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# Treatment of neurogenic detrusor overactivity in spinal cord injured patients by conditional electrical stimulation

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## ABSTRACT

**Purpose:** The feasibility of automatic event driven electrical stimulation of the dorsal penile/clitoral nerve in treatment of neurogenic detrusor overactivity (NDO) was evaluated in individuals with spinal cord injury (SCI).

**Materials and Methods:** The study included 2 women and 14 men with NDO, bladder capacities below 500 ml, age over 18 years and complete or incomplete suprasacral SCI. Detrusor pressure ( $P_{det}$ ) was recorded during an ordinary natural bladder filling. In a similar subsequent recording  $P_{det}$  was used to trigger electrical stimulation when the pressure exceeded 10 cmH<sub>2</sub>O.

**Results:** Of the 16 patients enrolled in this study 13 had an increased bladder capacity together with a storage pressure decrease as a result of automatic event driven electrical stimulation. In two patients the stimulation could not inhibit the first undesired contraction and leakage occurred and finally one patient could not tolerate the stimulation. During the stimulated filling  $P_{det}$  never exceeded 55 cmH<sub>2</sub>O and the storage pressure is thus sufficiently low to prevent kidney damage. An average bladder capacity increase of 53% was obtained.

**Conclusions:** This study demonstrates the feasibility of automatic event driven electrical stimulation in the treatment of NDO. Although the setup in this experiment is not suitable in a clinical setting, the treatment modality is promising and it warrants further investigation.

**KEY WORDS:** spinal cord injuries, electric stimulation, neurogenic bladder

## Introduction

Neurogenic bladder dysfunction after spinal cord injury (SCI) is a major medical and social problem for which there is no ideal treatment. After suprasacral SCI cortical control over the sacral reflex voiding center is impaired and in the majority of patients neurogenic detrusor overactivity (NDO) and/or detrusor-sphincter dyssynergia (DSD) emerges [1,2]. Detrusor overactivity is a urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked, while DSD is defined as a detrusor contraction concurrent with involuntary contraction of the urethral and/or periurethral striated muscle [3]. Patients with SCI who have NDO and/or DSD often have transient high intravesical pressures, low bladder capacity and incontinence. Recurrent urinary tract infections and vesicoureteral reflux may lead to upper tract damage. Therefore, the primary goal of NDO management is to reestablish low pressure storage and prevent recurrent bladder infections to preserve renal function. A secondary goal is to increase storage capacity.

First line treatment for NDO is the oral administration of anticholinergic drugs, such as oxybutynin and tolterodine. This treatment is often combined with clean intermittent self-catheterization to empty the bladder and decrease residual urine. However, many patients are refractory to the medication or have dose limiting side effects. Alternative therapies are used when conservative methods fail. These therapies include the oral administration of  $\alpha$ -adrenoceptor antagonists [4], intravesical installation of capsaicin or resiniferatoxin [5], injection of botulinum toxin in the detrusor muscle [6], bladder augmentation cystoplasty [7] and detrusor deafferentation [8]. An option that does not require ablative and irreversible surgery is electrical stimulation. This approach depends on a physiological process known as neuromodulation, in which activity in 1 neural pathway modulates activity in another through synaptic interaction [9]. It has been shown that electrical stimulation of pudendal nerve afferents can inhibit bladder contractions in patients with SCI and bladder capacity can be increased by continuous [10] as well as conditional stimulation [11, 12].

Implants such as the InterStim® system have made this treatment modality commercially available. Common to these implantable systems is that they use continuous stimulation. Detrusor inhibition is in principal only necessary during an involuntary contraction and, thus, stimulation could be turned off between contractions. Such a stimulation scheme could have a number of advantages. Power consumption may be decreased and, thus, extend battery lifetime. Furthermore, continuous stimulation of a reflex may lead to habituation, which would be minimized or prevented by conditional stimulation. In this study we examined the effect of the automatic, event driven electrical stimulation of pudendal nerve afferents on bladder capacity in patients with SCI.

