

Recent Update of SCS

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The Need

- Many patients achieve satisfactory pain control with spinal cord stimulation, however, with position changes they may experience
 - *Painful or uncomfortable stimulation*
 - *Loss of stimulation*
 - *Change in paresthesia amplitude or coverage*
- Patients respond by adjusting their stimulation frequently
- This problem, common to all manufacturers, has not been adequately addressed until now

All SCS Manufacturers Warn of Unpleasant Stimulation as a Result of Posture Changes

St. Jude:

- “Changes in posture or abrupt movements may result in a decrease or increase in the perceived level of stimulation. Perception of higher levels of stimulation has been described by some patients as uncomfortable, painful, or jolting.”
 - STJ Eon mini Clinician Manual, page 5, 2007

Boston Scientific:

- “Patients should be advised that changes in posture or abrupt movements may cause decreases, or uncomfortable or painful increases, in the perceived stimulation level.”
 - Boston Scientific Precision® Physician Implant Manual, page 10, 2008

Medtronic:

- “Postural changes and other activities, may cause shocking or jolting.”
 - Medtronic Neurostimulation Systems for Pain Therapy Brief Disclosure, 2007

Published Sources Confirm the Problem

Cameron and Alo, 1998

“We found posture to have a significant effect on the charge per pulse when electrode lead are implanted in the thoracic region.”

Olin, Kidd, and North, 1998

“Assuming that patients will (as most do) use their stimulators in a variety of body positions, they will require some method to adjust amplitude frequently throughout the day.”

Abejon and Feler, 2007

“Therefore, to maintain a constant or nearly constant electric field at the level of neural substrate and avoid the potential consequence of postural changes, the amplitude should be varied with each change in posture.”

Patient Surveys

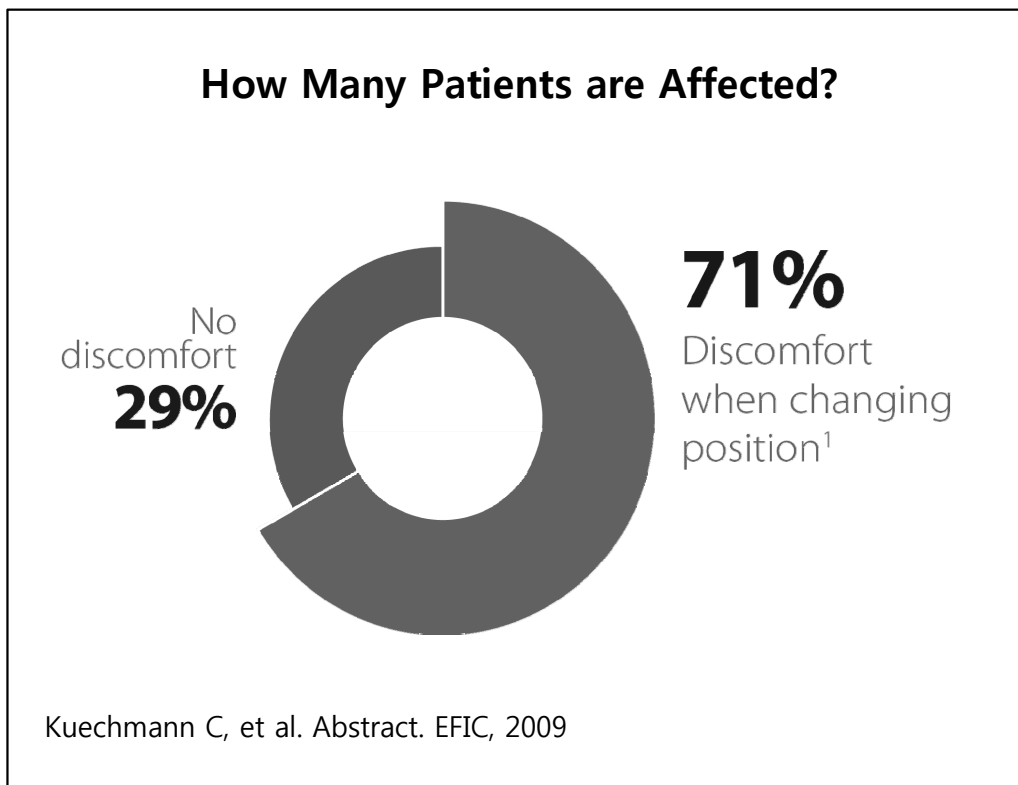
Medtronic conducted independent survey research to better understand patient experience with stimulation-related discomfort related to position changes

Patient Programmer Use to Address Position Change-Related Stimulation: Study Method

- 119 patients completed survey
 - High response rate of 31%
- 20 patients completed in-depth qualitative interviews
- Patients surveyed
 - used all 3 manufacturers' devices
 - were representative of the clinical population

Kuechmann C, et al. Abstract. EFIC, 2009.

