Sacral Neuromodulation: Applications in Pelvic Floor Disorders

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Objectives

- Understand the indications for sacral neuromodulation
- Select patients who are candidates for sacral neuomodulation
- Counsel a patient on the clinical protocol for sacral neuromodulation.
- Understand how sacral neuomodulation affects other medical/ surgical procedures and conditions

No disclosures

Neuromodulation

- Deep brain stimulation
  - Parkinson's
  - Tremor
  - Dystonia
- Vagal nerve stimulation
  - Epilepsy
- Other areas- depression, OCD, Tourette's Chronic pain
- Pelvic floor disorders- urinary, bowel

Sacral Nerve Stimulation

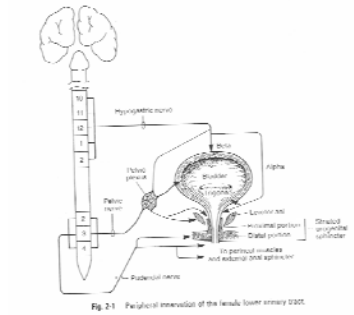
- **Definition** - stimulation of the sacral nerves to modulate the neural reflexes that influence the bladder, sphincter and pelvic floor.

Sacral Nerve Stimulation

History of Sacral Nerve Stimulation

- 1981 – Department of Urology, University of California at San Francisco initiated clinical program.
- 1985-92 – Multi-center trial conducted by Urosystems, Inc.
- 1994 – Medtronic CE mark (approval to market in Europe) for InterStim® in Europe for treatment of urge incontinence, retention, and urgency-frequency.
- 1997 – FDA grants Medtronic approval of the InterStim System for treatment of urge incontinence in the US.
- 1999 - FDA approval of the InterStim System for treatment of symptoms of urgency-frequency and urinary retention.

Normal micturition/ storage



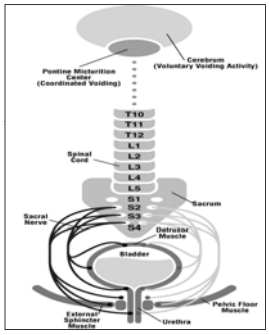
Guarding reflexes

- two guarding reflexes that work to prevent incontinence
- One guarding reflex is between the bladder and the smooth muscle of the urethra which is mediated by the *efferent* pathways of the sympathetic system.
- second guarding reflex, between the *afferent* nerves in the bladder and the *efferent* pathways in the pudendal nerve, leads to contraction of the skeletal component of the urethra.

Afferent pathways

- Bladder afferent pathways
  - are mediated by unmyelinated C fibers and small myelinated A fibers
  - Pudendal afferent input can *turn on* voiding reflexes by suppressing the guarding reflex pathways
  - pudendal afferent input can also *turn off* overactive voiding by blocking ascending sensory pathways.

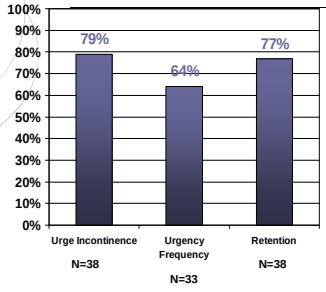
SNS mechanism of action



Indications for Urinary control

- Urinary frequency
- Urge incontinence
- Urinary retention
- Not yet FDA approved for IC, underlying neurological conditions (MS), < 16 years of age, pregnancy, anal incontinence

InterStim® Therapy: Clinical Efficacy[1]



Urge Incontinence
- 45% remained completely dry
- 34% experienced ≥ 50% reduction in leaking episodes

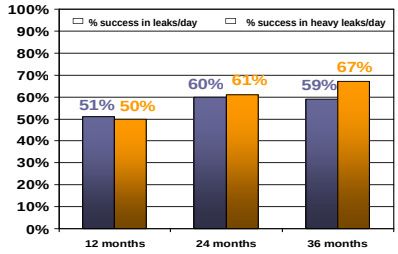
Urgency Frequency
- 31% returned to normal voids (4 to 7 voids/day)
- 33% experienced ≥ 50% reduction in voids

Retention
- 61% eliminated use of catheters
- 16% experienced ≥ 50% amount of urine emptied from catheter usage

1. MDT-103 Study, Medtronic data on file.

Urge Incontinence: Sustained Results Over Time[1]

