Urgent-SQ Implant: Safety and Efficacy, 18 Years After First Implantation.

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Research article

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Abstract

Background: To evaluate the long term follow up in terms of safety and usability of the Urgent-SQ system (implantable tibial nerve stimulator) based on 1 year, 9 year follow up and novel results 18 years after first implantation in 2002.

Materials & Methods: Since 2002, eight patients were implanted with the Urgent-SQ system. Seven patients were included in previous follow up studies, 1 patient had loss of efficacy before 1 year of follow up. During this study all patients who were included in the previous follow-up studies (n=7) were contacted to be interviewed regarding efficacy, usability and safety.

Results: Five out of seven patients were available for assessment, mean age 72 years ± 8 (range 65-82). Two patients were considered lost to follow up. None of the interviewed patients reported safety issues, new adverse events or discomfort. One of the patients was able to visit the hospital for efficacy. However, treatment could not be performed due to deficiency of the external or internal component. All patients did not perform self-stimulation anymore due to external stimulator deficiency (n=2) or loss of effect (n=3).

Conclusion: 18 year follow up of the Urgent-SQ implant demonstrates a high safety profile. However efficacy after 18 years is lacking in 60% whereas in 40% the therapy cannot be applied because the external stimulator is deficient. This most likely depicts the end of the lifecycle of the device.

Introduction

Overactive bladder syndrome (OAB) is a condition characterized by “urinary urgency, often accompanied with frequency and nocturia, with or without urgency urinary incontinence in the absence of proven infection or other obvious pathology” according to the ICS terminology. [1] The prevalence of OAB is rising with age and approximately 43% of women 40 years and older do have signs of OAB. Besides, women are twice as likely affected by OAB. [2, 3]

In the treatment of OAB, percutaneous electrical stimulation of the tibial nerve (PTNS) is one of the regular third line therapies after behavioral therapy and medication. PTNS efficacy was proven in sham-controlled studies and has efficacy ranges between 55%-80%. [4–6] Since a few years the field of tibial nerve stimulation became of interest for several companies with small implanted tibial nerve stimulators. However, the first pilot study with a tibial nerve implant was already performed between 2002 and 2004 with the Urgent-SQ device.

The Urgent-SQ system consists of an external stimulator and an internal body. The external stimulator is an external electromagnetic pulse generator and has radio-frequency transmission. The internal body of the Urgent-SQ consist of an electromagnetic pulse receiver and a body with two leads containing monopolar electrodes (Fig. 1.). [7]

Results published by van der Pal et al. were promising. The 1 year follow up demonstrated significant improvement of voiding and quality of life parameters. [8] Subsequently, the 9 year follow up study by
Janssen et al demonstrated the high safety profile of the Urgent-SQ system. This latter open label study reported that 3 patients were still using the system. Six of the seven patients still had sensory and loco-motor responses on stimulation. [7]

The aim of this study is to evaluate the long term follow up in terms of usability and safety of the Urgent-SQ system based on previous published results and novel results.

**Patients & Methods**

This 18 year follow up study included all patients \( (n = 7) \) who were included in the 1-year and 9 year follow up paper. [7, 8] These patients underwent an implantation procedure with the Urgent-SQ between 2002 and 2004. In total, eight patients were implanted with the Urgent-SQ system. One of the implanted patients had unexplainable loss of efficacy after 6 months of follow up. This patient underwent an explantation of the implant, was dropped out of all studies and was considered unsuccessful. [8]

During this study, patients were interviewed through a standardized discussion with a physician by phone. This discussion consisted of questions regarding efficacy, durability and safety of the Urgent-SQ system. The hospital’s local ethical committee approved the study. The results were compared to the former published papers (1-year and 9 year follow up). Table 1. summarizes the questions patients were asked. Second, patients who reported sensory and loco-motor responses at 9 year follow up \( (n = 3) \) were asked to visit the hospital. During this visit physical examination was performed including stimulation of the implant with FineTech-Brindley External Controller© due to absence of the original Urgent-SQ external controller.