## Materials and Methods

Methods, definitions and units conform to the standards recommended by the International Continence Society except where specifically noted. The study was approved by the local ethics committee and informed consent was obtained from all patients. A total of 16 patients with SCI were included (table 1). Inclusion criteria were NDO with bladder capacity less than 500 ml, age greater than 18 years and complete or incomplete suprasacral SCI. Participants were not asked to change bladder management prior to participating in this study, for example medication use. Stimulation was performed with a custom-made, battery driven stimulator using pairs of round, self-adhesive, platinum PALS® surface electrodes 3.2 cm in diameter placed on the base of the penis or on the clitoris. The parameters were 20 pulses per second and pulse width 200  $\mu$ seconds. Stimulation amplitude was gradually increased until the bulbocavernosus reflex (BCR) was elicited. This was determined by observation or palpation of an anal sphincter contraction. During event driven stimulation an amplitude of  $2 \times \text{BCR}$  was used. This amplitude was chosen based on the study of Previnaire et al. [14]. They reported the relationship between detrusor inhibition and current amplitude when stimulating the dorsal penile/clitoral nerve via surface electrodes. Other studies evaluating conditional stimulation also used the same amplitude [11, 12]. Natural bladder filling was used to avoid artifacts caused by artificial high filling rates and patients were encouraged to drink. Vesical pressure ( $P_{\text{ves}}$ ) and abdominal pressure ( $P_{\text{abd}}$ ) were measured using an 8Fr water filled catheter and a 9Fr water filled rectal balloon catheter, respectively. The catheters were connected via external pressure transducers to a custom-made portable device [15]. Electrical stimulation was automatically applied based on calculated detrusor pressure ( $P_{\text{det}}$ ) (fig. 1). Each patient underwent 2 filling sessions, that is 1) control filling and 2) filling with stimulation enabled. Stimulation was applied when  $P_{\text{det}}$  exceeded 10 cmH<sub>2</sub>O. It was stopped in certain cases, namely 1) automatically when  $P_{\text{det}}$  remained below 10 cmH<sub>2</sub>O for 10 seconds, 2) manually when leakage was

detected by visual inspection and 3) manually when stimulation time exceeded 2 minutes without a decrease in pressure. Additional control filling was performed in 7 patients. To evaluate the effect of penile/clitoral nerve stimulation 4 parameters were calculated/extracted per subject, including 1) average  $P_{det}$  peak pressure during contractions in control filling, 2) average  $P_{det}$  peak pressure during suppressed contractions in stimulated filling, 3) bladder volume at first contraction during stimulated filling, calculated on the assumption of constant urine production during bladder filling, and 4) bladder volume at the time of leakage in stimulated filling, measured as the volume leaked plus residual urine at the end of bladder filling (fig. 2).

Table 1. Patient characteristics	
No. men/women	14/2
Time since SCI	3 months – 36 years
SCI Level	C4/5 - L4/5
No. SCI Completeness:*	
Complete	8
Incomplete	6
No. Main bladder emptying	
Clean intermittent self-	13
Diaper	2
Suprapubic tapping	1
No. bladder management	11
*Completeness was classified according to the ASIA protocol <sup>13</sup>	

A change in peak storage pressure and a change in bladder capacity as a result of stimulation were calculated as the ratios, average  $P_{det}$  peak pressure during suppressed contractions in stimulated filling/average  $P_{det}$  peak pressure during contractions in control filling and 1 – bladder volume at first contraction during stimulated filling/bladder volume at the time of leakage in stimulated filling, respectively. To evaluate the efficacy of stimulation a certain success criterion was used, that is a good responder is a patient in whom electrical stimulation inhibited at least the first unstable detrusor contraction, thereby, preserving continence. The capacity increase was calculated based on the assumption that, had the patient not undergone stimulation, the first uninhibited detrusor contraction would have led to leakage. Consequently the time from the first inhibited contraction until leakage was regarded as the increase in filling time. Under the assumption of constant urine production during the time of stimulated filling the relative increase in filling time equaled the relative increase in capacity. The order of control and stimulated filling was not randomized since the bladder exceeds normal capacity during stimulated filling. Increased bladder wall stretch would more likely bias a subsequent control filling than the opposite order of fillings.