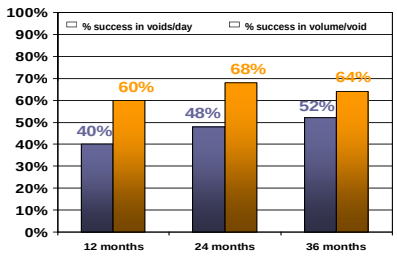
Percentage of patients achieving clinical success with InterStim® Therapy (≥ 50% improvement) by visit for severity of leaking parameters



1. Medtronic Post Approval Study, Medtronic data on file.

Urgency Frequency: Sustained Results Over Time[1]

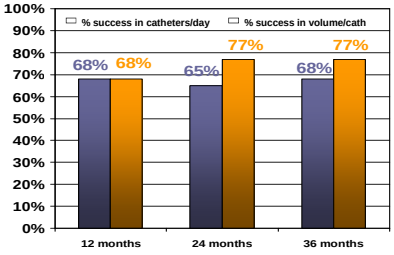
Percentage of patients achieving clinical success with InterStim® Therapy (≥ 50% improvement) by visit and diary parameters



1. Medtronic Post Approval Study, Medtronic data on file.

Retention: Sustained Results Over Time[1]

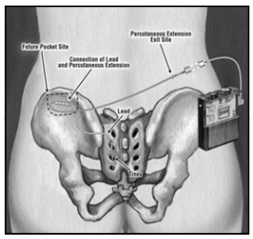
Percentage of patients achieving clinical success with InterStim® Therapy (≥ 50% improvement) by visit and diary parameters



1. Medtronic Post Approval Study, Medtronic data on file.

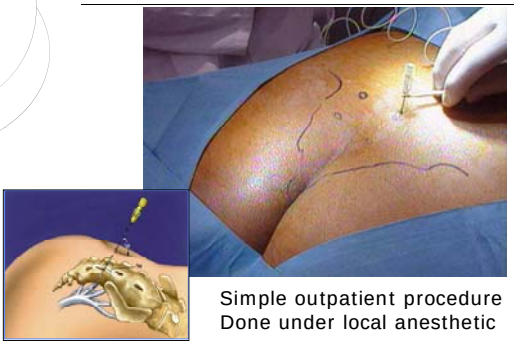
Test Stimulation Procedure

- A lead (percutaneous or tined) is surgically implanted near the sacral nerve (S2, S3, or S4)
- Lead is connected to an external device worn on the patient's belt for a period of 3-7 days
- Patient will record his/her voiding behavior in a diary



Test Stimulation & Implantation

Needle Placement: Testing for Motor/Sensory Responses



Simple outpatient procedure
Done under local anesthetic

Test Stimulation

Test Stimulation & Implantation

Voiding Diary Documentation

Please record date and time and answer every question each time you go to the toilet and/or have a leaking episode.

	Date:	5/6/98	5/6/98	5/6/98	5/6/98
	Time:	7 a.m.	10 a.m.	a.m.	a.m.
		p.m.	p.m.	12 p.m.	2 p.m.
1. Volume voided into measuring cup.		300 ml	250 ml	250 ml	500 ml
2. Volume measured by catheter.		ml	ml	ml	ml
3. Please rate any leaking episode you experienced:		None	None	None	None
Urgency = a few drops		(Slight)	Slight	Slight	Slight
Moderate = 1-2 Tablespoons (15-30 ml); soaks pad/diaper or outer clothing		Moderate	(Moderate)	Moderate	Moderate
Heavy =		Heavy	Heavy	(Heavy)	Heavy
4. Did leaking cause you to replace your pad/diaper?		No	No	No	No
		Yes	(Yes)	Yes	Yes
5. Did you feel empty after voiding?		No	No	No	(No)
		(Yes)	Yes	(Yes)	Yes
6. Degree of urgency prior to voiding?		None	None	None	None
		(Mild)	Mild	Mild	Mild
		Moderate	(Moderate)	Moderate	Moderate
		Severe	Severe	Severe	Severe

