

First review correction

Comment	Answer	Changes made
Editor		
I found the title was more than 12 words. The title should be no more than 12 words;	Thank you for this comment. We did not notice the title should be no more than 12 words. We shortened the title to 14 words. In our opinion the number of words cannot be further reduced without removing substantial content of the title describing our study. Moreover, we recognized some studies in the World Journal of Orthopedics exceed the 12 words. Therefore, we hope you to accept our title of 14 words.	<u>Title page, title changed to:</u> Highly Cross-Linked versus Conventional Polyethylene Inserts in Total Hip Arthroplasty, a five-year RSA RCT.
I found no "Author contribution" section. Please provide the author contributions	We apologize that we did forget this section. We added this to our manuscript. Thank you.	<u>Added to Title Page:</u> Authors' contributions statement: All authors contributed to the study conception and design. D. Haverkamp and D. Hoornenborg were involved in the initial surgery procedures. Writing of the study protocol was performed by D. Haverkamp. Data collection and analysis were performed by J. van Loon and I.N. Sierevelt. The first draft of the manuscript was written by J. van Loon. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.
I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor	Our apologies for the inconvenience. We added the original files. Thank you for your comment.	<u>Added as separate files:</u> <ul style="list-style-type: none"> - Figure 1: file '56927 - Figure 1.png' - Figure 2: file '56927 - Figure 2.doc' - Figures 3 to 6: file '56927 - Figure 3-6.pptx'
I found the authors did not add the PMID and	When available, all PMID and DOI were added for the	<u>Changes made:</u> When available, all PMID and DOI

<p>DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout</p>	<p>references.</p>	<p>were added for the references.</p>
<p>I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text</p>	<p>We apologize that we did forget this section. We added this to our manuscript. Thank you.</p>	<p><u>Added after Conclusions section:</u> ARTICLE HIGHLIGHTS <i>Research background</i> Highly cross-linked polyethylene (HXLPE) inlay in THA is presumed to give lower wear rates in vivo, compared to convention polyethylene. <i>Research motivation</i> More in vivo studies are needed in literature, especially when using Röntgen Stereophotogrammetric Analysis (RSA), to confirm the advantage of HXLPE over conventional PE. <i>Research objectives</i> The objective of the study was to compare wear the HXLPE (REXPOL) and conventional PE acetabular inlay with similar ceramic head articulation, within the first five years after implantation. <i>Research methods</i> A double blind randomised controlled trial (RCT) was performed to investigate wear of REXPOL, a HXLPE, with conventional PE within the first five years after implantation using Röntgen Stereophotogrammetric Analysis (RSA). <i>Research results</i> The HXLPE (REXPOL) showed less wear in latero-medial direction. Significant wear rates of the conventional PE were seen in latero-medial and center-proximal direction and in volume and corrected volume, whereas the REXPOL did not show this outcome over time at all. <i>Research conclusions</i> Total 3D wear is less in THAs inserted with REXPOL (HXLPE) inlay than conventional PE inlay after five years. <i>Research perspectives</i> Further investigation of the wear on long-term and factors that might influence wear rates should be done, to confirm that the HXLPE (REXPOL) can reduce the risk of osteolysis and as</p>

		a result reduce revision rates in THA as well. In addition, investigation of the impact of wear reduction
The author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces	We applied the correct citation method throughout the whole manuscript.	<u>Changes made:</u> We applied the correct citation method throughout the whole manuscript.
Reviewer 1		
Materials and methods: One or two figures that show the RSA measurement of installed tantalum markers would make the readership to easily understand your study and would improve the quality of your work.	Thank you for this comment, indeed an additional picture helps to understand our study. We added an additional picture of the measurements after insertion of the tantalum markers. This figure was combined with the original Figure 1.	<u>Figure 1:</u> Changed to new figure '56927 - Figure 1' <u>Figure legend, changes in bold:</u> Model of RSA technique on right sided acetabular component after insertion of tantalum markers, by measurement of the penetration of the head in proximal-distal (A-axis), medial-lateral (B-axis) and anterior-posterior migration (C-axis) direction
Who measured the wear rates and functional scores?	As stated in the RSA outcomes section (Materials and Methods): line 177 wear was measured and analysis was done by the independent RSAcore, at the Department of Orthopedics at the LUMC, The Netherlands. The functional outcomes were done by a research nurse, involved in the standard follow-up routine care of our studies.	<u>Added in line 201:</u> 'The pain and activity of daily living (ADL) domains of the Hip Injury and Osteoarthritis Outcome Score (HOOS) were assessed pre-operatively, and after five years by a research nurse. '
In the 'Result', you don't have to enumerate the whole data. They are already all in the table. But you should describe the trend of data. You need to describe about the cup inclination, LLD, abductor offset, and plastic thickness.	Thank you for this important comment. We admit that the results section was an enumeration of the results instead of appointing which results were seen. Therefore, we made some changes to the manuscript. Regarding <u>cup inclination</u> , no measurements were done during follow-up. Cup inclination was not measured in our study, since our study design was not focused on	<u>Changes made in RESULT section (in bold):</u> A total of 51 consecutive patients were included in this study at baseline. Figure 2 shows a flow chart of all the patients during this study. Seven patients were excluded, and the remaining 44 patients were included in our analysis; 22 in the REXPOL and 22 in the Standard PE insert group. During follow-up five patients in the REXPOL group were lost to follow-up and three in the Standard PE group. The patient demographics and baseline characteristics of both groups