Patients Surveyed Were Representative of the Clinical Population	
Demographics of Respondents	
Gender	51% Female
Age	51% >50 years
Years implanted	51% <2 years
Type of pain controlled	63% Leg pain 54% Back pain 24% CRPS 25% Other
Kuechmann C, et al. Abstract. EFIC, 2009	



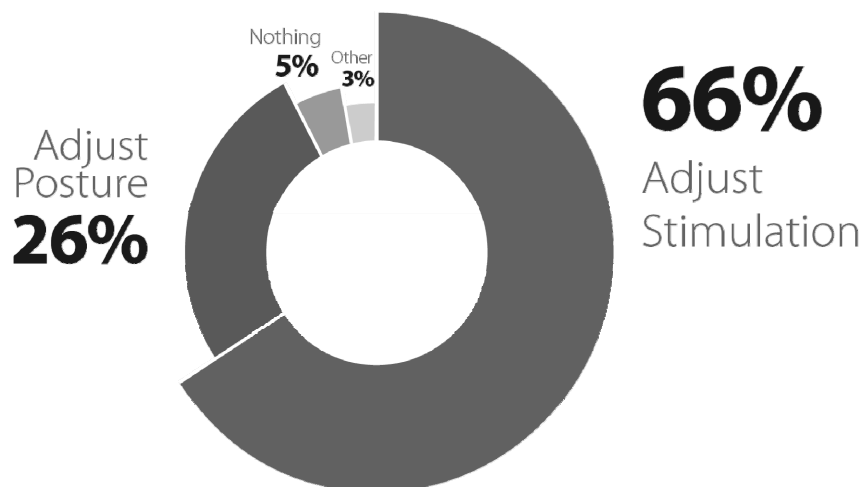
When Does Stimulation Become Uncomfortable?



When I lie down	58% (49)
When I sleep	18% (15)
When my activity increases	16% (13)
When I stand or sit after lying	14% (12)
	n=84

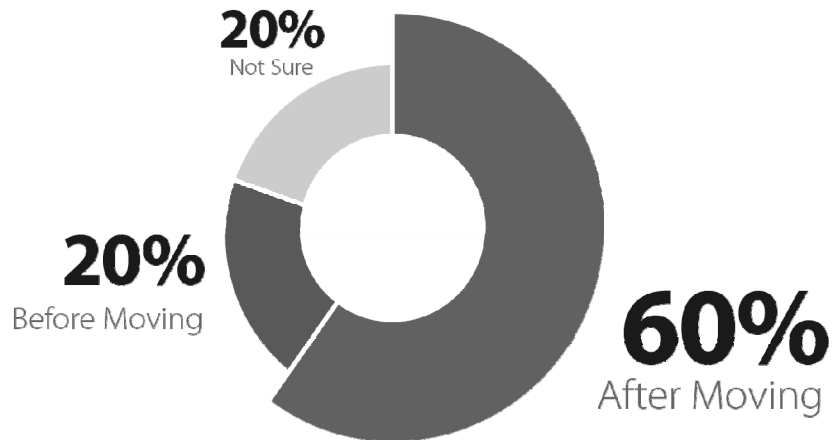
Kuechmann C, et al. Abstract. EFIC, 2009

How Do Patients Respond?



