ORIGINAL CONTRIBUTION

Long-term Durability of Sacral Nerve Stimulation Therapy for Chronic Fecal Incontinence

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BACKGROUND: Limited data have been published regarding the long-term results of sacral nerve stimulation, or sacral neuromodulation, for severe fecal incontinence.

OBJECTIVES: The aim was to assess the outcome of sacral nerve stimulation with the use of precise tools and data collection, focusing on the long-term durability of the therapy. Five-year data were analyzed.

DESIGN: Patients entered in a multicenter, prospective study for fecal incontinence were followed at 3, 6, and 12 months and annually after device implantation.

PATIENTS: Patients with chronic fecal incontinence in whom conservative treatments had failed or who were not candidates for more conservative treatments were selected.

INTERVENTIONS: Patients with ≥50% improvement over baseline in fecal incontinence episodes per week during a 14-day test stimulation period received sacral nerve stimulation therapy.

MAIN OUTCOME MEASURES: Patients were assessed with a 14-day bowel diary and Fecal Incontinence Quality of Life and Fecal Incontinence Severity Index questionnaires. Therapeutic success was defined as ≥50% improvement over baseline in fecal incontinence episodes per week. All adverse events were collected.

RESULTS: A total of 120 patients (110 women; mean age, 60.5 years) underwent implantation. Seventy-six of these patients (63%) were followed a minimum of 5 years (maximum, longer than 8 years) and are the basis for this report. Fecal incontinence episodes per week decreased from a mean of 9.1 at baseline to 1.7 at 5 years, with 89% (n = 64/72) having ≥50% improvement ($p < 0.0001$) and 36% (n = 26/72) having complete continence. Fecal Incontinence Quality of Life scores also significantly improved for all 4 scales between baseline and 5 years (n = 70; $p < 0.0001$). Twenty-seven of the 76 (35.5%) patients required a device revision, replacement, or explant.

CONCLUSIONS: The therapeutic effect and improved quality of life for fecal incontinence is maintained 5 years after sacral nerve stimulation implantation and beyond. Device revision, replacement, or explant rate was acceptable, but future efforts should be aimed at improvement.

KEY WORDS: InterStim therapy; Sacral nerve stimulation; Sacral neuromodulation; Fecal incontinence.

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Fecal incontinence (FI) is a distressing problem affecting 8% to 18% of the adult population.[1–3] The most common risk factors for FI are anterior sphincter defects secondary to obstetrical trauma.[4,5] Traditionally, sphincter defects were treated with an overlapping sphincter repair. However, poor long-term functional outcome, as reported in several articles, has prompted caregivers to seek alternative therapies that provide durable long-term results.[6,7]

Sacral nerve stimulation (SNS), also referred to as sacral neuromodulation, was first reported to treat FI by Matzel et al[8] in the *Lancet* in 1995. Significant improvement in bowel control was noted and led to widespread use worldwide. Over the past 15 years, institutions outside the United States have reported impressive safety and efficacy results.[9] Another attractive benefit of SNS versus most other therapies is that implantation involves a 2-stage procedure. During stage 1, the efficacy of the device can be ascertained before the chronic components are placed during stage 2.

Even though the successful use of the SNS technique for FI has been reported since 1995,[8] few long-term studies have been published. Many lack both rigorous follow-up and validated study tools. The aim of this study is to assess the outcome of SNS by using precise tools and data collection with a focus on the long-term durability of the therapy.

PATIENTS AND METHODS

Study Design and Objectives

This prospective, nonrandomized, US Food and Drug Administration (FDA)-regulated study was conducted in 14 centers in the United States, 1 in Canada, and 1 in Australia from 2002 through 2012. Patients with chronic FI in whom conservative treatments had failed or who were not candidates for more conservative treatments received SNS with the use of InterStim Therapy (FDA-approved in March 2011, Medtronic, Minneapolis, MN) and were thereafter followed at predetermined intervals to evaluate the efficacy and safety of the therapy. Previous publications from this study provide additional detail regarding study procedures.[10–13] The study protocol was approved by the FDA and institutional review boards at all participating institutions. The present article provides an overview of the 120 patients who received the SNS therapy, but focuses on the long-term durability of the therapy in the patients who were followed for at least 5 years after device implantation at the time of data cutoff for this article (February 22, 2012).

Study Patients

Candidates for SNS who provided informed consent and met inclusion and exclusion criteria, as previously described,[12] were enrolled. All patients experienced chronic FI, defined as more than 2 episodes of incontinence of fecal material per week for a duration of longer than 6 months (1 year after vaginal childbirth), had failed or were not candidates for more conservative medical treatments, and were 18 years of age or older with no upper limit.

Assessments at Baseline and at Follow-up Visits

Baseline assessments[11,12] were performed and qualified patients underwent a staged implant procedure with a percutaneous subchronic test stimulation for a period of 10 to 14 days to determine the effectiveness of the therapy. Patients who showed ≥50% improvement in incontinent bowel episodes were eligible to receive the chronic implant. All patients undergoing implantation were followed at 1 month, 3 months, 6 months, and annually until exited from the study. Therapeutic success was defined as a ≥50% improvement in incontinent bowel episodes per week.

Bowel Diary

A bowel episode diary was completed at baseline and at each scheduled follow-up visit (with the exception of the 1-month visit) for 10 to 14 days to assess the efficacy of the therapy. The diary contained 5 questions pertaining to each bowel episode: amount of incontinence, urgency, ability to defer defecation, occurrence of the episode during sleep, and stool consistency. Stool consistency was graded by using the validated Bristol Stool Scale,[14] and patients were excluded at baseline if they had stool consistency of liquid (Bristol 7) or mush quality (Bristol 6).

Fecal Incontinence Quality of Life

The patient's quality of life was measured at baseline and each follow-up visit (with the exception of the 1-month visit) by using the validated Fecal Incontinence Quality of Life (FIQOL) questionnaire[15] as previously described.[10]

Fecal Incontinence Severity Index

In addition, the patient's perception and physician scoring of symptom severity was measured by using the Fecal Incontinence Severity Index (FISI).[16] Patients were also asked to rate their bowel health on a scale of 0 to 10, with 0 being the worst imaginable state and 10 being the best imaginable state, and report on their use of minipads, panty liners, or other protective undergarments.

