Peer Review File

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Reviewer A

1. Methods: Inclusion criteria should be added: age of patients, dimensions of the lung nodules, histology (all the histologies? Only primary lung tumors? Also metastasis?)
→Data were added in lines 150-155. The contents of Table 1 were also updated.

2. Methods: It could be interesting to have more info about the baseline characteristics of the patients, since it could be possible that some comorbidities (COPD, emphysema etc) could impact on the accordance/discordance of the preoperative and intraoperative images.
→Comorbidities are listed in Table 1. It is possible that comorbidities affect the 3D images, but the small number of comorbidities made statistical examination difficult.

3. Introduction: a more broad overview of the existing experiences on the image-assisted systems should be given, also considering the already published papers on this topic (e.g. Wu Z, Huang Z, Qin Y, Jiao W. Progress in three-dimensional computed tomography reconstruction in anatomic pulmonary segmentectomy. Thorac Cancer. 2022 Jul;13(13):1881-1887. doi: 10.1111/1759-7714.14443.)
→Thank you for your suggestions. We have added several references that mention various image support systems, including the specified papers (7, 10-13, 16).

4. Paragraph 2.2: it would be interesting to get more details about the creation of the 3D model for segmentectomy, also with the aim of making it more reproducible. Moreover, it would be interesting to know more about the time used for 3D image processing.
→In this study, we decided to align the images based on the position of the ribs so that the images could be compared as accurately and reproducibly as possible; this is described in lines a-b of Method. We also noted the time required to create the 3D images, which can be done in about 5 minutes. We believe this is another advantage of the deflation simulation algorithm.

5. The delineation of the segments was based on the direction of the pulmonary arteries. An article by Tokuno (Tokuno J, Chen-Yoshikawa TF, Nakao M, Matsuda T, Date H. Resection Process Map: A novel dynamic simulation system for pulmonary resection. J Thorac Cardiovasc Surg. 2020 Mar;159(3):1130-1138. doi: 10.1016/j.jtcvs.2019.07.136)

showed an accuracy of the virtual dynamic images to identify all the vascular branches, on 3D reconstruction by the SYNAPSE VINCENT of the 98.6%. In your experience, Intersegmental line concordance could not be obtained in some of the patients who underwent lower lobe S6 segmentectomy, and comparison of the 3D image and intraoperative images showed that the function of the deflation system to deflate lungs was not sufficient in the lower lobe. Did you find any problems of the system in identifying the vascular branches? Did you match these findings? Those patients had emphysema or other comorbidities which could explain this discordance? Why do you think the reconstructions of lower lobes are less accurate? It could be interesting to add something about the percentage of accuracy in identifying all the vascular branches, on 3D reconstruction by the SYNAPSE VINCENT and to match them with the accordance/discordance of the predicted intersegmental planes.

→There was no problem in detecting blood vessels or constructing 3D images, and the deflation algorithm was determined by analyzing CT data from human pneumothorax lungs and cone beam CT data from intraoperative lungs, but the accuracy may have been insufficient due to the insufficient number of CT images used as samples. Discussion was updated.

Reviewer B

Thank you for asking me to review this paper, interesting as it is innovative. The subject matter is relevant, as more and more lung segmentation studies are being performed using softwares, prior to performing anatomical segmentectomies, but in my opinion there are some critical issues.

I think it would be necessary to describe the algorithm in more detail, indicating the variables that are taken into consideration, as we know that the lung can desufflate differently from one patient to another, depending on the air trapping that may be related to the quality of the lung.

My main concern is about the very small sample size of this retrospective study.

Authors do not define parameters used to define partial agreement versus disagreement; the figures do not make this clear.

Finally, the discussion is poor, it should be expanded by describing the techniques for identifying the intersegmental plane, reporting the results described in the literature.

In conclusion, I believe major revisions are needed to make the paper acceptable for publication.

→Thank you for your comments on this paper. As you mentioned, we believe that the degree of lung collapse is influenced by pre-existing conditions such as emphysema or interstitial pneumonia. Our ultimate goal is to create a deflation system that includes such conditions in the algorithm, but at the time of this report, the algorithm is being constructed using lung samples from pneumothorax patients. At the time of this report, the algorithm is being developed using a sample lung from a pneumothorax patient. In the future, we will train the algorithm on many images of collapsed lungs, accumulate case examples, and aim to develop more accurate 3D images.

We have tried to quantitatively evaluate the degree of agreement between the intraoperative movie and the 3D image as much as possible. In order to compare the three-dimensional structure of the lungs with the two-dimensional images, we aligned the images based on the ribs to avoid angle deviation as much as possible. This was the limitation of this paper because it is inevitable that the evaluation is subjective to some extent. If the positioning part could also be done mechanically, image comparisons would be more quantitative and reproducible, but a new algorithm needs to be developed.

The Discussion section has been expanded by adding references showing existing techniques to delineate intersegmental lines.

Reviewer C

1. Throughout the whole article (18 times to be exact), it is called a novel deflation system. This insinuates that the ‘system’ deflates the lung, but it is a simulation of the deflation of a lung based on CT-images. I would propose you call it a ‘lung deflation simulation algorithm’ or an ‘algorithm that simulates lung deflation’ - and states the intersegmental lines of course, the most important part.

→The name of the system has been changed to 'the lung deflation simulation algorithm'.

2. The videos are cool, but they lack resolution and it does not show that is actually performed by the algorithm. As this is also missing in the methods, I have no idea how the algorithm could work. It does not become clear from the article what SYNAPSE VINCENT is or does and therefore the complete work cannot be put into perspective or perform any kind of comparison to similar work in the past or future.

