

**Peer review file**

**Article information:** <http://dx.doi.org/10.21037/jtd-21-211>

**Comment 1:** I agree with the introductory paragraph, patients with early stage lesions may be better managed with wedge resection rather than anatomic resections. Localization methods are sometimes required. A generous surgical margin is better than a small margin from a recurrence standpoint. This is particularly important for primary lung cancer since cure is the goal. What factors enhance an adequate surgical margin is therefore important.

**Reply 1:** We agree with your assessment. We also believe that the distance of the tumor from the pleural surface and the localization of the lesion are important, although there is no clear conclusion as to what factors are associated with adequate surgical margins.

**Changes in the text:** We added text to Introduction as advised (see Page 3, line 64-66).

**Comment 2:** The indication for pulmonary localization was made by thoracic surgeons. This includes a lot of surgical decision making which is not captured in this study. Some more clarity on this decision making would be useful. For example, it excludes patients in which a wedge resection is not possible based on location or size. The selection criteria are so broad as to be practically useless since they are all “or” inclusion criteria. Criteria which applied to all of the lesions would be more useful. For example, all lesions were < 2cm in diameter.

**Reply 2:** Thank you for your suggestion. In accordance with the Reviewer's comment, we have revised the selection criteria.

**Changes in the text:** We deleted the text from Page 4, line 84-86 and added new selection criteria (see Page 4, line 86-91).

**Comment 3:** Were all lesions >4mm from the pleural surface? It appears pleural based lesions were not included (distance to pleural surface was never 0). I assume this was because they could be visualized at the time of surgery, but this was not stated.

**Reply 3:** All lesions were more than 4 mm away from the pleural surface, so the selection criteria were modified.

**Changes in the text:** We have modified the selection criteria (see Page 4, line 90-91).

**Comment 4:** Distance to the pleural edge is not defined. I'm assuming it was from the edge of the lesion to the pleural surface, but the distance from the lipiodiol to the lesion was measured from their centers, not the edge of the lesion, so I'm not sure.

**Reply 4:** The distance to the pleural edge was specified in the selection criteria as the distance from the edge of the nodules to the pleural surface.

**Changes in the text:** We have modified the selection criteria (see Page 4, line 90-91).

**Comment 5:** Depth-to-size ratio is not defined. I'm not sure why they are displayed as a ratio. I would assume a greater depth and a larger size would make a negative margin more difficult. Therefore, they are more cumulative factors rather than trade-off factors.

**Reply 5:** The reviewer's comment is correct. We excluded the depth-to-size ratio because we thought it might confuse the reader.

**Changes in the text:** We have modified Table 2 and Table 4.

**Comment 6:** What is an automatic suturing device? Is that a stapler?

**Reply 6:** In accordance with the reviewer's comment, we have changed this to endoscopic stapler.

**Changes in the text:** We have modified the text (see Page 6, line 124).

**Comment 7:** The difference between a 11mm and a 9mm margin can't be much. I wonder if you could measure factors impacting surgical margin along a continuous distribution?

**Reply 7:** You have raised an important point; however, there are several papers that show a significant difference in recurrence rates when a 10 mm surgical margin is used as the cutoff value. In addition, we believe that the number of cases in this study is insufficient to measure the factors affecting the surgical margin along a continuous distribution.

El-Sherif A, Fernando HC, Santos R, et al. Margin and local recurrence after sublobar resection of non-small cell lung cancer. *Ann Surg Oncol* 2007; 14: 2400–5.

Wolf A, Swanson SJ, Yip R, et al. The impact of margins on outcomes after wedge resection for stage I non-small cell lung cancer. *Ann Thorac Surg* 2017; 104: 1171-8.

**Comment 8:** The distance to the pleural surface and tumor size was larger for those lesions with a margin < 10mm although neither factor individually was statistically significant. Both of these factors are certainly factors that influence surgical margins and should be mentioned.

**Reply 8:** We agree that this point requires clarification, and have added the following text to the Result.

**Changes in the text:** We added text to Results as advised (see Page 7, line 169-171).

**Comment 9:** Time required for marking is in mm? I'm assuming minutes?

**Reply 9:** This error has been corrected in accordance with the reviewer's comment.

**Changes in the text:** We have modified Table 3.

**Comment 10:** An increasing 3D deviation certainly makes sense that it would lead to closer margins. I'm not sure what an optimal cut-off of 1.4 cm means.

**Reply 10:** We have removed the ROC curve and its description from this paper because it may confuse the reader.

**Changes in the text:** We deleted the text from Page 8, line 176-179.

**Comment 11:** "In percutaneous preoperative marking, direct puncture of lung lesions may cause pleural dissemination and should be avoided." This needs a citation as it is critical to the whole paper.

**Reply 11:** We agree with the relevance of this reference, and have added it to the Discussion.

**Changes in the text:** We have added the reference (see Page 10, line 239).

**Comment 12:** Not injecting into the lesion increases the 3D deviation. Is there a way to minimize this? Is there a way to inject deep to the target lesion so you know if you resect the lipiodol you will resect the lesion with adequate surgical margins?

**Reply 12:** One solution may be to perform a transbronchial approach like VAL-MAP, which is being developed in Japan, and to perform multiple markings on a single lesion. However, the disadvantage of VAL-MAP is that, unlike Lipiodol, it cannot determine the depth of the target lesion. We believe that the development of a transbronchial approach using a contrast agent such as Lipiodol may contribute to accurate preoperative marking in the future.

Sato M, Omasa M, Chen F, et al: Use of virtual assisted lung mapping (VAL-MAP), a bronchoscopic multispot dye-marking technique using virtual images, for precise navigation of thoracoscopic sublobar lung resection. J Thorac Cardiovasc Surg

**Comment 13:** I don't understand this sentence: "Based on the results of this study, we are considering a change from wedge resection to resection or addition of lipiodol injection for a case with a 3D deviation >1.4 cm."

**Reply 13:** We have removed the ROC curve and its description from this paper because it may confuse the reader.

**Changes in the text:** We deleted the text from Page 11, line 254-256.

**Comment 14:** Another way to say this is “imprecise localization, may lead to smaller surgical margins”. I think the reasons for imprecise localization need to be enumerated. There are other factors that may also cause smaller surgical margins that your paper was not powered to detect.

**Reply 14:** We agree that this point requires clarification, and have added the following text to the Discussion.

**Changes in the text:** We have rewritten our text (see Page10-11, line 250-253) to be more in line with your comments.