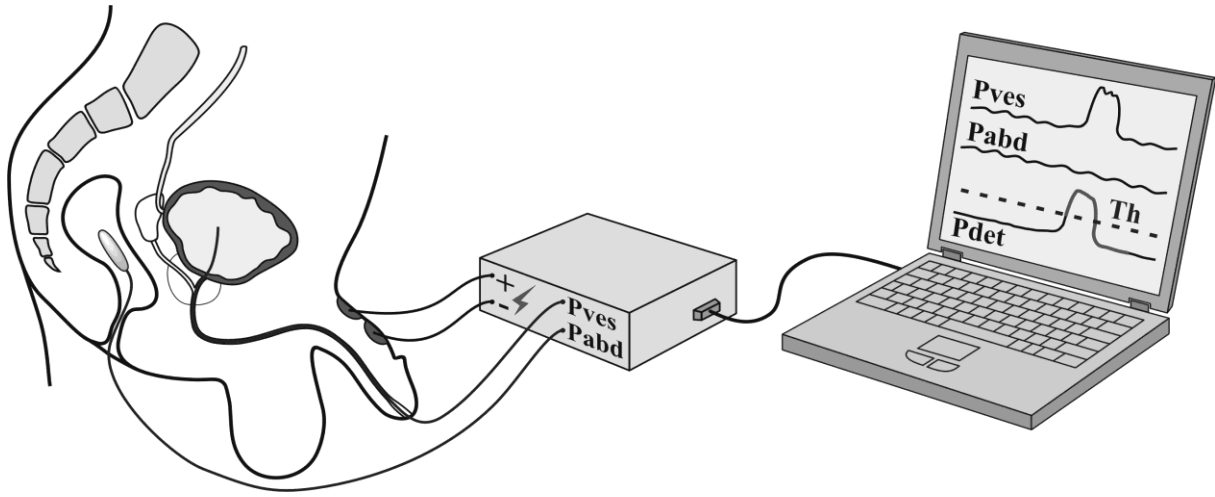


FIG. 1. Experimental setup for recording  $P_{ves}$  and  $P_{abd}$  with automatic, pressure activated stimulation control. Recording unit can be connected to personal computer for online monitoring of pressure lines and for setting threshold (Th).

## Results

Penile/clitoral nerve stimulation was well tolerated in 15 of the 16 patients. Of these 15 patients 13 fulfilled the success criterion of having at least 1 inhibited detrusor contraction. One patient had leakage, although stimulation decreased peak storage pressure by 65% compared with control filling, and 1 did not respond to stimulation. The 3 patients who did not meet the success criterion were excluded from the calculation of average values (table 2). Figure 2 shows recorded data on 1 patient. In control filling NDO occurred after 25 minutes of natural bladder filling, causing transient, high intravesical pressure with a peak of 89 cmH<sub>2</sub>O. Leakage (100 ml) occurred at this time with a subsequent residual volume of 90 ml. In stimulated filling NDO occurred after 54 minutes. Estimated bladder volume at this time was 348 ml (fig. 2). Stimulation with 60 mA was automatically applied as  $P_{det}$  exceeded the 10 cmH<sub>2</sub>O threshold and the effect of stimulation was a sudden decrease in pressure.  $P_{det}$  decreased to below the threshold 8 seconds after the onset of stimulation and it remained there more than 10 seconds, causing stimulation to stop automatically. During the next 21 minutes an additional 9 detrusor contractions occurred and the sequence of events described was repeated at each contraction. Eventually stimulation was unable to keep detrusor pressure below the threshold. After 2 minutes with constant high pressure stimulation was stopped manually. The result was an immediate leakage of 130 ml with a subsequent residual volume of 357 ml (fig. 2). Average peak storage pressure during the stimulation time was 28 cmH<sub>2</sub>O (fig. 2). Automatic, event driven stimulation in this patient resulted in a peak storage pressure decrease of 69%, concurrent with an extended filling time of 21 minutes. The later was equivalent to a relative increase in filling time of 40% and, therefore, also equivalent to a bladder capacity increase of 40%. Table 2 lists summarized data on all patients. Figure 3 shows individual as well as overall average peak storage pressures during contractions in control and stimulated fillings. Figure 4 shows individual as well as overall average bladder volumes at the time of the first contraction and at the time of leakage.

