Minimally invasive electrical stimulation for treatment of fecal and urinary incontinence: scientific background and clinical applications

Workshop 35

Tuesday, August 24, 0900-1200

Time	Time	Topic	Speaker
0900	0905	Introduction	John Heesakkers
0905	0930	Basic principles of electrical stimulation	Nico Rijkhoff
0930	0940	Discussion	
0940	1005	Experimental electrical stimulation in animals and humans	Sivert Lindstrom
1005	1030	Discussion	
1030	1100	Coffee break	
1100	1130	Minimally invasive electrical stimulation for urinary incontinence	John Heesakkers
1130	1135	Discussion	
1135	1155	Minimally invasive electrical stimulation for fecal incontinence	Klaus Matzel
1155	1200	Discussion	

Aims of course/workshop

Lower urinary tract disorders and colorectal diseases like faecal incontinence often are caused by neurological disorders. One solution is functional restoration via the pathways of the nervous system by electrical stimulation of the involved nervous tracts. New basic and clinical research suggest that peripheral and more superficial techniques can successfully applied to correct functional urogenital and anorectal disorders. These new techniques allow more general applicability. This workshop provide the basic science that creates the foundation for electrical stimulation. Latest non-invasive and minimal invasive techniques and results are presented.
The aim is to provide insight in basic and clinical electrophysiological mechanisms of electrical stimulation. The objectives are: to understand the basics of electrical stimulation with emphasis on neuroplasticity and therapeutic stimulation; to realise that electrical stimulation can be applied in various forms; to have knowledge about different types of stimulation in clinical practice and be able to appreciate the efficacy.

Educational Objectives

The educational value of our workshop is that it shows that as well urinary and fecal incontinence co-exist and are bothersome. The underlying pathophysiological mechanisms show that there are many similarities between urinary and fecal incontinence from a innervational point of view but that the end organ differs. Electrical stimulation of the nervous system is a logic way of correcting disorders. Latest developments show that more superficial and therapeutic ways of stimulation have high efficacy and are less expensive, making it a technique that can be applied in a more general way. Moreover since the pelvic innervation of the urinary and anorectal tract are similar beneficial effects can be expected on both organ systems. Therefore it is worthwhile to explore and explain the background of electrical stimulation on both tracts in an integrative way.

Content

The treatment of lower urinary tract and anorectal dysfunction traditionally consists of medical treatment or surgical interventions.
Functional lower urinary tract and anorectal disorders often are caused by problems of the whole innervational tract of the mentioned end organs. Logically this implies that the solution for these problems also should be by restoring the function of the lower urinary tract and the excretory part of the intestinal system via the nervous pathways. This workshop tries to give insight in newest developments of treatment with minimally electrical stimulation.
Electrical stimulation can be done at various nerves like the sacral roots or the pudendal nerve. Also nerves that convene in the pelvis and therefore might be expected to have an effect on the pelvic organs, are explored. The best known example is the posterior tibial nerve. The general concept is that afferent stimulation should be applied in order to have central cerebral processing followed by a correcting efferent effect to the end organs. Stimulation can be applied continuously or discontinuously in order to have the maximal effect. With discontinuous stimulation technical difficult and expensive implants could be avoided and more patients could benefit from the techniques. There are theories stating that periodical stimulation is better than continuous because habituation of the nervous system is less likely to occur and neuroplastic effects are more efficiently applied. The workshop will address all these items as well as the clinical results of the applied techniques.

Nico Rijkhoff will lecture about basic principles of electrical stimulation and how it can be applied in living organisms. The best ways to effectively apply stimulation is addressed as well as the best techniques to pass the skin impedance. **Sivert Lindstrom** will continue with the known basic facts about electrical stimulation in animals and humans. The effects of nerve stimulation at several sites and organs of the body, the way of stimulation, the effects of differences in stimulation frequency etc. are topics that are discussed. Emphasis is put on discontinuous as opposed to continuous stimulation to look at the effect on neuroplasticity.
The clinical application of minimally invasive stimulation of urinary incontinence will de addressed by **John Heesakkers**. Electrical stimulation in physiotherapy practice and the minimal invasive approaches like percutaneous and transcutaneous stimulation are discussed. Electrical stimulation is also applied in anorectal disorders like fecal incontinence. The most extensively studied way of electrical stimulation for faecal incontinence is neuromodulation of the sacral roots. New ways of stimulation like several types of pudendal nerve stimulation and also posterior tibial nerve stimulation have been introduced lately. The results from these therapies on anorectal disorders will be presented in this workshop by **Klaus Matzel**

Nerve activation using electrical stimulation: Basic aspects

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Electrical stimulation of nervous tissue has been shown to be an effective treatment option for patients with refractory urinary disorders such as retention and incontinence. In addition patients with fecal incontinence can also benefit from electrical stimulation. While there are still open question in neuromodulation, which involves, among others reflexes, long-term potentiation and plasticity, the basics of electrical nerve stimulation is well understood and covered by an extensive body knowledge including theory and experimental data. In this lecture I will present a summary of the basic principles in electrical stimulation with a focus on non-implanted stimulation electrodes.

