

## Peer Review File

Article information: <http://dx.doi.org/10.21037/shc-21-1>.

### Review A:

Comment 1: This is an interesting manuscript documenting important information regarding operative characteristics of core needle biopsies. The authors could improve their submission by:

1. Giving more information regarding how they performed their meta analysis.
2. The authors should clarify that their statistical analysis/data met the requirements of the Cochran protocol.

Reply 1: Thank you very much for the comments.

In contrast to meta-analysis, we authored a narrative review which does not answer a specific research question by statistical analysis but rather discusses the topic from a theoretical point of view. Therefore, narrative reviews do not necessarily list the methodological approaches as we did not perform statistical analysis. For this review, we conducted a detailed literature search using PubMed for articles on core needle biopsy, lung cancer classification, morphologic subtypes of lung cancer, biomarkers, tumor heterogeneity and genetics of lung cancer.

We added a Methods paragraph in the revised manuscript describing the PubMed literature search on page 5, lines 100-104.

### Review B:

Comment 1: I noticed many medically and grammatically inappropriate expression. First, in the lung oncology field, nodule and tumor implies masses smaller than 3cm and 3cm or larger, respectively.

The title, therefore, should be changed to the revised one if the authors included the lung mass 3cm or larger. Authors should revise the term “nodule” in the manuscript to proper expression. Needless to say, the expression “ tumor nodule” in the manuscript should be changed.

Reply 1: Thank you very much for the comments and highlighting these important issues.

We agree, it is crucial to use the correct terminology for lung nodules and tumors and define the difference. We have revised our manuscript accordingly and changed the title using the more comprising term “lung cancer” instead of “lung nodules”.

Furthermore, the distinction of lung nodule and lung tumor by the size of 3cm has been added in the abstract; page 2, lines 30-31. Additionally, the definition of lung nodule and tumor has been integrated in the introduction section on page 4, lines 79-81. In addition, reference 14 has been added on page 4, line 81. This publication provides a glossary of terms for thoracic imaging.

The terms nodule and tumor have now been discriminated throughout the revised manuscript. The changes are highlighted throughout the manuscript with yellow color.

The misleading expression "tumor nodule" has been changed to "lung nodule or tumor" on page 6, line 145 and page 7, line 167.

Comment 2: In addition, the expression of "biopsy sections and resections" is inappropriate. Biopsy sections and resections generally imply the biopsied tissue and the behavior of resection, respectively.

The expression of "the primary tumor and metastases" also implies the tissue and action of metastasis, respectively.

"Biopsies and resection specimens" is the same.

Reply 2: Thank you for pointing out these differences. The expression "biopsy section" has not been used in the manuscript. However, we have revised the manuscript to improve the accuracy of terminology and to avoid inappropriate expressions and potential misunderstanding. We have highlighted all changes in the second revision of the manuscript with yellow color. We use the terms "biopsy specimen", "surgical specimen" and "surgical resection specimen" in the revised manuscript.

Furthermore, we have slightly changed the sentence of page 12, lines 277- 278, to "... the primary tumor and **their** metastasis."

Comment 3: "Mattson et al. reported also" and "Vignot et al. observed also" should be described as "Mattson et al. also reported"and "Vignot et al. also observed".

Reply 3: We changed the sentences according to the comment on page 11, line 263 and page 12, line 280.

Comment 4: The expression "punctured part of the tumor" does not imply the tumor location in the lung but the puncture site of the tumor such as tumor center or tumor edge.

Reply 4: We added on page 7, line 155 "(central or peripheral areas within the tumor)" for clarification.

Comment 5: Figure 1: There are no scale bars in the figures. solid (e)→and solid (e)?

Reply 5: The scale bars have been present in the Figure and the scale described in the figure legend. However, the scale bars were too small and therefore easily overlooked. We have now increased the thickness of the bars to enhance their visibility.

We are sorry, because we do not understand the comment " solid (e)→and solid (e)?"

Comment 6: Finally many sentences should be revised for readers to correctly understand the meanings. Lines 30-1, 35-6, 72-6, 182-4,

Reply 6: Unfortunately, we are not able to identify these lines for sure. Perhaps the reviewer received a manuscript version with line numberings different from our submitted manuscript? We would need help for the identification of these lines, e.g. by giving a part of the text suggested for improvement.

Nevertheless, we have tried to improve the clarity of sentences on page 3-4, lines 73-75 and page 8, lines 191-193 in the revised manuscript.