IJUH
The International Journal of Urologic History©
www.ijuh.org



# History of Sacral Neuromodulation in Urology

**Raymond Lay, Adam Visca, Gareth Warren, Ronald Rabinowitz, Divya Ajay***

*From the School of Medicine and Dentistry, University of Rochester, Rochester, NY (RL, AV); Department of Urology, University of Rochester Medical Center, Rochester, NY (GW, RR, DA)*

**Correspondence: Department of Urology, University of Rochester Medical Center, 601 Elmwood Ave, Rochester, NY 14642; email: divya_ajay@URMC.Rochester.edu*

**Introduction**: Approximately 16.5% of the U.S. population is estimated to have overactive bladder (OAB), significantly impacting their daily life. Sacral nerve stimulation (SNS) has been a successful method of treating urge incontinence, urgency, frequency, and non-obstructive retention since its development. This article reviews the development of SNS from its inception to the procedure we know it as today.

**Sources and Methods**: We conducted a literature review using the PubMed database, Google Scholar, and JSTOR regarding the history of SNS and the discoveries leading to its development.

**Results**: As our ability to incorporate electricity into medical practice improved in the mid-1900s, the pressing question in urology was whether it could be used in treatment of the neurogenic bladder. Initial efforts focused on direct detrusor stimulation and pelvic nerve stimulation, with limited efficacy. In the 1970s, Drs. Emil Tanagho and Richard Schmidt found that stimulation of sacral nerves in dog models resulted in a detrusor contraction response, resulting in the voiding of urine. They focused on improving these techniques and published a paper in 1989 on the first use of SNS on human subjects, paving the way for our modern-day procedure. Eventually, Medtronic developed the InterStim system, which received FDA approval in 1997 for the treatment of urge incontinence. The basic SNS technique has since remained largely the same. In 2019, the Axonics Sacral Neuromodulation System was also approved for treatment of OAB symptoms as an alternative to the InterStim system. Given the efficacy of SNS in the treatment of OAB, further iterations of SNS devices were recently developed, such as devices with rechargeable batteries and prolonged battery life.

**Conclusions:** Since Tanagho and Schmidt first described its use, SNS has been and continues to be a successful method for treating OAB. Going forward, SNS will remain a viable option for the treatment of urge incontinence and retention.

**Keywords:** History, Sacral Nerve Stimulation, Electrical Stimulation, Bladder Control, Emil Tanagho

Approximately 16.5% of U.S. adults, or 1 in 6 people, are estimated to have overactive bladder (OAB) symptoms, with the prevalence increasing with age.(1) OAB can significantly affect quality of life, causing some to stay home and reduce their overall activity due to fear of losing control of their bladder function while in public. OAB is also known to increase the incidence of urinary tract infections, perineal skin infections, depression, falls and fractures. (2)

As our ability to use electricity improved, so too did our ability to incorporate it into medicine, eventually leading to the invention of sacral nerve stimulation (SNS) for the treatment of OAB as well as fecal incontinence. Currently, the American Urological Association guidelines for treatment of the condition consist of a three-tiered algorithm, with behavioral therapy as the first-line treatment, pharmacological therapy with anti-cholinergics or beta-3 agonists as second-line treatment, and finally SNS, posterior tibial nerve stimulation, or botulinum toxin injection as the third-line treatment.(3) Here, we delve into the history of SNS and the developments that led to the technology we use today.

## SOURCES

We conducted a literature review using the PubMed database (www.ncbi.nlm.nih.gov), Google Scholar (www.scholar.google.com), and JSTOR (www.jstor.org). PubMed and Google Scholar were used to identify contemporary medical literature on the use of electricity in medicine and urology, sacral nerve stimulation, and the relevant discoveries leading up to these topics. The digital storage site JSTOR was used to identify journal articles on the history of electricity in medicine. FDA

**Figure 1.** The Magneto-Electric Machine was available to both physicians and the general consumer, marketed to be able to cure a wide range of diseases, including tuberculosis, gangrene, and spinal deformities. (Courtesy of Lancaster Medical Heritage Museum, Lancaster, PA)

Establishment Registration & Device Listing database was accessed for device approvals.

