Safety and Effectiveness of the Recharge-Free Axonics Sacral Neuromodulation System

Abstract

Purpose: Approved in 2019, the initial Axonics sacral nerve modulation (SNM) system, was a rechargeable neurostimulator R15, with a 15+ year expected life. The FDA approved the Axonics recharge-free neurostimulator (F15) in 2022. The R15 is well-studied with demonstrated safety and effectiveness out to 2 years. The purpose of this study is to describe the safety and effectiveness of the F15 SNM System in patients with urinary urgency incontinence (UUI) and fecal incontinence (FI) who have a minimum of one-year follow-up.

Methods: Multicenter study evaluating the safety, effectiveness and device performance of the recharge free Axonics F15 SNM System in improving UUI and FI symptoms at a minimum of 1-year post implant. Participants implanted with the Axonics F15 SNM System prior to September 2023 were identified. Participants who consented were assessed using a patient satisfaction questionnaire and review of neurostimulator performance. UUI participants completed a 3-day bladder diary. The primary outcome measures included patient satisfaction, device parameters, leak reduction (UUI only), and safety obtained via medical record and patient report.

Results: Sixty-nine (69) patients implanted for at least 1 year were consented and completed a study follow-up visit. The average follow-up was 21.4 months post-implant for this cohort. Medical records for 398 patients were also reviewed for device and/or procedure-related complications.

Participant satisfaction with therapy was high with 94% reported as satisfied, 90% indicating a ≥50% improvement; 69% indicating a ≥75% improvement in symptoms and 94% of participants confirming they would likely undergo the therapy again.

Based on device settings, the expected battery life for participants was an average of 17.5 years (median 18.6). There were no unanticipated adverse events and no serious device or procedure-related adverse events for the participants who completed the study visit.

Conclusions: The long-lived, recharge-free Axonics F15 SNM System is safe and effective, with participants reporting high satisfaction with therapy and low rate of complications. The median battery life expectancy was calculated to be 18.6 years for participants completing the study visit.

Runninghead: Long-term outcomes for the recharge-free Axonics SNM System

MeSH Keywords: Urinary urgency incontinence, overactive bladder, Fecal incontinence implantable neurostimulator, impedance, programming, recharge-free

Introduction

Overactive bladder (OAB), including urinary urgency incontinence (UUI) and urinary frequency (UF), is a common condition affecting an estimated 40 million adults.[1,2] Sacral neuromodulation (SNM) is a guideline-recommended advanced therapy for refractory OAB[3] with proven success in UUI patients that have failed conservative treatments.[4-6]

Fecal incontinence (FI) is an undertreated condition that can have a severe impact on quality of life. Treatment options are limited and are dependent on the underlying etiology. Both European and American guidelines recommend SNM for patients who have failed conservative therapy.[7,8] A recent update to the American Society of Colon and Rectal Surgeons (ASCRS) guidelines for the evaluation and treatment of FI now recommends SNM as a first-line surgical therapy in patients who have failed conservative therapy.[8]

The recharge-free Axonics F15 SNM System (Figure 1) was FDA approved in the United States in March of 2022 and is the smallest (10cc volume) and longest-lived non-rechargeable SNM device available. The F15 system is designed to last 10-20+ years in the body depending on stimulation parameters (amplitude, pulse width, frequency and impedance). The purpose of this study is to describe the safety, effectiveness and device performance in terms of longevity of the Axonics F15 SNM System in patients with UUI or FI who have been implanted for a minimum of one year. Additionally, the Axonics Clinician Programmer (CP) contains a proprietary algorithm that prioritizes and recommends patient stimulation settings based on information gathered during the lead implant procedure. This study also evaluates how likely the algorithm is to predict effective stimulation settings.

Methods and Materials

Multicenter study evaluating the safety, effectiveness and device performance of the Axonics F15 SNM System. Approval of the protocol was obtained by a central Institutional Review Board (WCG IRB). Patients implanted with the Axonics F15 SNM System over 12 months ago were identified by the study sites. Patients who were successfully contacted and agreed to participate signed an informed consent, completed a patient satisfaction questionnaire, and had their neurostimulator settings and device performance reviewed. UUI patients also completed a 3-day bladder diary.

