**Peer Review File**

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**Reviewer A**

Comments:
1) “These procedures were undertaken only by one operator, the corresponding author, with procedural uniformity, in a randomized fashion over Groups.” I didn't understand what the author meant by the phrase "...in a randomized fashion over Groups." could you clarify?

Reply and Changes in the text:
The order of each experimental procedure was assigned randomly from one group to the other, not confined to only one group. The author added the following sentence to Page 9, Line 136-137 (highlighted portion): The order of each experimental procedure was assigned randomly from one group to the other, not confined to only one group.

2) “The airway pressure was gradually increased, and the minimum positive airway pressure causing air leakage from the defect (seal-breaking burst pressure; SBBP) was recorded by visual assessment for each sample and then compared between the groups.”

Wouldn't assessing the loss of resistance during insufflation give much more repeatable results than a visual assessment? The visual evaluation is subjective, it would be advisable to have an other samples evaluated by a second observer.

Reply and Changes in the text:
Recording seal-breaking burst pressure by visual assessment is a clear-cut and much more sensitive method than the reviewer anticipates. With a gradual increase in airway pressure, the first small bubble slowly appears at the edge of the covering material on the lung soaked in normal saline and then gains force with the edge of the sheet coming off. Assessing the loss of resistance of intra-airway pressure, as the reviewer mentions, requires a far more sensitive electric manometer because the amount of air leak from a 20×30 mm pleural defect is too small to detect as a fall of intra-airway pressure, and it is difficult and impractical to adopt along with the protocol of this experimental study. The author added Video 1, demonstrating such experimental procedures, to the manuscript for reference.

3) Group 9 and group 1 differ only in the size of the non-woven PGA felt, is that right? Is fibrin sealant used in both? It's not entirely clear to me from the text.

Reply and Changes in the text (highlighted portion):
As shown in Fig.1, a 20 ×30 mm standardized pleural defect was covered with

different synthetic bioabsorbable sheets (three pieces of 15 ×30 mm in Groups 1, 2, 3, 4, 5, and 6; one piece of 40 ×30 mm in Groups 7, 8, and 9). Since TachoSil® cannot be applied one sheet over another because of its thickness of 5 mm, the 20×30 mm standardized pleural defects were covered not with three pieces of 15×30 mm TachoSil® but with one piece of 30×40 mm TachoSil®, as in Groups 7 and 8. For a valid comparison within Experiment 3, Group 9 (one piece of 0.15 mm-thick PGA felt with a size of 40×30 mm) was added instead of Group 1 (three pieces of 0.15 mm-thick PGA felt with a size of 15×30 mm).

Based on this reviewer's question, the description in Page 13, Line 198-204 was modified and complemented as follows: As TachoSil® cannot be applied one sheet over another because of its thickness of 5 mm, the 20×30 mm standardized pleural defects were covered not with three pieces of 30×15 mm TachoSil® but with one piece of 30×40 mm TachoSil® in Groups 7 [TachoSil] and 8 [FS+TachoSil]. For valid comparison within Experiment 3, Group 9 [1p-PGA0.15] (one piece of 0.15 mm-thick PGA felt with a size of 40×30 mm) was added instead of Group 1 [PGA0.15] (three pieces of 0.15 mm-thick PGA felt with a size of 15×30 mm).

4) It seems that the better performing groups also have higher variance, how does the author interpret this trend?

Reply:
First, significant differences between groups were confirmed based on the valid biostatistical assessment that was supervised by a biostatistician. It is possible that the trend indicated by the reviewer was caused by some variability in the manually created 20×30 mm pleural defects.

**Reviewer B**

It is my pleasure to review this article. The authors conducted comparative experimental study in ex-vivo porcine lung model using variable clinically usable synthetic bioabsorbable sheets.

This study suggests effective combined techniques in choosing bioabsorbable sheets and fibrin sealants against troublesome air leakage in pulmonary surgery.

I think this paper has minor concerns to be discussed, listed as follows:

1. In line 28, Histologic significant clot penetration seems subjective findings without showing experimental result that can be described in the result/discussion section.

Reply: The author agrees with the reviewer's comment. The sentence (Histologically, clot penetration into the tissue was significant in Groups 8 and 9.) was omitted from the Abstract section.

2. In experimental settings, any observers or assistance for objective and qualified data acquisition seems to require, even though the author's own contributed experimental studies.

