肺癌手術新發展
Recent Advances in Surgical Treatment of Lung Cancer

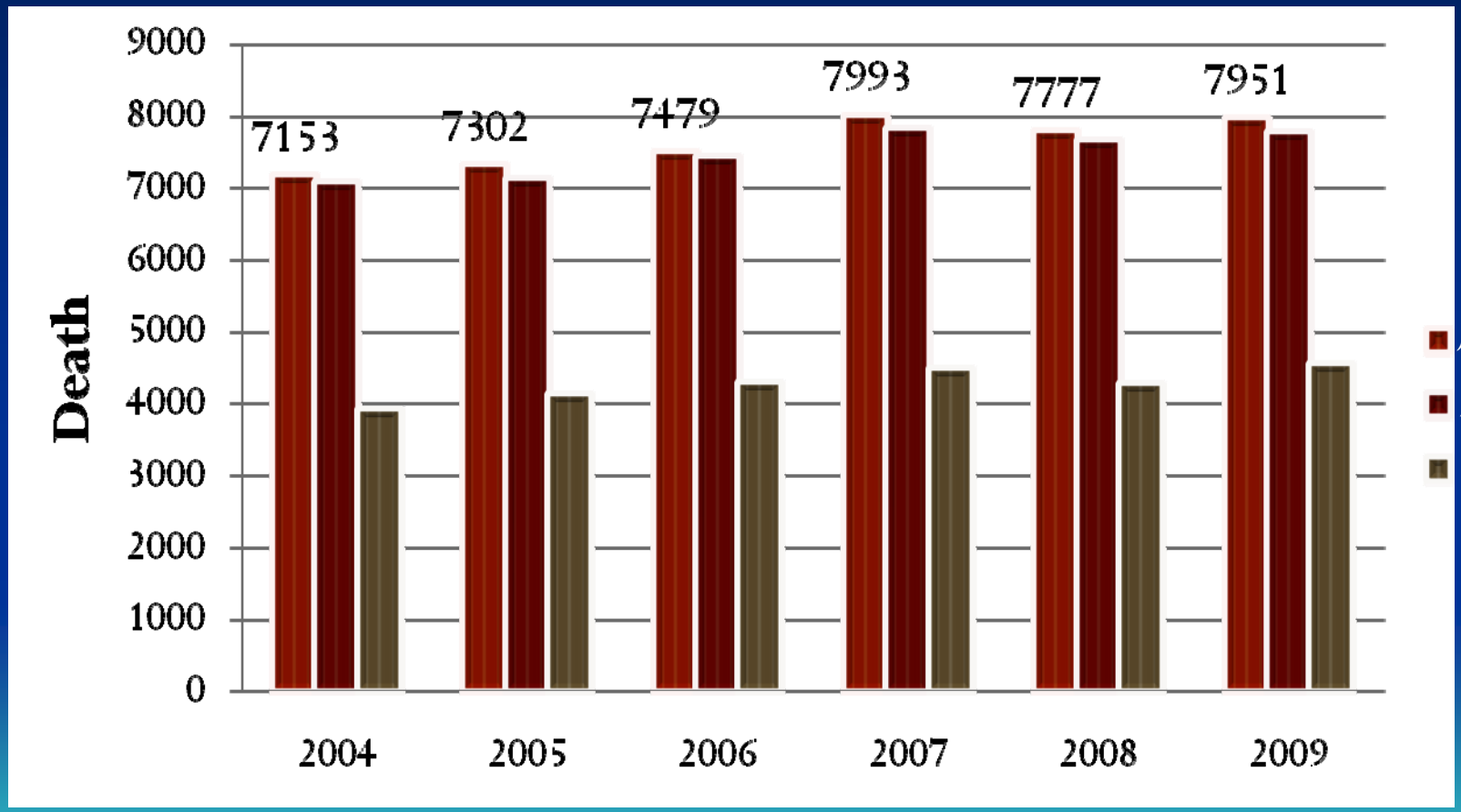
陳晉興 醫師

臺大醫學系外科　副教授
臺大醫院實驗外科　主任
臺大醫院胸腔外科　主治醫師

綱要

- 肺癌簡介
- 肺癌微創手術治療新進展
  - 減少胸壁創傷: 胸腔鏡手術
  - 減少肺臟切除範圍(sublobar resection)
  - 減少麻醉創傷：免插氣管內管之胸腔鏡手術
- 合併治療新進展
  - 爭議性肺癌手術
  - 合併標靶治療

肺癌：近年來台灣癌症死亡原因之第一名



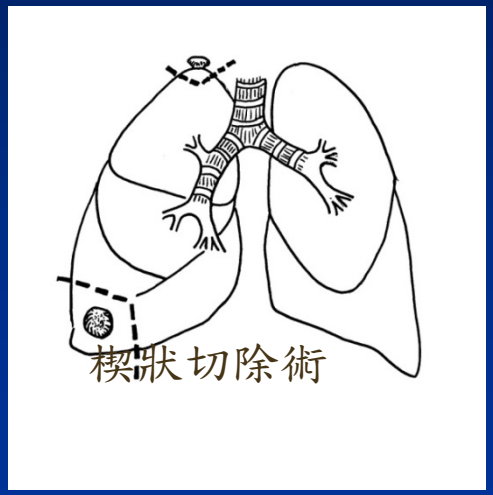
資料來源：行政院衛生署

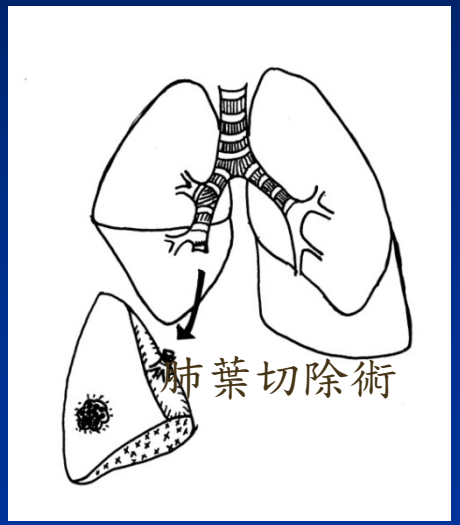
非小細胞肺癌：

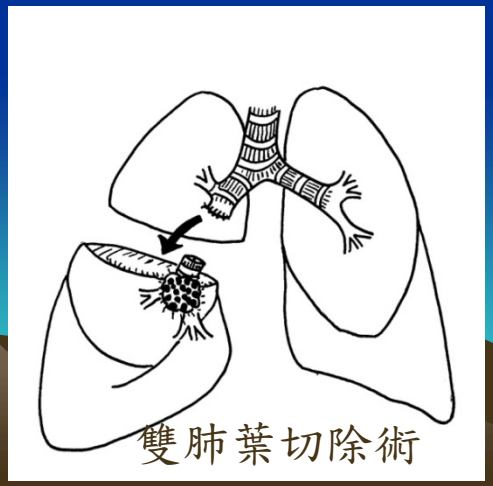
- 約佔所有肺癌之85-90%
- 外科手術之角色:
  - 根除性切除：提供早期肺癌病患最佳根治及存活機會
  - 確定診斷與分期
  - 症狀解除

