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Two-year outcomes of the ARTISAN-SNM study for the treatment of urinary urgency incontinence using the Axonics rechargeable sacral neuromodulation system

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Abstract

Aims: Sacral neuromodulation (SNM) is a guideline-recommended treatment with proven therapeutic benefit for urinary urgency incontinence (UUI) patients.

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Axonics Modulation Technologies

The Axonics® System is the first Food and Drug Administration-approved rechargeable SNM system and is designed to deliver therapy for a minimum of 15 years. The ARTISAN-SNM study was designed to evaluate UUI participants treated with the Axonics System. Two-year follow-up results are presented.

Methods: One hundred and twenty-nine UUI participants underwent implantation with the Axonics System. Therapeutic response rate, participant quality of life (QoL), and satisfaction were determined using 3-day voiding diaries, ICIQ-OABqol, and satisfaction questionnaires. Participants were considered responders if they had a 50% or greater reduction in UUI episodes post-treatment. As-treated and Completers analyses are presented.

Results: At 2 years, 93% of the participants ($n = 121$ Completers at 2 years) were therapy responders, of which 82% achieved $\geq 75\%$ reduction in UUI episodes and 37% were dry (100% reduction). Daily UUI episodes reduced from 5.6 ± 0.3 at baseline to 1.0 ± 0.2 at 2 years. Statistically significant improvements in ICIQ-OABqol were reported. All participants were able to recharge their device and 94% of participants reported that the recharging frequency and duration were acceptable. Participant demographics nor condition severity were correlated with clinical outcomes or recharging experience. No unanticipated or serious device-related adverse events occurred.

Conclusions: At 2 years, participants treated with the Axonics System demonstrated sustained safety and efficacy, high levels of satisfaction with therapy and recharging. Participant-related factors were not associated with efficacy or recharging outcomes, indicating the reported results are applicable to a diverse population.

KEYWORDS
clinical trial, implantable neurostimulator, overactive bladder, sacral neuromodulation, urinary urgency incontinence

1 | INTRODUCTION

Urinary urgency incontinence (UUI) associated with overactive bladder (OAB) is a widespread condition affecting millions of adults.[1,2] The chronic nature of this condition necessitates life-long treatment for sustained symptom relief and quality of life improvement. Sacral neuromodulation (SNM) is a guideline-recommended third-line therapy[3] with proven success in UUI patients that have failed conservative treatments.[4,5]

The Axonics® System is the first Food and Drug Administration-approved rechargeable SNM system for the treatment of both bladder and bowel symptoms including OAB, nonobstructive urinary retention (UR), and fecal incontinence (FI), and is designed to provide therapy for a minimum of 15 years (Figure 1).

The ARTISAN-SNM study is a prospective, single-arm, multicenter, pivotal study designed to assess the safety and efficacy of the Axonics System for treating UUI patients.[6,7] This article reports 2-year clinical and recharging outcomes for the Axonics System.

FIGURE 1 The Axonics System is comprised of a rechargeable, implantable neurostimulator with an approximate size of 5 cc. The system is approved in the United States, Europe, Canada, and Australia and has conditional approval for full-body magnetic resonance imaging at 1.5 T and 3 T

2 | METHODS

Study design and inclusion/exclusion (IE) criteria have been detailed previously[6] (Table S1). Ethics committees at all centers approved the study protocol and all study participants provided informed consent.

All participants were implanted with the Axonics quadripolar tined lead and implantable neurostimulator (INS) in a single, nonstaged procedure (i.e., an external trial system was not used).[6,7] SNM best practices[8] were followed for surgical placement of the tined lead along sacral nerve root S3 (preferred) or S4, which required a positive response on at least two electrodes at less than 4 mA. INS placement was near the upper buttocks. Intraoperative motor responses and postoperative sensory responses were used to program the study participants to optimal settings.

