Product Review: Non-Invasive Neuromodulation for the Treatment of the Most Difficult Pain Conditions

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Inside today's intelligent devices and an applied example using the InterX.

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The Fast-Paced Growth of Neuromodulation

The use of neuromodulation as a treatment in a wide array of pain-related disorders has expanded ever since the concept of spinal cord stimulation (SCS) was introduced and operationalized many years ago. Fellow *PPM* board member C. Norman Shealy, MD, PhD, has been credited as a pioneer in this field, when, in the 1960s, he implanted the first dorsal column stimulation device, which many believe to be the precursor for today's SCS devices.

Neuromodulation can be thought of as any treatment that alters nerve activity and represents an advanced form of conventional electrostimulation, also called neurostimulation. Essentially, electrostimulation serves as the *action* while neuromodulation serves as the *effect*.

The treatment has become an intriguing option for the more problematic cases involving chronic intractable pain – and is even being used to help manage exacerbated respiratory conditions related to COVID via vagus nerve stimulation.

In fact, we continue to witness the fast-paced growth of this form of treatment, which has now become an industry of its own.[1] According to the market research company Neurotech Reports, the field of neurotechnology – which includes neuromodulation, neuroprosthetics, neurorehabilitation, and neurosensing – will reach $13 billion in 2022, and the largest segment of this market is indeed neuromodulation systems, which will grow from $4.7 billion in 2018 to $7.6 billion in 2022.[2]

On the flip-side of implantable stimulators (ie, SCS) are non-invasive peripheral nerve stimulators, which will be the focus of this review, starting with how these devices differ.

Intelligent Devices for Peripheral Neurostimulation

A new generation of electrotherapeutics is evolving with the explicit function(s) of neuromodulating or communicating with the CNS. By using sophisticated circuitry and electrical signaling with the intent of altering or modulating nerve function, researchers, scientists, and now clinical providers can begin to tap into a new kind of healing that was once considered futuristic.

Electrostimulation devices entering the marketplace today come with advancements in the form of artificial intelligence (AI), microelectromechanical systems (MEMS), and machine learning applications.

As an example, MEMS technology has driven the latest diabetes remote monitoring systems – these systems do not require needlesticks and perform continuous blood glucose monitoring from a single patch location. MEMS are also driving the next generation of peripheral pain neuromodulation devices – such as the InterX device (InterX 5002; Interx Technologies, Plano, TX), which I will review herein.

This device produces high amplitude, high density, and high-frequency stimulation with a pulsing current. In comparison to a transcutaneous electrical nerve stimulation (TENS) device, the electrical density of InterX is 170-220 mA vs 15-40 mA of TENS. But the real secret is "in the sauce" – that is, the device's micro-engineering and circuitry. In keeping with the trend toward personalized medicine, the InterX device allows treatment customization with no two patient treatments being alike.

Figure 1. InterX 5002 hand-held device.

Click to enlarge

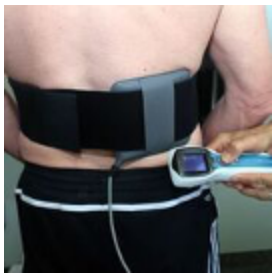
How it Works

The AI technology built into the InterX 5002 device allows the provider to simply scan a treatment area and let the device both select the treatment area and the appropriate dosage requirements based on a continuous feedback loop system based on skin resistance levels. The device continuously updates and creates new algorithms (machine learning in action) to maximize treatment effects on any given patient.

As a result of the changing electronic inputs and outputs, there is no anticipation of tissue accommodation (ie, tolerance), which has been a common concern with earlier generation electrotherapy devices.

Figure 1 shows the device itself (InterX 5002) and Figures 2 and 3 show the various attachments that come with the device. Of note, there is a home model as well (InterX 1000).

Figure 2. InterX device attached to a larger pad for an increasing area of treatment.



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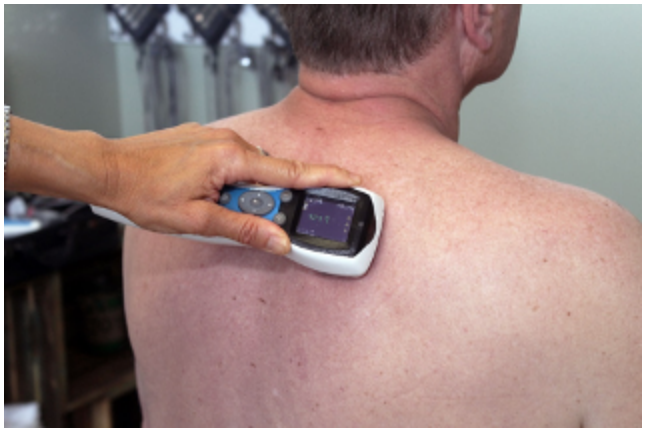
Studies vs Experience: A Provider Perspective

Before getting into the user experience details, I'd like to step back for a moment and reinforce that we often see conflicting studies when innovative devices and treatments emerge from the pipeline. Unclear results can be disconcerting for providers looking to use new therapeutics – especially if the amount of concordant research alone is used as a determinant of an intervention's effectiveness. Experienced practitioners are smarter than that – we know that the litmus test is in the actual sampling or evaluating how a treatment works in practice.