## RESULTS AND DISCUSSION

### Combining Electricity and Medicine

Ancient Egyptians initially described electric shocks from fish and eels in 2750 BCE, and the first description of electrostimulation dates to 400 BCE, when Ancient Grecians placed electric eels in footbaths to soothe arthritic pain and promote circulation. In 47 CE, Roman physician Scribonius Largus described in his list of 271 prescriptions, *Compositiones*, the use of a bioelectric fish to relieve headaches and gouty pain. (4) Electrostimulation practices boomed with the discovery of static electricity in the medical era of Franklinism in the mid-1800s. Around this time, Guillaume-Benjamin-Amand Duchenne, fascinated by electrophysiology, created a portable device that was able to stimulate individual muscles to avoid the usual tissue damage and pain that electrostimulation was known to cause. Known as localized faradization, he was able to study a plethora of neuromuscular diseases with this method, with Duchenne muscular dystrophy ultimately being named after him.(5)

From the 1870s-1920s, the medical battery was created to treat pains through application of electricity to target tissue, similar to the Ancient Greeks. With such easy access to electricity, however, medical quackery ran rampant with the creation of electric products touted as being cure-alls, claiming to treat anything from balding to obesity (Figure 1).(6) In 1937, building on the medical battery, Newman, Fender, and Saunders developed radio frequency induction, which called for the use of tuned primary and secondary coils to create a stimulating waveform. This allowed for better control of the amplitude so that multiple types of delicate biological tissue, including the bladder, could be stimulated with increased precision, thus creating a new interest in electrotherapy.(7, 8) However, this method was limited due to the bulkiness of the equipment. It was not until the late 1950s that the development of transistors allowed for smaller devices to be made, resulting in the creation of the cardiac pacemaker in 1958, along with the development of newfound interest in creating implantable bladder devices. (7, 9)

### Electrophysiology work on the bladder

In 1950, Corey et al. described a method to measure electropotential changes in the healthy human bladder, demonstrating the average rate and duration of bladder contraction upon application of electric stimulation (Figure 2).(10)

This new method paired with the ability to implant devices allowed urologic researchers to begin evaluating the optimal location to induce bladder contraction in patients with neurogenic bladders: the bladder itself, the pelvic floor, or the spinal cord. Initial efforts focused on regaining bladder control in paraplegic patients experiencing urinary retention.

In 1954, Dr. Edward J. McGuire studied the effects of direct electrical stimulation to the bladder on dogs using a variety of electrodes, stimulating multiple areas of the outer bladder and measuring the subsequent response, though high voltages were required for successful stimulation.(11) The same year, Boyce et al. implanted coils prepared by McGuire into the bladders of paraplegic patients with neurogenic bladder. The trial enrolled three subjects, only one of whom had a successful outcome. (12) Bradley, Chou, and French also tested implantation of a radio transmitter unit into the bladder in 1963, first in dogs (Figure 3, left), then in 7 patients who all had bladder incontinence. Overall, while electrostimulation led to bladder contraction, it did not correlate with actual bladder emptying in all but two of the patients, showing that direct bladder stimulation may not be the best approach for inducing micturition. This method also had intolerable side-effects, including fibrosis of the bladder. (13)

In 1959, Burghele et al. attempted to promote micturition by direct stimulation of the pelvic nerves in dogs (Figure 3, right). It was found that while pelvic nerve stimulation did result in detrusor contraction, it also simultaneously stimulated the pudendal nerve, leading to contraction of the external urethral sphincter (EUS), preventing bladder emptying.(14) To prevent the activation of the EUS, Holmquist in 1968 described a method of severing the pudendal nerve to allow relaxation of the external sphincter while the detrusor muscle was being activated. He also suggested placing an additional electrode to stimulate the urethra until "fatigue stimulation" is achieved, allowing the EUS to relax after current discontinuation. However, Holmquist concluded that the use of pelvic nerve stimulation was limited in humans due to the need to perform a pudendectomy (essentially eliminating the ability to achieve erections), difficult access for electrode placement for that time period, and limited use in patients with neurogenic bladders due to nerve atrophy. (15)

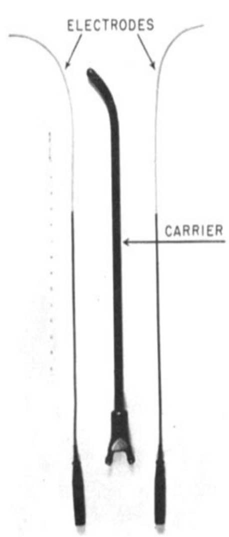


**Figure 2.** In 1950, Corey et al. inserted electrodes with a carrier and into the urethra to stimulate the bladder wall and subsequently measure parameters of bladder wall contraction. (10)

