CANADIAN NEUROMODULATION SOCIETY
Société Canadienne de Neuromodulation

Dear CNS Members,

Greetings! I hope everybody is keeping well during these unprecedented times.
Last fall, when I introduced the CNS newsletter, I mentioned that the world of neuromodulation is a rapidly evolving field and we need a forum to share news and views. No one would have imagined how drastically the world would change just a few months from then. But even during these strange times we feel the need to provide a platform to share ideas, opinions and experience.
I would therefore very much like to thank **Professor Taufik Valiante** and **Professor Sandeep Amin** for sharing their innovative work with our readers!

If you like to share something, please send me an email at **Yasmine.hoydonckx@uhn.ca** and I will include it into our fall newsletter.

Stay safe!

Yasmine Hoydonckx MD FIPP
Editor – Newsletter, CNS
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A word from our President

It is my pleasure to welcome you to the Canadian Neuromodulation Society. We are a non-profit group of clinicians and scientists dedicated to improving patients' lives through neuromodulation. Our mission is to educate each other and the public, research new and better therapies, and improve access to neuromodulation technology across Canada to patients in need.

Over the next two years it is important that we continue to grow as a society and advocate for our patients. We can do this through interprovincial and international research collaborations, sharing our valuable and unique experiences, and highlighting our successes in improving our patient's lives.

Neuromodulation is an exciting field. The indications for treatment continue to expand and the technology is advancing at a rapid pace. I encourage you to *join* the Canadian Neuromodulation Society so that we can continue to teach each other and help more and more patients.

Our annual meeting is the culmination of the year's scientific and teaching activities, and a great opportunity to share ideas with colleagues from across Canada and around the world. This year, we have been forced to forgo our annual meeting in September 2020 in order to keep our members, sponsors, and invited guests safe.

We very much look forward to seeing all of you in 2021!

President

Dr Keith MacDougall, MD FRCSC

“My lab”

An Introduction to CRANIA

The **C**ente**R** for **A**dvancing **N**eurotechnological **I**nnovation to **A**pplication (**CRANIA**), a partnership between University Health Network, Canada’s largest academic hospital, and the University of Toronto brings together research, clinical and academic experts from multiple disciplines to develop and commercialize new technologies and treatments for people living with brain diseases and disorders.

Our research and clinical teams are currently working on several fronts to develop new technological solutions for those living with a variety of neurological and spinal cord diseases and conditions, including spinal cord injury, epilepsy, Parkinson’s disease, stroke, Alzheimer’s, chronic pain, depression, concussion and brain injury.

At CRANIA we study, develop and partner with diverse industry, academic and investor stakeholders to accelerate translational neuromodulation research programs, so that new, improved or existing neurotechnologies – including neural implants and neuromodulation techniques and tools – can be delivered to the market to help address the significant unmet patient and market need.

Moreover, these brain technology applications and products would improve the lives of the one in three people worldwide who will suffer from a brain disease, injury or disorder in their lifetime. As an evolving, fully-integrated, world-leading neuromodulation center of excellence, we look forward to engage and collaborate with our current and future partners to advance neuro-devices and first-to-clinic neuromodulation therapies and related electroceuticals that can positively impact the lives of patients, families and healthcare providers in the next 5 years.

Dr. Taufik Valiante MD, PhD FRCS(C)
Director CRANIA
Associate Professor
Department of Neurosurgery – University of Toronto
https://crania.ca

“What’s out there?”

Hybrid Neurostimulation trial – Surfing between waveforms directed to the Dorsal Column and Dorsal Root Ganglion during the Trial Period

Electrical stimulation of the nervous system, better known as neuromodulation is an important component in the armamentarium of neuropathic pain. Spinal cord stimulation has been proven safe and effective, all while minimizing the costs of treating chronic pain patients with neuromodulation when compared to other modalities. Dorsal root ganglion stimulation is another form of spinal cord stimulation, differs slightly by the selective method of treating intractable pain in the trunk and limbs, specifically in patients with complex regional pain syndrome, diabetic peripheral neuropathy and phantom limb pain by achieving paresthesia free stimulation to the targeted regions of pain. The dorsal root ganglion has anatomic specificity of stimulation and its concordance of pain and paresthesia overlap. The dorsal root ganglion provides a unique filter to sensory input from the periphery and modulation of the signals at the dorsal root ganglion can provide significant relief for patients with certain neuropathic states.

