

Impacto económico dos neuromoduladores recarregáveis – Muda o paradigma?

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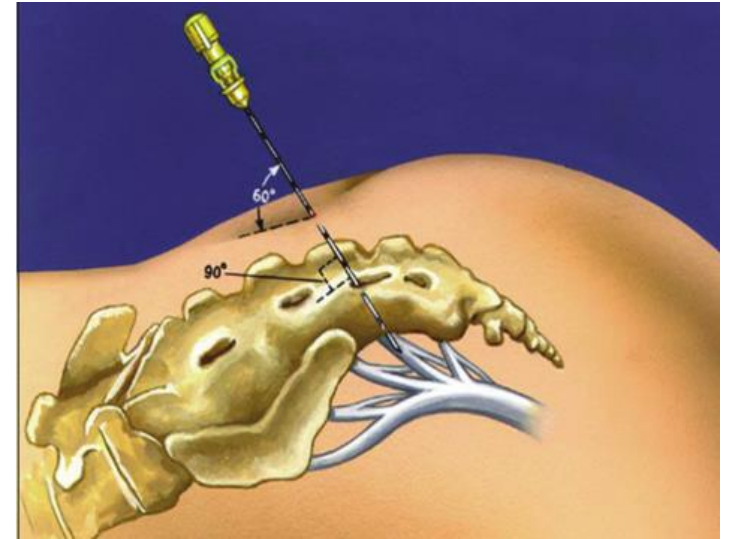
SNM - indications

- Urological

- Refractory OAB – 75%
 - Wet -1997
 - Dry -1999
- No obstructive urinary retention –NOUR -1999 – 25%

- Proctological

- Fecal incontinence -2011
- Chronic constipation -Europe



OAB treatment

- First-line treatment
 - **Behavioural therapies** -bladder training (BT) and pelvic floor muscle therapy (PFMT)
 - **Lifestyle changes** -fluid and caffeine intake, diet, weight loss, *management of bowel regularity, and optimization of other comorbidities*
 - **Patient education** -motivation and adherence to the previous strategies
- Second-line treatment
 - Pharmacological
- Third-line treatment
 - BTXA
 - SNM

SMN vs BTXA



- Which is the preferred/first, third line option remains open to debate
- Failed BTXA therapy
 - due to either lack of efficacy, urinary retention, or adverse reaction
 - patients may be candidates for SNM.

SNM - safety

- The most common adverse event
 - pain at the implant site
 - in most studies varies between 3% and 42%
- Other adverse events reported
 - lead migration (1–21%)
 - bowel dysfunction (4–7%)
 - infection(4–10%).

Banakhar MA, Al-Shaiji T, Hassouna M. Sacral neuromodulation and refractory overactive bladder: an emerging tool for an old problem. Ther Adv Urol. 2012;4:179–185.

SNM - efficacy

- Success rates, have been reported between 64% and 88%.

Table 1: Results of SNM treatment in OAB patients [Hassouna *et al.* 2000; Hijaz *et al.* 2006; Sutherland *et al.* 2007; van Kerrebroeck *et al.* 2007; van Voskuilen *et al.* 2006, 2007; Weil *et al.* 2000].

Study	General improvement (%)	Void/day (%)	Volume/void (%)	Follow up (months)
Hassouna <i>et al.</i> [2000]	88	-46	77	12
Hijaz <i>et al.</i> [2006]	75	NA	NA	16
Sutherland <i>et al.</i> [2007]	69	-35	NA	22
van Kerrebroeck <i>et al.</i> [2007]	NA	-23	79	49
van Voskuilen <i>et al.</i> [2006]	80	-38	44	15
van Voskuilen <i>et al.</i> [2007]	64	NA	NA	64
Weil <i>et al.</i> [2000]	56 (100% continence)	NA	NA	6

Banakhar MA, Al-Shaiji T, Hassouna M. Sacral neuromodulation and refractory overactive bladder: an emerging tool for an old problem. *Ther Adv Urol.* 2012;4:179–185.

