

Peer Review File

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Review Comments

Reviewer A

Review of the paper entitled: "Vein first strategy for VATS lung segmentectomy under use of Three-Dimensional Computed tomography" by Hiroyuki Oizumi et al. Department of Thoracic Surgery, Higashi-Yamato Hospital, Tokyo, Japan. I read with interest this paper and the associated videos of this study on a novel vein-first approach to lung segmentectomy. The authors showed that this approach is feasible and useful for the upper lobe segments and in some lower lobe segments even if in these cases surgery is more complex. In my opinion and for my experience the vein-first strategy is the current practice for upper lobe segments because the approach to the artery and bronchus is easier when the vein is dissected. Regarding the lower lobe segmentectomies I have some doubts about the real advantages of this strategy because I think we can expose the patient to an increased risk of intraoperative bleeding, increased operative time, post-operative prolonged air leak and consequently prolonged length of stay. I think that the right approach of segmentectomy should be the simplest and the fastest and not a mere surgical exercise. In fact, the authors suggest using the vein first strategy for lower lobe segmentectomies when the fissure is incomplete, but in these cases I perform a wedge with adequate lymph node dissection as suggested by the CALGB 140503 study. This is my main comment and I have also other suggestions to improve the paper:

To Reviewer A

Thank you for your comments. We understand and agree with your opinions about the indications or preferences of procedures. We always think of simple maneuvers, as complex procedures may cause some adhesions that may disturb future operations. However, this is a how-to-do-it article, and knowing optional ways and their utilization will increase the range of the surgeons' skills. We have revised our original manuscript according to each of your comments.

1) check the whole paper for typos and I suggest using the same style;

Answer 1): Thank you for the comments regarding the typos and style.

Change 1): We revised the manuscript.

2) authors should insert the number of the CALGB randomized controlled study (140503);

Answer 2): Thank you for the comment. We revised the manuscript.

Change 2): We added the number 140503 (line 38, page 4).

3) the authors started to perform segmentectomy with this approach in 2009 and they stated that they try to standardize this approach applying to all segmentectomy. During these 13-14 years the authors should harvest several data and so I suggest inserting some pre-operative and post-operative data about indication and results of this approach. For example: type of segmentectomy, conversion to lobectomy rate, conversion to open rate, complications, bleeding, operative time and so on;

Answer 3): Thank you for the valuable comment regarding the peri-operative data. This is a Surgical Technique article, and majority of patients received the operation in our previous hospital. Those are the reasons we omitted to describe the perioperative data. The IRB approval number is not yet stated as it's not yet been issued at this present time. We will add it later.

Change 3): We added the information about the number of operations since 2009, bleeding, operative time and duration of chest drainage in the comment, which includes the data of our previous hospital (lines 202-211, page 13). Also, we added two coauthors of our previous hospital (lines 1-7, page 1).

4) what about prolonged air leak (PAL)? PAL is an issue of segmentectomy and almost of complex segmentectomy and so I suggest inserting some data about it. Moreover, I saw in the videos that large part of lung parenchyma was dissected with energy device exposing patients to an increased risk of PAL;

Answer 4): Thank you for the valuable comment. We observed the PAL (7 or more days) in 12 patients among 425 who received VATS anatomic segmentectomy since 2009.

Change 4): We added this information (lines 208-209, page 13).

5) the quality of the first video is poor and I suggest inserting more landmarks identification point;

Answer 5): Thank you for your comment. In fact, some of the videos are not of good quality, as they include older videos of the early phase taken from our DVDs, which introduce the basic techniques of our VATS segmentectomy using old devices. However, we believe this omnibus format video will give the readers a good understanding of our original style and the basics of surgical technique and its developments.

Change 5): We extended the video time of the left S3 segmentectomy, which we did in 2011, and added more landmarks.

6) in the second part of the first video about s9-10 at the minute 2:52 is not clear what * means

Answer 6): We are sorry for not describing enough. B* means the subsuperior segmental bronchus. DOI:<https://doi.org/10.1016/j.athoracsur.2017.07.007>

Change 6): We revised the video subtitle to “B9+10 stump preserving subsuperior bronchus (B*)”.

7) in the second video the authors performed a lower lobe subsegmentectomy with the first structure dissected and sutured is the bronchus, then they dissected the artery and lastly the vein. Could the authors explain this incongruence?