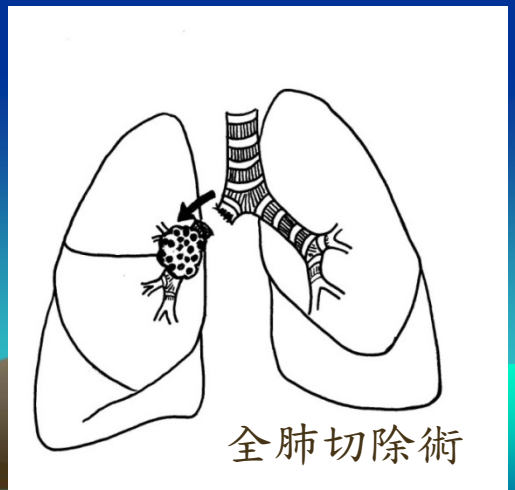
肺癌手術基本概念：

1. 肺臟切除不再重生
2. 手術危險性與切除範圍成正比









肺癌手術後肺活量短期減少 40-70%; 長期減少10-40%，如何減少短期傷害？

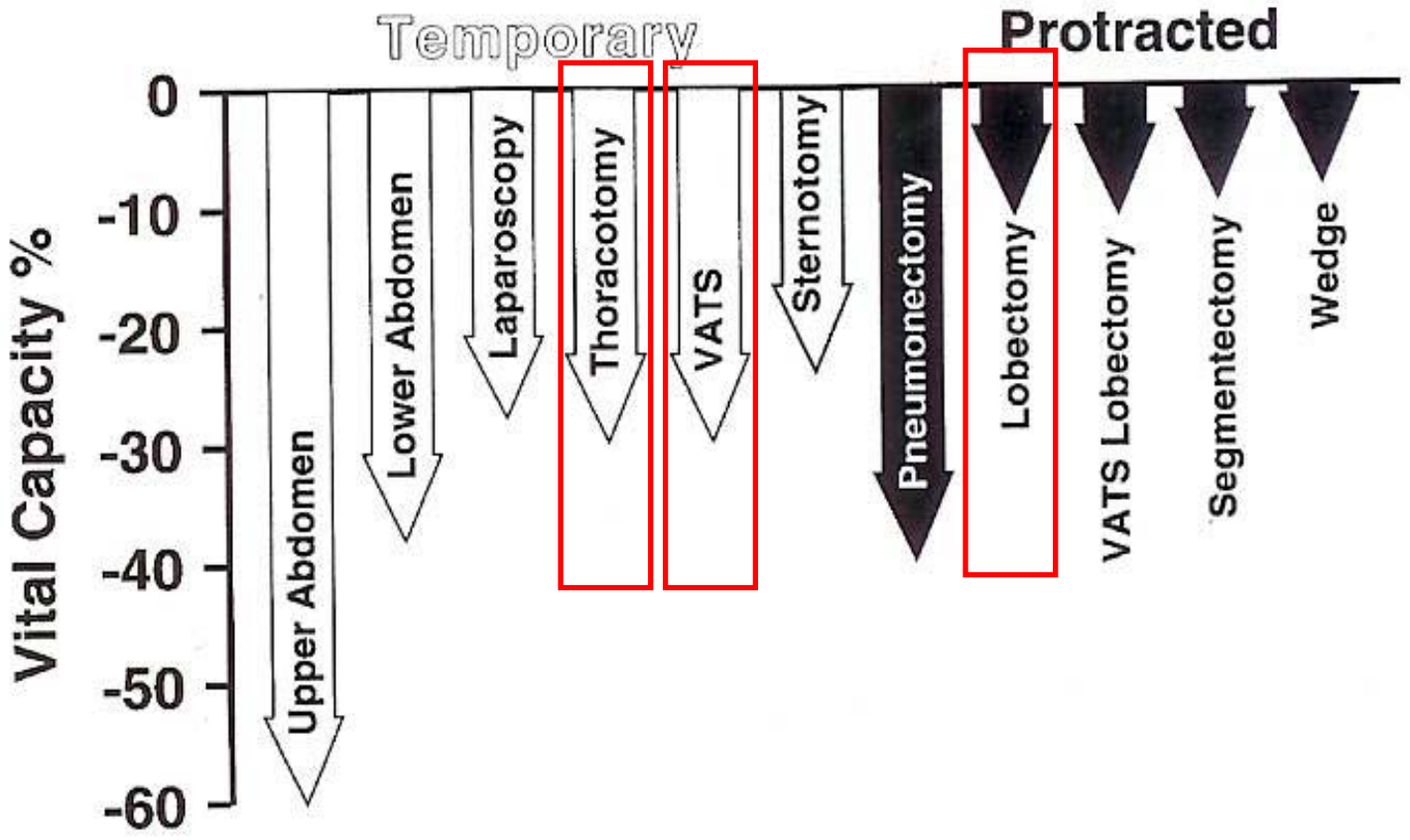


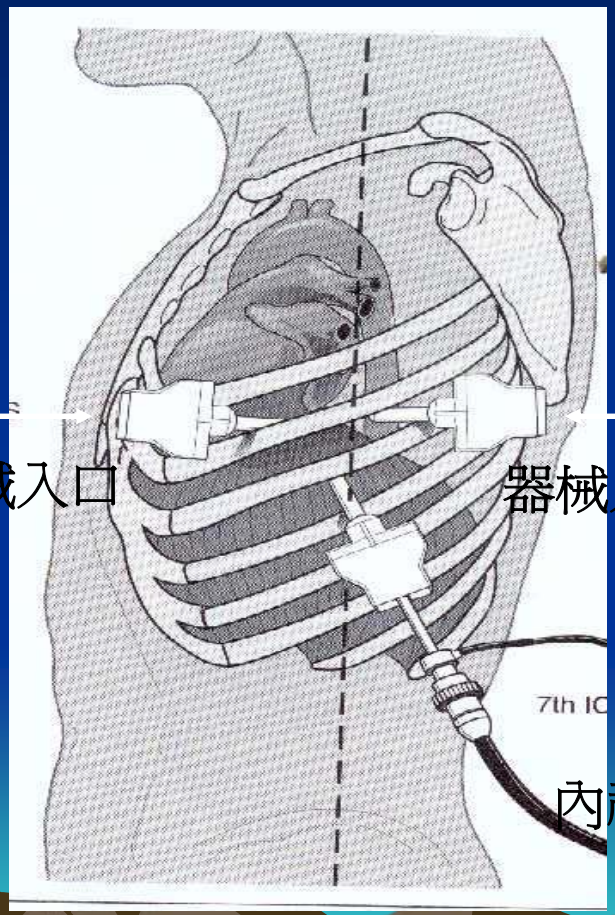
Fig. 19-1. Effect of surgical procedures on vital capacity. VATS, video-assisted thoracoscopic surgery.

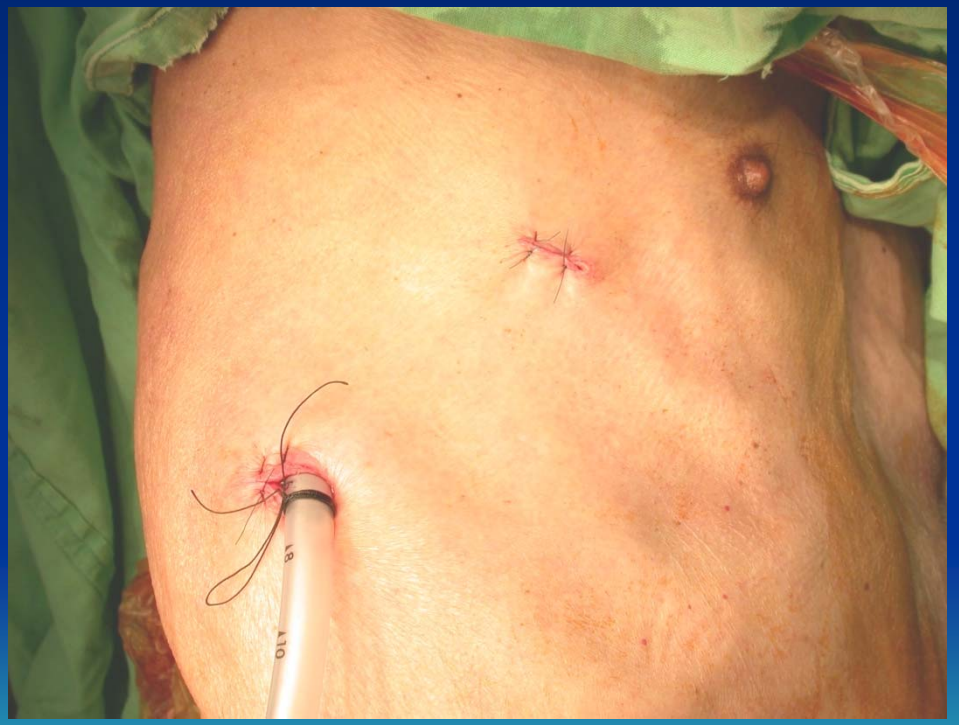
肺癌手術及麻醉之進展趨勢：

- 肺癌手術及麻醉之風險：
  - 老年病患居多，心肺功能不佳
  - 術前進行化療或放射線治療，惡化身體狀況
  - 切除肺臟及胸壁肌肉，嚴重影響肺功能
  - 全身麻醉及插管使用呼吸器之併發症
- 肺癌手術及麻醉進展趨勢：
  - 減少胸壁創傷: 胸腔鏡手術
  - 減少肺實質切除: 肺節切除術及楔狀切除術
  - 減少麻醉創傷：免插氣管內管之胸腔鏡手術