SNM after BTXA

- To date, there has been little data on the efficacy of SNM after BTXA.
- Smits et al reported
 - 70% success rate for first-stage SNM (n=20).
 - 79% success at 1 year with the Permanent implantable pulse generator (IPG) (n=14)

Smits MAC, Oerlemans D, Marcelissen TAT, Kerrebroeck PEV Van, De Wachter SGG. Voiding Dysfunction Sacral Neuromodulation in Patients with Idiopathic Overactive Bladder after Initial Botulinum Toxin Therapy. *J Urol.* 2013;190:2148-2152. doi:10.1016/j.juro.2013.07.017.

SNM after BTXA

- Success rate of 70 % in BTXA-naïve patients (n=47)
 - 63.9 % for prior BTXA (n=36). P=0,5
 - 64.0 % for prior “ineffective” BTXA (n=25) P=0,6
- First-stage SNM success rate
 - 68 % (n=19) \leq 2 BTXA treatments,
 - 58 % (n=17) \geq 3 BTXA treatments (P=0.5).

Hoag N, Plagakis S, Pillay S, Edwards AW, Gani J. Sacral neuromodulation for refractory overactive bladder after prior intravesical onabotulinumtoxinA treatment. *Neurourol Urodyn*. 2017. doi:10.1002/nau.23117.

SNM - cost-effectiveness related to BTXA

- SNM as the first therapeutic option for refractory idiopathic OAB-wet
 - is cost effective after 3 years
 - €21,259/QALY), (ICUR < 40.000 €/QALY)
 - and becomes dominant at 10 years
 - less costly— €333.22 saved
 - more effective— 0.59 QALY gained

Bertapelle MP, Vottero M, Popolo G Del, et al. Sacral neuromodulation and Botulinum toxin A for refractory idiopathic overactive bladder: a cost-utility analysis in the perspective of Italian Healthcare System. *World J Urol.* 2015. doi:10.1007/s00345-014-1401-7.

Table 2 Cost-utility analysis

Year	Costs (€)	QALYs	ICUR (€/QALY)
<i>Year 1</i>			
SNM strategy	12,423.36	0.85	
BoNT/A strategy	6,500.17	0.79	
SNM strategy versus BoNT/A strategy	5,923.19	0.05	109,333.34
<i>Year 2</i>			
SNM strategy	14,712.09	1.68	
BoNT/A strategy	9,933.04	1.57	
SNM strategy versus BoNT/A strategy	4,779.06	0.11	44,322.80
<i>Year 3</i>			
SNM strategy	16,901.10	2.49	
BoNT/A strategy	13,249.41	2.32	
SNM strategy versus BoNT/A strategy	3,651.69	0.17	21,258.72

SNM - cost-effectiveness

Bertapelle MP, Vottero M, Popolo G Del, et al. Sacral neuromodulation and Botulinum toxin A for refractory idiopathic overactive bladder: a cost-utility analysis in the perspective of Italian Healthcare System. *World J Urol.* 2015. doi:10.1007/s00345-014-1401-7.

<i>Year 10</i>			
SNM strategy	32,975.47	7.52	
BoNT/A strategy	33,308.69	6.93	
SNM strategy versus BoNT/A strategy	-333.22	0.59	SNM dominant

cost effective (ICUR < 40.000 €/QALY)

SNM strategy, clinical pathway starting with sacral neuromodulation (SNM); BoNT/A, clinical pathway starting with Botulinum toxin A (BoNT/A) injections; *QALY* quality-adjusted life year, *ICER* incremental cost-effectiveness ratio

SNM - cost-effectiveness

In Europe, the relative cost-effectiveness of SNM and BTXA has been investigated in Spain (1), Holland (2) and UK (3)

1. Arlandis S, Castro D, Errando C et al (2011) Cost-effectiveness of sacral neuromodulation compared to Botulinum neurotoxin A or continued medical management in refractory overactive bladder. Value Health 14:219–2287.
2. Leong RK, de Wachter SG, Joore MA et al (2011) Cost-effectiveness analysis of sacral neuromodulation and Botulinum toxin A treatment for patients with idiopathic overactive bladder. BJU Int 108:558–5648.
3. Walleser S, Betts C, Hallas N et al (2012) Sacral nerve modulation (SNM) for the treatment of idiopathic refractory overactive bladder: cost-effective in the UK compared to optimal medical therapy, Botulinum toxin A (BoNT-A) and percutaneous tibial nerve stimulation (PTNS). Value Health 15:A354–A3559.

