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# Neuromodulation in Management of Overactive Bladder

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## 1. Introduction

Symptoms of urgency and frequency, with or without incontinence, are collectively referred to as overactive bladder (OAB), that is particularly bothersome and worsens quality of life (QOL) (Cardozo et al., 2005). Patients' QOL is substantially impacted by OAB as social, psychological, occupational, domestic, physical, and sexual functioning are all affected (Abrams et al., 2000). Pharmacotherapy (anticholinergics) is the main treatment options in OAB. However, uncertainty still exists as to whether the effects of anticholinergics are worthwhile and which ones and which is the best route of administration. Neuromodulation is one of the non-drug alternatives of OAB managements like bladder training, pelvic floor muscle training (PFMT), and a combination of bladder training with biofeedback (Bergmans et al., 2005). Neuromodulation involves the use of either implanted or external electrodes to stimulate reflex inhibition of pelvic efferents or activation of hypogastric efferents to down regulate detrusor muscle activity (Alhasso et al., 2006). But, neuromodulation has not been widely accepted as first-line therapy because of few physiological and evidence based data. Patients with OAB are commonly treated using anticholinergics despite many adverse events (mainly dry mouth and constipation) (Abrams et al., 2006), possible poor medication adherence, and insufficient treatment satisfaction.

I review the current reports regarding neuromodulation and evaluate its efficacy and management mainly focused on interferential therapy (IF) in the treatment of OAB with and without urinary incontinence (wet & dry OAB).

## 2. Interferential therapy

### 2.1 History

IF utilizing effects of low frequency electrical stimulation was first conducted on the lower urinary tract in the treatment of urinary incontinence or urinary frequency, resulted in a clinical improvement (McQuire, 1975). The utility of this therapy for conditions such as urinary frequency, urge incontinence (UUI) and stress incontinence (SUI) was subsequently reported by several researchers (Dougall, 1985; Laycock and Green, 1988; Switzer and Hendriks, 1988). Yasuda reported the efficacy of IF over sham stimulation in double-blind cross over trial in Japanese patients regarding frequency, urgency and urinary incontinence

(UI) and revealed clinical efficacy of IF for neurogenic detrusor overactivity, idiopathic OAB and psychogenic pollakisuria (Yasuda et al., 1994). Suzuki reported the long term efficacy of IF with a mean follow-up of 6.7 months in 16 patients, with improvement rate 71.4% (Suzuki et al., 1994). Oh-oka reported clinical safety and efficacy of IF in the elderly wet OAB patients followed by treatment failure of anticholinergics (Oh-oka, 2008).

## 2.2 Basic principles/mechanisms

IF assumes the interference of two medium frequency currents producing a low frequency effect equal to the difference between the two currents around 4000Hz, that are applied to the body from different directions using four surface electrodes placed in the lower abdomen and lower buttocks, after that an interferential wave can be generated by the crossing of these two currents in the pelvic organs (bladder and pelvic floor). The mechanism for the treatment of OAB, including UUI, has been reported to include, 1) inhibition of efferent activities of the pelvic nerve through the somatosensory nerve stimulation in the pudendal region (action on the micturition center in the brainstem and the spinal cord) (Kimura et al., 1994; Sato et al., 1992), 2) increasing the pelvic blood flow (Nikolova, 1984), and 3) improving the urine storage function of the bladder and urinary tract through the sympathetic nerve (hypogastric nerve) (Kaeckenbeeck, 1983). Of these, mechanism 1) appears to be most essential.