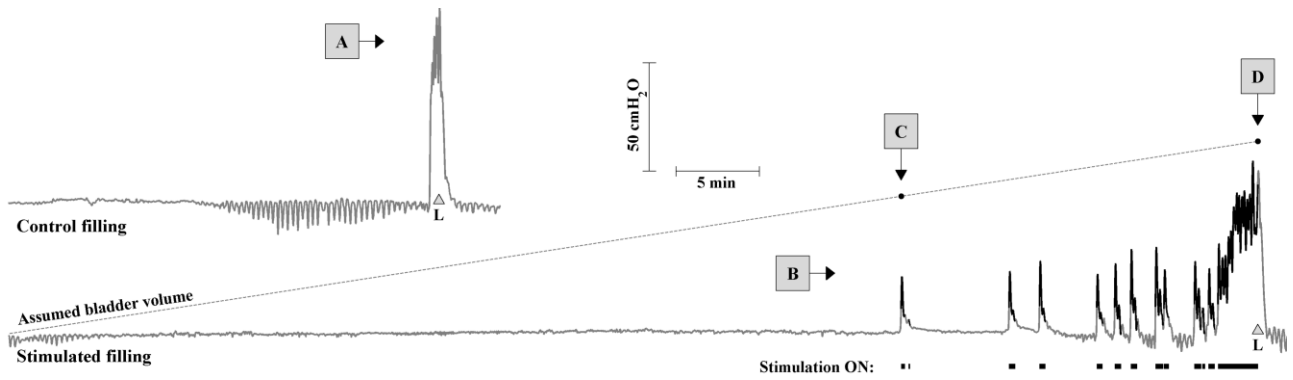


FIG. 2. Two fillings in 1 patient, recorded consecutively. Stimulation was turned on automatically when  $P_{det}$  exceeded 10  $cmH_2O$  and it had clear inhibitory effect on detrusor contraction. Stimulation was turned off automatically when  $P_{det}$  had remained under threshold for 10 seconds. At end of stimulated filling stimulation had been on more than 2 minutes without decrease in pressure and, thus, it was manually disabled. Result was immediate leakage (L). A, average  $P_{det}$  peak during control filling contractions. B, average  $P_{det}$  peak during stimulated filling suppressed contractions. C, bladder volume at stimulated filling first contraction. D, bladder volume at stimulated filling leakage.

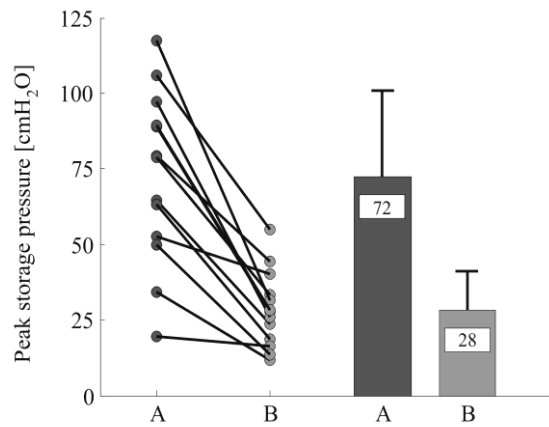


FIGURE 3: Average peak of  $P_{det}$  during contractions in the control filling (A) and during suppressed contractions in the stimulated filling (B). Circles indicate individual values, boxes are mean values and T-bars are standard deviation.