**Initial studies of SNS**

In 1972, Nashold et al. electrically stimulated the sacral nerves of 36 dogs and cats with bladder paralysis, finding that the S1-S3 nerves produced the strongest bladder contraction. While only a portion of the animals successfully voided, this new method of bladder stimulation eventually paved the way for our current modern-day methods of SNS. The same year, Nashold et al. described a method in which an electrode was implanted to the S1-S2 region of 4 patients, and 3 of the 4 patients experienced adequate emptying of the bladder every 3-4 hours with stimulation. However, the patients also experienced uncomfortable autonomic effects, such as diaphoresis, erection, and fever. (16, 17) In 1975, Dr. Emil Tanagho and Dr. Richard Schmidt attempted to solve this issue by more precisely targeting the nerve fibers controlling micturition. Their first innovation was the discovery that the stimulation of the ventral portion of the S2 nerve root in dogs created the strongest detrusor contraction response, though this was also associated with external sphincter contraction. Aware of the inherent problem of sphincter contraction with general sacral nerve stimulation, they performed a dorsal rhizotomy to remove sensation that reflexively led to sphincter closure. They also divided the S2 ventral root to avoid stimulating somatic sphincter fibers. In these studies, however, they were unable to completely localize the detrusor contraction response, and they frequently got responses of defecation, pelvic artery dilation, and erections, limiting the utility of their results. (18-20)

In 1982, Tanagho and Schmidt refined their

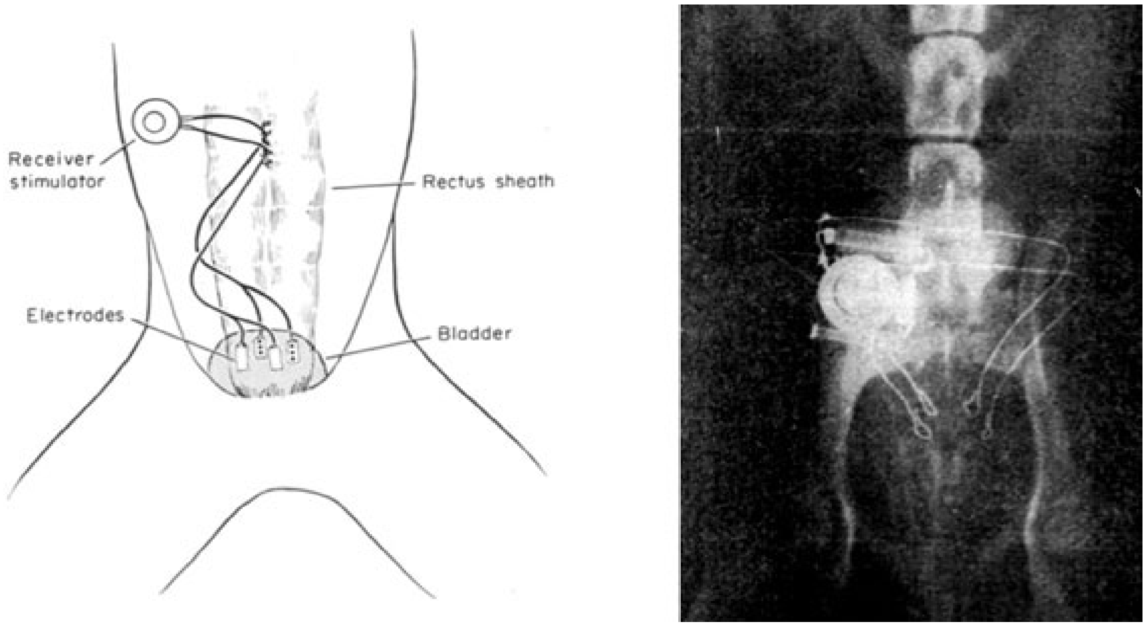


**Figure 3. (left)** Diagram of direct electrostimulation of the bladder in the dog, 1962-63.(13) **(Right)** 1959 X-ray showing electrodes implanted *in vivo* in the canine model by Burghele et al. (14)

technique of stimulating the ventral component of sacral nerves in dogs. This time, they performed a selective neurotomy of the somatic fibers in the sacral root before the fibers form the pudendal nerve. When testing this new method on paraplegic dogs with fully neurogenic bladders, they found that stimulation successfully caused bladder emptying for 4-10 months in several dogs. (21)