| Table 1                                      |
|----------------------------------------------|
| Primary subjective outcomes of safety and daily life usability of the Urgent-SQ device. |
| Do you still use the Urgent-SQ implant? If not, since when? |
| What is the reason for not using the implant anymore? |
| Did you concern any safety issues the past years? (i.e. explantation) |
| Do you have any walking or mobility difficulties? |
| Do you experience any pain or discomfort at the site of the implant? |
| Can you see or palpate the implant? |

**Results**

Results were obtained from 5/7 patients (60% female), mean age during 18 year follow up was 72 years ± 8 (range 65–82). Two patients could not be contacted and were considered lost to follow up. Both patients were responders after 1 year of follow up. During 9 year follow up one of them was still using the system.
All five patients, included in this follow up study, did not use the system anymore due to external stimulator deficiency \((n = 2)\) or loss of effect \((n = 3)\). Patients who reported external stimulator deficiency were satisfied with the treatment and used it frequently until deficiency. After quitting the therapy the complains of urge/ urge-incontinence increased again in all patients \((n = 5)\). Patients are on different treatment nowadays varying from botulin toxin, to medication or alternative medicine. Only patient 2 (Table 2) was able to come over to the hospital. During physical examination the implant was not visible from the outside. Palpation of the ankle and implant area was not painful. Unfortunately, we did not see any sensory and/or loco-motor responses during test stimulation.

### Table 2

|       |       | 1 year follow up | 9 year follow up | 18 year follow |
|-------|-------|------------------|------------------|--------------|
|       |       | Response | Pain | In use | Response | Pain | In use | Response | Pain | In use |
| P1    | M     | +        | -    | +      | +        | -    | -      | n/a      | -    | -      |
| P2    | F     | +        | -    | +      | +        | -    | +      | -        | -    | -      |
| P3    | F     | +        | -    | +      | -        | -    | -      | n/a      | n/a  | n/a    |
| P4    | F     | +        | -    | +      | +        | -    | +      | n/a      | n/a  | n/a    |
| P5    | M     | +        | -    | +      | +        | -    | -      | -        | -    | -      |
| P6    | F     | -        | -    | -      | -        | -    | -      | n/a      | -    | -      |
| P7    | F     | +        | -    | +      | +        | -    | +      | n/a      | -    | -      |
| P8    | F     | -        | -    | -      | -        | -    | -      | -        | -    | -      |

* Age during 18 year follow up moment.

\[\hat{\text{1}}]: Treatment not effective anymore
\[\hat{\text{2}}]: Device deficiency
\[\hat{\text{3}}]: Started treatment again after 9 year follow up control
P3 and P4 were considered lost to follow up in the present study.
P6 had unexplained loss of efficacy within 1 year after implantation;
P8 was explanted after 1 year of FU

Regarding safety, all patients \((n = 5)\) reported no explantations or other surgical interventions during the extended follow up period. Other serious adverse events or adverse event due to the implant, external stimulator or implant procedure were not mentioned. Patients did not report any local problems at the site of the implant. None of the patients had problems with discomfort or pain at the implant site during resting state, nor during walking/ exercises. Most of the patients \((3/5)\) could feel the implant from the outside, but could not see the implant. During palpation by themselves, No patient reported any pain or discomfort. These results are largely in line with the published 9 year follow up data. There was one patient who reported sporadic spontaneous sensory response during 9 year follow up, but this was not
reported during the present study. Table 2 shows an evaluation of the results regarding response, pain and patients who still use the Urgent-SQ system comparing to 1 year and 9 year follow up studies.

**Discussion**

In this study, the primary goal was to evaluate safety and usability of the at that time experimental Urgent-SQ implant after a maximum of 18 years after implantation. Patients ($n = 5$) reported no (serious) adverse events during follow up period. None of the patients ($n = 5$) who were included in this study reported any complaints or discomfort at the implant site. Therefore, we conclude that the Urgent-SQ is a well-tolerated implant on the longer term.

