

# A Progressive Treatment for a Chronic Progressive Disease:

## THE WAR AGAINST COMPLEX REGIONAL PAIN SYNDROME

BY BENJAMIN KEIZER, PHD, LINDSAY SPOSATO, MS, OTR/L, AND KATHLEEN YANCOSEK, PHD, OTR/L, CHT

“I just don’t believe it, my pain level is only a 2 right now,” said Thomas at the conclusion of the treatment, slipping on his customized ankle/foot brace. Prior to today’s session, Thomas, a 52-year-old Caucasian man, reported a pain level around 7 or 8 out of 10. As we first observed Thomas, his body language expressed fear and anticipation of pain as he gingerly stood from his chair and started out of the office and down the clinic hallway. However, unexpected as it may have been to Thomas, with each successive step he appeared more confident that his pain had diminished substantially in the last 60 minutes. When asked about his familiar pain, Thomas said, “Imagine you are sitting in your chair with the worst case of “pins and needles” [paresthesia] that you can think of. Now imagine standing up and walking down a hallway and every time

**Imagine standing up and walking down a hallway and every time one of your feet hits the ground you feel like you are walking in burning lava.**

one of your feet hits the ground you feel like you are walking in burning lava.” For Thomas, that was life with complex regional pain syndrome (CRPS), and the recent treatment provided relief from the “lava.”

CRPS, formerly called reflex sympathetic dystrophy (RSD), typically develops as a local-

ized pain disorder within four to six weeks of a traumatic injury to an upper or lower extremity. Although many traumatic injuries can initially result in CRPS symptoms, most resolve over time without treatment. Adding mystery to this challenging disease state, CRPS may also occur spontaneously without an inciting event (1). Consider how incredibly painful a CRPS pain experience can be. According to the McGill Pain Index, CRPS is one of the most painful conditions that exists. Indeed, the McGill Pain Index score ranks CRPS higher in pain severity than childbirth without

training or even amputation of a finger or toe (2).

It was still shocking to Thomas how a few moments changed the trajectory of his life. Several years ago Thomas was undergoing aortic valve replacement and bypass surgery when his heart suddenly shut down. He developed serious complications, including kidney failure, liver failure, and fluid in his lungs. He was kept in a medical coma while his chest remained open for four days to allow a mechanical pump (right ventricular assist device) to assist with heart function. Thomas remained in a coma for the next 14 days and nearly died five times. He spent 30 days in the intensive care unit and an additional three weeks in an inpatient rehabilitation unit. Doctors estimated a 5% chance of survival. Due to unexpected complications, Thomas lost the use of his right leg and left arm.

Thomas eventually regained full use of his left arm. However, despite intensive rehabilitation, his right leg did not fare as well. Indeed, the aortic valve replacement and bypass surgery resulted in permanent left drop foot and CRPS in both his right foot and anterior lower leg. In Thomas’ case (and is often the case with CRPS), the medication regimen of oxycodone/acetaminophen and pregabalin was ineffective. Thomas was eventually admitted to the inpatient unit for a five-day continuous subanesthetic ketamine infusion. The ketamine infusion was successful, and he returned to his previous level of functioning.

Clinical symptoms of CRPS fall within four categories: A) sensory, B) vasomotor, C) sudomotor, and D) trophic. Sensory symptoms include allodynia (painful response to a stimulus that should not be painful) or hyperesthesia (heightened response to a painful stimulus) (3). Vasomotor symptoms include changes in skin color and temperature. The affected extremity may present as red and hot to the touch (i.e., “warm CRPS”), or may be pale/blue-tinged and cold (i.e., “cold CRPS”). In terms of temperature, approximately 70% of patients initially present with warm CRPS, with the other 30% presenting with cold CRPS (4). In this case, Thomas presented with cold CRPS, a condition



that has been shown to exhibit a worse prognosis when compared to warm CRPS (5). The sudomotor symptoms of CRPS include swelling and sweating asymmetry between the affected and unaffected extremity (3). Trophic symptoms include changes in skin texture (i.e., shiny skin), changes in fingernails (may grow more quickly, or become curved or rigid), or increases or decreases in hair growth (1,3). CRPS may also result in loss of range of motion and cause tremor or weakness (2,5).

CRPS is differentiated between Type I and Type II. A diagnosis of CRPS I is made when no nerve damage has occurred to the affected area. In contrast, the distinguishing factor of CRPS II is nerve damage to the affected area (3).

For unknown reasons Thomas' CRPS returned with

vengeance one year later. The CRPS not only returned, but progressed to his left leg, which was cold to the touch and exhibited the same blue/purple freckling and hair loss that his right leg had re-developed. How did this happen? The cause of CRPS remains unknown; however, acceptable theories support a multifactorial origin, with potential contributors being post-traumatic inflammation, neural plasticity, overactivity of the sympathetic nervous system, genetics, and psychosocial factors (1).

