



The role of the neurometer CPT/C in sacral neuromodulation

Sakral nöromodülasyonunda Neurometer® CPT/C®'nin rolü

Abdullah Ahmed Ghazi¹ , Malak Abuzgaya¹ , Mai Banakhar² , Magdy Hassouna¹

Cite this article as: Ghazi AA, Abuzgaya M, Banakhar M, Hassouna M. The role of the neurometer CPT/C in sacral neuromodulation. Turk J Urol 2018; 44(1): 70-4.

ABSTRACT

Objective: The aim of the current research project was to study the role of the Neurometer® as a tool to predict responders to sacral neuromodulation therapy (SNM).

Material and methods: This was a prospective, open study in male and female patients, aged 18 and over with voiding dysfunction [non-obstructive retention and/or frequency/ urgency syndrome]. The first group underwent a screening test to evaluate percutaneous nerve functions (PNE) and to determine whether they are candidates for SNM with the InterStim®. Prior to PNE testing, all patients were evaluated with the pain tolerance test (PTT) using the electro-diagnostic Neurometer® CPT/C device. An InterStim® implant was placed in patients who were responders to PNE testing underwent. On the other hand, non-responders underwent a staged implant placement. The second group consisted of patients who already had InterStim® implanted for voiding dysfunction. During the routine office follow-up, the patients implanted with Interstim® underwent a PTT using the Neurometer® CPT/C device. All the testing using the Neurometer CPT/C was performed on the day of the PNE for the first group, and the day of the routine follow-up visit for the second group. All of the results for the Neurometer® testing were kept blinded from the PNE results, and those of the outcome of the follow-up visit. The study received approval by the Research Ethics Board of the University Health Network (No. 14-8196).

Results: We recruited a total of 123 patients. The results presented here include 110 patients who completed the study, 48 of whom were in the first group, and 62 in the second group. The statistical analysis used was as follows: Group 1: Simple linear regression analysis and the linear discriminate analysis were performed. It was found that for patients without the InterStim® implant with a combined CPT/CPD of 800 and above, the Neurometer® could predict the test screening results with an accuracy of 71%. Group 2: Same analysis and tests were conducted for patients with the InterStim® implant, and the results showed that if the patient had a combined CPT/CPD of 600 and above, the Neurometer® could predict the patients satisfaction or dissatisfaction with an accuracy of 72%.

Conclusion: Neurometer® may play a role in predicting test trial positive responders and patient satisfaction after the placement of InterStim® implant.

Keywords: Electrical nerve stimulation; electrodiagnosis; frequency-urgency syndrome; urinary urge incontinence; Percutaneous Nerve Evaluation (PNE); response to sacral nerve stimulation test trial; sacral neuromodulation; sensory nerve pain threshold.

ÖZ

Amaç: Güncel araştırma projesinin amacı sakral nöromodülasyon tedavisine (SNM) yanıt verenleri öngörmeye bir araç olarak Neurometer®'in rolünü incelemektir.

Gereç ve yöntemler: Bu çalışma işeme disfonksiyonu [obstrüktif olmayan retansiyon ve/veya sık işeme-acil işeme hissi sendromu] olan 18 yaş üstü erkek ve kadın hastalarda yapılan prospektif, açık uçlu bir çalışma idi. Birinci grup hasta InterStim® ile SNM için uygun olup olmadıklarını belirlemede perkütan sinir değerlendirmesiyle (PSD) tarama testinden geçen hastalardı. PSD testinden önce elektrodyagnostik Neurometer® CPT/C cihazı kullanılarak ağrı tolerans testinden geçirilmişlerdir. PSD testine yanıt veren hastalara bir InterStim® implant takılmıştır. Diğer taraftan yanıt vermeyenlere aşamalı implantasyon işlemi uygulanmıştır. İkinci gruba daha önceden işeme disfonksiyonları için InterStim® implantı takılmıştır. Rutin takip sırasında Interstim® implante edilmiş hastalar Neurometer® CPT/C cihazı kullanılarak ağrı tolerans testinden geçirilmiştir. Neurometer® CPT/C testlerinin tümü birinci grupta PSD testinin yapıldığı gün, ikinci gruba ise rutin kontrol günü uygulanmıştır. Neurometer® testinin tüm sonuçları, ağrı tolerans testi sonuçları ve kontrol vizitinin sonucu gizli tutulmuştur. Üniversitede Sağlık Araştırma Etik Kurulu çalışma onayı alınmıştır (No. 14-8196).

