Difference in the Yields of Bronchial Washing Cytology before and after Forceps Biopsy for Lung Cancer Diagnosis

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Objectives: Fiberoptic bronchoscopy (FOB) has been one of the essential procedures used in the diagnosis of lung cancer. Diagnostic yields of FOB related procedures such as bronchial washing (BW), bronchial brushing (BB), and transbronchial biopsy (TBBx) depend on the location and extent of the tumors. The yields of BW vary among different studies (39-79%). Some reported that the yield might increase in post-bronchoscopic sputum. Since samples from BW are obtained directly from the respiratory tract, we hypothesized that post bronchoscopic forceps biopsy BW might further increase the yield as well. The objective of this study was to compare the diagnostic yields of bronchial washing before and after forceps biopsy for lung cancer.

Material and Method: 114 patients, 70 with endobronchial lesions (42 exophytic lesions, 28 submucosal lesions) and 44 with non-endobronchial lesions, suspected to have lung cancers were evaluated at Siriraj Hospital between March and October 2000. All the patients underwent FOB with initial BW then forceps biopsy (BBx or TBBx) of the lesions followed by re-BW. The cytological specimens were blinded to the cytopathologists. Positive cytologic results of each procedural specimen were compared to final malignancy diagnosis (by positive specimens from FOB, transthoracic needle aspiration, surgery, clinical and radiological follow-up) to determine the sensitivity of each test.

Statistical analysis: Chi-square test comparing sensitivity of each test.

Results: 82/114 patients (39 patients had exophytic lesions, 24 patients had submucosal lesions, and 19 patients had peripheral lung lesions) had a final diagnosis of malignancy. The sensitivity of initial BW before forceps biopsy was 37.8% (31/82), re-BW after forceps biopsy was 37.8% (31/82), both initial BW and re-BW was 46.3% (38/82), and forceps biopsy alone was 79.3% (65/82). There was no statistically significant difference (p>0.05) in the sensitivity of initial BW, re-BW and combined initial BW and re-BW. No major complications such as massive hemorrhage, respiratory failure, or death occurred.

Conclusion: The diagnostic yields of BW before and after forceps biopsy for malignancy were not different in our study. However, the yield seemed to be higher when combined pre and post-forceps biopsy BW was used.

Keywords: Bronchial washing, Cytology, Forceps biopsy, Transbronchial biopsy, Bronchoscopy, Lung cancer, Diagnostic yields

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Fiberoptic bronchoscopy (FOB) is widely used to diagnose primary and metastatic lung cancers. Various bronchoscopic related procedures, including bronchial biopsy (BBx), transbronchial biopsy (TBBx), needle aspiration for cytology, bronchial washing (BW), or bronchial brushing (BB) aid in the diagnosis. How-
From the 114 patients who participated in the study, the one who did not have a definite diagnosis from the procedures above went on to have transthoracic needle aspiration for cytology and/or surgery. Only a few patients had clinical evidence of metastatic diseases upon follow up.

The sensitivity of each BW procedure is the proportion of the number of specimens having malignant cytology diagnosis compared to the total number of specimens with a definite diagnosis of malignancy. The sensitivity of the biopsy procedure is the proportion of the number of malignant histology diagnosis specimens compared to the total number of specimens with definite diagnosis of malignancy.

**Statistical analysis**

Chi-square test and McNemar’s test were used to compare the sensitivity of each procedure. A value of \( p <0.05 \) was considered statistically significant.

**Results**

114 patients, 71 male and 43 female, aged 23-88 years old (mean \( \pm \)SD = 58±10.2) had final diagnoses from various procedures (FOB related procedures, open lung biopsy or lung resection, tissue biopsy of metastatic site). Of these 114 patients, 82 had diagnoses of malignancy, 22 had tuberculosis, one had aspergilloma, one had leiomyoma, and eight had benign conditions such as pneumonia, bronchiectasis or interstitial lung disease as shown in Table 1. The most common CXR findings were lung masses 52.6% (60/114). The rest were interstitial infiltration 16.7% (19/114), atelectasis 11.4% (13/114) and hilar mass 8.8% (10/114) respectively as shown in Table 2.

