

# Outcomes of Lumbar to Sacral Nerve Rerouting for Spina Bifida

Kenneth M. Peters, Benjamin Girdler, Cindy Turzewski, Gary Trock, Kevin Feber, William Nantau, Brian Bush, Jose Gonzalez, Evan Kass, Juan de Benito and Ananias Diokno

From the Ministrelli Program for Urology Research and Education (MPURE), and Department of Urology (KMP, BG, CT, KF, JG, EK, JdeB, AD), Department of Clinical Neurophysiology (WN, BB) and Department of Neurology (GT), William Beaumont Hospital, Royal Oak, Michigan

## Abbreviations and Acronyms

DR = dorsal root

EMG = electromyography

VR = ventral root

Submitted for publication November 25, 2009.  
Funded by Ministrelli Program for Urology Research and Education (MPURE)-Philanthropy.  
Study received institutional human investigation committee approval.

Additional clinical information can be found at <https://www.beaumont-hospitals.com/urology-clinical-trials>.

See Editorial on page 417.

**Purpose:** Restoring bladder and bowel function in spina bifida by creation of a skin-central nervous system-bladder reflex arc via lumbar to sacral nerve rerouting has a reported success rate of 87% in China. We report 1-year results of the first North American trial on nerve rerouting.

**Materials and Methods:** Nine subjects were enrolled in the study. Intradural lumbar to sacral nerve rerouting was performed. Subjects underwent urodynamic testing with stimulation of the cutaneous dermatome and careful neurological followup. Adverse events were closely monitored along with changes in bowel and bladder function.

**Results:** At 1 year 7 patients (78%) had a reproducible increase in bladder pressure with stimulation of the dermatome. Two patients were able to stop catheterization and all safely stopped antimuscarinics. No patient achieved complete urinary continence. The majority of subjects reported improved bowel function. One patient was continent of stool at baseline and 4 were continent at 1 year. Of the patients 89% had variable weakness of lower extremity muscle groups at 1 month. One child had persistent foot drop and the remainder returned to baseline by 12 months.

**Conclusions:** At 1 year a novel reflex arc with stimulation of the appropriate dermatome was seen in the majority of subjects. Improvements in voiding and bowel function were noted. Lower extremity weakness was mostly self-limited, except in 1 subject with a persistent foot drop. More patients and longer followup are needed to assess the risk/benefit ratio of this novel procedure.

**Key Words:** nerve transfer; spina bifida cystica; spina bifida occulta; urinary bladder, neurogenic

SPINA bifida is a congenital defect affecting approximately 0.2/1,000 live births in the United States.<sup>1</sup> Xiao et al introduced the concept of an artificial voiding reflex by intradural microanastomosis of a healthy lumbar motor root to a sacral motor recipient root.<sup>2</sup> By performing the procedure at the intradural root level the sensory limb is left intact, allowing for voluntary initiation of void-

ing by stimulating the appropriate cutaneous dermatome.

Initial studies done in rats involved microanastomosis of the left L4 ventral root to the left L6 ventral root.<sup>2,3</sup> After scratching the skin surface afferent information travels through the intact L4 DR and initiates the reflex. Further studies have established this technique in higher taxonomic species,<sup>4</sup> and recently have

been brought from bench to clinical practice in humans, involving microsurgical anastomosis of the L5 and S2/3 ventral roots.<sup>5,6</sup> Initially described in patients with spinal cord injury in 2003, the principle was expanded to spina bifida, with 85% of patients regaining satisfactory bladder control and continence postoperatively. Xiao updated the intradural artificial reflex arc experience with 110 patients with spina bifida in 2005, reporting an 87% success rate at 1 year.<sup>7</sup>

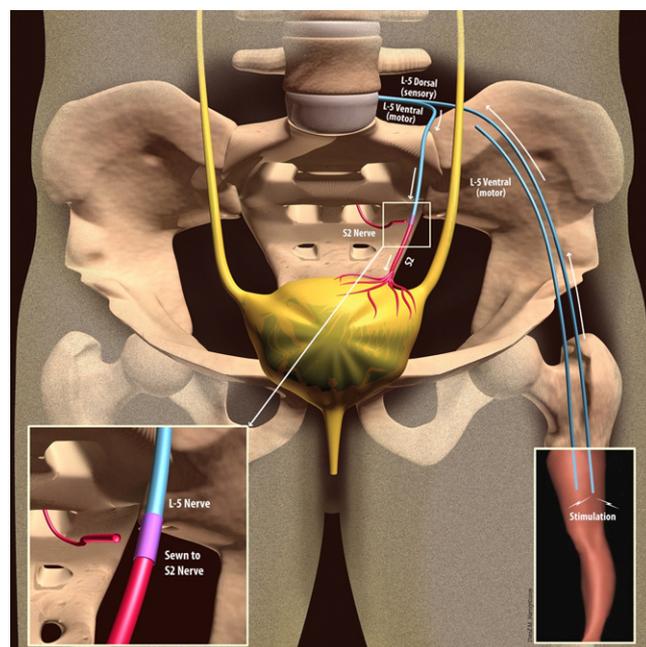
All of the human data reported in spina bifida have been gathered in China, and there is a need to study this rerouting concept in the United States. Thus, we designed the first known North American pilot study to investigate the safety and efficacy of this procedure in patients with spina bifida. We report our 1-year data on the first 9 consecutive patients treated at our institution.

