



Pre-clinical study of Novel Asymmetrical Linear Staple (NALS) devices for cancer surgery



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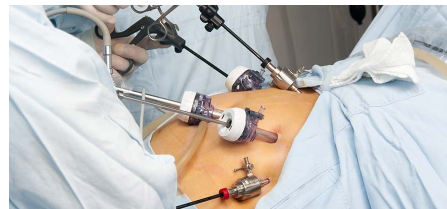
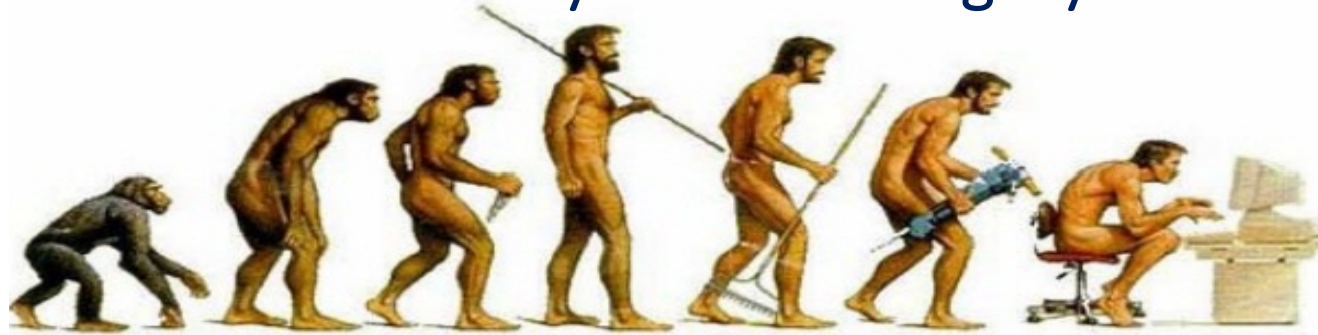
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Current develop of surgical treatment of cancer within 2 decades

➔ Just focus to the minimally invasive surgery



Open Surgery

2005 ~

Minimally invasive surgery

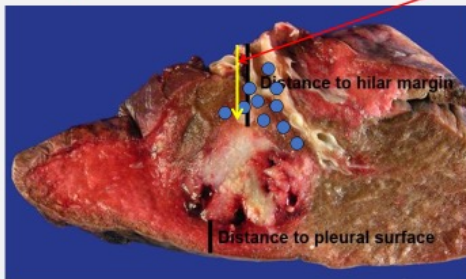


Overlook: R0 Resection

The major purpose of cancer surgery

Unmet need in stapler: Cancer safety margin

More than 1.5~2cm from main mass or Tumor/margin ratio > 1



● : Malignant daughter cell

Optimal Distance of Malignant Negative Margin in Excision of Nonsmall Cell Lung Cancer: A Multicenter Prospective Study

Noriyoshi Sawahata, MD, Mitsunori Ohta, MD, Akishio Matsuzawa, MD, Kazumichi Nakagawa, MD, Hiroshi Hirata, MD, Hajime Maeda, MD, and Hikaru Matsuda, MD, PhD, for the Thoracic Surgery Study Group of Osaka University

Background: Complete excision of nonsmall cell lung cancer is necessary during a limited resection procedure, as a malignant positive margin can lead to disease relapse. Because there is some information available regarding the optimal size of a malignant negative margin, we conducted a multicenter, prospective study to more fully elucidate this issue in cancer.

Methods: Two hundred five pulmonary resected (122 nonsmall cell lung cancer and 83 resected bronchiectasis) were resected, of which 110 nonsmall cell lung cancer lesions were analyzed. Malignant status was considered positive when either a cytologic or histologic technique revealed the margin to be malignant. Maximum tumor diameter (from 1 to 41 cm with an average of 13.3 mm), margin distance (from 0 to 23 mm with an average of 5.2 mm), tumor location, extent of resection, control rate, and performance of a bronchoscopy were the variables.

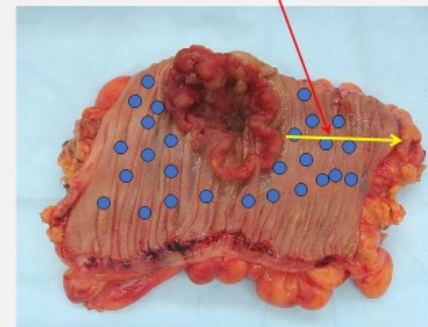
Results: Seventy-two of the sample lesions (65%) were malignant negative. The negative group had smaller maximum tumor diameter, greater margin distance, in situ or more easily resectable regions, and more often regional lymph node. Using a multivariate analysis, maximum tumor diameter and margin distance were found to be independent factors. The number of malignant positive margins was 17 (15%) when the margin distance was greater than 20 mm, and the number of malignant positive margins was 12 (11%) when the margin distance had a margin distance greater than the maximum tumor diameter.

Conclusions: Malignant positive margins were not found when the margin distance was greater than the maximum tumor diameter, which was considered to be the optimal margin distance for preventing against margin relapse.

Ueno Thorax Surg 2006;77:453-26
© 2006 by The Society of Thoracic Surgeons

Colon cancer safety margin

More than 3cm from main mass



● : Malignant daughter cell



Table 1 Surgical margin for cancer surgery from the literature sources.

