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Direct bladder stimulation with suture electrodes promotes voiding in a spinal animal model: A technical report

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Abstract—To determine the efficacy of a new electrode for direct bladder stimulation, five male cats were instrumented during anesthesia. Multistranded, 316LVM, stainless-steel, wire electrodes were implanted on the bladder wall serosa above the trigone area. The electrodes were made with a needle attached to the end that was cut off after suturing the electrode in place. Additional instrumentation included tubes for pressure recording and filling, and hook electrodes for leg and pelvic floor EMG recording. Bladder filling and stimulation studies were conducted in tethered animals 1 to 2 weeks following recovery. Chronic studies were conducted following recovery in tethered animals. To test these electrodes in a spinal cord injury (SCI) model, a T-1 level complete lesion was performed on the above instrumented animals. Spinal animals had successful direct bladder stimulation that induced active contractions and voiding both before and after SCI, but voiding rates were higher more than 2 weeks after SCI and at larger initial bladder volumes. Optimum stimulation parameters consisted of 40 pulses per second, 300 μs to 1 ms pulse duration, a stimulation period of 3 to 4 s, and 10 to 40 mA. Urethral resistance, indicated by a urethral function measure, showed that stimulation had no adverse effect on urethral function, and fluoroscopy showed an open membranous urethra during stimulation and voiding. The cat has a small penile urethra that is the flow rate controlling zone. The suture electrode did not corrode, erode into the bladder, or become dislodged, and appears suitable for chronic implantation.

Key words: *cystometry, electrical stimulation, functional electrical stimulation, neural prosthetics, neurogenic bladder, spinal cord injury, urodynamic studies.*

INTRODUCTION

Sacral ventral root stimulation in conjunction with sacral dorsal root rhizotomy has been effective in promoting voiding with minimal residual volume in spinal cord injured (SCI) patients (1–4). However, extensive surgery is required to implant the electrodes in the lower lumbar or sacral canal. Direct bladder stimulation with implantable stimulators has also been investigated for promoting micturition. Direct bladder stimulation in animal models has been shown to be effective (2); however, many clinical studies have shown poor results. Cited problems in the clinical studies have included high urethral resistance due to activation of the striated urethral sphincter, poor bladder emptying, the need for high stimulating currents, and activation of lower limb muscles, pain, and electrode erosion into the bladder (2,5–10). One group (11,12) reported effective stimulation-driven voiding in 29 of 32 patients. These subjects were unable to void on their own due to SCI and other neurological deficits. Eight small platinum disk electrodes were sutured into the bladder wall, and the most effective loca-

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tion of the electrodes was adjacent to the ureters where the neurovascular bundle innervates the bladder. Concerns with this study (11,12) include the large number of electrodes on the bladder wall and the lack of long-term results. In addition, this work does not address the high urethral resistance problem cited in many other studies (2,5–10).

We are investigating electrodes that might improve direct bladder stimulation techniques. We reported that sacral nerve electrodes and "woven-eye" bladder wall electrodes were effective for activation of the bladder in animal models (13,14). Currently, we are evaluating a suture type electrode that might have the following advantages: 1) an extended length that could be placed across the entire neurovascular bundle that innervates the bladder, 2) implantation in the outer serosal layer that would not erode into the bladder, and 3) a simple electrode requiring little additional implantation procedures, such as suturing, and that might be implanted through a laparoscope. Studies were conducted in male cats both before and after SCI. Urodynamic responses to stimulation, electrode characteristics, and aspects of this animal model are described.

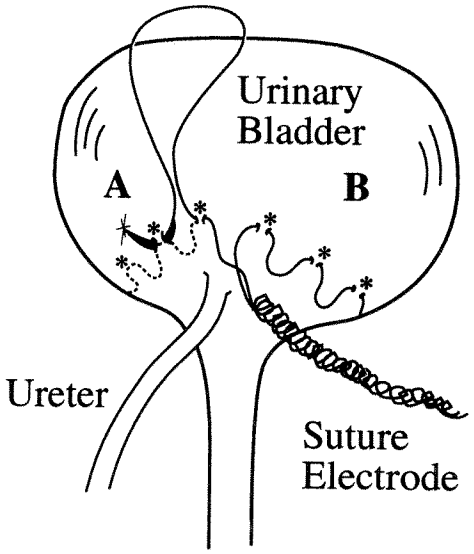

Figure 1.
Bladder wall instrumentation with two suture electrodes: lateral view. A. Illustrates the implantation of the suture electrode; B. Implanted sutured electrode with needle cut off. * indicates suture site.