Adverse events were collected at test stimulation, device implantation, scheduled or unscheduled follow-up visits, or during additional surgical procedures, when they occurred. They were recorded on standardized adverse events case report forms and were included in the analysis. An independent Adverse Events Committee adjudicated each adverse event for seriousness and relatedness to the device, therapy, or implant procedure.

Statistical Analysis

The software package SAS version 9.2 (SAS Institute, Inc, Cary, NC) was used for all data analyses. The exact binomial test for a 1-sample proportion was used to compare the proportion of patients achieving ≥50% reduction in weekly FI episodes, FI days, or urgent FI episodes against a null value of 50%. A more conservative sensitivity analysis was also conducted to address missing data, which imputed missing 5-year data for the number of FI episodes per week as follows: if a patient discontinued from the study because of a lack of efficacy, a device/therapy-related adverse event, or a death (regardless of relatedness to the device or therapy), the patient's baseline diary was carried forward in the analysis; otherwise, if a patient discontinued from the study, missed the 5-year visit, or did not complete a 5-year diary for reasons unrelated to the device or therapy, the patient's last (ie, most recent) diary was used in place of missing 5-year data.

A comparison of baseline characteristics, with the use of the Wilcoxon rank sum test for continuous data and a Fisher exact test for categorical data, was done between patients with ≥50% improvement at 5 years and those patients with <50% improvement at 5 years or those who exited because of the lack of efficacy before the 5-year visit.

Changes from baseline to the 5-year follow-up in FI symptoms and quality-of-life measures were evaluated with either the paired *t* test or the Wilcoxon signed rank test after testing for data normality. Patients' responses to a survey question on pad use were summarized at baseline and follow-up visits.

Device/therapy-related adverse events were summarized by number of events and the percentage of patients experiencing each event. The number of patients with device revisions, replacements, and permanent explants was summarized. Three analyses of time to first event were conducted by using actuarial life table methods with yearly intervals to examine the cumulative probability of having 1) a device revision or replacement, 2) a permanent device explant, and 3) a device revision, replacement, or explant (any surgical intervention) after implant.

RESULTS

Patients

A total of 285 patients with chronic FI were evaluated for potential enrollment at 16 institutions, of whom 152 were excluded from further participation in the study, primarily because they did not meet the study criteria for degree of FI as previously outlined.[12] One-hundred thirty-three patients underwent acute test stimulation, and 120 achieved ≥50% improvement in incontinent bowel episodes during the test stimulation phase and successfully underwent implantation of the device. Previous surgical procedures, baseline demographics, origins of FI, and concurrent medical disorders have been reported previously.[11,12]

Seventy-six of the 120 patients who received the chronic implant were followed for a minimum of 5 years postimplantation and are the focus of this report. Seventy-four of these 76 patients who were enrolled in the study for at least 5 years completed a 5-year follow-up visit, some of whom also completed 6-, 7-, and 8-year postimplantation follow-up visits (Fig. 1).

Forty-four patients exited the study before reaching their 5-year visit. Twenty-eight of these patients (63.6%) had achieved at least a 50% improvement in weekly incontinent episodes at their last follow-up visit (Table 1). The reasons for study exit for these 44 patients include terminal illness of the local principal investigator[11] with further patient follow-up not possible (n = 14); and device/therapy-related adverse events (AEs) (n = 8), lack of efficacy (n = 7), death (n = 5), other patient-related reasons (n = 10).

Therapy Durability

Effect on FI Symptoms. The majority of patients with long-term follow-up showed therapeutic efficacy at each follow-up visit after implantation of the InterStim system. At 5 years postimplantation, 89% (64/72) of patients contributing bowel diary data had at least a 50% improvement from baseline in weekly incontinent episodes ($p < 0.0001$; Fig. 2). In addition, 36% (26/72) of patients at 5 years postimplantation had achieved total continence. The average number of weekly incontinent episodes decreased from 9.1 at baseline to 1.7 at 5 years ($p < 0.0001$). This improvement from baseline was observed past 5 years; however, significance testing was not conducted after the 5-year follow-up visit.

A sensitivity analysis of the 5-year efficacy results was conducted for weekly incontinent episodes to account for the missing data for 48 of the patients who had undergone implantation. Under this method of imputation, with 20 patients using the baseline observation and 28 patients using the last observation carried forward, 69% (83/120) of patients achieved at least a 50% improvement from baseline in weekly incontinent episodes ($p < 0.0001$).

Similar long-term improvements in weekly incontinent days and weekly urgent incontinent episodes were observed for patients who were followed in the study for at least 5 years. At the 5-year follow-up visit, 86% (62/72) of patients had at least a 50% improvement in the number of weekly incontinent days from baseline ($p < 0.0001$), and 79% (57/72) of patients had at least a 50% improvement in the number of weekly urgent incontinent episodes from baseline ($p < 0.0001$). The majority of patients receiving SNS therapy long-term showed a sustained improvement in FI.

Analysis of the response to the therapy in patients who completed both 1-year and 5-year bowel episode diaries (n = 70) showed that at 1 year, 62 patients (89%) had