Study participants were trained on how to recharge their device at home, with instructions to recharge every 1 to 2 weeks. Briefly, participants place the wireless charging device in a belt which is then placed over the implanted neurostimulator.

Efficacy data were collected using a 3-day voiding diary, health-related quality of life (QoL) questionnaire (ICIQ-OABqol), and a satisfaction questionnaire.[6,7] A 10-point minimally important difference in ICIQ-OABqol score from baseline is considered clinically meaningful in this study.[9,10] All participants completed the Cleveland Clinic Florida Fecal Incontinence Score (CCF-FIS) at baseline to assess their bowel symptoms. The CCF-FIS was also collected at follow-up in participants with a baseline CCF-FIS score of 6 or more, which is associated with the presence of bothersome fecal incontinence.[11] Safety was assessed by reported adverse events (AEs) through 2 years and adjudicated by an independent data and safety monitoring board.

Participants were defined as therapy responders if they had a 50% or greater reduction in UUI episodes on their voiding diary at follow-up as compared to baseline. Additional analyses consisted of the absolute and percent change in all UUI episodes and large UUI episodes at follow-up compared to baseline. All efficacy results for urinary incontinence were assessed using urgency incontinence episodes only (i.e., stress incontinence episodes were not used). QoL outcomes (ICIQ-OABqol) and participant satisfaction questionnaires were also evaluated.

Two analysis methods were used for evaluating efficacy including an As-treated analysis and a Completers analysis, with Completers being the primary analysis method. In the As-treated analysis, all implanted participants were included regardless of whether they completed the 2-year study visit. Participants that were exited before or did not complete the 2-year visit were assumed to be treatment failures and symptoms at the follow-up visit were assumed to be the same as that at baseline. In the Completers analysis, only participants that completed the 2-year study visit were included. Analysis was also performed in the "Test Responders" cohort, defined as participants who were therapy responders at 1 month. The analyses performed in the all implanted cohort is more rigorous than in existing literature,[4,5,12] where therapeutic efficacy is frequently reported only for participants who had a positive clinical response during an external trial period.

A posthoc Spearman's correlation analysis was performed to test the association between participant demographic factors of age and body mass index (BMI), and clinical factors such as duration of disease, prior third line therapy on efficacy and recharging outcomes. The participant-reported recharging duration per week was calculated using the formula: (Recharging duration/number of days between charging) × 7 days/week. A posthoc analysis was also performed to test whether having a prior test system before enrollment in the study affected the overall responder rate reported in this study.

3 | RESULTS

3.1 | Study demographics and baseline symptoms

A total of 129 participants met the IE criteria and underwent an implant with the Axonics System in a single, nonstaged procedure.[6,7] No study participants were intraoperative test failures. Of the 129 participants, a total of 113 participants were Test Responders at 1 month (defined as ≥50% reduction in UUI symptoms at 1 month). Baseline demographics have been published previously[6] and are listed in Table S2. Average participant age was 59.3-years old (21–86 years) and 98% of participants were female.[6,7]

Average UUI episodes per day at baseline was 5.6 ± 0.3 (± standard error). In addition, 81 participants (63%) reported at least one large leak per day at baseline. Urinary frequency (UF) was defined as eight or greater voids per day and 103 participants (80%) had UF at baseline, reporting an average of 11.6 ± 0.3 voids per day. Fecal incontinence, as confirmed by a score of 6 or more on the CCF-FIS, was present in 42 participants (33%) at baseline, with an average CCF-FIS score of 9.3 ± 0.5.

A total of 121 of the 129 participants (94%) completed the 2-year follow-up visit. Details on the eight exited participants are provided in the safety section.

