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Specific Tips for General Controversies in Sacral Neuromodulation

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Abstract The field of Sacral Neuromodulation is continually evolving and still in its infancy. Common dilemmas experienced with this therapy will be discussed in this article, including ways to avoid and manage them. The focus will be on test evaluations performed with either peripheral nerve evaluation (PNE) or staged procedure, the clinical effectiveness and safety of unilateral versus bilateral test stimulation for both the PNE and staged procedures, and best methods to determine the success of the trial phase. We will also discuss how to deal with the problem of declining efficacy of the device over time. The article presents a discussion on future technological innovations to enhance techniques and mode of positioning and use of leads, which along with a refined understanding of how neuromodulation is effective for different problems, will lead to better outcomes.

Keywords Sacral Neuromodulation · Staged procedure · PNE · LUTS

Introduction

While Sacral Neuromodulation has been shown to be of significant benefit for certain bladder and bowel symptoms, the field is continually evolving as we learn more about the therapy and what differences may be important in any given scenario. New tools and techniques are bound to help resolve issues those of us who use the therapy may commonly encounter, such as how best to trial patients, how to interpret the motor and sensory results when they are atypical, how to determine success of a trial phase, and how to improve outcomes among patients who may not respond ideally to initial therapy. Given the current state of the art, this article is intended to explore some common dilemmas and to make recommendations based on our prior experience. We will also discuss possible future innovations which could help achieve better outcomes in challenging cases.

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Peripheral Nerve Evaluation (PNE) Versus Staged Trial for Therapy Screening

We have been strongly in both camps over time. Currently, we are supportive of a stratified approach, wherein we would offer PNE to most patients, and a staged trial as the initial test to a minority. Patients who undergo an unsuccessful PNE are generally candidates for a staged trial. PNE has the advantage of being less invasive, and less resource intensive, but generally is done with only local anesthesia, having a potential to be more uncomfortable for patients, and is less sensitive as a test than the staged trial. Patients ideally suited for PNE are adults who can cooperate and remain relaxed during the normal discomfort and stress of the procedure. Certainly, some will "self select" when given a choice, just as they might for other minor procedures such as vasectomy or intravesical injection. Having a comfortable bedside manner, setting the mood with compassion and humor, and letting the patient have some control (choose the music, say "when") can also go a long way to making this a good experience. It is also important to

read the patient properly, and stop after one side is done if there has been a struggle or unusual discomfort. It makes a difference how well your clinic is set up to conduct the trial. We, for example, have a fluoro unit and table, and identify the nerve target in the same way we do in the OR. This makes up for normal variations of body habitus that can result in extra pokes and prolonged procedure times in those individuals for whom boney landmarks do not typically line up. We can also gauge the depth and location of the needle tip and numb the periosteum in the relevant area before touching with the needle, which can prevent "winding-up" of the patient's sensitivity and anxiety. Since we generally know which foramen we are accessing with fluoro before we test for motor and sensory responses, it can help if the patient is not relaxing his or her pelvic and gluteal muscles and obscuring the motor response and allow more comfortable reliance on predominately sensory feedback. Since our aim is to provide a "taste" of the therapy, we do not have to be as precise with exact lead positioning and thresholds, which allows expediency. Since we use fluoro, we can use the exact same techniques to identify the position for a future tined lead placement and minimize the risk of a less successful outcome with the more invasive procedure. In general, this discussion implies if you are new to the therapy, a low volume implanter, or less confident in your ability to be precise and efficient with an unsedated patient, and do not have fluoro available to help you, you may be better of doing a staged trial first.

