Comparison of Conventional and Kilohertz Frequency Epidural Stimulation in Patients Undergoing Trialing for Spinal Cord Stimulation: Clinical Considerations

Chandan G. Reddy[1], Brian D. Dalm[1], Oliver E. Flouty[1], George T. Gillies[2], Matthew A. Howard III[1], Timothy J. Brennan[3]

■ OBJECTIVE: **Compare therapeutic response of patients to conventional versus high-frequency spinal cord stimulation (SCS).**

■ METHODS: **Twelve patients with back and leg pain who met standard clinical criteria for a trial of conventional SCS (low-frequency stimulation [LFS]) participated in a half-day session of high-frequency stimulation (HFS) during their weeklong conventional trial. HFS consisted of frequencies ranging from 50 Hz to 4 kHz, or 100 Hz to10 kHz, at constant voltage settings increasing from 0.5 V to 10 V. Visual Analog Scale scores from 0 to10 were recorded, along with notes of any clinical discomfort and open patient comments.**

■ RESULTS: **Two of 12 patients had no benefit from either LFS or HFS. In the remaining 10 patients, paresthesias were significantly altered by HFS, and four experienced complete elimination of paresthesias. Five patients preferred HFS to LFS, with an additional three preferring both equally. Abrupt sensation to the onset of HFS was described in six patients, and in ten patients, HFS allowed maximum voltage stimulation of 10 V without discomfort. The four patients who did not have a successful trial of stimulation had significantly longer duration of pain compared to the eight patients who went on to permanent implant (11.2 vs. 4.3 years, $P = 0.04$).**

■ CONCLUSIONS: **HFS significantly altered the feeling of paresthesias in the majority of patients (ten of 12), was preferred to LFS in five of 12 patients, and non-inferior to LFS in eight of 12 patients. Both 4 kHz and 10 kHz stimulation allowed patients to benefit from HFS. HFS allowed maximum voltage stimulation without discomfort.**

INTRODUCTION

Spinal cord stimulation (SCS) is projected to be a $2.3 billion component of the overall neuromodulation market in 2016.[1] At present, 35,000 people are implanted with spinal cord stimulators globally each year.[2] Failed back surgery syndrome (FBSS) indications for SCS account for roughly 70% of these implantations.[3]

Recent attention has been brought to high-frequency epidural stimulation as a potential superior modality for relief of back pain.[4-6] Alternate stimulation parameters have also been suggested.[7,8] These modalities propose to offer pain relief without paresthesias. The technological tradeoff for higher-frequency stimulation may be greater use of battery power than conventional SCS.

Despite newer evidence suggesting the advantages of higher-frequency stimulation, the majority of patients implanted today have conventional stimulators that operate with lower-frequency parameters. Few studies have been performed to explore the relative clinical advantages of higher-frequency spinal cord stimulation. Kapural[6] recently reported the results of a large, randomized, controlled trial of 198 patients comparing high-frequency stimulation to traditional SCS, suggesting superior back and leg pain relief in the high-frequency group. Smith[9] reported improvement of 2 patients initially treated with low-frequency (40 Hz) and then switched to high-frequency (1 kHz) stimulation. Perruchoud[10] presented a randomized, double-blind, placebo-controlled trial in 40 patients comparing the effects of 5

Key words
- High-frequency stimulation
- Kilohertz frequency stimulation
- Spinal cord stimulation

Abbreviations and Acronyms
CRPS: Complex regional pain syndrome
FBSS: Failed back surgery syndrome
HFS: High-frequency stimulation
LFS: Low-frequency stimulation
SCS: Spinal cord stimulation
VAS: Visual analog scale

Departments of [1]Neurosurgery and [3]Anesthesia, University of Iowa Carver College of Medicine, Iowa City, IA, USA; and [2]Mechanical and Aerospace Engineering, University of Virginia, Charlottesville, VA, USA

To whom correspondence should be addressed: Chandan G. Reddy, M.D. [E-mail: chandan-reddy@uiowa.edu]

Citation: World Neurosurg. (2016) 88:586-591.
http://dx.doi.org/10.1016/j.wneu.2015.10.088

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Table 1. Baseline Patient Characteristics

