thereafter, a Medtronic SCS, single octrode lead was advanced under live-fluoroscopic guidance with final lead position at T6. An intra-operative stimulation trial was then conducted to ensure appropriate coverage of the affected pelvic regions. Leads were then secured with an anchoring device and attached to external pulse generators. The patient was discharged home the same day and told to return in 1 week to evaluate the efficacy of the trial. The trial was deemed a success at week's end by the patient and practitioner (decreased pain and/or increased functional status); he was scheduled for permanent implantation. There were no complications during the trial phase of the procedure.

NL subsequently underwent permanent implant of 2 ANS SCS octrode leads. The epidural space was accessed at L2/3 and L3/4 for the dual-lead, permanent implant. Final lead position of the permanent implant was as follows: both leads at the inferior end-plate of the T6 vertebral body in the midline. The patient suffered lead migration [right lead migrated caudally to T9] and subsequent loss of adequate coverage. The leads were subsequently repositioned (Figure 3) and coverage of the affected areas was recaptured. NL reported 50% pain relief at 10-month follow-up. The

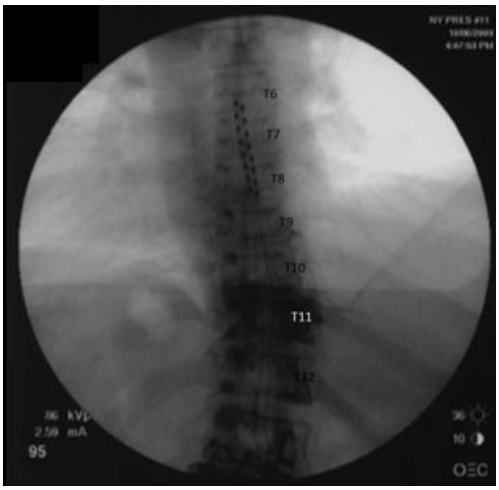

Figure 3. Patient—NL, diagnosis—rectal pain, final lead placement—T6, (patient had lead migration after permanent implant with subsequent position adjustment. This image represents the most recent image documenting lead position).

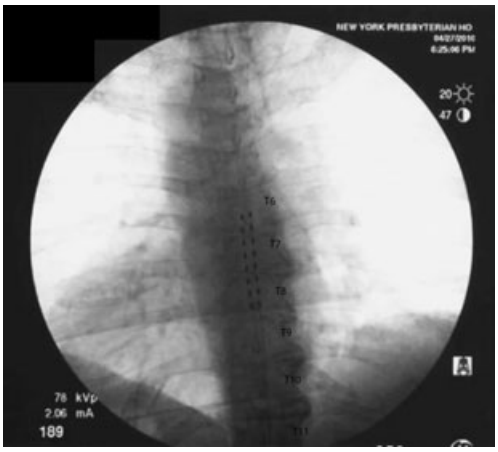

Figure 4. Patient—CN, diagnosis—rectal pain, final lead placement—T6.

patient is utilizing fewer breakthroughs opioid medication, as evidenced by an increased interval between prescription refills, and he ascribes to being able to perform more activities of daily living. Additionally, he reports coverage in the low back as well as in the lower extremities.

Patient #4

CN: 73-year-old female with a history of rectal pain. The patient described her rectal pain as burning in nature and exacerbated by most activities. Prior to SCS, the patient was treated with a hypogastric block that was unsuccessful in relieving her pain.

The trial was performed with fluoroscopy, utilizing the standard, percutaneous technique to insert the leads. The patient was positioned prone, with the lumbar spine prepared in a typical sterile fashion and sterilely draped. A 14-gauge Touhy needle was then advanced at L2/3 with intermittent fluoroscopic guidance into the epidural space. Position of the needle tip in the epidural space was confirmed both with fluoroscopy and using the loss-of-resistance-to-air technique. Thereafter, a Medtronic SCS, single octrode lead was advanced under live-fluoroscopic guidance with final lead position at T6. An intra-operative stimulation trial was then conducted to ensure appropriate coverage of the affected pelvic regions. Leads were then secured with an anchoring device and attached to external pulse generators. The patient was discharged home the same day and told to return in 1 week to evaluate the efficacy of the trial. The trial was deemed a success at week's end by the patient and practitioner (decreased pain and/or increased functional status); she was scheduled for permanent implantation.