In the group of 82 patients with final diagnoses of malignancy, 39 patients had exophytic lesion, 24 patients had submucosal lesion and 19 patients had non-endobronchial lesion, see Fig. 1. These diagnoses were made from bronchial washing in nine patients, from forceps biopsy in 38

<table>
<thead>
<tr>
<th>Other diagnoses</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycobacterial infection</td>
<td>22</td>
</tr>
<tr>
<td>Aspergilloma</td>
<td>1</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>4</td>
</tr>
<tr>
<td>Interstitial lung diseases</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>1</td>
</tr>
</tbody>
</table>

**Material and Method**

We enrolled 114 patients who were suspected of having lung cancer. They underwent FOB at the Division of Respiratory Disease and Tuberculosis, Siriraj Hospital between March 1 and October 31, 2000. We excluded patients with contraindications for FOB such as coagulopathy, uncooperativeness, or the patients who did not consent to participate in the study. All the patients underwent FOB (using 2% Lidocaine as a topical anesthetic agent) according to the following procedure: Initial BW pre-forceps biopsy followed by 2-4 times of bronchial biopsy for cases with visualized endobronchial lesions (both exophytic and submucosal infiltration) and transbronchial biopsy for cases with non-visualized lesions (non-endobronchial lesion) and then repeated BW post forceps-biopsy. The transbronchial biopsy was done without fluoroscopy. The amount of 0.9% saline instilled for BW was not limited each time but at least 15 milliliters (ml) of returned BW fluid was required for each specimen. The BW fluid was sent for cytological examination and microbial culture (aerobic bacteria, mycobacteria and fungus). The biopsy tissue was sent for histological examination. We recorded the amount of bleeding, color of returned BW fluid and complications of the procedures such as pneumothorax, hypoxemia, arrhythmia, etc.

Only two pathologists reviewed the cytological and histological specimens. They were both blinded to the pre and post-forceps biopsy BW specimens. The cytological results were classified as positive for malignancy only when the results were read as “suspicious for malignancy” or as “malignancy”, the other readings were considered negative for malignancy.

From the 114 patients who participated in the study, the one who did not have a definite diagnosis from the procedures above went on to have transthoracic needle aspiration for cytology and/or surgery. Only a few patients had clinical evidence of metastatic diseases upon follow up.

The sensitivity of each BW procedure is the proportion of the number of specimens having malignant cytology diagnosis compared to the total number of specimens with a definite diagnosis of malignancy. The sensitivity of the biopsy procedure is the proportion of the number of malignant histology diagnosis specimens compared to the total number of specimens with definite diagnosis of malignancy.

**Statistical analysis**

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**Results**

114 patients, 71 male and 43 female, aged 23-88 years old (mean \( \pm \)SD = 58±10.2) had final diagnoses from various procedures (FOB related procedures, open lung biopsy or lung resection, tissue biopsy of metastatic site). Of these 114 patients, 82 had diagnoses of malignancy, 22 had tuberculosis, one had aspergilloma, one had leiomyoma, and eight had benign conditions such as pneumonia, bronchiectasis or interstitial lung disease as shown in Table 1. The most common CXR findings were lung masses 52.6% (60/114). The rest were interstitial infiltration 16.7% (19/114), atelectasis 11.4% (13/114) and hilar mass 8.8% (10/114) respectively as shown in Table 2.

In the group of 82 patients with final diagnoses of malignancy, 39 patients had exophytic lesion, 24 patients had submucosal lesion and 19 patients had non-endobronchial lesion, see Fig. 1. These diagnoses were made from bronchial washing in nine patients, from forceps biopsy in 38
patients, from both bronchial washing and forceps biopsy in 29 patients, from transthoracic needle biopsy in two patients, from surgery in three patients and by clinical evidence of malignancy upon follow up in only one patient. The overall sources of positive diagnosis of lung cancer are shown in Table 3.

The sensitivity of BW pre-forceps biopsy alone was 37.8% (31/82). The sensitivity of BW post-forceps biopsy was 37.8% (31/82); note that the members of this group were not all the same as the members of the pre-forceps biopsy group, Fig. 2. For the combined pre and post-forceps biopsy results, the sensitivity of BW was 46.3% (38/82). For the group that had only forceps biopsy, the sensitivity was up to 79.3% (65/82). When we combined the positive pre-forceps biopsy BW, positive post-forceps biopsy BW and the positive forceps biopsy groups together, the sensitivity increased to as high as 90.2% (74/82) as shown in Table 4.

We found no statistically significant difference (p>0.05) between the sensitivity of positive BW for pre and post-forceps biopsy (McNemar’s test). This finding was also the same when the results were analyzed according to different lesion characteristics (exophytic (p=0.08), submucosal (p=0.10) or non-endobronchial (p=0.25)) as shown in Fig. 3.