ORCID IDs of the authors:

A.A.G. 0000-0002-9358-8696;
M.A. 0000-0001-6447-3825;
M.B. 0000-0002-2341-1270;
M.H. 0000-0002-1096-3391

¹Department of Urology,
Toronto Western Hospital,
University of Toronto, Toronto,
Canada

²Department of Urology, King
Abdulaziz University, Faculty
of Medicine, Jeddah, Saudi
Arabia

Submitted:
23.02.2017

Accepted:
19.07.2017

Available Online Date:
19.12.2018

Correspondence:
Magdy Hassouna
E-mail:
Magdy.Hassouna@uhn.ca

©Copyright 2018 by Turkish
Association of Urology

Available online at
www.turkishjournalofurology.com

Bulgular: Toplam 123 hasta çalışmaya alınmıştır. Burada, birinci gruptan 48, ikinci gruptan 62 olmak üzere çalışmayı tamamlayan 110 hastaya ait sonuçlar sunulmuştur. Aşağıda belirtilen istatistiksel analiz kullanılmıştır: Grup 1: basit doğrusu regresyon analizi ve doğrusal ayırt edici analiz uygulanmıştır. Kombine CPT/CPD'si 800 ve yukarı InterStim® implantı olmayan hastalarda Neurometer® tarama testinin sonuçlarını %71 doğrulukla öngörebildiği saptanmıştır. Grup 2: Stim® implantı olan hastalarda aynı analiz ve testler uygulanmış ve sonuçlar hastalarda CPT/CPD 600 ve daha fazla olduğu takdirde Neurometer®'in hasta memnuniyet veya memnuniyetsizliğini %72 doğrulukla öngörebildiğini göstermiştir.

Sonuç Neurometer®, testi pozitif çıkacak olan hastaları ve implant takıldıktan sonra işlem başarısı ve hasta memnuniyetini öngörmeye rol oynayabilir.

Anahtar Kelimeler: Elektrikle sinir uyarımı; elektrodyagnoz; sık işeme-acil işeme hissi sendromu; sıkışma inkontinansı; Perkütan Yolla Sinir Değerlendirmesi (PSD); sakral sinir uyarımı testine yanıt; sakral nöromodülasyon; duysal sinir ağrı eşiği.

Introduction

Sacral neuromodulation (SNM) is considered as a successful therapy for voiding dysfunction. Before permanent implantation, the patient must undergo a stimulation test called Percutaneous Nerve Evaluation (PNE). The patients' response (measured as an improvement in voiding function) determines whether they will receive a permanent device implantation. Up to 50% of screened patients are not eligible for implantation due to a lack of improvement observed during the stimulation test trial PNE, as recorded in the voiding diary.^[1-3] One of the major reasons for this is inefficient electrode placement in the sacral foramen and/or lead migration.^[4]

The aim of the current research project is to study the role of the Neurometer® CPT/C device as a tool to predict the responders to SNM therapy in both the screening, and the follow-up phases of the treatment.

