Reviewer’s report

Title: Retention of metals in periprosthetic tissues of patients with metal-on-metal total hip arthroplasty is reflected in the synovial fluid to blood cobalt transfer ratio in the presence of a pseudotumour

Version: 0 Date: 06 May 2020

Reviewer's report:

My biggest concern is that conclusion are being drawn from results that were not statistically significant (Lines 347-350): lots of emphasis of paper on findings that could be due to chance alone. Also appears in the abstract. Related to lines 234-251 & Table 4 nothing statistically different. Also relevant for discussion lines 292-322. Is the paper appropriately powered for this pseudotumour analysis?

Another concern is that the authors mention controls which have not been described in the methods (first use of the word control(s) is in the results line 193).

Other more minor comments:

Abstract:
- "ceased their use" implies not used at all anymore. Metal resurfacing is still used for appropriate patients and hence this should be edited accordingly.

Intro:
- Reference 6 refered to as recent, but is from 2005, which pre-dates much of the work on metal ions.
- The quality of written English is generally acceptable as is. However the aim is not clear and should be re-worded (usual to have the effect of XXXX on YYY, but there is no "on" clause and hence is unclear).

Methods:
- It appears 3 patients were analysed differently (line 118: no MARS MRI, line 136: not clear if they were not tested for infection, or if they had infection, the wording could be interpreted either way). Also not clear if this is the same three patients. Is it appropriate to include these patients?

Statistical analysis:
- Was a power analysis done? The study appears to be under-powered for the analysis of pseudotumour types.
- Please clearly define the independent and dependent variables for the statistical analyses. Currently not clear. (lines 182-185)

Results:
- line 200: in previous sentence, it appears that the authors have approximated to 1 significant figure (to 100, and 1000). In line 200 they approximate to 3 significant figures. Why is the
reporting more accurate in the second sentence? The same level of precision should be used for similar measures.
- line 211: B-Co not defined - blood cobalt? Same with B-Cr. AO/AS/IS/IO also not defined in body of text, same for SF, ST, WB etc. Please define in main text, not just figure legends. Please check all acronyms defined at first use in body of text.
- Tables 3 and 4. Please report the n per group in the table for clarity.

Discussion
- Line 265: is it possible to correlate the Ti data with the clinical notes on taper wear to confirm this hypothesis

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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