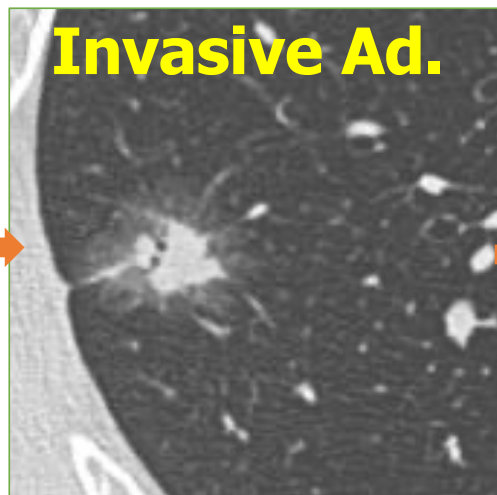
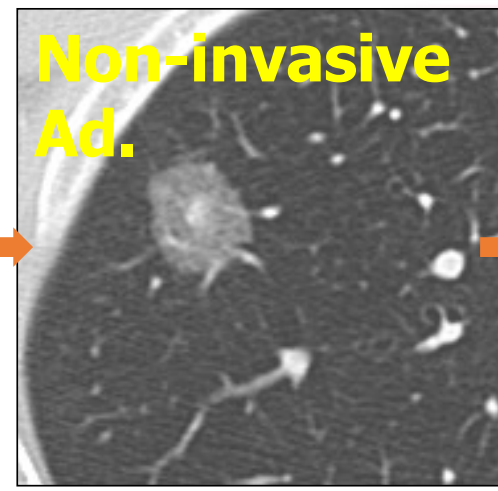
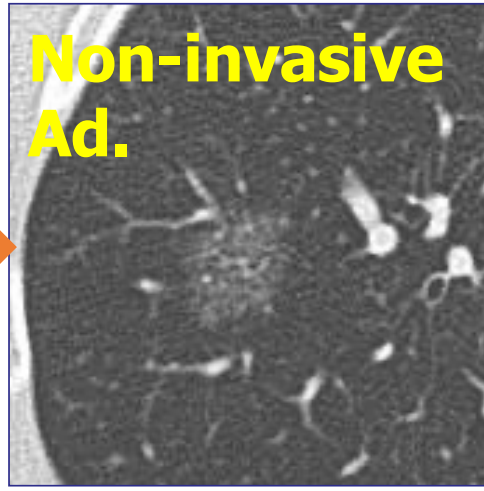
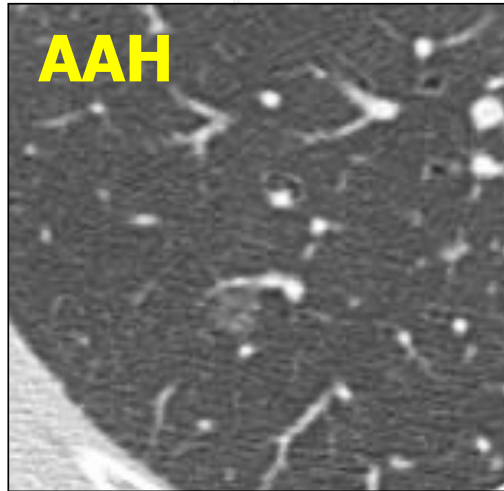
| Anatomic site | Surgical margin | Authors |
|---------------------------|-----------------|---------------------------------------------------------|
| Esophagus | 0.1 cm | Chan et al. ¹¹ |
| Gastroesophageal Junction | 5 cm | Barbour et al. ¹⁶ |
| Stomach (proximal end) | 2-4 cm | Tsujitani et al. ¹⁵ |
| Colon | 3 cm | Shimada et al. ¹⁴ |
| Rectum | 1-2 cm | Bujko et al. ¹⁰ , Moore et al. ¹³ |
| Liver | | |
| HCC | 1 cm | Shi et al. ²⁷ , Ker et al. ¹⁸ |
| CCC | 2 cm | Saioum and Castaing ²⁸ |
| CLM | 1-3 mm | Hou et al. ²⁵ , Konopke et al. ²³ |

CCC = cholangiocellular carcinoma; CLM = colorectal cancer metastasis; HCC = hepatocellular carcinoma.

➔ To reduce the risk of remnant cancer cell in patient's body after operation, surgeon resect enough organ to prevent recurrence of cancer.



In terms of Lung adenocarcinoma: AAH-adenocarcinoma

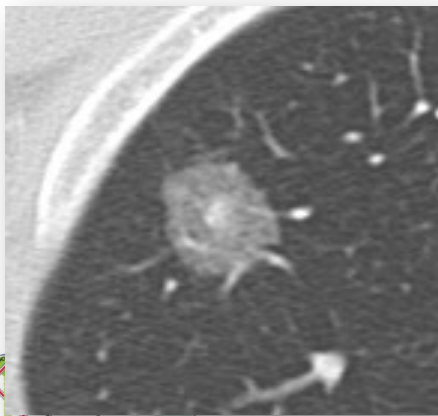


What is the condition of non-invasive tumor on CT?

JCOG0201

Radiological-pathological correlation in lung adenocarcinoma ≤ 2.0 cm in size

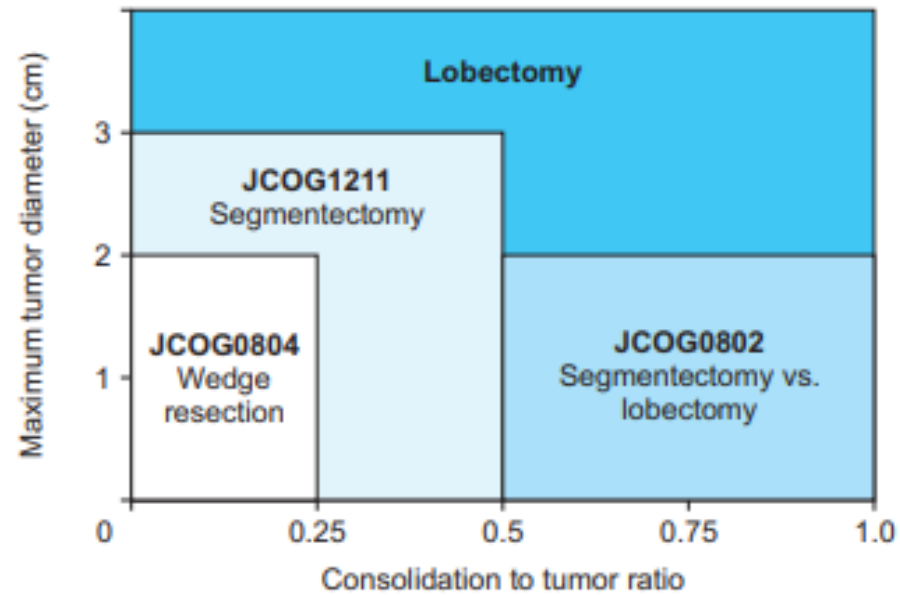
- **545 adenocarcinomas ≤ 2 cm**
- **Lobectomy with mediastinal dissection**
- **Non-invasive = No nodal involvement, vascular invasion, and lymphatic invasion**



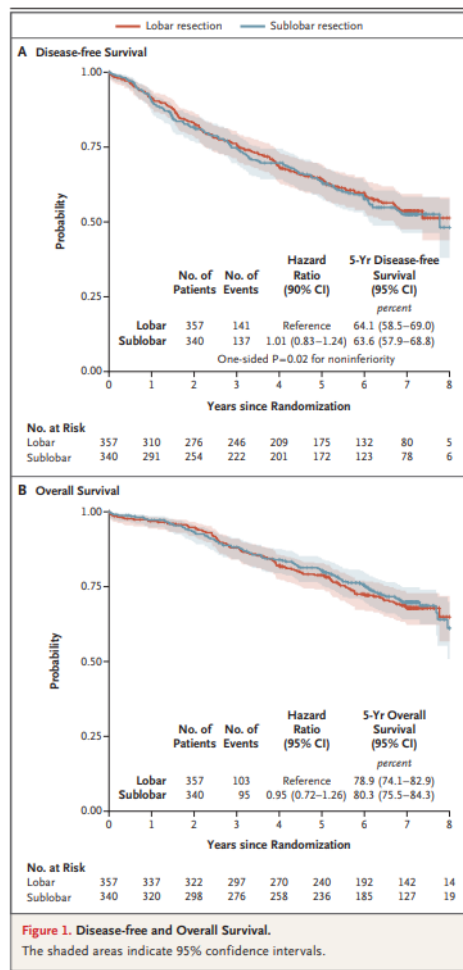
**C/T ratio ≤ 0.25 were considered to be non-invasive.
(specificity 98.7%)**

Suzuki K, et al. JTO 2011;6:751-6.