## 2.3 Clinical efficacy

A 20-minute treatment session was conducted twice a week for the first 3 weeks, and once every two weeks thereafter in Japan. Ease of usage and external application without giving harm to the superficial tissues are the main advantages of IF. The current and the intensity is well tolerated by the patients (Laycock and Green, 1988). Appropriate treatment frequencies of IF in patients with wet & dry OAB are generally 5 to 20Hz for reflex detrusor inhibition, but low frequencies such as 5 Hz may cause irritation (Yamanishi & Yasuda, 1988; Goode et al., 2003), which can be resolved by reducing electric current. In patients with stress incontinence (SUI), frequencies ranging 20 to 50 Hz have been reported to be effective for urethra and pelvic floor (Yamanishi & Yasuda, 1988; Aukee et al., 2002). The frequency and period of stimulation vary according to investigators, from twice daily to once weekly, for 15 to 30 min. each, and from a month to 6 weeks, or 3-5 months (Yamanishi et al., 1997; Sand et al., 1995; Yamanishi et al., 2008). The optimal number of sessions required is still unknown, at least 10 treatments are recommended before the evaluation of clinical efficacy (Sand et al., 1995), and a session of 4-6 weeks is conventionally employed (Yamanishi et al., 1997; Li et al., 1992). For about the intensity of stimulation, the maximal tolerable intensity is usually employed (Yamanishi et al., 1997; Sand et al., 1995; Plevnik and Janez, 1979).

Yasuda et al. reported clinical efficacy of IF for patients with neurogenic detrusor overactivity (DO), idiopathic OAB and psychogenic pollakisuria. Subjective variables (patients' impression > good, improvement in urgency) and objective variables (improvement in pollakisuria, incontinence, 1-hr. pad test, overall improvement) had all improved significantly over sham stimulation. Furthermore, improvement was statistically significant in patients with neurogenic bladder (n=32, p<0.01) and urodynamic SUI (n=17, p<0.01) (Yasuda et al., 1994). Suzuki et al. reported clinical efficacy of IF with mean follow-

up of  $6.7 \pm 3.9$  months in 16 patients with neurogenic DO, idiopathic OAB and psychogenic pollakisuria. Clinical efficacy of subjective variables (categorical scale of urinary frequency, urgency, patients' impression > good and overall improvement) were 46.7%, 53.3%, 81.3% and 71.4%, respectively. As for objective variables (urinary frequency, categorical scale of urinary incontinence (UI) frequency, incontinence volume) were 46.2%, 70.0% and 70.0%, respectively (Suzuki et al, 1994). Oh-oka reported the clinical efficacy of IF in 80 elderly non-neurogenic (idiopathic) OAB patients (69-78, median age 72.0) with UUI prospectively, for whom anticholinergics (propiverine hydrochloride) were not effective, who were provided with IF alone for three months (Table 1). In this paper he commented not only QOL score, but changes in lifestyle and plasma osmotic pressure (OP), brain natriuretic peptide (BNP). The average hours spent outdoors in one day, the one-day average radius of action increased, and the ADL scale score decreased; all these improvements were significant. Interviews from patients showed that all patients experienced increases in their amount of outdoor activities, time spent for shopping and hobbies, and time spent with their friends and close relatives. Also, OP increased significantly while BNP decreased significantly. These data indicate even in the absence of clinically evident cardiac disorders, OP and BNP levels can be high and that such levels are lowered in a relatively short period of time. IF can improve clinical symptoms of 'wet OAB' with relatively rapidly and thereby can improve ADL levels, implying a reduced load on left ventricular function. These features suggest that IF is a favorable treatment for the elderly, and for more than 1 year continuation of all 80 patients at their own request revealed satisfactorily compliance of IF (Oh-oka, 2008).

