Neuromodulation in Bladder Dysfunction

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electrostimulation to modulate and restore

- respiration
- upper limbs
- pain
- sacral area
- stand up and walk

Spinelli, 2009
Detrusor Over activity

![Graph showing detrusor activity with various measurements such as Vinfus, Pves, Pdet, Pabd, and Qura. The graph includes data points for UR and VB with corresponding values.]
Detrusor Hyper-reflexia (NDO)
Obstructive Voiding in a Female
Complex interaction between Pelvic/sacral nerves and Spinal cord and CNS.
POSTERIOR TIBIAL NERVE STIMULATION
Tibial nerve stimulation

Percutaneous vs. Transcutaneous

• Increase in publications over last 12 years for IDO

• Increase in publications over last 4 years for NDO
How does it work?
Posterior Tibial Nerve Stimulation

- Less invasive
- 12 weekly sessions of 30 minutes each
- Cheaper
- Efficacy
  - 60-70% in non-selected patients
  - 50% success rate in our neurological patient if failed all other treatment
## Literature Review

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>PTNS Events</th>
<th>PTNS Total</th>
<th>Sham Events</th>
<th>Sham Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finazzi Agro 2005</td>
<td>6</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>17.6%</td>
<td>13.00 [0.85, 198.14]</td>
</tr>
<tr>
<td>Finazzi Agro 2010</td>
<td>12</td>
<td>17</td>
<td>0</td>
<td>15</td>
<td>17.4%</td>
<td>22.22 [1.43, 345.99]</td>
</tr>
<tr>
<td>SuMIT 2010</td>
<td>60</td>
<td>110</td>
<td>23</td>
<td>110</td>
<td>47.4%</td>
<td>2.61 [1.75, 3.90]</td>
</tr>
<tr>
<td>Vohra 2002</td>
<td>9</td>
<td>11</td>
<td>0</td>
<td>10</td>
<td>17.6%</td>
<td>17.42 [1.14, 265.34]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>146</strong></td>
<td></td>
<td><strong>143</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>7.02 [1.69, 29.17]</strong></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>87</strong></td>
<td></td>
<td><strong>23</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\text{Tau}^2 = 1.07$; $\chi^2 = 6.18$, df = 3 ($P = 0.10$); $I^2 = 51$

Test for overall effect: $Z = 2.68$ ($P = 0.007$)
SuMIT trial

- Multi-center double-blind RCT (sham controlled)
- Level I evidence
  - PTNS safe and effective in OAB management
  - 54.5% reported improved vs. 20.9% sham subjects

Regulatory Body Approvals

- 2000 FDA
- 2010 NICE IPAC 362
Percutaneous posterior tibial nerve stimulation as an effective treatment of refractory lower urinary tract symptoms in patients with multiple sclerosis: preliminary data from a multicentre, prospective, open label trial

C Gobbi¹, GA Digesu¹,²,³,⁴, V Khullar³, S El Neil⁴, G Caccia² and C Zecca¹

Table 2. Study outcomes

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Pre-PTNS</th>
<th>Post-PTNS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime frequency*</td>
<td>9 (6–11)</td>
<td>6 (5–10)</td>
<td>0.04</td>
</tr>
<tr>
<td>Nocturia*</td>
<td>3 (2–4)</td>
<td>1 (0–3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Voided volume**</td>
<td>182 ml (±50)</td>
<td>225 ml (±50)</td>
<td>0.003</td>
</tr>
<tr>
<td>Post-micturition residual**</td>
<td>98 ml (±124)</td>
<td>43 ml (±45)</td>
<td>0.02</td>
</tr>
<tr>
<td>PPBC*</td>
<td>5 (5;6)</td>
<td>2 (2;3)</td>
<td>0.003</td>
</tr>
<tr>
<td>PPIUS*</td>
<td>4 (3;4)</td>
<td>2 (1;3)</td>
<td>0.005</td>
</tr>
<tr>
<td>UB-VAS (cm)*</td>
<td>10 (8;10)</td>
<td>6 (4;8)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Transcutaneous Posterior Tibial Nerve Stimulation for Treatment of the Overactive Bladder Syndrome in Multiple Sclerosis: Results of a Multicenter Prospective Study

Marianne de Sèze, M.D., Ph.D., Patrick Raibaut, Philippe Gallien, Alexia Even-Schneider, Pierre Denys, Veronique Bonniaud, Xavier Gamé, and Gérard Amarenco
Acute Urodynamic Effects of Percutaneous Posterior Tibial Nerve Stimulation on Neurogenic Detrusor Overactivity in Patients With Parkinson’s Disease

Sibel Canbaz Kabav, Sahin Kabav,* Mehmet Yucel, and Hilmi Ozden

Fig. 2. Graphics of the effects of PTNS on urodynamic variables for the comparison of baseline and after PTNS findings in PD patients.
Sacral Neuromodulation
NHNN Indications for SNM

