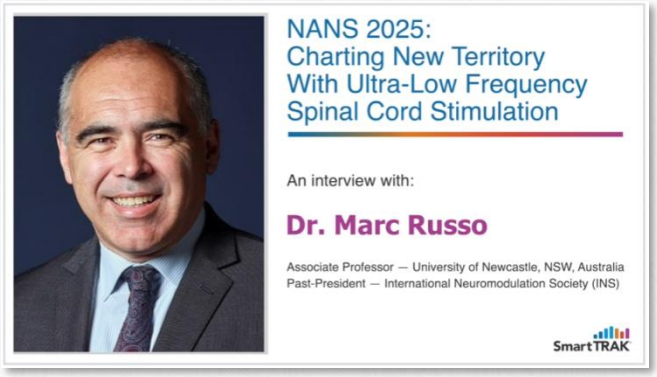
NANS 2025: Charting New Territory With Ultra-Low Frequency Spinal Cord Stimulation

Dr. Marc Russo discusses his research on ultra-low frequency SCS and its potential to treat nociceptive back pain in an interview with SmartTRAK at NANS 2025.

By Anne Staylor | Executive Editor, VP & GM of Neuro Therapies



While spinal cord stimulation (SCS) has been a standard treatment for chronic neuropathic pain conditions for over 30 years, SCS technologies to date have not demonstrated efficacy in the treatment of chronic low back pain that is predominantly nociceptive in origin. At the recent North American Neuromodulation Society (NANS) 2025 Annual Meeting in Orlando, Dr. Marc Russo, a professor at the University of Newcastle in Australia, presented data evaluating the use of ultra-low frequency (ULF) SCS (Presidio Medical) for the treatment of nociceptive chronic low back pain, which affects a much larger segment of the population than those affected by chronic neuropathic pain.

While chronic low back pain can have a mix of both nociceptive and neuropathic pain, a technology that can effectively treat nociceptive pain, or even both types of pain, could be a game changer. In an interview with *SmartTRAK*, Dr. Russo discusses ULF SCS, its mechanism of action and how this research is charting new territory in the treatment of chronic low back pain.

To find our more about ULF SCS and Dr. Russo's latest research, listen to the interview by visiting https://vimeo.com/1053613852. A transcript of the interview is also provided below.

SmartTRAK: Anne Staylor here with SmartTRAK. Today, I'm at the North American Neuromodulation Society Annual Meeting and I have the opportunity to speak with Dr. Marc Russo, a professor at the University of Newcastle in Australia.

Hi, Dr. Russo. So nice to see you again.

Dr. Marc Russo: Hi, Anne. Likewise.

I always like to talk to you about innovation. You seem to be on the leading edge of these things all the time. So here at the meeting, you've presented on a new technology that you've been studying, ultra-low frequency spinal cord stimulation. You presented a study. Let's start by having you provide an overview about what ultra-low frequency is for spinal cord stimulation and then we'll get into the study. Can you start with that?

Dr. Marc Russo: Yes. Absolutely. And I think we really have to set the scene by talking about the original research work that looked at how we could actually interact with nervous system tissue. So that work goes all the way back to the work of Huxley back in 1961. And in that, they showed that if you used a frequency of 50 hertz, 100 hertz, 200 hertz, you could depolarize axonal tissue. So that meant that you would activate that tissue. And it was later on in 1967 with the gate control theory that it became clear if we activated axons in the dorsal column, we could then use the inhibitory circuits to inhibit pain transmission. Now, people forget that the back part of their paper also showed that if you used extremely low frequency, well below one hertz, you would actually not activate axons. You would directly, is an important word, directly inhibit axons.

So the depolarization, is that what you're talking about?

Dr. Marc Russo: Yes, but it would be inhibitory, not excitatory. Now at the time, because that is a little bit like direct current inhibition, there are issues related to what happens to the electrode, which can degrade over time. There are issues that can happen if you're not charge balanced with then changes to the local tissue. So at the time, it couldn't be used clinically, so it just sat there and got shelved and we went on, created the entire field of spinal cord stimulation based on exciting tissue, which would be bad for pain, unless you can use an inhibitory circuit.

