Response to Recent JAMA Article on Spinal Cord Stimulation

I am writing to you today because both myself and the International Neuromodulation Society (INS) Executive Officers have been flooded with calls from members who, like us, are concerned about the methodological flaws in a recent study on SCS published in the prestigious journal JAMA (Journal of American Medical Association) and the likelihood for a range of patients, doctors and healthcare delivery systems to reach erroneous conclusions on the evidence base for spinal cord stimulation (SCS) based on this one study.[1]

The flaws are so manifold and the statements of the authors so disparaging of the whole field that I feel it is important that all members of the INS have the facts available to them to help dispel this misinformation. In particular I would urge each and everyone of you to use your social media and networking channels to educate those around you as to the true nature of how this study was conducted as I've enumerated in the points below. Together in a concerted effort we can ensure that this vital information is delivered where it is needed before payers use this flawed study as justification to cease covering SCS.

A formal letter to the Editor of JAMA will be forthcoming from signatories of multiple medical societies including the INS but INDIVIDUAL activity will have more effect in the court of public opinion. Patient access to neuromodulation, including pain relief, must be a first and last priority of both practitioners and the societies that represent them.

The study, in short, purported to be a randomised blinded "placebo-controlled" study of clinical SCS on disability in patients with leg pain after spine surgery. It found no difference between the two groups at 90 days on Oswestry Disability Index (ODI). The authors have subsequently made multiple media statements that SCS "doesn't work".

Here are the major flaws that make any conclusions from the study inapplicable to how we conduct spinal cord stimulation around the world

1. The subjects were trialled with tonic waveform SCS when the actual study was run with burst SCS. There is no data and no reason to assume that a response to tonic SCS means that the patient has been shown to be a responder to burst SCS to gain entry into the study.

2. Only a 30% pain reduction was required to enter study yet we know SCS delivers 60-100% pain relief; HENCE many placebo responders would have been included in the initial cohort. 30% reduction in pain should never be allowed as entry criteria for a SCS study.

3. The trial was conducted with pain reduction as the measure to gain entry but then the primary outcome measure for the study was switched to Oswestry Disability Index change at 90 days. Disability reduction follows (not leads) pain reduction so, if pain relief was not allowed to be optimised (as we will see), then the investigators will have manufactured a placebo outcome.

4. Manufacturer guidelines on therapy delivery were NOT followed. Simple burst waveform at 50-70% of paresthesia threshold was deployed, not the manufacturer's algorithm. The patient controller was REMOVED from the patients so they could do no adjustments themselves to optimise their therapy, nor turn off the device if they experienced discomfort. This however is mandatory, to ensure that no overstimulation occurs under any circumstances. Patients were not given the opportunity to have any optimisation of pain relief within the 90 day period. It seems to have not been recognised by the investigators that SCS is a titrated therapy not a fixed therapy.

5. Researchers should be experienced in the field and highly experienced in the specifics of the therapy under investigation. The implanters had no prior experience of managing paresthesia free SCS. The study nurse who did all the programming had never programmed patients prior to this study. This raises the question of whether sufficient experience was present to run a study of this kind.

6. There were no washout periods at all during the study when crossing over to the other group, hence carryover effects bleed into the next treatment group and wash results to a single common level. Carry over effects are proven to be real in SCS.[2]

7. Only 90 day results were chosen as a primary endpoint when the purpose of SCS studies is to assess BEYOND the possible placebo response time of 3 months and assess outcomes at one, two and five years. The primary endpoint was chosen within the possible placebo response period of 90 days.[3]

8. Subjects were told in the informed consent document that they would receive "stimulation". It is reasonable to assume that subjects believed they were to receive standard clinical care SCS. However they were not remotely allowed to have an optimised algorithm that was individually titrated to their needs and which they could control and optimise themselves with the patient remote programmer. They were given a version of the therapy that is not actually practised by clinicians anywhere in the world currently. This raises the issue of proper informed consent and whether the study has breached ethical guidelines on subject information and consent.

What can be gleaned from the above is that the study has major methodological flaws that call into question whether any conclusion at all can be relied upon. Certainly it would seem prudent to rely on multi year outcome studies, meta-analyses and registry data of true clinical care SCS to guide patients, clinicians and healthcare systems.

I urge you to communicate your own critique of this study to your social and medical networks so that information is accessible to those who need it.

The INS will continue to demand high quality research in the field of neuromodulation including not only efficacy but cost-effectiveness and quality of life outcomes across the board.

Best wishes,

Marc A. Russo, MBBS DA (UK) FANZCA FFPMANZCA
President, International Neuromodulation Society

References

1. Hara S, Andresen H, Solheim O, et al. Effect of Spinal Cord Burst Stimulation vs Placebo Stimulation on Disability in Patients With Chronic Radicular Pain After Lumbar Spine Surgery: A Randomized Clinical Trial. JAMA. 2022;328(15):1506–1514. doi:10.1001/jama.2022.18231

2. Perruchoud, C., Eldabe, S., Batterham, A.M., Madzinga, G., Brookes, M., Durrer, A., Rosato, M., Bovet, N., West, S., Bovy, M., Rutschmann, B., Gulve, A., Garner, F. and Buchser, E. (2013), Analgesic Efficacy of High-Frequency Spinal Cord Stimulation. Neuromodulation: Technology at the Neural Interface, 16: 363-369. https://doi.org/10.1111/ner.12027

3. Gilligan C, Volschenk W, Russo M, Green M, Gilmore C, Mehta V, Deckers K, De Smedt K, Latif U, Georgius P, Gentile J, Mitchell B, Langhorst M, Huygen F, Baranidharan G, Patel V, Mironer E, Ross E, Carayannopoulos A, Hayek S, Gulve A, Van Buyten JP, Tohmeh A, Fischgrund J, Lad S, Ahadian F, Deer T, Klemme W, Rauck R, Rathmell J, Maislin G, Heemels JP, Eldabe S; ReActiv8-B Investigators. Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial. Neuromodulation. 2021 Dec 18:S1094-7159(21)06386-8. https://doi.org/10.1016/j.neurom.2021.10.011