The clinical effect of nerve stimulation is brought about by generation of action potentials in nerve fibers which propagate over the axon to the terminal (synapse) where a neurotransmitter is released to affect an organ or another nerve. Action potentials can be initiated by a creating fast changing electrical potential field along a nerve fiber usually by sending an electrical current through 2 conducting contacts (electrodes) placed near the target nerves. This electrical current reduces the membrane potential of the nerve fiber (depolarization). When the depolarization exceeds a certain amount (the threshold), an action potential is generated. Several stimulation parameters like amplitude, pulse width, pulse rate, pulse shape and pulse polarity affect the process of action potential generation. Other important parameters are electrode dimensions and the electrode-nerve distance.

The influences of the different parameters will be summarized in the presentation.

Minimal and non-invasive ways of electrostimulation in the Urinary Tract

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Several types of stimulation are applied in the lower urnary tract. To the non-invasive and minimally invasive techniques belong: intravesical stimulation, intravaginal or intrarectal stimulation, transcutaneous or percutaneous stimulation of branches of the sacral nerve or the pudendal nerve, and percutaneous stimulation of the posterior tibial nerve.

Intravesical electrical stimulation. Intravesical electrostimulation involves direct intraluminal electrical stimulation via a catheter with a special stimulation electrode. The bladder is filled with sodium chloride to serve as a cathode and an indifferent electrode is placed on the thigh or arm. The technique has been used mostly in children with incomplete nerve lesions, resulting in absent bladder sensation and/or insufficient detrusor contractions. Intravesical electrostimulation is usually combined with intensive bladder training, which may partly account for the successful outcome.

Transvaginal stimulation. Based on experiences with anal stimulation for fecal and urinary incontinence transvaginal stimulation for urinary incontinence was evaluated in 1977 by Fall. Since then several reports on transvaginal electrical stimulation have been published. In animal experiments performed to illuminate the working mechanism of this technique Lindstrom et al observed that detrusor relaxation was accomplished by activation of sympathetic hypogastric inhibitory neurons and by central inhibition of pelvic parasympathetic excitatory neurons. Overall the transvaginal mode of treatment is not well accepted by most patients. To achieve an acceptable therapy outcome stimulation at high intensity is needed, which cannot be easily tolerated by women with normal sensation in the pelvic region. Consequently further reports of this treatment modality are scarce.

Functional or maximal electrical stimulation.
This is a technique that uses an anal plug and electrodes over the sacrum that can change vesical and urethral pressures. This technique is called acute maximal FES when high stimulation levels can be used because of sensory losses associated with spinal cord injury. Others tried to maximize stimulation in a procedure called maximal electrical stimulation by stimulating with an intensity as high as tolerable and also increasing the number of stimulation sites when possible. Therefore, women were stimulated anally as well as transvaginally at the same time. Reported results vary considerably, also because different criteria for success were used. The physical and psychological discomfort of this treatment limited the acceptance of functional or maximal electrical stimulation.

Penile and clitoral stimulation. As the most superficial branch of the pudendal nerve, the dorsal nerve of the penis or clitoris is near the skin surface and can be used for stimulation as well. In experimental studies the acute effects of dorsal penile nerve stimulation seem promising, especially for improving bladder capacity and for suppressing detrusor overactivity.

Transcutaneous Electrical Nerve Stimulation (TENS)

Fall was the first to report a study in patients with IC using suprapubic TENS. Favorable outcome was considered to be due to pain relief. Studies were performed in patients with idiopathic lower urinary tract dysfunction. In this form of TENS 2 electrodes are positioned suprapubically 10 to 15 cm apart. Stimulation is given at maximum tolerable intensity up to 2 hours twice daily since there proves to be a carryover effect, ie lasting improvement after the withdrawal of stimulation. Frequencies vary from 2 -150 Hz. Low frequency TENS is reported to give earlier results in some patients but muscle twitches are highly unpleasant. Because suprapubic TENS has proved to be an easily applicable treatment it was thought that the application of TENS over the S2 or S3 dermatome might improve clinical results. This treatment option has been studied extensively using clinical as well as urodynamic parameters. These studies revealed a positive effect on detrusor overactivity a delay in the first desire to void and increased bladder capacity on urodynamics.

