

Novel Asymmetrical Linear Stapler (NALS) for pathologic evaluation of true resection margin tissue

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Background: The use of limited resection for lung cancer has increased with the accumulation of knowledge about early lung cancer. To decrease locoregional recurrence after a limited resection, it is important to confirm R0 resection at the true resection margin. In this study, we report a novel linear stapler that preserves the true resection margin tissue after organ resection.

Methods: We used a Novel Asymmetrical Linear Stapler (NALS) made by Meditlip. On the resected organ side of NALS, there is a single row of titanium fasteners. To verify the utility of NALS and to compare its preservation of the resection margin tissue to a conventional stapler, we performed wedge resection of the lung in a porcine animal model and examined the pathology of the true resection margin.

Results: Using NALS, we successfully divided and closed the lung tissues, as with the conventional stapler. There was no bleeding on either side or no air leakage from the remnant stapled tissue. The distance between the cutting edge and the titanium fasteners was 3.10 mm with NALS, which was sufficient to resect the true resection margin tissue for pathology evaluation. There was no squeezing artifact at the true resection margin on microscopic evaluation with NALS. With the conventional stapler, it is difficult to evaluate the pathology at the true resection margin due to the severe squeezing artifact.

Conclusions: NALS preserves the true resection margin tissue and thus should be useful for evaluating the resection margin with a frozen section biopsy in oncology surgery.

Keywords: Non-small cell lung cancer (NSCLC); limited resection; resection margin; surgical stapler

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Introduction

Surgical resection is the standard treatment for resectable non-small cell lung cancer (NSCLC). The extent of resection has gradually decreased as studies on surgery for lung cancer have accumulated. In the 1950s, the standard resection for lung cancer was a pneumonectomy. In 1960, Cahalan successfully performed a lobectomy with regional lymph node dissection in 48 cases (1). Subsequently,

lobectomy was universally accepted and became the standard surgery for lung cancer. However, some patients who had poor pulmonary function required a wedge resection or segmentectomy, i.e., a limited resection, for small peripheral lung cancers (2,3). Limited resection for peripheral early lung cancer was performed not only in patients with poor pulmonary function but also in patients with normal pulmonary function (4,5). In 1995, the Lung Cancer Study Group reported a randomized trial of limited resection for



Figure 1 The novel asymmetrical linear stapler used for evaluating pathology.

T1N0 stage NSCLC that compared limited resection with a lobectomy, and concluded that locoregional recurrence increased after a limited resection (6). However, this result was confounded by several factors. About 25% of the patients had squamous cell carcinoma and the characteristics of the tumors and distance between the resection margin and tumor were not reported. Consequently, limited resection continued to be studied and performed for early NSCLC, particularly tumors smaller than 2 cm (7-12).

The development of chest computed tomography (CT) resulted in the increased diagnosis of ground glass nodules (GGNs) (13). The GGNs in a thin section in chest CTs are generally correlated with clinical features (14). In 2011, the Japan Clinical Oncology Group reported that the specificity for noninvasiveness is 98.7% in adenocarcinoma ≤ 2.0 cm with a consolidations/tumor (C/T) ratio ≤ 0.25 (15). By contrast, a prospective multicenter study reported that pure GGNs and heterogeneous GGNs do not develop into invasive adenocarcinoma within a mean follow-up duration of 4.3 years (16). Based on these findings, limited resection is generally accepted for GGNs ≤ 2 cm with a C/T ratio ≤ 0.25 .

To decrease locoregional recurrence after a limited resection, it is important to confirm that there are no malignant cells in the resection margin. The conventional triple row stapler does not provide intact resection margin tissue for frozen section biopsy due to the tissue damage caused by the titanium fastener. To examine the pathology, the staples in the resection margin must be removed. However, the resection margin tissues are damaged by the stapler itself in almost all cases, which results in profound difficulty with the pathology examination. To resolve this problem, a stapler that preserves the resection margin is required for more accurate cancer surgery.

In this study, we report a new type of linear stapler that preserves the true resection margin tissue after an organ resection. We evaluated its feasibility and accuracy for

assessing true resection margins.

Methods

Novel Asymmetrical Linear Stapler (NALS) for resection margin evaluation

Meditulip (Osong, South Korea) recently developed a NALS for evaluating the resection margin (Figure 1). A conventional linear stapler has two or three symmetrical rows of titanium fasteners on either side of the resection, and a cutter for organ resection between the rows of titanium fasteners. In comparison, NALS has an asymmetrical structure. Figure 2 shows a cross-sectional view of NALS, demonstrating its mechanism. The three rows of titanium fasteners on the remnant organ side are the same as with a conventional linear stapler. These three rows of fasteners close the remnant side tissues securely. In comparison, on the resected organ side, there is a single row of titanium fasteners located farthest from the endocutter in the stapler device. With this design, the stapler can provide tissue for a frozen section biopsy at the true resection margin, without the titanium fasteners injuring the tissue. NALS also has a tissue stabilizer (the blue material in Figure 2) that presses the true resection margin tissue to protect the tissue from the forward force of the cutter during firing.