Paresthesia based stimulation, better known as tonic stimulation delivers electrical stimulation to the sensory fibers of the dorsal column where the fibers synapse at the spinal cord with smaller sensory nerve fibers and based on the gate theory by Melzack and Hall, activation of these synapses inhibit the transmission of painful sensation.

Spinal cord stimulation is approved to treat chronic intractable pain of the trunk and limbs. SCS delivers electrical pulses *via* spinal epidural electrode arrays (leads) in the posterior epidural space at vertebral levels commonly T8/9 and 10 associated with perceived pain. **Traditional SCS devices** are capable of delivering pulse frequencies in the range 2 to 1,200 Hz, with typical application of approximately 40 to 60 Hz. The objective of these relatively low-frequency SCS devices is to produce paresthesia (a tingling sensation) that overlaps the pain distribution, with the intent of masking pain perception. Intraoperative paresthesia mapping is thus required, wherein patient feedback is solicited while adjusting stimulation location, pulse frequency, pulse width, and amplitude. Thus, traditional SCS success depends on adequacy and durability of paresthesia coverage as well as patient tolerance of the induced sensations.

HF10 therapy involves application of short-duration (30 µs), high-frequency (10 kHz), low-amplitude (1 to 5 mA) pulses to the spinal epidural space in such a manner as to not produce paresthesia, thus obviating the requirement of paresthesia mapping.The **SENZA-RCT study** (Nevro) in 2015 showed at 3 months, 84.5% of implanted HF10 therapy subjects were responders for back pain and 83.1% for leg pain, and 43.8% of traditional SCS subjects were responders for back pain and 55.5% for leg pain ($P < 0.001$ for both back and leg pain comparisons). The relative ratio for responders was 1.9 (95% CI, 1.4 to 2.5) for back pain and 1.5 (95% CI, 1.2 to 1.9) for leg pain. The superiority of HF10 therapy over traditional SCS for leg and back pain was sustained through 12 months ($P < 0.001$). HF10 therapy subjects did not experience paresthesia. The SENZA-RCT was a performed with a rechargeable IPG.

The **SUNBURST study** (Abbott) demonstrated that burst stimulation is noninferior to tonic stimulation ($p < 0.001$). Superiority of burst was also achieved ($p < 0.017$). Significantly more subjects (70.8%) preferred burst stimulation over tonic stimulation ($p < 0.001$). Preference was sustained through one year: 68.2% of subjects preferred burst stimulation, 23.9% of subjects preferred tonic, and 8.0% of subjects had no preference. No unanticipated adverse events were reported and the safety profile was similar to other spinal cord stimulation studies. This study involved a primary non-rechargeable IPG.

The Dorsal root ganglion is physiologically in the peripheral, lying in the medial to lateral aspects beneath the pedicle of the vertebral body of the neural foramen. The Dorsal root ganglion is somatotopically organized becoming an ideal target for neuro stimulation with significant less electrical dosage delivered to the central nervous system than traditional dorsal column stimulation. **The ACCURATE study** (Abbott) demonstrates that compared to tonic stimulation, DRG provides significantly less and statistically significant neuro-electrical footprint to the central nervous system and less unrequired paresthesia, with the added benefit of less battery consumption. Changes in body mass, position, and posture create changes in the movement of CSF which alters the distance of the electrodes from the dorsal column with traditional spinal cord stimulation. With DRG, the distance between the electrode and neuronal elements are more consistent and further allowing for a more precise titration of therapy. The stimulation parameters involve use of micro current in the form of micro amps compared to milliamps for dorsal column stimulation.

The **Accurate study** found that people with chronic pain in a lower limb from CRPS experienced superior pain relief after 12 months with DRG stimulation with a primary 74.2 percent of people experienced meaningful pain relief with DRG stimulation, compared to 53 percent who received traditional spinal cord stimulation.

- One-third had more than 80 percent pain relief and no tingling sensation, which is a common side effect with traditional spinal cord stimulation.
- DRG stimulation led to a better quality of life compared to traditional spinal cord stimulation.