explaining why wear occurs. Moreover, all cups were placed within the normal range of inclination. If malposition would occur, this would have been stated in the article. Therefore, we stated that further research is needed, based on other designs, to find potential predictive factors for wear, such as inclination.

Regarding LLD and abductor offset, we stated in the Materials and Methods section, that we aimed the leg length and femoral offset to be identical to the contralateral side. If LLD >1 cm or there was a change in offset, we scored these outcomes as complications in our clinic. As mentioned in the manuscript, these complications did not occur in this study. Moreover, as explained above, we chose to not include both variables as outcomes, since our research questions was focused on comparing wear rates and not to determine potential factors predicting wear rates. Therefore, these outcomes would not have added value to our research question.

At last, plastic thickness is actually a derived value of all outcomes measured by our RSA analysis, like wear in directions and volumes, which is one of the principals of RSA. Measurement of the plastic thickness is subordinate to RSA when calculating wear of PE, as explained in our Methods sections. Therefore, we chose to not measure the plastic thickness on its own. Since thickness of the inlay is related to cup size, we tested if cup size differed between

where comparable and are shown in Table 2. In both groups no revisions were needed during follow-up.

RSA migration

The total wear of the inlay measured from baseline showed less wear in all directions in the REXPOL group, which was significant in the REXPOL group in latero-medial direction. All results of the total wear measured from baseline are shown in Table 3. Due to significant interaction between cup type and follow-up time, the wear pattern during follow-up of the REXPOL and Standard PE inlay were analysed separately. **These wear patterns over the years showed greater wear in all directions in the conventional PE group, which is visualized in the Figures 3 to 6. The corresponding wear rates over this time period in Table 4, showed that in all directions and volumes calculated, conventional PE had significant wear rates, whereas REXPOL did not show this outcome over time.** At the RSA photo's no signs of osteolysis were seen.

Functional outcomes

The functional questionnaires were measured at the time point of five years, to detect potential differences in functional outcomes. These results are shown in Table 5, **showing no significant differences.**

Added line 236 in Results section:

No significant differences were seen in cup sizes between both groups.

	<p>both groups. Initially this was stated in line 234-235 as that patient demographics and baseline characteristics were comparable between both groups. Since we share the opinion that this needs to be better clarified we added the line 236 as stated aside.</p>	
<p>Is there any difference in wear rate between bedding-in time and steady-state?</p>	<p>We thank you for this comment. During bedding-in time you would expect very low wear rates. Moreover, migration of the prosthesis can be seen during this period as well. However, our research question was focused on if change in wear would occur after five years. Therefore, we think that only visualization of wear over time by our figures was important, which might visualize the difference in wear between bedding-in and steady-state as well. Since this was not the focus of our study and the study protocol and follow-up time were not focused on determination of a difference in this, we did not mention this in our study.</p>	<p><u>No changes made</u></p>
<p>In the "Discussion", you need to shorten the content of line 296-326.</p>	<p>We thank you for this comment and feedback. We share the opinion that this section was too long and tried to shorten it. Since one of the greatest long-term risks of polyethylene wear is wear induced osteolysis, which can be seen or expected based on the 5-years outcomes, we think this concern should be discussed in this article as well. Since our research question was based on difference in wear between PE and HXLPE, the resulting possible outcome of (wear induced) osteolysis is therefore relevant for our research question.</p>	<p><u>We shortened the discussion section, especially on the lines 296-326 as mentioned.</u></p> <p>Discussion section is reduced with approximately 250 words.</p>
<p>The outcome of your study was evaluated at the time point of five</p>	<p>Our research question was to determine differences in wear at five years follow-up.</p>	<p><u>No changes made</u></p>