Answer 7): We “at first” managed two veins to expose the artery and bronchus, as described in the text (line 189-192). There are subtitles of managing intersegmental veins at the minutes 00:40 and 00:54. The target bronchus and artery were deeply located; therefore, we first dissected the lung parenchyma along the intersegmental vein between S8 and S7, which reached the confluence point, and then we dissected the parenchyma along the intersegmental vein between S8a and S8b. Finally, the target bronchus and artery became visible. We included the 3D-CT at the minutes 00:25.

Change 7): We also added this information in the video legends (lines 296-298, page 18).

To Reviewer B

Thank you for your comments. We agree with your opinion of some limitations and we have used your comments to revise our original manuscript.

1. When the ICG method had not been used for the identification of the inter-segmental line, I thought that the vein first strategy was useful because the inter-segmental vein becomes the demarcation of the inter-segmental line. However, the ICG method has been used worldwide in recent years. If the ICG method is applied for the division of the inter-segmental plane, I wonder if the vein first strategy would be needed. I hope to get the authors' comments regarding these points.

Answer 1: Thank you for your question regarding the benefit of vein-first in using the systemic ICG fluorescence method. The vein-first strategy has two merits even in the ICG method era: 1) When the segmental artery is located deeply in the parenchyma, the precise assessment of hilar structure using 3D-CT, finding the neighboring vein, and dissection along the vein can lead to the target segmental artery. We demonstrated the representative case in Video 2. 2) When we use the systemic ICG method,

we need to divide the intersegmental plane only by staplers. In our experience, segmentectomy using the ICG method is less precise around the hilar structures and tends to resect larger areas to avoid some mistakes. Recent developments of staples for thick tissue, such as black stapler cartridges, made it possible to catch and divide the thick tissue; however, it is sometimes still hard to hold the correct point as the opening angle is limited. It is also hard to keep the grasp point as it slips at the thicker hilum side. The dissection along the intersegmental vein makes the parenchyma thinner to apply staplers, and it also facilitates the stapler cartridge or anvil to be fixed in the appropriate position, and may prevent extra parenchymal convergences.

Change 1: We added comments regarding the ICG method in the discussion (lines 255-268, page 16).

2. It was unclear how the number of the patients could receive segmentectomy or subsegmentectomy with the vein first strategy because there were some variations in branch types of the pulmonary veins and the authors did not describe the actual number of segmentectomies performed with this method although the authors described that nobody had undergone right S7, S8 segmentectomy. Therefore, I think that it is better to add the approximate number of patients who can receive the vein first strategy for each segment for readers' understanding.

Answer 2: Thank you for the constructive comment. Actually, we recently experienced a vein-first right S8 and right S7 segmentectomy in a type of case where S7 (B7) is located posteriorly to the common basal vein. Therefore, we have revised the description regarding S7 and S8. We have performed 536 total thoracoscopic segmentectomies since 2004. We began this method in 2009 and have performed 425 cases. It depends on understanding the 3D anatomy from the CT data. The equipment and surgical techniques for 3D reconstruction have gradually changed, and the performance of this method has gradually increased and become more established. Therefore, the pure number of vein-first is not countable.

Change 2: We added the number of thoracoscopic anatomic segmentectomies since 2009 (line 206, page 13), and changed the sentence about right S7, S8 (lines 121-123, page 8).

3. I think that a conventional first step of segmentectomy is basically the artery first strategy. Although the authors emphasized the merit of vein-first strategy, it is better to describe why the authors started this method in the introduction section. I thought that the authors' reason for starting this method was vague.

Answer 3: Thank you for the comment. The segmentectomy is based on managing the bronchus; therefore, the artery beside the bronchus was conventionally the first step.

To perform a precise anatomical segmentectomy, if we treat the artery and bronchus first, we usually need to dissect the intersegmental plane later, seeking venous branches. If we dissect the intersegmental veins first and divide the *intra*-segmental veins, the bronchus and arteries will spontaneously be peeled off and become apparent easily. We realized that this would ultimately eliminate unnecessary maneuvers when we catch the anatomy by 3D-CT. It led us to apply the technique to various segments.

Change 3: We added the sentence in the introduction section (lines 43-49, page 4).

Minor comments-

1. There were some mistakes of font style. Please check them before submission.

Answer 1: Thank you for pointing out the mistakes.

Change 1: We rechecked the entire manuscript and have changed them respectively.

2. Although the authors described "vein first strategy" as "vein-first approach" or "vein-first method", what do these differences mean? Please be consistent with word choice, grammar, and hyphens.

Answer 2: Thank you for pointing out those differences. We unified the words to vein-first but used “approach” in some sentences.

