Conclusion: Minor revision
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)

1. 2. 3. The Title, Abstract and Key words, cover the main aspects of the work, it spark interest to the right audience in this domain

4. Background: The given background in the Introduction easy to follow. It cite the recent appropriate papers. It provide a hypothesis or aim of the study well located in relation to the state of the art of existing works

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? The methods section does not provide enough detail; so that the approach used is clear to readers, the authors are invited to provide more details on the elements used in the image analysis and reconstruction algorithm. They do not give enough information on the effects of tissue interfaces on the waves or on the tarnsfert matrix used (if applicable) in order to define the parameters of the optical wave solicited in each layer.

[Response]

Thanks to the reviewer for their kind suggestions. We have added more details in the section of methods (LIGHT PROPAGATION MODEL-BASED OMT ALGORITHM) to make this article clearer. As to each layer of the neural network (in the section of MACHINE LEARNING-BASED OMT ALGORITHM), the network is trained to solve the RTE directly, and the effects of tissue interfaces on the waves cannot be defined in each layer.

6. 7. Results and Discussion: Effectively, the authors discuss a flexible approach giving a 3D optical image in depth with an optimized calculation time (real time). The Discussion address the main findings, and give proper recognition and a real contribution to similar work in this field

8 Illustrations and tables. The Results refer to the figures in a logical order. On the other hand, Figures 3 and 4 have to be redone with an overall revision of the legends and scales.

[Response]

Thanks and done.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Not applicable

10 Units. Does the manuscript meet the requirements of use of SI units? Seriously missing in the text and on the axes of the images (figures 2 & 3 for example)

[Response]

Thanks to the reviewer for their suggestions. Based on these helpful suggestions, we have carefully revised the paper. It is worth noting that there are not axes in some images on figures 2 & 3, because the axes are not given in the original picture.

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes. In genetral, the authors discuss in this paper an imaging modality based on the optical molecular tomography (OMT) in the near-infrared light, to reconstruct the three-dimensional information in biological tissue. However, I invite the authors to take note of the remarks expressed above in order to improve the overall content of the article and

which in no way affects the quality of this work.

[Response]

Thanks for the helpful suggestions.

Conclusion: Minor revision

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

This is a generally well-written review on machine learning and OMT. The topic is of very high interest. It can be an advanced method for in vivo tissue imaging and potentially can change biological and medical sciences. This paper can be improved in following points. There are many environmental, dietary, and other factors that influence the microbiome, immune system, and pathogenic mechanisms. The authors should discuss molecular changes induced by these factors that can be detected by OMT. In these contexts, as a future direction, research on dietary / lifestyle factors, microbiome, immunity, and molecular tissue biomarkers is needed. The authors should discuss molecular pathological epidemiology (MPE), which can pathologically, epidemiologically investigate those factors in relation to molecular pathologies, immunity, and clinical outcomes. MPE's strengths and challenges have been discussed in Gut 2018, Annu Rev Pathol 2019, etc. I believe MPE research can be a promising direction and OMT can make a big role..

[Response]

Thanks for this kind comment. We have added additional content about the application of OMT on MPE research in the section of PERSPECTIVES.