Reply and Changes in the text:
Several personnel of CSL Behring Co. participated in the experiment for setup, assistance, and observation during objective and qualified data acquisition. The author added the following remarks in Page 26, Line 434-437: The author is also grateful to Ms. Nakamura, Inada, and Tamura for histological processing and several personnel of CSL Behring Co. for setup, assistance, and observation of the experiment.

3. In line 104~107, between Group 1 and Group 2, 3; 0.3ml differences in usage of fibrin sealants are minimal, but does not matter to compare the groups in study design?

Reply and Changes in the text (highlighted portion):
As explained in Page 10, Line 148-151 (A total of 1.2 ml of each component solution was used in Groups 1, 4, 5, 6, 8, and 9, which was more than a sufficient amount. In Groups that used thicker sheets, such as Groups 2 and 3, a total of 1.5 ml of each component solution was used with further impregnation of the sheets.) The amount of fibrin sealant used was appropriate for the study protocol. For better comprehension, Table 1 has been added as a succinct summary that explains group characteristics, including sheets, thickness, and fibrin sealant amount.

Table 1 Group characteristics

| Groups | Sheet | Thickness (mm) | Applied fibrin sealant (cc) |
|---|---|---|---|
| 1 (PGA0.15) | 0.15 mm-PGA felt | 0.15 | 1.2 |
| 2 (PGA0.3) | 0.3 mm-PGA felt | 0.3 | 1.5 |
| 3 (PGA0.5) | 0.5 mm-PGA felt | 0.5 | 1.5 |
| 4 (ORC) | ORC sheet | 0.15 | 1.2 |
| 5 (W-PGA0.11) | Vicryl Mesh Woven | 0.11 | 1.2 |
| 6 (K-PGA0.18) | Vicryl Mesh Knitted | 0.18 | 1.2 |
| 7 (TachoSil) | TachoSil | 5 | 0 |
| 8 (FS+TachoSil) | Fibrin sealant + TachoSil | 5 | 1.2 |
| 9 (1p-PGA0.15) | 0.15 mm-Neoveil (1 piece) | 0.15 | 1.2 |

4. In Fig. 1, consistency of width/height for pleural defect and sheets might be helpful.

Reply and Changes in the text:

Video 1, which demonstrates the modality of creating standardized pleural defects, was added to verify the consistency of the width/height for pleural defects. The following sentences have been added on Page 8, Line 118-119 (highlighted portion): - by one operator through both the previous [10] and the present study with minimal

variance. Furthermore, in Page 32, Line 528-534, the Figure legend section was modified as follows, adding “the standardized”:
1A: Modality with three pieces
In Groups 1, 2, 3, 4, 5, and 6, three pieces of 15×30 mm sheets were attached over and over, with their margin doubled to cover the 5 mm-width outer margin of the standardized 20×30 mm pleural defects.
1B: Modality with one piece
In Groups 7, 8, and 9, one piece of 40×30 mm sheet was attached to cover the 5 mm-width outer margin of the standardized 20×30 mm pleural defects.

5. In Fig 2, 3 and Table 2, SBBP = full term.

Reply:
“SBBP” in Fig. 3, 4 was fully spelled as “seal-breaking burst pressure” as Figure footnote.

6. In Fig 4, What means the group 10 in this study?

Reply and Changes in the text:
The naming of the groups was wrong. The figure legend for Fig. 4 (new Fig. 3C) has been corrected as follows (highlighted portion) on page 34, Line 555-557:
3C: Experiment 3
SBBP in Group 7 was significantly lower than that in Groups 8 and 9, respectively (* $p < 0.05$). There was no significant difference between Groups 8 and 9 ($p = 0.981$).

7. In Fig 6, Descripted parameters are not clearly visible due to word size and alignment.

Reply:
The description of the parameters in Fig. 6 (new Fig. 4) has been improved.

8. In Fig 7, Different depths with descriptors or borders of materials and alveolar tissues can be indicated within the photos.

Reply:
The magnifications in Fig. 7A and 7 B (new Fig. 5A and 5 B) were identical. The difference in the width of “NS” (Neoveil® sheet) and “TS” (TachoSil®) is related to the original thickness of the Neoveil® sheet (0.15 mm) and TachoSil® (5 mm). The difference in the width of “CP” (clot penetration into the tissue) is related to randomized photo clipping and some fluctuation in the depth of clot penetration.

**Reviewer C**

The authors, Dr. Itano, have made interesting study evaluating the material

characteristics used for alveolar air leakage with fibrin sealant. The study was well designed and showed interesting, clinically useful data and I consider it has value to be published from academic journal. However, I recommend the author to make minor revision of this manuscript.