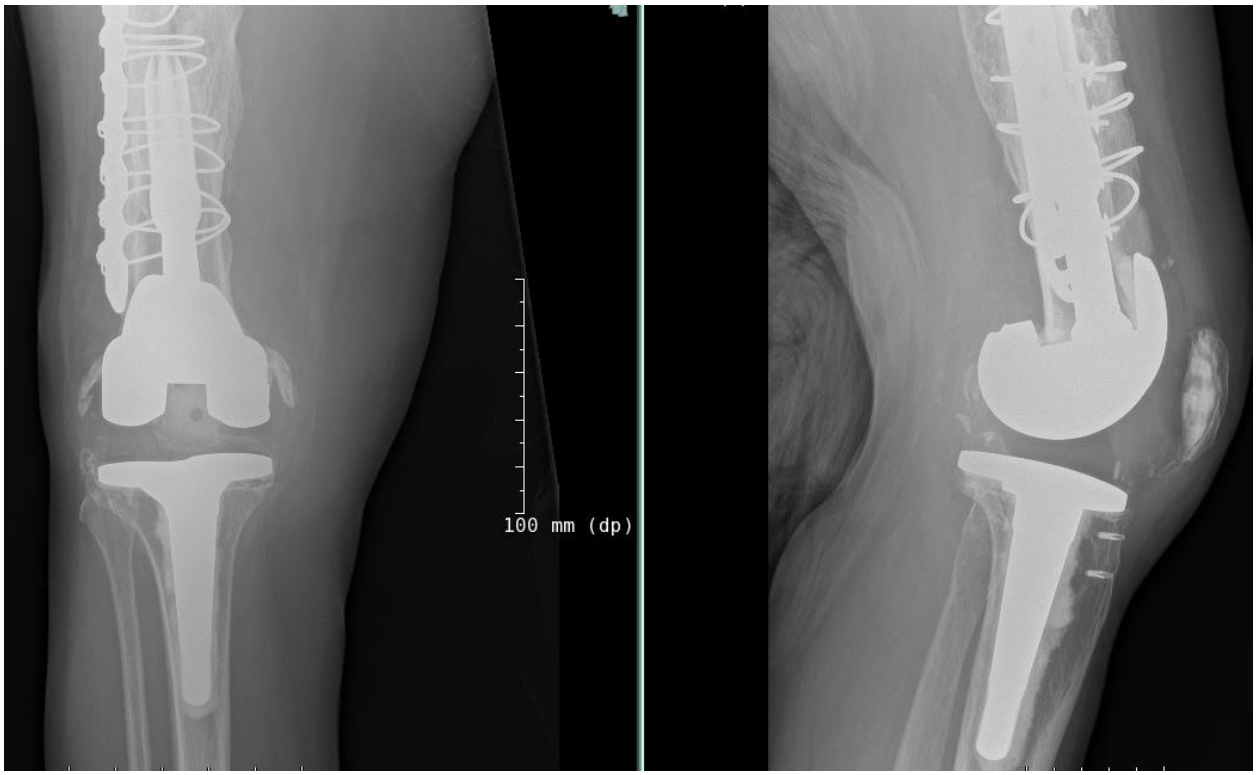
While all the modalities and waveforms described above provide some form of relief in patients with chronic neuropathic pain the choice of device and waveforms needs to be made by the clinician in conjunction with the patient. While the data as outlined above is supportive for the different modalities there is advantage is choosing DRG stimulation in patients with CRPS and focal neuropathic states. The decision making is straight forward in patients with normal spinal anatomy and focal pain. Scenarios will emerge when the spinal anatomy due to either previous surgery or degenerative spinal and foraminal stenosis is potentially not accommodating to the placement of a DRG leads. Also in patients with mixed pain states where there is axial and focal pain sometimes it is difficult to predict the potential superiority of one therapy over the other. Piggybacking an existing trial with a different external pulse generator to provide a different waveform and frequency has been a common practice for many clinical practices when the leads and external pulse generator of one device fails to provide adequate relief. This may serve as salvage therapy in patients with suboptimal relief. This however cannot be done in a patient with failed DRG trial to switch the external pulse generator given the unique anatomic location of the leads and differences in stimulation parameters. Currently there is no hardware (Internal pulse generator) that exists that is capable delivering of all the different modalities mentioned above.