		baseline (pre IF)	post IF	p value
<i>frequency of IF treatment required to show optimal effects</i>	eight treatments (median)			
<i>average weekly frequency of incontinence (times/week)</i>		13.3 ± 5.2	3.6 ± 3.5	< 0.0001
<i>60-min. pad test (gr.)</i>		17.5 ± 2.1	3.1 ± 2.1	< 0.0001
<i>daytime voiding episodes (times)</i>		8.3 ± 2.4	7.0 ± 1.8	< 0.0001
<i>nighttime voiding episodes (times)</i>		1.8 ± 1.0	1.4 ± 1.0	0.0004
<i>daytime voided volume (mL)</i>		1199 ± 230	1220 ± 320	NS
<i>nighttime voided volume (mL)</i>		514 ± 185	464 ± 157	NS
<i>IPSS</i>		12.1 ± 5.3	6.3 ± 3.3	< 0.0001
<i>QOL index</i>		5.2 ± 0.8	2.4 ± 1.1	< 0.0001
<i>Uroflowmetry variable</i>				
<i>voided vol. (mL)</i>		170.2 ± 84.8	254.2 ± 60.6	< 0.0001
<i>maximum flow rate (mL/sec.)</i>		18.1 ± 6.8	25.7 ± 6.6	< 0.0001
<i>average flow rate (mL/sec.)</i>		8.9 ± 4.1	12.1 ± 3.5	< 0.0001
<i>postvoid residual urine volume (mL)</i>		17.5 ± 24.0	14.5 ± 23.1	NS
<i>specific gravity of urine</i>		1.019 ± 0.007	1.016 ± 0.006	NS
<i>The average hours spent outdoors in one day (hours)</i>		1.5 ± 1.3	3.0 ± 1.4	< 0.0001
<i>the one-day average radius of action (meters)</i>		400 ± 300	1200 ± 500	< 0.0001
<i>ADL scale score</i>		8.0 ± 1.2	3.4 ± 1.5	< 0.0001
<i>Plasma osmotic pressure (mOsm/L)</i>		295.1 ± 7.8	297.8 ± 3.6	< 0.0001
<i>brain natriuretic peptide (pg/mL)</i>		41.3 ± 38.7	19.2 ± 11.1	< 0.0001
IF; interferential therapy, IPSS; International Prostate Symptom Score, QOL; Quality of Life, ADL; Activities of Daily Living, NS; not significant				
This data was modified from prior published work (Oh-oka, 2008, 2010)				

Table 1. Anticholinergic resistant elderly wet OAB patients after 12 weeks of IF

Before and after IF, the follows were examined. 1) frequency of IF treatment required to show optimal effects, 2) average weekly episodes of incontinence, 3) 60-min. pad test, 4) episodes and voided volume in the daytime and nighttime, 5) fluid intake volume, 6) International Prostate Symptom Score (IPSS), QOL index, 7) Uroflowmetry, 8) postvoid residual urine volume (PVR), 9) specific gravity of urine, 10) average hours spent outdoors, 11) average radius of action and activities of daily life score, 12) standing blood pressure (BP) and heart rate, 13) clinical laboratory findings, 14) adverse events, 15) plasma osmotic pressure (OP), and 16) Brain natriuretic peptide. And the patients showed improvements for eight treatments (median). Improvement was observed in the followings; 2), 3), 4) voiding frequency, 6), 7) voided volume, maximal and average flow rate, 10), 11), 12) BP, 15) OP, and 16).

Demirtürk F et al. reported comparison to the effects of interferential current (0-100 Hz, 15 min., 3 times/week) and biofeedback applications (Kegel exercise, 15 min., 3 times/day) on incontinence severity in patients with 40 USI women and resulted both treatment modalities seemed to have similar effects on pad test (95% CI: -1.48 - 4.59), pelvic muscle strength (95% CI: -9.29 -1.78) and quality of life (95% CI: -11.91 - 5.31) outcomes (Demirtürk et al., 2008).

## 2.4 Challenges/future prospects

Currently, only interferential therapy using the Uromaster® is approved for use in the treatment of OAB and UI in Japan. IF reports regarding clinical efficacy or basic research in OAB are very few, and good, randomized, placebo controlled studies have rarely performed. Applying uniformly set treatment modalities (treatment parameters and schedules), long term data on the clinical outcome, also concerning the patients' characteristics (definition and duration of symptoms, previous treatment) is very important and urgently necessary (van Balken et al., 2004). Also combination effect with PFMT or anticholinergics should be further analyzed strictly to manage OAB for the future. On the other hand, advantages of IF include; the absence of complications such as increased episodes and (nighttime) voided volume resulting from more water intake to counter dry mouth, which is an bothersome adverse event observed with the use of anticholinergics including propiverine hydrochloride; and satisfactory compliance that can be achieved in patients who are not indicated for oral treatment or are incapable of oral ingestion. IF is suitable for short-term electrical stimulation for home use (portable IF devices are available, that are unauthorized for medical equipment in Japan).

