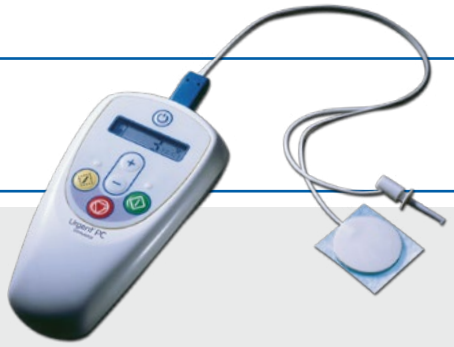
Urgent® PC

CLINICAL SUMMARY

PTNS FOR URINARY INCONTINENCE



The Urgent® PC Neuromodulation System provides percutaneous tibial nerve stimulation (PTNS) for Overactive Bladder (OAB) and associated symptoms of Urinary urgency, Urinary frequency, Urinary urge incontinence.

LONG TERM DATA

Percutaneous tibial nerve stimulation (PTNS) for the long-term treatment of overactive bladder: Three-year results of the STEP Study

Peters, K., et al. (2013). J Urol, 189(6), 2194-201.

Study Design & Patient Selection:

- 50 responders from the randomized, double-blind SUmiT Trial followed 3 years
- Assigned a fixed-schedule 14-week tapering protocol, followed by a personal treatment plan

Outcomes:

- 29 continued treatment for up to 3 years
- Average of 1.1 treatments per month
- Bayesian model estimated ~77% maintained moderate or marked improvement
- All improvements from baseline were significant ($p<0.0001$)
- Median voids/day from 12.0 (IQR 10.3 – 13.7) to 8.7 (7.3 – 11.3)
- Median voids/night from 2.7 (IQR 1.7 – 3.3) to 1.7 (IQR 1.0 – 2.7)
- Median urge incontinence episodes/day from 3.3 (IQR 0.7 – 6.0) to 0.3 (IQR 0.0- 1.0)
- QoL parameters remained markedly improved

Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder

MacDiarmid, S., et al. (2010). J Urol, 183, 234-40.

Study Design & Patient Selection:

- 33 patients who responded to PTNS were followed for up to 12 months
- Treatment was tapered to individuals for sustained relief of OAB symptoms
- Evaluation at 6 and 12 months using voiding diaries, global and safety assessments

Outcomes:

- 30/33 (90%) continued treatment for 6 months and sustained improvements
- 24/33 (73%) continued treatment for 12 months and sustained improvements
- Patients received a mean of 12.1 ± 4.9 additional treatments over an average of 263 days; mean of 21 days between treatments
- All outcome measure changes from baseline were significant ($p<0.05$)
- Significant QoL improvement from 12 weeks to 12 months ($p<0.01$) and from 6 months to 12 months ($p<0.01$)
- No serious adverse events or device malfunctions

COMPARED TO SHAM

Randomized trial of percutaneous tibial nerve stimulation versus sham efficacy in the treatment of overactive bladder syndrome: Results from the SUmiT Trial

Peters, K., et al. (2010). J Urol, 183, 1438-43.

Study Design & Patient Selection:

- 23-center, double-blind, randomized, controlled trial
- 12-week study; 220 patients (174 female, 46 male)
- Randomized 1:1 to 12 weeks of treatment with PTNS or sham therapy

Outcomes:

- 103 PTNS patients and 105 sham patients evaluated
- Patient Global Response Assessment
  - 54.5% of PTNS patients reported moderate or marked improvement in bladder symptoms compared to 20.9% of sham patients ($p<0.001$)
  - PTNS patients had a statistically significant improvement compared to sham patients for urinary urgency ($p=0.003$), urinary frequency ($p<0.001$) and urinary urge incontinence ($p=0.02$)
- No serious device related adverse events or malfunctions were reported

Percutaneous tibial nerve stimulation effects on detrusor overactivity incontinence are not due to a placebo effect: A randomized, double-blind, placebo controlled trial

Finazzi-Agrò, E. et al. (2010). J Urol, 184, 2001-6.

Study Design & Patient Selection:

- Prospective, single-site, double-blinded
- 35 female patients with urge incontinence and detrusor overactivity
- Patients received twelve 30-minute treatments
  - Placebo group (17): stimulator was turned on for a few seconds then turned off for the remainder of session
  - PTNS group (18): treated per protocol

Outcomes:

- Patients with >50% decrease in incontinence episodes were considered responders
  - 71% PTNS patients
  - 0% placebo patients
- Improvements in incontinence episodes, number of voids, voided volume and incontinence quality of life scores were statistically significant in the PTNS group but not in the placebo group

COMPARED TO DRUGS

Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: Results from the Overactive Bladder Innovative Therapy Trial

Peters, K., et al. (2009). J Urol, 182, 1055-61.

