

Contrasting the Percutaneous Nerve Evaluation Versus Staged Implantation in Sacral Neuromodulation

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Abstract Sacral neuromodulation is increasingly used for the treatment of voiding dysfunction, pelvic pain syndromes, and gastrointestinal disorders. While increased use of this technology has led to a greater understanding of its potential as well as its limitations, difficulty persists in identifying the patients that will benefit most. Either of two trial stimulation techniques is performed before placement of a permanent neuromodulator: the monopolar percutaneous nerve evaluation and the timed quadripolar staged trial. The preponderance of recent literature asserts the superior sensitivity of the staged trial over percutaneous nerve evaluation. However, the techniques offer disparate advantages, and other issues, such as cost-effectiveness, remain largely unexplored. The role of sacral neuromodulation will continue to expand as physicians and patients become increasingly aware of its therapeutic potential. Widespread adoption of this clinically superior technique will most rapidly help the greatest number of patients.

Keywords Sacral neuromodulation · Interstim · Percutaneous nerve evaluation · PNE · Staged implantation · Overactive bladder · OAB · Urge incontinence · Voiding dysfunction · Pelvic pain · Interstitial cystitis · Painful bladder syndrome · Cost-effective

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Introduction

Sacral neuromodulation (SNM) is a vitally useful alternative therapy for many patients with a variety of refractory voiding dysfunctions. In 1997, the U.S. Food and Drug Administration (FDA) approved SNM for urgency incontinence, and in 1999 for refractory urgency–frequency syndrome and nonobstructive chronic urinary retention [1, 2]. Non-FDA approved uses are also increasing. Several investigators report significant benefits of neuromodulation for pelvic pain disorders, fecal incontinence, fecal retention, and pediatric voiding dysfunction. While the exact mechanism of action is unknown, neuromodulation is thought to alter the pathological imbalance of sacral reflexes controlling bladder storage and emptying. Because it is difficult to predict therapeutic response, a trial phase of SNM is performed before placement of the implantable pulse generator (IPG). Two different testing methods are widely used and their relative value debated: the percutaneous nerve evaluation (PNE) and the staged implantation using permanent leads. This review discusses the relative merits of each technique as reported in the voiding dysfunction and pelvic pain literature.

Test Phase Techniques

Percutaneous Nerve Evaluation

The traditional PNE is an office-based technique that uses a temporary monopolar lead without an intrinsic retention mechanism, allowing for minimally traumatic deployment and retrieval. Most commonly, the lead is placed bilaterally via the S3 foramen under local anesthesia without the assistance of fluoroscopy. Correct lead placement is determined by a levator ani motor response, plantar flexion

of the ipsilateral great toe, and induction of perineal sensory activation [3]. Some groups advocate subsequent stimulation of the next caudal foramen to assess for S2 stimulated leg rotation, thereby offering additional confirmation of appropriate S3 placement of the test lead. The temporary lead is retained for the duration of the test phase by fixation to the skin surface with adhesive. The test phase is usually 4 to 7 days, limited primarily by lead migration and the patient's ability to restrict activity. PNE lead migration is particularly problematic among obese and active patients [3]. Following a successful test phase, the temporary lead is easily withdrawn (as well as any therapeutic effect), and the patient is taken to the operating room for fluoroscopically guided insertion of a permanent quadripolar tined lead and IPG in one setting. The device is then programmed, hoping to duplicate or improve upon the response to the temporary lead.

Staged Implantation

The staged implantation technique was first described in 1997 [3] in response to those patients that initially failed a PNE trial. This technique most commonly involves fluoroscopically guided unilateral placement of a permanent quadripolar tined lead in the operating room with the patient under sedation. Formerly, the lead lacked an intrinsic retention mechanism and was secured to the dorsolumbar fascia to decrease the rate of lead migration. This method of lead fixation was supplanted by the development of a self-retaining quadripolar tined lead in 2003 [4]. Intraoperative bipolar testing can be performed with the permanent lead, though it is not widely practiced. As with the PNE lead, intraoperative testing is typically performed with monopolar stimulation seeking a levator ani and ipsilateral great toe motor response and perineal sensory stimulation. While a suboptimal response to intraoperative monopolar stimulation may preclude placement of a PNE lead, this is not the case with a quadripolar lead. Postoperatively, the quadripolar lead affords far greater programming versatility as compared to the monopolar temporary lead, and thus, higher likelihood for therapeutic effect. Additional program options may be gained by placement of a second, contralateral, quadripolar lead. The permanent lead is then connected to extension wires that are tunneled through the subcutaneous tissue, further mitigating the risk of lead migration and infection [5, 6]. In contrast to the PNE lead, the incidence of lead migration is significantly reduced with these maneuvers, though cases of tined lead migration are reported [7]. The test phase may be extended as long as several weeks while optimizing programming [5]. If the test phase produces significant improvement in the symptoms, the patient is brought back to the operating room and the IPG is placed. The original quadripolar leads are not moved, and the demonstrably

successful test settings may be immediately programmed into the permanent device for uninterrupted treatment.

