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DETAILED ANALYSIS OF ADVERSE EVENTS AND SURGICAL INTERVENTION IN A LARGE PROSPECTIVE TRIAL OF SACRAL NEUROMODULATION THERAPY FOR OVERACTIVE BLADDER PATIENTS

Hypothesis / aims of study
The InSite trial is a prospective, multicenter post-approval study in subjects receiving sacral neuromodulation (SNM) therapy with the InterStim® System for bothersome symptoms of overactive bladder (OAB). One of the primary aims of the study is to report on the safety of the tined lead out to five years. The purpose of this abstract is to provide a detailed analysis of device-related adverse events and surgical intervention out to 12 months.

Study design, materials and methods
Device-related adverse events and surgical intervention from full system implant through 12 months visit were analyzed for all subjects who completed test stimulation with a tined lead and then received a full system implant. An adverse event (AE) was defined as any undesirable experience (sign, symptom, illness, or other medical event) occurring to the patient, and that appears or worsens during the clinical study whether or not associated with the study product(s) or related procedures. A serious adverse event (SAE) was defined as any event that resulted in in-patient hospitalization or prolongation of an existing hospitalization, was life threatening, resulted in patient death, or resulted in persistent or significant disability/incapacity or impairment of a body function or permanent damage to a body structure, necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure, or resulted in fetal distress, fetal death or congenital anomaly or birth defect. A Clinical Events Committee (CEC) consisting of 3 physicians adjudicated the etiology and seriousness of all the adverse events. The CEC reviewed the reported AEs from all follow-up visits to 12 months and determined the severity and etiology of the AE. A consensus was required for adjudication and any discrepancy required re-evaluation of the AE and possible review of the source documents. For the purpose of this abstract, we specifically evaluated the device-related adverse events which are caused or contributed (with a reasonable possibility) by/to the device or the procedure to implant, explant, or program the device. Surgical interventions included device revision, replacement, or explant with no replacement.

Results
Of the 340 subjects who went through test stimulation, 272 received an SNM implant. For subjects implanted with full system, 91% were female and mean age was 57 years. Device-related adverse events occurred in 30% (82/272) of subjects 12-months post-implant, with only one considered serious (implant site erosion). Over half (56%) of the device-related AEs reported post-implant occurred between implant and the 3-month visit. A summary of the most frequent device related adverse events (undesirable change in stimulation (12%, 32/272); implant site pain (7%, 20/272); and implant site infection (3%, 9/272)) and events of lead migration/dislodgment and lead fracture are provided in the table below. As shown in the table, only 1 undesirable change in stimulation event in 1 subject (0.4%) required surgical intervention which was resolved with a lead replacement. The report of undesirable change in stimulation was often minor and was resolved in the majority of cases with minor reprogramming or temporary discontinuation of stimulation. Of the 20 subjects with implant site pain, 10 (4%) required surgical intervention, 2 of whom had the device explanted. The remaining 10 subjects only required minor interventions to resolve the events. Nine subjects experienced 12 events of a surgical site infection: 7 events were resolved by surgical intervention, 4 events were resolved with antibiotics, and 1 event required antibiotics, wound debridement and revision. Three adverse events of lead migration/dislodgment were reported in 3 subjects (1%), all of which were resolved by replacement. Four adverse events of lead fracture were reported in 4 subjects (1%), and all of which were resolved by replacement.

Besides adverse events, surgical interventions could be due to patient request, battery replacement or lack of efficacy. The overall surgical intervention rate from implant through 12 months was 13% (35/272) with the most common adverse event reasons being implant site pain (4%) and implant site infection (3%). Surgical intervention due to lack/loss of efficacy was 4%. Permanent explantation occurred in 5% of patients.

Interpretation of results and concluding message
Although the 12-month device-related adverse event rate reported appears high at 30%, most AE's reported were of a minor nature and were able to be resolved without surgical intervention. It is important to note however that surgical intervention was required in 13% of patients, with the majority being revision or replacement.

Table: Summary of Device-related Adverse Events*

	Adverse events		**Requiring surgical intervention on the device as an intervention§**	
AE type†	**Number of events**	**Number of subjects**	**Number of events**	**Number of subjects**
Undesirable change in stimulation	36	32	1	1
Implant site pain	26	20	13	10
Implant site infection	12	9	7	7
Lead fracture	4	4	4	4
Lead migration/dislodgment	3	3	3	3

*Other device-related AEs not displayed in the table occurred in ≤1% of subjects.

§Besides surgical intervention on the device, interventions may include other medical or non-surgical therapy or programming adjustments.
†A subject could have multiple types of events.

Disclosures
Funding: Clinical trial sponsored by Medtronic **Clinical Trial:** Yes **Registration Number:** ClinicalTrials.gov, NCT00547378 **RCT:** No **Subjects:** HUMAN **Ethics Committee:** WIRB and local committees at participating institutions **Helsinki:** Yes **Informed Consent:** Yes