## 3. Pelvic floor electrical stimulation

### 3.1 History

Caldwell reported the successful implantation of an anal sphincter stimulator for fecal incontinence, which proved to be effective for urinary incontinence (Caldwell, 1963). Anal plug electrodes were subsequently modified. Later Fall et al. provided reports regarding transvaginal electrical stimulation with urinary incontinence and interstitial cystitis (Fall et al., 1977, 1980, 1984).

### 3.2 Basic principles/mechanisms

Vaginal, anal, and surface electrodes are used for pelvic floor electrical stimulation. Vaginal electrode is popular for women, and anal electrode is usually used for men. The mechanism

of these techniques was detrusor relaxation induced by afferent pathways including activation of hypogastric inhibitory neurons, inhibition of pelvic excitatory neurons with pudendal nerves (Lindström, 1983).

### 3.3 Clinical efficacy

Because of poor tolerability due to pain or discomfort of intravaginal and anal plug electrodes, surface electrical stimulation of dorsal nerve of penis or clitoris (transcutaneous electrical stimulation [TENS]) has been often adopted as low invasive modality for DO. The alternative TENS treatments was thought S2 or S3 dermatome, which might improve clinical outcome (Walsh et al, 1999). Comparison of neuromodulation to sham TENS, no TENS, other TENS including suprapubic or tibial nerve TENS, and medical treatment including anticholinergics is important. These studies resulted in a positive effect on detrusor instability (DI), an improvement in the first desire to void and increased bladder capacity on urodynamics. Some DI patients become stable, while in others the volume at first contraction improved significantly. For permanently decreasing incontinence TENS alone might be insufficient. Superiority of clinical efficacy between oxybutynin and electrical stimulation (intravaginal or TENS) in controversial (Soomro et al, 2001; Wang et al, 2006), but the prevalence of electrical stimulation devices might not enough (Walsh et al, 1999). Arruda RM et al. reported the effectiveness of oxybutynin, functional electrostimulation (transvaginal) and pelvic floor training for treatment of 64 women with DO after completion of 12 weeks of treatment and resulted all three treatments were equally effective for improvement rate of subjective symptoms, urgency and urodynamic cure (Arruda et al., 2008).

### 3.4 Challenges/future prospects

Intravaginal and anal plug are sometimes intolerable for many patients due to discomfort, mucosal injury (Yamanishi et al., 1997; Yamanishi & Yasuda, 1998) and high intensity stimulation for acceptable outcome, surface electrodes like TENS have been employed as less invasive treatment for OAB.

## 4. Electrical tibial nerve stimulation of the lower limb

### 4.1 History

During experimental studies in nonhuman primates with spinal cord injury to improve bipolar anal sphincter Stimulation, McGuire et al. found that detrusor activity inhibition was equally achieved by applying a positive current to the anal sphincter with a negative electrode placed over the posterior tibial nerve (McGuire et al., 1983). Similar results were obtained by applying current on the common peroneal or posterior tibial nerve and a ground electrode placed over the same nerves contralaterally. The idea of stimulating tibial nerve was based on the traditional Chinese practice of using acupuncture points to inhibit bladder activity (McGuire et al., 1983). Transcutaneous posterior tibial nerve stimulation was then evaluated in clinical trials with variable results.

### 4.2 Basic principles/mechanisms

Percutaneous tibial nerve stimulation (PTNS) delivers neuromodulation to the pelvic floor through the S2-4 junction of the sacral nerve plexus via the less invasive route of the

posterior tibial nerve. Using the fine needle electrode insertion above the ankle, the tibial nerve is accessed. This area has projections to the sacral nerve plexus, creating a feedback-loop that modulates bladder innervation (Kohli & Rosenblatt, 2002).

### **4.3 Clinical efficacy**

Govier et al. reported a safety and efficacy of PTNS for refractive OAB and/or pelvic floor dysfunction (Govier et al., 2001). Klingler et al. demonstrated reduction in pain and urodynamic improvement of DI, total bladder capacity, first bladder sensation, bladder volume at normal desire to void, and urinary frequency (Klingler et al., 2000). Peters et al. demonstrated the objective effectiveness of PTNS in OAB symptoms compared to extended-release tolterodine (Peters et al., 2009). PTNS is also effective for disease related DO (DO in multiple sclerosis, Parkinson's disease).