Major point:

The author used many pronominal names for each material, such as “Group 1” for 0.15 mm-thick PGA. It makes their manuscript much difficult to read. I recommend the author to use some original abbreviation (ex. “PGA0.15” for 0.15 mm-thick non-woven polyglycolic acid, “k-PGA0.18” for 0.18 mm-thick knitted polyglycolic acid, “w-PGA0.11” for 0.11 mm-thick woven polyglycolic acid, and so on) for readability instead of the terms “Group”.

In addition, the details of each experiment should be added to the subsection titles (ex. 2.5 Experiment 1 [Evaluation for influence of PGA felt thickness], written in Page 7, Line 124).

Reply:

According to the reviewer’s recommendation, the abbreviation for each group was created and

added in the text and figures. Further, Table 1 was newly created and added to the manuscript (as shown above), that concisely describes the group characteristics, including the above abbreviation, thickness, and the amount of fibrin sealant used.

Minor point:

In Page 9, Line 174-178, the value of SBBP of Group 2 was not shown despite the ones of Group 1 and Group 3 were described. Please add it.

Reply and Changes in the text (highlighted portion):

The value of SBBP of Group 2 was added in Page15, Line 233 (highlighted portion) as the followings: and showed a trend toward higher pressure than Group 2 [PGA0.3] ($37.7 \pm 11$ $cmH_2O$) ($P = 0.161$).

The sentence concerning their study limitation written in Page 11, Line 226 to Page 12, Line 233 should be moved to the part just before the ‘conclusion section’.

Reply:

According to “Guidelines for Authors” of Journal of Thoracic Disease, the following structured discussion is recommended: For Original Article, we recommend that authors use a structured discussion to increase the readability: a) Key finding, b) Strengths and limitations, c) Comparison with similar research, d) Explanations of findings, e) Implications and actions needed.

If this structure should be observed, it is a little difficult to move the section of study limitation from the above (b) to (e).

The word of “using the ROC”, written in Page 15, Line 304 may be misspelling of “using the ORC”. Please check it.

Reply and Changes in the text:
In Page 24, Line 397, “ROC” was corrected to” ORC”. Thank you for your kind indication.

**Reviewer D**

This manuscript was attractive and interesting. It is acceptable to publish.

**Reviewer E**

This is a well-written article, investigating the optimal methods for applying bioabsorbable sheets to lung defects and comparing the bursting pressures in an ex-vivo model. The authors provide a well-structured discussion, reflecting on the physical characteristics of the different materials which are hypothesized to contribute to the measured results. Thereby, this article adds to the current literature into lung sealing techniques, providing comparative data for further research and development.

However, I still have some questions mainly relating to the methodology that require some further clarification.

1. Methodological comments
a. Were the heart-lung blocks used immediately in the experiment? Can you specify the maximal warm-ischemia time?

Reply and Changes in the text:
The author added the below phrases (highlighted portion) in Page 7, Line 99-102: After humane euthanization, the heart–lung blocks were retrieved, kept at 4 °C, and used for experiments with no perfusion within 2 days after retrieval. The maximum warm ischemic time was approximately 15 min.

b. Can the author specify the precise methods used for linear pressure increase in the lung? How was uniformity ensured? What manometer was used (digital, analog) and what the sampling interval was? (e.g., per 1cm$H_2O$)

Reply and Changes in the text:
The author added the below phrases (highlighted portion) in Page 8, Line 111-113: , which was monitored using a digital manometer with a graphical display demonstrating sequential linear pressure changes over time (Video 1). Further, Video 1 was added to the manuscript, that demonstrates the experimental procedure including measurement

of seal-breaking burst pressure by a digital manometer with the graphical display demonstrating sequential, linear pressure changes over-time.

c. Please specify the temperature of the water which was used to immerse the specimens.

Reply: The temperature of the water which was used to immerse the specimens is normal room temperature around 20 degrees.

Changes in the text in Page 9, Line 127-128 (highlighted portion):
The covered surface was maintained at rest for 5 min and then gently immersed in normal saline solution at room temperature (approximately 20 °C),

d. Were baseline measurements taken of the leakage capabilities of the lung lesions (such as leaking pressures or air leak in mL/min), to demonstrate clinically relevant air leakage and show overall comparability between the groups? I am curious to see if the 1mm deep lesions made with electric cautery produce clinically relevant air leaks.