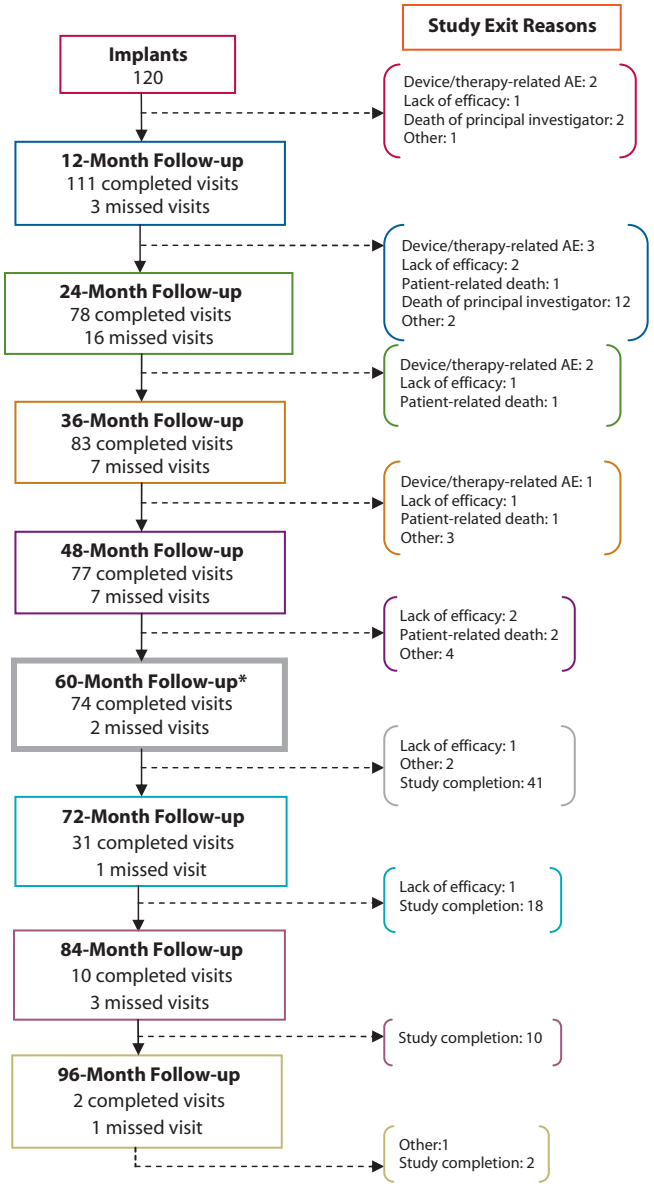


FIGURE 1. Summary of follow-up visits and study exit reasons for all study patients. AE = adverse event.

≥50% improvement, and 62 (89%) of the 70 had success at 5 years. For the 8 patients who were not categorized as successful at 1 year, 5 patients became successful at 5 years. An additional 5 patients who were successful at 1 year were not successful at 5 years, but continued to use the therapy.

Of the 57 patients contributing bowel diary data at each annual visit through 5 years postimplantation, 43 (75.4%) achieved therapeutic success at every visit. Seven patients achieved success at 4 of the 5 visits, and the remaining 7 patients achieved success at either 3 (n = 3), 2 (n = 2), or 1 (n = 2) of the 5 visits.

A comparison of baseline characteristics of the 64 patients with ≥50% improvement at 5 years and the 15 patients with <50% improvement at 5 years (n = 8) or those who exited because of lack of efficacy before the 5-year visit (n = 7) showed significance in 2 areas: average percentage of improvement at test stimulation (90% vs 80%; $p = 0.0072$) and the percentage of patients completely continent during test stimulation (47% vs 7%; $p = 0.0035$; Table 2 and Table 3). A scatterplot was used to explore the relationship between test stimulation and long-term efficacy, demonstrating that patients experienced long-term success across a wide range of improvement at test stimulation (Fig. 3).

Effect on Quality of Life, Symptom Severity, Bowel Health and Pad Use. Long-term improvements in patients' quality of life after SNS have been previously reported.[10] The results from the present analysis show that the improvements in average FIQOL component scales were also observed in this cohort of patients with at least 5 years of follow-up and maintained through long-term follow-up in the study (Fig. 4). Improvements in all 4 scales of the FIQOL from baseline to 5 years postimplantation were statistically significant (Table 4).

The FISI (both surgeon- and patient-weighted scores) decreased after implant, and the reduction was sustained long-term for patients with at least 5 years of follow-up in the study (Fig. 5). With the use of the patient weighting, the mean FISI decreased from 37.95 at baseline to 28.33 at the 5-year follow-up ($p < 0.0001$); similarly, with the surgeon weighting, mean FISI decreased from 38.58 at baseline to 29.26 at the 5-year visit ($p < 0.0001$) (Table 5).

Improvements in self-rated bowel health postimplantation were also sustained long-term for patients with at least 5 years of follow-up in the study (Fig. 6). Self-rated bowel health (0–10 scale) improved significantly from 3.55 at baseline to 7.29 at 5 years postimplantation ($p < 0.0001$).

Patient use of minipads and panty liners or other protective undergarments was also reduced through long-term follow-up. At baseline, before device implantation, 65% of patients with at least 5 years of follow-up in the study reported using some form of undergarment protection all of the time (Fig. 7). At 5 years postimplantation, the percentage of these patients who reported using undergarment protection all of the time decreased to 37%. In addition, 30% of patients reported no use of undergarment protection at the 5-year follow-up in comparison with 3% before device implantation.

Safety

The entire group of 120 patients who had received implants accumulated 559 device-years of experience, ranging from 0.2 to 9.3 years, with a mean postimplantation follow-up time of 4.7 years. The 76 patients who remained in the study for a minimum of 5 years, and who are the focus of this report, accumulated 468 device-years of experience,

TABLE 1. Percentage of improvement in weekly incontinent episodes at last visit before exit for patients who discontinued before 5-year follow-up visit

	Categorized percentage of improvement					
Last visit	*100%*	*75%–99%*	*50%–74%*	*0%–49%*	*≤0%*	*Total*
Test stimulation	0	0	1	1[a]	0	2
3-mo	0	0	0	2	1	3
6-mo	3	2	0	1	0	6
1-y	6	6	5	2	5	24
2-y	0	0	0	1	1	2
3-y	1	1	0	0	1	3
4-y	0	1	2	0	1	4
Total	10	10	8	7	9	44

[a]Patient was implanted because of meeting implant criteria for ≥50% improvement in weekly incontinent days.

averaging 6.2 years of follow-up. The 44 patients who discontinued before their 5-year follow-up visit averaged 2.1 years of follow-up per patient. Over the course of the study, the 76 patients with at least 5 years of follow-up experienced 218 of the 307 total device/therapy-related adverse events.

Table 6 summarizes the 307 device/therapy-related adverse events that occurred during the course of the study, with the most frequently occurring device/therapy-related adverse events listed individually in the table. Overall, these events include implant site pain (n = 53), paresthesia (n = 30), change in sensation of stimulation (n = 21), implant site infection (n = 12), urinary incontinence (n = 10), neurostimulator battery depletion (n = 9), diarrhea (n = 8), pain in extremity (n = 7), undesirable change in stimulation (n = 7), and buttock pain (n = 6) with the majority of these events (80%) successfully treated noninvasively with medication, other medical therapy, reprogramming, or no intervention. If looking only at the events that occurred at least 3 years after the date of initial implant (n = 73), the most frequent events were implant site pain (n = 14), change in sensation of stimulation (n = 9), paresthesia (n = 8), battery depletion (n = 6), implant migration (n = 3), and undesirable change in stimulation (n = 3).