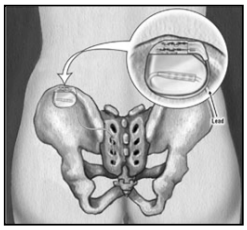
5/6/1998	5/6/1998	5/6/1998	5/6/1998
a.m.	a.m.	a.m.	a.m.
12 p.m.	2 p.m.	4 p.m.	7 p.m.
250 ml	500 ml	300 ml	250 ml
ml	ml	ml	ml
None	None	None	None
Slight	Slight	(Slight)	Slight
Moderate	Moderate	Moderate	(Moderate)
(Heavy)	(Heavy)	Heavy	Heavy
No	No	No	No
(Yes)	(Yes)	(Yes)	Yes
No	No	No	(No)
Yes	Yes	(Yes)	Yes
None	(None)	None	None
Mild	Mild	(Mild)	(Mild)
(Moderate)	Moderate	Moderate	Moderate
Severe	Severe	Severe	Severe

Test Stimulation Evaluation

- Patient should demonstrate an improvement of 50% in at least one of the following:
  - **Urge incontinence:** number of leaking episodes per day; severity of leaking episodes; or number of pads used per day due to incontinence
  - **Urgency-frequency:** number of voids per day; micturition volume per void; degree of urgency
  - **Retention:** catheterized volume per catheterization
- Should return towards baseline voiding behavior after completion of test stimulation.

Implant Procedure

- After successful test stimulation period, the physician may implant the InterStim System
- A pocket is typically created for the neurostimulator in the upper buttock



Technique

- Implantation technique
  - Open procedure to sacral periosteum
  - Open procedure to lumbo-sacral fascia
  - Tined lead (2003)

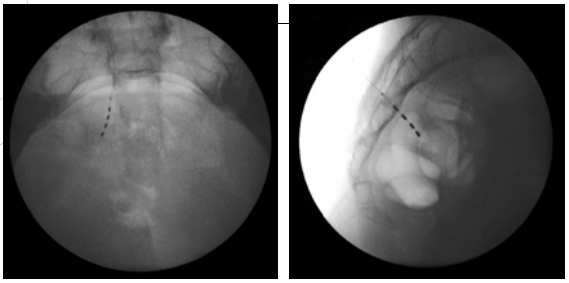
Implantation of Interstim® System

Programming

Sacral Nerve Stimulation

Test Stimulation & Implantation

Electrode Location: Chronic Lead



Which type of trial is best?

- Bilateral lead test stimulation better than unilateral in refractory voiding
  - 69/124 pts went onto to stage two
  - 55/124 pts went onto stage two
- Tined lead better than percutaneous
  - Tined lead - 67% response
  - Percutaneous – 40% response
  - Tined lead enables longer test time
  - Less lead migration

Blandon RE et al. Re-operation rates after permanent sacral nerve stimulation for refractory voiding dysfunction in women. BJU Int 2008.
Pham K et al. Unilateral versus bilateral stage I neuromodulation lead placement for the treatment of refractory voiding dysfunction. Neurourol Urodyn. 2008.

Implantation: Ranking of Adverse Events in first 12 Months Post-implant

- Pain at neurostimulator site 15.3%
- New pain 9.0%
- Suspected lead migration 8.4%
- Infection 6.1%
- Transient electric shock 5.5%
- Pain at lead site 5.4%
- Adverse change in bowel function 3.0%
- Note: Additional events occurred – each less than 2.0%

Source: MDT-103 Study 1993-1998, data on file Medtronic

Integration into Practice

- Treatment of OAB
  - Behavioral
    - Bladder retraining, dietary changes
  - Pelvic muscle exercises
  - Biofeedback
  - Medications
  - InterStim
- Treatment of urinary retention
  - Medications
  - Self catheterization

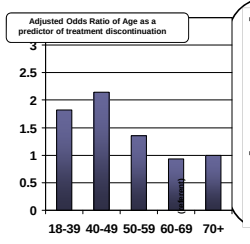
Should we keep OAB meds?

- Anti-cholinergics are available to prescribe
- established brand names on the market

YES……., BUT……..