SNM - cost-effectiveness

as well as in the USA (4) and Canada (5)

- all of them suggesting that

SNM is cost-effective in the medium and long-term

4. Ganz M, Clemens JQ, Anger J et al (2011) A Markov model comparing sacral neuromodulation and Botulinum toxin-A for medicare patients with idiopathic overactive bladder refractory to conservative care. Value Health 14:A211–A214

5. Hassouna M, Corcos J, Dwyer N et al (2012) Cost-effectiveness of sacral neuromodulation in refractory overactive bladder: a Canadian perspective. J Urol 187(4S):e117

Neuromoduladores recarregáveis

– Muda o paradigma?



Neurourology and Urodynamics

**Cost Profiles and Budget Impact of Rechargeable Versus
Non-Rechargeable Sacral Neuromodulation Devices in the
Treatment of Overactive Bladder Syndrome**

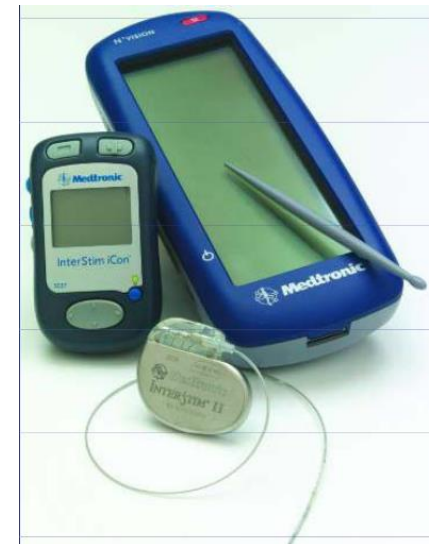
Noblett et al.

Neurourology and Urodynamics 2017 DOI 10.1002/nau

Non-rechargeable - Interstim II



- Current SNM device are not rechargeable, and require neurostimulator replacement every 3–6 years.
- Long term success rate proven to 5 years
- Acceptable cost-effectiveness profile
- Substantial upfront costs
- Replacement expenditures are the major cost contributor



Rechargeable devices

An **increased battery life** is a desirable feature not only for patients, but also for healthcare payers.

Rechargeable neurostimulation systems are currently being developed and tested

Cost profiles

- Analyze and compare the cost profiles of rechargeable versus non-rechargeable SNM devices
- Estimate the resulting long-term budget impact to payers
- Based on hypothetical scenarios

- Rechargeable strategy
 - reported lifetime of rechargeable spinal cord stimulation (SCS) systems (Eon Mini™ Rechargeable IPG; Nevro Senza SCS System)
- Non-rechargeable strategy
 - Reported lifetime of the established InterStim from the



InSite trial

Neurourology and Urodynamics 34:224–230 (2015)

**Results of a Prospective, Randomized, Multicenter Study
Evaluating Sacral Neuromodulation With InterStim
Therapy Compared to Standard Medical Therapy at
6-Months in Subjects With Mild Symptoms of
Overactive Bladder**