When considering the entire group of 120 patients, a total of 47 patients (39.2%) had at least 1 device revision, replacement, or explant throughout the duration of the study. There were a total of 10 device revisions in 10 patients (9 neurostimulators and 1 lead), 40 device replacements in 29 patients (neurostimulator, lead, extension, or a combination thereof), and 22 system explants in 22 patients. The most common reason for a surgical revision was device migration (n = 8), the most common reason for a device replacement was battery depletion (n = 12), and the most common reason for a system explant was lack of efficacy (n = 11). Within the cohort of 76 patients followed through 5-years postimplantation (mean, 6.2 years), 27 (35.5%) had at least 1 device revision, replacement, and/or explant during the study, including 6

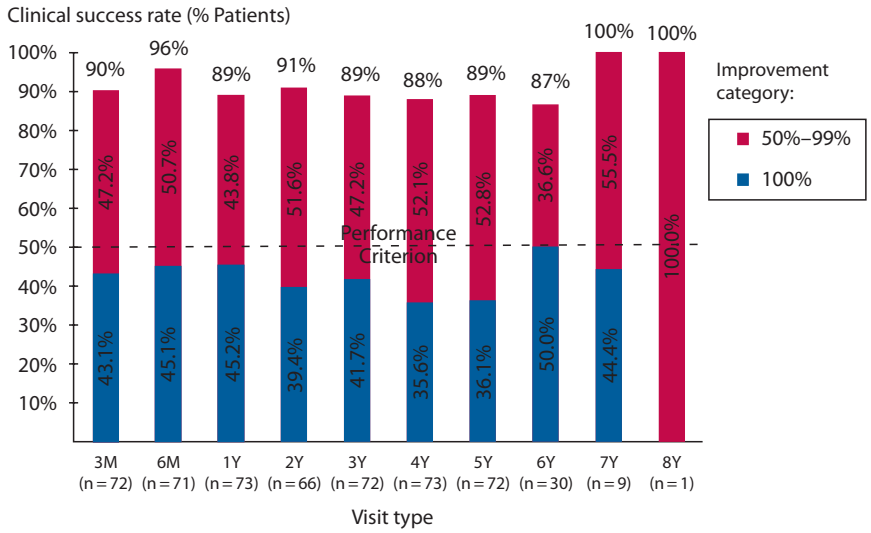


FIGURE 2. Proportion of patients with therapeutic success and a categorized percentage of improvement in weekly incontinent episodes at each visit for patients with at least 5 years of follow-up. (Note: All exact binomial tests, conducted through 5 years, had *p*-values < 0.0001.) M = month; Y = year.

TABLE 2. Comparison of continuous variables between patients with ≥50% improvement at 60 months with those patients with <50% improvement at 60 months or those who exited owing to the lack of efficacy

	≥50% at 60 mo (n = 64)			<50% at 60 mo or exited owing to lack of efficacy (n = 15)			
Variable	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*	*p (Wilcoxon rank-sum)*
Weekly incontinent episodes at baseline	64	9.3	6.5	15	10.9	7.5	0.3264
% Improvement at test stimulation	64	0.9	0.1	15	0.8	0.2	0.0072
Age, y	64	57.9	12.1	15	63.8	12.0	0.0927
BMI	62	28.3	5.8	15	28.5	6.0	0.9180
Years with FI	64	6.7	8.7	15	5.5	10.7	0.1026
No. of pregnancies	64	3.2	1.9	15	3.2	1.9	0.8186
No. of childbirths	64	2.4	1.7	15	2.4	1.2	0.7095
FIQOL scale 1: lifestyle	63	2.3	0.8	15	2.1	0.9	0.4276
FIQOL scale 2: coping/behavior	63	1.4	0.5	15	1.7	0.6	0.2127
FIQOL scale 3: depression/self-perception	63	2.6	0.8	15	2.5	0.8	0.7415
FIQOL scale 4: embarrassment	63	1.6	0.6	15	1.6	0.7	1.0000

FI = fecal incontinence; FIQOL = Fecal Incontinence Quality of Life.

patients with a neurostimulator revision, 24 patients with at least 1 device replacement, and 3 patients with system explants. Moreover, a device replacement owing to battery depletion was the only surgical intervention in 7 (25.9%) of the 27 patients (mean implant time, 4.9 years; range, 2–6.3). Therefore, of the 76 patients followed through 5 years postimplantation, 26.3% had a device revision, replacement, or explant for reasons other than expected battery depletion.

TABLE 3. Comparison of categorical variables between patients with ≥50% improvement at 60 months with those patients with <50% improvement at 60 months or those who exited owing to the lack of efficacy

		≥50% at 60 mo (n = 64)		<50% at 60 mo or exited owing to lack of efficacy (n = 15)		
Variable	*Category*	*Count*	*%*	*Count*	*%*	*p (Fisher exact)*
Continent at test stimulation	Yes	30	46.9	1	6.7	0.0035
Mode at implant	Continuous	31	62.0	8	66.7	1.0000
	Cyclic	19	38.0	4	33.3	
Sex	Female	60	93.8	14	93.3	1.0000
	Male	4	6.3	1	6.7	
Origin	Injury	2	3.1			0.8094
	Obstetric trauma	25	39.1	7	46.7	
	Other	21	32.8	6	40.0	
	Postsurgical	16	25.0	2	13.3	
Type of incontinence	Other	10	15.6	4	26.7	0.4084
	Passive	32	50.0	8	53.3	
	Urge	22	34.4	3	20.0	
Rectopexy	Yes	4	6.3	2	13.3	0.3188
Anal sphincteroplasty	Yes	19	29.7	4	26.7	1.0000
Pelvic floor repair	Yes	3	4.7	1	6.7	0.5771
Rectocele repair	Yes	6	9.4	2	13.3	0.6428
Cystocele repair	Yes	9	14.1	1	6.7	0.6774
Enterocele repair	Yes	1	1.6	1	6.7	0.3457
Hysterectomy	Yes	38	59.4	8	53.3	0.7737
Biofeedback	Yes	27	42.2	7	46.7	0.7790
Psychological counseling	Yes	5	7.8			0.5771
Irritable bowel syndrome	Yes	10	15.6	5	33.3	0.1456
Psychological disease	Yes	14	21.9	6	40.0	0.1885
Internal anal sphincter defect	Yes	10	15.6	5	33.3	0.1456
External anal sphincter defect	Yes	4	6.3	3	20.0	0.1216
Pudendal latency: left	Normal	41	70.7	12	85.7	
	Pathologic (>2.4 ms)	17	29.3	2	14.3	0.3275
Pudendal latency: right	Normal	40	66.7	10	71.4	
	Pathologic (>2.4 ms)	20	33.3	4	28.6	1.0000
FI medications at baseline	Yes	11	17.2	6	40.0	0.0785

FI = fecal incontinence.