Change 2: We unified the words to vein-first.

To Reviewer C

Thank you for your favorable comments.

1. Line 52: ‘... makes... ‘ I think this sentence needs to be revised.

Answer 1: Thank you for your comment regarding the sentence.

Change 1: We have changed the sentence.

2. The authors mention in line 33: ‘... managing the vein first sometimes...’ suggesting that dissecting vein first is sometimes handy, but not always. Do I understand this correctly? In that case the authors should specify in which situations vein first is better than conventional method and mention here, also maybe the title should be adjusted making it clear that vein first is not an alternative to the conventional strategy, but a technique only applicable in a subset of cases.

Answer 2: Thank you for your comment. This method mainly benefits patients with the inter-segmental vein in their hilum. We described it at the [Operative procedures] section as follows; “We first dissect the hilar parenchyma along the *inter*-segmental vein if anatomically possible”. To catch the anatomy correctly, a precise assessment of 2D and 3D-CT is necessary.

Change 2: We added the sentence in the introduction section (lines 43-49, page 4).

3. What is the opinion of the authors about the method of dissecting artery and bronchus and after ICG resecting parenchyma including the vein branches to the specific segment?

Answer 3: Thank you for your comment. Such a style of segmentectomy has become popular, and we also perform it in some emphysematous or poor-risk patients. However, we think we should preserve more lung for less invasive cancers, metastases and non-malignant diseases. Additionally, one of the statements of the recent ESTS recommendation for segmentectomy is, "Except simple and clear anatomy, the control of the vein is best done within the parenchyma and not at the hilum level as a segmental vein can drain >1 segment." We believe preserving the intersegmental vein by assessing the venous branches by 3D-CT can maintain the physiological function of the remnant lung parenchyma in appropriate cases.

Change 3: We added the sentences in the discussion (lines 249-253, pages 15-16).

4. Line 81 R is missing at the start of this line.

Answer 4: Thank you for pointing out our mistake.

Change 4: We revised the word.

5. Line 170 and further: the layout is different than first part of this manuscript.

Answer 5: Thank you for pointing out this.

Change 5: We revised the font style etc.

6. Line 214: figure legend mentions segmentectomy of S3, please mention the side. The same applies for Line 219 Figure 2 and line 223 figure 3.

Answer 6: Thank you for pointing out these mistakes.

Change 6: We revised the manuscript (lines 279, 282, 284, page 17).

7. Figure 1 Artery and Bronchus please check layout

Answer 7: Thank you for pointing this out. We guess that you mean both of them are not clear.

Change 7: We added the arrows in the figure 1.

To Reviewer D

Thank you for your favorable comment and suggestions. We have used your comments to revise our original manuscript.

1) Title should be reconsidered again. Please do not use abbreviation, such as “VATS”. “Three-Dimensional” and “Computed tomography” should be revised.

Answer 1): Thank you for your comment regarding the title.

Change 1): We changed the title as follows: Vein-first strategy for thoracoscopic lung segmentectomy under use of three-dimensional reconstruction of computed tomography.

2) On line 52, please check the typos, such as “makes the hilum makes the hilar side released”.

Answer 2): Thank you for pointing out these.

Change 2): We rechecked the entire manuscript and have changed them (line 86, page 6 etc.).

3) English should be checked again by a native professional editor who is familiar with scientific writing.

Answer 3): Thank you for the comment. We received a check of a native English speaker and revised the manuscript.

4) Abbreviations should be spelled out when they are firstly used in the text. For example, VATS and 3D-CT on line 34.

Answer 4): Thank you for the comment. The abbreviation of 3D-CT is already spelled out in the abstract. We did not spell out the abbreviation of the segment such as S1, as it seems to make the manuscript redundant.

Change 4): We changed “VATS” to “thoracoscopic”.

5) The font is different on line 170-179. Please check.

Answer 5): Thank you for pointing out this.

Change 5): We changed the font style.

6) On line 188, “Circulating Tumor Cells” is correct?

Answer 6): Thank you for your comment.

Change 6): We have corrected the words uncapitalized (line 236, page 15).

7) If the authors want to publish this draft as a surgical technique paper, the reviewer strongly recommend adding more surgical schema about each surgical technique.

Answer 7): Thank you for your comment. We understand your recommendation.

Change 7): We added two figures about left S9 and S10 segmentectomies (lines 162, 167, page 11 and 287, 288, pages 17-18).