Clinical outcome measures included patient satisfaction, safety data, device parameters (initial and current device settings and impedance values), and number and severity of incontinent leakage episodes (UUI patients only). Device settings and impedance values were used to calculate the expected longevity of the device. Program settings based on the CP algorithm were evaluated at baseline and follow-up. When available, the medical records of patients who could not be contacted or did not agree to complete a follow-up visit were reviewed for device-related complications, revisions, or explants. Additionally, a patient care management database managed by the Sponsor was reviewed for any other follow-up information available for these patients.

Standard summary statistics were calculated for demographic data and device parameters, including mean, standard deviation, median, range and/or frequency distributions. Mean and standard error were calculated for bladder diary data. Statistical significance for changes in bladder diary data between baseline and follow-up was determined using a one-sided paired t-test with $\alpha=0.025$. All statistical tests performed assumed significance at $p<0.025$.

Results

Study Demographics and Follow-up

Sixty-nine (69) patients implanted ≥ 1 year ago provided informed consent and completed a study follow-up visit. The average time from implant to study visit was 21.4 months (11.7–35.5). Of these 69 patients, 23 (33%) completed a follow-up visit ≥24 months post-implant. The medical records of 398 additional patients implanted ≥ 1 year ago who were unable to be contacted or did not agree to complete a follow-up visit were reviewed for safety data.

Of the 69 participants who completed a study follow-up visit, 62 had a primary indication of urinary urgency incontinence (UUI) and 7 had a primary indication of fecal incontinence (FI). The average age was 70 years old (35-89 years) and 97% were female (Table 1).

Sixty-eight (68) participants completed a participant satisfaction questionnaire; one participant inadvertently completed the incorrect questionnaire at the follow-up visit. Device parameters were collected for 94% (65/69) of participants immediately post-procedure and 99% (68/69) of participants at follow-up. Of the 62 UUI participants, 39 (63%) completed a 3-day bladder diary reporting UUI leakage episodes at both baseline (prior to implant) and follow-up.

Effectiveness Outcomes

Participant satisfaction was high with 94% (64/68) reported as satisfied with therapy, 90% (61/68) indicating a ≥50% improvement and 69% (47/68) indicating a ≥75% improvement in symptoms. Additionally, 94% of participants (64/68) confirmed they would likely undergo the therapy again and 96% (65/68) indicated they would recommend the procedure to family or friends.

For the 39 UUI participants who completed a bladder diary, a significant reduction ($p<0.001$) in incontinence leak episodes was observed (Figure 3). The average number of incontinent leak episodes reduced from 5.6 episodes at baseline down to 1.5 at the follow-up visit (Figure 2).

Device parameters recorded were amplitude of stimulation, pulse width, frequency, and impedance values (Table 2). One hundred percent (100%; 65/65) of participants were initially programmed to one of the Clinician Programmer (CP) recommended programs and 94% (64/68) were on one of the CP recommended programs at follow-up (Figure 3). Based on device settings, the expected battery life for study participants was calculated to range from 4.6–24.7 years with an average 17.5 years (median 18.6 years) with 75% having greater than 15-year battery life and

28% having greater than 20-year battery life (Figure 4). All patients were programmed to continuous stimulation (none were on cyclic stimulation).

Safety Outcomes

There were no intraoperative complications or unanticipated adverse events reported in the 69 study participants. Six (6) late (>30 days post-implant) serious adverse events (SAEs) occurred which were considered unrelated to the study device or procedure. No device or procedure-related SAEs were reported. Six (6) non-serious adverse events occurred in 4 participants which were considered device and/or procedure related (Table 3). All events considered device- or procedure- related were resolved without clinical sequelae and none required surgical intervention, revision, or explant of the study device. There were no reports of lead migration, lead fractures or impedance issues.