The term **hybrid trial** refers to the use of combined dorsal column leads and DRG leads in a patient with considerations outlined above. The trial procedure is performed with the placement of percutaneous dorsal column leads and DRG leads at the appropriate levels. The patient's paresthesia mapping is performed on the day of the procedure. One of the two modalities is initiated for the first half of the trial period. The percentage of relief and function is recorded for the dorsal column leads and subsequently the DRG leads or vice versa. The patient's receptiveness and tolerance to the initial mapping and paresthesia overlap can help with choosing the initial mode of stimulation. All no time should both modalities activated at the same time due to lack of feasibility to use both modalities simultaneously even if that were to be successful. This is based on lack of hardware that can accommodate both tonic stimulation leads and DRG. Combining both therapies would require two separate IPGs.

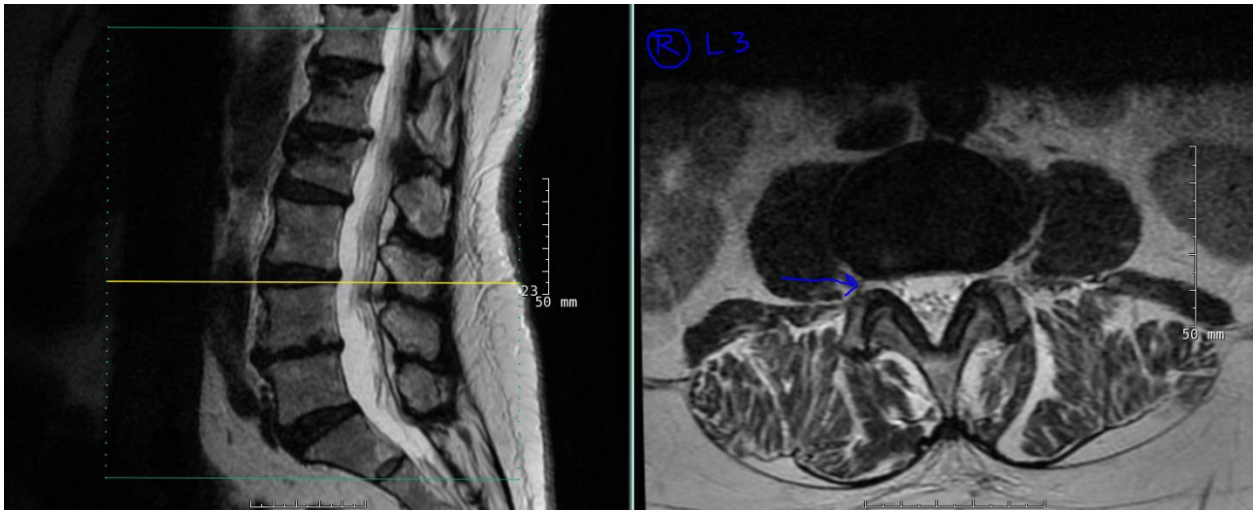
Case scenario

74 yr. old lady with H/O lumbar laminectomy L4-5, compression fractures L1/2 and vertebroplasty with intractable right lower extremity neuropathic pain predominantly in the knee.