CN subsequently underwent permanent implant of 2 Medtronic octrode leads. The epidural space was accessed at L2/3 and L3/4 for the dual-lead permanent implant. Final lead position for the permanent implant was at the T6 vertebral body in the midline (Figure 4). CN reported 50% pain relief at 3-month follow-up. Her opioid medication needs have decreased (the patient now takes methadone 5 mg po tid prn, decreased from 5 mg po tid to 2.5 mg po bid prn), and her overall activity level has increased. There were no complications during the trial or implant phase of the procedures.

Patient #5

DF: 71-year-old female presented with complaints of vaginal and rectal pain for 16 years. She stated her pain began in 1994 after a hemorrhoidectomy and increased in 1999 after undergoing abdominal and pelvic adhesion removal. Her pain was described as constant, 5/10 pain intensity, and burning and stabbing in nature. It was exacerbated by sitting and position change and improved with rest, ice, analgesics, and massage. The patient had been evaluated by multiple gynecologists, completed physical therapy, tried several different medications, and attempted multiple injection therapies (including traditional epidural injections, caudal epidurals, and pudendal nerve blocks) with no relief.

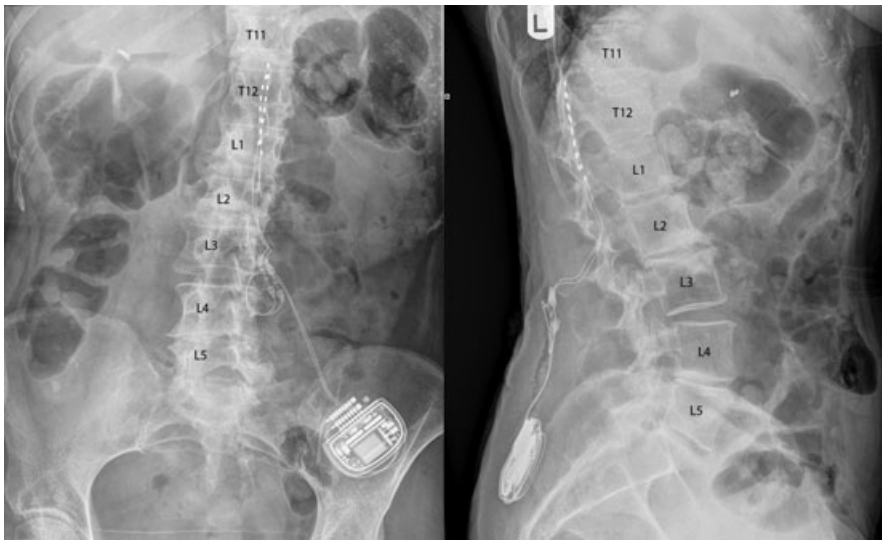

Figure 5. Patient—DF, diagnosis—sacral/rectal neuritis and vulvodynia, final lead placement—conus/T12 (left—anterior-posterior image; right—lateral image).

Electromyography and nerve conduction studies revealed a bilateral S2 radiculopathy. No lesions amenable to surgery were found on imaging studies. Her physical exam revealed loss of sensation at S1, S2, and S3—consistent with sacral neuritis. She had mild difficulty walking on her toes, but was able to walk on her heels unimpaired. The patient was tender diffusely over the bladder and buttocks. Straight leg raise was negative bilaterally, and motor findings and atrophy were absent. The patient was ultimately diagnosed with sacral/rectal neuritis and vulvodynia.

The patient elected to undergo a trial of SCS at the level of the conus in May 2010, which resulting in > 50% pain relief. She subsequently decided to proceed with permanent implantation of a SCS, which was completed in June 2010. Leads were placed at the T12-L1 level, straddling the conus (Figure 5). Postoperative follow-up in July 2010 revealed a pain rating of 1/10. She reported the stimulation was working very well, and her level of activity had increased, and her use of analgesic medications had decreased significantly.

