Peer Review File

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Reviewer A

Comment 1: I find the concept of "anatomic wedge resection" intriguing. However, for small nodules where sufficient margin can be achieved, would you consider permitting an aggressive approach with "non-anatomic wedge resection"?

Reply 1: The term "anatomic wedge resection" is my own construct. It was meant to describe the procedure performed by Qiu and colleagues where they are not bound by intersegmental planes, but the boundaries of resection are based on tumor location and margin (a wedge). I used the term "anatomic" to give this type of wedge resection an oncologic empowerment, meaning it is effective from an oncologic standpoint.

At this current juncture, given the US data regarding lobar v sublobar resection, I would perform a wedge resection only in very select patients that required a minimal intervention, such as a very comorbid or frail patient or one with extremely limited pulmonary function as an alternative to SBRT.

Changes in the text: None.

Comment 2: Depending on the location of the tumor, it might be possible to obtain a volume of tissue equivalent to that of segmentectomy or subsegmentectomy. To date, there are no randomized prospective trials comparing segmentectomy and wedge resection for small lung cancer. If possible, I would appreciate it if you could address this issue.

Reply 2: Correct, there are no direct randomized trials comparing wedge resection with segmentectomy. However, the data from CALGB 140503 Alliance Trial contained wedge resections vs lobectomy and were found to be non-inferior. Essentially, the same as a segment. However, this is debated outcome and further research is needed.

Changes in the text: The manuscript already contains a mention of this trial and how wedge resections were considered here: line 31 "With some controversy and variable interpretation of the data, the CALGB 140503 Alliance trial also reported that non-anatomic wedge resection was equivalent to segmentectomy. Practically, wedge resections made up a large portion of the reported United Status registry data for sublobar resections (what American surgeons were actually doing) and therefore, were included in the study."

Reviewer B

Comment 1: In Page 2 Line 60-62, author suggest that it will be interesting to see if small millimeter differences in margin distance contribute to disease recurrence and the the authors are well positioned to help clarify this question. I agree the suggestion conceptually. But I am not quite sure if it is really clinically relevant to examine the differences. It would be quite difficult to cut the soft lung parenchyma within millimeter differences in the 3-dimensional settings.

Reply 1: The millimeter differences in the tumor margin would be evaluated on postoperative pathology and compared retrospectively. Surely, this cannot be done in the operating room. So yes, conceptually, it would may be interesting information to know. What may change if millimeter differences were correlated to recurrence, would be a preference for lobectomy in cases of close(r) margin distances. Of course, this is what lobectomy vs segmentectomy is intended to evaluate and has yet to demonstrate a difference. So, I would guess there is no meaningful difference.

If it makes no difference, are we sure the rule of 2 cm is to be respected. This could not be done with the APL cohort as all these patients underwent completion lobectomy. But another question to consider.

Changes in the text: Line 75, "This said, margin distance essentially defines lobar vs sublobar resection, of which comparative trials have demonstrated relative parity of outcomes, such that a difference based on millimeters would be surprising."

Comment 2: Also, I suggest author to cite a paper on lung mapping techniques, such as VAL-MAP, in mentioning the surgical margin of limited lung resection.

Reply 2: Thank you for the suggestion. I have added a brief review in the paper and a new reference for a review of VAL-MAP.

Changes in the text: It must be noted that not all surgeons will have access to 3D imaging, which limits the generalizability of APL. Equally, alternative mapping techniques using 3D imaging, such as virtual-assisted lung mapping, have already be suggested (6). In this method, navigational bronchoscopic dye marking is performed to define the resection margin, which is then used to verify and optimize a subsequent 3D map for operative guidance. This type of mapping, however, is marred by its cumbersome process of two anesthetic events and imaging processes, as well as a loss of accuracy when targeting deep nodules (6).

Reference added: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6381264/

Reviewer C

Comment 1: I enjoyed reading your editorial, line 13 should read T1aN0 and T1bN0 Reply 1: Correct, thank you for this correction.

Changes in the text: Line 25, "(clinical stage 1A, cT1aN0 and cT1bN0)"

Reviewer D

Comment 1: I never have been heard about APL but i agree with your concept. In most of cases that the tumor is close to segmental plane, my surgical procedure is bisegmentectomy or extended segmentectomy. However, 3-D CT is crucial for APL. Many centers could not follow the procedure. Thank you for interesting procedure and new technique and long term outcomes must be required.

Reply 1: Thank you for your comments. I completely agree, and often perform a multiple segmentental resection in my practice (such as an LUL apical trisegmenectomy, my favorite, rather than a LUL S1, for example). Sometimes, I will do a segment, and the margin just appears close, and I will complete the lobe. The PFT data from the comparison trails suggest the differences in functional outcome are not as great as we thought, a 3-

6% difference. I also agree that 3D CT is needed and often not easy for the all surgeons, or even available to everyone at all instutitions. It is likely that it is not widely available. Certainly, long-term outcomes are crucial. Will be interesting to see.

Changes in the text: Line 55, "It must be noted that not all surgeons will have access to 3D imaging, which limits the generalizability of this method."

Reviewer E

Comment 1: Excellent editorial on the original article by Qiu and colleagues. This is an important topic considering the widespread adoption and expansion of lung cancer screening. In this modern world, the identification of early-stage lung cancers will increase. As thoracic oncologists, we need to adapt and modernize our operative strategies. This editorial appropriately describes the strengths and weaknesses of the original article. My only recommendation is providing a citation for page 1 lines 7-8 sentence "In the 1930s, pneumonectomy was the standard of practice in all cases. In the 1950s lobectomy was posited as an alternative to preserve lung and reduce perioperative mortality."

Reply 1: Thank you for your comments. I have included a reference.

Changes in the text: Line 21, "In the 1940s and 1950s lobectomy evolved as an alternative to preserve lung and reduce perioperative mortality." A new reference 1 was added.