METHODS

Instrumentation Surgery

Five male cats (weight 2 to 4 kg) were instrumented for subsequent direct bladder stimulation studies. Animals were sedated (IM ketamine hydrochloride 27 mg/kg and xylazine 1 mg/kg) followed by inhalation anesthesia (0.75 percent halothane and 0.8 L/min nitrous oxide). The bladder was surgically exposed via a midline incision, and suture electrodes were implanted on the bladder wall (**Figure 1**). The cable was 50-stranded, 1-mil stainless steel wire (316LVM, Cooner Wire Inc., Chatsworth, CA) coated with Teflon, and the electrode consisted of 7 cm of uninsulated wire with a 21 G curved needle attached to the end for suturing. A polypropylene (3-0) suture was tied into a knot at the end of the insulation to act as a stop against the bladder wall. Four electrodes were sutured to the base of the bladder (**Figure 1**). Suturing was started above the ureters and extended downward at an angle toward the bladder neck. One electrode was implanted posterior, and a second anterior, to the ureters. Approximately 4 cm of implanted wire was looped across the bladder wall so that the electrode could accommodate to filling. Implantation was in the serosa and outer smooth muscle layer. The suturing needle was cut off after implanting the electrode. Some of the electrodes were not secure and required one additional polypropylene suture to tie them to the bladder wall near the electrode insulation junction.

Additional instrumentation consisted of electromyography (EMG) recording hook electrodes (the same wire as the suture electrodes) inserted after making a 2-cm incision through the skin adjacent to the perineum. The electrodes were inserted with an 18 G needle in the leg biceps and pelvic floor. After careful palpation of the pelvic floor, the electrodes were inserted 1 to 1.5 cm deep, adjacent to the urethra in the bulbous urethral area. Additionally, two electrodes were placed under the skin in the back. These electrodes, with several inches of stripped insulation, served as grounding wires. Two small diameter Silastic tubes were also sutured into the dome of the bladder for bladder filling and pressure recording (14). A balloon catheter for abdominal pressure recording was placed in the abdomen. Electrode leads and catheters were tunneled and exteriorized and placed in an animal jacket for subsequent studies with tethering. Several of the animals had a bladder that was irritated and with small capacity after bladder instrumentation and were given Oxybutynin (1.5 mg BID) to increase bladder capacity

during the first 2 weeks after the surgery. The bladder catheters were also regularly flushed with antibiotic (Neosporin G.U. irrigant). Stimulation and cystometric studies were conducted 2–4 weeks after instrumentation.

Spinalization Procedures

A second survival surgery was conducted for spinalization 4–5 weeks after the animal instrumentation. The animals were reanesthetized and given an antihypertensive agent (8 mg per mouth, Nifedipine; 13–15) to reduce blood pressure increases associated with spinal injury procedures. The T-1 spinal cord dural space was surgically exposed. A small balloon was used for crushing the cord in the first two animals. However, this procedure was abandoned because the second cat developed some recovery of back leg function. The final three animals were spinalized using a hemostat compression for 20 s (13,14). These animals showed no recovery of back leg function. The animals were healthy for the 8–10 weeks that they were maintained in the study following spinal injury. An initial set of cystometric and stimulation studies were conducted 2–3 weeks, and a second set 4–7 weeks, after injury. Fluoroscopy was used on one day with radiopaque medium (Hypaque-76, Winthrop, NY) in the bladder. The lower urinary tract was observed during spontaneous and stimulation-induced voiding.

Urodynamic Studies

Urodynamic studies were conducted with the animals tethered in a urodynamic recording cage both before and after SCI. Pressures, EMG, and volume voided were recorded on an 8-channel recorder (Astromed, West Warwick, RI). Urine volume was collected in a funnel under the animal's cage and the weight of the fluid was recorded as a measure of the volume. Urine flow rate was assessed graphically by the slope of the volume voided record. Stimulation studies were conducted with an initial bladder volume one-half to two-thirds of cystometric capacity and isotonic saline at room temperature was used for filling. Cystometry was performed at 5 ml/min, until strong spontaneous bladder contractions associated with micturition occurred. Detrusor pressure was obtained by subtracting abdominal pressure from the recorded bladder pressure. Effects of stimulation on urethral functions were assessed with a urodynamic conductance factor, Area Equivalent Factor male (AEFm): AEFm (mm^2) = $3.7Q/P^{0.58}$, where AEFm estimates cross-sectional area of the flow controlling zone of the urethra during voiding in terms of detrusor pressure, P (cm H_2O) and flow rate, Q (ml/s). This factor has been found to be helpful in the evaluation of voiding difficulties due to obstruction (16,17) and stress urinary incontinence (18). This formula might have validity in urodynamic evaluation after SCI where reduced voiding is often seen due to membranous urethra contraction.

