

Dear Reviewers,

Thank you for your consideration and review of our article. We were able to accommodate all reviewer requests for modifications within the text and the figures. We look forward to your subsequent review of this revised manuscript for publication.

Below is a summary of changes according to your review.

Sincerely,

Daniel Skubleny

Reviewer 1:

1. Reformulated sentence
2. Revised introduction and added more general data and detail.
3. Clarified role of E-cadherin in relation to treatment response.
4. Add term neoadjuvant chemotherapy and treatment response to keywords.
5. Added appropriate reference
6. Corrected the sentence by removing extra NIR portion
7. Reformulated sentence per recommendation

Reviewer 2:

1. Figure legend was edited to include more detail and clarity. Meaning of solid and dotted lines stated.
2. Reordered the figures according to text appearance

Reviewer 3:

No comments

Reviewer 4:

1. Core tip reorganized
2. Added additional detail to introduction
3. Added flow chart figure
4. Added how to define and obtain normal tissues mentioned clearly.
5. The observers and magnifications are stated. A slide scanner was used at 20x magnification. The images were extracted at 10x using QuPath and scale bars are placed on the top left image.
6. Potential disadvantages to neoadjuvant chemo placed in the introduction. In addition to disadvantages related to morbidity/mortality we also note that neoadjuvant chemo may not be effect in microsatellite high tumour.

7. Edited and reworked discussion. Increased focus on immune microenvironment and added additional detail regarding the role/mechanism of CD4 and CD8 cells in anti-tumour response. Particular emphasis is placed on the essential role of CD4 cells.
8. Figure 1 images replaced and arrows added to more accurately represent the 25<sup>th</sup> and 75<sup>th</sup> percentile.