The medical records of the 398 patients who could not be contacted or did not agree to complete a follow-up visit were also reviewed for complications associated with the Axonics SNM System (Table 3). A total of 32 device- or procedure-related events were noted which included pain at implantable neurostimulator (INS) site (3.0%), infection at the INS or lead site (2.0%), lead migration (0.5%), INS migration (0.3%), lack of effectiveness (0.3%), and undesired stimulation (0.3%). There were no reported lead fractures or impedance issues.

Eleven (11) patients (2.8%) underwent a full system explant; four (4) per patient request (at days 308, 315, 513, and 566), four (4) due to pain at stimulator site (at days 91, 112, 140, 665), two (2) due to an infection (at days 22 and 40), and one (1) due to persistent procedural complications (at day 168). Four (4) patients (1.0%) had revisions: one (1) secondary to inadequate therapy response which occurred on post-operative day 616, one (1) due to INS displacement following a fall on post-operative day (POD) 385, and two (2) due to lead migrations resulting in lead revisions on postoperative day 377 and 482. There were no device-related re-hospitalizations reported.

Discussion

The safety and effectiveness of the rechargeable Axonics SNM System has been well established, with a 94% success rate in UUI patients at 2 years.[6] This is the first study evaluating the safety, effectiveness, and device performance of the recharge-free Axonics F15 System in patients suffering from UUI and FI. Sustained safety and effectiveness of the Axonics recharge-free system was demonstrated out to 2 years along with high degrees of patient satisfaction and 94% reporting they would undergo the therapy again. Additionally, UUI participants demonstrated a significant reduction in the number of incontinent leaks. The safety profile of the therapy in this study is also favorable and was similar to that reported for the rechargeable Axonics System[9], with no serious device or procedure-related adverse events and only 1% of participants required revision and 3% undergoing explant. Except for the explants due to infection, most explants occurred at greater than 6 months post-implant.

The Axonics F15 System is the longest-lived non-rechargeable sacral neuromodulation device commercially available. The longevity of the device is dependent on the neurostimulator settings (amplitude, pulse width, frequency, and impedance values). This data provides information of the average impedance values at a minimum of 1-year follow-up. The impedance values are similar to what has been reported with rechargeable Axonics SNM device[9] and will help to provide more information to the patient and physician on the longevity of the device. Based on programming settings recorded in this study, device longevity is projected to last a median of 18.6 years and over 20 years in 28% (19/68) of patients.

The Axonics Clinician Programmer contains a proprietary algorithm that considers the patient's intraoperative responses to recommend the top four program settings to use when setting the patient's initial stimulation parameters. The programming algorithm is intended to inform initial patient programming and reduce the need for patients to try different stimulation programs at home or to return to the office for reprogramming. This data demonstrates that the proprietary algorithm is highly predictive in suggesting an effective patient program with 100% going home on one of the top programs and 94% still on one of the top programs at long-term follow-up. This potentially decreases the burden on the patient and the physician to have their device reprogrammed. This is similar to the results demonstrated in the ARTISTRY Registry study which demonstrated that 95% of participants went home on one of the top two CP recommended programs and 92% were still on one of the top two CP recommended programs at one year[10].

Conclusion

The recharge free Axonics F15 SNM System provides long-term improvement to participants with urinary urgency incontinence and fecal incontinence. Patients reported high satisfaction with the recharge-free Axonics SNM System along with a favorable safety profile. The expected life of the device is the longest reported in the literature, and validation of the proprietary programming algorithm suggests patients will have little need to reprogram their device.