The staged trial has the advantage of sedation and more certain patient comfort. Some physicians are routinely doing the trial under general, which seems like too much anesthesia to me, except for certain patient scenarios such as morbid obesity and/or inability to control the airway in a prone position or extreme patient anxiety. Some anesthesia teams are also less comfortable with deep sedation. The staged trial has a higher likelihood of identifying an appropriate candidate for the therapy [1] and less likely to result in a successful screen and a post implant failure since what you see is what you get. It offers more potential for fine tuning of stimulation parameters due to multiple contacts being selectable, which may be needed and attractive for some patients. There is also the potential to conduct the trial for a longer period of time. We typically do the trials over 3–4 weeks and have not observed increased rates of infection related to this timeframe. The longer trial may be attractive for some syndromes such as fecal incontinence, urinary retention, or patients with primarily sensory urge with pelvic pain as a focus of their complaint. Patients who are very focused on their pain and/or with high anxiety would probably be best served with a staged approach with sedation. Deep sedation or general anesthesia required in these cases usually precludes obtaining sensory responses during the procedure and requires reliance on motor responses as a guide. Sensory responses can be monitored with light sedation, or by waking the patient up during the trial to gauge their response, but this can be challenging, unfeasible, or unreliable in many patients.

Many experts want to write-off the PNE as an inferior test and imply those who do it preferentially are motivated by the higher differential re-imbursement it brings in the USA. In trained hands, the PNE is a useful tool which gives the patients exposure to the therapy in an outpatient setting without the hassle of requiring a pre-op history and physical, fasting after midnight, having an intravenous line, dealing with the hospital or surgery center protocols and environment, giving up control for anesthesia, additional surgical risks, post-op nausea and altered sensorium, and requiring a driver and observation overnight by a family member. These all add up to a substantial cost and burden which can often be alleviated by a PNE. The staged trial makes sense when the patient prefers, in certain clinical scenarios, or as a backup to a failed PNE.

Future innovations for this dilemma include replacing the PNE lead with a more functional multipolar lead, which could have a retaining feature such as tines, or could be converted to a permanent lead in the OR. Another route for improvement would be to do away with the need for testing all together, if the likelihood of success with a tined lead placement or immediate response could be sufficiently predictive of long term success. Even if a measure such as a specific electromyographic (EMG) response [2] at the time of lead placement could be shown to predict a high rate of long-term success, patient selection would remain a factor. Perfect lead placement and ideal responses in a poor candidate for the therapy equals an ultimate failure. Perhaps the trial could be done away with in certain populations where success is predictably highest, such as fecal incontinence or OAB wet. This remains to be proven, of course.

Unilateral Versus Bilateral Testing

We almost always do bilateral tests for a PNE and unilateral for a staged implant. The bilateral PNE makes sense since the procedure is less precise, and the overall cost is much lower. The chance of hitting a bull's-eye on one side or the other is greater with more attempts. It does not necessarily mean the side that responds better is inherently best for long-term therapy. The difference could largely be due to the variable accuracy of the individual lead placements. We usually find the second side is quicker and smoother, since lots of the figuring is done on the first side. Therefore, we save the second side for our preferred side. If the patient has lateralizing pelvic or limb pain, we think it is important to aim for that side with chronic therapy. Therefore, we would tend to do the less painful side first so we can take what we have learned over to the other side where we think it matters most. We ask our patients to try the side they feel most comfortable with after immediate programming, and to switch to the second side after a few days only if

their symptoms have not been sufficiently improved. If they have been, there is less reason to switch. We do tend to place the tined lead on whichever side the PNE worked best on, but tell the patients the lead might wind up on the opposite side if we cannot get "ideal" placement.