Figure 3. Scatterplot of improvement at test stimulation versus long-term improvement for patients with 5-year data and those exited owing to the lack of efficacy (LOE), cutoff imposed of ≥–25% change at 5 years. A total of 17 patients had 100% improvement at test stimulation and the 60-month visit. [a]For patients who did not contribute 5-year data and discontinued because of a lack of efficacy, their last visit is shown in place of 5-year data.

Of the 72 patients with 5-year bowel diary data, 13 had at least 1 device revision and 59 had no device revisions before their 5-year follow-up visit. Of the 13 patients with at least 1 device revision, 10 (76.9%) achieved therapeutic success at 5 years postimplantation, with an average percentage of improvement of 66.6%. Of the 59 patients with no device revisions, 54 (91.5%) achieved therapeutic success at 5 years postimplantation, with an average percentage of improvement of 81.4% from baseline. The difference between these 2 groups in success rates at 5

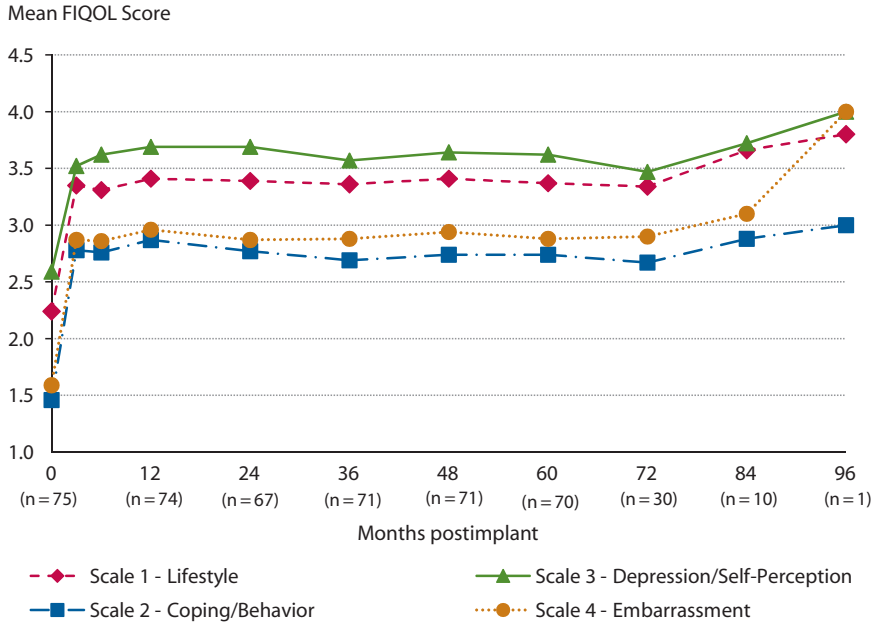


FIGURE 4. Mean Fecal Incontinence Quality of Life (FIQOL) component scales at each visit for patients with at least 5 years of follow-up (higher score indicates better quality of life).

TABLE 4. Changes in Fecal Incontinence Quality of Life component scales from baseline to 5 years postimplant for patients with at least 5 years of follow-up (higher score indicated better quality of life)

		Baseline		5 Years		5 Years – baseline	
FIQOL Scale	*N*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*p*[a]
Scale 1: lifestyle	67	2.26	0.79	3.36	0.68	1.10	<0.0001
Scale 2: coping/behavior	67	1.49	0.53	2.73	0.82	1.25	<0.0001
Scale 3: depression/self-perception	69	2.63	0.80	3.62	0.73	0.99	<0.0001
Scale 4: embarrassment	67	1.62	0.61	2.86	0.91	1.24	<0.0001[b]

[a]*p* values calculated by using paired *t* test except where noted.
[b]*p* value calculated by using Wilcoxon signed-rank test.

years postimplantation was not statistically significant ($p = 0.15$), nor was the difference in the percentage of improvement from baseline ($p = 0.49$).

An analysis of time to first device revision/replacement using the entire group of 120 patients who had received implants showed that the probability of a patient having a device revision or replacement (for any reason) by 1 year postimplantation was 10.3%, increasing to 24.4% after 5 years (Fig. 8). Likewise, a separate analysis of time to permanent device explant showed that the probability of a patient having an explant (for any reason) by 1 year postimplantation was 3.4%, increasing to 19.0% after 5 years. Overall, through 5 years of receiving SNS therapy, patients had a 35.6% chance of having any surgical intervention (device revision, replacement, or explant).

DISCUSSION

This study has confirmed the 5-year durability of SNS. Our data have been previously presented at 1 and 3 years for the entire group.[11,12] However, this study is unique in that it examines primarily patients who have a minimum of 5 years of follow-up after device implantation. It also represents one of the largest groups of carefully followed patients with FI and SNS. When considering FI research, an exact definition for "long-term" does not exist. There are some 10-year reports on overlapping sphincter repair that represent more of a snapshot in time for these patients without precise preoperative data for comparison.[6,7,17] In addition, a few investigators have reported their results longer than 5 years after FI therapies,[18,19] but no long-term studies are prospectively designed and systematically followed with the number of patients and rigor of this study.