PATHOPHYSIOLOGY AND POTENTIAL PATHOLOGIC CAUSES

Generally speaking, pain may be categorized into 1 of the 3 types: somatic, visceral, and neuropathic. Somatic pain originates from skin, muscles, some soft tissue, bones, and joints and is subsequently transmitted along sensory afferents and is thus well localized and perceived as sharp, burning, or aching.[5,17] Much like its name, visceral pain originates from internal viscous structures and is perceived as dull and aching. Being transmitted through sympathetic fibers of the autonomic nervous system, it is often poorly localized[18] and may be associated with autonomic dysfunction [eg, nausea, vomiting, sweating]. Neuropathic pain is a result of an insult or injury to the somatosensory nervous system (peripheral or central), whereby an insult to the nervous tissue leads a pain syndrome often characterized by dysesthesias, allodynia, and hyperesthesia.[5] In the case of CPP, it has been postulated that a disease state damages a particular organ leading to somatic or visceral pain, which over time develops into neuropathic pain.

Interstitial Cystitis/Painful Bladder Syndrome

As alluded to above, CPP is a broad diagnosis of exclusion that likely encompasses many other pathologic states and even more likely encompasses an evolution of those states to a neuropathic or CRPS-like state. IC/PBS is one such state that has received a great deal of attention owing to its prevalence. In 1999, reports from the Nurses Health Study found that over 6% of women in the U.S. were found to have "classic" IC.[19] More recently, in 2009, the Rand Interstitial Cystitis Epidemiology study detailed a prevalence of 3% to 6% in the general population.[20] It went on to report

that approximately 3.4 million U.S. women have signs and symptoms of IC/PBS, which equates to a prevalence of 2.7% in the female population.

IC/PBS is characterized by frequency, urgency, dysparenia, nocturia, and often pelvic and/or abdominal pain.[21] In 2002, the International Continence Society defined IC/PBS as:

- Suprapubic pain related to bladder filling (along with one or both of the following)—without a proven urinary tract infection.[22]
  1. Increased daytime frequency.
  2. Increased nighttime frequency.

In 2007, the European Society for the Study of Interstitial Cystitis (ESSIC) proposed the term "bladder pain syndrome" be used in parallel with or instead of IC in accordance with the criteria later:

- Chronic (> 6 months) pelvic pain.
- Pressure or discomfort perceived to be related to the urinary bladder.
- Accompanied by at least one other urinary symptom like persistent urge to void or frequency.[23]

While the exact etiology of IC/PBS is still unknown, many possible mechanisms have been proposed including autoimmune disorders, infection, pelvic floor dysfunction, toxins, and bladder wall defects. Many experts agree that a defect in the urothelial lining or glycosaminoglycan layer is most likely the primary cause.[10] When the urothelium is exposed to a particular noxious stimulus, mast cell activation occurs within the bladder wall—an influx of potassium ions upregulates afferent nerves, which in turn activate more mast cells. This positive-feedback situation leads to increased sensory nerve fiber activity in the bladder, chronic inflammation, and ultimately a neuropathic pain state involving the innervation of the bladder; pain is now manifested through visceral allodynia and hyperalgesia of the bladder and the adjacent pelvic organs.[24]

IC/PBS is diagnosed via cystoscopy and hydrodistention and may be accompanied with a biopsy when other probable causes of pain have been excluded. In symptomatic patients, small petechial hemorrhages called "glomerulations" on bladder distention can be indicative of the disease state.[25] 10% of patients with IC/PBS may present with a Hunter's ulcer evident on cystoscopy. In patients with longstanding IC/PBS, histological examination yields marked edema and injury to the blood vessels and nerves in the muscularis layer (consistent with neurogenic inflammation).[25] Along with deafferentation of and vasomotor injury to the bladder, IC/PBS bears a striking similarity to CRPS.[26–28] Without a thorough diagnostic evaluation, one could easily mistake it in a female patient for that of vaginitis, vestibulodynia, or pelvic floor dysfunction.[29]

Chronic Prostatitis (CP)/Prostadynia (PD)

Although IC/PBS can affect men (albeit the disease has a 5-fold predilection for women),[10] its counterpart in the male population with respect to prevalence is CP/PD. Despite likely being underreported secondary to the syndrome's vague constellation of bothersome symptoms (urinary frequency, dysuria, poor urinary flow, and genital or perineal pain), CP/PD still manages to make up a large portion of all cases of prostatitis.[22] In the U.S. alone, approximately 25% of men presenting with genitourinary tract problems are diagnosed with prostatitis, and up to 30% of those are ultimately diagnosed with CP/PD.[30,31]