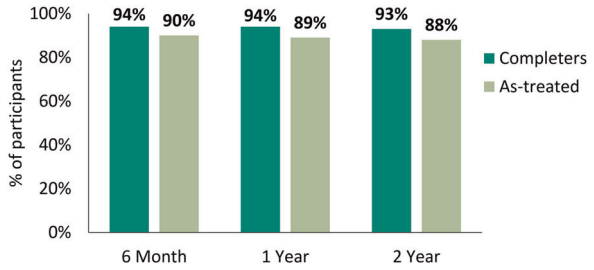

FIGURE 2 Therapy responder rates after Axonics System implant. Completers analysis was performed in participants who completed the follow-up visit. The As-treated analysis was performed in all participants—considering those who completed the follow-up visit and classifying any participants who were explanted or exited as treatment failures

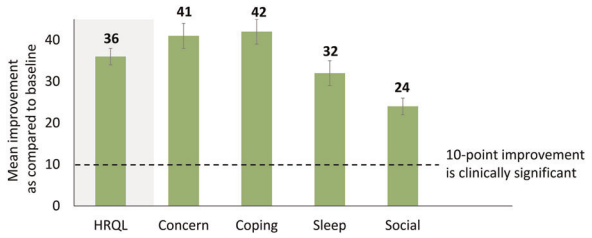

FIGURE 4 Completers analysis of ICIQ-OABqol questionnaire results. Standard error is presented. Score differences of more than 10 points were measured for all categories which mark a clinically meaningful improvement in participant quality of life.[9,10] HRQL, health-related quality of life; OAB, overactive bladder; qol, quality of life. All scores showed improvements that were statistically significant ($p < 0.0001$ for all comparisons, $n = 121$)

3.2 | Therapy responder rate and UUI symptom reduction

Of the 121 participants that completed the 2-year visit, 93% were therapy responders at 2 years (Figure 2, Completers analysis). Further, 97% of the Test Responders (106 of 109 available Test Responders) were therapy responders at 2 years. Across all 129 implanted participants (As-treated analysis), 88% were therapy responders at 2 years (Figure 2).

A significant overall UUI symptom reduction of 82% was seen at 2 years, with daily UUI episodes reducing from an average of 5.6 ± 0.3 at baseline to 1.0 ± 0.2 at 2 years ($p < 0.0001$) (Figure 3A, Completers analysis). Of the therapy responders at 2 years, 93 participants (82%) achieved greater than or equal to 75% reduction in UUI episodes per day (Figure 3B), 54% achieved greater than 90% reduction in UUI episodes per day, and 37% achieved full urinary continence (Figure 3B).

In the 81 participants that had large leaks at baseline, 76 were available at the 2-year follow-up. There was a significant change in large leaks, reducing from an average of 1.6 ± 0.2 at baseline to 0.1 ± 0.07 at 2 years ($p < 0.0001$). Using the Completers analysis, 88% of the participants had greater than or equal to 75% reduction in large leak episodes, and 82% achieved a 100% reduction in large leak episodes.

3.3 | Quality of life

At the 2-year visit, participants reported an average improvement of 36.1 points in health-related quality of life (HRQL) on the ICIQ-OABqol questionnaire ($p < 0.0001$), which represents a clinically meaningful improvement from baseline (Figure 4). All ICIQ-OABqol subscale categories showed statistically significant improvements in QoL, with increases of 41.4 points on Concern, 42.0