Due to the small number of patients and the technical failure of the external devices in this study, the results for long term efficacy of tibial nerve stimulation via an implant is difficult to interpret beyond 9 years. Patient 2 did not have sensory and/or loco-motor responses during this study visit, however the reason for failure is unclear. This may have to do with the internal components of the implant (i.e. leads or electromagnetic pulse receiver) or because of the fact that we were not stimulating the implant with the original external stimulator. However, the Urgent-SQ external stimulator used the same, but simplified, technology as the Brindley external stimulator.

All patients did subjectively report a worsening of symptoms after technical failure of the external stimulator. Comparing these results to other devices with longer follow up periods as well, we do see a large difference in efficacy outcome not in favor of the urgent-SQ. [9, 10] However, Peters et al reported a 41% (88/217) re-intervention rate in their long term SNM (sacral neuromodulation) study. In our follow up study ($n = 5$) we mentioned 2 patients (40%) who did respond to the therapy on the longer term but had to quit because of external stimulator deficiency. Nevertheless, it is hard to combine these results because of differences in technical specificities of the devices, number of patients and study designs.

The advantages of home-based treatment for OAB with a tibial implant could not be confirmed by this study beyond 9 years. However, this study is an open label follow up study, without technical support from the sponsor and had a small number of patients with a few patients loss to follow up. In addition, the longevity of the tibial implant should be one of the main concerns for newer implanted PTNS models. Recently, a pilot study confirmed the efficacy and improvement in quality of life on the longer term follow up (3-year) of a new tibial nerve implant.[11] In the future, a larger trial should confirm other theoretical benefits regarding home based tibial nerve stimulation by an implant. This study should confirm the beneficial concept of implant driven tibial nerve stimulation, being 1) closer stimulation to the tibial nerve, 2) no need for disposable materials and 3) on demand availability in a home-based setting for treatment.

**Conclusion**

This paper demonstrates the long term follow up of the Urgent-SQ implant. It shows a high safety profile without any new adverse or serious adverse events during the maximum 18 year follow up period. Technical failure of the external stimulator (40%) is the dominant factor of therapy failure beyond 9 years.
None of the patients in this cohort is currently using the Urgent-SQ implant for their treatment of OAB. Due to unavailability of the external stimulator, no revisions were possible. New technologies of tibial nerve stimulation by an implant do show promising results but should be confirmed on the longer-term.

**Abbreviations**

OAB: Overactive Bladder  
PTNS: Percutaneous Tibial Nerve stimulation  
SNM: Sacral neuromodulation

**Declarations**

**Ethical approval**

The study has been reviewed by the ethics committee of the Radboud University Nijmegen Medical Centre on the basis of the Dutch Code of conduct for health research, the Dutch Code of conduct for responsible use, the Dutch Personal Data Protection Act and the Medical Treatment Agreement Act. The ethics committee has passed a positive judgment on the study.

Consent to Participate was obtained by written procedure.  
Consent for publication: Images were taken from previous Urgent-SQ study, see reference.

**Author contributions:**

MtD: data collection, analysis, writing  
DJ: data collection, writing  
FM: writing  
MvB: writing  
JH: writing, Protocol/project development.

All authors have approved the manuscript and agree with submission to BMC Urology.

**Availability of data**

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

**Competing interests:**

Manon te Dorsthorst: Participation in the OASIS-trial, regarding the RENOVA implantable stimulation device for Tibial Nerve Stimulation (Firm: Bluewind)  
Dick Janssen: no conflict of interest.  
Michael van Balken: Participation in the OASIS-trial, regarding the RENOVA implantable stimulation device for Tibial Nerve Stimulation (Firm: Bluewind)
John Heesakkers: Participation in the OASIS-trial, regarding the RENOVA implantable stimulation device for Tibial Nerve Stimulation (Firm: Bluewind)
Frank Martens: Participation in the OASIS-trial, regarding the RENOVA implantable stimulation device for Tibial Nerve Stimulation (Firm: Bluewind)

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