<p>years. Some insight you have found while performing the study should be provided to the readership. The meanings and caveats of your study, as compared with previous studies, should be described with logic.</p>	<p>Therefore, we chose to show our insight we found on wear during the study only by the graphs figured in the article. We think that further mention of our insights would not have an additional value, especially since the next follow-up time after 2 years was 5 years.</p>	
<p>This study is based on a well-designed double-blinded prospective randomized controlled trial and have compared the wear rates of HXLPE to conventional PE by means of RSA. However, pre-existing articles, including long-term follow-up studies, have already reported that highly cross-linked PE show less wear than conventional PE. Many studies have reported the wear rate on the HXLPE and convention PE by means of RSA. The difference in the study design between this study and previous RSA studies comparing HXLPE to conventional PE may not be significant, and it may be hard for this article to provide new information. Moreover, wear rates of conventional PE have been reported to be low during mid-term follow-up, and several in vivo studies have reported that the increase in long-term wear rates are causing more significant problems. Since the follow-up period of this study is only 5 years, clinical significance may be limited.</p>	<p>Thank you for your expertise on this subject. To our knowledge and after a comprehensive search of literature, we think that research focussed on wear, especially based on RSA, the most precise method to measure wear, is still limited. The study of Callary et al. 2015 (mentioned in our study), is a review of all RSA based studies of HXLPE. They stated that only 12 primary THA cohorts, comprising 260 THA's with 2-10years follow-up were published in literature so far, with only 5 studies showing mid-term follow-up of 5 to 7 years and 2 studies having a long-term 10 years follow-up of 10-years. The studies of Broomfield et al. (2017) and Teeter et al. (2018) are the only additional RSA studies with 10-years follow-up reported after this review, with 39 and 100 THA's respectively. All other long-term studies, like Lachiewicz et al. (2016), Steiger et al. (2018) and Hanna et al. (2016) did not use RSA. The abovementioned status of literature shows that more studies on both mid-term and long-term are needed to confirm the advantage of HXLPE. Since our study is, as you mention: 'a well-designed double-blinded prospective randomized controlled trial', the value for literature is clear and this</p>	<p><u>No changes made</u></p>

	<p>article is clinically significant. We do share your opinion that longer term studies are needed as well, as stated in our '<i>Implications for further research</i>' section.</p>	
Reviewer 2		
<p>In Line 128 " Previous RSA studies showed a high degree of sensitivity and accuracy of measurements of migration; relatively small patient groups would show statistically significant outcome" This statement needs citation.</p>	<p>Thank you for this comment, we added the citation.</p>	<p><u>Citation added:</u> Valstar et al. 2005</p>
<p>Sample size calculation should be more clearly expressed</p>	<p>We added some extra information to explain how the sample size was calculated. We would like to thank you for this comment.</p>	<p><u>Changes made:</u> Added: 'Based on this difference in wear of 0.18 mm, a SD of 0.21 and a power of 80%, a sample size of 21 patients was required in each group, to find a statistically significant difference at a 0.05 significance level.'</p>
<p>In line 181, functional results are reported. It is irrelevant to the title and aim of the study. Functional results should be removed or title/aim should be revised by including this results.</p>	<p>We share your opinion that functional outcomes were not the aim of our study. Therefore, we do chose that measurement of functional outcomes was important to state as a secondary outcome. In theory, differences could occur on clinical functioning, without substantial differences in wear. Since this situation could change our opinion about using a PE or HXLPE insert or to continue the study or not, we made the decision to mention the outcomes to check for a potential difference (as stated in line 338-343 Since this outcome would not change the aim of the study, we chose not to mention it in our title.</p>	<p><u>No changes made</u></p>
<p>In Line 193, "Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 25.0 (SPSS Inc. Chicago, IL)." 25.0 version the SPSS is from different company. SPSS version or company</p>	<p>Thank you for this comment, we corrected the Statistical analysis section.</p>	<p><u>Changes made:</u> Statistical analyses were performed with IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, New York, USA).</p>

name should be corrected.		
Discussion section is too long and should be shortened. Current study aimed to compare wear of two insert.	We thank you for this comment and feedback. We share the opinion that this section was too long and tried to shorten it.	<u>We shortened the discussion section</u> , especially on the lines 296-326 as mentioned. Discussion section is reduced with approximately 250 words.
Between Line 287-300, revision rates and osteolysis are discussed. Are they relevant to your research question?	We thank you for this comment and feedback. Since one of the greatest long-term risks of polyethylene wear is wear induced osteolysis, which can be seen or expected based on the 5-years outcomes, we think this concern should be discussed in this article as well. Since our research question was based on difference in wear between PE and HXLPE, the resulting possible outcome of (wear induced) osteolysis is therefore relevant for our research question.	<u>No changes made</u>
Number of references is 47, as current paper is research article (not the review article). I advise reducing the number of references.	We reduced the number of references to a total of 36 references.	<u>Changes made:</u> We reduced the number of references to a total of 36 references.
I thank authors for this valuable retrospective study.	As stated above, this is a double-blinded prospective randomized controlled trial, which is very important for the interpretation and value of this paper. Therefore, we wanted to emphasize this again.	<u>No changes made</u>