- High rate of discontinuation
- Patient tolerability often challenging

OAB Pharmacotherapy: Predictors of Discontinuation



- **In a survey of 1,447 people receiving treatment for incontinence, younger patients (ages 40 – 49) were more than twice as likely to discontinue their therapy when compared to 70 year old repondents[1]**
- **Other predictors of therapy discontinuation were number of years with symptoms, and number of wetting accidents**

Source:
1. Campbell, U.B, Stang, P, Barron, R, Galt Associates, Inc., Allergan, Inc. Survey Assessment of Compliance and Satisfaction with Treatment for Urinary Incontinence. Poster Presentation, ICS Conference, 2005

Pharmacotherapy vs. InterStim® Therapy: A Theory

Pharmacotherapy: Mechanism of Action

- Targets efferent effects
- Poor side effect profile
- Poor patient compliance

SNS Therapy: Mechanism of Action

- Targets afferent effects & modulation of the pelvic floor
- General lack of side effects known associated with drug therapy

InterStim Therapy

- Should be considered after more conservative treatment options have failed and before surgical options are considered

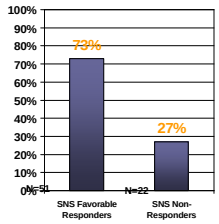
Patient Selection: Who Benefits Most?

In an independent investigation evaluating women with refractory, nonobstructive urinary urge incontinence after stress incontinence surgery, factors predictive of a **positive** response to SNS therapy included

- **Patients younger than 55 (p= 0.01)**
- **Test stimulation performed within 4 years of the surgical procedure (p=0.01)**
- **Evidence of pelvic floor muscle activity (p=0.01)**

1. Sherman, N. et al. Sacral Neuromodulation for the Treatment of Refractory Urge Incontinence after Stress Incontinence Surgery. Am Jrnl of Obst. & Gyn: (193) 2083-7, 2005.

Identifying the Refractory Patient: How Long Should a Patient Wait?



- Starkman et al.[1] reported a mean duration of symptoms of 4.6 years before implantation.
- Non-responders were found to have had a longer duration of symptoms (6.5 vs. 3.8 years)

1. Starkman, J.S. et al. Sacral Neuromodulation: Results from a Large Single Institutional Experience. Abstract No. 1296, AUA 2006 Meeting, Atlanta, GA.

Sacral nerve stimulation for anal- fecal incontinence

- randomized trial comparing sacral neuromodulation with optimal medical therapy
- 120 Pts (39-86 years) with severe FI (had complete eval) randomized to
  - sacral nerve stimulation (n=60) or best medical therapy (n=60)
  - SNS group- significant improvements (P<0.0001)
    - mean incontinent episodes per week decreased from 9.5 to 3.1 and mean incontinent days per week from 3.3 to 1
    - improvement in fecal incontinence quality of life index
  - Control group-no significant improvement in fecal continence and the fecal incontinence quality of life scores

Tjandra TT et al. Sacral nerve stimulation is more effective than optimal medical therapy for severe fecal incontinence: a randomized, controlled study. Dis Colon Rectum, 2008

Does SNS work for fecal incontinence in the presence of abnormal anatomy/ function?

- ? effectiveness of SNS in the setting of anal sphincter defects, previous sphincter repair, or pudendal neuropathy
- 55 pts underwent SNS
- The Fecal Incontinence Quality of Life score also showed a significant improvement on all 4 scales at 36 months
- No differences if had sphincter defect on endoanal ultrasound, pudendal neuropathy, or a previous sphincter repair

Brouwer R Duthie G Sacral nerve neuromodulation is effective treatment for fecal incontinence in the presence of a sphincter defect, pudendal neuropathy, or previous sphincter repair. Dis Colon Rectum. 2010

Sacral nerve stimulation for IC- BPS ?

- 32 women and 7 men with IC/PBS failed previous conventional therapy underwent sacral neuromodulation test stimulation.
- 22 pts implanted
- Long-term average follow-up of 59.9 months.
- Eleven (50.0%) devices required explantation
- Of 22 patients, 3 (13.6%) lost benefit over time.

Powell CR Kreder KJ. Long-term outcomes of urgency-frequency syndrome due to painful bladder syndrome treated with sacral neuromodulation and analysis of failures. J Urol 2010

Sacral nerve stimulation for pts with neurological conditions ?