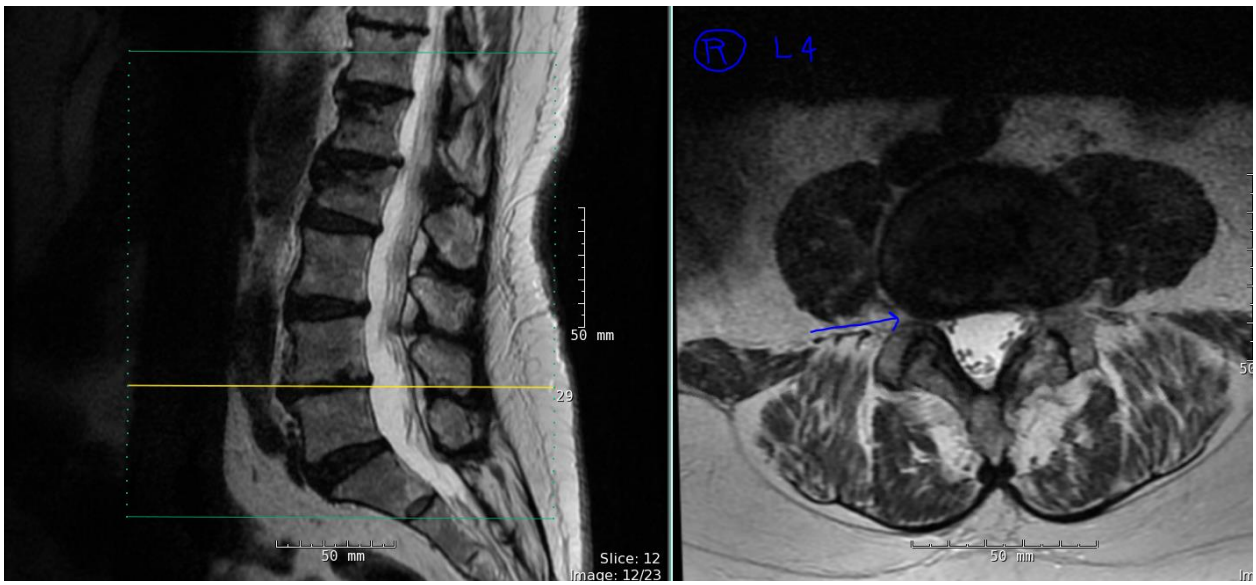
X-ray right knee



MRI L spine L3-4 neural foramen



MRI L spine L4-5 neural foramen



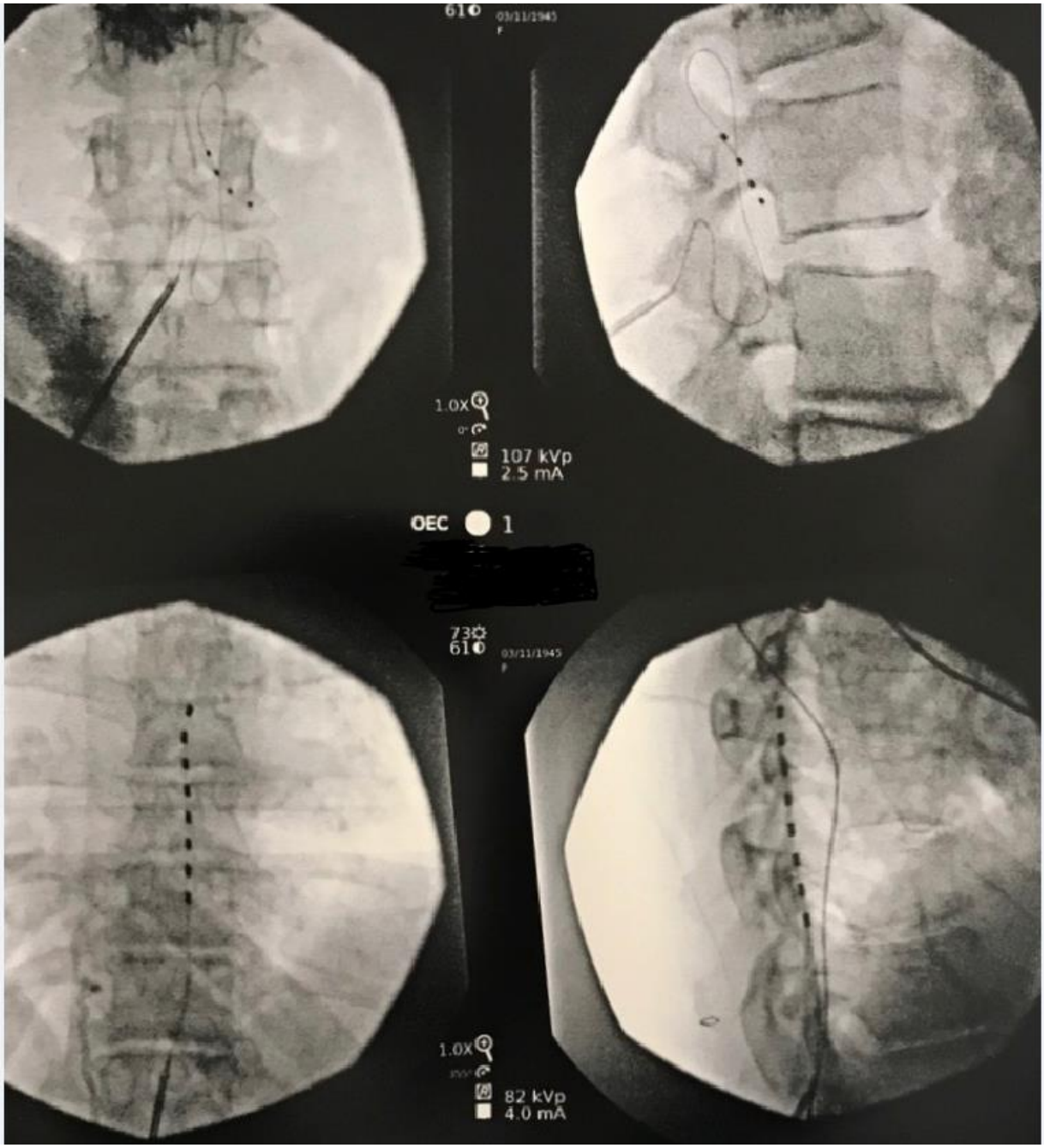
Patient underwent hybrid trial one dorsal column lead and one DRG lead right L3.