Surgical extent for early adenocarcinoma



CALGB 140503



The NEW ENGLAND JOURNAL of MEDICINE

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Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.

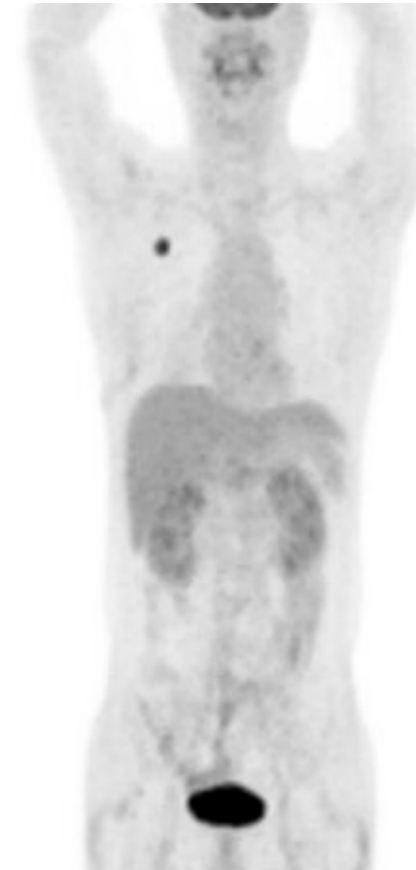
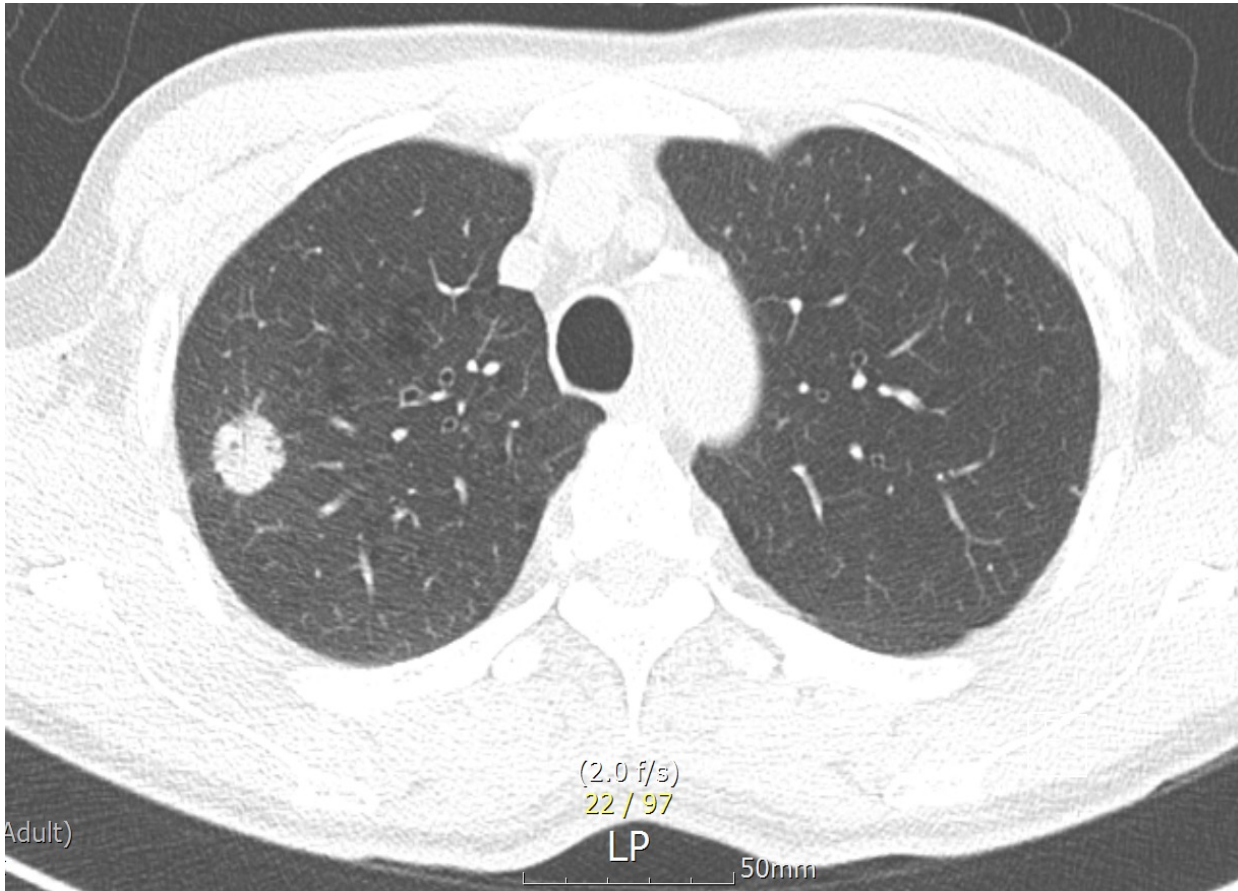
Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