PD has been considered a diagnosis of exclusion and a possible variant of IC as it may represent different manifestations of the same disease process.[32] While the pathophysiology of CP is also unknown, a great deal of effort has been put forth toward its classification. According to the National Institute of Health, there are 4 categories of prostatitis:

- Category I—Acute prostatitis: systemic symptoms like fever, chills, and/or hypotension 2nd to an underlying pathogen
- Category II—Chronic bacterial prostatitis: recurrent episodes of documented infections of the lower urinary tract with the same uropathogen, presenting with pelvic pain, urinary symptoms, and ejaculatory pain
- Category III—CP/pelvic pain syndrome: pain in a variety of areas (ie, perineum, rectum, prostate, penis, testicles, and/or abdomen) for 3 or more of the previous 6 months—as well as urinary symptoms, and painful ejaculation. No documented urinary tract infections from any uropathogens.
  - * This is the most common urological diagnosis in men over 50 and the 3rd most common in those under.
  - ○ IIIA: Inflammatory—white blood cells present in prostatic secretions

  - IIIB: Noninflammatory—affects 10% to 16% of men
- Category IV—Asymptomatic inflammatory prostatitis: asymptomatic and is often an incidental finding during evaluation for infertility or prostate cancer.[33–36]

Historically, it was thought that CP/PD was simply the result of inflammation; a hypothesis supported by the fact that symptomatic relief was often obtained with the administration of anti-inflammatory medications.[37] With further investigation, however, the disease process was also found to be associated with hypertrophy of smooth muscle, periurethral edema, and pelvic floor dysfunction resulting from increased tone in local musculature.[30] These phenomena have led to the supposition that the disease may actually also be due to an imbalance of the inflammatory cascade, proliferation of neurotrophin nerve growth factor (implicated in neurogenic inflammation), autoimmune processes, and central sensitization all contribute to the development of a neuropathic pain state.

Coccygodynia

Coccygodynia is a painful condition in or around the area of the coccyx, typically worsened with sitting, often stemming from trauma, infection, tumor, or osteoarthritis of the sacrococcygeal joint. There are, however, cases where the cause of pain is unidentifiable and is possibly being referred from surrounding visceral structures such as the rectum, sigmoid colon, the urogenital system (ie, IC/PBS or CP/PD), or spasm of the pelvic floor.[38] The idiopathic form comprises < 1% of all nontraumatic disorders of the spinal column.[39] There is a documented correlation between weight and incidence of coccygodynia, and as with IC/PBS, there is a predilection for the female population (5:1).[40,41]

Vulvodynia

First recognized in 1984, vulvodynia has been defined as vulvar discomfort occurring in the absence of either objective physical exam findings or a diagnosed neurological disorder.[42,43] Patients will often describe a sharp pain or burning that occurs in the vulva that may be constant, intermittent, or only provoked with contact. Provoked vestibulodynia, or vulvar vestibulitis, is the most common variant and is defined by pain triggered from a stimulus, which is normally painless (ie, wearing tight clothing, inserting tampons, etc.).[44] Reports suggest an in incidence of 15% to 16% of the female population; however, the true incidence may be higher.[25,45]

The exact etiology of the vulvodynia is debatable; however, the most strongly supported theory is the "muscular hypothesis" that suggests an increase in muscular tone in the superficial area of perineum leads to the symptomatology.[46] Neurogenic inflammation has also implicated, as biopsies of afflicted patients have revealed chronic inflammation of the mucosa along with neural hyperplasia.[47] Regardless of the etiology, some or all of the variants of vulvodynia likely possess a neuropathic component contributing to pain symptoms.

Anorectal Pain

Anorectal pain has been described in parallel with a multitude of conditions, the 3 most common being levator ani syndrome, coccygodynia, and proctalgia fugax.[48] Anorectal pain can either be idiopathic or secondary to an inflammatory, mechanical, neoplastic, or neurological process. Much like above-described pathologies, chronic, idiopathic anorectal pain is a diagnosis of exclusion. One must consider structural or malignant disorders like abscess, hemorrhoids, and cancer.[49] Like coccygodynia, the potential etiologies for the development of chronic, anorectal pain include spasm and general dysfunction of the pelvic floor muscles or a chronic, noxious event triggering a neuropathic pain state.