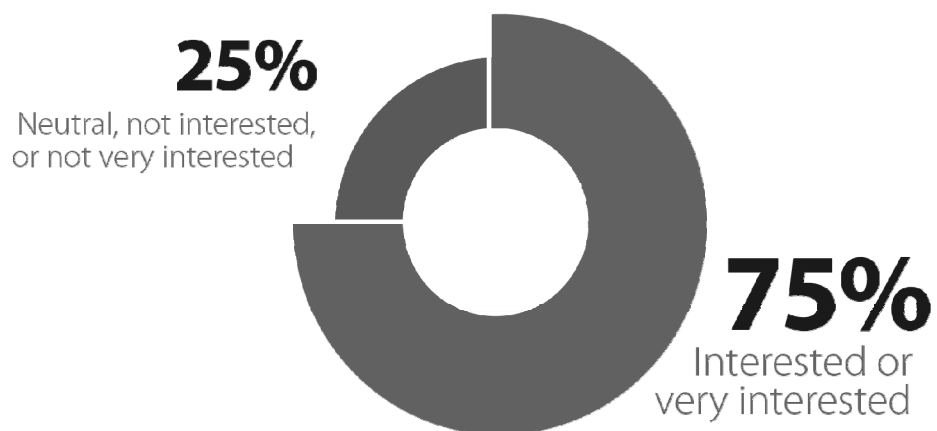
Kuechmann C, et al. Abstract. EFIC, 2009

When Do Patients Respond?



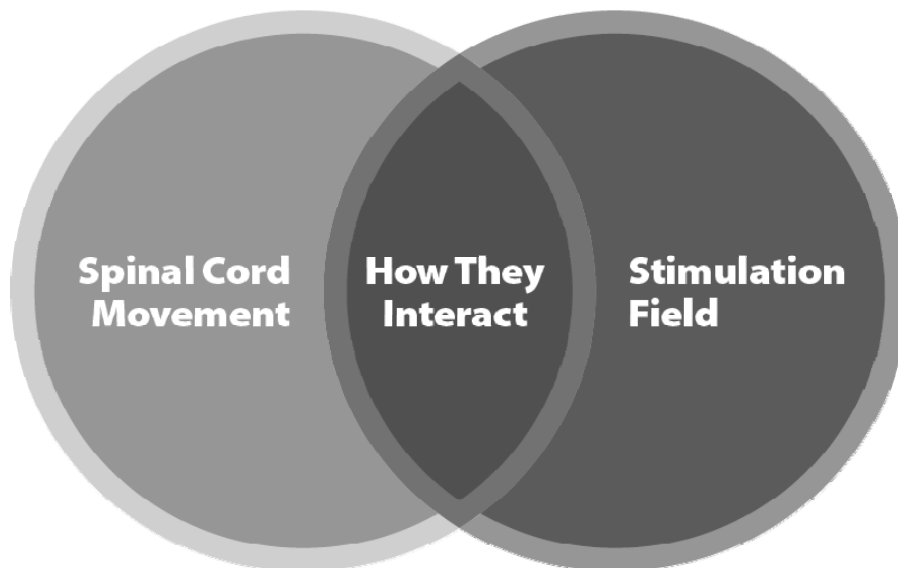
Kuechmann C, et al. Abstract. EFIC, 2009

How Many Patients Would Like a Solution?



Kuechmann C, et al. Abstract. EFIC, 2009

What Causes Uncomfortable Stimulation?



Spinal Cord Movement



- The dorsal cerebrospinal fluid (dCSF) fluid layer thickness determines the distance between the electrodes and the dorsal column

Spinal Cord Movement

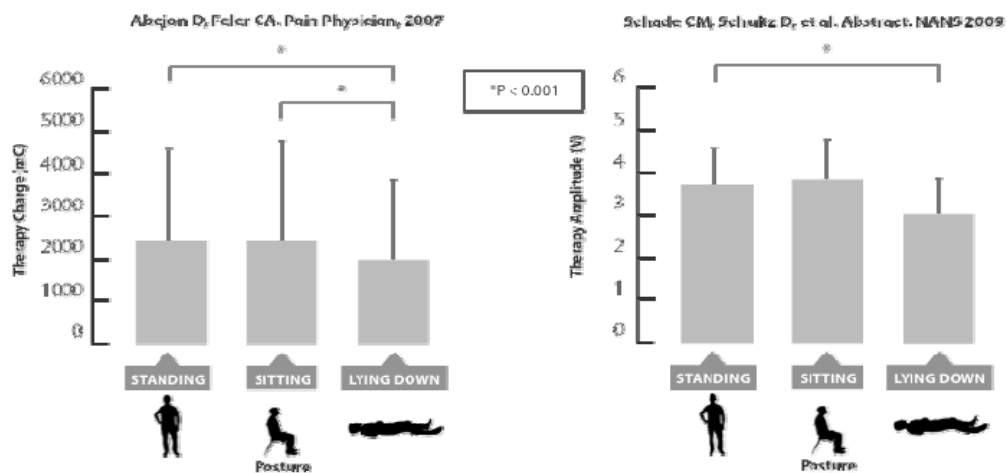
- Positional changes can result in spinal cord movement as much as 3 mm¹
- Overall patient stimulation comfort correlates to proximity of the cord to the electrodes, not impedance²