Reply: A standardized 20 mm×30 mm pleural defect with a depth of 1.0 mm was created by one operator through both the previous and the present study with minimal variance. This standardized pleural defect almost constantly has minimal air leak with lung blocks expanded with the airway pressure of 6 $cmH_2O$. As soon as beyond 6 $cmH_2O$, air leak from the pleural defect starts and increases more and more vigorously according to gradual linear increase of airway pressure without exception. That is, the baseline measurement of uncovered pleural defects in the present model shows bursting pressure of 6 $cmH_2O$ without exception. Since each covering procedure needs static status of expanded lungs and cannot be undertaken with ongoing air leak, expanded lungs with the airway pressure of 6 $cmH_2O$ should be the necessary baseline status. Video 1 was added for better comprehension, that demonstrates the air leak status from the uncovered pleural defect along with gradual increase of airway pressure. The following sentences were also added in Page 8, Line 118-123 (highlighted portion): - by one operator through both the previous [10] and the present study with minimal variance. This standardized pleural defect almost constantly has minimal air leak, with lung blocks expanded with an airway pressure of 6 $cmH_2O$. As soon as the pressure increases beyond 6 $cmH_2O$, air leakage from the pleural defect begins and increases more and more vigorously according to a gradual linear increase in airway pressure without exception.

e. Was any form of randomization or allocation concealment used, to prevent influences of biological variability of the lesion/lesion locations on the lung?

Reply and changes in the text (highlighted portion):
As explained by the added following sentences in Page 8, Line 118-123 (highlighted portion), the biological variability of the lesion (pleural defect) seems so small: - by one operator through both the previous [10] and the present study with minimal

variance. This standardized pleural defect almost constantly has minimal air leak, with lung blocks expanded with an airway pressure of 6 $cmH_2O$. As soon as the pressure increases beyond 6 $cmH_2O$, air leakage from the pleural defect begins and increases more and more vigorously according to a gradual linear increase in airway pressure without exception. Also, as explained in Page 8, Line 114-116 (Two pleural defects created per lung in the upper and lower lobes and four pleural defects per heart–lung block were used in the experiment. ), variability of lesion locations on the lung is minimal. Then, any form of randomization or allocation concealment was not used in the present study.

f. Two lesions are created per lung with the contralateral bronchus clamped. How was ensured that pressure drop in one of the lesions after bursting did not influence the other lesion?

Reply:
When the amount of air leak from the first defect site was relatively large and the pressure increase was negatively affected in the sealing experiment for the second defect, the hilum of the lung proximal to the first defect site was partially clamped using clamping devices, and the air leak was controlled. Such changes in intra-airway pressure were monitored using a digital manometer with a graphical display that demonstrated sequential pressure changes over time.

Changes in the text (highlighted portion):
To Page 9-10, Line 137-141, the following sentences were added: When the amount of air leak from the first defect site was relatively large and the pressure increase was negatively affected in the sealing experiment for the second defect, the hilum of the lung proximal to the first defect site was partially clamped using clamping devices, and the air leak was controlled.

g. Can the author comment on the application methods for TachoSil? I noted that pressure was only applied for 20s, while the instructions for use state 3-5min of pressure should be applied. Could we expect higher pressure resistance values with longer application time?

Reply:
In the experimental procedure, pressure was applied for 3 min immediately after the attachment of TachoSil until its collagen fleece became flat with gelatin-like change and tightly attached to the defect. The author re-checked the video and photo records this time and confirmed the above. We apologize for this mistake.
Changes in the text:
The sentence in Page 8, Line 129-132 as the following: In Groups 7 and 8, in which the TachoSil® sheet was used, the entire sheet was gently compressed to the lung using gauze for 20 sec immediately after the attachment of the sheet and kept at rest for 5 min, was corrected as the following (highlighted portion): In Groups 7 and 8, in

which the TachoSil® sheet was used, the entire sheet was gently compressed onto the lung using gauze for 3 min immediately after the attachment of the sheet and kept at rest for 5 min.

h. I am not too familiar with the Steel-Dwass post-hoc test after Kruskal-Wallis test across groups. Did you test across all possible combinations amongst the nine groups (so n=36 comparisons)? Or are the P-values shown in the graphs the only pairwise comparisons that were done?

Reply:
It is too complex and invalid to compare all nine groups simultaneously. The Kruskal-Wallis test with the Steel-Dwass post-hoc test was applied only within each experiment 1, 2, and 3. The statistical assessment in the present study was supervised and approved by the biostatistician Hiroshi Takahashi, BSc.