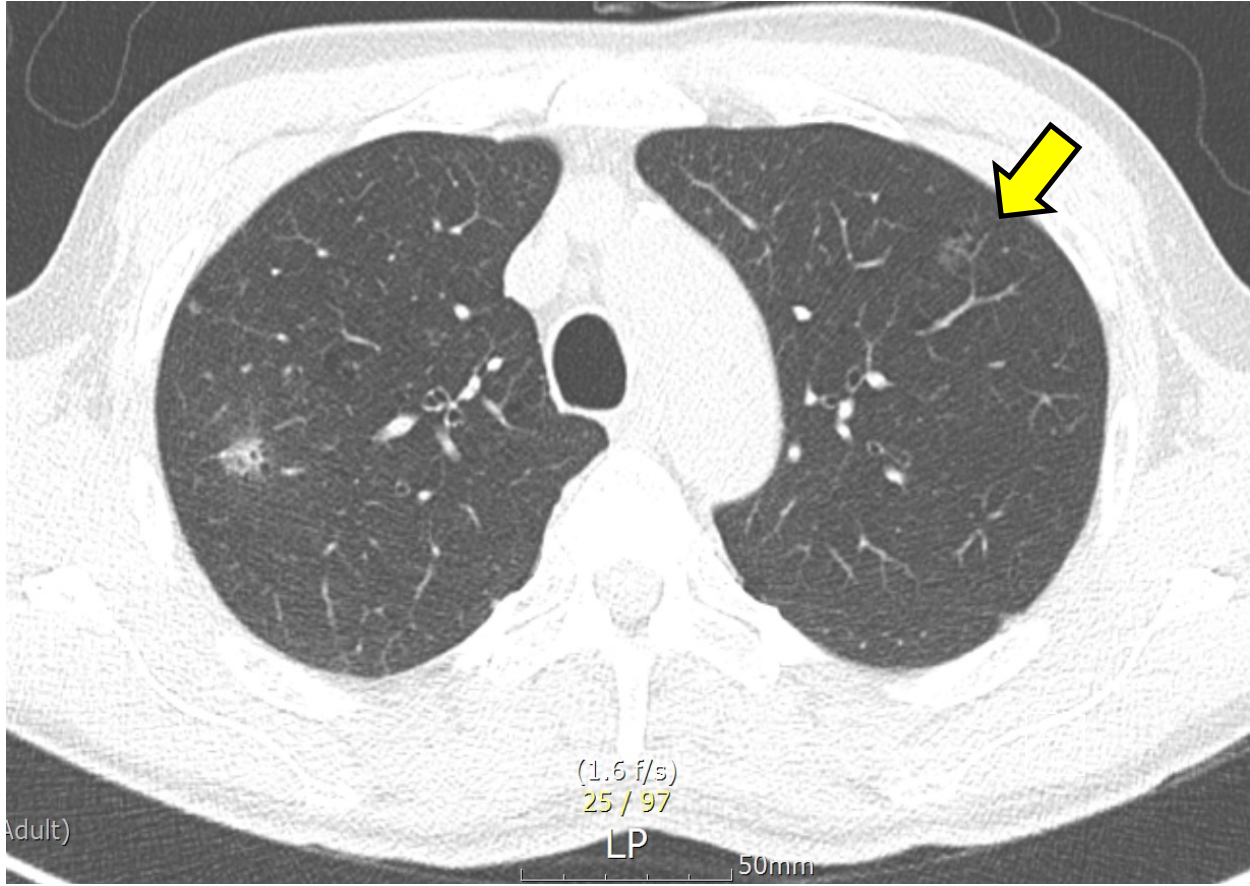
| Characteristic | Sublobar Resection (N=340) | Lobar Resection (N=357) | Total (N=697) |
|----------------|----------------------------|-------------------------|---------------|
| Age—yr | | | |
| Median | 68.3 | 67.6 | 67.9 |
| Range | 37.8–89.7 | 43.2–88.9 | 37.8–89.7 |

CONCLUSIONS

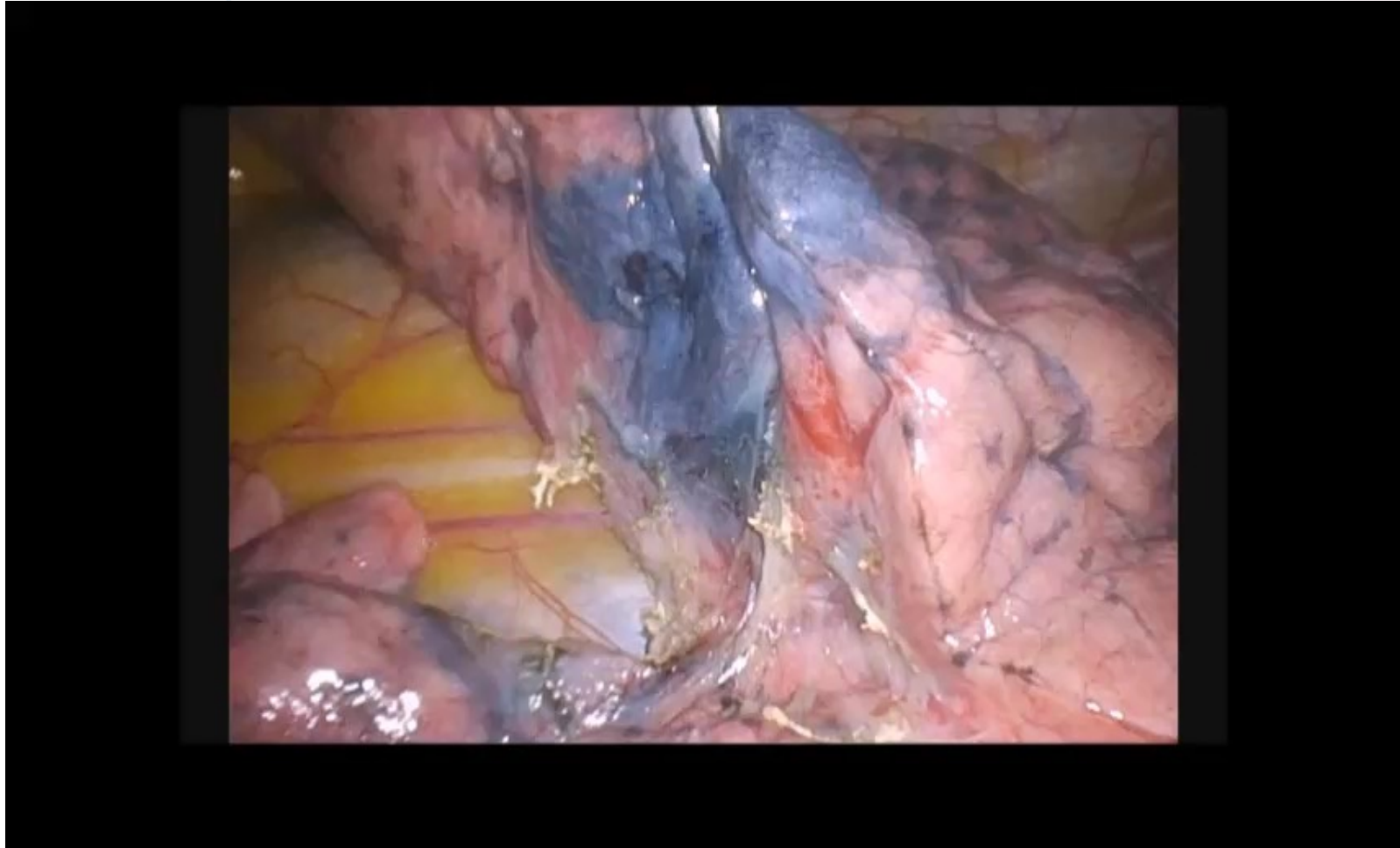
In patients with peripheral NSCLC with a tumor size of 2 cm or less and pathologically confirmed node-negative disease in the hilar and mediastinal lymph nodes, sublobar resection was not inferior to lobectomy with respect to disease-free survival. Overall survival was similar with the two procedures. (Funded by the National Cancer Institute and others; CALGB 140503 ClinicalTrials.gov number, NCT00499330.)