¹Holsheimer J, et al, Am J Neurol, 1994.

²Abejon D, Feler CA. Pain Physician, 2007

**Amplitude Change
is Related
to Spinal Cord Movement**

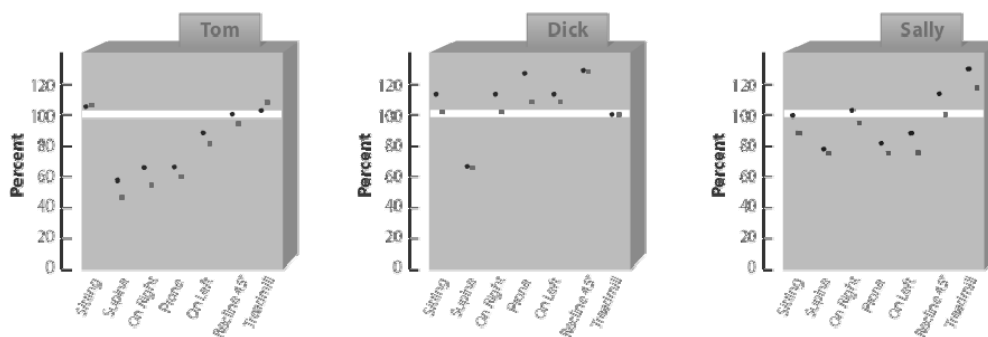
Amplitude



- Two studies confirm significantly lower values when comparing lying with standing or sitting
- Amplitude varies from position to position

