Author's response to reviews

Title: Implant Based Differences in Adverse Local Tissue Reaction in Failed Total Hip Arthroplasties: A Morphological and Immunohistochemical Study

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Author's response to reviews: see over
Dr. Giorgio Perino  
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Dear Editorial Board,

I have enclosed a revision of the manuscript entitled: "Implant Based Differences in Adverse Local Tissue Reaction in Failed Total Hip Arthroplasties: a Morphological and Immunohistochemical Study" which has been edited based on the reviewers’ suggestions. Changes in the text have been highlighted, responses to the reviewers’ questions have been placed below, and the original reviewer comments were placed in italics. All listed authors and acknowledged contributors have read and approved the final version of this manuscript. There are no conflicts of interest related to this manuscript.

We appreciate the opportunity to provide these revisions, and we believe that all reviewers’ concerns have been thoroughly addressed. We hope that this manuscript will add to the literature on the understanding of the occurrence and natural history of adverse local tissue reactions and generate hypotheses to stimulate further research on the subject. Thank you for your consideration of this revised manuscript. Please address all correspondence concerning this manuscript to me at the Hospital for Special Surgery and feel free to correspond with me by e-mail at perinog@hss.edu.

Sincerely,

Giorgio Perino, MD

Reviewer 2

I would recommend to diminish the strong statements about the novelty of ALTR as “a newly identified failure mode of THA”. This mode of failure is old, it is known for a long time, from the first studies of Willert and co-workers to Konttinen’s and Goodman’s studies (and several others). I mean the foreign body response in terms of findings of mixed inflammatory cell infiltrate, extensive soft-tissue necrosis, and vascular/perivascular changes. Of course, the novelty is clear and lies in approach, details, rules, overall interpretation strategy … great, but I strongly recommend respecting the contribution of other researchers. Therefore, it would be better to build the story on the history and what is known to date. The authors can involve the review published recently in Acta Biomater (Gallo et al, 2014), which calls for further progress in the field especially in terms of reducing the heterogeneity related to implant characteristics (incl. innovations) etc.
We appreciate the comments. We have improved the text to highlight the recent developments in ALTR, particularly with regards to the second generation MoM implants, and referred to the review by Gallo et al. for a comprehensive analysis and discussion of the topic as suggested. We have removed statements about ALTR being a “newly defined” mode of failure. The text has been modified as follows:

Line 90: This has resulted in increased MoM implant failures due to a distinct type of cellular/tissue reaction, originally reported as aseptic lymphocyte dominated vasculitis-associated lesions (ALVAL), now collectively referred in the literature as adverse local tissue reactions (ALTR) or adverse reaction to metallic debris (ARMD) [4-12].

Line 94: Previous histological analyses of retrieved periprosthetic tissue have shown evidence of corrosion products, metallic debris generated by abrasion and/or surface fatigue, extensive soft tissue necrosis, combined macrophagic and lymphocytic infiltrate with variable plasmacytic and eosinophilic components, and vascular wall changes [5,13-19].

Line 97: A comprehensive review describing features of periprosthetic inflammation to wear debris has been addressed in a recent review article by Gallo et al. [20].

Line 100: The constellation of pathologic findings observed in response to MoM implants was encompassed under the acronym ALVAL by Willert et al. to illustrate the unique lymphocytic component and probable vascular changes not seen in other typical modes of THA failure such as osteolysis or infection [14].

Line 443: Our observations are similar to previous studies that have illustrated the distinct histological aspects of the reaction, predominantly in MoM hip resurfacing implants or in mixed resurfacing and THA implants [10,13-19].

Line 458: This has been described frequently in ALTR from previous studies and represented the most common pattern we observed [13-18].

Line 472: Corroborative evidence of our interpretation was the presence of benign lymphocytic aggregates in the bone marrow associated with particle-laden macrophages as previously reported in hip resurfacing implants [15,39].

Line 489: Our data indicate these materials represent corrosion products from the taper junctions at the head-neck and neck-stem, which is consistent with previous studies [5,11,34].

2) Citation 27: correctly should be 1977 instead of 1997.

Line 684: This has been corrected from 1997 to 1977.
Editorial Comments

*Please include in your manuscript the full name of the ethics committee that approved your study (including the full name of the university if appropriate)*

We have added the full name of the ethical committee that approved this study. It was approved by the Institutional Review Board, which provides ethical approval for all clinical studies at the hospital. Line 133 now reads: Ethical committee approval was obtained prior to this study (Institutional Review Board, Hospital for Special Surgery, Protocol Number 26085).