Direct Bladder Stimulation Studies

Both bipolar and monopolar stimulation were evaluated in all five animals. For bipolar stimulation, both negative and positive electrodes were on the bladder wall, while for monopolar stimulation the negative electrode was on the bladder wall and the positive electrode was in the back (described above as implanted grounding electrodes). Capacitor-coupled stimulation was conducted for balanced charge injection pulses with two stimulators (S48, Grass, Quincy, MA). The stimulators were isolated from ground and were constant current units (13,15). Stimulating parameters such as current and pulse duration were set with a dial on the front of the stimulator, and were checked on an oscilloscope. A standard stimulation was 40 pps for 3 s with a pulse duration of 1 ms (14). Stimulating parameters evaluated in this study included the period, frequency, current, and pulse duration. Each parameter was studied independently, keeping other parameters constant.

Additional studies included electrode corrosion and postmortem evaluations. Two bladder wall electrodes were pulsed at the end of the study in a bipolar configuration for 115 hours using 40 pps with 25 mA and 1 ms pulse duration. Following euthanasia, pulsed electrodes and nonimplanted electrodes were viewed with light microscopy and with scanning electron microscopy (SEM, by EIC Laboratories, Norwood MA). Postmortem bladder wall thickness was evaluated after fixation with the installation of 20 ml formalin (HT50 Sigma, St. Louis, MO). Histological sections at the electrode site were stained with H&E. Data are presented as mean $\pm$ SD. Statistics were conducted using Student's t-test with paired data.

RESULTS

Cystometry and Spontaneous Voiding

Five male cats were instrumented before SCI, and urodynamic studies were conducted 2–4 weeks after surgery when oxybutynine administration had been

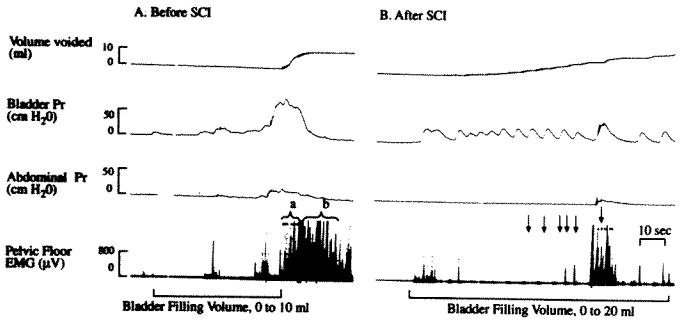

Figure 2.
Comparison of cystometry-induced micturition before and after SCI. A. Before SCI, showing voiding at a high flow rate. Records also show phasic pelvic floor activity during voiding (a) and stronger pelvic floor contractions at the end of voiding (b). B . After SCI, showing small bladder contractions with voiding at a low flow rate. Arrows indicate discharges of the pelvic floor. Record in B obtained 49 days following SCI.

stopped and bladder capacity had increased. In **Figure 2**, "A" shows cystometry-induced spontaneous micturition for one tethered cat with complete bladder emptying and at a high urine flow rate. A summary of micturition responses to cystometry for the five cats is shown in **Table 1.** Filling volumes for micturition ranged from 10 to 27 ml. Peak detrusor pressures during voiding were 32–75 cm H_2O and the peak urine flow rates were 0.6–2.2 ml/s (**Table 1**). Increased abdominal pressure during voiding was usually associated with the animal standing and assuming a voiding posture. Before SCI, the bulbous urethral EMG was unchanged during bladder filling in all of the animals, although movement-related changes occurred. Spiking in the EMG was seen during micturition, usually starting halfway through the voiding period and continuing to the end of voiding. As the detrusor pressure declined at the end of voiding, larger pelvic floor discharges were seen.

After SCI, an initial cystometry was conducted in the second to third week after injury. and a second cystometry was conducted after 5 weeks. For the first cystometry, numerous small bladder contractions occurred with little voiding. By 5 weeks after injury, bladder contractile activity increased. In **Figure 2,** "B" shows these stronger bladder contractions for one animal; however, the bladder contractions are short in duration and little voiding is shown. **Table 1** also shows this poor spontaneous voiding after SCI with rates from 0.1 to 0.2 ml/s and voiding that left high residual volume, ranging from 7 to 48 ml. Peak pressures ranged from 30 to 75 cm H_2O, and contractile activity typically started at 1–35 ml and continued to the end of bladder filling at 20–50 ml. After SCI, the bulbous urethral EMG was unchanged during bladder filling in all of the animals. The EMG showed small increases during bladder contractions with larger discharges at the end of bladder contractions and voiding.