Sacral Neuromodulation (SNM)

The causes of voiding dysfunction are often idiopathic, with no clear etiology.^[5] Pharmacological treatment of voiding dysfunction relies mainly on anticholinergic drugs, yet the bothersome adverse effects of these medications (such as dryness of mouth, constipation and blurred vision) discourage some patients from using them.^[6] Other modalities of treatment include behavioral therapy, such as pelvic floor training, restriction of fluid intake, and timed voiding.^[5] SNM has proven to be an effective treatment modality for voiding dysfunction refractory to drug therapy, and also urinary retention. SNM with InterStim® (Medtronic Inc., Minneapolis, Minnesota USA) is a Health Canada-approved medical device (Licence No. 14962) for the treatment of refractory overactive bladder, frequency-urgency syndrome and chronic urinary retention. It involves implantation of a lead electrode into the third sacral foramen adjacent to the third sacral nerve (S3) under local/general anesthesia using a minimally invasive procedure. The electrode is attached to an internal pulse generator (IPG), which is implanted in the subcutaneous tissue of the buttock area. The mechanism of action for SNM is still to be elucidated; however, it is believed that beneficial effects are due to the initiation of action potentials in somatic afferent nerves.^[7] Furthermore, SNM helps to attain normal voiding in patients with chronic urinary retention.

Percutaneous Nerve Evaluation (PNE)

The testing procedure involves placement of a thin insulated wire into the third sacral foramen to determine if a patient is a candidate for implantation of the permanent InterStim®.^[8] Patients who have a response to the test (defined as $\geq 50\%$ improvement in one or more of the voiding parameters compared to the baseline) are considered candidates for implantation of the InterStim®. The test trial involves either a PNE (which is an office-based test) or a staged procedure (which is performed in the operating room) for patients who are not candidates for office-based stimulation test (e.g. morbid obesity, difficult anatomy, previous sacral surgery or unable to tolerate the procedure under local anesthesia). The patient's response to the test determines if they are a candidate for the device implantation.

Neurometer CPT/C

The Neurometer® CPT/C, (Neurotron Inc., Baltimore, MD) is an investigative noninvasive, electrodiagnostic device that verifies the nerve integrity at a specific dermatome. It allows the operator to quantify the severity of detected abnormalities based on established normative values and a generated narrative report.^[9] The Neurometer® CPT/C tests the integrity of all three nerve fiber types (beta, delta and C) by testing the pain tolerance threshold (PTT) and plotting it on the interpretation curve to determine the functional status of the nerve. The Neurometer® CPT/C has three frequencies: 2000 Hz, 250 Hz, and 5 Hz. Patients who have voiding dysfunction have a higher activation of C afferent fibers than in patients with normal voiding.^[10] To determine the patient's pain tolerance threshold, C fibers are stimulated at 5 Hz. C fibers are normally quiescent under normal conditions and become reactivated under certain pathological conditions involving the lower urinary tract.^[11] Suppression of C fibers with normal or low pain tolerance threshold is required for effective SNM therapy.^[10] The device obtained an approval for use in our institution by Health Canada.

Material and methods

This was a prospective, open study in male and female patients, aged 18 and over with voiding dysfunction [non-obstructive retention, and/or frequency-urgency syndrome] who underwent a standard screening test trial with PNE to determine the candi-

dates for SNM using the InterStim® sacral nerve stimulator, and the patients who previously had the InterStim® implanted for voiding dysfunction.

The first group underwent a screening test trial with PNE to determine the candidates for SNM using InterStim® sacral nerve stimulator. Prior to PNE testing, all patients were evaluated for the PTT using the electrodiagnostic Neurometer® CPT/C device. The patients who were responders to PNE testing underwent InterStim® implantation. Patients who showed a poor response to the PNE underwent staged implantation procedure. The second group previously had the InterStim® implanted for voiding dysfunction. At routine office follow-up visits, those patients with implanted InterStim® had their symptoms evaluated subjectively and objectively using the voiding diary, and these symptoms were compared with the symptoms recorded in pre-implant (baseline) diary. During the same visit, they were tested for the PTT using Neurometer® CPT/C device.