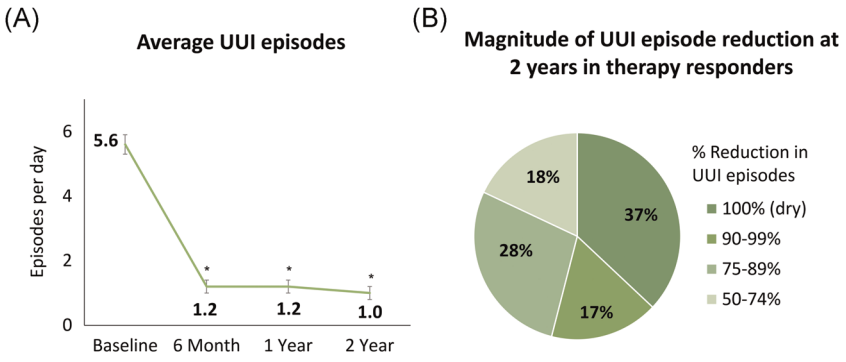

FIGURE 3 Urinary urgency incontinence (UUI) symptom reduction. (A) Completers analysis of average daily UUI episodes at Baseline ($n = 129$), 6 months ($n = 126$), 1 year ($n = 124$), and 2 years ($n = 121$). (B) UUI daily episode reduction in therapy responders only ($n = 113$) throughout the study. Standard error is presented. *$p < 0.0001$ compared to baseline

FIGURE 5 Completers analysis of participant satisfaction and recharging outcomes at 2 years ($n = 121$). (A) Therapy satisfaction. (B) Recharging outcomes. SNM, sacral neuromodulation

points on Coping, 31.9 points on Sleep, and 23.6 points on Social Interaction.

3.4 | Therapy satisfaction

Participants rated their overall satisfaction with SNM therapy throughout the 2-year study. At 2 years, 94% of the participants reported they were "satisfied" with their rechargeable SNM therapy, and 93% of participants reported that they would undergo the therapy again with the same expected outcomes (Figure 5A). These results are consistent with the satisfaction rates at 6 and 12 months, respectively.[6,7]

Participants also rated their therapy satisfaction for treating their FI symptoms. At 2 years, a total of 45 participants self-reported as having FI symptoms and 82% of these participants reported being "satisfied" with their SNM therapy for treating their bowel symptoms (Figure S1B).

3.5 | Additional outcome measures: Urgency, UF, and FI

Reduction in overall urgency episodes (urgent voids and/or leaks), UF, and FI symptoms were also reported throughout the study.

Participants experienced a significant improvement in urgency episodes per day, with a reduction from 10.6 ± 0.3 at baseline to 6.9 ± 0.3 at 2 years ($p < 0.0001$).

At 2 years, UF significantly reduced from 11.6 ± 0.3 to 8.5 ± 0.2 voids per day ($p < 0.0001$).

Forty-two of the 129 participants (33%) had FI at baseline with an average CCF-FIS score of 9.3 ± 0.5. At 2 years ($n = 42$), CCF-FIS was significantly reduced to 3.7 ± 0.5 ($p < 0.001$) (Figure S1A).

3.6 | Recharging experience

Participants reported on their experience with recharging their SNM system throughout the study. All participants reported being able to recharge throughout the 2-year study. At 2 years, 91% of participants rated recharging as "easy" (Figure 5B) and 94% rated recharging as "acceptable" (Figure 5B), results that are similar to the participant perception at 6 and 12 months.[6,7] A vast majority of the participants (88%) reported recharging session duration of less than 1 h, and 98% of participants reported at least 7 days between recharging sessions.

3.7 | Additional analysis

As mentioned in the Methods Section, a posthoc analysis was utilized to evaluate the association between participant factors with efficacy or recharging experience. Participant demographic and clinical factors were not correlated with the degree of UUI leak reduction (Spearman's $R = 0.3$). Participant demographic and clinical factors were also not correlated with recharging duration (Spearman's $R = 0.1$). These results suggest that participant factors do not affect clinical outcomes or recharging experience and the results presented here are generalizable to a broad population of patients.

A posthoc analysis was performed to test whether having a prior test system before enrollment in the study affected the overall responder rate. A total of nine study participants had a prior external trial stimulation system and had passed the trial but did not have a full implant. All nine subjects were responders at 1-month, 3-month, 6-month, 1-year, and 2-year visits (i.e., 100% responder rate). Removing these subjects from the responder rate analyses does not affect the reported responder rates (As-treated responder rate: 88%; Completers responder rate: 93%).

3.8 | Safety

Throughout the 2-year study, there were no unanticipated or serious device or procedure-related AEs. Device-related AEs occurred in 20 of the study

participants (16%), and procedure-related AEs occurred in 15 of the participants (12%).