Stimulation-Induced Voiding

Direct bladder stimulation resulted in prolonged bladder contraction and voiding both before and after SCI, as shown in **Figure 3. Table 1** summarizes the results for the five cats. Before SCI, peak detrusor responses to stimulation ranged from 22 to 74 cm H_2O. The initial filling volume for these stimulation studies ranged from 5 to 15 ml. The maximum voiding rates were 0.5–1.5 ml/s with a total volume voided with one stimulation period ranging from 5–15 ml and with minimal residual volume. The stimulating parameters for these

Table 1.
Urodynamic responses to cystometry and stimulation in the male cat before and after spinal cord injury.

	Filling Volume	Voided Volume	Pressure	Maximum Flow	AEFm
Cystometry:					
Before	17±7	14±5	50±17	1.2±0.6	0.44±0.13
After	34±11	8±6	46±18	0.1±0.04*	0.048±0.029*
Stimulation:					
Before	11±4	9±4	43±23	0.7±0.3	0.32±0.11
After	23±14	5±4	39±11	0.9±0.7	0.38±0.2

Means and SD for five animals for all data shown. Measures for each animal obtained as a typical record in response to a single stimulation period of 3-4 sec. Records after SCI obtained between 5 and 8 weeks after SCI. Volumes in ml; detrusor pressures (obtained at maximal urine flow rate) in cm H_2O; flow in ml/s; AEFm in mm^2.
*significantly different from cystometric results before SCI ($p \leq 0.05$).

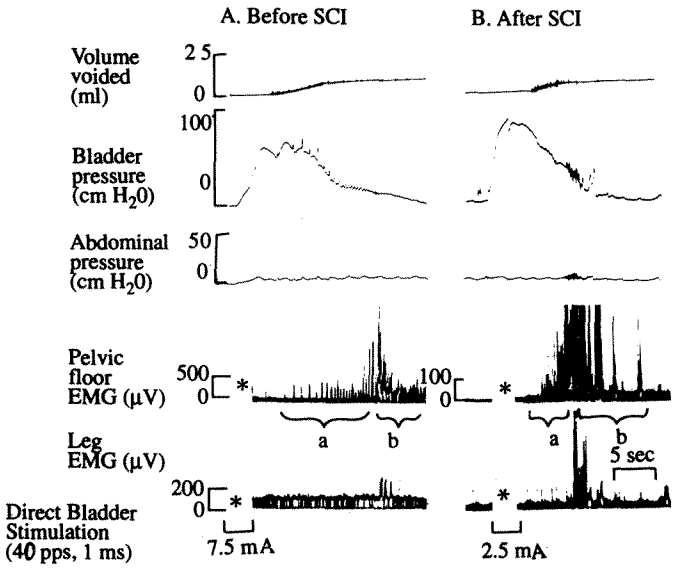

Figure 3.
Comparison of stimulation-induced voiding in one cat before and after SCI. A. Prolonged bladder contraction with 8 ml voided in response to 3 s of stimulation before SCI. Phasic pelvic floor contractions are shown during voiding (a) and stronger pelvic floor contractions are seen at the end of voiding (b). B. Responses to stimulation after SCI with 7 ml voided. Also shown is phasic activity percent (a), and strong pelvic floor contractions after voiding (b). Spinal animal 34 days postinjury. Note, similar urine flow rates in both records indicated by the slope of the volume voided record. * EMG not recorded during electrical stimulation.

voiding responses were 40 pps, 1 ms pulse duration, 3 s train with a current ranging from 7.5–40 mA. Before SCI, stimulation that induced strong bladder contractions in three of the five animals also caused discomfort. However, effective voiding was obtained at lower currents without noticeable discomfort to the animals as is shown in **Table 1.**

After SCI, three of the cats voided with stimulation in the first 2 weeks, and two of the cats did not respond to stimulation with voiding until the the third week. Average urodynamic responses are again summarized in **Table 1.** Maximal responses and stimulation parameters were similar to before SCI, again the current varied from 7.5–40 mA. Filling volumes ranged from 6–40 ml. Peak detrusor responses were 22 to 74 cm H_2O. The maximum voiding rates in response to stimulation 5–8 weeks after SCI ranged from 0.1 to 1.8 ml/s (**Table 1**). After 4–20 repeated stimulations, 3 animals completely emptied their bladders, but 2 animals retained a residual of 6 and 25 ml. These poorer voiding responses at smaller filling volumes may have been due to the shorter duration bladder contractions also seen at these smaller initial volumes (see fluoroscopic observations below). Another possible side effect of stimulation is leg movement, and this was seen in two cats during stimulation, and in two other cats at the end of voiding. An example of this is shown in **Figure 3** "B", where a strong discharge in the leg EMG is seen at the ending of voiding.