Siegel et al

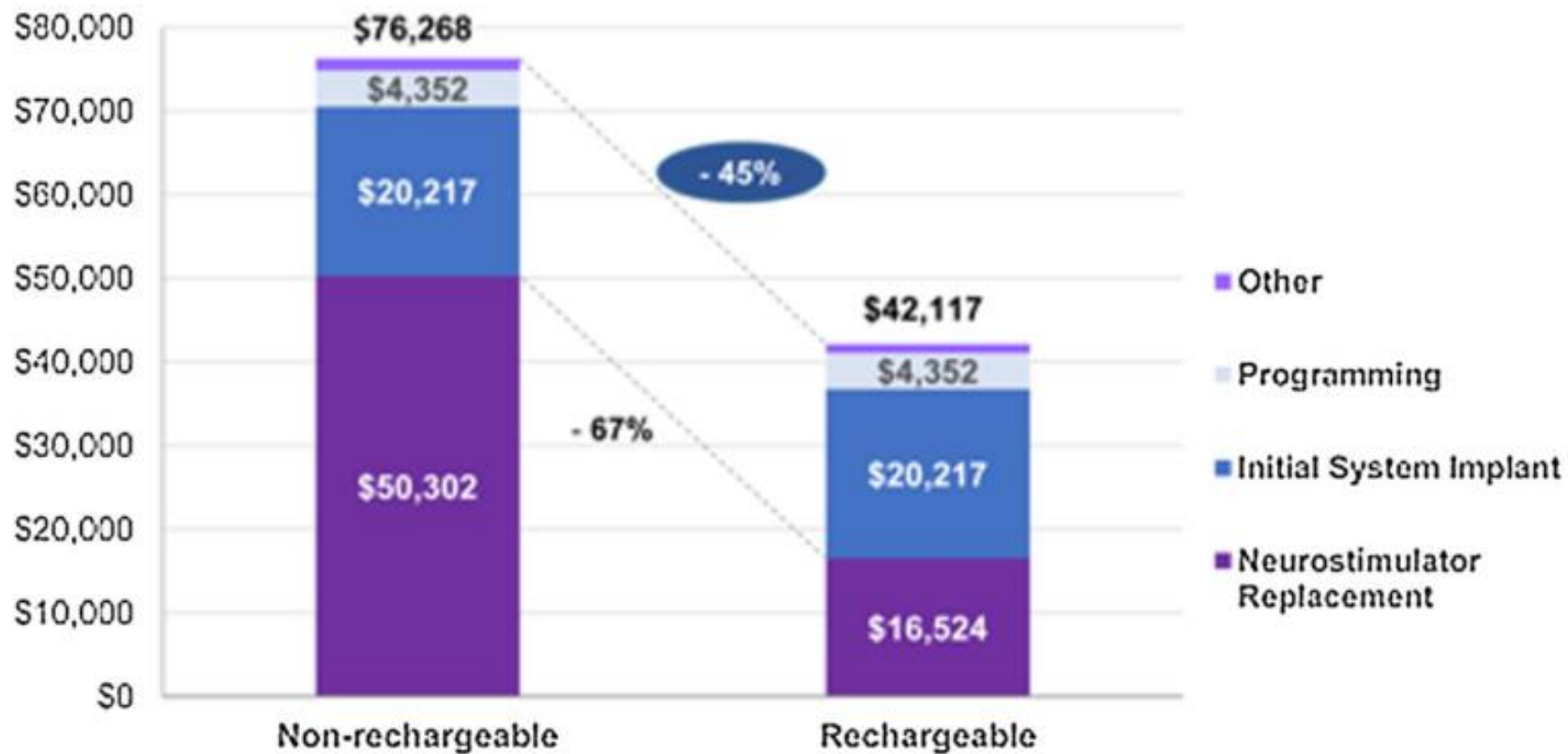


Fig. 1. Fifteen-year undiscounted costs per patient, non-rechargeable versus rechargeable device, and percentage change in total cost and neurostimulator replacement cost.