Percutaneous Tibial Nerve Stimulation (PTNS)

PTNS as a treatment option for lower urinary tract dysfunction was developed in 1997. Previously transcutaneous tibial nerve stimulation was described by McGuire. Also in China it is known already for centuries that it is possible to treat LUT disorders by stimulating the tibial nerve area at the ankle. PTNS is indicated for overactive bladder syndrome, non obstructive voiding retention and pelvic pain.

With PTNS a needle is inserted approximately 3 to 4 cm to the medial malleolus. A stick on electrode is placed on the same leg near the arch of the foot. The needle and electrode are connected to a stimulator (Urgent PC®, Uroplasty Inc, USA) with an intensity of 0 to 10 mA and a 20Hz pulse width of 200 usec. Stimulation is applied at an intensity well tolerated by the patient. Patients undergo 12 weekly outpatient treatment sessions of 30 minutes. If a good response occurs the patient is offered chronic treatment.

Neuromodulation is suggested to treat overactive bladder by restoring the balance between inhibitory and excitatory control systems, peripherally and centrally. Because the maximum effect of neuromodulation is not immediately obtained it is believed that neuromodulation induces learning changes (i.e. neural plasticity). For chronic non obstructive urinary retention, studies have shown subjective success in 58-59% of patients. More objective outcome measures improved over 50% in 41% of patients. In OAB subjective success was found in 59-64% of patients. Objective success, defined as over 50% decrease in incontinence episodes and/or micturition frequency, was found in 47-56% of patients. In a study on patients with OAB symptoms treated with PTNS for twelve weeks, a reduction in the number of urinary leakage episodes of 50% or more per 24 hours, could be obtained in 56%. Frequency / volume chart data and quality of life scores improved significantly. Increments in cystometric bladder capacity and in volume at DO were significant.

Subjects without DO at baseline responded better to PTNS. Patients with minor voiding dysfunction are more successful.
Peters et al published in 2010 in the Journal of Urology the first randomized controlled trial on PTNS. In this double blind sham controlled trial 220 patients were randomized. After 12 weeks treatment assessment was performed on: voiding diaries, QoL and Global response. In the sham group 21% of the patients had a moderate or marked response whereas this was 55% in the active treatment group. This clearly shows that in addition to a placebo effect there really is a substantial treatment effect of PTNS. Hopefully more studies of this kind will follow.

Minimally invasive electrical stimulation for fecal incontinence

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The most extensively studied an applied way of electrical stimulation for faecal incontinence is neuromodulation of the sacral roots. New ways of stimulation like pudendal nerve stimulation and posterior tibial nerve stimulation have only been introduced recently. Currently all these therapies are considered only if conservative therapies fail. The role of sacral nerve stimulation (SNS in the treatment algorithm is established, whereas the experience with the other new therapies are to limited to allow any statement regarding their role in the treatment armentarium – despite the fact that preliminary data are promising.

SACRAL NERVE STIMULATION / SACRAL NEUROMODULATION

Initially the use of SNS in the context of anorectal disorders was confined to fecal incontinence. The concept is the recruitment of residual function of the anorectal continence organ by electrical stimulation of its peripheral nerve supply. The technique used is the same as in Urology. The technique evolved to be of limited invasiveness with low morbidity.

Patients for permanent implantation of a neurostimulation device are selected by a therapeutic trial of a timely limited percutaneous test stimulation, usually for at least 2 weeks during which bowel habits are monitored. The results of the test stimulation is highly predictive for the clinical efficacy of chronic stimulation with a permanent device. The implantation of the permanent neurostimulation device is commonly advised if the frequency of episodes of faecal incontinence are alleviated by at least 50% during the test stimulation and if the improvement is reversible after stimulation discontinuation.

The surgical technique is standardized: Percutaneous nerve evaluation (PNE), is used to confirm a satisfactory nerve response and then to evaluate the clinical effect of temporary stimulation prior to the permanent implant. Two technical options are used for percutaneous nerve evaluation (PNE), the first being the more common one in Coloproctology: a temporary, percutaneously placed, lead (or multiple leads) is used for the test stimulation and removed at the end of this phase; or a quadripolar lead, the so-called “tined lead” electrode is operatively placed through a trochar with the help of fluoroscopy in a minimally invasive intervention. This electrode can stay in place and be used for permanent stimulation, if the test stimulation is effective. For screening, both types of leads are connected to an external pulse, the latter with a percutaneous extension cable. If screening is successful a permanent electrode and neurostimulator are implanted. In those with a foramen electrode already in place for screening the percutaneous extension is removed and only the pulse generator added (so-called “two-stage implant”). The pulse generator is placed subcutaneously most commonly in the gluteal area. The pulse generator is activated and stimulation parameters are set early after surgery by telemetry to low frequency stimulation.