Amplitude

- Adjusting for position is a key reason patients use their programmers

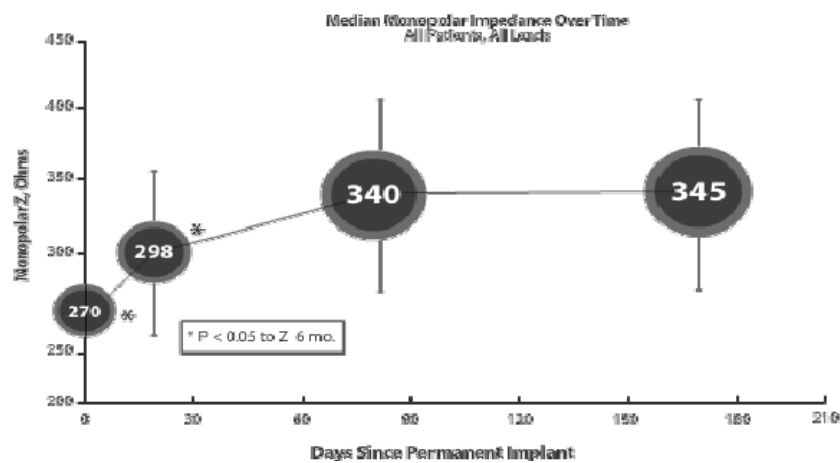


- Amplitude varies from position to position and from patient to patient

Schade CM, et al. Abstract. NANS 2009

Impedance Change is Not Related to Spinal Cord Movement

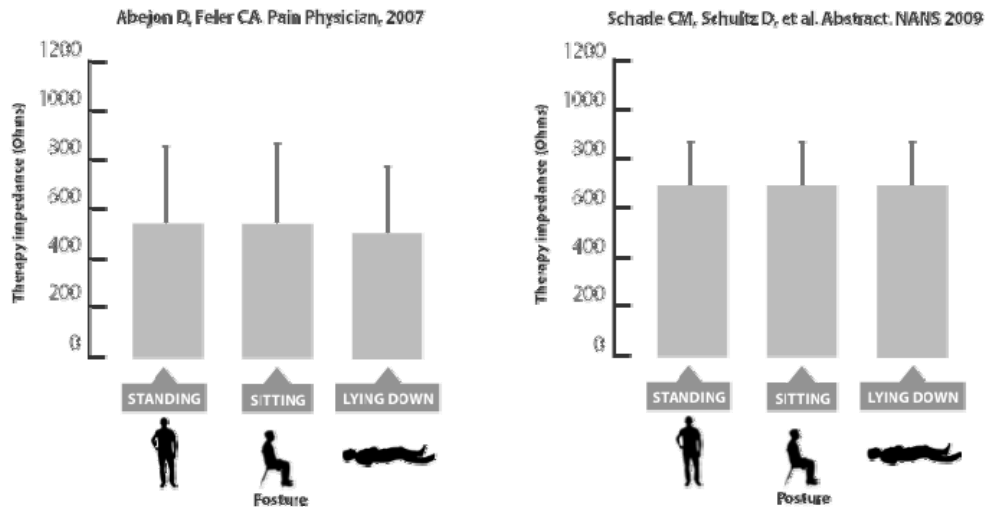
Relationship of Impedance Change to Scar Tissue



- Scar tissue buildup at the electrodes is limited to the first few weeks post-implant
- Automated adjustments for scar tissue-related impedance changes have little clinical impact

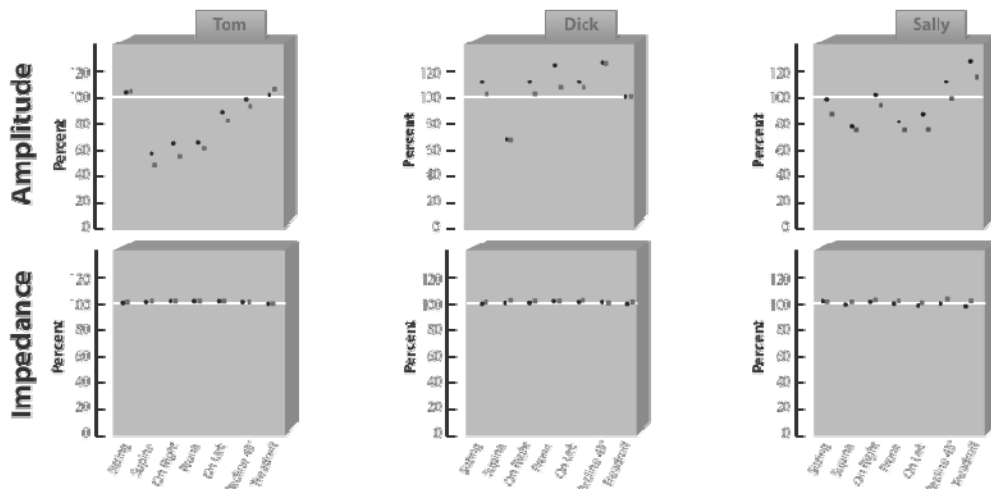
Oakley JC, et al. Poster. Am Soc Stereo & Funct Neurosurg, 2004. Available at: http://www.controlyourpain.com/printables/clinical_evidence/2.pdf. Accessed 11/20/09.

Impedance: Two Studies Confirm



- No statistically significant differences in posture related impedance have been found

Individual Patient-Preferred Amplitudes and Therapy Impedance by Posture Relative to Standing



- Amplitude varies from position to position and from patient to patient
- **Impedance remains relatively unchanged**