2. Discussion
a. Some concerns may be raised regarding the translatability of the findings, which the authors also point out, namely testing on linear pressure increase in contrast to cyclic ventilation cycles. Furthermore, results may not translate accordingly due to differences between patients and healthy porcine lungs, as demonstrated in the study by Gika et. al. (for reference: Masatoshi Gika and others, The short-term efficacy of fibrin glue combined with absorptive sheet material in visceral pleural defect repair, Interactive CardioVascular and Thoracic Surgery, Volume 6, Issue 1, February 2007, Pages 12–15). So, findings should be validated in models more closely resembling clinical practice (which could be a follow up study to the present paper).

Reply and Changes in the text (highlighted portion):
Regarding the testing of the linear pressure increase in contrast to the cyclic ventilation cycles, the following remarks have been added to “4.2 Strengths and limitations section in 4. Discussion”, Page 18, Line 293-304: In routine lung surgery, however, intraoperative air leak tests (sealing tests) are usually performed by sustaining a higher intra-airway pressure that is manually increased by anesthesiologists as the lung expands. If a small air leak is detected, it is completely controlled using meticulous mattress sutures and repeated air leak tests. Lung coverage with a bioabsorbable sheet and fibrin sealant is then added to these sites to prevent relapsing air leaks postoperatively. The author has adopted such “Zero leak policy” that never permits any small air leak persisting at the end of surgery. In this scenario, all patients who undergo lung resection have no postoperative air leak, and their chest tubes are removed within three days. Therefore, the experimental protocol of the present study to measure seal-breaking burst pressure along with a progressive linear increase in airway pressure might be clinically relevant, along with such “Zero leak policy”.
In the above study, a time-serial in vivo assessment of air leak amount was performed at multiple time points up to 24 h after coverage application. Regarding the appropriateness of multiple or single time points of measurement, the author added the

following remarks to Page 19, Line 305-312: This study is based on the above-mentioned “Zero leak policy” in clinical lung surgery practice, and its essential objectives do not focus on observing the in vivo time-serial process of persistent air leaks during or after surgery but on elucidating the pin-point minimum research question in which bioabsorbable sheets have higher SBBP and are optimal for combined application with fibrin sealant against alveolar air leakage. In this sense, measurements at a single time point in the protocol of the present study are clinically relevant.

Further, regarding the validity of using normal swine lungs in the present study instead of morbid lungs, author added the following remarks to Page 20, Line 318-325: With “Zero leak policy” the first choice of air leak control is meticulous mattress suture, and then repeated leak tests and coverage with bioabsorbable sheet and fibrin sealant on to the sutured site where air leak is completely controlled. Although air leak control in morbid lungs is generally more difficult, such basic handling of air leaks is not different between normal and morbid lungs. Considering that air leak control only by combined coverage with bioabsorbable sheet and fibrin sealant is not aimed in the above “Zero leak policy”, experiments using morbid lung model may not be mandatory.

b. Were any air leak measurements taken, to show air leak and air leak reduction effectiveness of the sealants? This outcome measure might be of more clinical relevance, for instance during measurements of air leak intraoperatively using the mechanical ventilator or postoperatively using digital chest drains. Maybe the author can elaborate on this in the discussion.

Reply:
Author added the following remarks to Page 19, Line 305-312 (the same response as the above comments 2-a of Reviewer E): This study is based on the above-mentioned “Zero leak policy” in clinical lung surgery practice, and its essential objectives do not focus on observing the in vivo time-serial process of persistent air leaks during or after surgery but on elucidating the pin-point minimum research question in which bioabsorbable sheets have higher SBBP and are optimal for combined application with fibrin sealant against alveolar air leakage. In this sense, measurements at a single time point in the protocol of the present study are clinically relevant.

3. The author may consider several suggestions regarding the style of the manuscript:
a. Photograph of the created lung lesions on the porcine lung; photograph of the applied sealing technique.

Reply:
A Video including the creation of a pleural defect and vigorous air leak from the uncovered pleural defect have been added as Video1 as follows (Page 8-9, Line 121-123): As soon as the pressure increases beyond 6 $cmH_2O$, air leakage from the pleural defect begins and increases more and more vigorously according to a gradual linear increase in airway pressure without exception (Video 1).

The photograph of the applied sealing technique of each group was added as Fig. 2 as follows (Page Line 13-14, 210-211): A macroscopic photograph of the sealing technique applied to each group in all the experiments is shown in Fig. 2.

b. Overview table of the relevant statistical comparisons done.