With the help of test stimulation, the spectrum of indications of SNS for incontinence been continuously expanded to patients suffering from fecal incontinence owing to a wide variety of causes resulting in a lack of function: weakness of the external anal sphincter, with concomitant urinary incontinence or a defect and/or deficit of the smooth-muscle internal anal sphincter; status post-rectal resection; limited structural defects of the external anal sphincter combined with limited defects of the internal anal sphincter; and neurogenic incontinence. The therapeutic effects of SNS have been demonstrated in multiple trials (Table 1). Patients are selected in a uniform way for implant. With chronic SNS the frequency of involuntary loss of bowel content is reduced, the ability to postpone defecation and quality of life is improved, and a substantial percentage of patients gain full continence. Longterm follow up demonstrates a sustainability of the clinical outcome. Morbidity of the procedure is low and complications are rare.

The spectrum of indications for SNS has now be expanded to include constipation. Two studies indicate that SNS can be an effective treatment for constipation in patients, who fail to respond to conservative management. Experience with this new indication for SNS and the total number of such patients treated remains limited. However, the relevance of selecting patients for permanent SNS on the basis of their response to a trial of this therapy has been demonstrated, as has persistent amelioration of constipation with SNS.

Despite the very positive clinical outcomes that have been reported for SNS therapy in defecatory disorders, our knowledge and understanding of its mechanism of action is incomplete. The effect of SNS on continence is complex and likely to be multifactorial, involving somatomotor, somatosensory and autonomic functions of the anorectal continence organ and modulation of peripheral and central functions. Clinical outcome of SNS has been correlated with results of anorectal physiology studies, but the effect of chronic stimulation varies greatly among published reports. Data are in part contradictory and inconclusive and sometimes not reproducible. Some studies have demonstrated increased resting anal pressure, but others have not. Several studies have documented an increase in anal squeeze pressure. The duration of voluntary contraction was shown to be increased. SNS appears to increase rectal sensitivity. Improvement in anal sensory function and sensibility of the perianal and perineal skin during SNS has been reported. Rectal manometry (24-hr) has indicated qualitative changes in anal and rectal motility: Reduction of spontaneous rectal motility complexe and spontaneous anal sphincter relaxation. Colonic manometry demonstrated an increase of the number of pancolonic propulsive, propagating pressure waves and their amplitude. However, understanding of the relative importance of each of these functions and their relevance in certain pathophysiologic conditions is unclear, both in general and in specific individuals treated with SNS.

PUDENDAL NERVE STIMULATION

In the field of anorectal dysfunctions the application of pudendal nerve stimlation is limited. Two techniques have been described, both as case reports.

BION MIcrostimulator

The use of a BION microstimulator as been reported in one patient not suitable for sacral nerve stimulation because of limited access to the sacral nerves due to substantial destruction and distortion of the bony structure of the sacrum and pelvic ring. Continous low frequency stimulation with the Bion microstimulator placed closed to the left pudendal nerve resulted in a reduction of symptoms: improved continence, decreased need of retrograde rectal irrigation for bowel emptying. No complications were observed.

INTERSTIM Device

The application of the INTERSTIM device for pudendal stimulation by a posterior approach with a slightly modification of the original equipment was described in two patients, in whom SNS did not result in sufficient symptomatic relief of fecal incontinence. With low frequency stimulation symptomatic improvement was superior to SNS in one patient, equal to SNS in the other one. The technique appeared to be feasible and no complications occurred.

POSTERIOR TIBIAL NERVE STIMULATION

Recently there is an increasing interest in the use of posterior tibial nerve stimulation to treat fecal incontinence. The studies are few with a limited number of patients. All trials apply intermittent, timely limited stimulation, but the studies designs, the applied techniques and the outcome measures vary. These proof-of-principle studies demonstrate a positive effect on fecal incontinence with a clear reduction in symptoms (Table 2).

The preliminary data are encouraging. Larger, well defined studies will be necessary to further clarify the potential of this approach and to determine its role in the treatment algorithm. Conceptually posterior tibial nerve stimulation can be considered as a therapy prior to or as a bridge to more invasive techniques.