The Neurometer® used in the present study was meant to measure a single numerical reading of the patient- adjusted PTT threshold that is recorded on the right and left sacral dermatomes. The intensity of the maximum tolerable neuroselective stimulus was defined as the PTT. The electrodes were located at the S3 dermatome near the anus, as shown in Figure 1. The PTT is a noninvasive atraumatic neuroselective evaluation test of pain tolerance under patient control. The CPT is the sum of the PTT thresholds that are recorded for the right and left sacral dermatomes. In the present study, the Neurometer® was used at a frequency of 5 Hz, which is specific for testing the threshold of perception of the C-fibers in the selected dermatome.^[10]

Statistical analysis

A statistical analysis of patients with and without an InterStim® implant was conducted to assess if the Neurometer® could be used as an adjunctive tool to screen and predict the outcomes

of the InterStim® therapy. The statistical test preformed was a linear discriminant analysis, which uses simple linear regression analysis to find out if the independent continuous variable(s) can predict the dependent categorical variable. In this analysis, the satisfaction of the patients and the trial results serve as two-level categorical- dependent variables since they have possible values: happy or unhappy, and positive or negative trial results. The two-level variables were separated into 0s and 1s to make the calculations and predictions simpler. Once the simple linear regression analysis was completed on Microsoft Excel, the slope (b1), intercept of the regression line (b0), and the numerical variable CPT/CPD value (x) was used in an equation (1) to predict the value of the dependent categorical variable (happy/unhappy, or positive/negative).

$$(1) \quad \hat{y} = b_0 + b_1(x)$$

Once the predicted -scores of each value have been calculated, we used the regression formula to classify scores, essentially categorizing them into different groups. The mean (of the predicted values were calculated in separate groups based on their x-value, either being a 1 or a 0 designated based on happy/unhappy, or positive/negative. A cutoff point (or midpoint value), defined as C, is determined to be able to separate the values into two separate categories-zeros or ones.

$$(2) \quad C = \frac{((n_0 \cdot \bar{x}_0) + (n_1 \cdot \bar{x}_1))}{(n_0 + n_1)}$$

The predicted y-hat score was classified as being in the group whose predicted score mean it is closest to. If a predicted y-hat score is *below* the midpoint value calculated as C in equation (2), it is classified as group 0. Conversely, if a predicted y-hat score is *above* the midpoint value calculated as C in equation (2), it is classified in Group 1. Once the calculations of predictions were completed, the percentages of accuracy of the predictions were calculated. To see if the predictions were accurate, the predicted groups (zeros or ones) must match the actual group (happy/unhappy, or positive/negative). A percentage was then determined from the amount of correct and incorrect predictions as shown in the equation (3) below.

$$(3) \quad \% \text{ Accuracy} = \frac{\text{correct}}{(\text{incorrect} + \text{correct})} \times 100$$

Results

We recruited a total of 123 patients, 60 of those were in Group 1, and 63 in Group 2. In Group 2, 12 patients had a negative PNE, and they were planned for a staged implant. They did not complete the study and excluded. In Group 2, one patient had a twin InterStim® implant, and was excluded.