### **4.4 Challenges/future prospects**

PTNS is less invasive, easily applicable, and well tolerated in all lower urinary tract conditions. Poor improvements in urodynamic studies, like other neuromodulation therapies, might be the main disadvantage, and it seems doubtful regarding the stable efficacy of chronic (over 10 to 12 weeks) treatment (van Balken et al., 2004). As in sacral root neuromodulation, PTNS seems less effective for improving chronic pelvic pain (van Balken et al., 2003).

## **5. Sacral nerve stimulation**

### **5.1 History**

In 1981 a group at the urological department at the University of California-San Francisco started a clinical program to evaluate the efficacy of sacral root electrode implantation in humans, leading to the humans (Tanagho & Schmidt, 1988; Schmidt, 1986). Since then, many reports regarding sacral nerve stimulation have been published as the technique has gained popularity.

### **5.2 Basic principles/mechanisms**

SNS involves continuous electrical stimulation of the sacral nerves to inhibit or activate the neural reflexes that influence the bladder, urethral sphincter, and pelvic floor (Shaker & Hassouna, 1988; van Kerrebroek et al., 2007; Oerlemans & van Kerrebroek, 2008). Thus, SNS has been indicated for various types of lower urinary tract dysfunction refractory to conservative treatment, such as wet & dry OAB, pelvic pain syndrome and urinary retention (UR) (Oerlemans & van Kerrebroek, 2008; Shaker & Hassouna, 1998). In patients with OAB, SNS would restore the balance between inhibitory and excitatory control systems at various sites in the peripheral and central nervous system. This would involve activation of somatosensory bladder afferents projecting into the pontine micturition center, and/or activation of the hypogastric sympathetic nerves (van der Pal et al., 2006). Also, Blok et al. reported changes in regional cerebral blood flow, using positron emission tomography, during chronic and acute sacral neuromodulation. They suggest chronic SNS influences,

presumably via the spinal cord, brain areas previously implicated in detrusor hyperactivity, awareness of bladder filling, the urge to void and the timing of micturition (Blok et al., 2006). Furthermore, SNS affects areas involved in alertness and awareness.

### 5.3 Clinical efficacy

A percutaneous nerve stimulation (PNE) of the S3 roots for 1-4 weeks is used to select responders of neuromodulation, and patients who are eligible for permanent implantation shift to a chronic stimulation system (Chartier-Kastler, 2008). To prolong test period safely (reduce the risk of infection and surgical invasiveness) and to avoid false-negative results due to lead migration, PNE with the permanent tined lead under local anesthesia is also available (Spinelli et al., 2005). Schmidt et al. reported success rate of 63% (test stimulation) in 155 patients with refractory UUI. Sustained clinical benefit was reported at 18 months after implantation (Schmidt et al., 1999). Jonas et al. reported efficacy with refractory idiopathic UR who are refractory to other treatments. Success rate of SNS was 83%, including 69% who stopped using catheters at 6 months after implantation (Jonas et al., 2001). Shaker and Hassouna reported a marked reduction in leakage episodes from 6.49 to 1.98 times per 24 hours, and eight of 18 patients became completely dry after an average follow-up was 18.8 months (Shaker & Hassouna, 1988). Sutherland et al. reported their one institution's 11-year experience with SNS in 104 patients including dry, wet OAB and mixed incontinence. With a mean follow up of 22 months (range 3-162 months), sustained subjective improvement was >50%, >80%, and >90% in 69%, 50%, and 35% of patients, respectively. By QOL survey, 60.5% of patients were satisfied with current urinary symptoms (Sutherland et al., 2007).