When looking specifically at the SNS literature regarding long-term outcome, Altomare et al[19] reported on 52 of 60 patients prospectively followed for a minimum of 5 years. Their results showed that 74% of patients had >50% improvement in incontinent episodes. Although the definition of success varies across studies, our results are comparable showing that 89% had a

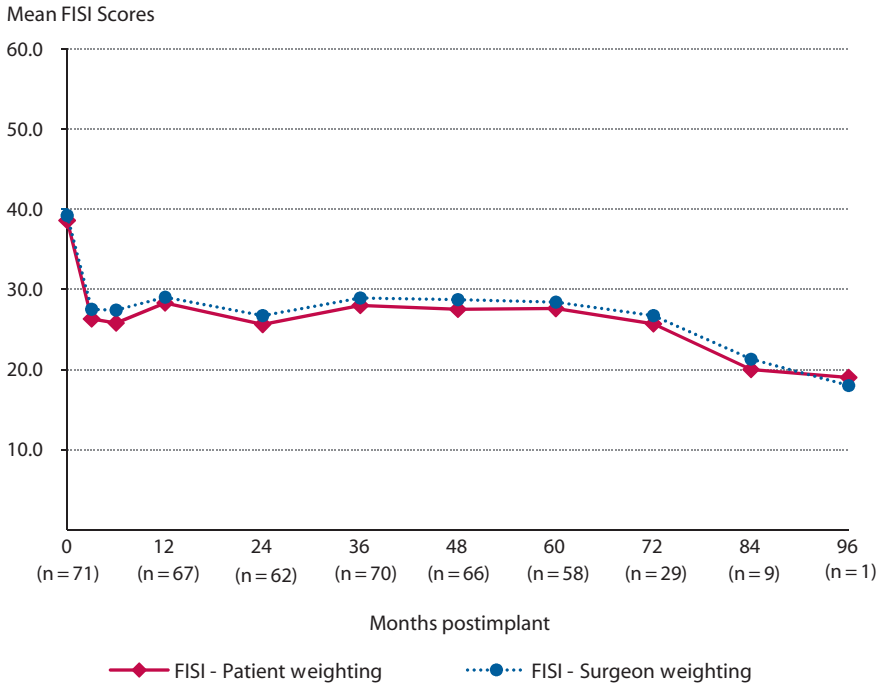


FIGURE 5. Mean Fecal Incontinence Severity Index (FISI) score at each visit for patients with at least 5 years of follow-up (higher score indicates greater severity).

TABLE 5. Changes in Fecal Incontinence Severity Index from baseline to 5 years

		Baseline		5 Years		5 Years – baseline	
FISI score	*N*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*p*[a]
Patient weighting	55	37.95	9.01	28.33	13.30	−9.62	<0.0001
Surgeon weighting	55	38.58	8.34	29.26	13.43	−9.33	<0.0001

[a]*p* values calculated by using paired *t* test.

sustained ≥50% reduction in FI episodes from baseline, 36% of whom were totally continent. George et al[20] reported on 23 patients followed for 114 months (range, 96–164) with full continence reported in 12 of 23 (48%). Matzel et al,[18] who reported the initial use of SNS for FI in the *Lancet* in 1995, have since reported the long-term results. They noted 9 of 12 patients who continued to use the SNS followed for 9.8 (range, 7–14) years. Looking at the median number of incontinent episodes per week, Matzel et al reported a decrease from 9 (range, 2–58) at baseline to 0 (range, 0–29; $p = 0.012$) in their 9 patients. This report is also similar to our data with an average of 9.1 weekly incontinent episodes at baseline that decreased to 1.7 at 5 years. Therefore, the results from the limited long-term studies on SNS, with fewer patients, are similar to our results.

There were no differences in baseline demographics between patients with ≥50% improvement at 5 years and those with <50% improvement at 5 years or who exited because of the lack of efficacy before 5 years. However, test stimulation appears to be a useful tool in assessing a patient's long-term response to the therapy. With a look at this relationship in more detail, the data show that, in general, patients can experience long-term success, as defined by the study, across a range of improvement during test stimulation (Fig. 3).

The observed success rate of 89% at 5 years postimplantation is likely overestimated, because some patients exited the study before 5 years owing to a stated lack of efficacy, and 36% of patients who exited before 5 years of follow-up showed less than 50% improvement from baseline at their last visit. However, the sensitivity analysis, which imputed either the baseline or last follow-up visit for a patient depending on the reason for study exit, showed a more conservative, although still statistically significant, success rate of 69% at 5 years postimplantation.

One interesting phenomenon in the present analysis was that, of the 8 patients who did not have ≥50% improvement in weekly incontinent episodes at 1 year, 5 became successful by 5 years. Further investigation as to why the 5 of 8 who were not successful at 1 year later became successful was not enlightening. However, it highlights that persistence with the device can lead to success in some patients whose initial results are suboptimal. There were also an additional 5 patients who were deemed successful at 1 year who did not meet the success criteria at 5 years. These patients are also puzzling. No definite reason could be elucidated with further investigation for the failure in these patients. Interestingly, they also continued to use the therapy, which may mean they perceived some benefit. Similarly, George et al[20] reported that 2 of 23 patients lost efficacy for unknown reasons at 48 and 60 months.

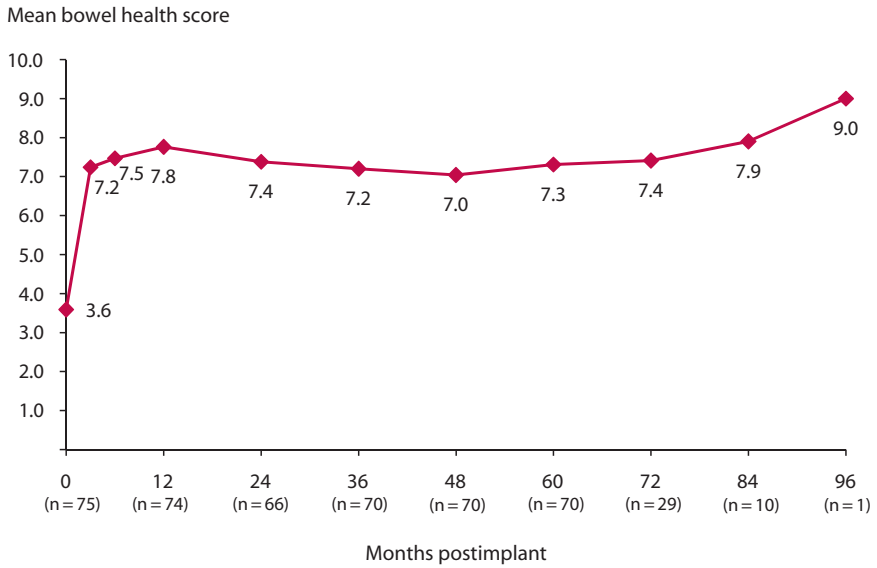


FIGURE 6. Mean bowel health score at each visit for patients with at least 5 years of follow-up (higher score indicates better bowel health).