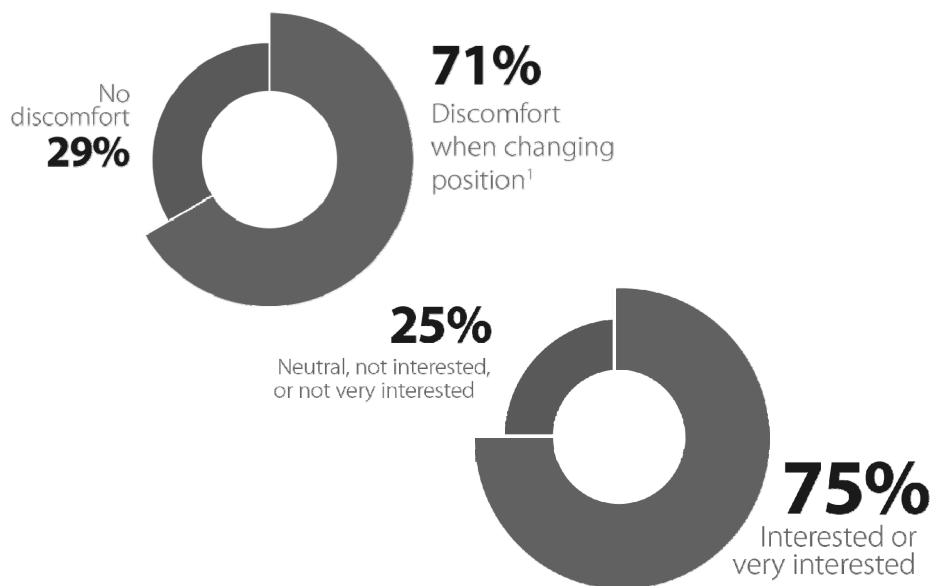
Schade CM, et al. Abstract. NANS 2009

It's Not about Constant Current *Or* Constant Voltage

- No peer reviewed published clinical trial has shown that either constant voltage or constant current is clinically more effective than the other
- Constant voltage and constant current are functionally equivalent
- They do not determine the outcome of the therapy

Abejon D, Feler CA. Pain Physician 2007

It's about the Patients



Kuechmann C, et al. Abstract. EFIC, 2009

What if...

- Everything you have done up to now is no longer the standard?
- There were a new standard?
- You could provide patients the choice of continuous motion?

[Decide whether to keep this transition slide in. Recommend deleting.]

What if a neurostimulation therapy now...

- **Listens**
 - and senses when your patient changes position
- **Learns**
 - from previous experience and remembers your patients' last comfortable setting
- **Responds**
 - by automatically adjusting to your patients' optimal settings in each position
- **Records**
 - to provide you with objective functional data

AdaptiveStim™ exclusively available with RestoreSensor™

- The first and only neurostimulator to automatically adapt to patients' optimum settings
- Addresses patient needs in a way that was previously unavailable



Medtronic Responded to the Need

Taking a **great**
therapy and making
it ***even better***



Accelerometer-based Technology

- Automatically detects changes in body position
- Adapts stimulation settings
 - to patient preferences
 - up to 6 positions
- Records patient activity level
 - providing objective data



RestoreSensor has all the features of RestoreUltra... and more

- MRI conditionally safe
 - FDA-approved labeling for 1.5-Tesla MRI head scans
- Highest energy output capabilities on the market
 - Industry-leading power output of 41.7 mA
- Smallest and thinnest (22 cc) 16-electrode neurostimulator available from Medtronic
 - More placement options and patient comfort
- Rechargeable device
 - 9-year device life

RestoreSensor Clinical Study

Medtronic-sponsored clinical study demonstrated **efficacy and safety**

Required by FDA for approval

Clinical Study Key Design Features

- Multicenter
 - 10 centers
- Prospective
- Open label
- Randomized
- Crossover



Schultz D, et al. *Pain Physician*. 2012. (in press)

Clinical Study Eligibility Criteria

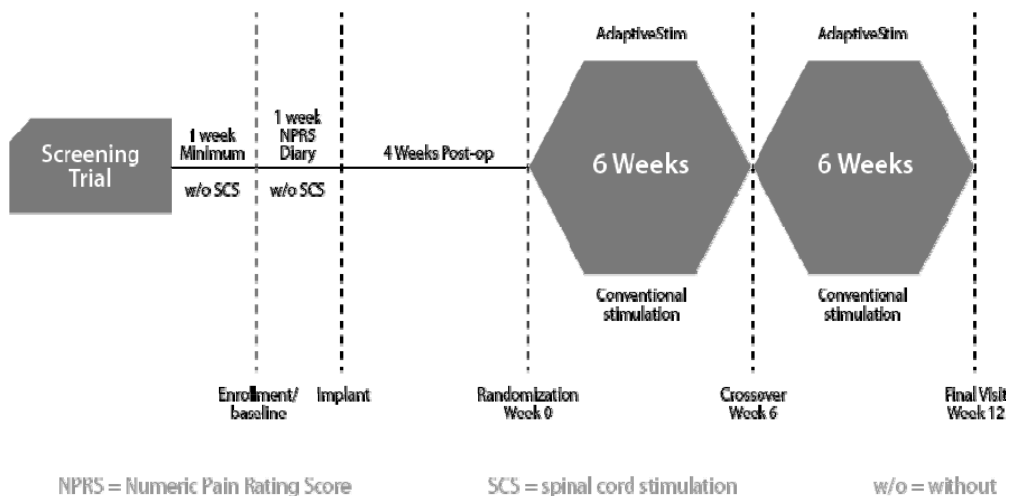
Real-world pain patients seen in the clinic daily