ANATOMICAL FEATURES

Visceral pain fibers, or the sympathetic nerve fibers, are known to often travel together with somatic. When treating a visceral pain syndrome like pancreatic cancer, the presynaptic pathways lending fibers to the prevertebral ganglion are the targets, that is, the celiac ganglion. If one were to attempt a neurolysis simply in the matching dermatomal distribution of the left flank, one would ignore these visceral pain fibers traveling within the sympathetic system and leave the patient's pain without significant improvement. The same should be considered with SCS as it pertains to CPP—as such, the anatomy of the sympathetic fibers should be noted.

Each spinal nerve receives sympathetic input in the form of unmyelinated, postganglionic fibers from the adjacent ganglion via the gray rami communicans (GRC). White rami communicans (WRC), present from T1 to L1 or L2, allow this input to continue into the spinal cord, now as myelinated, preganglionic fibers. This suggests that information carried via sympathetic fibers originating caudal to the L2 would enter the paravertebral chain at its respective level via a GRC, travel within the chain cephalad until at least L2 (or possibly several levels higher), whereby it will now seek its corresponding WRC, travel into the spinal cord and continue within the central nervous system.

Sympathetic input to the pelvis may also travel via the lumbar splanchnics. These contain preganglionic sympathetic and visceral afferent fibers that travel directly between the sympathetic trunk and the pelvic viscera via local ganglion. These originate at L1-L2, which obviously is much more cephalad than the sacral region.

Visceral pain fibers are theorized to travel a path via the corresponding sympathetic nerves of the region or organ in question, with their cell bodies in the thoracolumbar spinal ganglia and their central projections entering the spinal cord at L2 to as high as T2.[50] This could explain why patients with described pain that appears sympathetically maintained are not always responsive to conventional sympathetic blocks (ie, the ganglion impar or hypogastric plexus). It is for this reason we feel a lead placed sacrally could potentially leave a significant portion of pertinent fibers. One might create a dermatomally appropriate area and even capture a good share of the visceral and sympathetic fibers but still leave significant portion of those unaccounted for and yield a patient with incomplete stimulation.

TREATMENT WITH NEUROMODULATION

CPP is notoriously hard to treat in many cases. Obstacles to treatment include the aforementioned complex neuroanatomy of the pelvis, as well as psychologic comorbidities often associated with pelvic pain. Treatments targeting the hypothesized, proximal cause of pelvic pain often fail, either secondary to misdiagnosis or because a neuropathic pain syndrome has already evolved (ie, botulinum toxin injections in cases of surmised muscle dysfunction or antibiotics with a possible infectious cause). Typically, CPP enters the purview of the pain management physician after one or more specialists fail to divine the etiology of a patient's symptoms. Regional and sympathetic blocks are typically considered early, with SCS reserved for later in the treatment plan for those cases that are considered too refractory or severe.

Sacral Neuromodulation

To understand the use of neuromodulation in the pelvis, one must first understand its neuroanatomy. The pelvic viscera are parasympathetically innervated by the S2-S4 nerve roots and sympathetically innervated by the T12-L2 nerve roots. The parasympathetic outflow is transmitted via the pelvic splanchnic nerves (S2-4), which converge into the preganglionic pelvic splanchnic nerves. Sympathetic input to the pelvis arises from the thoracolumbar cord by way of the superior hypogastric plexus (which explains the popularity of this target for blocks in patients with CPP). Lastly, the somatic afferents and efferents to the pelvis originate from the S2-4 cord levels via the pudendal nerve—with S3 offering the primary supply to the anterior perineal musculature (Figures 6, 7).

Electrostimulation of the pelvic innervation and viscera has a long history in modern medicine. Saxtorph first reported its use in for the treatment of patients with contractile bladder and complete urinary retention in 1878.[51] This modality evolved to include the treatment of chronic neurogenic retention and hyperreflexia.[52] Eventually, electrostimulation gave way to neuromodulation in 1971 when Nashold et al.[53] described the first successful implantation of a SCS in the sacral spinal cord to initiate voiding in a patient with a spinal cord injury. In 1981, Tanagho and Schmidt subsequently demonstrated that stimulation of the S3 nerve root could be applied to a variety of GU pathologies (eg, incontinence and frequency) by modulating detrusor and sphincter action.[25,54] This research paved the way for the 1997 FDA approval of epidural sacral nerve root stimulation in the treatment of urinary urgency, frequency, urge incontinence, and retention.[54–56]