After many years of refining their SNS technique on dog models, in 1989, Tanagho and Schmidt compiled data from 22 patients who they treated from 1981-1987 using a combination of the previously described techniques of stimulation of the ventral S3-4, dorsal rhizotomy, and selective peripheral neurotomy. Like the results of their dog experiments, stimulation of the ventral portion of S2 combined with a dorsal rhizotomy and selective peripheral neurotomy significantly increased the ability to void successfully. Interestingly, the majority of patients treated did not have neurogenic bladder, but rather, OAB. Tanagho and Schmidt rationalized that because voiding dysfunctions commonly result from some degree of hyperactive bladder, the inhibitory effect of neurostimulation would reduce bladder spasticity, resulting in the use of SNS to treat urge symptoms. (22) Several of the patients in this study maintained continence during follow-up 4-5 years later, paving the way for modern-day SNS. (23) Eventually, with the development of smaller electrodes, Tanagho and Schmidt worked towards discovering a less invasive method of bladder control. Dr. Steven Siegel in 1992 described this as consisting of several phases, similar to current techniques. In the acute phase, a spinal needle was inserted into the sacral foramen, and a current was applied to stimulate various responses. The desired motor response included contraction of the anal sphincter, perineum, and buttocks ("bellows" response) as well as plantar flexion. The patient was also able to provide verbal feedback on sensation, described as a tingling, vibration, or pulling of the rectum, vagina, or scrotum. Once the desired response was obtained, a temporary electrode was put in the needle's place. The following sub-chronic phase involved testing the temporary electrode's therapeutic value over 3-5 days. Criteria for implanting a permanent device consisted of ≥50% improvement of 2 major symptom categories: pain, urinary frequency/urgency, voided volumes, and episodes/volumes of urinary incontinence. If successful, a permanent implant connected to a neurostimulator was then placed in a created subcutaneous pouch in the lower abdomen under general anesthesia. (24,25)

**The Rise of Sacral Neuromodulation**

Using this technique, Medtronic from Minneapolis, MN developed the InterStim system (Figure 4, left), eventually receiving European approval in 1994, Food and Drug Administration (FDA) approval in 1997 for treating urge incontinence, and FDA approval in 1999 for treating both urinary retention and urgency-frequency symptoms. (26) The InterStim system quickly became an accepted method for treatment of OAB.

In 2003, tined leads were introduced by Spinelli et al. to allow for percutaneous lead placement without incision or fascial anchoring, making the procedure much less invasive and reducing operation time. Since this discovery, the initial test phase can be performed using the temporary lead for percutaneous neuromodulation or permanent tined lead, producing better results due to reduced migration between testing and implantation. (27)

In 2006, InterStim II was developed, introducing a battery that was lighter and smaller by almost one half of the prior model, allowing for smaller incisions and pockets to be made (Figure 4, right). The production of smaller implants has served to further reduce operating times and post-operative pain. (28) Medtronic found other useful applications for this technology and in 2011, InterStim received FDA approval for the treatment of chronic fecal incontinence in patients who either fail or cannot tolerate conservative treatments. Other companies have followed suit. In 2019, Axonics' Sacral Neuromodulation System received FDA approval for treatment of urinary retention and OAB. The smaller Axonics system became the first rechargeable and MRI-compatible sacral neuromodulation device. In 2020, InterStim Micro was released to also introduce rechargeability and MRI-compatibility to the InterStim system. Finally, most recently in February 2022, InterStim X received FDA approval, providing a non-rechargeable battery lasting 10-15 years. (26)

Current adverse events include very low risk of infection, pain at the device site, uncomfortable stimulation sensations, and a reintervention rate of approximately 38% due to failed treatment or device malfunction. (26, 29) When comparing the success rate of SNS versus standard medical therapy for OAB symptoms after 6 months during the InSite trials (defined by ≥50% symptom reduction), SNS was found to be more effective for patients experiencing less severe OAB symptoms. With intent to treat analysis, the SNS group had a 61% success rate compared to 42% in the standard medical therapy group.(30) Additional benefits of SNS include therapeutic compliance, with low fall out rate of treatment as well as attrition rate for returning to clinic, thus offering a relatively safe and accessible option for patients. Future developments will only serve to improve the safety and efficacy of SNS as a treatment for OAB and urinary retention.

## CONCLUSIONS:

Since the discovery of electricity, humans have attempted to adapt it to medical applications. Now a safe and effective treatment for OAB and urinary retention, SNS is the result of many trials and iterations since electrostimulation was first tested on the bladders of dogs in 1954. Since Tanagho and Schmidt first described the procedure, the overall technique for SNS has not changed significantly, yet it remains an effective treatment method. Going forward, SNS will continue to be a viable option for the treatment of urge and fecal incontinence, OAB, and urinary retention.