Problems of urinary evacuation
- Urinary retention
- Voiding dysfunction post surgery

Problems of urinary storage
- Urgency/frequency (OAB/DO)

Combined problems
- Mixed incontinence (bladder and bowel)
- Double incontinence (stress and OAB/DO)
- Urogenital pain
Optimal Treatment

Improvement of >50% in patient’s symptoms

Minimal side effects and complications
Complex interaction between Pelvic/sacral nerves, Spinal cord, and CNS control centres ‘re-started’.
Percutaneous Nerve Evaluation Test (PNE)

Schematic drawing of cannulation of the left S3

The tip of the cannula (arrow) will ideally be placed against the corresponding sacral nerve when the cannula is inserted at an angle of 60° to the skin over the sacrum.
Cannula has been placed in the third sacral foramen on the left side.

Cannula is attached to an electrical cable to test the motor response of the anal sphincter.

Assess for 5-7 days.
60% show at least a 50% improvement in bladder symptoms but high false negative rate

2-stage Tined Lead Technique
Stage 1 SNM - Percutaneous
OUTCOMES
BLADDER SENSATISATION
Optimizing the duration of assessment of sacral neuromodulation in non-obstructive chronic urinary retention

![Bar Chart]

- Percent of patients (%)
  - 1-5: 58.3%
  - 6-10: 20.8%
  - 11-15: 8.3%
  - 16-20: 4.2%
  - 21-25: 4.2%
  - 26-31: 4.2%

The onset of bladder sensation (days)

Elneil, S. et al., 2013
Optimizing the duration of assessment of sacral neuromodulation in non-obstructive chronic urinary retention

Cumulative percentage of patient outcomes after stage-1 SNM

Elneil, S. et al., 2013
NHNN OAB/DO EXPERIENCE
Success rates vary 64-88% (12-15.5 months)

**Improvement in subjective parameters**
- 23-46% \(\downarrow\) the number of voids
- 56-90% \(\downarrow\) incontinence episodes
- 64-100% \(\downarrow\) frequency
- Sustained 5 years

**Improvement in objective parameters:**
- 52% \(\uparrow\) in bladder capacity
- \(\downarrow\) detrusor activity index (DAI)

**Cost-benefit analysis** (home study)
- £866 per patient/year for a projected 7.5 years by >50% improvement in OAB symptoms
**OAB/DO STUDY**

<table>
<thead>
<tr>
<th>Study Period:</th>
<th>August 2007 to July 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery:</td>
<td>2-stage SNM procedure</td>
</tr>
<tr>
<td>Assessment:</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>Bladder diary</td>
</tr>
<tr>
<td>Stage 1</td>
<td>Bladder diary,</td>
</tr>
<tr>
<td></td>
<td>Uroflowmetry &amp; PVR</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Bladder diary</td>
</tr>
<tr>
<td></td>
<td>Uroflowmetry &amp; PVR</td>
</tr>
</tbody>
</table>

**Success definition:**

>50% improvement in objective and subjective parameters
PATIENT DEMOGRAPHICS

Total Numbers: n = 37 with intractable DO

Gender: 33 Female 4 Male

Age: 46 ± 14 years (18-70 years)

Ethnicity: Caucasian: 32; Asian:1; Unknown:4

Duration of Symptoms: 16 ± 12 years

Type of DO: 33 IDO 4 NDO

Associated symptoms: Faecal incontinence in 9 patients
Voiding dysfunction in 16 patients
(following BTX injection trial)
PREVIOUS OAB/DO MANAGEMENT

• Refractory to anti-cholinergics
  – All patients in this study

• Previous intradetrusor BoNT/A injections
  – 23 patients (65%)
    45% had a 200iu dose
    >65% had 2 more treatment cycles

Elneil, S et al., IUGA Abstract 2013
PREVIOUS OAB/DO MANAGEMENT

History of symptoms 16 ± 12 years
Refractory to anti-cholinergics 37 patients
Previous intradetrusor botulinum toxin injections 23 patients (62%)
PREVIOUS POSITIVE RESPONSE TO BONT/A TREATMENT

- Successful stage-1: 71% (n=10)
- Failed stage-1: 29% (n=4)

PREVIOUS POOR RESPONSE TO BONT/A TREATMENT

- Successful stage-1: 46% (n=4)
- Failed stage-1: 54% (n=5)

[Fisher’s Exact Test; P=0.39]
STAGE 1 OUTCOMES IN INTRACTABLE OAB/DO
(Both anti-cholinergic and BoNT/A groups)

Success rate
- 26 patients (70.3%)

True failure (no response)
- 11 patients (29.7%)

Complications
- Infection: 3 (8%)
- Lead displacement/broken lead: 2 (5%)
- Severe pain at operation site: 2 (5%)
- Leg paraesthesia: 1 (3%)
- Severe Leg weakness: 1 (3%)

* patients underwent a re-do stage 1
** patients treated with physiotherapy
STAGE-2 PROCEDURES POST STAGE-1