Standard Posterolateral Thoracotomy:
傷口大，恢復慢，長期疼痛比例高

A. 如何減少胸壁創傷？
胸腔鏡手術





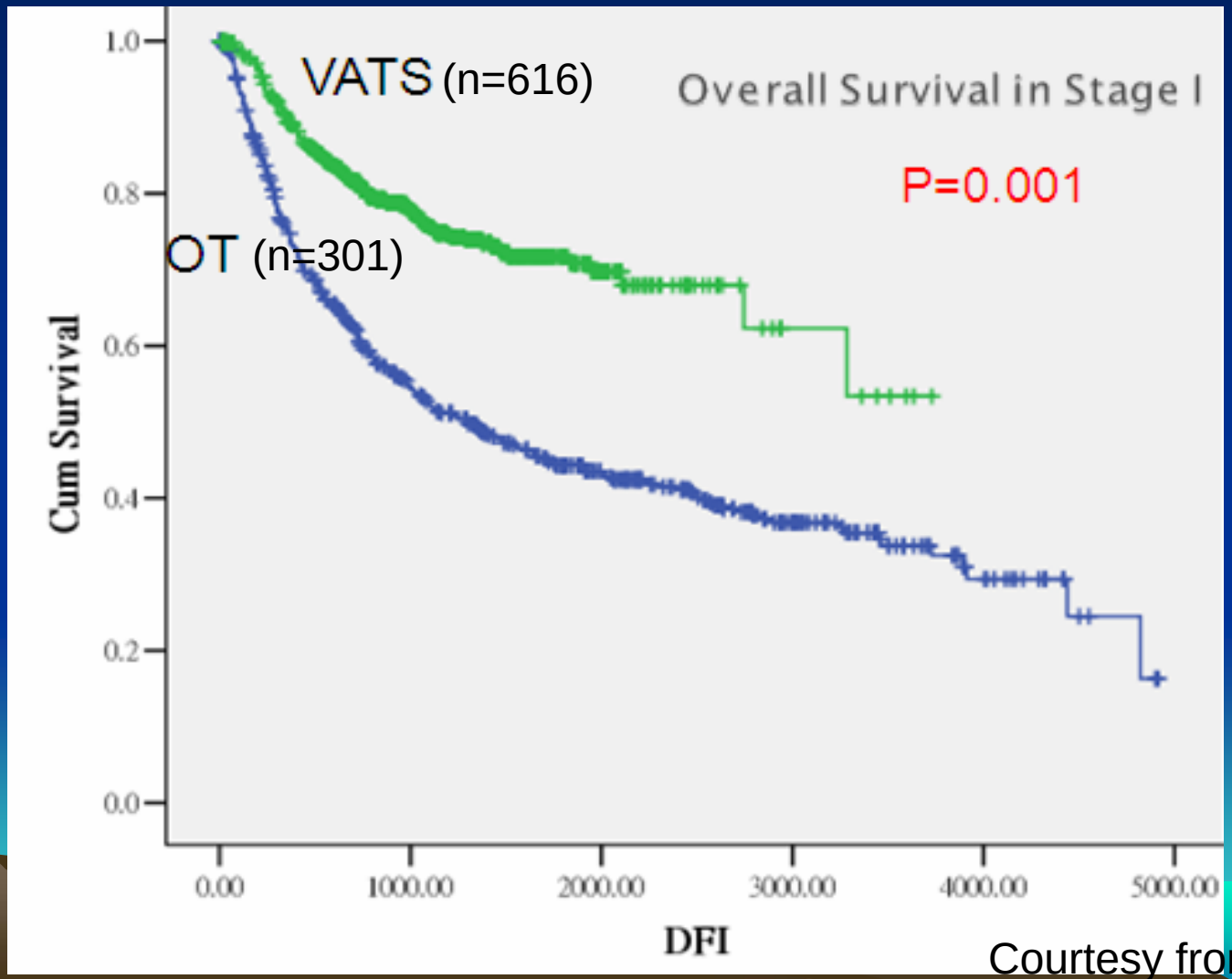
Lancet 1991

胸腔鏡肺葉切除術：優點

- 胸腔鏡肺葉切除術後之肺功能影響較小
- 胸腔鏡手術引發較少之發炎反應，對免疫功能較好
- 胸腔鏡肺葉切除術後長期生活品質較好

1. Kaseda S. Ann Thoracic Surg, 2000
2. Leaver HA. Eur J Clin Investi, 2000
3. Sugiura H. Surg Laparo Endo, 1999

VATS vs. Thoracotomy?
台大醫院肺癌手術經驗 (1997-2010)



Courtesy from Dr. Kuo SW

肺葉切除術：胸腔鏡或開胸手術？

- 目前胸腔鏡肺葉切除術已經有許多醫學中心使用於肺癌之手術治療.
- 安全性：與開胸手術類似，甚至更好
- 腫瘤學方面考量(JCO 2009 meta-analysis)：
  - 局部復發率沒有差別
  - 遠處轉移率較低
  - 5年死亡率較低

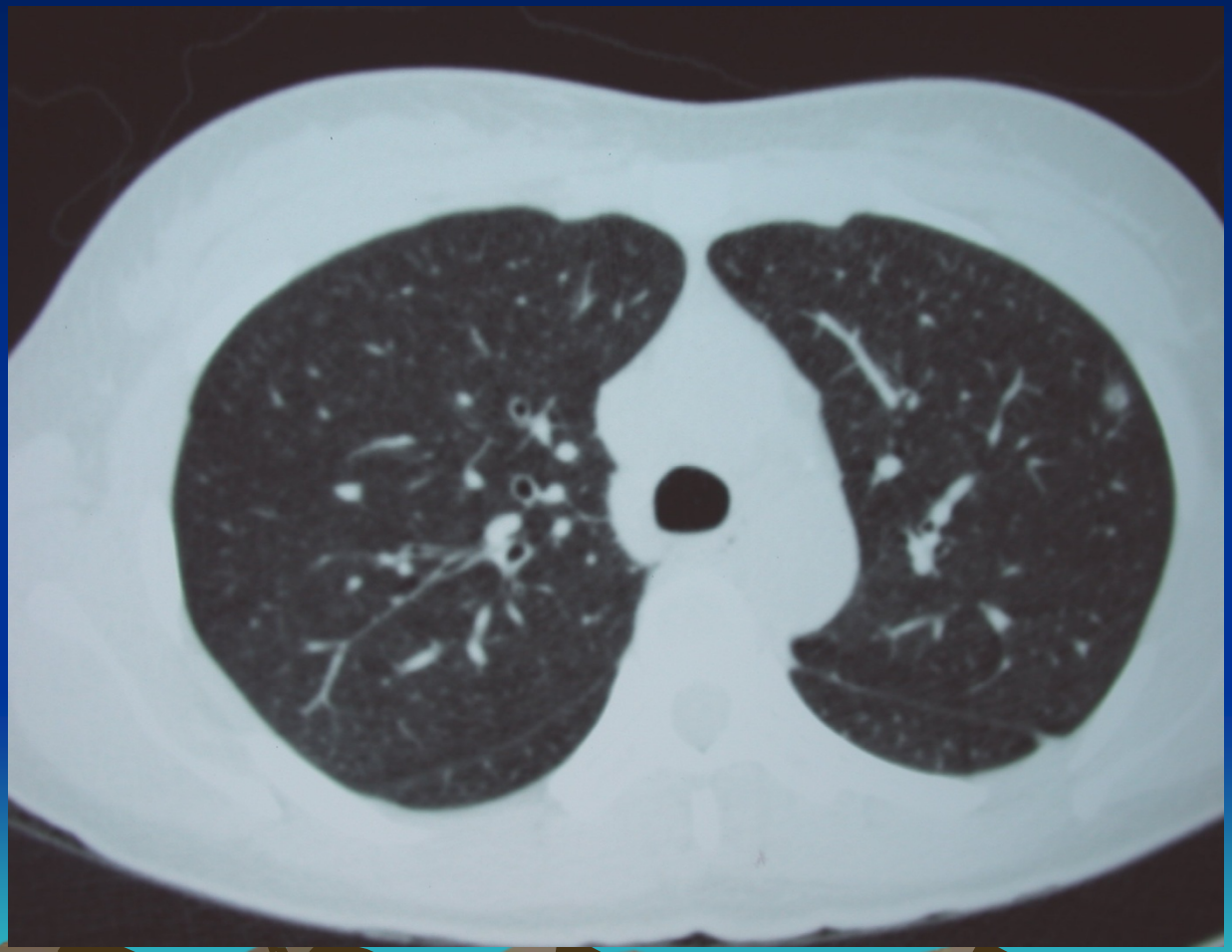
Yan TD. J Clin Oncol 2009.