We also analyzed the color of BW fluid post-forceps biopsy and the amount of instilled fluid for BW since these factors might have influenced the cytological results. The color of post-forceps biopsy BW fluid was divided into three groups: turbid, serosanguinous and bloody in color. In the turbid-colored

Table 2. Demographic data and CXR findings

<table>
<thead>
<tr>
<th>Demographic data (N = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>(Mean±SD = 58±10.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CXR findings</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung mass</td>
<td>60 (52.6)</td>
</tr>
<tr>
<td>Interstitial infiltrate</td>
<td>19 (16.7)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>13 (11.4)</td>
</tr>
<tr>
<td>Hilar mass</td>
<td>10 (8.8)</td>
</tr>
<tr>
<td>Lung nodule</td>
<td>6 (5.3)</td>
</tr>
<tr>
<td>Alveolar infiltration</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Normal</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Effusion</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>
group, 6.4% (2/31) of these specimens had positive cytology for malignancy and 15.6% (13/83) were negative for malignancy. In the serosanguinous group, 83.9% (26/31) were positive for malignancy and 69.9% (58/83) were negative for malignancy. In the bloody group, 9.7% (3/31) were positive for malignancy and 14.5% (12/83) were negative for malignancy. There was no statistically significant difference between the groups (p>0.05) as shown in Fig. 4. The amount of instilled fluid for BW was also analyzed as shown in Fig. 5. There was no significant difference in positive or negative cytology for malignancy among the groups that used small (21-44 ml) (p=0.11), moderate (41-60 ml) (p=0.13) or large (>60 ml) (p=0.11) amount of instilled fluid either.

The use of different bronchoscopists may have played a role in the different sensitivity of each procedure\(^7\). There were seven bronchoscopists involved in this study, and there was no significant difference in positive or negative cytology for malignancy among the groups that used small (21-44 ml) (p=0.11), moderate (41-60 ml) (p=0.13) or large (>60 ml) (p=0.11) amount of instilled fluid either.

In our study, no severe complications such as severe hypoxemia, respiratory failure, massive bleed-

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**Table 3.** Final diagnosis of malignancy by procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Exophytic Lesion</th>
<th>Submucosa lesion</th>
<th>Non-endobronchial lesion</th>
<th>Total N=82</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>-BW pre-forceps biopsy</td>
<td>17</td>
<td>43.6</td>
<td>7</td>
<td>36.8</td>
</tr>
<tr>
<td>-BW post-forceps biopsy</td>
<td>14</td>
<td>35.9</td>
<td>7</td>
<td>37.5</td>
</tr>
<tr>
<td>-BW pre+post-forceps biopsy</td>
<td>20</td>
<td>51.3</td>
<td>10</td>
<td>41.7</td>
</tr>
<tr>
<td>-Forceps biopsy</td>
<td>35</td>
<td>89.7</td>
<td>21</td>
<td>87.5</td>
</tr>
<tr>
<td>-BW pre+post-forceps biopsy + forceps biopsy</td>
<td>38</td>
<td>97.4</td>
<td>23</td>
<td>95.8</td>
</tr>
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**Table 4.** Sensitivity of each procedure among different types of lesions

<table>
<thead>
<tr>
<th>Procedures</th>
<th>N</th>
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<tbody>
<tr>
<td>BW only</td>
<td>9</td>
</tr>
<tr>
<td>BX only (TBBx, BBx)</td>
<td>38</td>
</tr>
<tr>
<td>BW + BX</td>
<td>29</td>
</tr>
<tr>
<td>FNA</td>
<td>2</td>
</tr>
<tr>
<td>Surgery</td>
<td>3</td>
</tr>
<tr>
<td>Clinical evidence of metastasis disease</td>
<td>1</td>
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</tbody>
</table>

Fig. 2  Sensitivity of bronchial washing (BW)
Fig. 3  Sensitivity of pre and post-biopsy bronchial washing (BW) per lesion characteristics

Fig. 4  Color of BW fluid after forceps biopsy VS cytologic result
Table 5. Different bronchoscopists and Cytologic yields