## METHODS

The institutional human investigation committee approved this study and consent was obtained from the parents of minors in the trial. We used a pretest posttest pilot study design with a convenience sample of patients with myelodysplasia undergoing intermittent catheterization. Subjects underwent rigorous preoperative evaluation. Voiding diaries, and bowel and bladder questionnaires were completed. Computerized urodynamic testing off antimuscarinics with patch EMG and cystoscopy using a flexible ureteroscope were done to evaluate the status of the bladder, urethra and bladder outlet. Renal/bladder ultrasound, post-void residual and renal function blood tests were done to establish the baseline anatomy and function of the upper tracts and lower tracts. Magnetic resonance imaging of the lumbosacral vertebral levels was obtained and reviewed to evaluate the status of the spine, cord and cauda equina. Detailed neurological examination by a board certified neurologist, EMG and nerve conduction studies were done to establish the viability of the lower lumbar and upper sacral roots to serve as a donor root and evaluate baseline lower extremity function.

Surgery was performed by urological surgeons with the aid of Xiao, the innovator of this procedure. Needle EMG electrodes were inserted into the lower extremity muscle groups, and intraoperative neurophysiological monitoring was used to identify triggered and spontaneous EMG responses throughout the procedure. A limited laminectomy at the level of the first intact spinous process was performed between L4 and S2.

The ventral root of the donor nerve was identified and confirmed via time locked, triggered compound muscle action potential response. Nerve hooks were used to microdissect the ventral root from its corresponding DR. It is critical to keep the DR intact to act as the initiator of the reflex. An attempt was made to split the donor nerve longitudinally when possible, keeping a portion intact to decrease the likelihood of foot drop. The donor ventral root was transected at the orifice of the dura and the S3 VR was transected near the cord. The distal stump of the



**Figure 1.** Left ventral lumbar (L5) to sacral (S2) nerve rerouting

donor VR was anastomosed to the proximal stump of the S3 VR using 8-zero absorbable suture (fig. 1). The lowest nerve root that exhibited a reproducible muscle EMG response with intraoperative stimulation was chosen as the donor nerve.

Treatment outcomes were determined by conducting clinical and functional examinations before and after the procedure. Voiding diaries, global response assessment questionnaires and Burwood bowel questionnaire were assessed.<sup>8</sup> The parents of minors in the study completed the questionnaires.

Attempted cutaneous stimulation of the novel reflex pathway was begun at 3 months with the opposite leg dermatome serving as a control. The appropriate dermatome as well as the dermatome above and below were stimulated by scratching the skin for at least 10 seconds while measuring bladder pressures during a cystometrogram. This procedure was repeated at 50 cc intervals until MCC was reached. A positive reflex was defined as a reproducible bladder contraction of at least 10 cm H<sub>2</sub>O with cutaneous stimulation of the appropriate dermatome. If a cutaneous reflex was found, the subject and family were taught how to stimulate this site and attempt voiding before catheterization. Antimuscarinics were stopped by 9 months to help facilitate bladder contraction. Urodynamics confirmed safe bladder pressures off antimuscarinics.

Adverse events were monitored at each visit, and neurological assessment was repeated at 1 month and 1 year. Given the small number of subjects, descriptive statistics are presented.