The mechanism behind sacral nerve stimulation's (SNS) ability to modulate micturition is still being elucidated. It may activate or reset the somatic afferents involved in sensory processing and the micturition reflex pathways in the spinal cord.[54] Additional theories surmise SNS may interfere with sympathetic signals to the bladder involved in the guarding and vesicosympathetic reflex, which control continence and

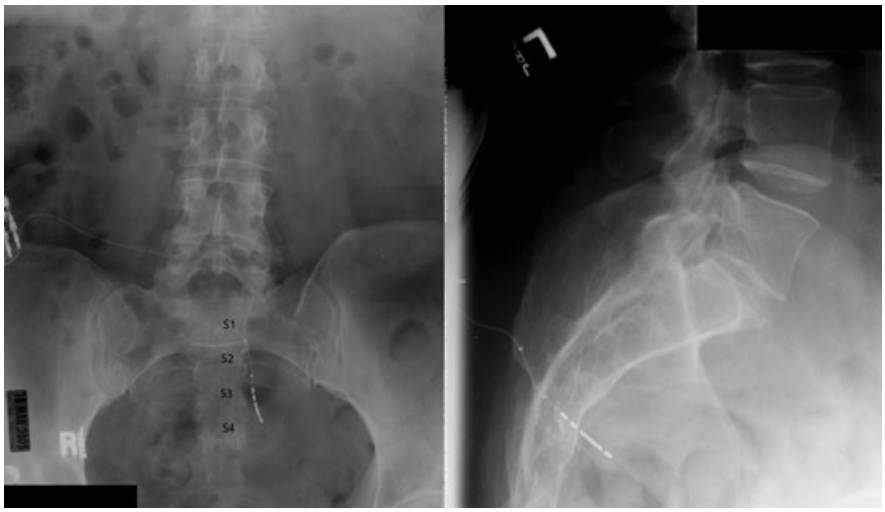

Figure 6. Picture of a Left S3 transforaminal lead placed via a retrograde approach (left—anterior-posterior image; right—lateral image).

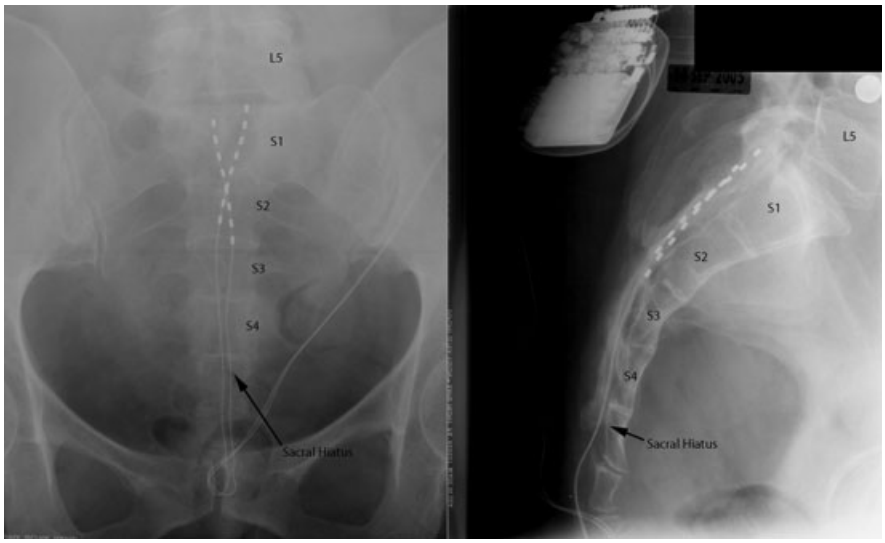

Figure 7. Picture of sacral leads placed via a caudal approach (left—anterior-posterior image; right—lateral image).

filling, respectively.[54,55] More recent studies have revealed SNS being correlated with increased activity in the brain (via PET) at the paraventricular gray, which is involved in activation or inhibition of the micturition reflex.[54,57]