Reply and Changes in the text (highlighted portion):
Table 2 has been added to the revised manuscript as follows (Page 16, Line 252-253): The SBBP (mean ± standard deviation; mmHg) of each group in all experiments is summarized in Table 2.

Table 2. SBBP of each Group

SBBP: Seal-breaking burst pressure

c. Reducing the amount of graphs and ensuring one or two graphs which present the main findings.

Reply and Changes in the text (highlighted portion):

| Groups | Sheet | SBBP (mmHg) |
|---|---|---|
| 1 (PGA0.15) | 0.15 mm-PGA felt | 57.1 ± 20 |
| 2 (PGA0.3) | 0.3 mm-PGA felt | 37.7 ± 11 |
| 3 ( PGA0.5) | 0.5 mm-PGA felt | 24.9 ± 4.5 |
| 4 (ORC) | ORC sheet | 17.0 ± 2.8 |
| 5 (W-PGA0.11) | Vicryl Mesh Woven | 30.9 ± 10 |
| 6 (K-PGA0.18) | Vicryl Mesh Knitted | 47.6 ± 12 |
| 7 (TachoSil) | TachoSil | 22.6 ± 3.1 |
| 8 (FS+TachoSil) | Fibrin sealant + TachoSil | 48.5 ± 12 |
| 9 (1p-PGA0.15) | 0.15 mm-Neoveil (1 piece) | 49.2 ± 16 |

According to the reviewer's suggestion, three graphs (Fig. 2, Fig. 3, and Fig. 4), which

are the main findings of this study, were combined into the new Fig. 3, and named as 3A, 3B, and 3C, respectively. One graph (Fig. 5) was omitted, and Fig. 6 was renamed as Fig. 4.

I am looking forward to your response and further considerations. Thank you for your efforts.

**Reviewer F**

This study details the treatment of pulmonary fistulas that occur during surgery in patients with lung cancer.

However, I believe the following points need further consideration.

1) Consideration has been given to air leak after lung cancer surgery. It is unclear whether it assumes air leakage from the interlobar pleura, which is a problem in actual clinical practice, or from the interlobar surface at the time of zonectomy. Considering the experimental system, is air leak from the pleural defects that may occur when the lung is grasped? This would need to be clearly stated.

Reply and Changes in the text (highlighted portion):
To the section of 1 Introduction, 1. 1 Background (Page 5-6, Line 69-78), the following remarks were added: In routine lung surgery, thoracic surgeons usually encounter air leaks from several sources in the lungs, such as (1) pleural defects, (2) lung parenchymal lacerations, (3) raw parenchymal stumps, and (4) stapled or sutured lines. The author adopts “Zero leak policy” that requires complete air leak control at the end of surgery. Meticulous mattress sutures with pledgets are frequently used as the first choice for controlling air leaks from the above sources, followed by repeated leak tests, and the sutured site is further reinforced by coverage with bioabsorbable sheet and fibrin sealant after almost complete control of air leaks. The experimental model of the previous [10] and the present study was determined to bear such a scenario in mind.

2) In patients with firm lung parenchyma, prolonged postoperative air leaks are rare. Rather, postoperative air leaks are often difficult to treat in cases of emphysema or pulmonary fibrosis. Therefore, it is important to consider the extent to which the findings of this study can be applied to cases of emphysema and pulmonary fibrosis from experimental results.

Reply:
Undoubtedly, morbid lungs, such as emphysema, interstitial lung disease, or a combination of both, are encountered much more frequently than normal lungs in routine lung surgery. Because air leak control in morbid lungs is difficult, the optimal methods determined in the present study are considered. Regarding the validity of using normal swine lungs instead morbid lung model in the present study, author added the

following remarks to Page 20, Line 318-325 (the same as the above reply to Comment 2-a of Reviewer E): With “Zero leak policy” the first choice of air leak control is meticulous mattress suture, and then repeated leak tests and coverage with bioabsorbable sheet and fibrin sealant on to the sutured site where air leak is completely controlled. Although air leak control in morbid lungs is generally more difficult, such basic handling of air leaks is not different between normal and morbid lungs. Considering that air leak control only by combined coverage with bioabsorbable sheet and fibrin sealant is not aimed in the above “Zero leak policy”, experiments using morbid lung model may not be mandatory.

3) In any case, there are ongoing studies from Reference 10 that indicate that the use of 0.15 mm Neoveil sheet in the Rub+Soak B method may be effective in treating air leaks that occur during lung cancer surgery. This is a very instructive and informative paper.

Reply:
Author appreciates the comment.