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Correspondence
Karen Noblett, MD
Chief Medical Officer
Axonics, Inc.
Irvine, California
Email: karen.noblett@bsci.com

Table 1. Baseline Demographics

Parameter	**All Subjects (N=69)** mean ± SD median (min-max) or % (n)
Age (years)	69.6 ± 9.5 72 (35 – 89)
Female	97.1% (67)
BMI (kg/m^2)	30.0 ± 6.4 29.7 (17.0 – 47.5)
Mean Follow-up (months)	21.4 ± 6.5 19.4 (11.7 – 35.5)

Table 2. Device Parameters

Parameter	**Post-Procedure (N=65)** mean ± SD median (min-max) or % (n)	**Follow-Up (N=68)** mean ± SD median (min-max) or % (n)
Amplitude	0.82 ± 0.42 0.75 (0.25 – 2.60)	0.98 ± 0.54 0.80 (0.25 – 2.90)
Pulse Width	210 ± 2.0 210 (210 – 220)	210 ± 32.0 210 (60 – 330)
Frequency	14 ± 0.0 14 (14 – 14)	14 ± 1.0 14 (14 – 21)
Impedance [1]	1211.3 ± 338.7 1172 (729 – 2362)	1497.9 ± 390.0 1504 (722 – 2397)
Mean change in Impedance [1]	---	291.2 ± 422.2 270 (-872 – 1218)

[1] Impedance values not available for 8 subjects at Post-Procedure.

Table 3. Complications Associated with Study Device or Implant Site

Event Description	**Study Participants (N = 69)** (%)	**Non-Participants (N=398)** (%)
Infection at INS or Lead Site	4.3	2.0
INS or Lead Erosion	0.0	0.0
INS Migration	0.0	0.3
Lead Migration	0.0	0.5
Lead Fracture	0.0	0.0
Undesirable/Uncomfortable Stimulation	1.4	0.3
Pain at INS Site or Lead Site	1.4	3.0
Lack of Effectiveness / Worsening of Symptoms	0.0	0.3
Other Incision/Implant Site Complication [1]	1.4	1.8
Revision	0.0	1.0
Explant	0.0	2.8
Re-Hospitalization	0.0	0.0

Percentage is number of events divided by N.

[1] Includes pain, erythema, swelling, superficial wound opening.

Figure 1. The Axonics F15 SNM System is comprised of a non-rechargeable implantable neurostimulator which provides electrical pulses to simulate the sacral nerve via a tined lead. The system was approved in the United States in March of 2022.

Figure 2. Average number of daily incontinent leak episodes as recorded in a 3-day bladder diary for UUI participants (N=39). A significant reduction in leaks ($p<0.001$) was observed between baseline and follow-up.

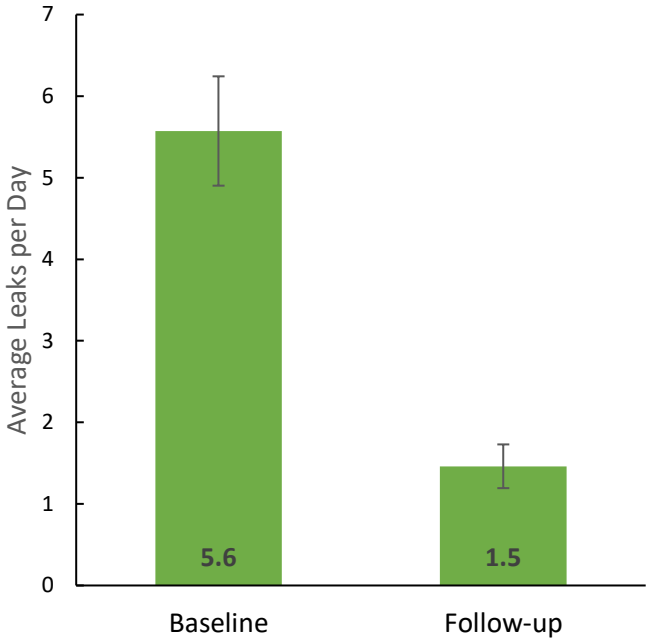


Figure 3. Active program settings **(A)** at post implant (N=64) and **(B)** after a minimum of 1-year follow-up (N=68). One hundred percent (100%) and 94% of participants were programmed to one of the Axonics Clinician Programmer (CP) recommended stimulation settings at post-implant and follow-up, respectively.