B. 如何減少肺實質切除？ Lobectomy or less?

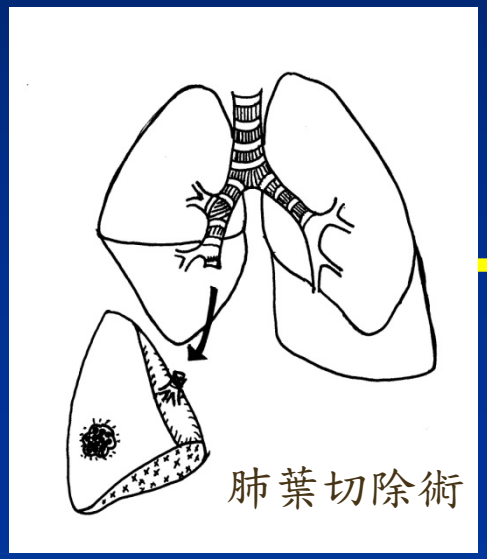
Lobectomy → Sublobar resection

1. Wedge resection (楔型切除術)
2. Segmentectomy (肺節切除術)

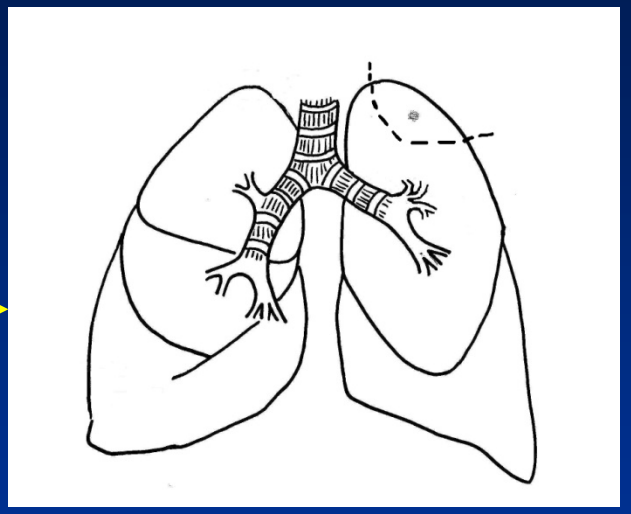
62 歲女性，胸部電腦斷層發現0.7公分結節，是否一定要接受肺葉切除？



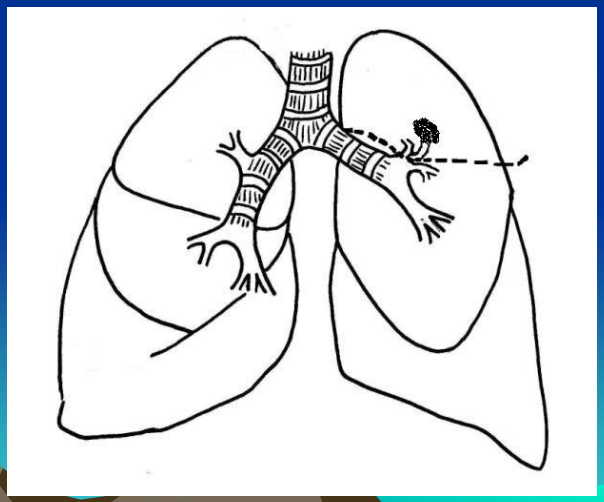
Sublobar resection for lung cancer



Lobectomy



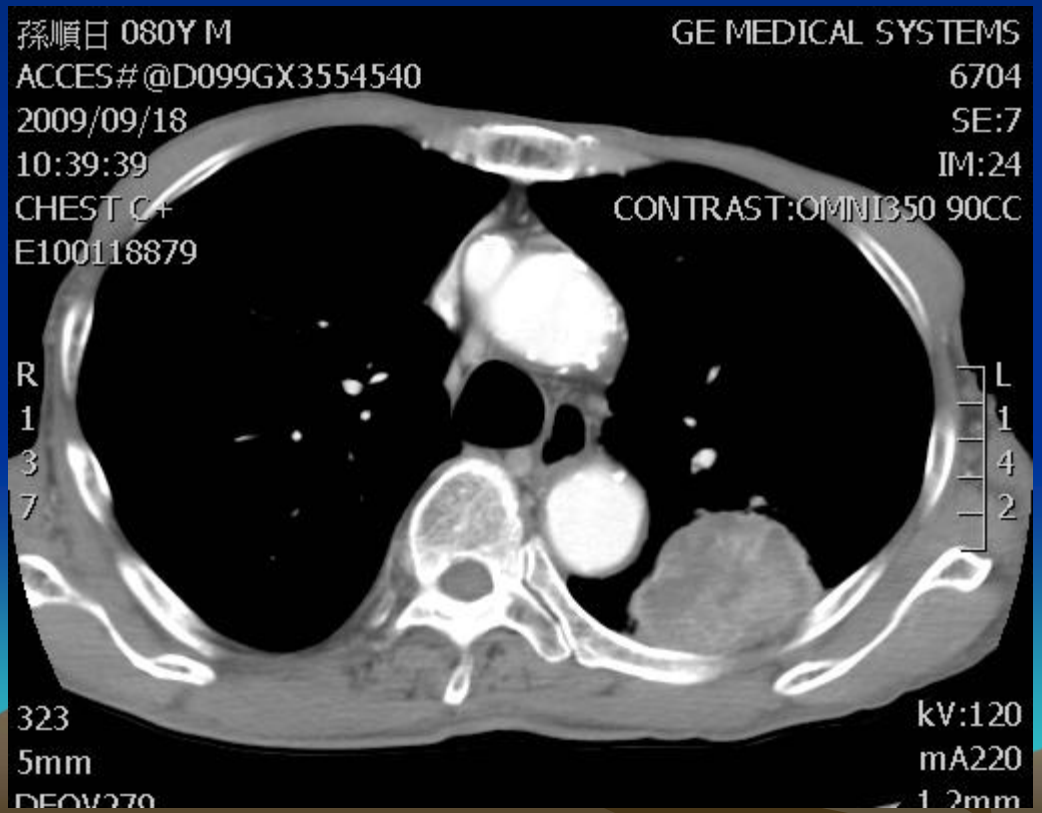
Wedge resection

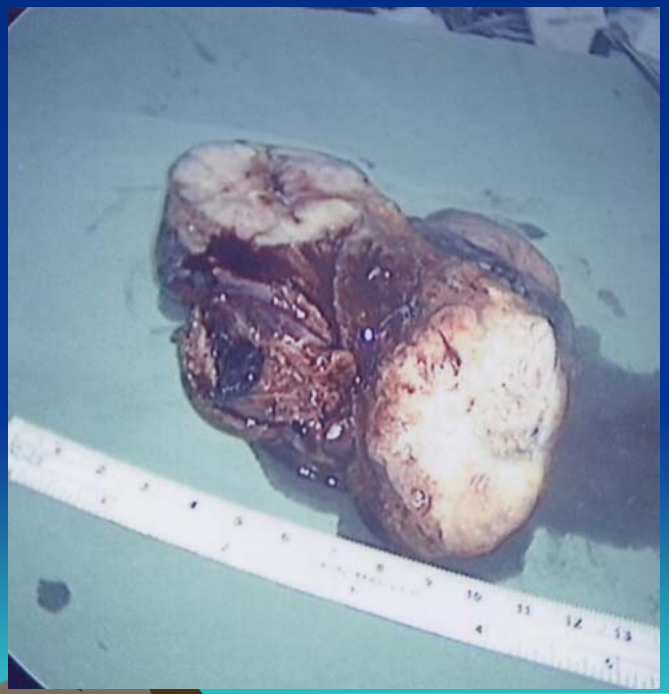


Segmentectomy

VATS LUL proper lobectomy

80歲男性, generalized weakness
CAD 心導管支架置放術後
須最近二月體重減輕8公斤,
s/p LUL proper lobectomy





Post-op CXR

術後6日出院，日常生活不受影響

VATS sublobar resection for lung cancer

- 包括楔狀切除(wedge resection)或肺節切除(segmentectomy)
- 局部復發率可能稍高，但長期存活率和肺葉切除術類似
- 楔狀切除或肺節切除之適應症：
  - Intentional: 腫瘤小於2公分, 特別是 Bronchioloalveolar cell carcinoma (BAC)
  - Compromised:年齡大或心肺功能差之病患

Bilfinger TV. Curr Opin Pulm Med 2008

TABLE 1. 5-yr Survival Data for Lobectomy vs. Sublobar Resection for NSCLC

Study	Trial Design	No. of Patients	Preoperative Staging	Stage	Operative Approach	Compromised vs. Intentional	Type of Sublobar Resection	Intraoperative Mediastinal Lymph Node Evaluation	Overall 5-yr Survival (%)		
									Lobectomy	Sublobar Resection	*p*
LCSG[1]	Prospective	247	CXR, bronchoscopy, selective CT scan	IA	100% thoracotomy	I	67% segment, 33% wedge	100%	69	60	0.08
Koike et al.[75]	Prospective	233	CT Scan	IA	N/R	I	81% segment, 19% wedge	65%	90	89	0.91