## RESULTS

Three males and 6 females underwent lumbar to sacral nerve rerouting (table 1). Median patient age

**Table 1.** Patient baseline characteristics

Pt No.—Age	Height (inches)	Wt (lbs)	Lesion Level	Defect Closed	Ventriculoperitoneal Shunt	History of Tethered Cord Release	Antimuscarinic	Incontinence	
								Stress	Urge
1—6	44.5	39.0	S3	Not applicable	No	No	No	Yes	No
2—7	50.5	62.0	L5/S1	In utero	Yes	Yes	Yes	No	Yes
3—13	52.5	136.0	L3/L4	Birth	Yes	Yes	Yes	No	Yes
4—7	51.3	87.0	L3	In utero	No	No	No	Yes	Yes
5—6	45.0	58.0	S3	Birth	No	Yes	Yes	Yes	No
6—17	63.3	110.0	L4	Birth	Yes	Yes	No	No	Yes
7—8	49.0	63	L5	In utero	Yes	No	Yes	Yes	Yes
8—8	44.5	51	L3/L4	Birth	Yes	No	Yes	Yes	Yes
9—37	72.0	155	L4	Birth	No	Yes	No	No	Yes

was 8 years (range 6 to 37). Five patients had the spinal defect closed at birth, 3 underwent intrauterine closure as part of a clinical trial and 1 had a myelolipoma but no cutaneous defect. All patients were ambulatory, with 4 requiring no assistance, 4 requiring ankle-foot orthotics and 1 requiring forearm crutches. At baseline only 2 subjects were able to void some urine by any means.

The procedure took an average of 183 minutes (range 127 to 278), mean blood loss was 57 cc (10 to 100) and there were no intraoperative complications. Active donor roots were found in all patients at various levels. The side of the donor and recipient nerves varied, and was dependent on intraoperative findings. Since this procedure involves sacrificing at least a portion of a nerve that innervates the lower extremity, postoperative weakness was expected. During surgery we had to sacrifice the whole donor nerve in 4 patients and half of a donor nerve in 5.

At 1-month neurological evaluation 8 patients had weakness in 1 or more lower extremity muscle groups in the expected dermatome distribution, 2 had major gait changes and 1 had persistent foot drop. The subject with foot drop had half of her donor nerve left intact during surgery. By 1 year all patients were at or near baseline function except for 1 with foot drop who had significant worsening of

her gait. No other long-term complications were identified.

Between months 6 and 9 a number of patients reported worsening of bowel and bladder incontinence, then began to have an increased awareness of bladder and bowel sensations, suggesting reinnervation of these structures. The majority of subjects reported improvement in bowel function before changes in bladder function.

Computerized urodynamics were performed while stimulating the appropriate dermatome, and bladder pressures were monitored to assess development of a cutaneous/bladder reflex. Patients were also asked to attempt to void, and uroflow volumes and post-void residuals were measured. Table 2 summarizes baseline and 12-month data. At 12 months 7 patients had a reproducible bladder reflex with cutaneous stimulation (fig. 2), with 1 present at 3 months, 4 at 6 months, 5 at 9 months and all 7 at 12 months. In addition, 7 patients could initiate a spontaneous void with an average voided volume of 133 cc (range 50 to 250), a mean post-void residual of 119 cc (10 to 380) and a maximum flow of 10 cc per second (4 to 25). Bladder compliance improved from 16.1 ml/cm H<sub>2</sub>O (range 6.6 to 28.6) at baseline to 21.8 ml/cm H<sub>2</sub>O (7.8 to 53.8) at 12 months. Two of three cases with a baseline compliance of less than

**Table 2.** Voiding and Urodynamic Data

Pt No.	Max Cystometric Capacity (cc)		Neurogenic Detrusor Overactivity		Sensation of Bladder Filling		Antimuscarinic		Reflex Present	Voiding	
	Baseline	12 Mos	Baseline	12 Mos	Baseline	12 Mos	Baseline	12 Mos		Baseline	12 Mos
1	252	180	No	No	No	Yes	No	No	No	No	Yes
2	200	402	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes
3	165	210	Yes	No	Yes	Yes	Yes	No	Yes	No	No
4	200	269	Yes	No	Yes	Yes	No	No	Yes	No	Yes
5	48	192	No	No	No	No	Yes	No	Yes	No	Yes
6	350	393	No	No	Yes	Yes	No	No	No	No	Yes
7	226	214	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No
8	189	155	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
9	269	268	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes



nor nerve will send a signal through the ventral nerve, resulting in a bladder contraction. This reflex was noted in 7 of our 9 subjects at 12-month followup, proving that this reinnervation can be demonstrated in humans. Interestingly 2 subjects (patients 1 and 6) began to void spontaneously and exhibited improvement in bowel function. However, we were unable to elicit a cutaneous reflex, possibly due to our inability to find the appropriate cutaneous site along the dermatome to activate the bladder, although the brain ultimately has the ability to control bladder function.