RUL PCNB: Adenocarcinoma











Pathology

RUL: adenocarcinoma, papillary (70%), acinar (30%)

size 2.5 x 1.7cm

lymph node metastasis (-)

LUL, lingular: minimally invasive adenocarcinoma

size 0.6 x 0.3cm

clear resection margin

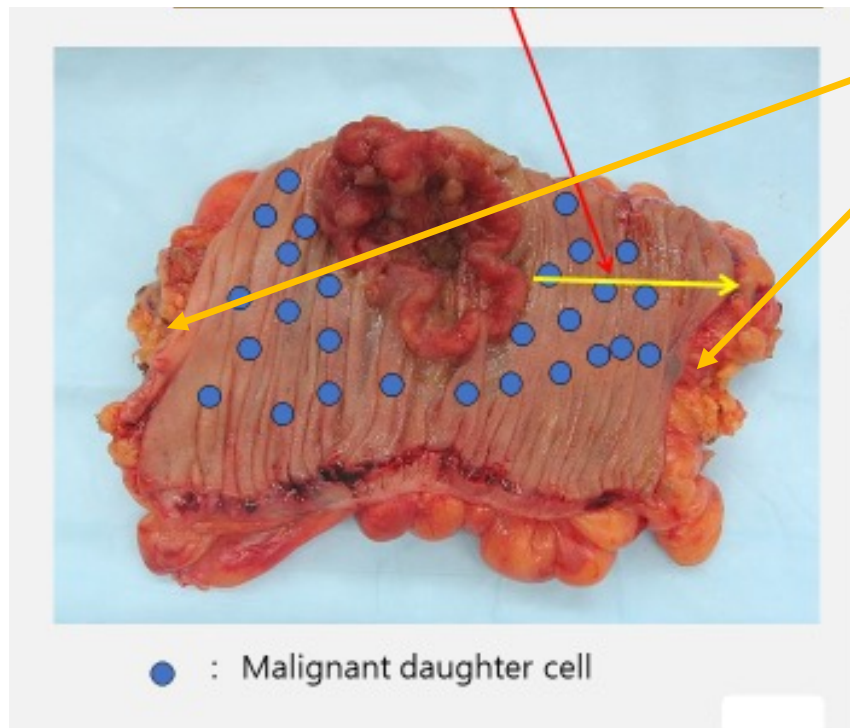
anterior: minimally invasive adenocarcinoma

size 0.6 x 0.2cm

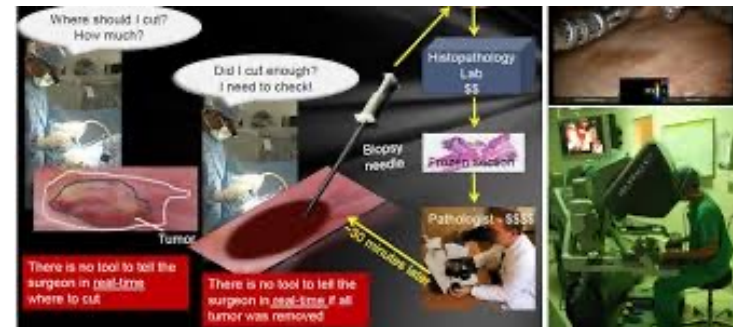
clear resection margin



To confirm of complete resection of cancer
; Should do the **frozen section biopsy** at resection margin
tissue.



End margin of the resected organ tissue is true resection margin that must evaluate the existence of cancer cell during operation with frozen section biopsy.



<https://www.epic-assoc.com/wp-content/uploads/2015/02/EPIC-EVENT-REPORT-26-EPIC-Biophotonics-Workshop-Intra-Operative-Assessment-of-Tumor-Resection-Margins.pdf>

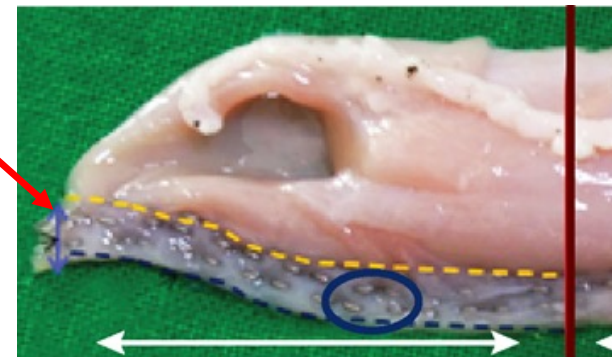
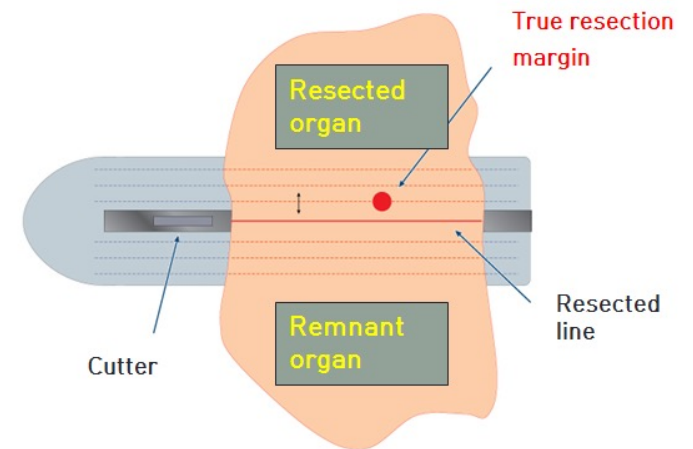
After confirm of **tumor negative in true resection margin**,
surgeon cancer finish the operation.

➔ Confirm R0 resection

Problem

Unmet need in Surgical treatment of cancer with surgical stapler is inaccuracy of frozen section biopsy with conventional stapler.

- We cannot perform frozen section biopsy at the true resection margin tissue for frozen section biopsy in case of surgery that use surgical stapler to resect cancer organ.
- It's impossible do the frozen biopsy due to tissue damage by surgical stapler.



Problem of conventional stapler in cancer surgery



There are publications pointing out the problems of frozen section examination when a stapler was used and suggesting attempts to confirm R0 resection intra-operatively

- ✓ US pathologist: Evaluation of margins by frozen section may be problematic, especially when stapler cartridges have been used on both sides.

State of issue for resection margin



William D. Travis

MD
Memorial Sloan Kettering Cancer Center
New York, New York

William D. Travis, MD, is an attending thoracic pathologist with a special interest in thoracic neoplastic and non-neoplastic lung disorders. I have worked on classification of thoracic disorders and served as Chair of the 1999 WHO Classification of Lung and Pleural Tumors; lead editor of the 2004 WHO Classification: Pathology and Genetics of Tumors of the Lung, Pleura, Thymus and Heart; co-chair of the 2002 American Thoracic Society and European Respiratory Society International Multidisciplinary Consensus Classification of Idiopathic Interstitial Pneumonias; co-chair of the ATS Workshop on Nonspecific Interstitial Pneumonia; and co-chair of the Pathology/Radiology Panel of the 2004 ASCO/IASLC Adenocarcinoma/Bronchioloalveolar Carcinoma Workshop.