Test Phase Response Differs by Technique: Analysis by Clinical Indication

Subjective Response in Voiding Dysfunction

Patients reporting at least 50% improvement in symptoms during the test phase are traditionally considered a success. While this criterion is arbitrary, it is a commonly used surrogate to define success in both PNE and staged trials. Regardless, patients receiving the IPG implantation following a similarly defined successful trial, whether PNE or staged, may have similar long-term therapeutic benefit [6]. This suggests similar specificity among the two techniques. Thus, a sensitive endpoint in determining the relative merits of staged versus PNE trials is progression rate to IPG implantation.

Several groups demonstrated that staged trials have a greater rate of IPG implantation among neuromodulation-naïve patients. In 2008, Bannowsky et al. [8] reported their experience with SNM in patients with voiding dysfunction. In their study, 42 patients received bilateral PNE and 11 received bilateral tined leads. 82% of staged patients progressed to IPG placement, while only 47% of patients receiving PNE progressed to permanent implantation. Hijaz et al. [9] reported a progression from staged trial to IPG implantation in 161 of 214 patients (75.2%), though 14.6% of these patients were treated for interstitial cystitis. Blandon et al. [10] recently described their experience of 105 test procedures in 95 female patients with voiding dysfunction. Thirty patients underwent PNE and 75 patients received staged leads, 11 of which predated the tined lead and were instead anchored to the dorsolumbar fascia. The final 64 patients received self-retaining tined leads. The staged leads afforded a longer screening time of 3.4 weeks versus 1 week for PNE. Of patients receiving tined leads, 67% progressed to IPG implantation compared to 36% of patients with leads anchored to fascia and 40% of patients receiving PNE ($P=0.01$). Another study evaluated 30 patients aged 55 years and older with refractory urge incontinence randomized to either PNE or a staged technique [11]. The likelihood of progressing to IPG was significantly greater in the staged cohort (15 of 17 patients; 88%) compared to the PNE group (6 of 13 patients; 46%).

Additionally, many patients failing a PNE test will respond to a staged trial and proceed to IPG placement. In 2007, Siegel's group [12] reported on their considerable 11-year experience of 155 leads in 104 patients. Eighty-two nontined leads were placed after PNE trial and 73 quadripolar tined leads were implanted as part of a staged procedure. Seventeen of 28 patients failing the first trial and

undergoing a successful second trial had initially received PNE. Similarly, four of five patients requiring a third trial finally found success with a tined staged implant, and all five patients undergoing a fourth trial ultimately found success following a tined staged implant.

Based on our review, IPG implantation rates, as predicated on patient-defined symptom improvement, approach 40% to 50% in PNE and 70% to 90% in tined-lead staged trials. The lower rate of PNE progression to IPG implantation can be attributed to several factors. First, monopolar PNE programming is limited to changes in pulse width, frequency, amplitude, and either continuous or intermittent stimulation. In contrast, quadripolar leads have greater range of programming options with a variety of stimulation patterns. The staged technique exploits this advantage to the patient's benefit. Second, there is a significant incidence of PNE lead migration. The true rate of migration is unknown because imaging is not routinely performed for all PNE failures. A novel PNE tunneling technique that reduces PNE lead migration and confers greater progression to IPG implantation is described. However, it is unclear how many surgeons have adopted this modification [13]. Finally, these limitations shorten the PNE trial phase duration, thus further limiting the trial phase to observe any potential benefit of neuromodulation.

Unilateral Versus Bilateral Test Phase

Though several articles address the issue of unilateral versus bilateral stimulation, the comparative efficacy is not well studied and conflicting evidence abounds. In their series of 20 patients with voiding dysfunction, Kessler et al. [6] found that the only 2 long-term failures among 16 permanent placements occurred in patients with unilateral stimulation. In contrast, Scheepens et al. [14] noted no significant difference in progression to second stage or long-term outcome between unilateral and bilateral nontined temporary leads in patients with voiding dysfunction. A retrospective comparison of 55 patients undergoing unilateral test stimulation versus 69 patients undergoing bilateral test stimulation respectively for refractory voiding dysfunction revealed greater progression to permanent implant in the bilateral group (76%) compared to the unilateral group (58%) [15]. Although bilateral stimulation may offer more programming flexibility, it remains to be seen whether this translates to superior clinical effect.

Attempts to Quantify Response Based on Testing Technique

In an effort to objectively measure a physiologic difference between the two trial methods, Bannowsky et al. [8•] performed urodynamic studies on 30 patients with urinary

retention and 23 with overactive bladder (OAB) syndrome during the testing phase. All but one patient underwent bilateral stimulation. Conventional PNE was received by 42 patients (25 in retention, 17 with urgency–frequency) while 11 patients (5 in retention, 6 with urgency–frequency) underwent a staged trial.