Further investigation will be necessary to clarify and confirm synergy between bladder and external sphincter with voiding. The sphincter EMG data were inadequate due to artifact caused by stimulating the dermatome, and we are currently using a dual electrode catheter to monitor bladder and sphincter pressures simultaneously. Renal function remained stable during this trial and no new hydro-nephrosis was identified.

Surprisingly many subjects reported an increased sensation of bladder and bowel. Although at baseline most patients reported sensation of bladder filling that occurred near cystometric capacity (table 2), at 6 to 9 months postoperatively the character of this sensation changed in that they had early sensations of bladder and bowel fullness, and with stimulation of the dermatome would announce they needed to urinate. This result was difficult to capture on case report forms. The development of new sensory function is interesting and difficult to explain, and challenges our current understanding of neurourology. Interestingly many subjects learned to void without stimulation of the dermatome, suggesting some remodeling at the level of the micturition center of the brain. Functional magnetic resonance imaging preoperatively and postoperatively may help to elucidate what occurs at a central level.

A difficult aspect of this study is how success should be defined, given that there is a constellation of symptoms associated with neurogenic bladder and bowel. Does the benefit of the procedure outweigh the inherent risks, particularly to the lower extremity? Is success defined as eliciting a detrusor contraction with stimulation of the dermatome? If this is the definition of success, then this surgery clearly works for the majority of patients. In addition, a number of patients have noticed a change in their voiding and bowel function, with several reporting improvements including increased sensation of the bowel and bladder, new ability to initiate voiding, improved bowel function, less detrusor overactivity and the ability to stop antimuscarinics. Are these changes enough to define success? Our clinical success at 12 months is less than the 85%

previously reported.<sup>7</sup> However, these are interim data and may change with time.

Despite these encouraging findings, at 12 months only 2 subjects have stopped catheterization and many still have issues associated with incontinence. Additionally most had significant postoperative weakness that required months to return to baseline. Also, 1 child has persistent foot drop that has permanently changed the way in which she ambulates despite splitting the nerve and keeping half of L5 intact. Importantly the negatives associated with this surgery continue to improve, and no patient has plateaued regarding improvement in bowel and bladder function. The fact that 7 of 9 patients would undergo the procedure again, despite modest improvements in symptoms, reveals the willingness of patients to seek new treatments for bowel and bladder dysfunction.

Limitations of this study include the small number of subjects and relatively short followup of 12 months. In addition, given that we were dealing primarily with children, it was difficult to obtain ideal urodynamic testing. Several factors account for this problem, including cooperation of the children in tolerating prolonged urodynamic testing. This testing entailed repeated stimulation of the cutaneous dermatome while monitoring bladder and abdominal pressures, and trying to get the children to attempt to void with urodynamic catheters in place.

Another limitation of the study was lack of objective measures of continence such as pad weight. In addition, it was difficult to assess sphincter function due to artifact on the EMG tracing caused by scratching. Regarding bowel function, we had no objective measure of sphincteric activity such as anal manometry or good measure of sensory function. Also, there was no control group to assess the effect of scheduled followup visits on bowel and bladder habits. Finally self-administered questionnaires by parent proxy may provide an inaccurate measure in a subjective scoring system.

Despite these limitations, it is clear that somatic to visceral nerve rerouting can be achieved. More patients with longer followup are needed to determine the true benefit of this procedure. If additional studies show this to be an effective treatment to restore bowel and bladder function, it could have a positive impact on the cost of medical care and quality of life for those suffering from many causes of neurogenic bladder and bowel.

## CONCLUSIONS

This is the first known North American trial on lumbar to sacral nerve rerouting to restore bladder and bowel function in patients with spina bifida. Although the majority of subjects experienced lower

extremity weakness immediately postoperatively, most returned to baseline within 12 months. The exception was 1 patient with a persistent foot drop. Seven subjects had a reproducible bladder contraction with stimulation of the appropriate dermatome, proving the development of a somatic to visceral reflex. The impact of this surgery on improvement in quality of life still needs to be determined. This

procedure should remain on a research protocol, and more patients and longer followup are needed to understand fully the associated risk/benefit ratio.