- All patients were indicated for SCS to treat chronic trunk and/or limb pain
- No minimum required pain score
- No demonstrated need for position-based stimulation adjustments



Schultz D, et al. 2012. (in press)

Clinical Study Design Sequence & Process



Schultz D, et al. *Pain Physician*. 2012. (in press)

Clinical Study Primary Efficacy Endpoint

To demonstrate that AdaptiveStim with RestoreSensor provides clinical benefits of improved pain relief and/or improved convenience compared with conventional stimulation

Schultz D, et al. *Pain Physician*. 2012. (in press)

Clinical Study Patients

- **Enrollment:**

- 79 enrolled
- 76 implanted and randomized
- 74 intention-to-treat analysis
- 71 completed the study


- **Pain etiology***


- 80% radicular pain syndrome
- 61% degenerative disk disease
- 44% postlaminectomy pain
- 37% failed back syndrome

*Patients could have more than one etiology

Schultz D, et al. *Pain Physician*. 2012. (in press)

Primary Efficacy Results Improved Pain Relief and/or Convenience

Better pain relief 

Better convenience 

With AdaptiveStim™ ON compared with OFF	Discontinued patients included in ITT	Much worse pain relief	Somewhat worse pain relief	No difference in pain relief	Somewhat better pain relief	Much better pain relief	Total
Discontinued patients included in ITT	3	<div style="border: 1px solid black; padding: 5px; text-align: center;"> $\frac{64}{74}$ = 86.5% success </div>					3
Much less convenient							1
Somewhat less convenient							2
No difference in convenience			1	1			2
Somewhat more convenient				1	7	5	13
Much more convenient				1	16	34	51
Total	3	1	1	6	23	40	74

Schultz D, et al. *Pain Physician*. 2012. (in press)

Overall Study Results

RestoreSensor effectively provides improved pain relief and/or convenience

- 86.5% (64) met primary efficacy objective in the intention-to-treat analysis (n=74)
- 90.1% (64) achieved success in the per protocol analysis (n=71)
 - 3 patients did not complete the study
- Study results were statistically significant, $p < 0.001$

Schultz D, et al. *Pain Physician*. 2012. (in press)

Safety Outcome

RestoreSensor has been demonstrated to be safe – and effective

- No increase in adverse events compared to other SCS studies
- No difference in adverse events between study arms
- Low numbers of device-related serious adverse events, 3.9% (3)

Schultz D, et al. *Pain Physician*. 2012. (in press)

Patient-Reported Benefits

- **90.1% (64) intended to use AdaptiveStim**
 - all or most of the time
 - or to turn on/off as needed
- **87.3% (62) preferred AdaptiveStim**
- Specific reported improvements*
 - 80.3% (57) comfort
 - 57.8% (41) control of therapy

Total n=71

*Most patients reported more than one improvement

Schultz D, et al. *Pain Physician*. 2012. (in press)

Examples of Patient-Reported Comments*

"Pain relief much better with AdaptiveStim especially at work where heavy change of position is required frequently."

"I didn't have to adjust it, it did it for me."

"My pain was controlled much better. I don't have to manually make adjustments."

"The internal adjustments allow for more consistent pain relief"

"Rather than fixing the setting all the time, it was already done."

"Much easier to go through the day without thinking about it!
Sleeping much better!"

*Patients independently wrote comments on Case Report Forms.