SNS has shown consistent efficacy in the treatment of bladder dysfunction, incontinence, urinary retention/frequency, and even with fecal incontinence;[54,56,58–61] it has also shown great promise in treating the symptoms of IC/PBS. Hohenfellner et al.[62] described that while the concomitant voiding symptoms of the syndrome could be relieved, pain was less likely to be relieved. As use of the technology evolved, SNS had been expanded from a traditionally unilateral approach to a more aggressive bilateral one, as pain with IC/PBS is seldom unilateral.[63] Many subsequent smaller studies were able to demonstrate reductions in both pain and narcotic requirements with the more aggressive approach to SNS[64] (Maher et al. reported on 15 patients with IC that found an approximate reduction in pain of 27% with SNS,[65] Seigel et al. reported a 60% significant improvement in pain in 10 patients at a median follow-up of 19 months with SNS, while Everaert et al. had success in 11 patient for

almost 3 years [in both men and women] with SNS).[66,67]

The placement of leads in SNS requires a percutaneous, retrograde approach (caudally directed) that is technically challenging and has an increased risk of complication [ie, dural puncture and intrathecal electrode implantation]. Alo et al.[68] were the first to report on this technique. After accessing the epidural space, he describes advancing the leads in a caudally under fluoroscopic guidance. He then went on to place leads along the lumbar and sacral nerve roots via the neuroforamen. In subsequent case reports, he described more specific placement in the sacral region (ie, bilateral S2/3 placement of leads) as well as a lateral approach to the interlaminar space, still with retrograde advancement of the leads.[69–72] Feler et al.[25,73] have also reported favorable findings with SNS with retrograde placement of SCS leads. He utilized as many as 4 leads, targeting sacral nerve roots selectively by advancing the leads into the neuroforamen of each root.

In addition to IC/PBS, SNS has proven to be an effective treatment for other pathologies including CP/PD, coccygodynia, vulvodynia, anorectal pain, and even pelvic pain from general pelvic floor dysfunction and spinal cord infarction.[5,10,25,33,49,60,74,75] Despite all of the positive data supporting the use of SNS, critics point out that some patterns of referred pain remain refractory to the modality, that the extent of pain control varies greatly from one study to the next, that studies have failed to consistently demonstrate an overall improvement in quality of life for patients,[63,75] and that general complication rates with SNS have been reported as high as 18.2%.[76]

NOVEL TARGETS

Because some patterns of pain are refractory to SNS and the effect of neuromodulation may decrease over time secondary to epidural scarring, physicians continually search for additional locations for lead placement. In 2006, Kapural et al.[77] reported on a T11-L1 placement of leads in 6 patients with CPP who experienced both significant improvements of pain and reductions of opioid requirements. Kapural's work suggests that there are alternatives for lead placement when SNS fails to provide pain relief. Later, novel targets for lead placement in patients with CPP are described—alluding to the reported case series above which demonstrated positive results in mid-thoracic and conus lead placement.

Mid-Thoracic Neurostimulation (Patients #1 to 4)

SCS lead placement in the mid-thoracic region for CPP at face value would seem counterintuitive when considering the innervation of the pelvis and the basic orientation of the spinal cord. Neuromodulation this far rostral would seem more appropriate for affecting thoracic dermatomes; however, this region has been targeted and successfully utilized to provide relief for visceral pain. In 2011, Kapural et al.[78] demonstrated that leads placed at the T5-6 levels reduced pain scores in patients with severe chronic pancreatitis. As described previously, visceral pain fibers have a complex path that may not follow the basic dermatomal distributions that we generally cling to when deciding on lead placement for pain patterns that may explain successes in neuromodulation in this region.

We propose that this cephalad placement of leads may provide pain relief for patients afflicted with CPP by stimulating visceral/sympathetic fibers that may escape stimulation by more sacrally placed leads. While the exact mechanism remains unclear, it may have to do with the anatomy of the dorsal columns. The dorsal columns are arranged such that the fibers lie medially to laterally depending upon how caudally they exit the spinal cord. For example, fibers entering the spinal cord in the lumbar region would lie medial to fibers entering the spinal cord in the thoracic region. It stands to reason then that sacral fibers would present medially for the entirety of the cord; this anatomy should theoretically allow for the stimulation of these fibers at any point along their progression down the spinal cord. It has been documented that stimulation of the dorsal columns as cephalad as T11 can provide appropriate coverage for the treatment of CPP,[77] most likely by stimulation of the sacrally exiting fibers of the dorsal columns. This case series presents a similar pattern of sacral-fiber coverage with an even more cephalad placement of leads at T6 and T7. To our knowledge, no studies or publications exist that suggest such a placement.