To shorten operation time and decrease pain complaints at the stimulator site buttock placement was advocated. The unilateral SNS might result in malposition of the electrode or local fibrosis. Hohenfellner et al. recommended clinical efficacy of bilateral SNS than unilateral SNS (Hohenfellner et al., 1998). Aboseif et al. reported the efficacy and QOL improvement of SNS in patients with idiopathic, chronic, non-obstructive functional UR. Permanent implants were performed 20 patients who revealed more than 50% improvement in symptoms during the PNE test. Eighteen patients were subsequently able to void and no longer required intermittent catheterization. Average voided volumes increased from 48 to 198 ml and PVR reduced from 315 to 60 ml. Eighteen patients reported more than a 50% improvement in QOL (Aboseif et al., 2002). New approaches of bilateral caudal neuromodulation might yield excellent outcome in patients with urinary retention refractory to traditional, unilateral S3 stimulation (Maher et al., 2007).

### 5.4 Challenges/future prospects

Sacral nerve stimulation (SNS) is an established treatment for OAB. Adverse events related to SNS can be the physical presence of the device or adverse stimulation. Van Kerrebroek et al. reported adverse events seemed to occur in 102 patients (67%) at 5-year follow-up, and the most frequent events being new pain or undesirable change of stimulation (27%) (van Kerrebroek et al., 2007). Adverse stimulation does not necessarily require surgical intervention. It is often resolved by changing stimulation factors (pulse width, amplitude,

mode of polarity etc.). Pain in implant site or scar pain could be adequately treated by antimicrobial agents, while device pain might require relocation of the device components. Hijaz et al. reported 10.5% of patients were explanted due to loss of efficacy or infection. In 16.1% of the patients, adverse events (implant site discomfort in 2.5%, lead migration in 0.6% and infection in 2.5%) or decreased efficacy (10.5%) could be managed successfully (Hijaz et al., 2006).

## **6. Magnetic stimulation**

### **6.1 History**

Magnetic stimulation has been used for experimental and clinical testing on the central and peripheral nervous systems (Barker et al., 1987). Compared to electrical stimulation, magnetic stimulation is useful to stimulate deep proximal nerves with little pain due to magnetic penetration of all body tissues without alteration. Also patients are not necessary to take off clothes during treatment because the magnetic field passes through clothes.

### **6.2 Basic principles/mechanisms**

A varying magnetic field will induce an electrical field in any specified loop in its vicinity. The roots of sacral nerves S2-S4 provide the primary autonomic and somatic innervations of the urinary tract, including pelvic floor, urethra, bladder and other pelvic organs, and stimulation of these roots is an efficient way to modulate the pelvic floor and control functions of pelvic organs (Shafik, 2000). Magnetic stimulation can be applied both at the sacral root (Sheriff et al., 1996; Fujishiro et al., 2002) and the peri-anal region (Yamanishi et al., 2000; Galloway et al., 1999). However, the commercially available stimulator is usually a chair type and stimulates the peri-anal region including pelvic floor muscles because of difficulty to fix the coil to the sacral root for a long time.

### **6.3 Clinical efficacy**

Reductions in the frequency of leakage and urodynamic improvement of maximum bladder capacity in UUI and increase in maximum urethral closing pressure in USI by continuous magnetic stimulation have been reported (Yamanishi et al, 2000a, 2000b). Unsal et al. reported the clinical efficacy of extracorporeal magnetic stimulation for the treatment of SUI and UUI in women (Unsal et al., 2003). Fujishiro et al. reported an investigational study and placebo controlled trial to evaluate the potential efficacy of magnetic stimulation of the sacral roots for the treatment of stress incontinence. They concluded significant efficacy for the treatment of UUI and SUI (Fujishiro et al., 2000 & 2002). Yamanishi et al reported a randomized comparative study investigating the urodynamic effects of functional magnetic stimulation (FMS) and functional electrical stimulation (FES) on the inhibition of detrusor overactivity, and concluded that both treatments were effective in the increase of first desire to void and maximum cystometric capacity. But the increase in the maximum cystometric capacity was significantly greater in FMS than FES group, also the inhibition of detrusor overactivity appeared greater in FMS than FES group (Yamanishi et al, 2000). Suzuki et al. reported the effect of functional continuous magnetic stimulation (FCMS) on urgency incontinence using a randomized, sham-controlled, crossover evaluation in 39 UUI patients.