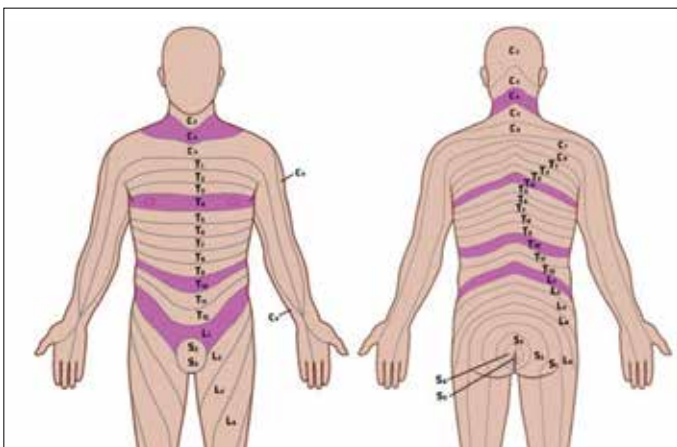


Figure 1. Dermatome map

After the simple linear regression analysis and linear discriminant analysis were performed for both groups, it was found that in Group 1, for a combined CPT/CPD of 800 and above, the Neurometer® could predict the trial test screening results with an accuracy of 71%. In Group 2, the results showed that if the patient had a combined CPT/CPD of 600 and above, the Neurometer® could predict the level of satisfaction or dissatisfaction with the InterStim® implant with an accuracy of 72%.

Discussion

The relative simplicity of the technique, and the low patient morbidity associated with proper selection and sacral implantation makes this therapy an attractive therapeutic option.^[3] However, SNM therapy has moderately high rate of complications, reaching up to 18.2%.^[12]

The patients with voiding dysfunction have to undergo a PNE or a staged implantation procedure to evaluate their eligibility for the InterStim® implant. Both options (PNE and staged implantation) are unpleasant to the patients; however, the proposed hypothesis behind using Neurometer is to offer a noninvasive procedure that can replace the routine invasive screening techniques.

The present study is a follow-up to a pilot study on 27 patients conducted at our site to test the feasibility of the Neurometer® as an adjunct to the PNE screening test for SNM using InterStim® sacral nerve modulator.^[13] The patients with voiding dysfunction have a higher activity of C afferent fibers than normal individual.^[10] Despite theories indicating an increased or altered afferent sensitivity in lower urinary tract dysfunction, there is no reliable method to measure the bladder sensation.^[14]

The patient's PTT recorded during the test with the Neurometer® is based on stimulating the C fibers at 5 Hz. Neurometer® CPT is the only commercially available instrument applying this technology for the evaluation of sensory nerve function.^[15] Measurement of CPT in the genital area has been reported previously for the transvaginal^[16] and transurethral regions.^[14, 17] To our knowledge, this is the first study which evaluated the bladder/urethral sensation using a transdermal approach targeted at S2-4 distribution (Figure 1).

The present study did not address the values of the C-afferent activity in the same dermatome in patients presenting with non-voiding dysfunction. This represents a likely objective of a subsequent study to establish the 'normal' values in non-voiding dysfunction patients.

In conclusion, based on the prediction values presented in this study, the Neurometer® may play a role in predicting both

test trial positive responders, and the patient satisfaction after implant. The screening test with PNE or staged implant is still the gold standard for the proper selection for patients with voiding dysfunction prior to the permanent implant with the InterStim® therapy. However, using the Neurometer® is considered a simple noninvasive test to follow patients with permanent InterStim® implant to test the C-afferent activity status.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of the University Health Network (No. 14-8196).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.A.G., N.B., M.H.; Design - M.H.; Supervision - A.A.G., M.H.; Resources - A.A.G., M.H.; Materials - A.A.G., M.H.; Data Collection and/or Processing - M.A., M.B.; Analysis and/or Interpretation - A.A.G.; Literature Search - A.A.G.; Writing Manuscript - A.A.G., M.H.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Bu çalışma için etik komite onayı Üniversite Sağlık Ağı'ndan (No. 14-8196) alınmıştır.

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - A.A.G., N.B., M.H.; Tasarım - M.H.; Denetleme - A.A.G., M.H.; Kaynaklar - A.A.G., M.H.; Malzemeler - A.A.G., M.H.; Veri Toplanması ve/veya İşlemesi - M.A., M.B.; Analiz ve/veya Yorum - A.A.G.; Literatür Taraması - A.A.G.; Yazıyı Yazan - A.A.G., M.H.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