Conus Placement (Patient #5)

SCS lead placement over the conus is not a novel idea; however, there have yet to be reported successes with the therapy. Placement of SCS leads at the conus seems to theoretically be ideal for the treatment of CPP. The conus is present at the L1-L2 region and is the termination of the spinal cord. It represents a point of

confluence for information to and from the pelvis via the cauda equina. The anatomy suggests the conus to be an ideal location for stimulation as a lead placed there could capture the maximal amount of innervation to the pelvis and thus minimize the amount of nociceptive input that could escape through alternate pathways.

Placement of SCS leads at the conus is not without its drawbacks. Firstly, its mobility within the spinal column makes it difficult to provide a consistent pattern of paresthesias. Secondly, there is an increased volume of cerebrospinal fluid between the epidural space and the neural tissue at the conus. This phenomenon means higher voltages may be required to access the dorsal columns, leading to inadvertent stimulation of the segmental roots. Segmental root stimulation is often associated with patients reporting discomfort and inability to tolerate the neuromodulation.

DISCUSSION

Refractory pain models that are characterized by neuropathic symptoms in any part of the body have historically been a challenge to treat for even the most astute pain physicians. While SCS is limited in its ability to mitigate malignant[28] and nociceptive pain,[79] its efficacy in treating neuropathic and sympathetically associated pain is well documented.[2,3,80–82] This is precisely the reason that SCS has been growing in popularity as a treatment modality, and its utility continues to extend beyond the treatment of intractable back pain and into the realm of patients afflicted with refractory, neuropathic pain disorders. It has been proposed that patients with CPP tend to display symptomatology (burning, dysesthesias, allodynia) analogous to other neuropathic pain disorders such as CRPS[11] and would, therefore, in some cases be ideal candidates for treatment with SCS. The authors would like to qualify, however, that SCS for pelvic pain remains experimental and empirical at this stage lest a better prognostic test or parameters for successful outcomes with SCS are described.

With neuropathic pelvic pain, the sacral portion of the cord theoretically appears to be the most ideal target for SCS. However, even though the pelvis receives both somatic and visceral innervation from the sacral spinal cord (not to mention the obvious correspondence to the dermatomal map), the unpredictable course of the sympathetic nervous system, and the fibers that accompany it, means it could escape coverage by a SCS placed over the sacral cord and potentially provide less than adequate pain relief. While some patients have responded well to sacrally placed leads, others have not, which makes coming to a consensus about optimal lead placement difficult. Whether this phenomenon is because of a failure to capture input not traveling along the sacral nerve roots is still a matter for debate.

The preceding case series demonstrated adequate and appropriate coverage of CPP with SCS lead placement at the T6 and T7 regions (Patients #1 to 4). Despite having different presentations and multiple etiologies, all of the patients received coverage to the affected regions with the previously undocumented, more-cephalad placement of epidural leads at T6 and T7. And while neuromodulation this rostral would seem beyond the reach of the sacral fibers complicit in the transmission of pain from this region, the organization of the spinal cord, as well as that of sympathetic nerve fibers, allowed for paresthesias to be achieved and sustained for relief.

The case series also presents a case of lead placement at the level of the conus (Patient #5), where in theory a dermatomal match to the pelvis should exist. Despite being a confluence of all sacral innervation, several potential pitfalls to placement of SCS leads at the conus exist. Not only is epidural to spinal cord space the greatest in this region, but the mobility of the conus within the spinal column makes consistent capture difficult. Nonetheless, we present a case where stimulation was not only possible, but effective.

A limitation we found in our presentation of these cases was the lack of standardization of pain medication utilized between the patients as well as the specific interventions performed prior to the consideration of SCS trialing. Additionally, while the presentation of the patients in the cases was collectively similar (ie, refractory pain located in the pelvic region), there were varied lengths of time relating to the existence of symptoms, and the specific etiologies/course of prior treatments were mixed.

CONCLUSION

As CPP has become an accepted diagnosis with increasing prevalence, discovering proven and successful treatment options has become a paramount concern. Not only are the symptoms of CPP crippling to the patient, but the disease is also frustrating to the pain physician as it is an entity often resilient to traditional pain medications and conventional interventions.

It has been shown that SCS yields significant improvements in CPP; we present support for successful symptom control with lead placement at the conus or the mid-thoracic region to provide pain physicians with additional options for lead placement.

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