Bilateral tined leads for testing is cost prohibitive in certain settings (a surgery center, for example) and may not be covered by insurance. There is a paucity of data indicating any advantage of bilateral stimulation over unilateral for a patient group. Only a single pilot study indicated that some patient populations might get benefit from bilateral stimulation after unilateral therapy failure [3]. In our experience, we are tempted to place bilateral staged leads when we cannot get an "ideal" response on either side, in order to increase the potential for one side to be favorable over the other. It seems inherently obvious that optimizing a lead placement on one side is better than two suboptimally placed leads. We also face a dilemma when patients have a defined neuropathology on one side versus the other. Which is the better side for treatment, the neurologically affected or the normal side? We are unable to predict at this point, so we would prefer to test both. There are some situations where testing at different levels (S3 and S4) might make sense. We call these patients the "missing S3" meaning they have a lot of foot compared to bellows at S3 despite our best attempts to direct the lead caudally, and all bellows and no toe at S4. It might be best just to go for S4 in this circumstance, or immediately try a pudendal placement, which would require pre-consent and the simultaneous availability of EMG [4]. If one is set up to place a pudendal lead, it begs the question as to whether simultaneous "optimal" placement of a sacral and pudendal lead for a trial might be helpful for some patients. We do not believe that this idea has already been adequately tested. In general, we think the best policy is to make every attempt to place a single S3 lead in an optimal fashion for the staged trial, and that bilateral leads or multiple level leads should be considered only in rare instances and remains experimental.

Future innovation might allow manipulation of the stimulation pattern in order to achieve sub-sensory testing, which could help achieve the holy grail of a true double-blinded placebo-controlled randomized trial for the effectiveness of unilateral SNM, bilateral SNM versus unilateral, and pudendal versus sacral. Bilateral testing would easily become more attractive if the patient could retain two leads and switch from one to the other for chronic therapy if and when there may be flagging responses due to lead migration or damage or CNS accommodation. The patient could be programmed to whichever side works best initially, switched to the opposite side when needed, or to both sides if there was an objectively demonstrable benefit, without performing a second operation. This would not preclude switching back again later on. Such a strategy of redundancy would give the patient more programming options, increase the likelihood of long-term success, and reduce costs by potentially eliminating a future revision surgery. The currently available devices cannot accommodate two leads and would require complete systems duplication in order to achieve this goal, which would be cost prohibitive as a routine way of delivering the therapy.

Motor Versus Sensory Responses

There has been debate about which is more critical, motor or sensory responses. Two small studies have shown that a positive motor response was more predictive of success of test stimulation than a sensory response [5, 6]. Given that the purported mechanism of action is sensory afferent neuromodulation, it seems likely that the sensory response should be the most critical, and the motor response is a corollary or marker for where the patient will feel the stimulation. As per the discussion above, sensory responses tend to be more easily measureable during a PNE, and motor responses are easier to observe during a staged lead implant with heavy sedation or general anesthesia. Sensory responses can be monitored during staged implant, but at a cost of potential patient discomfort or extra time and confusion that comes with waiting for the patient to wake up from sedation to weigh in with their altered sensorium. This may not be the case for all conditions. Our strong bias is that both motor and sensory responses are critical pieces to the puzzle of ideal lead placement, and ultimately deriving both will result in better overall outcomes than one versus the other. For example, it might just be that the motor response is indeed the critical thing to monitor for someone with fecal incontinence due to a traumatic injury to the anal sphincter, and no other dysfunctions. However, a patient with OAB dry and a component of pelvic pain might require lead placement with very specific sensory responses in order to get a benefit. Since this is unknown, we tend to favor optimizing the lead placement for all conditions, since there does not appear to be a downside to getting all four contacts close to the nerve with the correct pattern of motor thresholds at equally low thresholds (under 2 V).

Since we do our cases under heavy sedation, we have learned to "predict" the sensory responses the patient will feel in the recovery room based on the pattern and timing of the motor responses, once the lead appears to be in an ideal position with fluoro. For example, if the toe response comes first (at a lower threshold), and then perhaps all toes or bottom of the foot, and then at a higher threshold the bellows is observed, the patient is likely to say they feel the stimulation in the leg. If the bellows happens at a lower threshold, and then the toe comes after at a slightly higher threshold, they are likely to feel the stimulation in the genital or perineal area. If there is lots of bellows at lower thresholds, and then the toe comes at much higher thresholds, or there is no toe at all, the patient is likely to feel the stimulation in the rectum. Having all four contacts

yielding the same responses at low thresholds means the lead has been placed next to the relevant portion of the S3 nerve that will result in comfortable stimulation without collateral triggering of other structures (the piriformis muscle, for example). This may be especially necessary for syndromes like OAB dry with or without pelvic pain and may also prove to be critical for future indications such as interstitial cystitis or constipation/irritable bowel syndrome. It was interesting that in a recent meeting with a group of European implanters, many of whom were colo-rectal surgeons, the consensus was that patient sensation in the rectum was preferable to genital sensation. This remains an unanswered question and may involve different answers for different diagnostic categories.