Uncomfortable change in stimulation was the most common device-related AE, which occurred in 11 participants (9%), and was either resolved with a simple adjustment of the stimulation amplitude via the remote control in two participants or device reprogramming in nine participants. One participant (<1%) reported an event of discomfort/heating near the charging area and this was resolved with retraining on proper charging technique. Two participants (<2%) reported pain at the INS site, one of which was resolved with surgical intervention (details below) and one resolved with medication.

A total of 14 surgical interventions were performed in 11 study participants (9%) which included lead revision, INS revision, and device explant. Lead revisions were performed in three participants (2%) due to lead migration ($n = 1$ at 3 months postimplant) or high impedances ($n = 2$). The lead revisions resulted in a return of efficacy in all cases. INS revision was performed in four participants (3%); one INS revision was performed to resolve an infection at the INS site (after the INS explant), one due to pain at the INS site, and INS migration/rotation in two participants. The etiology for INS migration/rotation was an abdominoplasty surgery which altered the anatomy around the INS site. A total of five participants (<4%) were explanted without an INS reimplant. The reasons for explant were infection at INS site in one participant, pain unrelated to the device in one participant, and insufficient efficacy in three participants.

A total of eight participants (6%) exited the study before the 2-year visit. Study exit reasons included system explant (five participants), lost to follow-up (one participant), insufficient efficacy and device hibernation (one participant), and death unrelated to the study device or procedure (one participant).

A total of 13 MRIs were performed in 12 study participants (9%) during the study, with eight MRIs performed on the body/spine/torso and the remaining five MRIs performed on the head/neck. The reasons for MRI were pre-existing conditions such as back pain, medical evaluation of diagnoses of cancer or neurologic conditions, or events such as falls/accidents. No adverse events or lead migrations were reported after any of the MRIs.

4 | DISCUSSION

The ARTISAN-SNM study evaluated the safety and efficacy of the rechargeable Axonics System in patients suffering from UUI. Sustained safety and efficacy of the Axonics rechargeable system was demonstrated at 2 years, along with high degrees of patient satisfaction and acceptability of recharging. The durable therapeutic efficacy and charging satisfaction contrasts with published opinions that have raised concerns about patient satisfaction and compliance with rechargeable therapy.[13] The safety profile of the therapy is also very favorable, with a relatively low rate of explants and revisions due to AEs. In the InSite study of nonrechargeable SNM, 4% of participants had lead migrations, with the majority taking place between 12- and 24-months post-implant.[14] The only lead migration seen in the ARTISAN-SNM study was between 1 and 3 months,[7] and no lead migrations occurred between 12 and 24 months which demonstrates the reliable performance of the Axonics System. Additionally, the minimal occurrence of pain at the implant site was anticipated and the results are extremely favorable, especially relative to studies of the larger, nonrechargeable system.[5,14]

The ARTISAN-SNM study had extremely high rates of therapy success, symptom reduction, and satisfaction throughout the study, with 93% of participants continuing to respond to therapy at 2 years. High responder rates were consistent across all study visits even when analyzed in all implanted participants, which included the participants who were initial therapy failures and those who had been exited from the study. This "As-treated" analysis provides a more conservative assessment of therapy outcomes, yet the therapeutic response of this study remains high at 2 years, further demonstrating the robustness of the results and acceptability of rechargeable therapy. Additionally, the majority of the therapy responders (82%) had a 75% or higher urge leak reduction, and 37% of the therapy responders were dry. The magnitude of these results shows that most of the participants were well-above the traditional criteria for therapy success defined as a greater than 50% reduction in UUI episodes. The high clinical efficacy of the study results is likely influenced by the use of optimal lead placement techniques,[8,15–17] minimal lead migrations, and the constant-current stimulation provided by the Axonics System. Additional studies are necessary to understand the impact of these and other factors on therapy success.