Several months later, Thomas was desperate. His pain medicine physician referred him for acupuncture, and Thomas received 17 treatments with some pain relief (average 25% reduction). However, the relief was short lived, lasting anywhere from several hours to the rest of the day

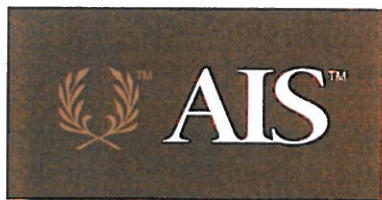
after the treatment. Both Thomas and his pain medicine physician were desperate for more significant relief and agreed that completing another ketamine infusion was probably the best treatment option. However, there was another non-invasive option.

Benjamin Keizer, PhD, a pain psychologist, worked extensively with military service members with lower extremity CRPS following combat injury and had been experimenting with using two non-invasive electrical stimulation devices synergistically—the Alpha-Stim® Cranial Electrotherapy Stimulation (CES) and the InterX® Therapy device. At his initial visit one year earlier, Thomas completed a psychological evaluation to assess his suitability for a spinal cord stimulator. Due to his high risk of developing an adverse reaction to a surgical intervention, his pain medicine physician made the decision not to implant a spinal cord stimulator. A chance meeting in the waiting room of the Interdisciplinary Pain Clinic and a follow-up conversation with Thomas' pain medicine physician set the wheels in motion to see if this non-invasive treatment might be an option.

Alpha-Stim CES refers to the application of a small amount of electrical current transcranially, via electrodes

attached to the ears. The electrical current is controlled through a handheld device, with treatment lasting approximately 20 minutes to one hour. Originally dubbed “electro-sleep,” the intended purpose of CES devices was to induce sleep as part of the “sleep cure” that was popular in early 20th century psychology. Later, researchers demonstrated that CES was not only effective for inducing restful sleep, but it was effective for treating stress-related symptoms as well. Today, the FDA recognizes CES devices for the treatment of anxiety, insomnia, and depression (6). More recent research indicates that CES is effective for pain management, as it stimulates regions of the brain that regulate pain messages, including the cingulate gyrus, insula, and prefrontal cortex (7,8). The ability of CES to modulate pain was demonstrated in a 2013 double-blind randomized controlled trial of individuals with fibromyalgia. In this study, the intervention group that received CES had significantly greater decreases in pain levels than those who received usual care or treatment with a sham device (8).

InterX Therapy, also a type of neurostimulation, has been developed specifically for the treatment of acute and chronic pain. While Alpha-Stim CES is delivered tran-



Leading the Way  
in Intrathecal PainCare™

50,000+  
**Safety in Numbers...**  
Learn More about Ours.

*Patient Safety. First!™*

Call AIS™ today at 877.443.4006  
[www.aispaincare.com](http://www.aispaincare.com)