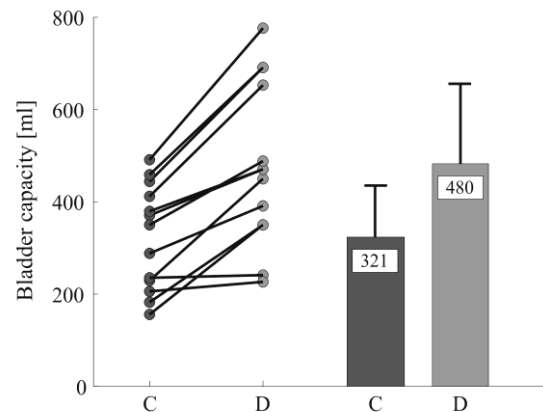


FIGURE 4: Bladder volume at 1<sup>st</sup> contraction (C) and at leakage (D) in the stimulated filling. Circles indicate individual values, boxes are mean values and T-bars are standard deviation.

Several patients with incomplete injuries reported that the sensation of electrical stimulation was different when received during a detrusor contraction compared with when the necessary stimulation intensity was initially examined. No patient experienced  $2 \times$  BCR intensity as being painful. However, 4 patients described stimulation as being slightly unpleasant. Interestingly the same patients reported that, while being stimulated during a detrusor contraction, the sensation of urge disappeared and they preferred the stimulation over the urge. An additional control filling was performed in 7 patients in our study. No apparent carryover effect of stimulation was observed since the prestimulated control was similar to the poststimulated control.

TABLE 2. Storage pressure, bladder capacity, filling time and stimulation parameters

	Mean $\pm$ SD
Stimulation amplitude ( $2 \times$ threshold to elicit BCR) (mA)	$53 \pm 11$
Av P <sub>det</sub> peak (cmH <sub>2</sub> O):	
During control filling contractions	$72 \pm 28$
During stimulated filling suppressed contractions	$28 \pm 13$
% Peak storage pressure decrease	$58 \pm 18$
Vol (ml):	
Estimated at first contraction	$321 \pm 114$
Measured at leakage	$480 \pm 176$
Bladder capacity increase:	
Absolute (ml)	$158 \pm 89$
% Relative	$53 \pm 36$
No. stimulated filling inhibited contractions	$16 \pm 17$
Time in stimulated filling (mins):	
First contraction	$41 \pm 23$
Leakage	$62 \pm 25$
% Stimulation on time/leakage time	$13.6 \pm 10.2$
Urine production rate (ml/min)	$8.7 \pm 4.2$
Values in 13 patients who fulfilled the success criteria of at least 1 inhibited detrusor contraction.	