Campione et al.[58]	Retrospective	120	CT scan and bone scan	IA	100% thoracotomy	C	100% segment	100%	65	62	0.2
Marin-Ucar et al.[18]	Retrospective	34	CT scan	IA and IB	76% thoracotomy, 24% VATS	C	100% segment	100%	64	70	N/R
El-Sherif et al[19]	Retrospective	784	CT scan	IA and IB	N/R	C	41% segment, 59% wedge	67% sublobar, 97% lobe	54	40	0.0038
Iwasaki et al.[25]	Retrospective	86	CT scan	I, II, IIIA	77% thoracotomy, 23% VATS	Mixed	100% extended segment	100%	73	70	0.76
Kilic et al.[6]	Retrospective	184	CT scan, selective PET, and mediastinoscopy	IA and IB	69% thoracotomy, 31% VATS	C	100% segment	100%	47	46	0.28

C, compromised; I, intentional; CT, computerized tomography; PET, positron emission tomography; segment, segmentectomy; wedge, wedge resection; lobe, lobectomy; N/R, not recorded; VATS, video-assisted thoracoscopic surgery.

A. lobectomy 和 sublobar resection in early cancer: 長期存活類似

B. Segmentectomy 比 wedge resection: sementectomy較好

J Thorac Oncol 2010

C. 如何減少麻醉創傷？

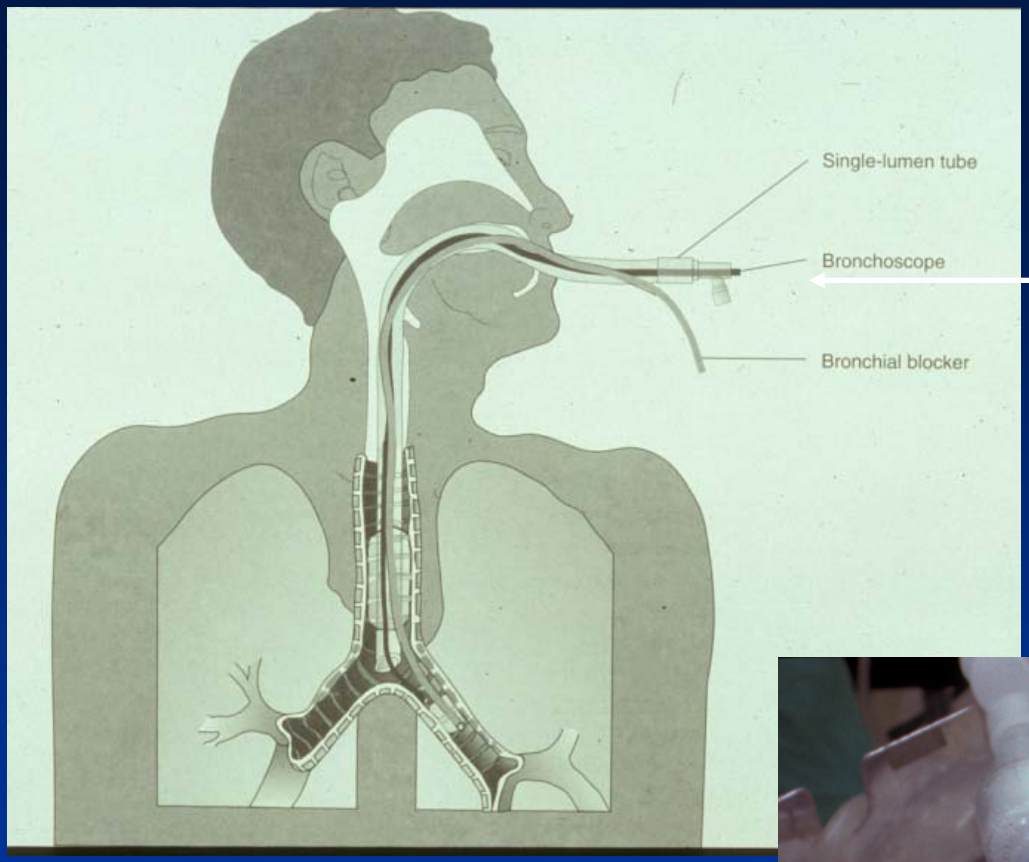
傳統胸腔鏡手術之麻醉

- General anesthesia with muscle paralysis
- Endotracheal intubation with one lung ventilation

-> 醫師輕鬆，病患危險增加：

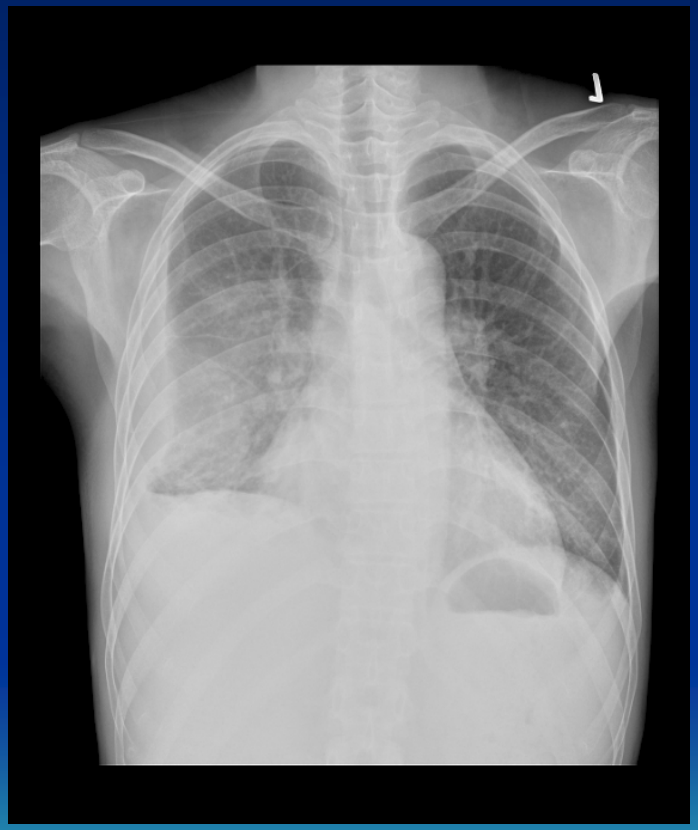
  - Increased risk of pneumonia
  - Impaired cardiac performance
  - Barotrauma by ventilator
  - Pulmonary atelectasis
  - Intubation-related complication