He is Director of the ACGME-accredited Thoracic Pathology Fellowship Program at Memorial Sloan-Kettering Cancer Center. He is the lead editor of the upcoming 4th Edition of the 2015 WHO Classification: Pathology and Genetics of Tumors of the Lung, Pleura, Thymus and Heart. And, he is the lead author of the upcoming 2013 American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias.

He will serve on the IASLC Board of Directors for four years, starting at the WCLC in 2013.

STATE OF THE ART: CONCISE REVIEW

International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma

What can be Expected of Pathologists at Frozen Section?

For a limited resection to be adequate oncologically, a precise pre- and intraoperative diagnosis is critical. The accuracy of intraoperative frozen section analysis in determining whether small lung adenocarcinomas have an invasive component still needs to be defined. The predictive value of frozen section ranges from 93 to 100% but not all articles clearly report the accuracy of frozen section analysis.^{45-47,449}

Evaluation of margins by frozen section may be problematic, especially when stapler cartridges have been used on both sides. Scraping or washing of staple lines with subsequent cytological analysis has been attempted.^{450,451} When a sublobar resection is performed, frozen section analysis of an interlobar, hilar, or any suspicious lymph node is a useful staging evaluation, and when positive nodes are found, a lobectomy is indicated when there is no functional cardiopulmonary limitation.

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December 6, 2023



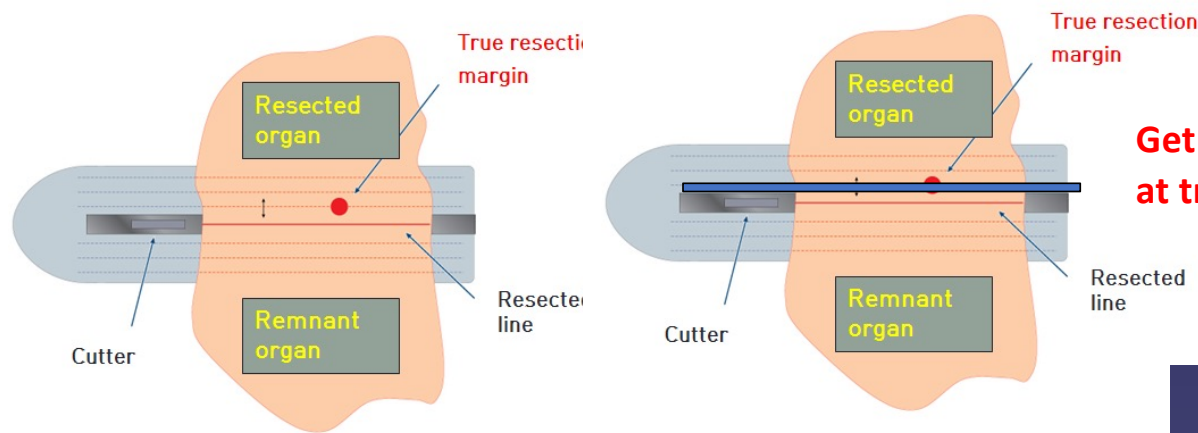


MEDITULIP
MAKING SURGICAL HISTORY

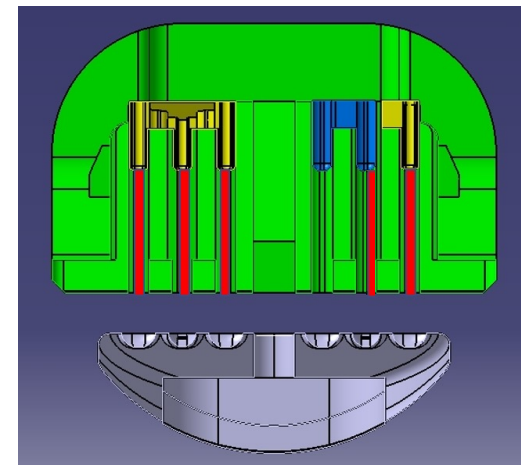
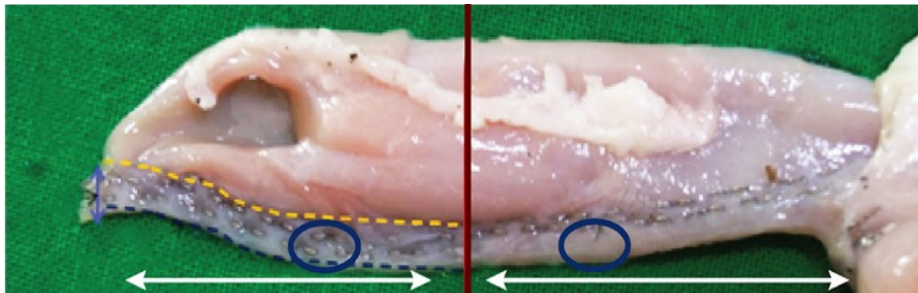
Solution

Novel Asymmetrical Linear
Stapler (NALS)

Novel Asymmetrical Linear Stapler (NALS)



Get rid of titanium fastener at true resection margin.





MEDITULIP
MAKING SURGICAL HISTORY



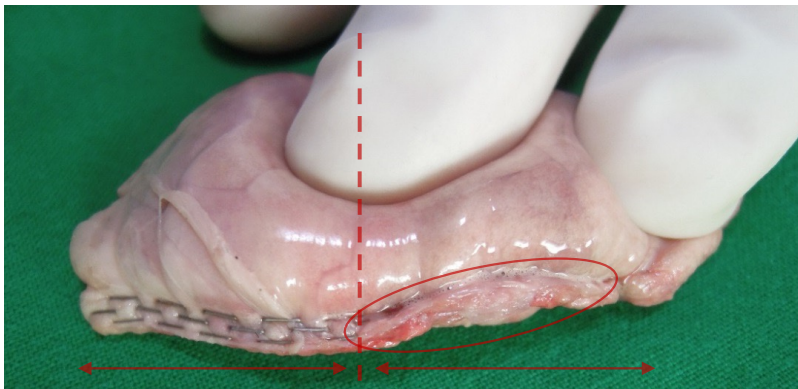
Endo blossom (3X3, Blue)
Complete sealing of bowel with
perfect B shape close of fastener.

NALS Endo blossom (3X2, Blue)
Complete sealing and provide enough
tissue for frozen section biopsy
evaluation at true resection margin of
specimen.

