Reviewer's report

Title: Spinal fusion leads to a statistical significant increase in serum titanium levels

Version: 4 Date: 24 June 2012

Reviewer: Teija Lund

Reviewer's report:

Major compulsory revisions:

1. The study design is a prospective observational study of the serum titanium levels of 15 patients who underwent a spinal fusion. The authors have also included a control group of 16 healthy adults. There was a statistically significant difference between these two groups at baseline regarding at least age and serum titanium levels. The authors might have considered a case-control design, especially when previous literature suggests that serum titanium levels might increase with age. With the present study design, the control group does not add much to the information gained from the study.

2. The serum titanium levels of the control group are significantly higher at baseline compared to the study group. It would have been interesting to measure their titanium levels at least at the 3- and 12-month follow-up time points to detect any possible variations over time.

3. There seem to be a lot of individual variation in the serum titanium levels amongst the study subjects over the time points studied herein. This makes it difficult to make any definite conclusions. The problem is likely due to the small study sample. How large are the normal variations of serum titanium level over time?

4. Further, as all serum titanium levels in the patient population at all follow-up time points were within the normal range, conclusions need to be cautious. In the discussion, the authors state that in their opinion, "all systemic effects caused by titanium ions are therefore possible after spinal fusion." This conclusion is not aligned with the clinically non-significant, although statistically significant results.

5. In the "Results" section, the authors state that there was no statistically significant difference of the serum titanium levels between the 3- and 12-month time points. However, in the "Discussion" the authors state that such a difference was noticed, and that it could be explained by the patients´ increased mobility. Which one of the statements is accurate?

6. In the "Background" and "Discussion", the authors state that in a previous study, Travis et al. noticed a correlation between serum titanium levels and the number of fused segments, but not between the serum titanium levels and the amount of "hardware". Did the authors of the present study find any correlation
between the number of fused levels and the serum titanium levels? Again the small sample size probably makes it difficult to find any significant correlations.

7. The authors have not reported the p-values of all significant changes in the serum titanium levels. E.g. the statistically significant changes in the study population between the baseline and the 3- and 12- month follow-up points, respectively. These are the main results of their study.

Minor essential revisions:

8. The manuscript needs some language edition.

9. Some linguistic mistakes appear repeatedly: e.g. the correct form is "statistically significant", not "statistical significant"; further, "pseudarthrosis" is used instead of "none arthrosis".

10. The authors should check the manuscript for any typos.

Discretionary revisions:

- 

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests regarding the present study.