In some situations, during the staged lead implant, there may be minimal or no motor response. Since the therapy is usually done in neurologically normal patients, who presumably do not have saddle anesthesia and walked into the office, the finding is most likely due to poor positing of the foramen needle (needs to be higher or medial in the foramen, or both), or the motor response is being masked by "buns of steel" or extremely high tone pelvic floor muscle dysfunction (PFMD). Conducting the trial on the other side or at a different level might help to resolve the problem. Instead of hooking the test clip on, tapping the foramen needle at an approximate rate of one pulse per second can be helpful in looking for a very subtle motor movement, and may also allow more ready identification of bellows or toe movements with stimulation versus respiratory effort or other extraneous factors. If no motor movement can be derived, it might make sense to waken the patient to get sensory input (good luck if the problem is due to extremely high tone PFMD), or if available, EMG would be a definite help to see if a compound motor action potential (cMap) is identified in relation to the stimulation, which should ultimately indicate the lead is in the right position. If EMG is not available immediately, it could be employed with planning on a future trial. It might also make sense to try one level lower, usually S4, where there is ordinarily a bigger bellows than in S3, and to go with that level if identified.

Future innovations could include a dumbed down EMG monitoring device as part of the testing system, making this type of information more generally available to the average implanter. Other improvements could be the development of a lead guidance mechanism based on real-time EMG monitoring. A refinement of our understanding when precise lead placement may be more or less critical, and if or when certain motor or sensory responses might be most desirable would also be of great benefit in guiding lead placement.

How to Determine Success of a Trial Phase

There is a critical difference between the "conversion rate" and long-term success. The key to the trial achieving long-term success is using objective data (diary info) [7] and to make sure there is a sufficient benefit based on pre- and post trial comparison. The 50 % threshold is somewhat arbitrary, based on FDA standards for evaluating devices. There is certainly room for clinical judgment in patients who do not quite meet that threshold, but the decision should be based on measureable and substantial objective changes. It is helpful to monitor other responses which may provide supporting evidence. We have used the patient-perceived changes in bowel function as a marker of a true positive response. Patients may not expect to note less constipation or fecal urgency, or improved fecal continence when they think they are having a procedure for their bladder problem, and noting this, along with improvements in bladder symptoms, has been a reliable indicator of overall success. Improvement of pain is also an important secondary benefit, but we are uncomfortable completing an implant based on that subjective report alone, and would advise against it. Today's subjective rating of "5/10" can turn into a "10" too easily, with little left to justify the implant in retrospect. As with any elective surgery, it makes sense to let the patient motivate the surgeon, and not the other way around. There have been many patients who present for consultation after an unsuccessful implant, and when they are asked what happened during the trial, they say "my surgeon said it would be good for me". In this circumstance, without a documented objective benefit, it makes sense to go back to square one and repeat their staged trial.

Future innovation which could help this situation is for the *diary data* to me more fully incorporated into the patient software, which could also be automatically calculated, reported, and compared along with other information collected during the initial trial, implant, previous, contemporary and longitudinal assessment, and at the time of revision. This would require a tool such as an app which would be easy to use and integrate with lead position and responses documented at the time of implant, device use, and programming data. It might help to provide clues as to when or why the therapy becomes less effective, or ongoing evidence of benefit in a group of patients who could, if agreed, be monitored over time without presenting to the office. Failing patients could be identified for clinical attention. Then, the difference between conversion rate and success could be readily quantified for specific patient groups and implanters. Such a system would require a substantial compliance from patients and their caregivers.