There was no increase in the EMG record for the five cats immediately following stimulation either before or after SCI (see A and B of **Figure 3**). Detrusor pressures were as high as 60 cm H_2O immediately following stimulation without increased urethral resistance indicated by the EMG signal. Spiking or phasic EMG responses were recorded during voiding and declining bladder pressures toward the end of voiding. This phasic activity was more prominent before than after SCI (see A and B of **Figure 3**). At the end of voiding, as bladder pressure declined, large pelvic floor contractions were seen both before and after SCI.

A urodynamic factor estimating urethral cross-sectional area, AEFm, showed that stimulation had little effect on urethral resistance (**Table 1**). At maximal flow, values for AEFm were not significantly different between cystometric-induced spontaneous voiding before SCI and stimulation-induced voiding both before and after SCI. Poor spontaneous voiding during cystometry after SCI is reflected in the small AEFm and low urine flow rates. As shown in **Figure 2** "B," the short duration of the bladder contractions during cystometry after SCI probably contributed to this poor voiding response.

Effective direct bladder stimulation techniques were determined. The application of negative polarity to the anterior bladder wall electrodes and positive to the posterior electrodes was superior in three of five cats both before and after SCI. This was indicated by higher peak detrusor pressures at lower currents. Stimulation using all four electrodes resulted in higher peak detrusor pressures than any combination of only two electrodes. Also, monopolar electrodes with negative electrodes on the bladder wall and positive electrodes along the back resulted in pain before SCI and in increased abdominal skeletal muscle movement after SCI. Subsequent evaluation of stimulating parameters were done using the observed optimum bipolar electrode arrangement with all of the electrodes on the bladder wall.

The frequency response study was conducted with a 1 ms pulse duration, 3–4 s stimulation periods, and at a current from 13–25 mA that was not varied in an individual animal. Maximum responses occurred at 40–60 pps in

four animals and 20 pps in the fifth animal; similar responses were obtained before and after SCI. For the pulse duration study only three cats were evaluated and 300 μs and 1 ms durations were compared. The 300 μs pulse duration induced similar peak detrusor pressures as 1 ms. However, the shorter pulse duration required 30–100 percent higher currents. Before SCI, there was no apparent difference in a discomfort threshold for the animal between the two pulse durations at similar peak detrusor responses.

Longer stimulation periods of 20–40 s also induced bladder contractions with voiding during stimulation in three of the five animals tested (**Figure 4**). For these three animals, voiding was induced during stimulation both before and after SCI, at pressures from 40–70 cm H_2O, Voiding was induced at 10 and 40 pps and was comparable to the 40 pps, 3–4 s stimulation periods. Responses in the two remaining animals were more varied. In one animal before SCI, the highest current used was 20 mA when the animal indicated slight discomfort. There was slight abdominal contraction with no bladder contraction and further studies were not conducted. In this same animal, 41 days after SCI the 20 s stimulation period at 25 mA induced a bladder contraction of 50 cm H_2O with an abdominal pressure of 15 cm H_2O. The initial volume in the bladder was approximately, 20 ml and the maximum volume voided with the single stimulation period was 6 ml. The maximal urine flow rate was 0.38 ml/s. A second cat voided in response to the 20–40 s stimulation with a low flow rate before SCI. After SCI, voiding during this

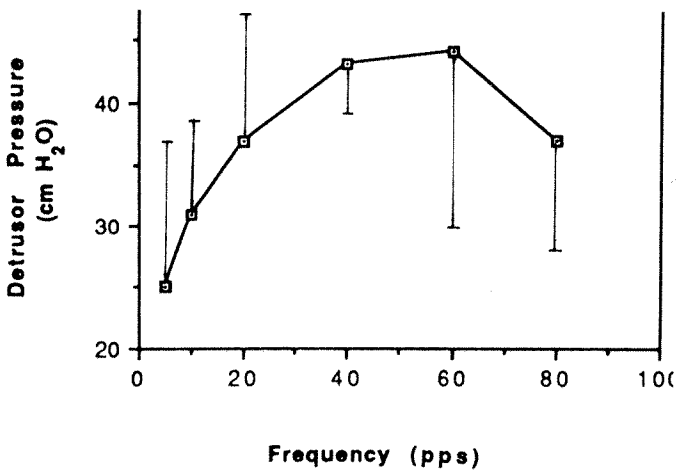

Figure 4.
Urodynamic responses to 20 s of continuous stimulation showing voiding during stimulation. A. Before SCI. B. After SCI. * the EMG was turned off during stimulation.

long-term stimulation was not observed in spite of pressures as high as 60 cm H_2O. Unfortunately, this cat was not viewed with fluoroscopy to further explain this response.