References

1. Janknegt RA, Weil EH, Eerdman PH. Improving neuromodulation technique for refractory voiding dysfunctions: two-stage implant. *Urology* 1997;49:358-62. [\[CrossRef\]](#)
2. Peters KM, Carey JM, Konstandt DB. Sacral neuromodulation for the treatment of refractory interstitial cystitis: outcomes based on technique. *Int Urogynecol J Pelvic Floor Dysfunct* 2003;14:223-8. [\[CrossRef\]](#)
3. Al-zahrani AA, Elzayat EA, Gajewski JB. Long-term outcome and surgical interventions after sacral neuromodulation implant

- for lower urinary tract symptoms: 14-year experience at 1 center. *J Urol* 2011;185:981-6. [\[CrossRef\]](#)
4. McLennan M. The Role of electrodiagnostic techniques in the reprogramming of patients with delayed suboptimal response to sacral nerve stimulation. *Int Urogynecol J Pelvic Floor Dysfunct* 2003;14:98-103. [\[CrossRef\]](#)
 5. Staskin DR, Wein AJ, Andersson KE, Bauer SB, Blaivas JG, Burgio KL, et al. Overview consensus statement. *Urology* 2002;60(5 Suppl 1):1-6.
 6. Gleason DM, Susset J, White C, Munoz DR, Sand PK. Evaluation of a new once-daily formulation of oxbutynin for the treatment of urinary urge incontinence. Ditropan XL Study Group. *Urology* 1999;54:420-3. [\[CrossRef\]](#)
 7. de Groat WC, Tai C. Impact of Bioelectronic Medicine on the Neural Regulation of Pelvic Visceral Function. *Bioelectron Med* 2015;25-36.
 8. Banakhar M, Al-Shaiji T, Hassouna M. Challenges in Sacral Neuromodulation, *Topics in Neuromodulation Treatment*, Dr. José Carrillo-Ruiz (Ed.), ISBN: 978-953-51-0395-0, InTech. 2012. Available from: <http://www.intechopen.com/books/topics-in-neuromodulation-treatment/challenges-in-sacral-neuromodulation>.
 9. Neurometer® Clinical and Research Update (2010-2011). Available from: <http://www.neurotron.com/>.
 10. Shaker H, Wang Y, Loung D, Balbaa L, Fehlings MG, Hassouna MM. Role of C-afferent fibres in the mechanism of action of sacral nerve root neuromodulation in chronic spinal cord injury. *BJU Int* 2000;85:905-10. [\[CrossRef\]](#)
 11. Steers WD. Pathophysiology of Overactive Bladder and Urge Urinary Incontinence. *Rev Urol* 2002;4(Suppl 4):S7-S18.
 12. Siegel SW, Catanzaro F, Dijkema HE. Long-term results of a multicenter study on sacral nerve stimulation for treatment of urinary urge incontinence, urgency-frequency, and retention. *Urology* 2000;56:87-91. [\[CrossRef\]](#)
 13. Hassouna M, Alsannan B, Banakhar M. Role of the Neurometer as adjunct to screening for Sacral Neuromodulation therapy. Abstract at Canadian Neuromodulation Society 2012.
 14. Vijaya G, Digesu GA, Derpapas A, Hendricken C, Fernando R, Khullar V. Antimuscarinic effects on current perception threshold: a prospective placebo control study. *Neurourol Urodyn* 2012;31:75-9. [\[CrossRef\]](#)
 15. AAEM Technology reviews, Guidelines in Electrodiagnostic Medicine ©1999 American Association of Electrodiagnostic Medicine, chapter 11, Page S248.
 16. Lowenstein L, Davis C, Jesse K, Durazo-Arvizu R, Kenton K. Comparison between sensory testing modalities for the evaluation of afferent nerve functioning in the genital area. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20:83-7. [\[CrossRef\]](#)
 17. Kenton K, Lowenstein L, Simmons J, Brubaker L. Aging and overactive bladder may be associated with loss of urethral sensation in women. *Neurourol Urodyn* 2007;26:981-4. [\[CrossRef\]](#)