Letter to the Editor

# Letter to the editor regarding "Two-year results of a double-blind multicenter randomized controlled non-inferiority trial of polyetheretherketone (PEEK) versus silicon nitride spinal fusion cages in patients with symptomatic degenerative lumbar disc disorders"

**Roel F. M. R. Kersten[1,2], F. Cumhur Öner[2], Mark P. Arts[3], Marian Mitroiu[4], Kit C. B. Roes[5], Arthur de Gast[1], Steven M. van Gaalen[1,6]**

[1]Clinical Orthopedic Research Center – midden Nederland (CORC-mN), Department of Orthopedics, Diakonessenhuis Utrecht/Zeist, The Netherlands; [2]Department of Orthopedics, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; [3]Department of Neurosurgery, Haaglanden Medical Center, The Hague, The Netherlands; [4]Department of Biostatistics and Research Support, Clinical Trial Methodology, Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands; [5]Department of Health Evidence, Section Biostatistics, Radboud University Medical Center, Radboud University, Nijmegen, The Netherlands; [6]Spinecenter.Amsterdam, Orthopedics, Acibadem International Medical Center, Amsterdam, The Netherlands

*Correspondence to:* Roel F. M. R. Kersten, MD. University Medical Center Utrecht, Department of Orthopedics, Heidelberglaan 100, 3584CX, Utrecht, The Netherlands. Email: rfmrkersten@gmail.com.

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Unpleasantly surprised we read the study by McEntire, Maslin and Bal (1). As the principal investigators of this study, comprising of the surgeons and staffs of the participating hospitals, we did not authorize the authors to publish these results. We strongly disagree with the post-hoc analysis performed by the authors, and therefore terminated our prior collaboration with McEntire *et al.* during the review process of this study. The correct version of the manuscript, discussing the authentic one and two-year results of our RCT, has recently been published in *The Global Spine Journal* (2). The original protocol criteria were used to analyze these results, published in 2014 (3).

McEntire and Bal are involved in SINXT Technologies (formerly known as Amedica), the manufacturer of the silicon nitride interbody cage. Our collaboration with Amedica started in 2011 with the design of the Silicon Nitride versus Peek (SNAP) trial, resulting in a joint publication of the SNAP research protocol (3). Furthermore an *in vivo* caprine study of silicon nitride versus PEEK cages was published with mutual consent (4). Amedica acted as the sponsor of these studies. An independent clinical research organization (CRO) managed the clinical trial together with the principal investigator's institutions. After analyzing the one and two-year results of our clinical RCT, we concluded there is insufficient evidence that the silicon nitride cage is non-inferior to the PEEK cage, using the original protocol criteria. Amedica (now called SINXT Technologies) disagreed, and presented a biased post-hoc analysis confirming the non-inferiority of silicon nitride compared to PEEK. Also, they excluded the principal investigators to publish their view of the results of the RCT by claiming exclusive rights for the study data. With this act, the authors did not adhere to the ethical and moral standards of Evidence Based Medicine (EBM). Firstly, they

acted contrary to article 36 of the Declaration of Helsinki, stating "Negative and inconclusive as well as positive results must be published or otherwise made publicly available". Also, restricting the principal investigators to publish the authentic results is deemed to be unreasonable according to the involved Medical Ethics Committee (METC) Directive on the Assessment of Clinical Trial Agreements. Moreover, the authors did not adhere to the revised International Committee of Medical Journal Editors (ICMJE) criteria. Lastly, it discloses a case of plagiarism by copying large parts of the Introduction, Methods, Results and Discussion sections combined with the figures and tables of the principal investigators (2).

Methodologically, their post-hoc analysis approach is a clear case of incorrect scientific practice. The design of the study (3), including the non-inferiority margin and assumptions, provided ample opportunity to challenge the margin and assumptions prior to having access to unblinded data and results. This did not happen, it only occurred at the moment the authors were fully aware of complete results. Their reasoning on what constitutes a non-inferiority margin is flawed: this margin is not the minimal clinically important difference (MCID) at individual patient level, but a margin that ensures non-inferiority at population level, as well as that it is sufficiently small to be robust against constancy of effects over time (5,6). Likewise, statistical power assessments at the design stage include that the standard deviation is not fixed but is estimated from the data. Post-hoc "power" calculations based on the observed standard deviation can be done, but they do not constitute an assessment of power of the study (7,8). The post-hoc analysis is fully data driven, therefore actual type 1 error (significance level) cannot be assessed and is likely inflated. The possibility to evaluate the primary results against any other non-inferiority margin than pre-defined is already perfectly possible based on our published paper (2) and does not justify an independent paper.

The EBM primary goal is to increase our scientific knowledge in order to improve public health and patients' care. However, SINXT Technologies did not act in the patients' best interest. In our opinion they have shown to be an unreliable partner and potentially damaged the public debate about interactions between commercial entities and research institutions. We strongly urge the editor to remove the publication of McEntire *et al.* from the Journal of Spine Surgery and all publicly available platforms and when deemed necessary take any further legal steps.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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