But now, with material science progressing with understanding how to charge balance and understanding that we don't want to do direct current, we want to go a little bit above that in terms of frequency, but still stay in the ultra-low frequency space, we can directly inhibit signals. And that has profound implications, because if you're directly inhibiting and shutting down a sodium channel, that neuronal tissue isn't worried if the pain is neuropathic, or nociceptive, or a mixture, mixed pain of neuropathic and nociceptive. Everything related to that pain will get shut down. So it suddenly means that we can actually use spinal cord stimulation, this is what our study's about, potentially to treat nociceptive pain.

When you talk about direct current, you're talking about in the epidural space, right?

Dr. Marc Russo: That's right. And we're not using direct current, so we're actually using a frequency of 0.08 hertz, meaning that we deliver a waveform. Not 50 waveforms a minute. 50 hertz, but we deliver one waveform over 12 seconds. That's a very long rolling wave.

Is the amplitude different then?

Dr. Marc Russo: The amplitude's a little bit different as well, so it's a very sinusoidal pattern to the waveform, so it doesn't look like a square wave and it's a sinusoidal wave. So there's a number of-

And is it sub-perception?

Dr. Marc Russo: Yes. It is. That's right. So it's paresthesia-free and we initially started with an earlier trial of a non-implanted system and we treated patients with neuropathic pain. A few of them had nociceptive pain mixed in. And to our utter amazement, their nociceptive pain disappeared and that caused us to then co-design a study with the sponsoring company to actually look at taking on nociceptive pain. And now with an actual chronic implant model, taking a dedicated specific pulse generator for delivering ultra-low frequency and then monitoring what happened. So I presented some early data. So the first 30 patients at three months, the full cohort will be 44 patients at two years, but presented this first data here at NANS in Orlando 2025. And really, we've never seen anything like this. We don't use, clinically, spinal cord stimulation for nociceptive pain, so we selected patients with what was felt by the clinician to be highly likely to be nociceptive pain based on clinical presentation, MRI scan, diagnostic blocks. So this was patients with low back pain, severe, more than three months, but nociceptive in nature rather than neuropathic.

Aren't some of them mixed?

Dr. Marc Russo: That's right. So a chunk of them had a mixture of nociceptive and neuropathic pain. The largest component had pure nociceptive pain. We had about 10% of patients that probably were a little bit more neuropathic than they were nociceptive. And so this is a clinician grading scale. We don't have a gold standard to define this, so we're taking a neural transmission pathophysiology and a clinical decision-making process. So we don't have a perfect system, but we used what we had and what we saw was that there was 87% of patients had 50% or more reduction in their pain.

Fifty percent or more?

Dr. Marc Russo: Yes, 53% of patients had 80% to 100% of their pain disappear. And then we had a cohort, a good third, the top third basically had abolition of their pain.

How do you measure nociceptive versus neuropathic? Neuropathic you can do nerve blocks, right?

Dr. Marc Russo: Sure. So look, at the end of the day, you're using the visual analog scale. And if you select our patients who only have what you believe to be nociceptive pain, then when their VAS falls, you record that as the change in nociceptive outcome.

But if you have the patient, how do you know? If you are entirely nociceptive, can you somehow just block the nerve and use it for acute pain like on a wound or some other variation of it, or does it have to be at the level of the spinal cord?

Dr. Marc Russo: It's a new frontier, so there are certainly more questions than there are answers. No. You can't use a nerve block to indicate whether pain is neuropathic or nociceptive, because if you block upstream, it's going to disappear.

I see. Everything.

Dr. Marc Russo: Yes. So that doesn't work. It's a very interesting question as to whether this could have applicability in acute pain. Acute pain is more predominantly going to be tissue-based or nociceptive in nature and I think the answer there is, well, we simply don't know at this stage. When you are doing direct inhibition, that means that you can shut down neural transmission. And if you kept cranking the dose up and up and up and up, you would first lose your pain, then you would lose sensation, then you would lose motor power. So one of the critical things is that we've identified an amplitude range within which we are only getting a selective loss of pain transmission. We're not getting any anesthesia, any numbness. We're certainly not getting any motor weakness. And those are areas that you wouldn't want to go to on a chronic basis. Could you use those higher doses that we have not used? Could you use those higher doses in a post-operative setting? I think those questions will come, but that research might be 5 or 10 years away.