All patients underwent preoperative and postoperative voiding diaries and videourodynamics. Both PNE and staged implantation groups improved in reduction of pad consumption and urge episodes. Among the patients with OAB, bladder capacity was increased by 30% with PNE and 52% with staged trials, while capacity at first urge was significantly improved only in the staged cohort. Both PNE and staged trials decreased detrusor instability by about 75%. Patients with nonobstructed urinary retention also fared better with the staged implantation technique. They demonstrated greater increase in maximum detrusor pressure (94%) over baseline, and 66% reduction in residual urine allowing for either voluntary micturition or reduction in catheterization frequency. Overall, they observed a permanent implantation rate of 47% among patients receiving PNE and significantly greater (82%) in staged implantation. While they retrospectively describe a heterogeneous nonrandomized cohort, the findings suggest a more robust response following the staged trial technique.

Comparison of Techniques in Interstitial Cystitis, Painful Bladder Syndrome, and Chronic Pelvic Pain

Since neuromodulation safety and efficacy first were established 10 years ago for voiding dysfunction, we have witnessed a surge of its utilization for various pelvic disorders. While not FDA-approved for these indications, many patients with refractory interstitial cystitis (IC), painful bladder syndrome (PBS), and chronic pelvic pain (CPP) now benefit from SNM and caudal epidural neuromodulation [16•, 17]. Similar to the voiding dysfunction patient population, the most optimal test modality has not been established for this patient population.

Peters et al. [17] reported outcomes of 21 patients with IC following bilateral PNE placement with confirmed motor and sensory responses during a 5 to 7 day test period. Of these patients, 14 (67%) had a positive response, 11 of whom (79%) progressed to the permanent lead placement, with a total implant rate of 52%. It is important to note that 100% of patients who had the permanent implant placed under sedation and confirmed sensory response did not require further reoperations or adjustments, whereas up to 43% patients who underwent implantation without sensory response verification required reoperation for lead adjustment and pocket revision. This suggests the importance of intraoperative confirmation for

optimal response to SNM. In the same paper, the authors also reported on 16 patients with IC receiving the unilateral staged technique with motor and sensory response confirmation following a 2-week testing period. All but one patient (94%) selected permanent generator placement and no reoperations were performed.

Another study reported similarly improved progression to IPG with the staged technique [18••]. In this study, 13 of 33 patients (39.4%) undergoing temporary PNE in the office progressed to the second stage, while 9 of 11 (81%) evaluated by staged quadripolar lead completed IPG implantation, including 5 who previously had failed PNE testing. Regardless of test modality, long-term success was equivalent among patients selecting permanent implantation.

Reproducibility of test-phase efficacy following IPG placement may also differ by technique among patients treated for pelvic pain disorders. One series reported as many as 33% of patients lost efficacy when the permanent lead and IPG were placed following a successful PNE trial, whereas in a staged trial, the therapeutic effect was maintained in all but 14% [19].

It is unclear whether there is an advantage to either unilateral or bilateral neuromodulation in patients with pelvic pain syndromes. It seems logical to offer bilateral stimulation to patients with bilateral symptoms. Moreover, based on some reported series, bilateral stimulation may afford greater efficacy to patients with truly refractory pelvic pain syndromes. The paucity of data in this difficult-to-treat patient population with chronic refractory disorders underscores the need for properly designed clinical trials to fully explore the efficacy of various SNM programming parameters and implantation techniques.

Cost

While there is evidence that SNM is cost-effective for pharmacologically refractory voiding dysfunction as compared to either botulinum toxin injections or nonintervention [20••, 21], we are unaware of any cost-effectiveness analysis comparing PNE to staged implantation.

The 2009 Medicare reimbursement in Los Angeles, CA differed significantly based on implantation technique and facility. Unilateral staged implantation performed in the operating room reimbursed \$742.73 with subsequent IPG paying \$1055.85 for a total compensation of \$1798.58. Unilateral office-based PNE trial reimbursed \$1792.62, and, if successful, an additional \$1055.85 for the IPG placement for a total of \$2848.47.

Medicare clearly incentivizes the proliferation of the office-based PNE over the staged procedure. It may be argued that this remuneration structure unnecessarily increases Medicare costs and promotes abuse of a less sensitive intervention.

Alternatively, it may be argued that the widespread use of the less expensive PNE electrode exposes a greater number of medically refractory patients to potentially beneficial treatment. A formal cost–benefit analysis has not been reported and should be undertaken to answer these important questions.

Conclusions

We believe the preponderance of evidence clearly supports the superiority of staged evaluations as compared to the traditional PNE. Staged trials have a lower incidence of lead migration, and thus a prolonged trial phase. This allows for the exploration of varying and more sophisticated programming and greater progression to IPG implantation. Staged trials offer uninterrupted treatment before IPG placement and, because the trial lead is not removed, conservation of successful trial settings. Well-designed comparative studies evaluating unilateral versus bilateral stimulation and various programming options are needed to fully explore SNM as a treatment modality for various refractory voiding dysfunction and pelvic pain syndromes.

Disclosure No potential conflicts of interest relevant to this article were reported.

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