Patient	Age	Gender	Diagnosis	Etiology	Pain Distribution	Previous Back Surgeries	Device	Electrode Level	Time Between Pain Onset and Trial (years)	Successful Trial, Permanent Implant (Y/N)
1	43	M	Neuropathic	SCI	Back + Legs	1	Medtronic	T8-9	1.2	Y
2	70	F	FBSS	L3-5 fusion	Back + Legs	3	Medtronic	T7-9	17.6	N
3	72	F	Neuropathic	Phantom Limb, SCI	Back + Legs	1	St. Jude	T10-11	13.7	N
4	60	F	Neuropathic	CRPS	Back + Legs	1	Medtronic	T9-11	0.4	Y
5	47	F	FBSS	L4-5 fusion	Back + Legs	3	Medtronic	T8-9	9.8	N
6	53	F	Neuropathic	SCI	Back + Legs	1	St. Jude	T10-12	3.6	N
7	37	M	FBSS	L5-S1 fusion	Back + Legs	4	Medtronic	T8-10	1.5	Y
8	53	F	Neuropathic	CRPS	Back + Legs	0	Medtronic	T8-10	2.9	Y
9	49	M	FBSS	L5-S1 fusion	Back + Legs	2	Medtronic	T8-10	4.3	Y
10	56	M	FBSS	L5-S1 foraminotomy	Back + Legs	3	Medtronic	T8-10	2.5	Y
11	43	F	Neuropathic	Paraplegia, tectal glioma	Back + Legs	0	St. Jude	T9-10	3.5	Y
12	46	F	Neuropathic	Phantom Limb	Back + Legs	0	Medtronic	T8-9	18.1	Y

SCI, spinal cord injury; T, thoracic; FBSS, failed back surgery syndrome; CRPS, complex regional pain syndrome.

kHz stimulation to sham stimulation against a conventional stimulation baseline, finding mixed results in terms of the demonstrable benefits of HFSCS.

We seek to expand upon these findings and investigate the potential for clinical advantage by varying both stimulation frequency and voltage in patients undergoing a conventional trial of spinal cord stimulation. In particular, we propose to systematically measure the effect of spinal cord stimulation on clinical pain relief (visual analog scale [VAS]) at frequencies ranging from 50 Hz–10kHz and voltages from 0.5V–10V. Patient observations and discomfort were also noted.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board, Protocol No. 201201745.

Patients

Twelve sequential patients undergoing a weeklong trial for conventional SCS were enrolled in the study. By conventional, the authors refer to low-frequency stimulation, typically in the 40 Hz–200 Hz range. Patients had been selected by standard clinical selection criteria used at a tertiary care pain management center. To be eligible for inclusion, all patients had to have ongoing back and leg pain refractory to standard therapy and meeting standard clinical criteria for a trial of spinal cord stimulation. Diagnoses and baseline characteristics are illustrated in Table 1.

There were 4 men and 8 women, ranging in age from 37–72 years. There were 5 patients with FBSS and 7 patients with neuropathic pain of other causes (phantom limb, spinal cord injury, complex regional pain syndrome). All patients had a thoracic lead placement. During the weeklong trial, 9 patients had Medtronic (Medtronic Neuromodulation, Minneapolis, MN, USA) leads implanted, and 3 patients had St. Jude (St. Jude Medical, St. Paul, MN, USA) leads, as determined by the clinical trialing convention of our institution at the time.

High-Frequency Stimulation Protocol

Patients who consented for the study reported to our institutional general clinical research center for 1 half-day before lead explantation and were disconnected from the conventional stimulation unit. A high-frequency stimulation device was then attached to their externalized leads. For 5 of the initial patients, a Tucker Davis Technologies IZ-2 stimulator system (TDT Systems, Alchua, FL, USA) was used, allowing maximum frequencies of 4000 Hz. For the latter half of the study, an Agilent Model 33500-B Waveform Generator (Agilent Technologies, Loveland, CO, USA) was used in conjunction with a BAK Model BSI-1 Stimulus Isolator (BAK Electronics, Inc., Umatilla, FL, USA), allowing maximum frequencies of 10,000 Hz. A charge-balanced biphasic waveform was used.

All patients received constant voltage stimulation, ranging from 0.5–10 V, in increments of 1–1.5 V. Typically, patients were started at lower frequencies of stimulation and were blinded to the on/off status of the stimulator. For a given frequency, the maximum tolerable voltage was noted or 10 V, whichever came first. Note was also made of any clinical discomfort, and open patient comments were logged. For a given setting of voltage and frequency, stimulation was delivered for 2 minutes' duration, allowing sufficient rest between stimulus presentations to allow for any transient effects lasting <2 minutes to reverse. Typical frequencies of stimulation using the TDT system were 50 Hz, 100 Hz, 200 Hz, 400 Hz, 800 Hz, 1600 Hz, and 4000 Hz. Typical frequencies using the Agilent system were 100 Hz, 1000 Hz, 5000 Hz, and 10000 Hz. Slight deviations from protocol were made on a case-by-case basis, depending on patient tolerance. The specific