Author’s response to reviews

Title: Blood Test Shows High Accuracy in Detecting Stage I Non-Small Cell Lung Cancer.

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Author’s response to reviews:

February 8, 2020

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Rossano Lattanzio
Editor, BMC Cancer
https://bmccancer.biomedcentral.com/

Dear Dr. Rossano Lattanzio,

Enclosed, please find a revised manuscript (BCAN-D-19-03455R2) entitled "Blood Test Shows High Accuracy in Detecting Stage I Non-Small Cell Lung Cancer" by Cherylle Goebel, Christopher L. Louden, Robert Mckenna Jr., Osita Onugha, Andrew Wachtel, and Thomas Long.

We are honored that you have considered our publication to be potentially accepted. As you have indicated in your email dated February 2, 2020, I am submitting this revised manuscript for further review. Due date of the revised submission is on February 8, 2020. The comments from the BMC Editorial Office are very much appreciated by the authors. The Editor comments are addressed below.

Comment 1: Please remove any files from the file inventory that you do not wish to see published.

Reply: Removed Supplementary Figure 2 from attachment.
Comment 2: Please include a Conclusions heading for the Conclusions section.

Reply: The heading “Conclusions” has been added to the Conclusions Section, Line 8-9, Page 15.

Comment 3: Please include the full name of the ethics committee (and the institute to which it belongs) that approved the study in the "Ethics Approval and Consent to Participate" subsection of the Declarations.

Comment 4: For all research involving human subjects, informed consent to participate in the study should be obtained from participants (or their parent or guardian in the case of children under 16) and a statement to this effect should appear in the ‘Ethics approval and consent to participate’ section of the Declarations including whether the consent was written. When reporting on such studies, individual patient data should not be made available unless consent for publication has also been obtained. If the need for informed consent has been waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this with details, including the name of the Board or a reference to the relevant legislation in the ‘Ethics approval and consent to participate’ section of the Declarations.

Comment 5: The 'Consent for publication' section covers manuscripts that contain any individual person’s data in any form (including individual details, images or videos), for which consent to publish must be obtained from that person, or in the case of children, their parent or legal guardian. If your manuscript does not contain any individual person’s data, please state “Not applicable” in this section.

Reply to Comments 3-5: The Declarations Section, Line 7-11, Page 17 has been corrected to:
Ethics approval and consent to participate: All samples were collected through an IRB approved protocol (e.g., Protocol #AST-FPB-003, Western IRB) or a signed Waiver of Consent form. Individuals under the age of 18 or those who cannot consent for themselves were not included in the study. Our manuscript does not contain any individual person’s data such as individual details, images or videos. All samples were collected in the United States between 2013-2015.

Reply to Comments 3-5: The Sample Collection and Handling, Line 29-35, Page 8 has been updated to:
All samples were collected through an IRB approved protocol (e.g., Protocol #AST-FPB-003, Western IRB) or a signed Waiver of Consent form. Individuals under the age of 18 or those who cannot consent for themselves were not included in the study. Samples were collected in the United States between 2013-2015.

Additional Reply to Comments 3-5 for the Editor: The blood banks noted that they be using several sites using the same protocol. Many of these sites use their own IRB, so there is no single entity that approves the protocol. If the collection site IRB is used then they cannot release the name for contractual reasons. If the site does not have an IRB, then they use Western IRB (WIRB), 1019 39th Avenue SE Suite 120, Puyallup, WA 98374-2115.

Waivers of Consent are commonly issued if a facility determines they no longer need to retain clinical samples and they want to release them for research use. Due to the length of time elapsed since the clinical specimen was obtained and the minimal risk to the subject (e.g. these specimens were previously removed for clinical reasons), the IRB waives the requirement to obtain consent from the subject. This is a very common reason for issuing a waiver of consent. As with protocol approvals, the
IRB reviewing the waiver request is generally associated with the collection facility, but may also be performed by WIRB. BioIVT (Bioreclamation, Asterand, etc.) complies with US federal regulation 45 CFR Part 46.116 (i) for biospecimens obtained under a waiver of consent.

Comment 6: Please provide specific Authors' contributions using unique initials for all of the authors in an Authors' contributions section

Reply: The Declarations Section, Line 42-48, Page 17 has been revised to:
Authors’ Contributions: C.G. designed the study and performed result analysis. C.L.L. provided statistical analysis and algorithm development. C.G. wrote the initial draft of the manuscript and provided Table 1 and 2, Supplementary Figure 1, and Figure 1; C.L.L. provided the Tables 3-4, Figure 2, and Supplementary Table 1; C.L.L. provided content for machine learning and algorithm-related topics and reconfirmed all statistical results reported on the manuscript; R.M., O.O., A.W., and T.L. reviewed the manuscript and contributed in the Background and Conclusions sections.

Comment 7: If you wish to acknowledge someone by their full name in the Acknowledgements, please ensure you have obtained permission from them to do so.

Reply: Attached are signed permission from Nancy Lim and Andreas Goebel.

Comment 8: Please note that it is the responsibility of the author(s) to obtain permission from the copyright holder to reproduce figures or tables that have previously been published elsewhere. Do you require copyright permission to reproduce any of the figures? Please also include some clarification in the relevant legends as to any software used in the generation of the figures, including version number.

Reply: No copyright permission is required. All Tables were generated using Excel, Word from Microsoft Office Professional Plus 2019 and R Version 3.4.4. All images were purchased from adobe or created using PowerPoint.
Table 1 and Figure 1 was generated using Word.
Table 2 was generated using a PIVOT table in Excel.
Table 3, Table 4, Supplementary Table 1, and Figure 2 were generated using R Version 3.4.4. Supplementary Figure 1 was generated using PowerPoint, purchased Adobe images which were modified by C.G., and Word.

The following text: “Table was generated using R Version 3.4.4.” was added to:
Table 3, Line 47-48, Page 26
Table 4, Line 29-30, Page 28
Supplementary Table 1, Line 31, Page 30

The following text: “Figures were generated using R Version 3.4.4.” was added to: Figure 2, Line 57, Page 31

The following text was added to Algorithm and Statistical Analysis, Line 48-49, Page 9: Excel and R Version 3.4.4 were used for data analysis.

Comment 9: At this stage, please upload your proofread manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethrough or text in different colours.
All relevant tables and figures should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Should you wish to respond to these revision requests, please include the information in the designated input box only.

Reply: Attached is a final clean version of the manuscript. To the best of our knowledge, the revised manuscript conforms to the journal style found in the Submission Guidelines on the journal homepage. All Tables and Figures are final clean versions and uploaded as separate files.

A submission agreement from each author is also attached.

Please let me know if I can provide further information to address the Reviewer’s comments. Thank you for your consideration and time. I look forward to your response.

Respectfully,

Cherylle Goebel