Fluoroscopic Observations

Fluoroscopic observations of the urethra during spontaneous and stimulation-induced voiding was obtained in four of the five animals and showed an important role of the penile urethra in regulating urine flow. Typical lower urinary tract responses to stimulation in three cats, A, B, and C, are shown in **Figure 5**. Before electrical stimulation and with bladder filled to 50–60 percent of the cystometric capacity, the bladder neck is closed before stimulation (A1 in **Figure 5**). During a maximal stimulation at 40 pps for 5 s, the entire urethra, including the membranous section, is seen to open and voiding commences (A2). However, the penile urethra is narrow, restricting urine flow (A3). A view from a second cat again shows the small penile urethra during stimulation-induced voiding (B1). The urethral emptying reflex is shown for C, the third cat. C1 again shows the open urethra during stimulation-induced voiding. C2 shows the initial closure of the membranous urethra at the end of voiding. Subsequently, the urethra was seen to continue to contract distally, emptying the penile urethra of urine. There was also some proximal urethral contraction pushing urine back into the bladder. The long bladder neck appeared to close passively and more slowly. In additional fluoroscopic observations (not shown), urethral activity during spontaneous bladder contractions appeared the same as stimulation-induced contractions.

Poor voiding responses appeared on the fluoroscope to be related to the small penile urethra. Direct bladder stimulation at low stimulating currents associated with low bladder pressures was seen to open the urethra only up to the membranous or penile length of urethra. Stimulation was also less effective in promoting voiding at small bladder volumes. Short duration bladder contractions occurred at smaller bladder volumes and were seen on the fluoroscope to open the urethra only up to the membranous or penile sections.

Postmortem Studies

Postmortem, mid-bladder-wall thickness was 3.3 ± 1.1 mm for the five animals, and evaluation of the electrodes revealed that they lay in a thin connective sheath in the serosa over the bladder wall. Histological evaluation of electrode sites revealed mature fibrous con-

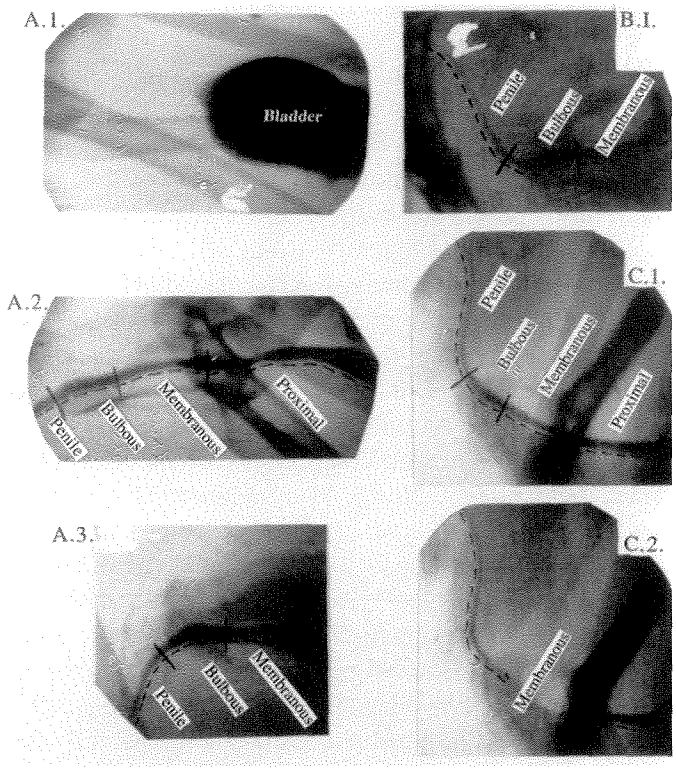

Figure 5.
Fluoroscopic views of the lower urinary tract during stimulation induced voiding from three different cats, A, B, C. A1. Bladder filled before electrical stimulation showing closed bladder neck. A2. Open urethra during 4–5 s of 40 pps stimulation at high current. A3. Subsequent view during continued voiding showing small cross-sectional area of penile urethra. B1. View of stimulation-induced voiding in a second cat showing a small penile urethra. C1. View of open urethra following direct bladder stimulation from a third cat. C2. Subsequent view showing urethral closure at the end of voiding. Urethral closure is initiated at the membranous urethra. Note, the bladder is to the right in each figure; the dashed line highlights the urethra and the solid lines through the urethra are the approximate dividing lines for each section of the urethra.

nective tissue around the electrode in three cats. Smooth muscle submucosal and urothelium under the electrode appeared the same as areas lateral to the electrode site. However, the urothelium and submucosal areas were thickened in all three animals showing inflammatory responses. Under light microscopy, all of the eight electrodes evaluated were shiny and without signs of corrosion after approximately 14 weeks of implantation and studies described here. In addition, two electrodes were continuously pulsed during the last 4.5 days (115 hours) before sacrificing the animals. Upon harvesting these electrodes, light microscopy observations revealed a shiny surface without loss of metal. However, based on SEM, the negative electrode had rare micro pits with little or no evidence of corrosion, whereas the positive electrodes had a few micro pits, which were increased in localized areas.

