Author's response to reviews

Title: Non-invasive Monitoring of Tissue Oxygenation During Laparoscopic Donor Nephrectomy

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Author's response to reviews: see over
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Dear Dr. Norton,

Attached is a revised copy of our manuscript (MS 1815448695165726) entitled “Non-invasive Monitoring of Tissue Oxygenation During Laparoscopic Donor Nephrectomy.” The authors would first like to thank the reviewers for the time taken to carefully consider this manuscript. We found the reviewers comments to be helpful and hope that the incorporation of their suggestions improves the quality of the manuscript.

Regarding Dr. Foster’s comments:

We appreciate Dr. Foster’s generous review.

Regarding Dr. Luke’s comments:

First, we would like to thank Dr. Luke for his thoughtful review. We believe that addressing Dr. Luke’s comments only helped to strengthen the quality of our manuscript. First we discuss the major comments made by Dr. Luke.

In the first paragraph of the Results section (Spectroscopic Evidence – Animal Model), we have added text explaining the rationale behind our chosen animal model.

"...porcine model. We chose the open porcine model so that pneumoperitoneum would not be a variable when considering the effect of blood oxygenation on the mean ROI values calculated from the 3-CCD camera. While the equipment employed in this study is used in an open fashion, it is designed for laparoscopic incorporation. An obvious model for altered tissue oxygenation would have been clamping the renal hilum; however, in our hands, it has been extremely difficult to partially clamp the hilum in a controlled fashion (progressive hilar clamping) or to allow the kidney to reperfuse in a controlled and partial manner. Without being able to control the tissue oxygenation or deoxygenation, we could not reliably collect enough data points for a clear correlation. Thus, the decreasing FiO₂ model was chosen for our validation experiment. This model directly enabled correlation of oxygen delivery with 3-CCD mean ROI values."

We have added a sixth paragraph to the Results section, where we briefly discuss our positive control with laparoscopic partial nephrectomies.
While not presented in this manuscript, we have also examined laparoscopic partial nephrectomies, where complete hilar clamping or renal arterial clamping is performed, and so, we have explored variation in oxygenation as a direct result of surgically-induced vasoconstriction. We do in fact see the mean ROI values decrease after clamping and then return to baseline ROI values after reperfusion (p ≤ 0.05 in all cases).

These results are currently submitted for publication in another manuscript. In these particular cases (n=10), we have calculated the mean ROI values for all kidneys prior to clamping (normal), during hilar clamping (ischemic), and after removal of the hilar clamps (reperfusion).

The reviewer also inquired about the impact of a bloody laparoscopic field on the ROI values. This technique is restricted to surface measurements of oxygenation, as visible light can penetrate only millimeters into the tissue being monitored. As such, only if the organ is exposed can measurements be made. This does not, however, require that all of the organ be exposed, but just enough to make calculations on three ROIs. If the entire field is blood-filled, some of the blood must be suctioned before measurements can be made. A comment regarding this has been added to the last paragraph of the discussion.

…”Similarly, bloody operating fields are only problematic if the entire region of interest is obscured; several small, exposed regions are sufficient for calculating mean ROI values…”

Finally, the reviewer comments that, “It is not clear whether organs with decreased ROI had any differences in immediate graft function vs. those with higher ROI.” The authors would like to highlight that this study only compares beginning and end ROI values for individual patients, this study does not compare the ROI values of multiple patients. Reasons for ROI value comparison of only individual patients include variability in abdominal illumination from case to case and variability in duration of pneumoperitoneum from case to case. The most important thing is that all of these patients experienced immediate graft function (like most laparoscopic donors), so no assessment of the relationship between immediate graft function and the mean ROI intensity value can be made. A comment regarding this is made at the end of the fifth paragraph in the Results section.

…”Note, intrapatient comparison of mean ROI values is not performed due to variability in abdominal illumination from case to case and variability in duration of pneumoperitoneum from case to case.

Next, we would like to address Dr. Luke’s minor comments.

1. The ROI abbreviation has been identified in the abstract as “region of interest”.

2. A sentence and reference regarding the underlying mechanism of 3-CCD enhancement has been added to page 6 – “The difference has been directly correlated with the spectral response of hemoglobin in both the blue and red regions of the visible spectrum.[6]”

3. At the end of the first paragraph in the Background section, we discuss the clinical utility of intra-operative tissue oxygenation determination.
"...The ability to intraoperatively monitor renal parenchymal oxygenation would be useful in a number of clinical situations in which prompt resolution may have a dramatic effect. One such example is encountered when during the course of the operation the blood supply to the organ becomes impaired by the technical maneuvers done during dissection (i.e., approaching the vessels from the posterior aspect). Prompt recognition of decreased oxygenation would allow for repositioning of the kidney and re-establishment of blood flow. Other examples include the determination of secondary renal arteries and the establishment of a baseline acceptable pneumoperitoneum, potentially useful in older donors."

4. The conclusion section has been appropriately shortened.

We hope that you will find our revised manuscript suitable for publication in *BMC Surgery*. Thank you for your consideration. Please do not hesitate to contact me with any questions.

Sincerely,

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