While research provides guidance on the mechanism of action (MOA), new clinical-grade pain devices rarely have enough evidence-based science behind them to cover all conditions, all patient populations, and all means of dosage/use. For me, and many practitioners, the decision to purchase an expensive piece of equipment comes only after actually trialing the device in my practice, with my patients.

Figure 3. InterX treatment to spine muscles.



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InterX Data to Date

The InterX device has appeared in a number of scientific studies presented and published since its market release in 2010. Twenty percent[3] of these studies failed to show a superiority effect with InterX use; the remainder found significant positive differences in the dependent or outcome variables used, including for:

changes in lymphocyte metabolism, gene expression and cytokine [4]

- acute pain s/p repaired ankle fracture[5]
- chronic low back pain[6]
- post-operative pain management in total knee or hip arthroplasty[7]
- chronic plantar fasciiti[8]
- pain management in post-operative total knee arthroplasty[9]
- C-spine trigger points[10]
- knee osteoarthritis[11]
- ow grade ankle sprain[12] (Razzano et al., 2018), and trochanteric hip fracture recovery[13]

A short trial (2 weeks or 5 treatments) of InterX did not show a difference in inflammatory response (cytokine activity) in a group of neck pain patients,[14] nor did it show superiority to TENS in a study using young college subjects and artificially inducing pain in a lab setting.[15]

A couple of important characteristics of these latter two trials are their limitations, as pointed out by the authors. The first was the small sample size and the second was the use of young healthy subjects in the study of pain versus using an older and sicker population that has pain secondary to disease and comorbid conditions. An older and sicker cohort would undoubtedly have demonstrated significant differences in the way they perceived, modulated, and transmitted pain when using (or not using) the device.

InterX Clinical Evaluation

Our research center in Ypsilanti, Michigan, has been collecting data and evaluating the InterX 5002 device with the informed consent of patients for approximately 8 months. Although our review has not completed as of yet, the device has demonstrated impressive resiliency and versatility in helping us treat painful conditions, ranging from chronic pain conditions such as osteoarthritis, psoriatic arthritis, fibromyalgia, and complex regional pain syndrome (CRPS) to post-operative pain and sports injuries.

We were all quite skeptical at first because the treatment seems so simple to administer, yet the device has provided pain relief to every patient who has trialed it, including our most treatment recalcitrant patients of all – those with CRPS.

In conjunction with the manufacturer and distributor of this device, we requested a sham unit be built to control for placebo. The comparative effectiveness between the sham and experimental treatment has been significant. In fact, it is important to note that it was next to impossible to recruit patients who had experienced InterX prior to our receiving the sham unit into the comparative trial because they simply said their sessions were too valuable and

did not want to risk *not* getting the actual treatment. As a result, we had to recruit patients who were unfamiliar with the device for our comparative trial. To date, we have looked at data on 38 non-blinded patients and 13 blinded patients.

We have applied the device to every peripheral joint in the body and have had success in conditions where we have experienced little before using other forms of treatment for difficult to treat disorders such as enthesopathies such as plantar fasciitis, lateral epicondylitis, Achilles tendinopathy, and insertional tendinopathies in general.

Final Thoughts on Product Review

In our view, the InterX 5002 device belongs in a class of technology used to treat the most difficult pain conditions. The device takes advantage of sophisticated AI technology that searches for and directs treatment to the areas needed the most, which adds an element of treatment consistency between providers while providing a personalized treatment session for the patient as no two sessions are necessarily identical.

The device also proves beneficial at a time when we are shifting to value-based reimbursement models, in which provider payments are linked to patient quality and outcome metrics. As fee-for-service plans become extinct, clinicians must select the best equipment possible to get their patients to better faster – in other words, quality providers will be those who achieve the best patient outcomes in the shortest amount of time.

Our sham comparisons have convinced us that InterX treatment meets these criteria and aligns with the positive feedback reported about its use around the globe. This is one time where we felt we were slow to bring this device in to test and should have done so years ago.

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Last updated on: October 15, 2020

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