<table>
<thead>
<tr>
<th>Bronchoscopists</th>
<th>Positive Cytology</th>
<th>Negative Cytology</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>1</td>
<td>12 (46.2)</td>
<td>14 (53.8)</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>2 (18.2)</td>
<td>9 (81.8)</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>7 (41.2)</td>
<td>10 (58.8)</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>8 (66.7)</td>
<td>4 (33.3)</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>4 (57.1)</td>
<td>3 (42.8)</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>0 (0)</td>
<td>3 (100.0)</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>4 (66.7)</td>
<td>2 (33.3)</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 6. Sensitivity of BW and Bx among different studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Endobronchial</th>
<th>Non-endobronchial</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Bx (%)</td>
<td>BW (%)</td>
</tr>
<tr>
<td>Chaudhary 1978(8)</td>
<td>95</td>
<td>78.8</td>
<td>77.9</td>
</tr>
<tr>
<td>Lundgren 1983(9)</td>
<td>47</td>
<td>80.9</td>
<td>46.8</td>
</tr>
<tr>
<td>Popp 1991(10)</td>
<td>99</td>
<td>92.9</td>
<td></td>
</tr>
<tr>
<td>Mak 1996(11)</td>
<td>125</td>
<td>76</td>
<td>49.6</td>
</tr>
<tr>
<td>Govert 1996(12)</td>
<td>177</td>
<td>80.8</td>
<td>42.9</td>
</tr>
<tr>
<td>Rosell 1998(13)</td>
<td>82</td>
<td>58.5</td>
<td>39.2</td>
</tr>
<tr>
<td>The present study (pre)</td>
<td>63</td>
<td>88.9</td>
<td>38.0</td>
</tr>
<tr>
<td>(post)</td>
<td></td>
<td>36.5</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 5. Amount of instilled fluid for BW VS cytologic result
ing or death occurred. Only one patient in our study who had a peripheral non-endobronchial lesion had pneumothorax post transbronchial lung biopsy.

Discussion

The sensitivity of BW for diagnosis of malignancy varied from 39-79% as shown in Table 6. Most of the malignancies were from endobronchial lesions. Only a few studies have been done to test the sensitivity of BW from non-endobronchial lesions. None of the studies has explored the sensitivity of pre and post-forceps biopsy BW. Very few studies reported a sensitivity increase in post bronchoscopy sputum and one reported an increased yield in bronchial biopsy rinsed fluid cytology.

The sensitivity of BW (either pre or post-forceps biopsy) in our study was 37.8%, which was not much different from the results of previous studies. The wide range of the sensitivity might be from the use of different techniques, different study populations, and different criteria for the cytological diagnosis of malignancy (some studies included “atypia” as part of malignancy).

In our study, we could not demonstrate a statistically significant difference in the sensitivity between pre and post-forceps biopsy BW regardless of the lesion characteristics (endobronchial or non-endobronchial lesions). This may be due to the small sample size used in this study. Nevertheless, we found a higher sensitivity for malignancy diagnosis when combined pre and post-forceps biopsy BW (46.3%) was used than when each of these procedures was used exclusively, though it was not statistically different. We also found that there were a few cases where the malignancy diagnosis could be demonstrated only from BW, either pre or post-forceps biopsy, but not from biopsy alone. This suggests that BW is helpful and should not be disregarded in assisting the diagnosis of malignancy using FOB.

Interestingly, in the non-endobronchial lesion subgroup analysis, we found higher sensitivity from post-forceps biopsy BW (42.1%), which was very close to the sensitivity of biopsies (47.4%), as compared to a lower sensitivity from pre-forceps biopsy BW (36.8%). This data may suggest that post-forceps biopsy BW may give a higher sensitivity than pre-forceps biopsy BW even though we could not demonstrate that there was a statistically significant difference.

Other factors that may influence the cytological results such as the color of BW fluid, the amount of instilled fluid in each washing and the use of different bronchoscopists was analyzed in this study. For the BW fluid color, most of the specimens were serosanguinous, the rest were turbid or bloody. The number of specimens with positive cytology for malignancy was not different from the number with negative cytology disregarding the color of the BW. The amount of blood in the BW fluid did not seem to interfere with the cytological readings. As for the fluid instilled for each BW, we found that the numbers of specimens with positive cytology were not different from the ones with negative cytology among the groups that used a small, moderate or large amount of instilled fluid. We did not find there was a statistically significant difference in the sensitivity of BW as performed by different bronchoscopists either.

We had no serious complications such as massive hemoptysis, respiratory failure, and severe hypoxemia in our study despite the longer duration of procedures using two BW. The only complication we had was pneumothorax from TBBx in a non-endobronchial case.

The advantages of our study were that both pre and post-forceps biopsy BW were from the same location, from the same patient, performed by the same bronchoscopist, on the same day. This reduced subject variability. However, a limitation of this study was the use of a small sample size.

From our study results, we found increased sensitivity of combined pre and post-forceps biopsy BW cytology compared to using either one exclusively. This may be a useful guide for improving the sensitivity of bronchoscopic methods for use in the diagnosis of lung cancer. Our future study plan is to evaluate the sensitivity of the combined pre and post-forceps biopsy BW fluid for diagnosis of lung cancer in a larger population.