To Reviewer E

Thank you for your comment and suggestions. We have used your comments to revise our original manuscript.

#Main drainage vein from left S1+2 is sometimes branched from central vein located in deep lung parenchyma between S1+2 and S3. It is difficult to dissect the drainage vein at first. Drainage vein

from S1 is branched from central vein from deep lung parenchyma. S1 segmentectomy were not also usually vein-first method. As described in text, S6 segmentectomy could not performed the vein-first-method. Author also described that right S7 or S8 segmentectomy is not the candidate for the vein-first strategy.

Therefore, the term of 'Vein-first method' was not suitable for their methods for segmentectomy.

Answer: Thank you for your comment. We do not mean the term of 'Vein-first method' to "transect or divide" it. We use the term "strategy" in that we first assess the presence of the target vein by 3D-CT, isolate and peel the inter- and intra-segmental veins, and then "divide" the target vein according to the location and distance from the lesion. We know the anatomy of the central vein type of left S1+2. Of course, we cannot divide the central vein first. We described, "We first dissect the hilar parenchyma along the *inter*-segmental vein if anatomically possible". Even in this situation, we precisely assess the thin-sliced CT, look for the thinner inter-segmental vein in the mediastinum side, and use it if it exists.

In addition, in Movie 2, because the segmental artery and bronchus are deeply located and difficult to reach, we first dissected the lung parenchyma along the intersegmental vein between S7 and S8, reaching the venous confluence point. Then, we dissected the parenchyma along the intersegmental vein between S8a and S8b. Finally, the target bronchus and artery became visible.

Change: We changed the term to "vein-first approach" in some sentences.

#Miss spell: ight S6 (line 81)

Answer: Thank you for pointing out this.

Change: We revised the spell (line 115, page 8).

To Reviewer F

Thank you for your comment and suggestions. We have used your comments to revise our original manuscript.

1. Would the author please discuss further the advantages of vein-first approach? There were brief mentions of advantage from an oncological standpoint as well as the ease of dissection due to the ability to manipulate the vein. From a technical standpoint and based on the author's description, is this an easier approach versus divisions of other hilar structures first?

Answer 1: It depends on the oncological feature or the characteristics of the lesion. For example, for S9 and S10 segmentectomy, the division between the S6 and basal segments may facilitate a simple procedure. However, extra-convergences of the lung parenchyma occur there. The merit of vein-first is that it can preserve the original connection and prevent extra convergences in those procedures. We quoted the references about the basal segmentectomy procedures.

Change 1: None

2. Are all lobectomy and segmentectomy pre-planned with 3D-CT? Is this standard practice for the authors? Can the authors comment on the ability to do this operation without the aid of 3D-CT (potentially at other institutions)? This would then speak for the replicability of the operations described.

Answer 2: We think 3D-CT is not essential for lobectomy; however, it is necessary for segmentectomy to grasp the precise hilar anatomy to perform correct anatomical segmentectomy via VATS. The report of 3D-CT use for segmentectomy is rapidly increasing. It may be difficult to perform our method without 3D-CT reconstruction; however, sagittal and coronal angle images may help grasp the intersegmental vein, etc.

Change 2: We added a comment about the status when 3D-CT is unavailable (lines 231-233, page14). Also, we added [Preoperative Preparations and Requirements] (lines 51-67, page4-5).

To Reviewer G

Thank you for your comment and suggestions. We have used your comments to revise our original manuscript.

1. Personally I don't see the utility to do the vein first in some easy segmentectomy (segmentectomy 6 for example). Your technique could be applied in some difficult cases where anatomy is not clear. At the end, what is the real value of vein first approach, it is not so clear after reading your article.

Answer 1: We had published several papers regarding individual basal segmentectomy, etc., and quoted them in the text. Also, we think the dissection along the vein facilitates the isolation and encircling of the target bronchus; thus, it makes the maneuver time-saving.

Change 1: In the introduction section, we added sentences about why we started this method (lines 43-49, page 4).

2. Then, one of the statements of the recent ESTS recommendation for segmentectomy is "Except simple and clear anatomy, the control of the vein is best done within the parenchyma and not at the hilum level as a segmental vein can drain >1 segment" and this statement was agreed by 96% of surgeons. So do you think that your technique is still valid? It should be mentioned in your article.

Answer 2: This is the crucial point of our technique. We recommend peeling the intersegmental vein as it drains more than two segments and dividing only the target segment draining vein.

Change 2: We added the sentences to clarify merit (lines 249-253, page 15-16).