胸腔手術之麻醉及插管
One lung ventilation



Double lumen
endotracheal tube

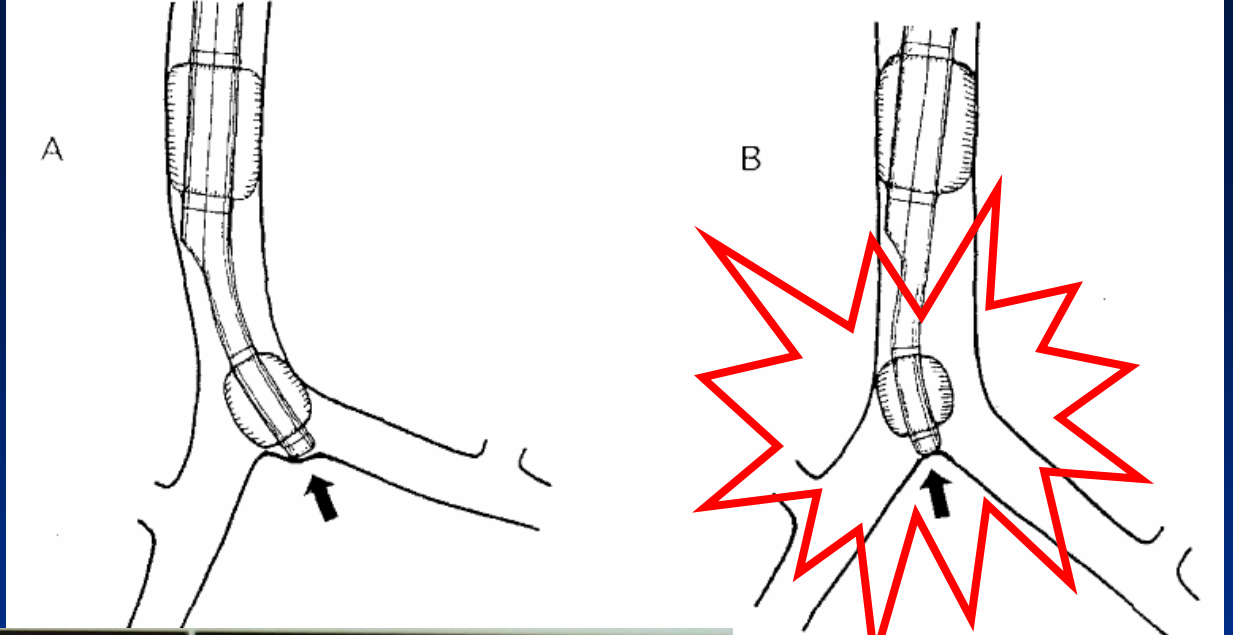
30 y/o female with IDDM and uremia Complicated with right empyema