References

ความแตกต่างของผลการวิจัยยังมีเรื่องแปลกโดยการตรวจเครื่องจากน้ำสั้น hồคลองก่อนและหลังการตัดชิ้นเนื้อปลอดผ่านทางกั้นส่องห้องคลอง

สุรีย์ สมประดิษฐ์, อุปนายิน เชนเวชกิจวานิชย์, ปานเทพ สุทธินนท์, สัมฤทธิ์ วงศ์บุญนนท์

วัตถุประสงค์: การส่องกล้องของหลอดรวมกับการตัดเครื่องที่เกี่ยวกับการตรวจกล้อง การตัดชิ้นเนื้อสั้น สุรีย์ สมประดิษฐ์ นำไปตรวจสอบวิจัยแล้วพบว่ามีนักเรียน 39 ถึง 79 คนเก็บตัวแทนและจำแนกกระจายตามที่อยู่ ได้ น้ำสั้นของหลอดรวมกับได้โดยตรงจากการส่องกล้องไม่ตอบสนองหลอดรวมที่มีความผิดปกติ อาจทำให้ผลการตรวจเพิ่มขึ้นโดยเฉพาะหลังการตัดชิ้นเนื้ออาการที่ไม่มีการหลอดคลองของหลอดรวมกับนักเรียน 39 คนมีความผิดปกติ อาจทำให้ผลการตรวจชิ้นเนื้อปลอดผ่านทางกั้นส่องห้องคลอง บริเวณที่มีการวิจัยชี้แจงโดยการส่องกล้องก่อนและหลังการตัดชิ้นเนื้อ

วัสดุและวิธีการ: ผู้ป่วยกลุ่มเล็กต่อการเป็นเรื่องสูงที่บุญกษัตริยะในบุญคุณวัน 114 คนได้รับการตรวจส่องกล้องของหลอดรวม ณ โรงพยาบาลราชวิถี ระหว่างเดือนมีนาคมถึงสิงหาคม พ.ศ. 2543 ในจำนวนนี้ผู้ป่วย 70 คนมีความผิดปกติในหลอดรวม โดยเป็นกลุ่ม 42 คน และมีความผิดปกติในหลอดรวม 28 คน ผู้ป่วย 44 คนมีเกินในเนื้อปลอก ผู้ป่วยเหล่านี้ได้รับการตรวจส่องกล้องของหลอดรวมและเก็บตัวอย่างบุญคุณวัน 39 คนตัวอย่างเนื้อปลอกที่มีเป็นแคลียร์ซึ่งมีการตรวจวิเคราะห์ในกลุ่มที่ต่างกันที่มีการรับผิดชอบกับผลการวิจัยและมีเรื่องบุญคุณวันสูง ด้วยวิธีดังต่อไปนี้

การวิเคราะห์ทางสถิติ: ใช้ Chi-square test

ผลการศึกษา: ผู้ป่วย 82 คนจาก 114 คนได้รับการวิเคราะห์เนื้อปลอก โดยมีเกินในหลอดรวม 39 คน มีเกินในหลอดรวม 24 คน มีเกินในหลอดรวม 15 คน มีเกินในชั้นเนื้อปลอก 19 คน การตรวจของหลอดเดิมจากการส่องกล้องก่อนการตัดชิ้นเนื้อปลอกมีความไว้ระคับ 37.8 การตรวจเครื่องจากน้ำสั้นต่ำลงหลอดเดิมจากการตัดชิ้นเนื้อปลอกมีความไว้ระคับ 79.3 การตรวจเครื่องจากน้ำสั้นที่เก็บตัวอย่างบุญคุณวันมีความไว้ระคับ 46.3 การตัดชิ้นเนื้อจากเนื้อปลอกหลอดรวมมีความไว้ระคับ 79.3 อีกตัวการตรวจเครื่องแบบชี้แจงโดยการตรวจของหลอดเดิมจากการส่องกล้องก่อนและหลังการตัดชิ้นเนื้อปลอกมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในแบบปัญหานครสะเทือน เช่น ปีติออกแบบ การระยะที่ทำให้ชี้แจงวิธีในการศึกษา

สรุป: การตรวจของหลอดน้ำสั้นหลอดรวมก่อนหรือหลังการตัดชิ้นเนื้อปลอกได้ชี้ว่าการตรวจเครื่องแบบชี้แจงโดยไม่แตกต่างกันแต่เฉพาะของการตรวจเครื่องน้ำสั้นหลอดรวมก่อนและหลังการตัดชิ้นเนื้อปลอกให้ชี้ว่าการวิเคราะห์เนื้อปลอกเพิ่มขึ้น