The demographics and clinical characteristics of the study participants suggest that the efficacy and safety results are applicable to a diverse patient population. Study participants had a wide range of ages (range: 21- to 86-year old) and BMI (range: 18–58). Participants were varied in their disease severity (baseline UUI range: 1.33–23 episodes per day), and duration of clinical diagnosis (6 months–54 years). There was no correlation between these various patient-related factors and the magnitude of urge leak reduction, indicating that therapy success is not dependent on these patient factors.

The diverse patient population in this study found that recharging with the Axonics System was easy and acceptable. A substantial proportion of the study participants (94%) were satisfied with their therapy and 94% rated recharging as acceptable. None of the tested patient demographics or clinical factors were found to impact patient recharging behavior. The recharging duration per week was similar from 3 months to 2 years, indicating no loss of battery capacity over time. The availability of a next-generation system (Axonics) with an even more favorable charging profile (once a month for an hour) should further improve the recharging experience.[18]

Strengths of the ARTISAN-SNM study include a prospective study design with 2-year safety and efficacy data in a large cohort of study participants. Additionally, this study showed sustained adoption of the Axonics rechargeable system. A limitation of the study was the absence of a placebo or control arm. Considering that SNM is a widely adopted treatment with proven long-term efficacy, concerns related to a placebo effect may not be applicable to evaluating the safety and efficacy of rechargeable SNM.

Benefits of using a rechargeable system include a reduced number of revision/replacement surgeries (due to the small INS size and device life of 15 years) as well as potentially increased patient comfort and projected lower healthcare costs.[19] This study shows that high patient satisfaction and significant, durable symptom reduction can be achieved with the rechargeable Axonics System without the significant tradeoffs historically reported for rechargeable systems.[13,20] Reasons for high satisfaction with recharging may include unique aspects of the Axonics rechargeable System, such as the small device size, the low recharging burden (short duration of recharging), and optimal implanting INS technique. Additionally, the Axonics recharging system was designed after extensive user-testing and feedback from the patient community, thus optimizing for real-life recharging experience. Having a long-lasting,[21] safe, and effective treatment for OAB/FI is especially important since recent literature has suggested an increased risk of long-term side-effects such as dementia in patients chronically taking anticholinergic medications.[22] Long-lasting, easy to use, third-line therapies such as SNM or percutaneous nerve stimulation could be considered as an early alternative to anticholinergic medications.

5 | CONCLUSION

The rechargeable Axonics System provides sustained benefits to participants with urinary urgency incontinence. Participants experienced safe and efficacious outcomes, with significant quality of life improvements. High levels of satisfaction with the therapy and recharging were reported throughout the 2-year study. Participant factors did not contribute to the efficacy or recharging outcomes, suggesting these results are applicable to a diverse patient population.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All named authors have contributed to study conception and design, article drafting and revisions, as well as read and approved the manuscript for submission.

PEER REVIEW

Prof. John Heesakkers led the peer-review process as the Associate Editor responsible for the paper.

DATA AVAILABILITY STATEMENT

The authors elect to not share data.

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REFERENCES

1. Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int*. 2011;108(7):1132-1138.
2. Milsom I, Coyne KS, Nicholson S, Kvasz M, Chen CI, Wein AJ. Global prevalence and economic burden of urgency urinary incontinence: a systematic review. *Eur Urol*. 2014;65(1):79-95.
3. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019. *J Urol*. 2019; 202(3):558-563.
4. Siegel S, Noblett K, Mangel J, et al. Five-year follow-up results of a prospective, multicenter study of patients with overactive bladder treated with sacral neuromodulation. *J Urol*. 2018; 199(1):229-236.
5. van Kerrebroeck PEV, van Voskuilen AC, Heesakkers JPFA, et al. Results of sacral neuromodulation therapy for urinary voiding dysfunction: outcomes of a prospective, worldwide clinical study. *J Urol*. 2007;178(5):2029-2034.