Study Design & Patient Selection:

- 11 U.S. centers
- 12-week study; 100 patients (94 female, 6 male)
- Randomized to either weekly PTNS therapy with Urgent PC or tolterodine tartrate extended release, 4mg/day

Outcomes:

- 79.5% of PTNS patients considered themselves cured or improved compared to 54.8% of drug patients
- Physicians considered 79.5% of PTNS patients cured or improved, compared with 60.5% of drug patients
- Comparable reductions in voiding episodes and urge incontinence were achieved in PTNS and drug patients
- No serious adverse events associated with either treatment
- Constipation and dry mouth reported less often with PTNS

Solifenacin succinate versus percutaneous tibial nerve stimulation in women with overactive bladder syndrome: Results of a randomized controlled crossover study

Vecchioli-Scaldazza, et al. (2013). Gynecol Obstet Invest, 75(4), 230-4.

Study Design & Patient Selection:

- Randomized, controlled, crossover study of 40 consecutive OAB patients (mean age 62; range 35-81)
- Group A: 5 mg/day of SS for 40 days, then 3-month washout, then 12 PTNS treatments
- Group B: 12 PTNS treatments, then 3-month washout, then 5 mg/day of SS for 40 days

Outcomes:

- Both groups had significant improvements in voids, nocturia, urge incontinence and voided volume ($p<0.05$)
- Subjective response was highly statistically significant for both treatments ($p<0.0009$)
- PTNS provided a greater reduction in daily voids and improvement in the QoL compared to SS
- "… the ease of execution, the minimal invasiveness tolerability and the low cost for the patient have determined a greater adherence and persistence of patients to therapy with PTNS."

Peripheral tibial neurostimulation (PTNS) versus tolterodine in the treatment of women with urge urinary incontinence and urge symptoms

Preyer, O., et al. (2009). Poster, International Urogynecological Assoc., Italy.

Study Design & Patient Selection:

- Prospective, single-site, 12-week follow-up
- 31 patients (16 PTNS – 12 weekly, 30-minute treatments; 15 tolterodine – 4 mg/day)

Outcomes:

- No statistical difference between PTNS and drug effectiveness for frequency, QoL, incontinent episodes or urge episodes
- Side-effects: 3.4% PTNS versus 20.7% tolterodine

CLINICAL EFFICACY

Peripheral afferent nerve stimulation for treatment of lower urinary tract irritative symptoms

Ruiz, B.C., et al. (2004). Eur Urol, 45, 65-9.

Study Design & Patient Selection:

- Retrospective, single-site, 21-month average follow-up
- 51 female patients

Outcomes:

- 69% excellent/favorable results
- No reported complications

- Improvement for 26 patients with frequency/urgency:
  - 32% reduction in daytime frequency
  - 52% reduction in nighttime frequency
- Improvement for 22 patients with incontinence:
  - 54% reduction in daytime leakage episodes
  - 67% reduction in nighttime leakage episodes

Posterior tibial nerve stimulation in patients who have failed anticholinergic therapy: Efficacy and time to response

Leong, F.C., et al. (2011). Female Pelvic Med Reconstr Surg, 17(2), 74-5.

Study Design & Patient Selection:

- Retrospective, single-site
- 141 female OAB patients with poor improvement on antimuscarinics
- Symptoms before treatment: urgency 83%, frequency 88.7%, nighttime voiding 68.8% and urge incontinence 78.7%

Outcomes:

- Patient satisfaction with level of improvement
  - As followed (116 patients): 79.3%
  - Intent-to-treat (141 patients): 67.4%

Symptom	Weeks to improvement (median)	Weeks to improvement (range)	Patients with "late" response >8 treatments
Nighttime Voiding	5	2-12	9.9%
Frequency	7	2-12	8.1%
Urgency	6	2-12	18%
Urge Incontinence	6	2-12	18.6%

- Long-term follow-up
  - 77.5% of patients completing initial series continued with long-term treatment (range 4-103 months)
  - Individualized treatment interval ranges from 1 to 3 months

Posterior tibial nerve stimulation in the treatment of urge incontinence

Vandoninck, V., et al. (2003). Neuro Urodyn, 22, 17-23.

Study Design & Patient Selection

- Prospective, multicenter, 12-week follow-up
- 35 patients (25 female, 10 male)

Outcomes:

- 63% subjective success
- 69% objective success (≥ 50% reduction in leakage episodes)
- 60% improved voiding frequency reduction
- Average I-QoL scores significantly improved

Percutaneous tibial nerve stimulation in the treatment of overactive bladder: Urodynamic data

Vandoninck, V., et al. (2003). Neuro Urodyn, 22, 227-32.