Animal Test Results



- ✓ With a conventional surgical linear stapler, the cellular structures were damaged by the staples piercing and squeezing the tissue (Squeezing artifact), thus making it impossible to accurately diagnose the presence of cancer cells on the true resection margin
- ✓ With MEDITULIP's Novel Asymmetrical Linear Stapler, no staple-induced tissue damage was observed, and in the histopathological examination, the intestinal mucosa and muscle layer in colon tissue was clearly observed, and the alveoli structure was preserved in the lung samples, allowing accurate diagnosis of R0 resection (no cancer on cut surface)



Tissue resection using conventional surgical linear stapler

Impossible to obtain tissue for pathologic examination

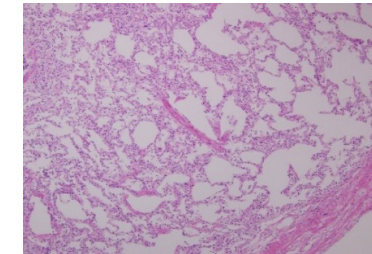
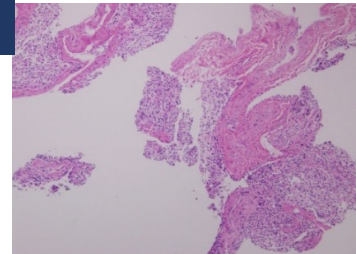
Tissue resection using MEDITULIP NALS

Possible to obtain tissue for pathologic examination

Surgical margin of conventional surgical linear stapler

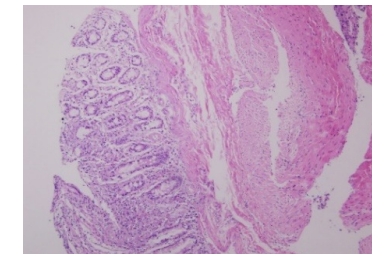
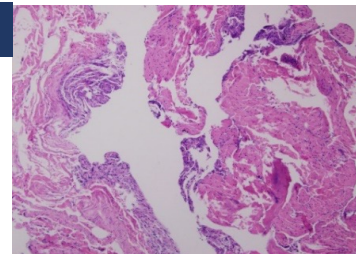
Surgical margin of MEDITULIP's Novel Asymmetrical Linear Stapler

Lung



Preserved alveoli structures

Colon



Preserved mucosa and muscle layer structures



Journal of Thoracic Disease

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

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

Shin-Kwang Kang[#], Jin San Bok[#], Hyun Jin Cho, Min-Woong Kang

Department of Thoracic and Cardiovascular Surgery, School of Medicine, Chungnam National University, Chungnam National University Hospital, Daejeon, South Korea

Contributions: (I) Conception and design: MW Kang; (II) Administrative support: MW Kang; (III) Provision of study materials or patients: MW Kang; (IV) Collection and assembly of data: JS Bok, SK Kang, HJ Cho; (V) Data analysis and interpretation: JS Bok, HJ Cho, SK Kang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*These authors contribute equally in this work.

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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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View this article at: <http://dx.doi.org/10.21037/jtd.2018.03.158>

Meditulip **complete** the development of NALS and new endo stapler for surgery

Endo Blossom



Endo Stem



December 2023



NALS Product Specifications



MEDITULIP provides stapler instruments and cartridges, both symmetric and asymmetric, to cover all tissue thicknesses and staple lengths

MEDITULIP Surgical Linear Stapler Series Code

| Reload Selection Chart | | | |
|------------------------|------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------|
| Vascular Range | | Medium Range | Thick Range |
| Extra Thin | Thin | | |
| | WHITE Thickness(=8mm) fastener(2 x 2 & 2.0mm) | NAVY Thickness(=12mm) fastener(=3 x 1 & 3.5mm) | DARK GREEN Thickness(=12mm) fastener(=3 x 1 & 4.5mm) |
| | | BLUE Thickness(=12mm) fastener(=3 x 3 & 3.5mm) | GREEN Thickness(=12mm) fastener(=3 x 3 & 4.5mm) |

Main Shaft

| TYPE | Shaft Length |
|---------------|--------------|
| ENDO STEM-150 | 150mm |
| ENDO STEM-60 | 60mm |