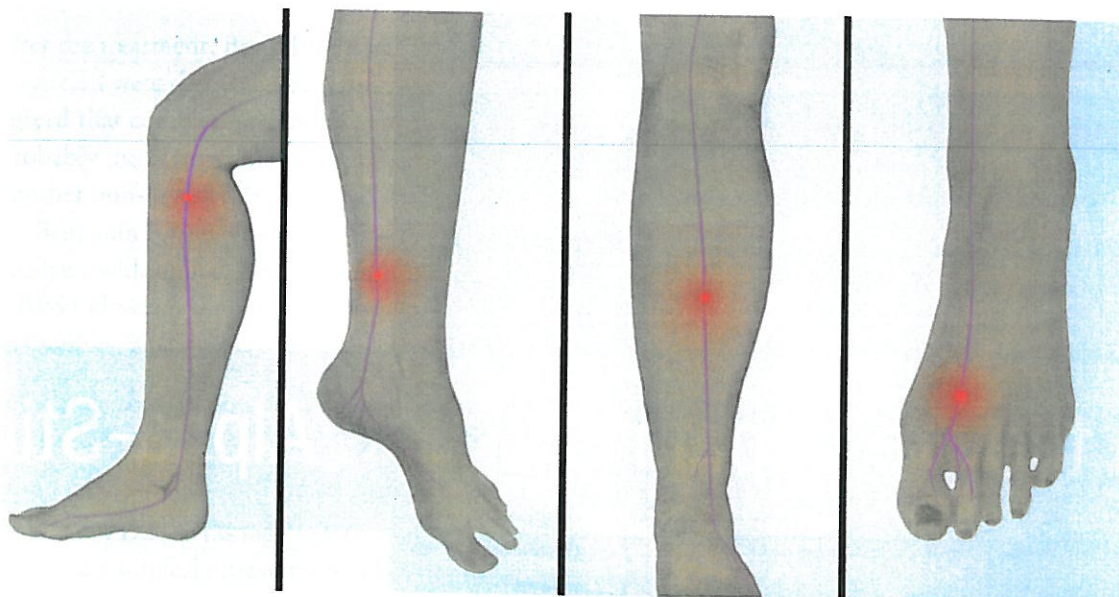


Figure 1. Neuroacupuncture points targeted with InterX® Therapy. From left to right: saphenous nerve, sural nerve, tibial nerve, deep peroneal nerve.



Figure 2. Left: Thomas' feet prior to the treatment in June 2015. Right: Thomas' feet following treatment in August 2015.

scranially, InterX Therapy is delivered on the skin of the involved area. InterX Therapy delivers high-amplitude, high-density stimulation through the use of a handheld device or its remote probes, with manufacturer recommended treatments of approximately 15-30 minutes. The number of sessions is left to the clinical judgment of the treating provider (9). Treatment also includes a dynamic component: When appropriate, the patient should complete stretches and/or exercises while stimulation is applied to the points of pain (10).

InterX Therapy is thought to control pain through a combination of several mechanisms. The neurostimulation causes endogenous opioid release, contributing to immediate reduction of pain. Pain relief often continues after the treatment, possibly due to a central nervous system response and neuropeptide/cytokine cascade effect. Additionally, pain perception may be reduced as part of a gate-control mechanism (11).

At least two randomized controlled trials have found InterX Therapy to be effective in pain management. In populations with postoperative ankle and femur fractures, participants who received InterX Therapy were found to have significantly less pain than those who were treated with a sham device (12,13).

### The Treatment Process

The InterX Therapy treatment for Thomas was initiated with the foot that exhibited the least amount of pain and progressed to the areas of most pain. First, the Alpha-Stim CES device was applied to the ears and the InterX device scanned the affected areas that caused the most pain. The working hypothesis was that the Alpha-Stim would initially decrease any central sensitization that was amplifying the signal coming to the brain from his lower extremities. Once the central sensitization decreased, subsequently applying the InterX Therapy would decrease sensitivity and increase range of motion.

Thomas' allodynia had progressed to the point that something as innocuous as a bedsheet resting gently on the CRPS-affected area caused significant pain. As the first treatment session progressed, Thomas realized that his range of motion was gradually increasing. During the active phase of InterX Therapy treatment, Thomas slowly moved the affected pain areas while the device was applied. By the end of the first treatment, the skin color on both feet began to change back to the original pre-CRPS color. Additionally, Thomas could move his toes and foot in a much larger range of motion and, most importantly for him, he experienced a decrease in his subjective pain experience by

approximately 75%.

By June 2015, Thomas participated in two additional treatment sessions that lasted approximately 60 to 75 minutes each. After the third session we procured both of the medical devices for him, taught him how to use the devices, and kept in contact with him during the learning process to answer any questions. Additionally, the acupuncturist treating Thomas gave him a diagram with acupuncture points to focus on during InterX Therapy treatments (Figure 1).

Thomas used the devices at home and his progress continued through his three-month follow-up in August 2015 (Figure 2). Given his success, Thomas was no longer being considered a candidate for a continuous subanesthetic ketamine infusion. Prior to the treatment, Thomas only tolerated working part time as a military intelligence analyst; however, Thomas returned to work full-time in June 2015.

Without a doubt, Thomas was a success story and we desperately want to see more CRPS patients follow this same trajectory. Unfortunately, controversy surrounds the therapeutic management of CRPS. Treatment with pharmacotherapy and noninvasive interventions such as mirror therapy, graded motor imagery, and pain-exposure physical therapy has yielded mixed results (1,14,15). Our hope is that this case provides preliminary support for the use of Alpha-Stim and Inter-X for rapid reduction in CRPS severity. These findings may also lead to hypotheses to drive development of additional novel noninvasive approaches for patients with CRPS.

**Acknowledgement:** The authors wish to thank Patrick Sonnenberg (licensed acupuncturist) for providing information about the neuroacupressure points, Joshua Yancosek for his rendering of the neuroacupressure points in Figure 1, and Bob D'Angelo for his photography of the authors.

**Disclaimer:** The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, the Department of Defense, or the US Government.