DISCUSSION

The Suture Electrode

The suture electrode was effective for direct bladder stimulation. The electrodes lay close to the bladder neurovascular bundles, yet did not have problems, such as erosion, migration, or excessive connective tissue formation limiting bladder filling. Implanting the electrodes with flexing (**Figure 1**) helped to allow for adjustment to bladder filling. One or no additional polypropylene sutures were required to hold the suture electrode on the bladder wall. Electrodes requiring no additional polypropylene sutures were looped and sutured in the same muscle location, and pulling on the cable showed that the electrode was secure. This implantation procedure is simpler than previously reported for direct bladder wall electrodes (5,8,11). Erosion of electrodes into the bladder has previously been reported as a problem (2,5). Since all of our electrodes were observed to lie in the outer serosa lining, erosion was not a problem in this animal model. An additional advantage of the suture electrode is that it extends over a portion of the bladder wall, which may help to activate the ramified pelvic nerves that innervate the bladder and require fewer electrodes on the bladder wall. For example, we previously reported that there was no difference between direct bladder stimulating with four and eight woven eye electrodes in the cat before SCI (14).

Pulsing the electrodes continuously for several days did not change the shiny luster on the electrode surface viewed with light microscopy and is similar to our previous observations on corrosion responses of pulsed 316LVM stainless steel woven eye electrodes (14). However, SEM evaluation here revealed some pit formations on the surface of the pair of electrodes pulsed for 115 hours. Although rates of corrosion can change over time, the large surface area of these electrodes results in charge injections densities lower than 20 $\mu C/cm^2$, which is generally not associated with an accelerated corrosion response (14,19).

Effective Stimulation Parameters

Current results are similar to our previous report using the woven eye electrode before SCI (14). For example, we confirm that bipolar stimulation with both electrodes on the bladder wall is more effective than monopolar stimulation with a positive distant electrode under the skin, because with monopolar stimulation, abdominal contraction and pain were seen before SCI, and muscle contraction associated with current spread to the distant electrode after SCI. Bipolar electrodes with positive and negative electrodes on the bladder wall did not appear to have these problems. Optimal bipolar arrangement in most of the cats had the negative electrode anterior, adjacent to the major neural enervation to the bladder, agreeing with work published by others (3,7,9). An effective stimulation protocol was capacitor-coupled monophasic pulses using the bipolar electrodes on the bladder wall and stimulating parameters of 40 pps, 300 μs to 1 ms pulse duration and 10–40 mA applied for 3–4 s resulting in post-stimulus voiding. Using the optimum stimulating parameters, the bladder was emptied with a single stimulation period before SCI and, in a majority of the cats, with repeated stimulations after SCI. Bladder reflexes are probably important in all stimulation-induced contractions. The sustained bladder contractions after the end of stimulation (**Figure 3**), both before and after SCI, indicate a strong reflex component to induced responses. Ebner et al. (20) recently showed that direct bladder stimulation with intravesical electrodes was mediated through sensory nerves and activation of micturition reflexes. One new result is related to short pulse durations. Previously, we reported that 250 μs before SCI in the cat resulted in pain at currents insufficient to induce peak bladder contractions obtained with longer pulse durations (14). Since it is advantageous to use short pulse durations as it reduces the total charge used for stimulation (20), we conducted the pulse duration study here comparing 300 μs and 1 ms. Although only three of the five animals were evaluated, results before SCI showed equally effective bladder contractions without pain for the two pulse durations. Between 30 and 100 percent higher currents were required for the 300 μs pulse duration to induce similar peak pressures as the 1 ms pulse duration. After SCI, there were similar responses.