Porcine animal model and operating procedure

A 6-month-old female Korean native black pig was prepared for the procedure. The animal was quarantined and acclimated in the preclinical animal experiment center in Osong, South Korea, for 1 week before the surgery. With the pig in the left lateral decubitus position, general anesthesia was induced with 2% sevoflurane. A lateral thoracotomy was performed to approach the thoracic cavity. Before performing a wedge resection, the thickness of the porcine lung tissue was measured with calipers, and then the proper site for the wedge resection was determined. Using NALS (a 60-mm long blue stapler with 3.5 mm staples), we performed a wide wedge resection in the right upper lobe to evaluate the stapler. To compare the extent of tissue damage to the true resection margin tissue, we used a popular commercial three-row stapler as a control (Figure 3).

This study was approved by the institutional review board of Osong Medical Innovation Foundation,

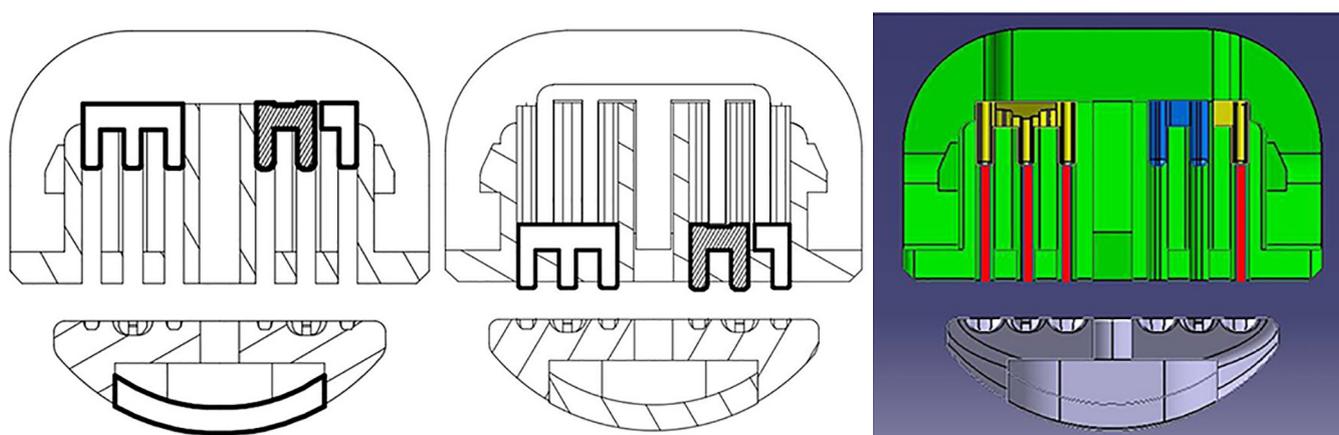


Figure 2 Cross-sectional view of the novel asymmetrical stapler device used for evaluating the resection margin tissue. Left side, pre-firing view; right, post firing view; red, titanium fastener; blue, tissue stabilizer for protecting true resection margin tissue from shearing stress by forward force of cutter during firing; yellow, pusher for titanium fastener.



Figure 3 Porcine animal experiment involving a wide wedge resection of the porcine lung with the novel asymmetrical stapler device.



Figure 4 Resected porcine lung with the novel asymmetrical stapler. There is only a single row of staples. The tissue between the staple row and cutting edge is the 'true' resection margin.

Cheongju, Chungbuk, Republic of Korea (KBIO-IACUC-2017-004).

Results

The right upper lung was widely resected using both staplers. Both use titanium fasteners of the same height and we used a commercial blue cartridge for medium tissue thickness.

With NALS, we successfully divided and closed the lung tissue (*Figure 4*). There was no bleeding on either side of the resection margin after the wedge resection. In the saline air-leakage test with 30 cmH₂O pressure, there was no air leakage from the remnant organ at the resection margin. The distance between the cutting edge and titanium fasteners was 3.10 mm, allowing a pathological evaluation of the true resection margin. This distance was sufficient to harvest the true resection margin tissue with a scalpel.

With the conventional three-row symmetrical stapler, it was impossible to resect true resection margin tissue without removing the titanium fasteners because the space from the cutting edge to the staples was too narrow. To evaluate the pathology, we had to remove the titanium fasteners and then resect the true resection margin tissue.