6. McCrery R, Lane F, Benson K, et al. Treatment of urinary urgency incontinence using a rechargeable SNM system: 6-month results of the ARTISAN-SNM Study. *J Urol*. 2020; 203(1):185-192.
7. Benson K, McCrery R, Taylor C, et al. One-year outcomes of the ARTISAN-SNM study with the Axonics System for the treatment of urinary urgency incontinence. *Neurourol Urodyn*. 2020;39(5):1482-1488.
8. Goldman HB, Lloyd JC, Noblett KL, et al. International Continence Society best practice statement for use of sacral neuromodulation. *Neurourol Urodyn*. 2018;37(5):1823-1848.
9. Coyne KS, Matza LS, Thompson CL, Kopp ZS, Khullar V. Determining the importance of change in the overactive bladder questionnaire. *J Urol*. 2006;176(2):627-632.
10. Noblett K, Siegel S, Mangel J, et al. Results of a prospective, multicenter study evaluating quality of life, safety, and efficacy of sacral neuromodulation at twelve months in subjects with symptoms of overactive bladder. *Neurourol Urodyn*. 2016; 35(2):246-251.
11. Richard N, Hudson M, Gyger G, Baron M, Sutton E, et al. Clinical correlates of faecal incontinence in systemic sclerosis: identifying therapeutic avenues. *Rheumatology (Oxford)*. 2017; 56(4):581-588.
12. Amundsen CL, Komesu YM, Chermansky C, et al. Two-year outcomes of sacral neuromodulation versus onabotulinumtoxinA for refractory urgency urinary incontinence: a randomized trial. *Eur Urol*. 2018;74(1):66-73.
13. de Wachter S, Knowles CH, Elterman DS, et al. New technologies and applications in sacral neuromodulation: an update. *Adv Ther*. 2020;37(2):637-643.
14. Siegel S, Noblett K, Mangel J, et al. Three-year follow-up results of a prospective, multicenter study in overactive bladder subjects treated with sacral neuromodulation. *Urology*. 2016; 94:57-63.
15. Adelstein SA, Lee W, Gioia K, et al. Outcomes in a contemporary cohort undergoing sacral neuromodulation using optimized lead placement technique. *Neurourol Urodyn*. 2019; 38(6):1595-1601.
16. Matzel KE, Chartier-Kastler E, Knowles CH, et al. Sacral neuromodulation: standardized electrode placement technique. *Neuromodulation*. 2017;20(8):816-824.
17. Vaganée D, Kessler TM, van de Borne S, de Win G, de Wachter S. Sacral neuromodulation using the standardized tined lead implantation technique with a curved vs a straight stylet: 2-year clinical outcomes and sensory responses to lead stimulation. *BJU Int*. 2019;123(5A):E7-E13.
18. Business Wire. Axonics® Announces U.S. Food & Drug Administration approval of next-generation implantable neurostimulator; November 4, 2020.
19. Noblett KL, Dmochowski RR, Vasavada SP, Garner AM, Liu S, Pietzsch JB. Cost profiles and budget impact of rechargeable versus non-rechargeable sacral neuromodulation devices in the treatment of overactive bladder syndrome. *Neurourol Urodyn*. 2017;36(3):727-733.
20. Khaleeq T, Hasegawa H, Samuel M, Ashkan K. Fixed-life or rechargeable battery for deep brain stimulation: Which do patients prefer? *Neuromodulation*. 2019;22(4):489-492.
21. Elterman DS. The novel Axonics® rechargeable sacral neuromodulation system: procedural and technical impressions from an initial North American experience. *Neurourol Urodyn*. 2018;37(S2):S1-S8.
22. Coupland CAC, Hill T, Dening T, Morriss R, Moore M, Hippisley-Cox J. Anticholinergic drug exposure and the risk of dementia: a nested case-control study. *JAMA Intern Med*. 2019;179:1084.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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