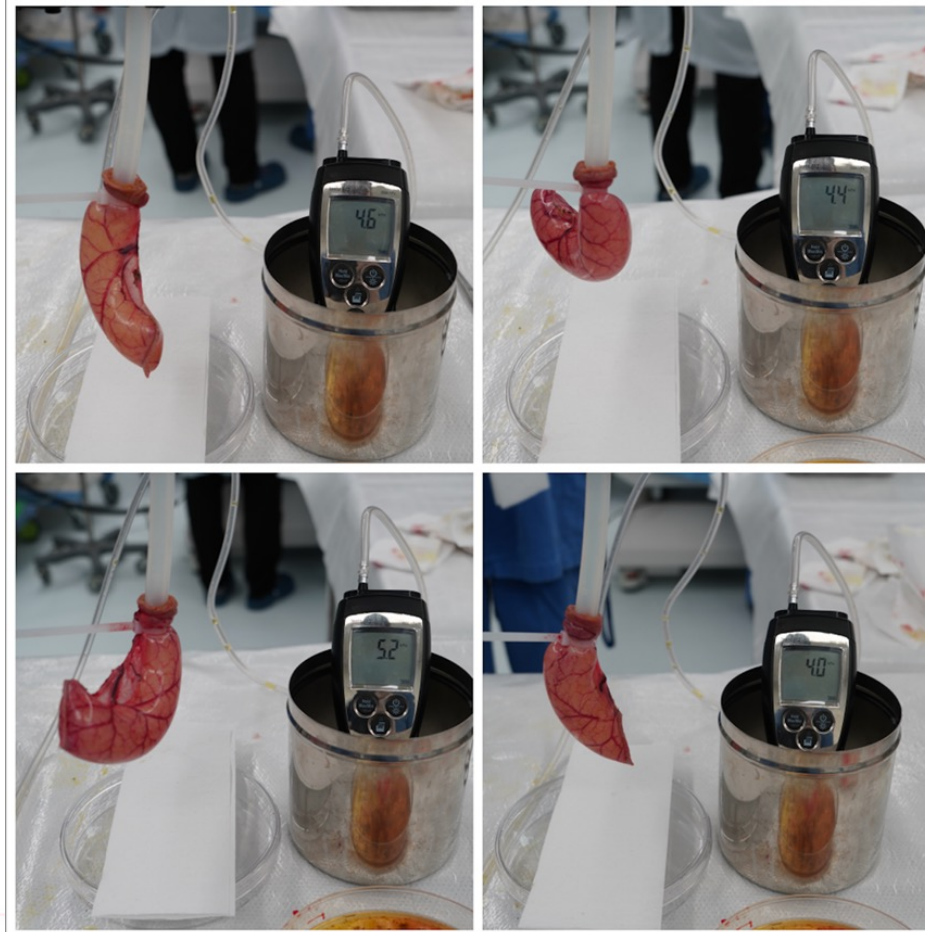


December 16, 2023

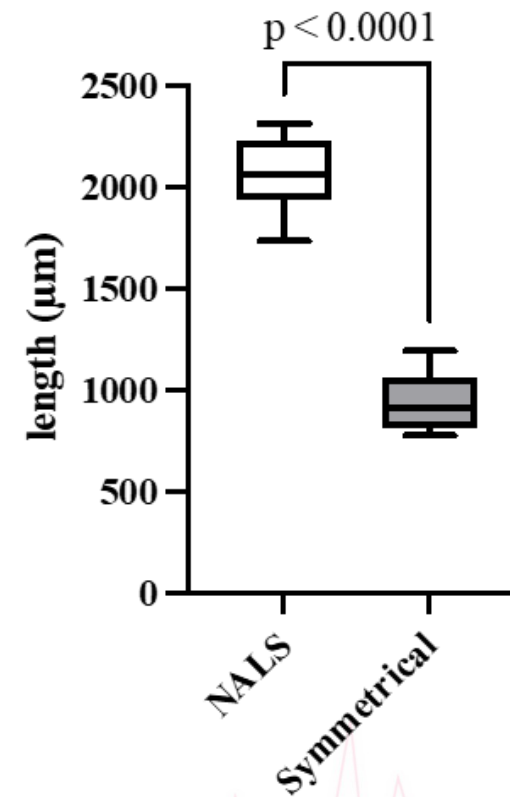
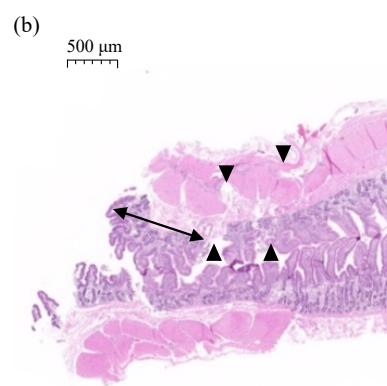
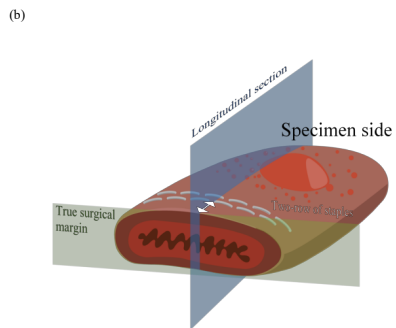
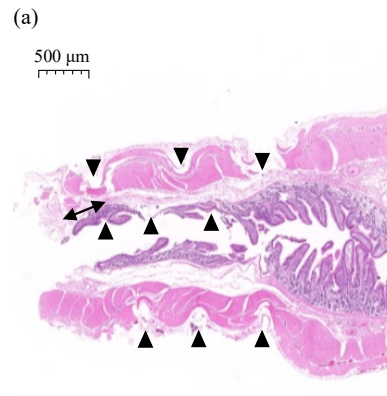
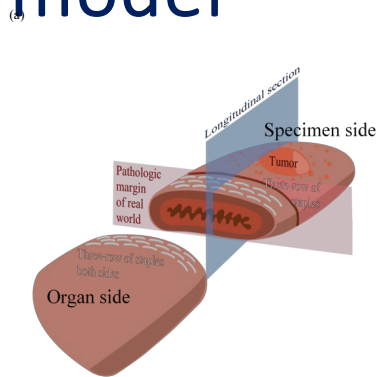


Investment Memo_Eng._Confidential

Burst pressure measurement by 2-row, 3-row staplers (NALS vs Conventional staples)



Comparison of the distance between the resection margin and the staple line for the resected porcine model



Attempts to confirm R0 resection



Japanese gastric surgeons manually removed staples from the cartridge in advance of surgery to obtain tissues for accurate pathologic evaluation of the true surgical margin intra-operatively

In vivo evaluation of a modified linear stapling device designed to facilitate accurate pathologic examination of the surgical margin

Hironori Tsujimoto¹ · Hitoshi Tsuda² · Shuichi Hiraki¹ · Shinsuke Nomura¹ · Nozomi Ito¹ · Kyohei Kanematsu¹ · Hiroyuki Horiguchi¹ · Suefumi Aosasa¹ · Junji Yamamoto¹ · Kazuo Hase¹

In conclusion, the proposed linear stapling device in which staples are removed beforehand is safe and could be useful for the pathologic evaluation of the true surgical margin.

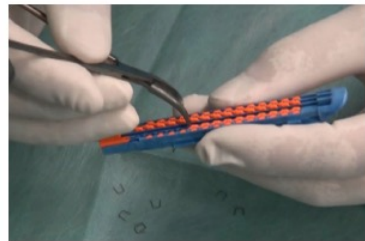


Fig. 1 Setup for the linear stapling device. An ECHELON FLEX™ Powered ENDOPATH® stapler (60 mm; Ethicon, Tokyo, Japan) was used. The cartridge cover was removed, and one line (stapler E2) or two lines (stapler E1) of staples were removed with sharp Péan forceps. Then, the cover was replaced, and the cartridge was attached to the stapling device

- ✓ Proved feasibility of tissue biopsy on the true resection margin by removing 1 or 2 rows of staples on the resected tissue side
- ✓ Proved 1 row is secure enough on resected organ
- ✓ Published after MEDITULIP's patent application (20th April 2015)

Published online: 22 July 2015

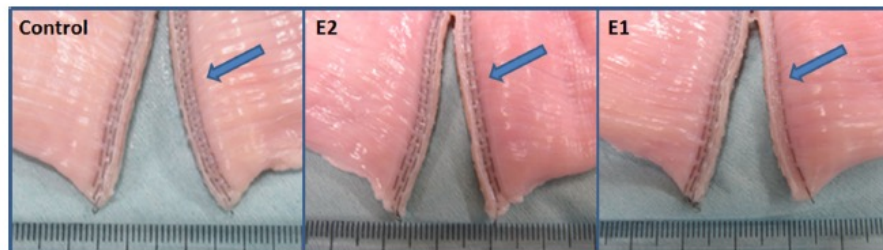
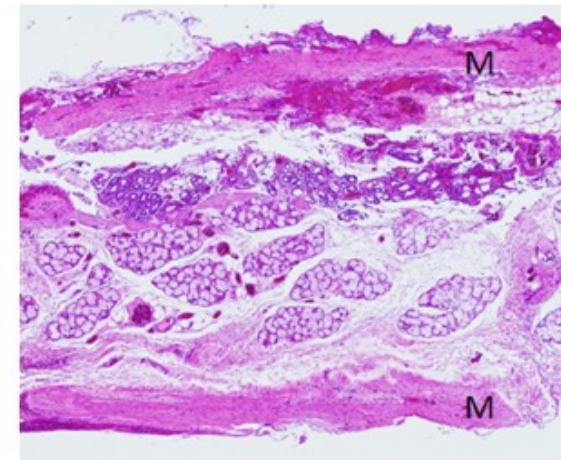


Fig. 2 Photographs of a porcine stomach resected with each of the three linear stapling devices (stapler E1, stapler E2, and control). The resected porcine stomach was successfully divided and stapled with all three staplers



Let's go together



csdockang1@gmail.com