Urodynamic Responses of Stimulation

Voiding in response to direct bladder stimulation was seen in this study, and we concluded that stimulation before and after SCI did not increase urethral resistance based on four urodynamic measures: 1) the pelvic floor EMG immediately following a 3–4 s stimulation period was not increased; 2) voiding was observed during stimulation (**Figure 4**); 3) the urodynamic factor, AEFm, showed no difference in uretheral resistance between spontaneous voiding before SCI and stimulation-induced voiding before or after SCI (**Table 1**); 4) fluoroscopy of the urethra during stimulation-induced voiding showed an open membranous urethra, and urethral mechanics appeared the same with spontaneous and stimulation-induced voiding. However, stimulation did not always induce voiding in spite of high bladder pressures. At smaller bladder volumes, stimulation-induced voiding was reduced or absent. This was seen in the relatively large number of stimulations required to empty the bladder after SCI and also, in some cats, residual urine after repeated stimulations. This poor voiding response at smaller filling volumes was probably due to short duration bladder contractions. For example, after SCI, cystometric-induced spontaneous voiding was poor, reflected in low AEFm values (**Table 1**), and this poor voiding was associated with short duration bladder contractions (**Figure 2**, "B"). Fluoroscopy of the urethra also revealed that the small penile urethra or membranous urethra did not open in some animals during the short bladder contractions at small filling volumes. A second observation of poor voiding was seen in some animals for the first few weeks following SCI. Voiding was not seen during stimulation or spontaneous bladder contractions during this early period. This time-dependent effect may have been a result of increased intrinsic urethral resistance in the early spinal cats. For example, it is difficult to empty the bladder of the spinal cats using suprapubic pressure early but not late after SCI (unpublished observations). A third observation of poor voiding responses was with the 20–40 s of continuous stimulation in one of the cats before and another after SCI. For the animal before SCI, stimulation induced low bladder pressures (<30 cm H_2O) probably insufficient to overcome urethral resistance. For the animal after SCI, fluoroscopic observations were not conducted in this animal to provide any further explanation.

In this animal model, we observed that the small penile urethra was a primary factor regulating urine flow. The small penile urethra as observed with fluoroscopy (**Figure 5**) would contribute to the high voiding pressures that were recorded in this study. Both stimulation-driven and spontaneous voiding before and after SCI had high bladder pressures ranging from 22–74 cm H_2O (**Table 1**). The penile urethra in the male cat is well known as a site

where obstructed voiding, including strictures, occurs (21,22).

Potential adverse responses to stimulation were investigated, such as bladder wall hypertrophy, pain, and leg and abdominal movements. The postmortem average wall thickness of 3.3 mm is thicker than the 1–2 mm thickness seen in normal cats (13). This response may be caused, in part, by the chronic catheters and effects of SCI in addition to the bladder wall electrodes and electrical stimulation. The bladder wall under the electrodes was unchanged from adjacent bladder wall, showing little tissue reaction to the electrodes. Discomfort is a concern with stimulation before SCI. This was limited by only using lower currents that did not cause pain. Leg spasms were also noted with stimulation and voiding in a few cats after SCI.

Animal Model of Spinal Cord Injury

In generalizing results from this study, it is important to take into consideration the lack of detrusor-sphincter-dyssynergia or high urethral resistance in this animal model. The high-level SCI cat does not appear to have the same high urethral resistance problem seen in upper-motor-neuron-lesioned SCI patients (23). For humans, urinary continence is obtained by a urinary continence reflex, indicated by increased pelvic floor EMG activity during bladder filling. After SCI, greatly increased membranous urethral contraction caused by exaggerated pelvic floor reflexes prevents voiding (23,24). In contrast, the continence reflex was not evident in the cats before or after SCI. There was no increase in the pelvic floor EMG during bladder filling. After SCI, there was an absence of increased EMG immediately following the end of electrical stimulation with bladder pressures as high as 60 cm H_2O. This observation was not due to inadequate amplification in our pelvic floor EMG signal: the rectified signals produced full-scale deflections during phasic urethral activity (**Figures 2–4**). These observations are particularly striking as others have described dyssynergia in the cat (25) and rat (26). For example, in the rat, increased EMG recordings from the membranous urethra have been used to describe a dyssynergic animal model (26). In comparison, our electrodes in the bulbous urethral area were not in the optimum location, which is the membranous urethra.

In this animal model, the urethra shows phasic activity that is not present in humans. Male cats conduct territorial marking by squirting their urine in jets. This squirting behavior appears to result from a combination of phasic contractions of the membranous urethra during urination and a nozzle effect of the narrow penile urethra (**Figure 5**; 21,22,27). Also, in this animal model the bladder is located up in the abdomen with a 4–5 cm preprostatic urethra (21,22), in contrast to the human where the bladder lies directly above the pelvic floor. Thus, bladder wall electrodes in the cat that are some distance from the pelvic floor would be less likely to induce pelvic floor contraction from electrical current spread than would similar electrodes in humans.

In conclusion, the suture electrode appears to be effective in activating the bladder in an SCI animal model. Several features of the electrode appear to make it advantageous. The electrode is simple to implant. The electrode stayed secured on the bladder wall without some of the erosion and migration problems previously reported (2,4,5). However, any clinical applications of the suture type electrode should take into consideration the cited limitation of this animal model. For example, clinical applications of direct bladder stimulation undoubtedly would require procedures to reduce or eliminate high urethral resistance. Several new treatments of high urethral resistance, such as implanted urethral stents (28), botulinus toxin injection into the membranous urethra (29), and improved sphincterotomy procedures (30), may increase the feasibility of direct bladder stimulation techniques.

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