→This deflation algorithm was established by analyzing CT data of human pneumothorax lungs and cone beam CT data of intraoperative lungs. The details of the algorithm are given in lines 133-138.

3. The added value of the system and how it could replace the current method is unclear.
→This image support system is valuable in that it constricts the 3D image of the lungs and allows the anatomy to be understood under conditions that more closely resemble the actual surgical field, as described in detail in lines 193-202.

Specific lines:
Line 92: invasive drug injection is somewhat overdone in my opinion. Surgery is invasive, an injection during surgery does not make it more or less invasive.
→The word 'invasive' has been removed.

Line 103-104: This is results.
→We have moved the description you mentioned to Results.

Line 108-109: How many patients were excluded based on this criteria? How well did the algorithm work in these cases?
→There were 28 patients who underwent Robot-assisted segmentectomy during the study period. Six of these patients did not have contrast-enhanced CT, and six were excluded because the intersegmental line was not clearly delineated by indocyanine green. Especially in cases where contrast-enhanced CT was not taken, 3D images were not created because it would be difficult to delineate the pulmonary vessels. Details are given in lines 150-153.

Line 112: How much time between scan and surgery? Was the CT-scan made specifically for this research (not all patients undergo contrast CT, at least not in our center)? If yes, what is to say about the added radiation?
→We routinely perform contrast CT imaging within approximately one month of the date of surgery. No patient has had contrast CT imaging just for research purposes. Details are given in lines 117-119.

Line 125: Why is this additionally? This is the whole intention of the algorithm in my opinion.
→We have corrected the wording in the section you mentioned.

Line 143: It should be stated why these 3 cases are highlighted. I see they represent agreement, partial agreement and no agreement, but this is not clear and now it looks as if these where the first three patients subjected to this research.

→We have tried to quantitatively evaluate the degree of agreement between the intraoperative movie and the 3D image as much as possible. In order to compare the three-dimensional structure of the lungs with the two-dimensional images, we aligned the images based on the ribs to avoid angle deviation as much as possible. This was the limitation of this paper because it is inevitable that the evaluation is subjective to some extent. If the positioning part could also be done mechanically, image comparisons would be more quantitative and reproducible, but a new algorithm needs to be developed. In the present study, Figures are representative of cases that can be typically evaluated for concordance among the cases reviewed.

Line 148: What is meant by blood flow control? I would suspect this is the ICG-injection, but this should then be stated more accurately.
→We have changed the wording of the sentence you mentioned and included it in lines 170-171.

Line 166: retrospectively? You stated before that all patients signed informed consent before participation. We would then suspect that the research was done prospectively and if not, why not and do you think this makes a difference in the comparison?
→In this study, we retrospectively evaluated past surgical cases. As a result, we confirmed that the accuracy of this method is comparable to existing methods for identifying intersegmental lines, and we plan to continue to study this method prospectively in the future.

Line 174-175: It does have a deflation function, but there is no real-time guidance and it does not provide landmarks for the surgeon that would make the injection of ICG unnecessary, because the actual segmental border is clear from the algorithm-produced images.
→This system can be manipulated intraoperatively to match the field of view and adjust angles in a timely manner. The ultimate goal is to replace the existing intersegmental line delineation technology in terms of accuracy.

Line 185-186: what is meant by processed?
→Changed word to 'detached', lines 214-215.

Additionally, 8 out of the 12 references you make are written by the authors of this article, which I think is quite exceptional and does not make the reader think you really compared

your work to others or looked into the usefulness of this system.
→In Discussion, the content was expanded by adding references to existing techniques for delineating intersegmental lines (7,10-13,16).

Reviewer D

Original and veer interesting work.
Innovating subject.
→Thank you for your detailed review of our report.
Thank you for your interest.

Reviewer E

We congratulate the authors on an interesting manuscript that highlights the feasibility of using software algorithms to predict lung segment delineation preceding or during surgery in deflated lung, as compared with intraoperative observations. This could be a useful tool to help the lung surgeon in performing more limited surgery.
While the use of software to provide guidance is interesting and has high potential as described by the authors, the retrospective and small nature of this study along with low detail on software details and technological novelty when compared to other literature makes this study of limited scientific value.
Based on the supplied information it is furthermore unfortunately not clear what algorithm is used to deflate the lung. The video shows what seems to be only a scaling factor, which would then be outdated when compared to other complex 3D transformation algorithms that are being developed by groups throughout the world.
While an interesting concept, additional work is needed to make this research of potential impact for the scientific community. In the reported state, it is not in a phase for it to be reported as clinically ready yet but also not scientifically thorough enough such that other can further develop the concept.
Concluding, we encourage the authors to further develop their work and look forward to a future manuscript which is more elaborate and clinically impactful.

→Thank you for your detailed review of our report.
This deflation algorithm was established by analyzing CT data of human pneumothorax lungs and cone beam CT data of intraoperative lungs. The details of the algorithm are given in lines 128-133.
As you mentioned, we believe that the degree of lung collapse is influenced by pre-existing conditions such as emphysema or interstitial pneumonia. Our ultimate goal is to

create a deflation system that includes such conditions in the algorithm, but at the time of this report, the algorithm is being constructed using lung samples from pneumothorax patients. At the time of this report, the algorithm is being developed using a sample lung from a pneumothorax patient. In the future, we will train the algorithm on many images of collapsed lungs, accumulate case examples, and aim to develop more accurate 3D images.