Neurourology and Urodynamics DOI 10.1002/nau

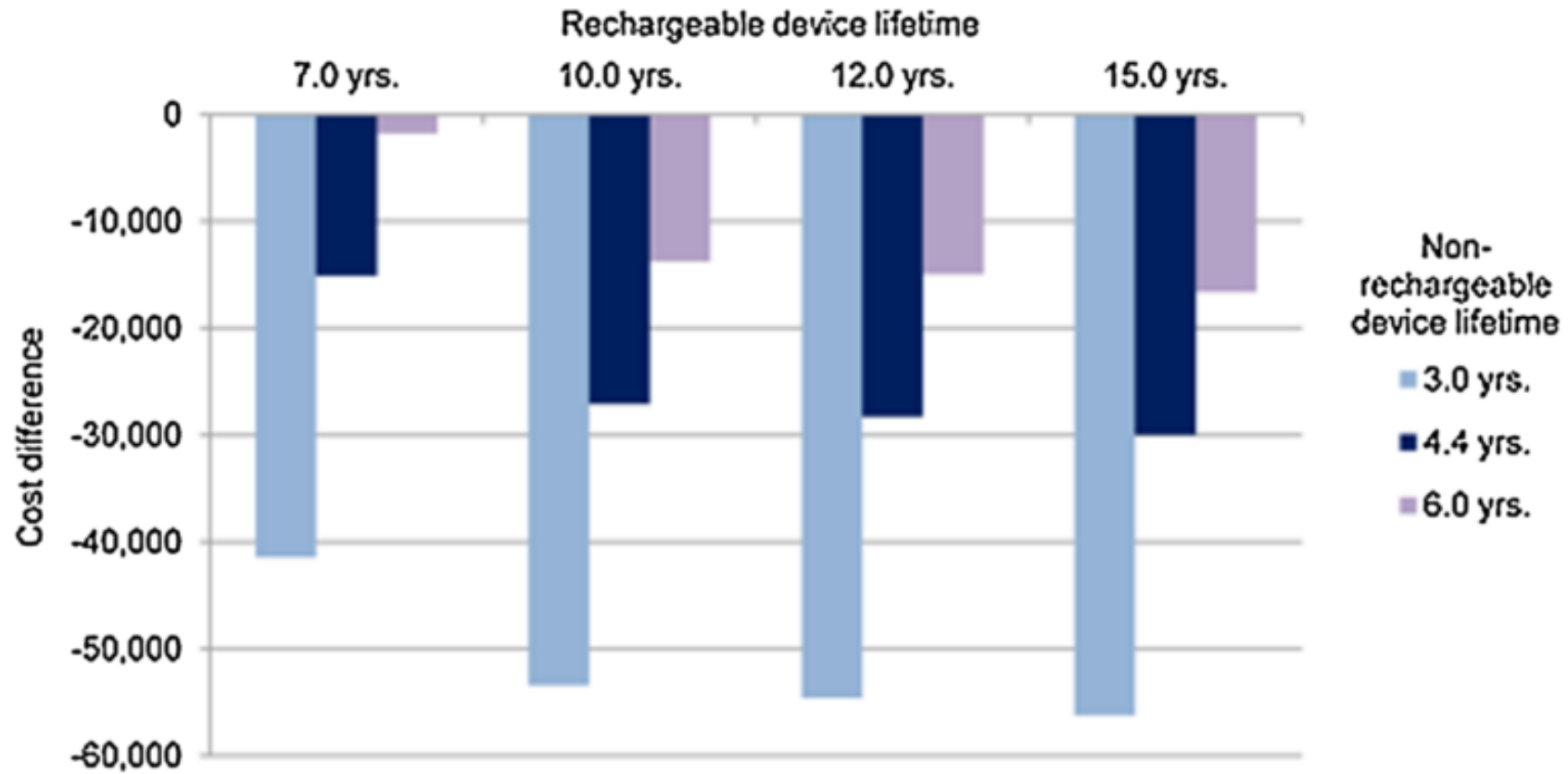


Fig. 2. Cost difference between non-rechargeable and rechargeable SNM device strategy at 15 years for various scenarios of respective battery lifetimes. A negative number denotes a saving associated with the rechargeable SNM device strategy. All amounts discounted.