Anatomic considerations were the right neural foraminal narrowing at L4-5 and laminectomy defect on the left.

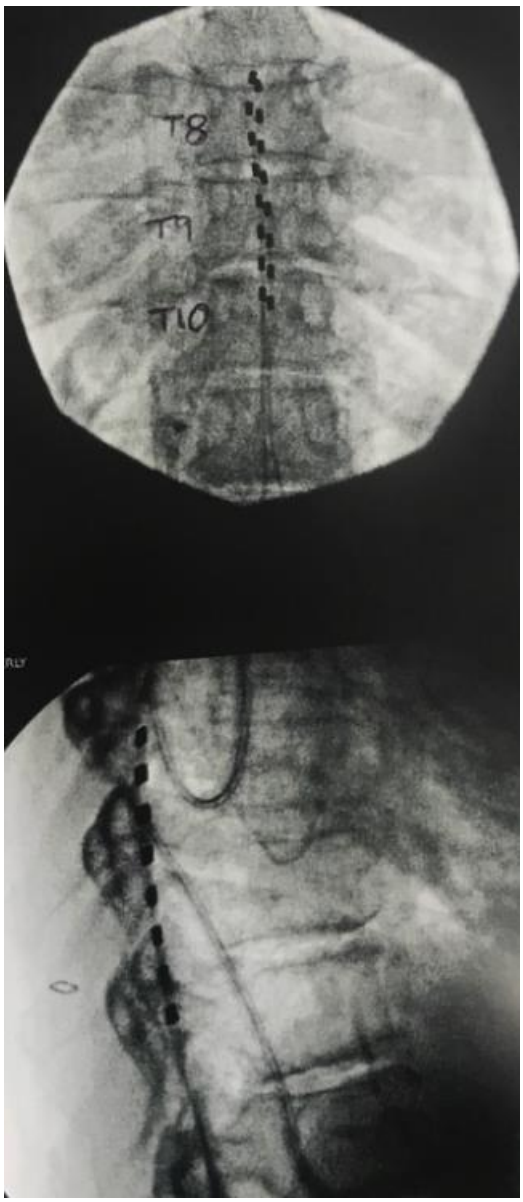
Plan was to place DRG leads at L3/L4 and dorsal column lead at T8/9/10, however due to the right L4 foraminal stenosis unable to pass DRG lead at L4.

Patient did not report significant relief with the DRG lead but 60% relief with dorsal column stimulation with the Burst DR waveform.

Trial SCS/DRG hybrid



Permanent SCS leads



Discussion:

As outlined in the case scenario above, this patient posed a unique challenge given the focal neuropathic pain, however with the underlying spine pathology of laminectomy and foraminal stenosis. The feasibility of successfully placing DRG leads at L3 and L4 was questionable given the anatomy. Placing a dorsal column lead in a patient with potential failure of DRG stimulation provided a backstop which prevented failure of neuromodulation therapy in this case. The ability to test a patient Tonic/Burst DR and DRG stimulation provides a unique opportunity to both patient and clinician to test the efficacy of relief of targeting waveforms at both the dorsal column and dorsal root ganglion prior to the permanent implant. Hybrid trial of spinal stimulation should be considered in special circumstances. Advancement in technology for the IPG to allow simultaneous application on both therapies can translate into permanent implantation using hybrid technology.