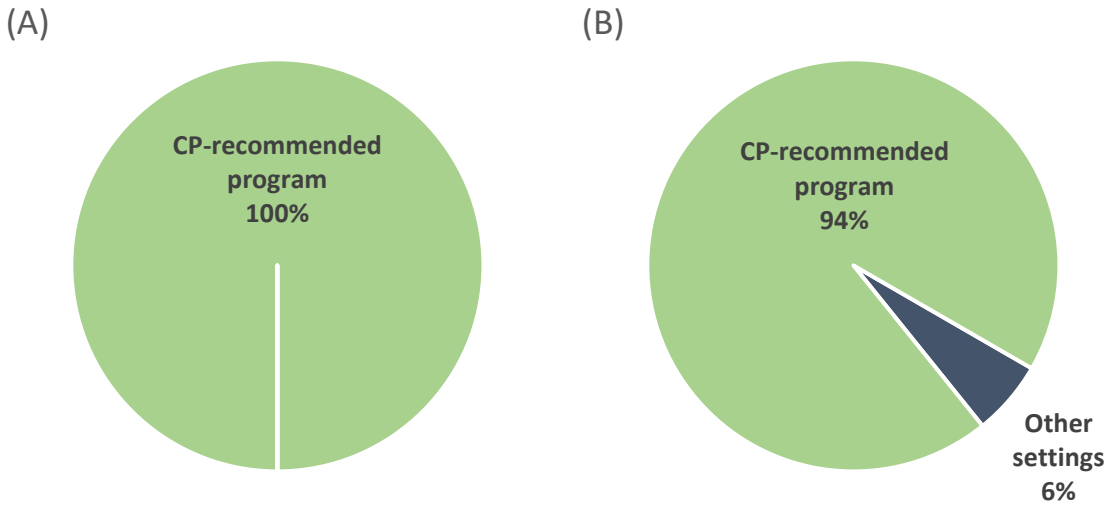
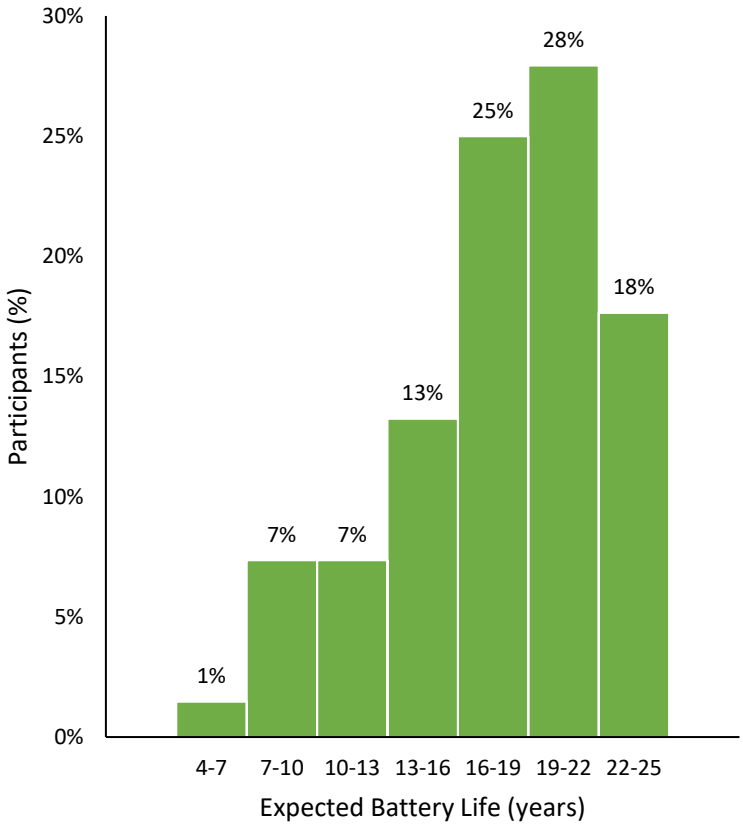


Figure 4. Calculated device life based on neurostimulator settings (amplitude, pulse width, frequency, and impedance) after a minimum of 1-year follow-up. Device longevity is projected to last a median of 18.6 years, and over 15 years in 75% (51/69) and over 20 years in 28% (19/68) of patients.



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