Budget Impact (Savings) to Payers , discounted

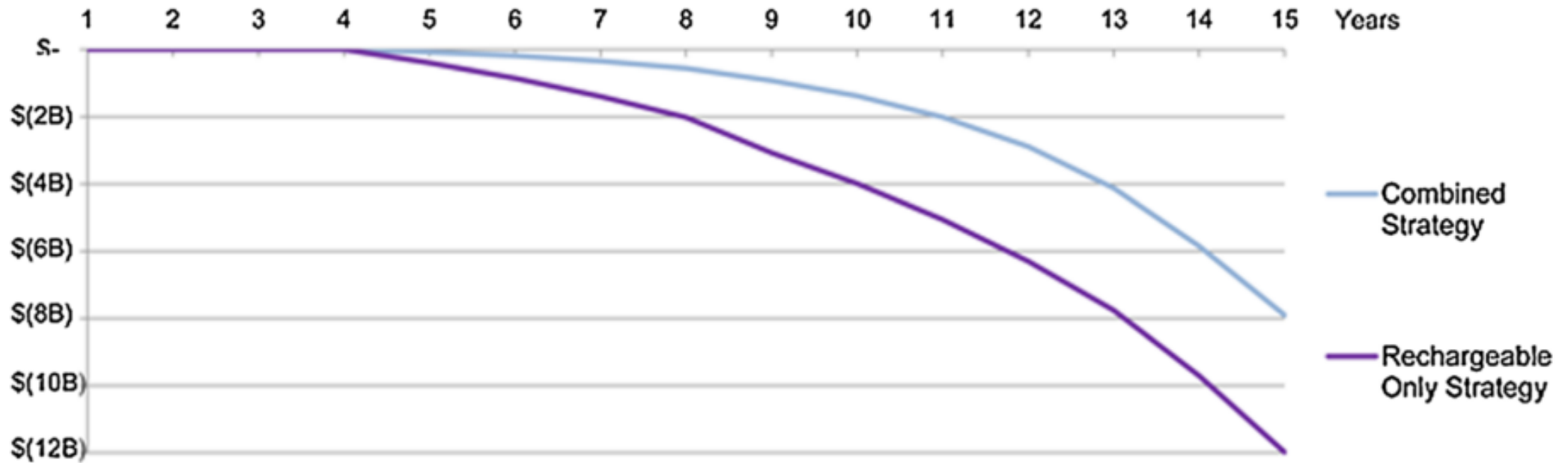


Fig. 3. Budget impact to United States payers for two adoption scenarios (gradual adoption of rechargeable devices vs. immediate full adoption scenario), considering new implants only. All amounts discounted.

Neurourology and Urodynamics DOI 10.1002/nau

Rechargeable devices

- Rechargeable SNM systems are not yet commercially available
- Long-term performance is based on the best available evidence from comparable rechargeable systems used in the field of SCS.
- Rechargeable neurostimulator devices for sacral neuromodulation may deliver significant cost savings

Rechargeable devices -Axonics



- The device was approved in 2016 for the treatment of OAB in Europe and Canada
- Consists of a small volume rechargeable neurostimulator (60% smaller than Interstim)
- Approved for head MRI like Interstim.
- The battery is rechargeable with a 15-year lifetime in the body
- There is no real-life data to support the efficacy up to 15 years
- Recharging, performed via a wireless charger, secured to the patient either by disposable carrier or a flexible belt, would be expected to take between 1 and 2 hours



Guzman-Negron JM, Goldman HB. New Devices and Technologies for the Management of Overactive Bladder. doi:10.1007/s11934-017-0739-y.

Axonics

- There is currently a prospective multicenter clinical study ([RELAX-OAB trial](#)) designed to confirm the performance of the Axonics SNM System

ClinicalTrials.gov

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Treatment of REfractory Overactive BLadder With the AXonics Sacral Neuromodulation System (RELAX-OAB)

This study is ongoing, but not recruiting participants.

Sponsor:

Axonics Modulation Technologies, Inc.

ClinicalTrials.gov Identifier:

NCT02620410

First Posted: December 3, 2015

Last Update Posted: July 19, 2017

Enrollment:	51
Study Start Date:	June 2016
Estimated Study Completion Date:	February 2019
Primary Completion Date:	June 2017 (Final data collection date for primary outcome measure)

Nuvectra

- Nuvectra Corporation submitted in 2/2017 to the FDA and CE Marking authorities for Virtis™ approval
- Is full body MRI compatible.
- Is **dual channel**, therefore can perform bilateral stimulation.
- Can last up to **10 years**.

VIRTIS

Pros and cons



- Rechargeable is not suitable for everyone
- InterStim can fit patients' lifestyles, providing FREEDOM to live without thinking about their therapy.
- At this time, there are no published data to the Axonics system.