Revision for Declining Efficacy

The initial approach for decreased efficacy should be to *reprogram* the patient in a systematic fashion. Once reprogramming options have been exhausted, it is reasonable to consider *lead revision* [8]. This is particularly true in cases where a prior PNE demonstrated better symptomatic control

than the permanent implant, which implies a "flub" in placing the permanent lead. Anterior-posterior and lateral sacral x-rays can be helpful in determining if there are obvious ways in which lead position could be improved (Fig. 1). Is the lead as high and medial in the foramen as possible? Do the contact points have characteristic spacing in the AP and lateral planes? Furthermore, sensory responses may also suggest a goal. If there is too much stimulation down the leg or in the foot, it implies the lead needs to be directed more caudally from the prior position, and if the stimulation is mainly in the rectum, it needs to be more cephlad in orientation. If thresholds are high, it suggests the lead must be too inferior or lateral when entering the foramen, or that the lead is not oriented parallel to the nerve. In the case of a successful PNE, with obvious problems identified with permanent lead placement, it is reasonable to correct the problems during revision and to connect to the implantable pulse generator (IPG) in a single stage revision. If, as discussed above, the response to the original trial is questionable in retrospect, it may be appropriate to perform a staged trial with the new lead, and to connect after diaries confirm symptom control. If further improvement is not demonstrated, it may then be appropriate to remove all implanted devices [9]. In performing the revision surgery, we prefer to leave the original lead in place in order to compare its position to the new lead. This usually entails putting the new lead on the opposite side, but it is also possible to place on the original side if the lead is too inferior or lateral in the foramen, as there is still room in the correct position for the new lead (Fig. 2). Placing on the same side might be preferable depending on lateralizing pain or other variables. After comparing the radiographic and motor responses/thresholds between the old and new leads, if we are confident of an improved placement, we will remove the old lead. This is another reason it may be preferable to place on the opposite side, since making a presacral incision to remove the original lead may displace or interfere with the anchoring of the new one.

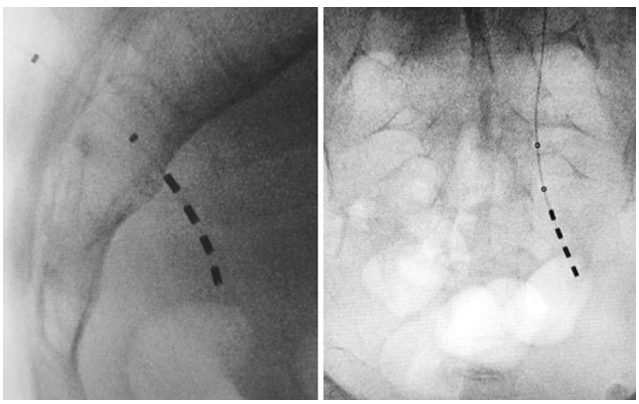

Fig. 1 In the lateral view, an optimally placed lead parallels the fusion plan of the sacral segments. The lead exits the foramen anteriorly about 1 cm above the fusion plane and curves caudally. The spacing of distal contacts appears to be closer together than the proximal ones due to the lead moving towards or away from the viewer in space depending on which side it is being viewed from. In the AP view, the lead enters the bone table very close to the medial edge of the foramena and courses down and out laterally. The spacing of distal contacts appears to be farther apart than the proximal ones due to the lead moving towards the viewer as it enters the foramen and then out laterally as it follows the nerve path