## Discussion

This study demonstrates the feasibility of automatic, event driven electrical stimulation of the pudendal afferent nerves in the treatment of NDO in patients with SCI. Transient high intravesical pressures are decreased due to a stimulation induced detrusor inhibition, which together with possible reflex mediated sphincter activation also accounts for the increased bladder capacity. There is no consensus on the exact value at which intravesical pressure becomes dangerous to kidney function. However, 40 cmH<sub>2</sub>O is frequently used in the literature [16]. It is our goal to keep intravesical pressure below this safety level during the filling phase. Peak storage pressure in control filling was above the safety level in 11 of the 13 good responders. Stimulation brought peak storage pressure at or below the safety level in 8 of these 11 patients. Kirkham et al tested conditional electrical stimulation of pudendal afferent nerves with an artificial filling of 10 ml per minute and found an increase in bladder capacity of  $144\% \pm 127\%$  or  $230 \pm 143$  ml [12]. The relative increase was approximately 3 times higher than our results and the absolute increase was about 1.5 times higher but absolute capacity was 90 ml smaller. However, a direct comparison with our results is difficult since their patients were asked to discontinue any medication 4 days prior to participating. Dalmose et al described results similar to those of Kirkham et al [12] in a study of 10 patients with SCI, in whom conditional stimulation of pudendal afferent nerves was performed manually and an artificial filling rate of 60 ml per minute was used [11]. When using the calculation method of our study, Dalmose et al [11] noted a bladder capacity increase of  $167\% \pm 217\%$  or  $192 \pm 130$  ml. The relative and absolute increases were higher but again absolute capacity was smaller than in our study. These high relative and absolute capacity increases in the 2 studies were mostly due to initial small capacity in the patients. The average patient in the study of Kirkham et al [12] went from a bladder capacity of approximately 160 to 390 ml and in the study of Dalmose et al [11] from 157 to 349 ml. This should be compared with our average patient, who went from a bladder

capacity of 321 to 480 ml. The large initial capacity in our control was most likely due to the fact that the majority of patients in this study were on medication. A similar high initial capacity was reported by Læssøe et al when studying the effects of ejaculation by penile vibratory stimulation on bladder capacity in men with spinal cord lesions [17]. They found a significant increase in bladder capacity after 4 weeks of frequent treatment (ejaculation every third day). This method, which is therapeutic in nature, has also been tried with daily sessions of electrical stimulation of the penile/clitoral nerve but with variable success rates [18]. Mechanical and electrical stimulation may work through some of the same mechanisms but the relationship between short-term bladder inhibition and long lasting therapeutic modulation of bladder capacity is elusive. We observed no immediate carryover effect of electrical stimulation in the 7 patients who underwent an additional control filling. As mentioned, implants using continuous stimulation are commercially available. A 5-year followup study showed a 50% decrease in the number of good responders after 3 years of treatment [19]. This decrease might have been due to habituation of the involved reflexes. In our study stimulation was on for only 13.6% of the filling phase. Thus, the possible habituation effect is believed to have been decreased but further studies must verify this.

## **Conclusion**

The results of this study indicate that it is feasible to treat NDO by event driven electrical stimulation of the pudendal nerve. Peak storage pressure was brought down to what is believed to be a safe level and at the same time bladder capacity was increased. The risk of habituation was lowered since stimulation was only on during contractions. An extended filling time of  $20 \pm 13$  minutes was achieved, although patients were encouraged to drink. In ordinary life this period would likely be longer. With conditional stimulation patients can be warned at the time of the first contraction, which marks the onset of extended filling time. With a warning 20 minutes prior to leakage most patients would have sufficient time to find a toilet. Although the setup in this experiment is not suitable for the chronic setting, the treatment modality is promising. The timely decrease in the number of good responders among patients receiving continuous stimulation with an implant makes it relevant to investigate event driven stimulation. Steps are being taken to develop noncatheter based monitoring of bladder activity since this is needed to apply stimulation automatically in a chronic setting.

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## **REFERENCES**

1. Weld, K. J., Graney, M. J. and Dmochowski, R. R.: Clinical significance of detrusor sphincter dyssynergia type in patients with post-traumatic spinal cord injury. *Urology*, 56: 565, 2000
2. Weld, K. J. and Dmochowski, R. R.: Association of level of injury and bladder behavior in patients with post-traumatic spinal cord injury. *Urology*, 55: 490, 2000
3. Abrams, P., Cardozo, L., Fall, M., Griffiths, D., Rosier, P., Ulmsten, U., Van Kerrebroeck, P. et al: The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology*, 61: 37, 2003