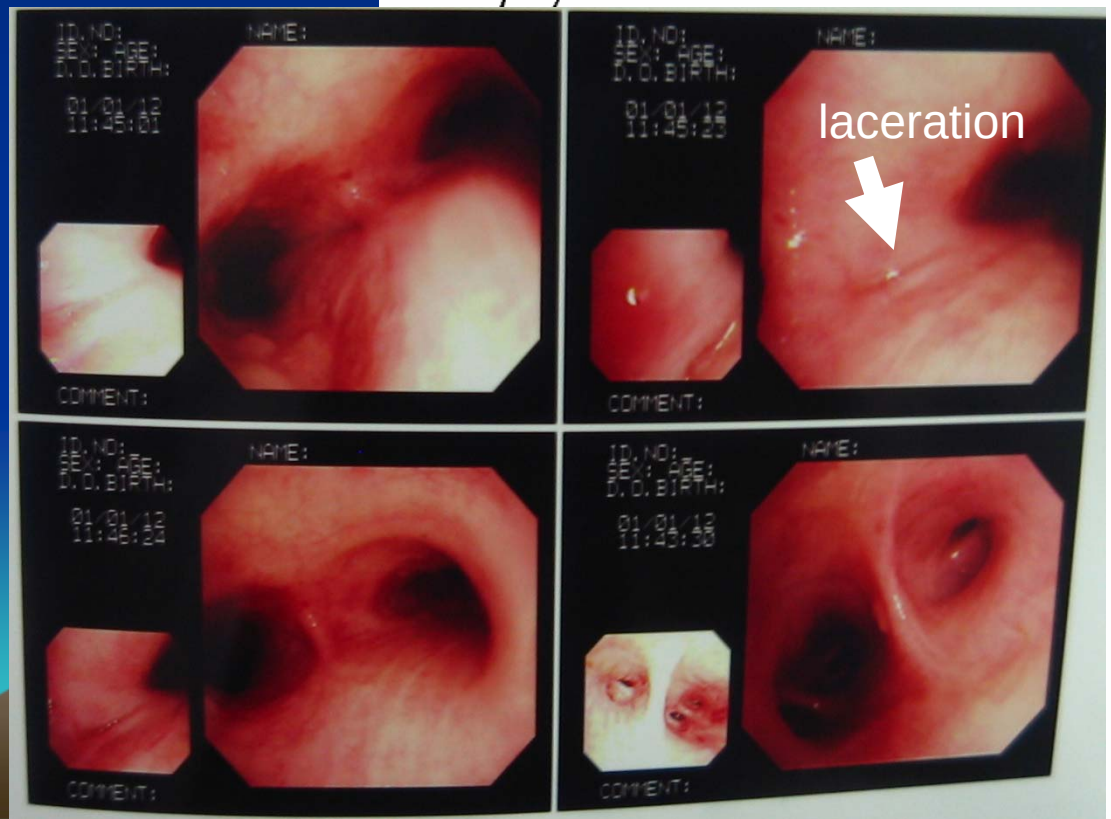


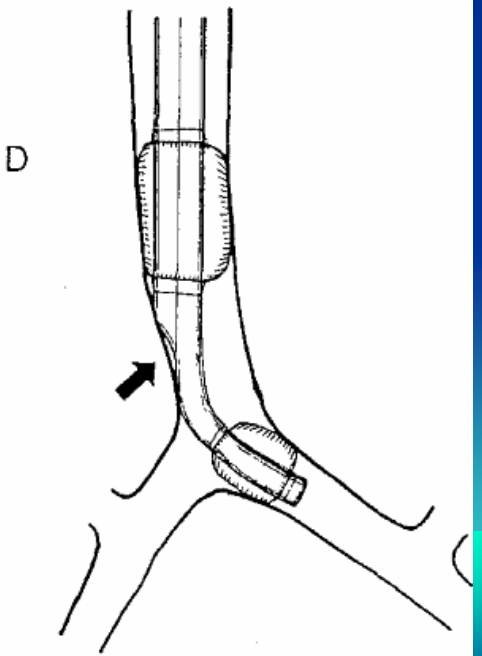
Before Double-lumen intubation

CPR for Tension pneumomediastinum after Double lumen intubation

Courtesy from Dr. Hsu HH


A
B

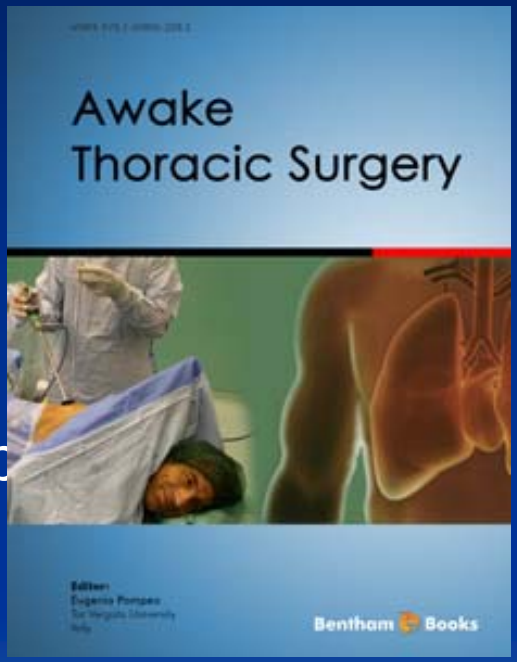

laceration


D

免插氣管內管胸腔鏡手術
Non-intubated (Awake) VATS

免氣管插管胸腔鏡(nonintubated VATS)手術之優點

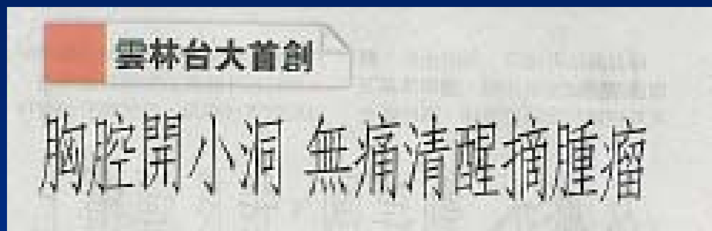
- 無插管之併發症
- 心血管之功能較不受影響
  - Improved myocardial blood flow
  - Improved LV function
  - Reduced heart rate and arrhythmia
- 術後肺功能恢復較好
  - Intact cough ability immediate after op
  - Improved post-op lung function
- COPD 術後發作之比例較低
  - Decreased bronchospasm
  - Decreased respiratory complications



Mineo TC. Eur J Cardiothorac Surg. 2007

夢想起點：台大醫院雲林分院
無痛清醒胸腔鏡手術

2009年8月開始



雲林台大首創

胸腔開小洞 無痛清醒摘腫瘤

迷你胸腔鏡手術

切除肺腫瘤 全程醒著看

無痛開胸 病患清醒傷口小

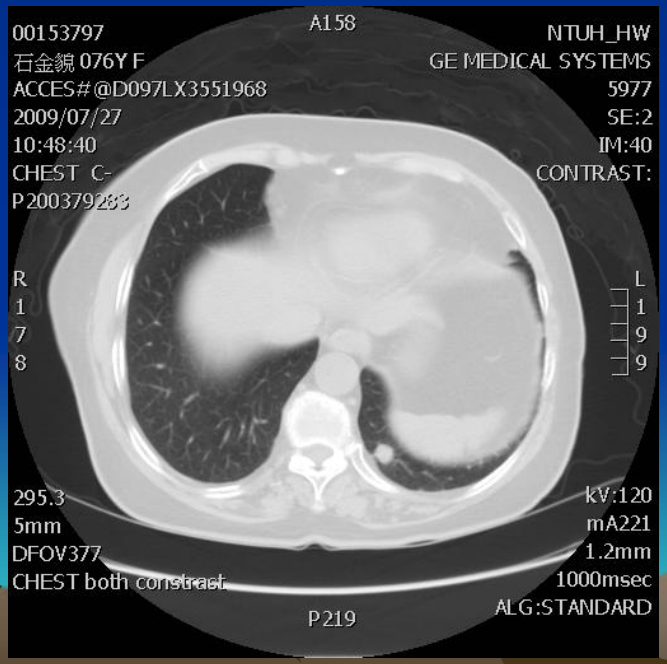
開口僅0.3公分 麻醉風險低

台大首創

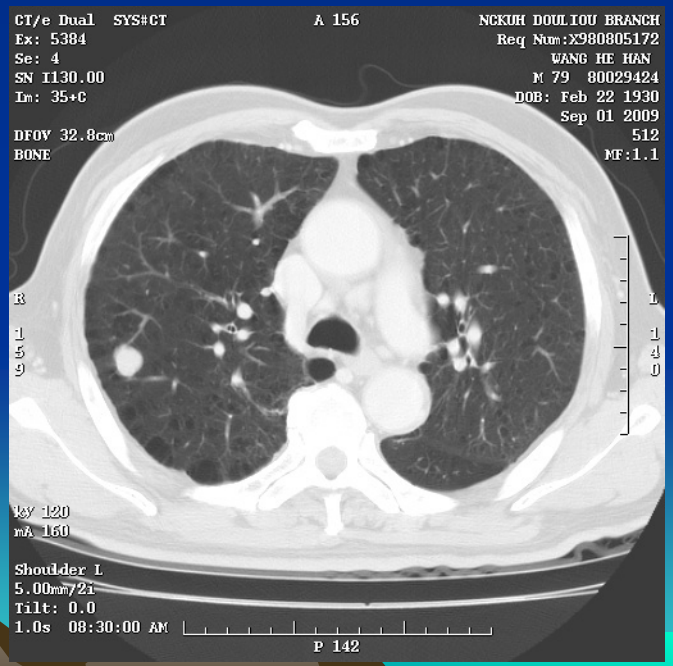
時間不能拖久

免氣管插管之迷你胸腔鏡切除肺腫瘤

76歲女性，大腸癌術後
左下肺1公分腫瘤



81歲男性, COPD
雙側肺腫瘤，無診斷



Awake needlescopic VATS video

Nonintubated Needlescopic Video-Assisted Thoracic Surgery for Management of Peripheral Lung Nodules

Yu-Ding Tseng, MD, Ya-Jung Cheng, MD, Ming-Hui Hung, MD, Ke-Cheng Chen, MD, and Jin-Shing Chen, MD, PhD