Table 1. Sacral nerve stimulation, published results since 1999, including prospective series with 10 or more patients

Authors	Year	Number of patients	Follow-up (months)	**Incontinent episodes per week**		**Incontinence-score (CCIS)**	
				Before SNS (baseline)	After SNS (last FU)	Before SNS (baseline)	After SNS (last FU)
Rosen et al.	2001	16	15*	6	2	nr	ns
Ganio et al.	2001	16	15,5	5,8	0	nr	ns
Matzel et al.	2003	16	32.5	nr	nr	16	2
Altomare et al.	2004	14	14*	7	0.5	15	2
Matzel et al.	2004	34	24*	16,4	2,0	nr	ns
Jarrett el al.	2004	46	12*	7	1	14	6
Rasmussen et al.	2004	34	6	nr	nr	18	7
Leroi et al.	2005	34	7*	3,5*	0,5*	16*	10*
Kenefick et al.	2006	19	24*	12	0	nr	ns
Holzer et al.	2007	29	35*	2,3	0,67	nr	ns
Hetzer et al.	2007	37	13	nr	nr	14	5
Tan et al.	2007	53	12	9,5	3,1	16	1,2
Melenhorst et al.	2007	100	25,5	10,4	1,5	nr	ns
Meurette et al.	2008	15	15	nr	nr	nr	9,4
Vallet et al.	2008	32	37	nr	nr	16,1	6,9
Altomare et al.	2009	60	74	3,5	0,7	15	5
El-Gazzaz et al.	2009	24	28*	4,5	1,5	12	4,7
Wexner et al.	2010	120	28	9,4	1,4	nr	nr
Gallas et al.	2010	200	12*	4*	nr	14*	6,5*
Michelsen et al.	2010	126	24	8,3	0,6	16	10

Parameter	Queralto *et al.* (2006)	Vitton *el al.* (2009)	De la Portilla *et al.* (2009)	*Govaert et al. (2009)*	Boyle *et al.* (2010)
Study type	Prospective, single centre	Prospective, single centre	Prospective, single centre	Prospective, 3 European sites	centre
Technique	Transcutaneous stimulation adhesive skin electrode	Transcutaneous stimulation	Percutaneous stimulation, needle electrode	Percutaneous stimulation, needle electrode	Percutaneous stimulation, needle electrode
Indication	Idiopathic FI	FI due to IBD	FI > 4/28 days CCIS >10 intact EAS IAS defect: 8	FI Intact sphincter: 16 EAS defect: 6	FI urge IAS disruption:10 EAS disruption:17 Both disrupted: 9
Number of patients	10	12	16	22	31
Follow-up (months)	1 month 4 months	3 months	3 months 8 months 6 months (without stim.)	1.5 months (n:22) 3 months 6 months 12 months	Median 9 months (range 3–14)
Outcomes	Pre CCIS; mean 11.4 (4-18) CCIS improved in 8/10 Mean CCIS improve-ment: 60 % CCIS: mean 5,4 (1-15)	Pre CCIS; mean 13.1 (7-17) 5/12 reported symptomatic improvement (VAS: n=2: 4/5; n=2:3/5; n=1:1/5) CCIS: mean 12.3 (1-16) Time to defer: improved in 3/12 patients	Pre CCIS; mean 13.2 (7-20) <u>3 months (n:16)</u> 10/16: success CCIS: mean 9.0 (1-19) <u>8 months (n:11)</u> CCIS: mean 6.0 (0-13) <u>9 months (n:11)</u> CCIS: mean 7.4 (2-13)	Pre CCIS; mean 11.6 (10-14) <u>1.5 months (n:22)</u> 18/22: improved 14/22: improved > 50% CCIS: mean 8,2 (7-10) <u>3 months (n:18)</u> CCIS: mean 5.9 (5-7) <u>6 months (n:17)</u> CCIS: mean 5.4 (3-8) <u>12 months (n:14)</u> 13/22: improved > 50% CCIS: mean 5.9 (4-8)	<u>FI episodes:</u> 22/31: > 50% 12/31: continent Pre: median 4/w (0/30) Post: median: 0/w (0-27) <u>CCIS:</u> improved 21/31 Pre: median: 13 (5-20) Post: median: 7 (0-20) Median improvement: 2 <u>Urgency:</u> improved 20/31
Quality of life	NR	5/12 improvement QoL: (n=1:60%; n=2:70%, n=2:80%)	Significant improvement in FIQS in all domains‡	Sign. improved domains 12 months: FIQS: Lifestyle, Coping/ Behaviour, Embarressment	NR

				SF 36: all except vitality	