Some of the devices, like the high frequency, patients don't always know if it's working until three days later and then of course, Boston has a variation of sub-perception where they have FAST and you can assess it and the patients can determine that they have pain relief sooner than that from what I understand. And so in this situation, how fast is their pain relief?

Dr. Marc Russo: It was variable. So we saw some patients that had quite rapid reduction in pain within four hours. We had other patients whose pain relief came on after the first 24 hours. And that may be reflective of the fact that we started off in the original study with fairly low doses, so low amplitude and then you titrate up to sort out what happens as you go up. So I think we're still learning our way in that regard.

So patient selection sounds like that might be really important for this kind of a study, because determining-

Dr. Marc Russo: Well, it certainly is when you're mechanistically wanting to make the statement that spinal cord stimulation can treat nociceptive pain. You must only recruit patients with that. The first non-chronic implant study, we did the opposite. We were wanting to stay in the safe territory of exploring what happens to patients with neuropathic pain. So they had almost

consistently pure neuropathic pain. We got similar results.

Really?

Dr. Marc Russo: The results I just gave you, the 80 and the 50, we got the same result for neuropathic pain. So it raises the issue that are we dealing with something that is a treatment that is pain agnostic? In which case it would make the life of a pain physician much easier in terms of patient selection. It treats what's wrong with you.

Yes. But to make that claim for nociceptive pain, you think they need to be purely nociceptive in order to be able to go to FDA with that kind of a claim?

Dr. Marc Russo: Absolutely. Yes. Absolutely. If you're going to be on label, you better make sure that that's your patient population. So that's our study in Australia. There are plans for a much larger study to be conducted in the United States in the future.

Are you going to be the primary investigator on that?

Dr. Marc Russo: No. I think that'll be a United States-based person.

I see. So for your study, you said you had 34. Is that what you said you had?

Dr. Marc Russo: So we've got results for 30 patients at three months and the full cohort will be 44 patients at two years.

I see. So then you're just going to follow the same patients out for that long?

Dr. Marc Russo: Correct. Correct.

So are you the only person that's doing a study in this right now that you know of?

Dr. Marc Russo: Well, I was one of the investigators on this particular study, but I had a whole series of colleagues based in both Victoria and South Australia as part of that. So there'll be future studies, which will be multinational, looking at how this is deployed, what the results are over the long term. It's very much charting new territory, so there will inevitably be learnings, bumps on the way and so forth. But at this stage, the promise that was contained back in 1961, but never be able to be utilized, at this early stage is looking like it's bearing fruit and definitely worthy of further research and investigation.

If it's that low in frequency, I'm sure the battery life on that would be very long. I'm just thinking out loud. I hear people talking about rechargeable and non-rechargeable, how many times they have to recharge and battery longevity. I know for DRG stimulation, for example, it uses very, very little amount of battery, so this could change a lot.

Dr. Marc Russo: Yes. So the physics of ultra-low frequency is a little bit different as regards battery, so you can't exactly extrapolate from higher frequency world, but nevertheless, it is a fairly efficient system.

So you're presenting three months here. When are we going to see your next results?

Dr. Marc Russo: Well, we'll probably do a six-month cut of the data and a twelve-month cut of the data, so that'll be a little way away, but I'm looking forward to tracking this over time. Obviously, we're very interested in looking at adverse events, serious adverse events. Gratifyingly, we really have not seen anything of significance in this regard, but the proof of the pudding is your long-term data as regards that.

And so there's no different leads? They obviously have their own type of lead, but is there something-

Dr. Marc Russo: It's unique material coatings related to the electrode and then it's a unique bias setting and a unique formation of the pulse generator. There's nothing off-the-shelf here from commercial vendors. This is specifically developed from the ground up.

Well, I look forward to hearing more about these results at your next presentation, six and 12 months.

Dr. Marc Russo: Always a pleasure talking, Anne.