Schultz D, et al. *Pain Physician*. 2012. (in press))

Physician-Reported Assessments

- Ten investigators collectively reported that 88.7% (63) of patients clinically benefitted from AdaptiveStim
- Clinicians found initial programming easy or very easy for 86.8% of patients
- Most patients preferred manufacturer default settings
- Patients and physicians agreed that AdaptiveStim was highly beneficial

Total n = 71 (completed case analysis)

Schultz D, et al. *Pain Physician*. 2012. (in press)

In Summary...

RestoreSensor: Clinical Implications

- Listens, learns, responds and records patient therapy needs
- Automatically adjusts to the patient – instead of the patient adjusting to the stimulator
- Enables patients to regain greater normalcy
- For my patients, it's *"Set it and forget it"*

One Clinical Study Patient's Comments

"With AdaptiveStim, I can set it and forget it."

Marty, RestoreSensor clinical study patient

Using AdaptiveStim exclusively available with RestoreSensor since 2010



References

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- Schade CM, Schultz D, Tamayo N, et al. Automatic adaptation of spinal cord stimulation intensity in response to posture changes. Abstract. North American Neuromodulation Society, Las Vegas, NV: Dec 2-6, 2009.
- Schade CM, Schultz D, Tamayo N, et al. Automatic adaptation of neurostimulation therapy in response to changes in patient position. Results of the posture responsive spinal cord stimulation (PRS) research study. *Pain Physician*. 2011;14:407-417.
- Schultz D, Webster L, Kosek P, Dar U, Tan Y, Sun, M. Sensor-driven position-adaptive spinal cord stimulation for chronic pain. *Pain Physician*. 2012. In press.
- Medtronic advanced pain therapy using neurostimulation for chronic pain. Clinical summary. 2011; M221494A006.

Brief Disclosure

Indications, Safety, and Warnings

- Product manuals must be reviewed prior to use for detailed disclosure.

Indications

•A Medtronic implantable neurostimulation system is indicated for spinal cord stimulation (SCS) system as an aid in the management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain associated with the following conditions: Failed Back Syndrome (FBS) or low back syndrome or failed back, Radicular pain syndrome or radiculopathies resulting in pain secondary to FBSS or herniated disk, Postlaminectomy pain, Multiple back operations, Unsuccessful disk surgery, Degenerative Disk Disease (DDD)/herniated disk pain refractory to conservative and surgical therapies, Peripheral causalgia, Epidural fibrosis, Arachnoiditis or lumbar adhesive arachnoiditis, Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or causalgia

Contraindications

- Diathermy** - Do not use shortwave diathermy, microwave or therapeutic ultrasound diathermy (all now referred to as diathermy) on patients implanted with a neurostimulation system. Energy from diathermy can be transferred through the implanted system and cause tissue damage at the locations of the implanted electrodes, resulting in severe injury or death.

Warnings

- Sources of strong electromagnetic interference (eg, defibrillation, diathermy, electrocautery, MRI, RF ablation, and therapeutic ultrasound) can interact with the neurostimulation system, resulting in serious patient injury or death. These and other sources of EMI can also result in system damage, operational changes to the neurostimulator or unexpected changes in stimulation. Rupture or piercing of the neurostimulator can result in severe burns. An implanted cardiac device (eg, pacemaker, defibrillator) may damage a neurostimulator, and the electrical pulses from the neurostimulator may result in an inappropriate response of the cardiac device.

Precautions

- The safety and effectiveness of this therapy has not been established for pediatric use (patients under the age of 18), pregnancy, unborn fetus, or delivery. Patients should be detoxified from narcotics prior to lead placement. Clinicians and patients should follow programming guidelines and precautions provided in product manuals. Patients should avoid activities that may put undue stress on the implanted neurostimulation system components. Patients should not scuba dive below 10 meters of water or enter hyperbaric chambers above 2.0 atmosphere absolute (ATA). Electromagnetic interference, postural changes, and other activities may cause shocking or jolting.

Adverse Events

- Adverse events may include: undesirable change in stimulation described by some patients as uncomfortable, jolting or shocking; hematoma, epidural hemorrhage, paralysis, seroma, CSF leakage, infection, erosion, allergic response, hardware malfunction or migration, pain at implant site, loss of pain relief, chest wall stimulation, and surgical risks.
- For further information, please call Medtronic at (800) 328-0810 and/or consult medtronic.com

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