Pros and cons

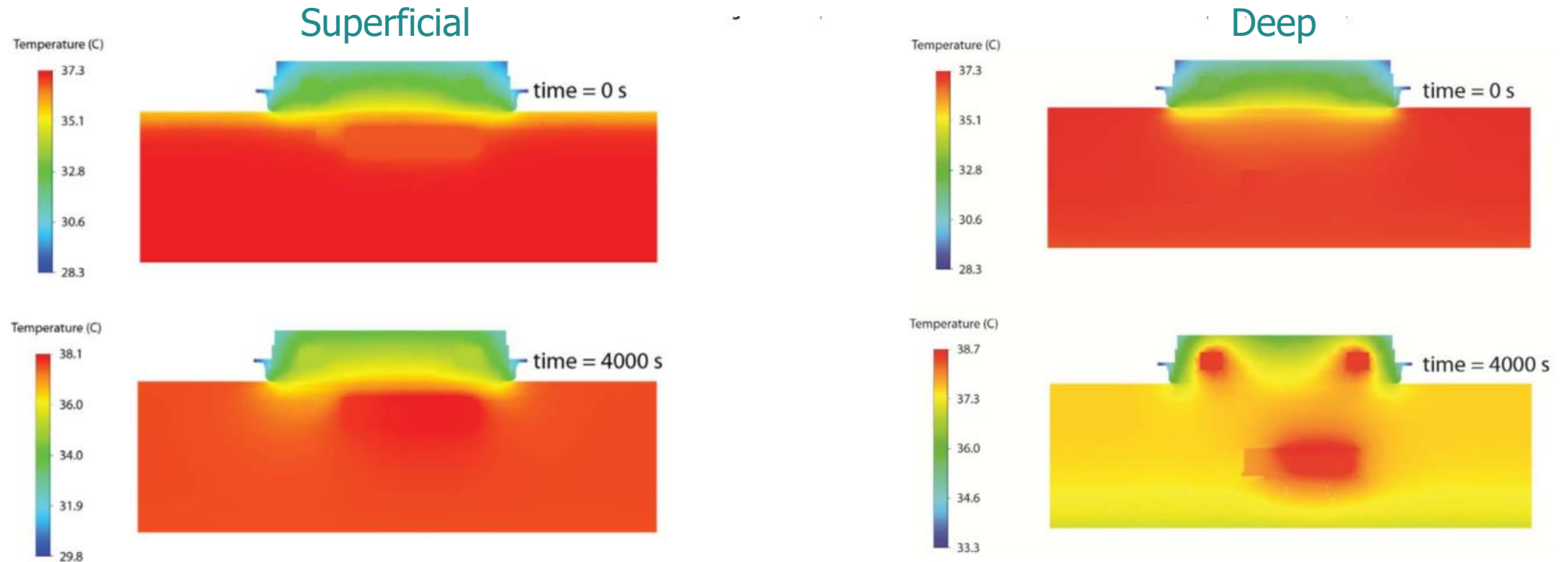


- **Coupling** with patient programmer or recharger might be more difficult with a smaller device
- The **position, changes in depths** and the **orientation** of the device may vary with time
- As a result, **the efficiency of the recharge** may decreased and more heat may be generated over time

Plourde B, Vallez L, Nelson-Cheeseman B, Abraham J. Transcutaneous Recharge: A Comparison of Numerical Simulation to In Vivo Experiments. *Neuromodulation*. 2017. doi:10.1111/ner.12627.

Pros and cons

- Numerical simulation to predict tissue temperatures in **changes in depths** and **orientation**
- The results show that temperatures do not rise to a level which can cause thermal injury.
- That level is generally considered to be 43°C.



Abraham JP, Plourde BD. Validation of Numerically Simulated Tissue Temperatures during Transcutaneous Recharge of Neurostimulation Systems. *Neuromodulation*. 2016. doi:10.1111/ner.12331.

Conclusions

- Today SNM is Interstim II
 - Safe
 - Long term success rate proven to 5 years, even in failed-BTXA
 - Cost-effective in the medium and long-term
- Rechargeable SNM
 - Not suitable for everyone
 - Probably in the next 2 years – Axonics, Interstim recarregável
 - May deliver significant cost savings




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