Author's response to reviews

Title: Histological, histomorphometric and microtomographic analyses of retrieval hip resurfacing arthroplasty failed at different times.

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Author's response to reviews: see over
Reviewer: Takuma Yamasaki

1) Retrieval femoral heads were analyzed and compared among 3 groups according to the period until the revision surgery. However, each group has only 3 specimens, and it might be difficult to perform statistical evaluations among these groups.

We agree with the reviewer that our study presented the limitation of the small number of cases but the primary objective of the study was not to define the pathophysiology of HR prosthesis failure, but to evaluate if these techniques might be applied in this field of research and give further insight into the failure mechanisms of these implants. Moreover, we agree that performing statistical evaluation with so few specimens might be a limitation. However, one way to resolve this limit is to perform analysis by using the exact test to compute probability. Bootstraps and Monte Carlo methods are the most commonly applied. We decided to reanalyze data by using non-parametric Kruskal-Wallis and Mann-Whitney tests followed by the Monte Carlo exact test to compare data. All results were updated according to this analysis (page 8, line 205-207 and page 10, line 240-247).

2) In group 3, I wonder whether the retrieval femoral heads assumed total necrosis or not. It should be mentioned that the retrieval femoral heads became total necrosis or bone atrophy with partial necrosis after stress shielding using histological findings.

Following the reviewer’s suggestions we have clarified in the manuscript that through the use of histology in each examined retrieval femoral heads of Group 3 a decrease in bone mass (bone atrophy) with partial necrosis was observed (page 9, line 231-232 and page 11 line 281-283). In addition, in Group 3 the reduction of bone mass was confirmed by histomorphometrical and microtomographical analysis in which a decrease BV/TV and Tb.N and an increase in Tb.Sp were seen.

3) In Figure 2, histological photographs with different magnification are shown. The histological findings should be presented with the same magnification.

We agree with reviewer’s observation and we have changed the resolution of figure 2c in order to have for each group a figure at 10x and one at 20x of resolution.

4) The author mentioned about blood supply to the femoral head and surgical approach. In this study, all patients were treated with postero-lateral approach. The failure rate due to bone necrosis (group 2 and group 3) was quite low (only 0.6%). It is not suitable to recommend anterior approach instead of posterior approach to reduce bone necrosis.

We agree with reviewer’s observation. We do not recommend using a blood supply-sparing approach, we hypothesize that these approach may improve implant survival in the long-term. In our series the failure rate due to bone necrosis was very low. Similar results are reported in the literature where different surgical approaches do not seem to influence implant survival (McBryde CW, Revell MP, Thomas AM, Treacy RB, Pynsent PB. The influence of surgical approach on outcome in Birmingham hip resurfacing. Clin Orthop Relat Res. 2008 Apr;466(4):920-6). Therefore we had modified the manuscript (page 13, line 325-329).
Furthermore, this study does not support the suggestion “necrosis increases quantitatively with time after surgery”.

Following the reviewer’s suggestions we have removed the affirmation “These results suggest that necrosis increases quantitatively with time after surgery” that was present only in the abstract.
Reviewer: Sokichi Maniwa

Minor Essential revisions

(General opinion)

This paper is very interesting and important because no studies have used histomorphometric and microtomographic evaluation to study the retrieved metal-on-metal hip resurfacing. But the advantage of your methodology (combination of 2D and 3D quantitative measurements) is not so clear. I would like you to exaggerate the superiority of your method over the other methods in the past.

Thank you very much for your comments. The main goal of this study was to examine the characteristics of bone quality and its microarchitecture in a serial of femoral head that failed at different experimental times by adopting quantitative histomorphometry and μCT in order to evaluate whether these 2D and 3D measurement techniques might be applied in this field of research and give further insight into the failure mechanisms of these implants. Following the reviewer’s suggestions we tried to make this point more comprehensible, at the end of the INTRODUCTION paragraph (page 4, line 90-95), at the beginning of the DISCUSSION (page 11, line 262-264) and in the CONCLUSION paragraph (page 14, line 352-356).