With NALS, there was no squeezing artifact at the true resection margin on microscopic examination and all of the alveolar structures were preserved for evaluation. By contrast, with the conventional stapler, there was severe squeezing artifact and subsequent tissue damage caused by the titanium fasteners making the evaluation extremely difficult (*Figure 5*).

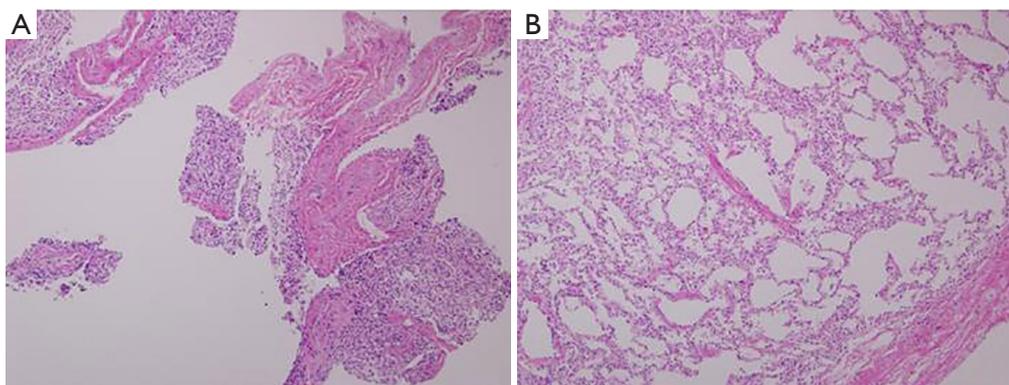


Figure 5 Pathologic findings of the true resection margin tissue (H&E, $\times 100$). (A) The resection margin tissue with the conventional stapler showing a severe squeezing artifact; (B) the resection margin tissue with the novel asymmetrical stapler; the alveolar structure was well preserved and no squeezing artifact is seen.

Discussion

An R0 resection, i.e., a microscopically negative resection margin, is an important factor in oncology surgery. This means that there are no malignant cells remaining in the patient after the operation. For an R0 resection, tissue from the true resection margin must be evaluated during the operation. To do so, a frozen section biopsy can be performed at the true resection margin. In conventional open surgery without a linear stapler device, it is easy to obtain fresh undamaged true resection margin tissue. However, when resecting the lung with a linear stapler device, it is impossible to get undamaged true resection margin tissue due to the tissue damage caused by the titanium fasteners. This is very problematic, because it makes it impossible to evaluate the true resection margin. This concern has been raised by both surgeons and pathologists (17). Therefore, this problem needs to be solved to ensure more accurate surgical treatment of cancer patients.

With the development of chest CT, the diagnosis of early NSCLC has improved, which has resulted in an increase in limited resection in patients who can tolerate a lobectomy. The oncological outcomes in recent studies support this trend (18-20). Hence, we are concerned with the failure to obtain an R0 resection with a limited lung resection in early lung cancer.

Previous studies have reported that the distance between the resection margin and the tumor is important for preventing locoregional recurrence (21,22). However, even when the distance between the resection margin and tumor exceeds the tumor size, locoregional recurrence sometimes occurs. To decrease locoregional recurrence, a frozen

section biopsy of the true resection margin tissue should be performed to confirm R0 resection. With a conventional stapler, it is difficult to examine the resection margins precisely, due to squeezing artifacts. In comparison, NALS effectively preserves the true resection margin tissue. It is also easy to cut the true resection margin tissue after the stapler is applied, because there is sufficient space to resect the tissue with a scalpel (more than 3 mm). In addition, there is no bleeding from the resected lung fastened with a single row of titanium fasteners during the operation. Therefore, a single row of staples is sufficient for the resected lung side.

A recent study of gastric cancer reported a manually removed modified stapler similar to NALS for evaluation of the true resection margin (23). With that modified stapler, true resection margin tissue could be harvested in gastric cancer without a squeezing artifact. Therefore, this type of linear stapler device is useful for evaluating the true resection margin in both lung and solid cancer surgery.

This animal study had several limitations. First, we performed a wide wedge resection in a single pig. Although we demonstrated the feasibility of NALS, we could not determine the statistical difference between it and the conventional stapler. Second, the wedge resection was performed in a pig and not in human tissue. Therefore, more studies of human tissue are required to evaluate potential safety issues.

Conclusions

NALS, which preserves the true resection margin, is useful for evaluating the resection margin with a frozen section

biopsy in oncology surgery. Particularly, with a limited resection, such as sublobar resection, in early lung cancer, this stapler device is useful for evaluating the resection margin.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the institutional review board of Osong Medical Innovation Foundation, Cheongju, Chungbuk, Republic of Korea (KBIO-IACUC-2017-004).

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