Study Design & Patient Selection:

- Prospective, multicenter, 12-week follow-up
- 90 patients (67 female, 23 male)

Outcomes:

- 56% with ≥50% reduction in leakage episodes
- 38% dry
- 64% subjective success

Percutaneous afferent neuromodulation for the refractory overactive bladder: Results of a multicenter study

By Govier, F.E., et al. (2001). J Urol, 165, 1193-8.

Study Design & Patient Selection:

- Prospective, multicenter, 12-week follow-up
- 53 patients (48 female, 5 male)

Outcomes:

- 71% overall success
- ≥25% reduction in daytime/nighttime frequency
- 35% reduction urge incontinence or leak episodes
- Statistically significant improvements in QoL
- 3 minor adverse events resolved spontaneously

Posterior tibial nerve stimulation as neuromodulative treatment of lower urinary tract dysfunction

van Balken, M.R., et al. (2001). J Urol, 166, 914-8.

Study Design & Patient Selection:

- Prospective, multicenter, 12-week follow-up
- 37 patients (27 female, 10 male), 91% failed drug therapy; 49% with prior surgery

Outcomes:

- 59% subjective success
- Rare side-effects of minor bleeding at needle site or temporary pain

Use of peripheral neuromodulation of the S3 region for a treatment of detrusor overactivity: A urodynamic-based study

Klingler, H.C., et al. (2000). Urol, 56, 766-71.

Study Design & Patient Selection:

- Prospective, single-site, 11-month follow-up
- 15 patients (11 female, 4 male)

Outcomes:

- 47% considered cured
- 20% demonstrated significant improvement
- 48% reduction in daytime voids to normal pattern
- 68% reduction in nighttime voids
- 41% reduction in mean number leakage episodes
- 1 minor hematoma at needle insertion site

META-ANALYSIS

Percutaneous tibial nerve stimulation (PTNS): A literature-based assessment

MacDiarmid, S.A., & Staskin, D.R. (2009). Curr Bld Dysf Rept, 4, 29-33.

Analysis Design & Paper Selection:

- 17 studies were reviewed for inclusion in a meta-analysis; 7 met the inclusion criteria for 1+ measured outcomes
- Total patients = 244

Outcomes:

- 71% of patients improved (174 of 244, 7 studies, p<0.001)

Criteria	Mean Improvement	Patients	Studies	p-value
Daytime Voids	23%	244	7	p<0.001
Nighttime Voids	41%	151	5	p<0.002
Voiding Volume	43%	182	5	p<0.001
Incontinence Episodes	45%	167	4	p=0.023
I-QoL	17%	122	3	p=0.033

Effectiveness of percutaneous posterior tibial nerve stimulation for overactive bladder: A systematic review and meta-analysis

Burton C., et al. (2012). Neuro Urodyn, 31, 1206-16.

Study Design & Patient Selection:

- Systematic literature search of relevant key words for studies through April 2011
- 16 studies selected for inclusion
  - 4 randomized, controlled trials compared to Sham
  - 2 randomized, controlled trials compared to antimuscarinics
  - 10 prospective non-randomized studies
- Total patients = 940 (701 female, 239 male)

Outcomes:

- Pooled subjective success rate of 61.4% (95% CI 53-72%)
- Pooled objective success rate of 60.6% (95% CI 84-75%)
- Statistically superior to Sham [RR 7.02 CI 1.69 – 29.17]
- No significant differences in the change in bladder diary parameters compared to antimuscarinics; PTNS associated with a better side-effect profile

COST-EFFECTIVENESS

Cost of neuromodulation therapies for overactive bladder: Percutaneous tibial nerve stimulation versus sacral nerve stimulation

Martinson, M., et al. (2013). J Urol, 189(1), 210-6.

Study Design & Patient Selection:

- Markov model constructed to simulate 2-year cost and effectiveness of PTNS and sacral nerve stimulation (SNS)
- Cost based on average U.S. Medicare national physician payments and ambulatory payment classification and diagnosis related group payments
- Effectiveness based on a review of clinical literature

Outcomes:

- Initial costs: $1,773 for 12 PTNS treatments vs. $1,857 for test SNS and $22,970 for the implant
- 2-year costs for patients remaining on therapy: $4,867 for PTNS vs. $24,342 for SNS
- 71% PTNS and 90% SNS continued for 2 years with ICER of $99,872
- 1% more continue SNS but average cost per additional patient is >$500,000

About PTNS Treatment: The Urgent® PC Neuromodulation System, from Cogentix Medical, provides percutaneous tibial nerve stimulation (PTNS) for the treatment of overactive bladder and associated symptoms of urinary urgency, urinary frequency and urge incontinence. The device technology and treatment protocol are founded on the SANS device (Stoller's Afferent Nerve Stimulator).

USA:
5420 Feltl Road
Minnetonka, MN 55343

Tel.: 866 258 2182
Fax: 866 255 4522

LABORIE

www.laborie.com

20100G 07/18