**Figure 4. (left)** The first InterStim System developed, 1990's (25) **(Right)** Modern-day (2006) InterStim II, with size comparison to a €2 coin. (WikiMedia Commons, Public Domain)

## REFERENCES


1. Reynolds WS, Fowke J, and Dmochowski R: The burden of overactive bladder on US public health. Current Bladder Dysfunction Reports 2016; **11**: 8.
2. Brown JS, McGhan WF, and Chokroverty S: Comorbidities associated with overactive bladder. Am J Manag Care 2000. **6**: S574.
3. Lightner DJ, et al: Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019. J Urol 2019; **202**: 558.
4. Kellaway P: The part played by electric fish in the early history of bioelectricity and electrotherapy. Bulletin of the History of Medicine 1946; **20**: 112.
5. Parent A: Duchenne De Boulogne: a pioneer in neurology and medical photography. Canadian J of Neurological Sciences 2005; **32**: 369.
6. Wexler A: The medical battery in the United States (1870–1920): Electrotherapy at home and in the clinic. J History Med and Allied Sci 2017; **72**: 166.
7. Newman H, Fender F, and Saunders W: High frequency transmission of stimulating impulses. Surgery 1937; **2**: 359.
8. Melick WF: Electrical stimulation in urology. J Urol 1970; **103**: 815.
9. Aquilina O: A brief history of cardiac pacing. Images Paediatric Cardiology 2006; **8**: 17.
10. Corey E, et al: Electro-potential changes in human urinary bladder: A method of measurement. J Applied Physiology 1951; **3**: 631.
11. McGuire W: Response of the neurogenic bladder to various electric stimuli. Research thesis, Dept. of Surgery, Bowman Gray School of Medicine, 1955.
12. Boyce WH, Lathem JE, and Hunt LD: Research Related to the Development of an Artificial Electrical Stimulator for the Paralyzed Humanbladder: A Review. J Urol 1964. **91**: 41.
13. Bradley WE, et al: An experimental study of the treatment of the neurogenic bladder. J Urol 1963; **90**: 575.
14. Burghele T, Ichim V, and Demetrescu M: Experimental studies on the physiology of micturition and the emptying of the urinary bladder in patients with lesions of the spinal cord: artificial micturition through distant electromagnetic induction. Rumanian Medical Review 1959; **3**: 48.
15. Holmquist B: Electromicturition by pelvic nerve stimulation in dogs. Scandinavian J Urol and Nephrology 1968; **2**: 1.
16. Nashold BS, et al: Electromicturition in paraplegia: implantation of a spinal neuroprosthesis. Archives of Surgery 1972; **104**: 195.
17. Nashold Jr BS, Friedman H, and Boyarsky S: Electrical activation of micturition by spinal cord stimulation. J Surgical Research 1971; **11**: 144.
18. Jones L, et al: Urodynamic evaluation of a chronically implanted bladder pacemaker. Investigative Urology 1976; **13**: 375.
19. Schmidt R, Bruschini H, and Tanagho E: Sacral root stimulation in controlled micturition. Peripheral somatic neurotomy and stimulated voiding. Investigative Urology 1979; **17**: 130.
20. Schmidt RA and Tanagho EA: Feasibility of controlled micturition through electric stimulation. Urologia Internationalis 1979; **34**:199.
21. Tanagho EA and Schmidt RA: Bladder pacemaker: scientific basis and clinical future. Urology 1982; **20**: 614.
22. Schmidt RA: Applications of neurostimulation in urology. Neurourology and Urodynamics 1988; **7**: 585.
23. Tanagho EA, Schmidt RA, and Orvis BR: Neural stimulation for control of voiding dysfunction: a preliminary report in 22 patients with serious neuropathic voiding disorders. J Urology 1989; **142**: 340.
24. Siegel, S: Management of voiding dysfunction with an implantable neuroprosthesis. The Urologic Clinics of North America 1992; **19**: 163.
25. Gajewski JB, et al: The history of sacral neuromodulation in Canada. Canadian Urological Assoc Journal 2020; **14**: 87.
26. United States Food and Drug Admnistration, Devices@FDA, 2022. Available at https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm
27. Spinelli M, et al: New sacral neuromodulation lead for percutaneous implantation using local anesthesia: description and first experience. J Urology 2003; **170**: 1905.
28. Spinelli M, and Sievert KD: Latest technologic and surgical developments in using InterStim™ therapy for sacral neuromodulation: impact on treatment success and safety. European Urology 2008; **54**: 1287.
29. Chughtai B, et al: Failures of sacral neuromodulation for incontinence. JAMA Surgery 2018; **153**: 493.
30. Siegel S, et al: Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared to standard medical therapy at 6-months in subjects with mild symptoms of overactive bladder. Neurourology and Urodynamics 2015; **34**: 224.