Author’s response to reviews

Title: Fetal Cardiac Function at Intrauterine Transfusion Assessed by Automated Analysis of Color Tissue Doppler Recordings

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Response to reviewers’ comments
“Fetal Cardiac Function at Intrauterine Transfusion Assessed by Automated Analysis of Color Tissue Doppler Recordings“
Herling et al.

Reviewer #1:
In this study the authors sought to assess the changes in fetal myocardial function by IUT using automated analysis of cine-loops of the fetal heart obtained by color tissue Doppler imaging. The study is interesting however many comments have to be addressed.

The design of the study is well described however the results are confusing.

- First of all the sample of the study, the authors reported 70 study then, 68 pre and post IUT and in another paragraph 136 ultrasound examinations. A consort diagram could be useful and the description for the included studies should be described.

Thank you for the valuable comment. A consort diagram/flowchart (new figure 2) have been provided to clarify participant flow in the included examinations.
Could the authors report the main results also for the patient and not only for US examinations may be before and after the first IUT?

To improve this, we have now presented data on the degree of anemia in the patients that had first time transfusions and available ultrasound examination and how their myocardial velocities changed with transfusion (row 180-185).

In the table 1, 29% didn't have anemia, please explain

The non-invasive diagnosis of fetal anemia based on increased peak systolic velocity of middle cerebral artery needs to be verified by taking a blood sample from a fetal blood vessel (usually the umbilical vein). Therefore, it can occur that there is no actual anemia yet at the time of sampling (even though the hemoglobin value is decreasing the threshold level for anemia has not been reached). However, as the majority of fetuses have an on-going pathological process leading to destruction of the red blood cells and repeated blood sampling is associated with risk of fetal loss, we generally transfuse a smaller amount of blood to prolong the time until the next invasive procedure.

The authors reported Myocardial velocities before all 70 IUTs are presented in Table 2. Am, Sm and Em were all significantly increased in the LV and IVS, Table 2 in not clear: could the authors report the absolute values and the z score.

We agree with your comment and we have according to your suggestion added absolute values to the myocardial velocities in table 2.

- The authors reported : In the 161 sub-group of 12 first IUT fetuses, pre-transfusion z-scores of LV Em (1.03, 95% CI -0.12-1.95) how did you divide by groups . moreover 1.03 is a normal z-score could the authors explain why they reported that tended to be higher than normal ..,

Thank you very much for pointing out this error. We fully agree with you that a z-score of 1.03 is normal, and we have deleted the sentence stating that the z-score tended to be higher than normal.

Comparison of myocardial velocities before and after IUT could the authors report a table comparison with median IQ, or mean e DS, and the results.

We have added a table showing the significant differences between myocardial velocities before and after IUT including absolute velocities, z-scores, interquartile ranges.

All changes to the manuscript have been high-lighted in yellow to facilitate reading.