## References

- Birklein F, O'Neill D, Schlereth T. Complex regional pain syndrome: an optimistic perspective. *Neurology*. 2015;84(1):89-96.
- Wilkie DJ, Savedra MC, Holzemer WL, Tesler MD, Paul SM. Use of the McGill Pain Questionnaire to measure pain: a meta-analysis. *Nurs Res*. 1990; 39(1): 36-41.
- Harden RN, Bruehl S, Stanton-Hicks M. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Medicine*. 2007;8(4):326-331.
- Eberle T, Doganci B, Krämer HH, et al. Warm and cold complex regional pain syndromes Differences beyond skin temperature? *Neurology*. 2009;72(6): 505-512.
- Vaneker M, Wilder-Smith OH, Schrombges P, Oerlemans HM. Impairments as measured by ISS do not greatly change between one and eight years after CRPS 1 diagnosis. *Eur J Pain*. 2006;10(7):639-644.
- Electromedical Products International. Scientific and clinical literature examination for the Alpha-Stim AID cranial electrotherapy stimulator. Published 2014. Prepared for National Institute for Health and Care Excellence.
- Kirsch DL, Price LR, Nichols F, Marksberry JA, Platoni KT. Military service member and veteran self reports of efficacy of cranial electrotherapy stimulation for anxiety, posttraumatic stress disorder, insomnia, and depression. *US Army Med Dep J*. 2014;Oct-Dec:46-54.
- Taylor AG, Anderson JG, Riedel SL, Lewis JE, et al. A randomized, controlled, double-blind pilot study of the effects of cranial electrical stimulation on activity in brain pain processing regions in individuals with fibromyalgia. *Explore*. 2013;9(1):32-40.
- Neuro Resource Group. Frequently asked questions for patients. InterX Therapy. [http://www.interx.com/patient\\_faqs.php](http://www.interx.com/patient_faqs.php). Published 2013. Accessed December 29, 2015.
- Neuro Resource Group. InterX Therapy. [http://www.interx.com/docs/InterX\\_Introduction\\_Sheet.pdf](http://www.interx.com/docs/InterX_Introduction_Sheet.pdf). Published 2008. Accessed December 29, 2015.
- Neuro Resource Group. Frequently asked questions for professionals. InterX Therapy. [http://www.interx.com/professional\\_faqs.php](http://www.interx.com/professional_faqs.php). Published 2013. Accessed December 29, 2015.
- Gorodetskiy IG, Gorodnichenko AI, Tursin PS, Reshetnyak VK, Uskov ON. Use of noninvasive interactive neurostimulation to improve short-term recovery in patients with surgically repaired bimalleolar ankle fractures: a prospective, randomized clinical trial. *J Foot Ankle Surg*. 2010;49(5):432-437.
- Gorodetskiy IG, Gorodnichenko AI, Tursin PS, Reshetnyak VK, Uskov ON. Non-invasive interactive neurostimulation in the post-operative recovery of patients with a trochanteric fracture of the femur. *J Bone Joint Surgery Br*. 2007;89(11):1488-1494.
- Cossins L, Okell RW, Cameron H, Simpson B, Poole HM, Goebel A. Treatment of complex regional pain syndrome in adults: a systematic review of randomized controlled trials published from June 2000 to February 2012. *Eur J Pain*. 2013;17(2):158-173.
- O'Connell NE, Wand BM, McAuley J, Marston L, Moseley GL. Interventions for treating pain and disability in adults with complex regional pain syndrome: an overview of systematic reviews. *Cochrane Database of Syst Revs*. 2013;4:1-68



**Benjamin Keizer, PhD**, (left) works for the Army Medical Department as leader of the Rehabilitation and Performance Psychology group at the Center for the Intrepid (CFI), Fort Sam Houston, Texas. As one of the premier outpatient rehabilitation centers for the Department of Defense, the CFI provides advanced, interdisciplinary care for military service members who sustained serious injuries (e.g., amputation, limb-salvage, multi-trauma, major surgery). He earned his doctorate at the University of Louisville in counseling psychology before completing a two year post-doctoral fellowship in health psychology at San Antonio Military Medical Center.

**Lindsay Sposato, MS, OTR/L** (center) is a first lieutenant in the United States Army. She is a Senior Fellow in the Army-Baylor University Doctor of Science in Occupational Therapy Program. She is interested in the relationship between disability and employment. She has written about dignity therapy and is currently engaged in research about the psychosocial adaptation to limb salvage.

**Kathleen Yancosek, PhD**, (right) is a lieutenant colonel in the United States Army. She currently serves as the director of the CFI. She earned her doctorate at the University of Kentucky in Rehabilitation Science before completing a two year post-doctoral fellowship at the United States Army Research Institute of Environmental Medicine in Natick Massachusetts. Her research interests relate to rehabilitation of traumatic upper limb injuries.