Time period between stage 1 and 2

4 – 12 weeks

Stage-2 performed

22 of 26 patients

Stage-2 not performed

4 of 26 patients
(2 late infections, 2 personal choice)
STAGE-2 OUTCOMES

Follow-up

12 – 48 months

At 12 months follow-up

21 out of 22 patients who underwent stage-2 had successful resolution of OAB/DO symptoms (95%)

1 out of 22 patients only had a good response for FI symptoms and not their OAB/DO symptoms

Complications

1 in 22 (5%) had infection at battery site
Thus,

Two-stage SNM is a viable option in intractable OAB/DO, refractory to other therapeutic modalities

- 70% success following stage-1 SNM

- 95% sustained success rate at 12 months in those who continued onto stage-2 SNM
NHNN CUR EXPERIENCE
## Efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>Total</th>
<th>Patients with UI</th>
<th>Patients with U/F</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cured</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>US National Patient Registry [14]</td>
<td>81</td>
<td>&gt;50%</td>
<td>&gt;50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>27/43</td>
<td>10/19</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>62%</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>Amundsen &amp; Webster [20]</td>
<td>12</td>
<td>2/12</td>
<td>12/12</td>
<td>7.8 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Bosch &amp; Groen [11]</td>
<td>45</td>
<td>27/45</td>
<td>9/45</td>
<td>47.1 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Siegal et al. [12]</td>
<td>112</td>
<td>21/41</td>
<td>16/29</td>
<td>24-36 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>19/41</td>
<td>5/29</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>46%</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>Schmidt et al. [10]</td>
<td>34</td>
<td>16/34</td>
<td>14/25</td>
<td>6 months</td>
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<tr>
<td></td>
<td></td>
<td>47%</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>10/34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hassouna et al. [21]</td>
<td>25</td>
<td></td>
<td></td>
<td>24 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14/25</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>Elhilali et al. [13]</td>
<td>41</td>
<td>1/6</td>
<td></td>
<td>77.4 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Voskuilen et al. [8]</td>
<td>149</td>
<td>89/107</td>
<td></td>
<td>70 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>83%</td>
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</tbody>
</table>
# 2-stage SNM for CUR in women

Determination of prognostic factors that may affect outcome

<table>
<thead>
<tr>
<th></th>
<th>Success (n=136)</th>
<th>Failure (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>36.1±10.9</td>
<td>36.8±13.5</td>
<td>0.76</td>
</tr>
<tr>
<td><strong>Precipitating event for CUR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>64</td>
<td>16</td>
<td>1.00</td>
</tr>
<tr>
<td>No</td>
<td>72</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td><strong>Opiate treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48</td>
<td>13</td>
<td>0.84</td>
</tr>
<tr>
<td>No</td>
<td>80</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td><strong>UPP(cmH2O)</strong></td>
<td>99.2±26.4</td>
<td>102±30.8</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>SV(cm³)</strong></td>
<td>1.80(0.7-3.8)</td>
<td>1.9(1.0-2.6)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>EMG outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>11</td>
<td>4</td>
<td>0.48</td>
</tr>
<tr>
<td>Abnormal (Fowler’s Syndrome)</td>
<td>56</td>
<td>10 (n=66)</td>
<td></td>
</tr>
<tr>
<td>Equivocal</td>
<td>9</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not done</td>
<td>60</td>
<td>18 (n=78)</td>
<td></td>
</tr>
</tbody>
</table>
2-stage SNM for CUR in women
Determination of prognostic factors that may affect outcome

Patient’s characteristics and urethral physiological assessments had **NO IMPACT** on Stage-1 (P>0.05) or on Stage-2 outcomes (P>0.05).

Success rate

<table>
<thead>
<tr>
<th>Stage</th>
<th>Success</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>136/169</td>
<td>(80.5%)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>125/136</td>
<td>(92%)</td>
</tr>
</tbody>
</table>

Elneil, S et al., 2013 ICS Abstract
<table>
<thead>
<tr>
<th>Indication</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary retention</td>
<td>82%</td>
</tr>
<tr>
<td>Double incontinence</td>
<td>81%</td>
</tr>
<tr>
<td>Mixed incontinence (+USI Sx)</td>
<td>78%</td>
</tr>
<tr>
<td>Urgency/frequency (OAB/DO)</td>
<td>72%</td>
</tr>
<tr>
<td>Voiding dysfunction post surgery</td>
<td>67%</td>
</tr>
<tr>
<td>Urogenital pain</td>
<td>66%</td>
</tr>
</tbody>
</table>
NHNN 10 year experience (1996-2006)
Conclusion

- Success rates for traditional SNM and 2-stage SNM are comparable to reported data

- 2-stage SNM has reduced complication rate

- Resource utilisation is high, but worth the cost when balanced against other continence devices/procedures

- Estimate of cost: variable depending on the system used

- NICE approval for OAB and faecal incontinence – what about retention?