(Methods)

Authors divided the cases into 3 groups according to the time to fracture. Some authors divided the patients into 2 groups: the patients failed within one month and the patients failed after one month, for example (Steffen RT et al., 2010). Reasons for your classification should be mentioned in comparison with the other papers.

Our methodology, in which 2D and 3D measurement techniques were used, was applied to a small consecutive revision case series taking into account the time to revision because we wanted to assess whether these techniques might be applicable and useful for the evaluation of different bone microstructural changes at different failure times of HR prosthesis. We named our 3 groups as failure at less than 6 months (Group 1), failure between 6 months and 3 years (Group 2) and failure later than 3 years (Group 3). Gross fractures that occurred soon after surgery (Group 1), which presented a pattern involving the implant rim were classified as acute biomechanical fractures and may be related to the surgical technique leading to biomechanical changes in the femoral neck by the notch. The other two groups (Group 2 and Group 3) were defined as late fractures. These two groups were divided arbitrarily to highlight the possible presence of a phenomenon that progresses with time. We clarified this point in the paragraph METHODS, Patient Cohort (page 5, line 117-118) and DISCUSSION (page 11, line 267-269).

Page 5, line 111: I think that “Fractures were divided into three groups.”

We apologize for the mistake and we made the requested change (page 5, line 109).
More information about the existence of pseudotumor, ALVAL, and the extent of metallosis in each group should be expressed.

We had modified the manuscript and we made the requested change (page 5 line 118-123).

Were there any cases with malposition of the implant in retrieved specimen?

Yes there was a case of malposition. One patient of group 2 had a steep cup with an inclination angle of 67°. This was reported in Table 1, but now has been underlined in the text (page 5, line 122-123). Moreover, Table 1 reported also the presence/absence of the notching.

Page 6, line 156: Is Toluidine Blu correct?

We agree with reviewer’s observation and we corrected “Toluidine Blu” with “Toluidine Blue” (page 7, line 159).

(Discussion)

Page 12, line 308: If a vascular injury causes osteonecrosis in the central and bottom regions in group 1, the same finding also could be seen in the top region. But your study demonstrated less empty lacunae in the top region in group 1. I would like you to show the reason and further consideration. Page 13, line 319: Osteonecrosis started from the bottom in the specimen in groups 2 and 3. This finding is very interesting part of your study. I would like you to add more consideration from your observation or from the literature.

In our study we found that osteonecrosis of the femoral head seems to proceed from the bottom to the top. This controversial result might be explained by analyzing the surgical technique. During femoral head preparation the top region is always removed, thus eliminating the bone volume more subjected to osteonecrosis. Moreover, the residual blood supplied comes from the lateral femoral circumflex artery and a recent report (Zlotorowicz M 2012) shows two more possible sources of blood supply to the femoral head. These two vessels were identified as the anterior nutrient artery of the femoral neck which origins from the lateral femoral circumflex artery and the inferior branch of the deep branch of the superior gluteal artery (page 13, line 317-324). The complexity and inter-individual variability of the vascularization of proximal femur should be considered when interpreting our results. In addition, in the literature there are no works in which osteonecrosis progression, in different region of interest, of the femoral head was examined.

(Conclusion)

Purpose of your study was to evaluate the characteristics of bone quality and its microarchitecture in the retrieved specimen after hip resurfacing. I would like you to remark the answer to your original purpose in Conclusions.
As recommended by the reviewer we remarked on the original purpose of the study in the conclusion paragraph (page 14, line 352-356).

(References)

#19: “J of Microscopy” # “J Microscopy”

We corrected reference 19.

(Figures)

Are data expressed correctly as mean ± SD in figures 4, 5, and 6?

We apologize for the mistake, but data are singularly reported as dot plot.