- Case series of 28 patients with neurological conditions (MS, Parkinson's, other) underwent SNS
  - Decrease in incontinence, daytime frequency, nocturia, self-cath
- retrospective case-control study of 14 ambulatory women with MS, stage 1/2 sacral neuromodulation for urinary retention.
  - 12 of 14 patients (86%) were successfully implanted
  - mean f- up 4.32 +/- 1.32 years
  - Urine retention improved
    - mean postvoid residual = 50.5 +/- 21.18 ml
    - mean maximum uroflow = 17.7 +/- 7.9 ml/s

Wallace PA et al. Sacral neuromodulation in patients with underlying neurologic disease. Am J Obstet Gynecol. 2007.
Marinkovic SP Gillen LM. Sacral neuromodulation for multiple sclerosis patients with urinary retention and clean intermittent catheterization. Int Urogynecol J Pelvic Floor Dysfunct. 2010

Can you have a cardiac pacemaker?

- cross-talk between cardiac pacemakers and sacral neuromodulation
- case series of patients who underwent staged Interstim
  - with cardiac pacemakers or who later required cardiac pacemakers or implantable cardioverter defibrillator device
- No cross-talk was demonstrated by cardiac monitoring and post op telemetry
  - intraoperative
  - during programming

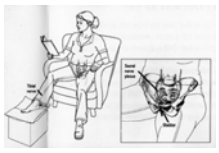
Wallace PA et al. Sacral nerve neuromodulation in patients with cardiac pacemakers. Am J Obstet Gynecol 2007.
Roth TM. Sacral neuromodulation and cardiac pacemakers. Int Urogynecol J Pelvic Floor Dysfunct. 2010
Molon G et al. ICD and Neuromodulation Devices: Is Peaceful Coexistence Possible? Pacing Clin Electrophysiol. Feb 2011

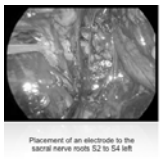
Can you have an MRI?

- do not perform MRI examinations on patients with implanted sacral nerve stimulator.
  - motion, dislocation or torquing of the implanted pulse generator (IPG), heating of the leads, damage to the IPG
- MRI at 1.5Tesla safe if the area to be imaged is out of the isocenter of the MRI scanner
- Eight MRI examinations in 6 pts , IPGs were put to "nominal" status
- Patients were monitored continuously, Devices were then re-programmed , voiding diaries repeated, no change in diaries, perception of stimulation or pts, devices working

Elkelini MS et al. Safety of MRI at 1.5Tesla in patients with implanted sacral nerve neurostimulator. Eur urol 2006.

Other neuromodulation techniques

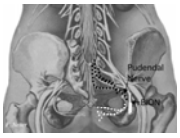




- Posterior tibial nerve stimulation
- LION (laparoscopic implantation of neurostimulator)- hypogastric plexus for bladder atonia
- Miniaturo (Accessa ®) AMS
  - Paraurethral neuro-modulation
  - Not available
  - Study ongoing in Netherlands

BION – pudendal nerve stimulation

- Stimulation activates afferent innervation over three sacral segments
- Efferent stimulation activates the external urethral and external anal sphincters, and the levator ani muscles
- The external components of this neural prosthesis



Pudendal nerve stimulation

- **a tined lead** placed at the pudendal nerve via the ischial-rectal approach
- majority of 84 patients (78.6% female; age 51.8 +/- 16.9 years) had IC/PBS or OAB
- **Pudendal response (≥50% improvement) occurred in 60/84 (71.4%)**
- **Almost all (93.2%) who had previously failed sacral neuromodulation responded to pudendal stimulation**
- Outcomes were evaluated in 55 continuing on CPNS (median follow up 24.1 months).
  - 5 revisions, 4 other re-operations, 5 explanted
- **significant improvements** in frequency ($P < 0.0001$), voided volume ($P < 0.0001$), incontinence ($P < 0.0001$), and urgency ($P = 0.0019$) occurred.
- **ICSI-PI scores significantly improved over 12 months** ($P < 0.0001$)

Peters KM et al. Chronic pudendal neuromodulation: Expanding available treatment options for refractory urologic symptoms. Neuro Urol 2009

Benefits of InterStim® Therapy

- Test stimulation period allows informed choice for patient and doctor
- Effective treatment in properly screened patients
- Safe
- Reversible
- Does not preclude use of alternative treatments
- Future indications?- CPP, sexual dysfunction

Summary

- Patients with conditions of urinary urgency-frequency, urge incontinence or urinary retention
- Sacral neuromodulation stimulation offers a minimally invasive alternative treatment for many patients with lower urinary tract dysfunction.
- Until recently, these patients' treatment options included major surgical procedures such as augmentation cystoplasty or urinary diversion.