## ACKNOWLEDGMENTS

C. G. Xiao provided guidance in developing the trial and expertise in training the surgeons involved.

## REFERENCES

1. Lary JM and Edmonds LD: Prevalence of spina bifida at birth—United States, 1983-1990: a comparison of two surveillance systems. *MMWR Morb Mortal Wkly Rep* 1996; **45**: 15.
2. Xiao CG, Schlossberg SM, Morgan CW et al: A possible new reflex pathway for micturition after spinal cord injury. *J Urol* 1990; **143**: 356A.
3. Xiao CG and Godec CJ: A possible new reflex pathway for micturition after SCI. *Paraplegia* 1994; **325**: 300.
4. Xiao CG, DeGroat WC, Godec CJ et al: Skin-CNS-bladder reflex pathway for micturition after spinal cord injury and its underlying mechanisms. *J Urol* 1999; **162**: 936.
5. Xiao CG, Du M-X, Dai C et al: An artificial somatic-central nervous system-autonomic reflex pathway for controllable micturition after spinal cord injury: preliminary results in 15 patients. *J Urol* 2003; **170**: 1237.
6. Xiao CG, Du M-X, Li B et al: An artificial somatic-autonomic reflex pathway procedure for bladder control in children with spina bifida. *J Urol* 2005; **173**: 2112.
7. Xiao CG: Rerouting for neurogenic bladder: historic review and introduction of a somatic-autonomic reflex pathway procedure for patients with spinal cord injury or spina bifida. *Eur Urol* 2006; **49**: 22.
8. Lynch AC, Wong C, Anthony A et al: Bowel dysfunction following spinal cord injury: a description of bowel function in a spinal cord-injured population and comparison with age and gender matched controls. *Spinal Cord* 2000; **38**: 717.

## EDITORIAL COMMENTS

The authors present the first North American experience with lumbar to sacral nerve rerouting for patients with spina bifida. The results from this study and previous animal and clinical studies by Xiao clearly demonstrate that nerve rerouting produces a somatic-autonomic or cutaneous/bladder reflex with stimulation of the lower extremity dermatome.<sup>1</sup> What is also clear is that the clinical benefit of the procedure is not at all similar to previous reports.

Although the authors did an excellent job of following the patients and characterizing their changes, the results are hard to validate without a control population going through the same rigorous surveillance regimen. In particular the improved bowel continence and minimal changes in bladder compliance may not be statistically significant. The fact that most patients were still on clean intermittent catheterization and none achieved complete urinary continence is troubling in light of the report

of 87% success with 110 children with spina bifida presented by Xiao.<sup>1</sup> One has to wonder if most of these children are not voiding volitionally or using the newly developed cutaneous reflex, and how much reinnervation has a role in this surgery. Is it possible that unilateral denervation of the S3 ventral motor nerve produced improved compliance and continence, as previously reported in numerous clinical series?<sup>2,3</sup>

I congratulate the authors for taking on this challenge. I hope this study leads to a rebirth or refocus regarding neurosurgical treatments of neuropathic bowel and bladder. I strongly agree with the authors that this procedure should remain on a research protocol only.

**Eric A. Kurzrock**

*Pediatric Urology*

*U. C. Davis Children's Hospital  
Sacramento, California*

## REFERENCES

1. Xiao CG: A somatic-autonomic reflex pathway procedure for neurogenic bladder and bowel: results on 92 patients with SCI and 110 children with spina bifida. In: *Proceedings of International Conference of Urology*. Shanghai, China, July 2-4, 2005.
2. Lucas MG, Thomas DG, Clarke S et al: Long-term follow-up of selective sacral neurectomy. *Br J Urol* 1988; **61**: 218.
3. Hohenfellner M, Pannek J, Botel U et al: Sacral bladder denervation for treatment of detrusor hyperreflexia and autonomic dysreflexia. *Urology* 2001; **58**: 28.

One of the most curious findings is the discrepancy between urodynamic data and subjective voiding. One patient exhibited a decrease in capacity and an absence of reflex arc, and yet he subjectively reported improved bladder and bowel function! I could not help but speculate that his voiding after the procedure could simply be the bladder emptying via intra-abdominal pressure generation against an open bladder neck, given his preoperative stress incontinence.

Xiao reported that more than 87% of 110 patients gained sensation and continence within 1 year (refer-

ence 7 in article). In comparison, the current patients undergoing the identical procedure with the help of Xiao himself only showed a modest improvement in objective urodynamic studies and subjective reporting. Unless the innovators provide a sound argument and data for the validity of the procedure, there is a great danger of its improper and rapid adaptation by patients and the medical community at large.

---

**John M. Park**

*Department of Urology  
University of Michigan Medical School  
Ann Arbor, Michigan*

---

## REPLY BY AUTHORS

We agree this is a challenging study on many levels. The intent of publishing these 1-year data was to understand the potential complications associated with lumbar to sacral nerve rerouting, demonstrate that a cutaneous to bladder reflex is achievable and, given

the nationwide interest in this procedure, reinforce the need to continue this rigorous research protocol until more is known about the risk-benefit profile. Hopefully our 36-month data will shed more light on the clinical usefulness of this innovative procedure.