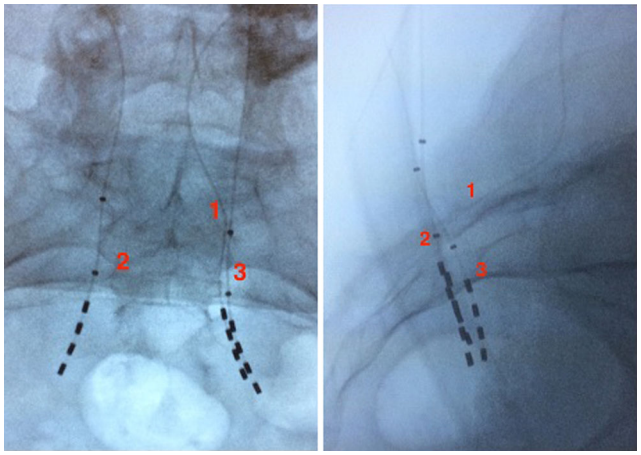

Fig. 2 These are films from a patient who has benefitted from SNM for over 20 years, but has required IPG and lead replacements over that timeframe to maintain the therapy. The originally implanted lead (*1*) was placed blindly via an open technique and resulted in very good symptom control for many years. The replacement lead (*2*) was placed using a tined lead under fluoro and did not result in the same degree of symptom control, but was deemed adequate for many years. The final lead revision (*3*) was placed back on the original side, and it is obviously positioned higher in the foramen on the lateral view than either of the prior leads. Not only was there sufficient room for it, its use has resulted in a greater degree of symptom control and patient satisfaction than either of the prior leads, indicating its optimized positioning was important to the outcome of the therapy. The previously placed leads (*1* and *2*) were removed prior to completion of the surgery

Future innovation could include the development and validation of an objective *scoring system* for lead placement. This would require proof that certain characteristics of lead placement (radiographic position in foramen, motor and sensory thresholds, pattern of motor responses, and location of sensation), individually or in aggregate, actually matter and result in better outcomes. If so, a "lead score" could be used to differentiate between a well placed lead which would be harder to improve upon technically, and a poorly placed lead which may be more readily improved. If an implanter has a lower average lead placement score, it might help promote a referral to a more experienced center if revision is required in a challenging situation, or trigger some attention and resources directed towards improving individual skills. If the lead score could be calculated on the fly at the time of lead implant, it could be used to decide if placement is adequate or whether further effort is warranted before final deployment. Defined patient groups with similar lead scores from different implanters might be studied in aggregate to measure the result of "optimized" therapy. Other desired developments include improved programming options. With the present voltage-based system, delivery of energy at more than one point along the nerve is limited by the fact that the energy will

preferentially go down the path of least impedance, even when the lead is programmed with more that one negative electrode. Having a current-based system could allow equal or specific and differential delivery at more than one location (30 % at electrode 1, 70 % at 3, for example). Constant current allows for automatic changes in amplitudes in order to maintain a specific current with local tissue changes such as degree of scaring or alteration of nerve function over time. Other changes in the implantable neurostimulator could present the ability to "shape" the field of energy into wider or narrower arrangements depending on the situation, direct the energy in one direction or the other, and alter the pulse pattern or waveform to achieve variable results depending on the demands of different clinical conditions. These changes theoretically increase the likelihood of successful initial lead placement and the ability to resolve patient problems with reprogramming rather than surgical revision. Issues of lead design may also play into the ability to maintain benefit and reduce the rate of revision. For example, leads and systems need to be MRI conditionally safe to avoid the need for explantation solely for this concern. Leads should be designed to be "body complaint" so they are less prone break from routine falls or bumps, and they need to be fully extractable from the pocket so the usual concerns can be mitigated easily if and when a revision or removal is needed.

Conclusion

Sacral neuromodulation has become a standard of care and an indispensable tool for the management of a potentially increasing number of urinary and bowel disorders. Certain dilemmas are common to the therapy, and this review has discussed ways in which the problems can be avoided or mitigated. Future evolution of devices, techniques, mode of delivery, and software, along with a refined understanding of how and why neuromodulation is effective for different problems, will lead to better outcomes with and greater confidence in choosing this mode of treatment.

Compliance with Ethical Standards

Conflict of Interest Ahmed S. El-Azab declares no potential conflicts of interest. Steven Siegel is a consultant, lecturer, and has authored/particpated in research sponsored by Medtronic. He is a consultant and has participated in research sponsored by NuVectra.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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