They concluded magnetic stimulation was effective on UUI in comparison to sham stimulation (Suzuki et al, 2007). However, Culligan et al. reported no differences in pelvic muscle strength between patients receiving active or sham extracorporeal magnetic innervation treatments (ExMI) in the early postpartum period (Culligan et al., 2005). Voorham-van der Zalm et al. reported the clinical results of extracorporeal magnetic innervation therapy (ExMI) of the pelvic floor muscles with functional changes in the pelvic floor musculature, urodynamics and quality of life, and concluded ExMI did not change pelvic floor function (Voorham-van der Zalm et al., 2006). There are varying outcomes of several studies on ExMI stress the need for critical studies on the effect and the mode of action of electrostimulation and magnetic stimulation.

#### **6.4 Challenges/future prospects**

This type of stimulation cannot be applied for prolonged periods and unsuitable for long-term treatment, although it may be helpful for preliminary assessment of candidates for chronic sacral root neuromodulation. It is unclear if the exact mechanism of action is magnetic, nerve root, peripheral nerve, or intramural nerve stimulation. No prospective randomized studies to date have been performed to demonstrate this therapy's use in larger groups regarding UUI or USI.

### **7. Conclusions**

Although the use of electrical stimulation and neuromodulation to treat patients with OAB has been widely investigated, in many reports important information is not enough and good randomized, placebo controlled studies are rare. The advent of various techniques of neuromodulation causes paradigm shift of treatment strategies of patients with OAB and other lower urinary tract dysfunction. We should compare various techniques and evaluate placebo effects overcoming unsolved aspects of the current treatment including neuromodulation. And our better approaches based on further understanding of voiding function and action mechanism of neuromodulatory techniques might lead more various types of patients with urinary tract dysfunction to more satisfactorily clinical outcomes. In consideration of these problems, I personally expect potential clinical efficacy of IF as short-term electrical stimulation, that has few adverse event, and improving not only QOL but ADL.

### **8. Acknowledgements**

I thank Tomonori Yamanishi from the department of Urology of Dokkyo University School of Medicine for valuable advices on this paper.

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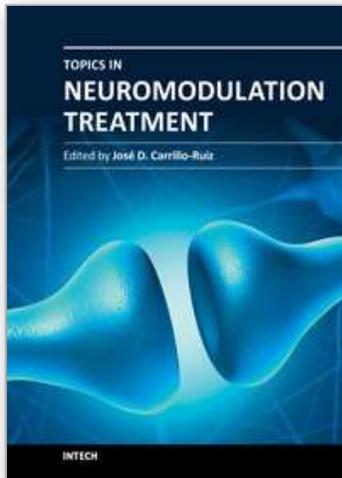
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### **Topics in Neuromodulation Treatment**

Edited by Dr. José Carrillo-Ruiz

ISBN 978-953-51-0395-0

Hard cover, 190 pages

**Publisher** InTech

**Published online** 23, March, 2012

**Published in print edition** March, 2012

"Topics in Neuromodulation Treatment" is a book that invites to the reader to make an update in this important and well-defined area involved in the Neuroscience world. The book pays attention in some aspects of the electrical therapy and also in the drug delivery management of several neurological illnesses including the classic ones like epilepsy, Parkinson's disease, pain, and other indications more recently incorporated to this important tool like bladder incontinency, heart ischemia and stroke. The manuscript is dedicated not only to the expert, but also to the scientist that begins in this amazing field. The authors are physicians of different specialties and they guarantee the clinical expertise to provide to the reader the best guide to treat the patient.

#### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Hitoshi Oh-Oka (2012). Neuromodulation in Management of Overactive Bladder, Topics in Neuromodulation Treatment, Dr. José Carrillo-Ruiz (Ed.), ISBN: 978-953-51-0395-0, InTech, Available from:  
<http://www.intechopen.com/books/topics-in-neuromodulation-treatment/neuromodulation-in-management-of-overactive-bladder>

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