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Response: Auto-Targeted Neurostimulation In Chronic Low Back Pain: Why Available Evidence Rejects Its Clinical Utility

Dear Editor:

Thank you for giving us the opportunity to respond to the invalid arguments raised by the company addressing our published study that examined the effectiveness of their device for treating chronic low back pain (1). Below we reply to the issues raised, showing that the company's claim regarding the effectiveness of the device is based on invalid data, attempts to change the study protocol a posteriori and hence to fraud the study in favor of the company's interest.

The company claims that they are able to tell from analyzing the 'scans' of the Soleve device that the placement of the device in some of the patients was improper. This was something that the company raised after they were informed that the clinical trial showed that the Soleve device was not superior over placebo (1). Importantly, we reported a clinical trial in the manuscript. A clinical trial reports on the effects of the treatment how it is used in clinical practice. We applied the device as it was used in clinical practice at the time the study took place, and neither the researchers, nor the therapists providing the treatment were able to verify how the company obtained those 'scans' (or what exactly the scans were telling us). Our research staff performing the study, was trained and supervised in an ongoing manner by the company, and hence, this claim could have been brought to our attention at a much earlier stage, if valid! Also, it remains unclear how those 'scans' were obtained, what type of information the scans provide, whether the scans generate valid data, or what exactly the scan findings imply. Moreover, no one of our research team ever saw any of those scans. Even if those 'scans' exist and generate valid data, it is clear that therapists using the Soleve device in clinical practice will not be able to access them in real time. Hence, therapists will not be able to use those scans to improve the treatment.

After being informed about the negative study outcome, the company had ample time to provide more information regarding those scans prior to the publication of the manuscript, but never did so. At best, those scans can be the basis for further research in this area. In their Letter to the Editor, Gorenberg and Kanner claim to provide data from such additional analysis. However, they report data from a subgroup analysis performed on the preliminary dataset of no more than 8 (out of

19) patients in the experimental control group. Those data are fraud: before preparing the submitted manuscript, the entire dataset was double-checked for errors and inconsistencies, in line with common research practice. This way, several small errors in the dataset were corrected, resulting in the final database as used for the definite statistical analysis (and reported in the manuscript). Hence, the data as presented by Gorenberg and Kanner are fraud.

Even if the results presented by Gorenberg and Kanner were valid, it would be unethical to report data from such a small subgroup of the experimental group. The number of people within that subgroup is too small to draw meaningful conclusions: they represent no more than 8 out of 19 patients (42%) that received the treatment. In fact this implies that the company reveals that their device does not operate correctly in 58% of the patients. This illustrates the lack of clinical utility of the device for clinical practice.

Another reason why this additional analysis cannot be used for clinical or scientific purposes, is that the scans were not part of the original study protocol either, as approved by the local ethical committee, agreed with the company and as published online at ClinicalTrials.gov (clinical trial registration number NCT02256410). Even if the scans would exist and would have been verifiable, using those scans to do additional analyses would be a severe study protocol violation, which would go against all research ethics and could be labeled as scientific fraud.

All therapists who administered the treatment were properly trained in the operation of the Soleve device. As acknowledged by the peer-reviewers of the manuscript, the study was conducted at the highest methodological level possible in an RCT: Pre-post measures, randomized-controlled design in which patients, a priori sample size calculation, clinical trial registration, clinician assessing the outcomes and the researcher performing the statistical analyses were all blind to patients' group status.

In the point-by-point reply we have shown that the study was performed in accordance with international research standards and research ethics, and that the manuscript represents the actual findings. Given the importance of the study findings, it is of prime importance that the study findings were published in a top-level scientific journal. Finally, we advocate that future studies using the Soleve device are performed with the same scientific independency and rigor as ours, because the obvious conflict of interest makes it unethical for the company to take part in such studies. The fact that they report fraud data in their Letter to the Editor clearly illustrates this notion.

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Response to Response

Soleve Image-Guided Targeted Hyperstimulation Analgesia Show Promising Clinical Results in Chronic Low Back Pain

The reanalysis presented in our letter to the editor has been executed, reported and sent to the Company by Nijs group. In fact, the graphical presentation, the results and the conclusion are quoted word for word from the report by Nijs group. This reanalysis was performed by Nijs group following a detailed face to face discussion of the findings.

Nijs found promising clinical results with the new device, which seems to reduce self-reported pain by approximately 50% in the experimental group, compared to the placebo control-group, thereby contradicting the published data in *Pain Physician* journal by the same author (1).

To avoid any doubt it is quoted here again:

Results
VAS pain: A significant Time x Group interaction was found for VAS-pain ($F(5, 117) = 2.708$, $p < .05$). This interaction is presented in Figure 2. Following this interaction, a simple-effects analysis revealed that pain levels of patients in the experimental group were significantly lower before session 5 ($p = .05$) but not lower before session 6 ($p > .05$).
Conclusions: We must be very cautious due to the small number of patients in this reanalysis. Looking at pain levels, the new device seems to reduce