4. Abrams, P., Amarenco, G., Bakke, A., Buczyński, A., Castro-Diaz, D., Harrison, S. et al: Tamsulosin: efficacy and safety in patients with neurogenic lower urinary tract dysfunction due to suprasacral spinal cord injury. *J Urol*, 170: 1242, 2003
5. Chancellor, M. B. and de Groat, W. C.: Intravesical capsaicin and resiniferatoxin therapy: spicing up the ways to treat the overactive bladder. *J Urol*, 162: 3, 1999
6. Schurch, B., Stöhrer, M., Kramer, G., Schmid, D. M., Gaul, G. and Hauri, D.: Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. *J Urol*, 164: 692, 2000
7. Quek, M. L. and Ginsberg, D. A.: Long-term urodynamics followup of bladder augmentation for neurogenic bladder. *J Urol*, 169: 195, 2003
8. Hohenfellner, M., Pannek, J., Botel, U., Dahms, S., Pfitzenmaier, J., Fichtner, J. et al: Sacral bladder denervation for treatment of detrusor hyperreflexia and autonomic dysreflexia. *Urology*, 58: 28, 2001
9. Craggs, M. and McFarlane, J.: Neuromodulation of the lower urinary tract. *Exp Physiol*, 84: 149, 1999
10. Wheeler, J. S., Jr., Walter, J. S. and Zaszczurynski, P. J.: Bladder inhibition by penile nerve stimulation in spinal cord injury patients. *J Urol*, 147: 100, 1992
11. Dalmose, A. L., Rijkhoff, N. J., Kirkeby, H. J., Nohr, M., Sinkjær, T. and Djurhuus, J.C.: Conditional stimulation of the dorsal penile/clitoral nerve may increase cystometric capacity in patients with spinal cord injury. *Neurourol Urodyn*, 22: 130, 2003
12. Kirkham, A. P., Shah, N. C., Knight, S. L., Shah, P. J. and Craggs, M. D.: The acute effects of continuous and conditional neuromodulation on the bladder in spinal cord injury. *Spinal Cord*, 39: 420, 2001
13. Maynard, F. M., Jr., Bracken, M. B., Creasey, G., Ditunno, J. F., Jr., Donovan, W. H., Ducker, T. B. et al: International Standards for Neurological and Functional Classification of Spinal Cord Injury. American Spinal Injury Association. *Spinal Cord*, 35: 266, 1997
14. Previnaire, J. G., Soler, J. M., Perrigot, M., Boileau, G., Delahaye, H., Schumacker, P. et al: Short-term effect of pudendal nerve electrical stimulation on detrusor hyperreflexia in spinal cord injury patients: importance of current strength. *Paraplegia*, 34: 95, 1996
15. Fjorback, M. V., Hansen, J., Dalmose, A. L., Rijkhoff, N. J. M. and Sinkjær, T.: A portable device for experimental treatment of neurogenic detrusor overactivity. *Neuromodulation*, 6: 158, 2003
16. McGuire, E. J., Woodside, J. R., Borden, T. A. and Weiss, R. M.: Prognostic value of urodynamic testing in myelodysplastic patients. *J Urol*, 126: 205, 1981
17. Læssøe, L., Sønksen, J., Bagi, P., Biering-Sørensen, F., Ohl, D. A., McGuire, E. J. et al: Effects of ejaculation by penile vibratory stimulation on bladder capacity in men with spinal cord lesions. *J Urol*, 169: 2216, 2003
18. Previnaire, J. G., Soler, J. M. and Perrigot, M.: Is there a place for pudendal nerve maximal electrical stimulation for the treatment of detrusor hyperreflexia in spinal cord injury patients? *Spinal Cord*, 36: 100, 1998
19. Bosch, R. and Groen, J.: Complete 5-year follow-up of sacral (S3) segmental nerve stimulation with an implantable electrode and pulse generator in 36 consecutive patients with refractory detrusor overactivity incontinence. *Neurourol Urodyn*, 21: 390, 2002