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References:

*Deer, Timothy R., Robert M. Levy, Jeffery Kramer, Lawrence Poree, Kasra Amirdelfan, Eric Grigsby, Peter Staats, et al.2017. "Dorsal Root Ganglion Stimulation Yielded Higher Treatment Success Rate for Complex Regional Pain Syndrome and Causalgia at 3 and 12 Months: A Randomized Comparative Trial." *Pain* 158 (4): 669–81.
*Gildenberg, Philip L. 2006. "History of Electrical Neuromodulation for Chronic Pain: Table 1." *Pain Medicine*. https://doi.org/10.1111/j.1526-4637.2006.00118.x.
Kemler, Marius A., Henrica C. W. De Vet, Gerard A. M. Barendse, Frans A. J. M. Van Den Wildenberg, and *Maarten Van Kleef. 2004. "The Effect of Spinal Cord Stimulation in Patients with Chronic Reflex Sympathetic Dystrophy: Two Years' Follow-up of the Randomized Controlled Trial." *Annals of Neurology* 55 (1): 13–18.
Krames, Elliot S. 2014. "The Role of the Dorsal Root Ganglion in the Development of Neuropathic Pain." *Pain Medicine*. https://doi.org/10.1111/pme.12413.
*Kumar, Krishna, Rod S. Taylor, Line Jacques, Sam Eldabe, Mario Meglio, Joan Molet, Simon Thomson, et al. 2007. "Spinal Cord Stimulation versus Conventional Medical Management for Neuropathic Pain: A Multicentre Randomised Controlled Trial in Patients with Failed Back Surgery Syndrome." *Pain* 132 (1-2): 179–88.
*Melzack, R., and P. D. Wall. 1965. "Pain Mechanisms: A New Theory." *Science* 150 (3699): 971–79.

North, Richard B., David H. Kidd, Farrokh Farrokhi, and Steven A. Piantadosi. 2005. "Spinal Cord Stimulation versus Repeated Lumbosacral Spine Surgery for Chronic Pain: A Randomized, Controlled Trial." *Neurosurgery* 56 (1): 98–106; discussion 106–7.
*Piedade, Guilherme Santos, Jan Vesper, Apostolos Chatzikalfas, and Philipp J. Slotty. 2019. "Cervical and High-Thoracic Dorsal Root Ganglion Stimulation in Chronic Neuropathic Pain." *Neuromodulation: Journal of the International Neuromodulation Society* 22 (8): 951–55.
*Taylor, Rod S. 2006. "Spinal Cord Stimulation in Complex Regional Pain Syndrome and Refractory Neuropathic Back and Leg Pain/Failed Back Surgery Syndrome: Results of a Systematic Review and Meta-Analysis." *Journal of Pain and Symptom Management*. https://doi.org/10.1016/j.jpainsymman.2005.12.010.
*Verrills, Paul, Bruce Mitchell, David Vivian, William Cusack, and Jeffery Kramer. 2019. "Dorsal Root Ganglion Stimulation Is Paresthesia-Independent: A Retrospective Study." *Neuromodulation: Journal of the International Neuromodulation Society* 22 (8): 937–42.

*Leonardo Kapural, M.D., Ph.D.; Cong Yu, M.D.; Matthew W. Doust, M.D.; Bradford E. Gliner, M.S.; Ricardo Vallejo, M.D., Ph.D.; et al Pain Medicine | October 2015 Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial

By the way ….

To make this newsletter happen, we would like to have your input!

You can send us your work/advancements/experience on the following topics:

- **What's out there?** : Short reviews of recent advances on neuromodulation topics.
- **This is how I do it**: Share with us your tips and tricks for performing neuromodulation procedures.
- **My clinic/program**: Brief report on the unique features of your neuromodulation clinic/program.
- **My lab**: Brief report on your neuromodulation research set-up.
- **Never too late to learn**: Any educational event that you are organizing including information about upcoming national/international meetings.
- **Curious cases**: Interesting case reports from your practice.
- **Letter to the Editor**: Response to articles or topics addressed in the CNS newsletter.

Please send an email to **Yasmine.hoydonckx@uhn.ca** and I will include it into our fall newsletter.