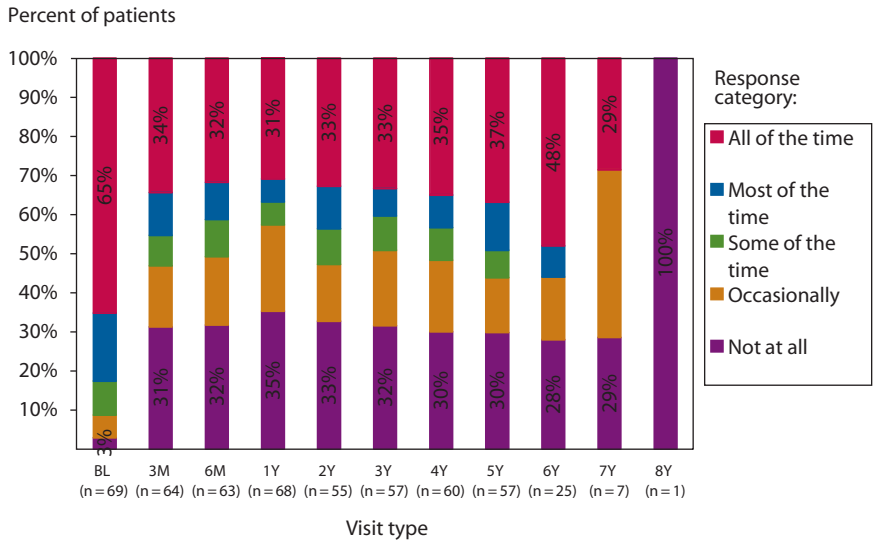


FIGURE 7. Distribution of pad use frequency at each visit for patients with at least 5 years of follow-up. BL = baseline; M = month; Y = year.

In contrast, both patients in that series had their device removed. Further study is needed to understand these 2 types of response patterns to optimize the outcome for future patients.

When considering FI, improvement in our patients' quality of life (QOL) should be the main focus, not simply improvement in an absolute number. Although some investigators feel that QOL is difficult to fully appreciate versus a definitive number (like the number of weekly FI episodes), validated tools such as the FIQOL have become acceptable methods to examine QOL. The improvements seen in this study at 1 year in all 4 scales of the FIQOL and sustained beyond 5 years are gratifying. Many early studies did not include QOL measurements (let alone those specific for FI), because the importance of this facet of study has only perhaps become apparent over the past decade. Altomare et al[19] used the SF36 and noted 39.8% improvement at 5 years postimplantation.

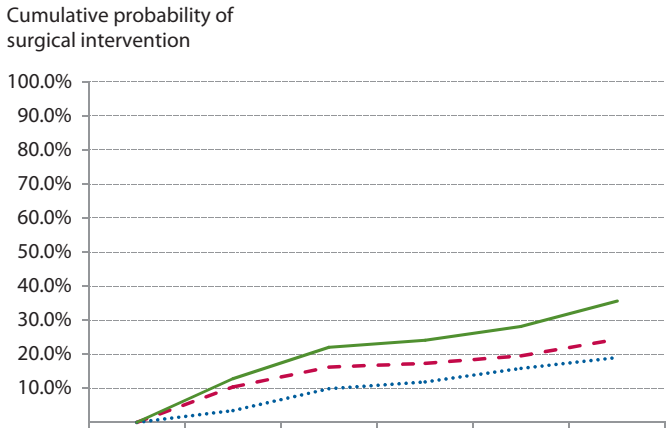
This study found that, overall, in the entire group of 120 patients, 47 (39.2%) patients needed a device revision, replacement, or explant. After at least 5 years of follow-up, 76 (63.3%) of 120 patients had a functioning device and remained in the study. When looking at the 5-year study group, 20 patients (26.3%) had a revision, replacement, or explant for reasons other than battery depletion. Our results are not dissimilar to the long-term SNS report from

TABLE 6. Device/therapy-related adverse events during the study

	All patients (n = 120)		*Patients with 5-y follow-up (n = 76)*		*AEs occurring after 3 y of follow-up (n = 90)*	
Adverse event	*No. of events (serious)*	*No. of patients (%)*	*No. of events (serious)*	*No. of patients (%)*	*No. of events (serious)*	*No. of patients (%)*
Implant site pain	53 (4)	39 (32.5)	36 (1)	26 (34.2)	14 (0)	12 (13.3)
Paresthesia	30 (0)	23 (19.2)	22 (0)	15 (19.7)	8 (0)	7 (7.8)
Change in sensation of stimulation	21 (0)	14 (11.7)	16 (0)	9 (11.8)	9 (0)	6 (6.7)
Implant site infection	12 (4)	12 (10.0)	5 (0)	5 (6.6)	1 (0)	1 (1.1)
Urinary incontinence	10 (0)	10 (8.3)	7 (0)	7 (9.2)	1 (0)	1 (1.1)
Neurostimulator battery depletion	9 (1)[a]	8 (6.7)	8 (1)	7 (9.2)	6 (1)	6 (6.7)
Diarrhea	8 (0)	8 (6.7)	7 (0)	7 (9.2)	1 (0)	1 (1.1)
Pain in extremity	7 (0)	7 (5.8)	5 (0)	5 (6.6)	0 (0)	0 (0.0)
Undesirable change in stimulation	7 (0)	7 (5.8)	6 (0)	6 (7.9)	3 (0)	3 (3.3)
Buttock pain	6 (0)	6 (5.0)	4 (0)	4 (5.3)	1 (0)	1 (1.1)
Migration of implant	3 (0)	3 (2.5)	3 (0)	3 (3.9)	3 (0)	3 (3.3)
Other	141 (11)	70 (58.3)	99 (6)	47 (61.8)	26 (3)	16 (1.8)
Total	307 (20)	93 (77.5)	218 (8)	60 (78.9)	73 (4)	38 (42.2)

AE = adverse event.

[a]Event was considered serious because of the patient being admitted to hospital for >24 hours; however, no complications occurred during or after the battery replacement.



	0	1	2	3	4	5
Revision/replacement	0.0%	10.3%	16.2%	17.3%	19.5%	24.4%
Permanent explant	0.0%	3.4%	9.8%	11.8%	15.8%	19.0%
Any surgical intervention	0.0%	12.8%	22.1%	24.1%	28.1%	35.6%

Time from implant (in years)

FIGURE 8. Plot of life table estimates of cumulative probability of all-cause surgical intervention (n = 120).

Matzel et al.[18] His group reported that 3 of 12 (25%) patients followed for a minimum of 7 years had their device removed for pain or neurological disease. Of the 9 with functioning devices (75%), the pulse generator required replacement in 8 patients at a mean of 7.4 years for battery depletion. Although battery depletion is an anticipated occurrence, the 26.3% unanticipated revision, replacement, or explant rate needs to be better understood and requires further study. Although this may be a rate comparable to other SNS studies, new techniques should focus on methods to reduce this percentage.

In our study, although there were 307 device/therapy-related AEs, only 20 were considered serious. Attempting to compare this finding with other published studies is difficult, because no other study imposed the rigors of AE collection in the same manner as this study.

This study has multiple strengths including its long-term follow-up, the number of patients, the quality of the data, and the use of accepted tools to objectively study the patients before and after therapy. One drawback of this study is that it was not a randomized study with a control arm. Although that would have added to the credibility of the data, the present FDA-sanctioned study still used a rigorous design with strict collection of data at baseline and then regularly through and past 5 years. In addition, an ideal control arm would have entailed implantation of the device without activation. Because implantation is a 2-stage procedure and permanent implantation is only done if a positive response is attained during stage 1, it would have been difficult to subject a patient to permanent implant during stage 2 without subsequently activating the device. Also, keeping the patient blinded to the lack of therapy in the control arm would have been difficult. Another limitation of this study is that there were no prescribed program settings for the device. Patients were able to adjust the stimulation as they needed with portable programmers between visits. Future studies will need to precisely record programming information and how it relates to battery depletion.

CONCLUSION

This prospective study looking at the durability of SNS therapy has shown that the therapeutic effect and improvements in QOL are maintained through 5 years postimplantation. In comparison of this study with other published SNS studies, the device revision rate is at least similar. Although battery depletion is anticipated, further study focusing on decreasing device revisions is needed. Where SNS fits into the current FI treatment algorithm also needs further study. Considering the sustained degree of FI and QOL improvement, an argument can be supported to consider SNS early in the treatment algorithm.

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REFERENCES

1. Goode PS, Burgio KL, Halli AD, et al. Prevalence and correlates of fecal incontinence in community-dwelling older adults. *J Am Geriatr Soc*. 2005;53:629–635.
2. Roberts RO, Jacobsen SJ, Reilly WT, Pemberton JH, Lieber MM, Talley NJ. Prevalence of combined fecal and urinary incontinence: a community-based study. *J Am Geriatr Soc*. 1999;47:837–841.
3. Whitehead WE, Borrud L, Goode PS, et al. Fecal incontinence in US adults: epidemiology and risk factors. *Gastroenterology*. 2009;137:512–517.e512.
4. Bharucha AE, Zinsmeister AR, Locke GR, et al. Risk factors for fecal incontinence: a population-based study in women. *Am J Gastroenterol*. 2006;101:1305–1312.
5. Madoff RD, Williams JG, Caushaj PF. Fecal incontinence. *N Engl J Med*. 1992;326:1002–1007.
6. Zutshi M, Tracey TH, Bast J, Halverson A, Na J. Ten-year outcome after anal sphincter repair for fecal incontinence. *Dis Colon Rectum*. 2009;52:1089–1094.
7. Bravo Gutierrez A, Madoff RD, Lowry AC, Parker SC, Buie WD, Baxter NN. Long-term results of anterior sphincteroplasty. *Dis Colon Rectum*. 2004;47:727–731.
8. Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. *Lancet*. 1995;346:1124–1127.
9. Hull TL. Sacral neuromodulation stimulation in fecal incontinence. *Int Urogynecol J*. 2010;21:1565–1568.
10. Devroede G, Giese C, Wexner SD, et al; SNS Study Group. Quality of life is markedly improved in patients with fecal incontinence after sacral nerve stimulation. *Female Pelvic Med Reconstr Surg*. 2012;18:103–112.
11. Mellgren A, Wexner SD, Coller JA, et al; SNS Study Group. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum*. 2011;54:1065–1075.
12. Wexner SD, Coller JA, Devroede G, et al. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. *Ann Surg*. 2010;251:441–449.
13. Wexner SD, Hull T, Edden Y, et al. Infection rates in a large investigational trial of sacral nerve stimulation for fecal incontinence. *J Gastrointest Surg*. 2010;14:1081–1089.
14. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol*. 1997;32:920–924.
15. Rockwood TH, Church JM, Fleshman JW, et al. Fecal Incontinence Quality of Life Scale: quality of life instrument for patients with fecal incontinence. *Dis Colon Rectum*. 2000;43:9–16.
16. Rockwood TH, Church JM, Fleshman JW, et al. Patient and surgeon ranking of the severity of symptoms associated with fecal incontinence: the fecal incontinence severity index. *Dis Colon Rectum*. 1999;42:1525–1532.
17. Oom DM, Gosselink MP, Schouten WR. Anterior sphincteroplasty for fecal incontinence: a single center experience in the era of sacral neuromodulation. *Dis Colon Rectum*. 2009;52:1681–1687.
18. Matzel KE, Lux P, Heuer S, Besendörfer M, Zhang W. Sacral nerve stimulation for faecal incontinence: long-term outcome. *Colorectal Dis*. 2009;11:636–641.
19. Altomare DF, Ratto C, Ganio E, Lolli P, Masin A, Villani RD. Long-term outcome of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum*. 2009;52:11–17.
20. George AT, Kalmar K, Panarese A, Dudding TC, Nicholls RJ, Vaizey CJ. Long-term outcomes of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum*. 2012;55:302–306.