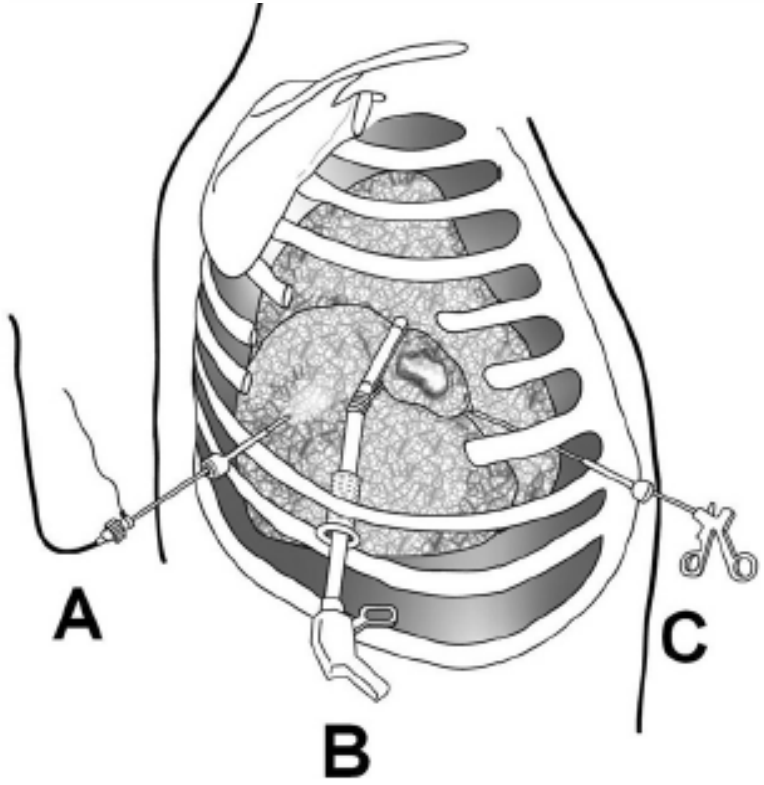
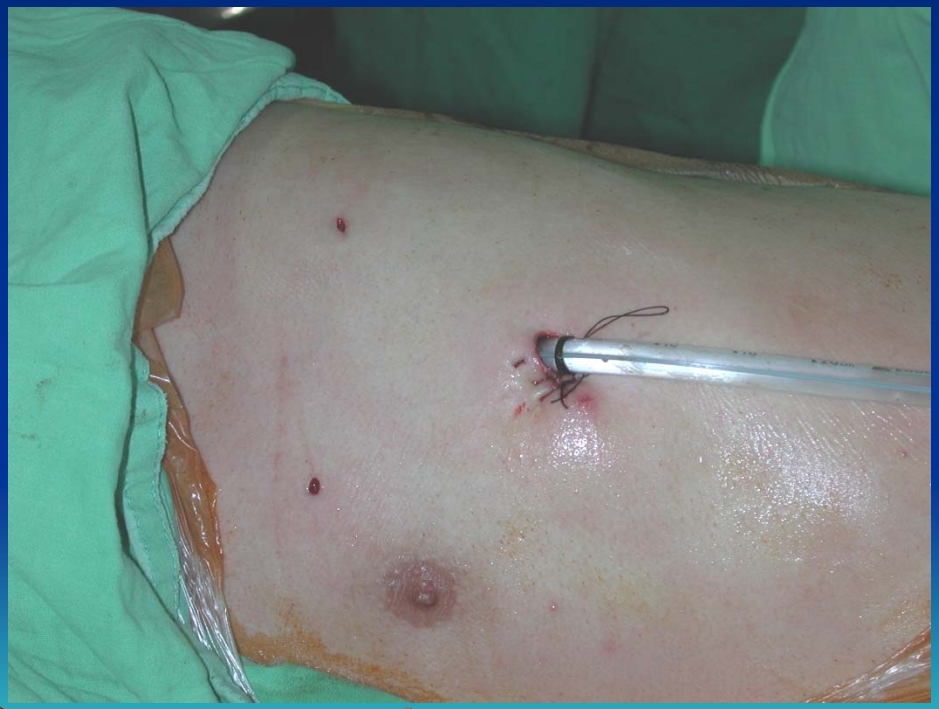


Fig 1. Positioning of needlescopic instruments for excision of a peripheral lung nodule. (A) The 3-mm thoracoscope; (B) the 10-mm endostapler; and (C) the 3-mm mini-endograsper.



Tseng YD, et al. Ann Thorac Surgery 2012

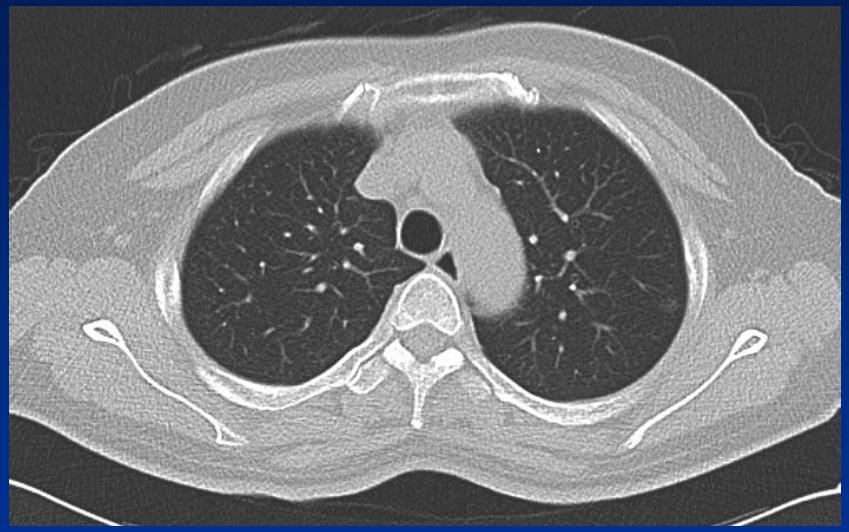
46 patients with peripheral lung nodules (2008-2011)

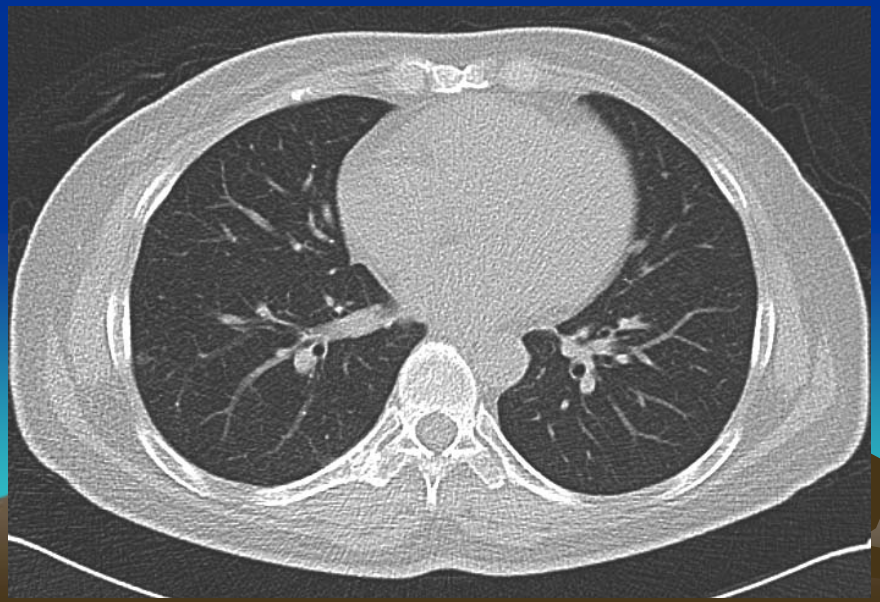
Table 4. Diagnoses of the Nodules

Diagnosis	No. (%) (N = 46)
Malignancy	8 (17.4)
Lung cancer	3 (6.5)
Metastatic cancer	5 (10.9)
Benign	38 (82.6)
Intrapulmonary anthracosis	11 (23.9)
Granulomatous inflammation	6 (13.0)
Hamartoma	5 (10.9)
Cryptococcus infection	5 (10.9)
Sclerosing hemangioma	5 (10.9)
Organizing fibrosis	3 (6.5)
Tuberculoma	2 (4.3)
Arteriovenous malformation	1 (2.2)

Diagnostic rate: 100%

Bilateral nonintubated VATS





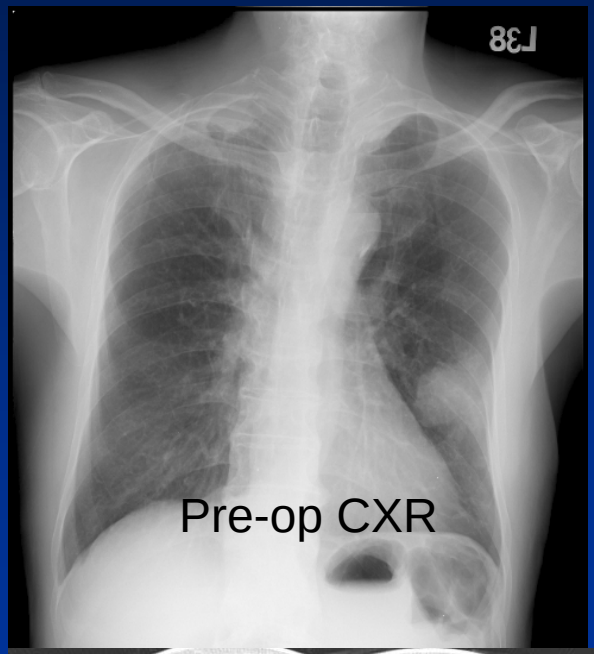
58 y/o female, Sjogren's syndrome

Final pathology:

1. Left: BAC
2. Right: benign nodule

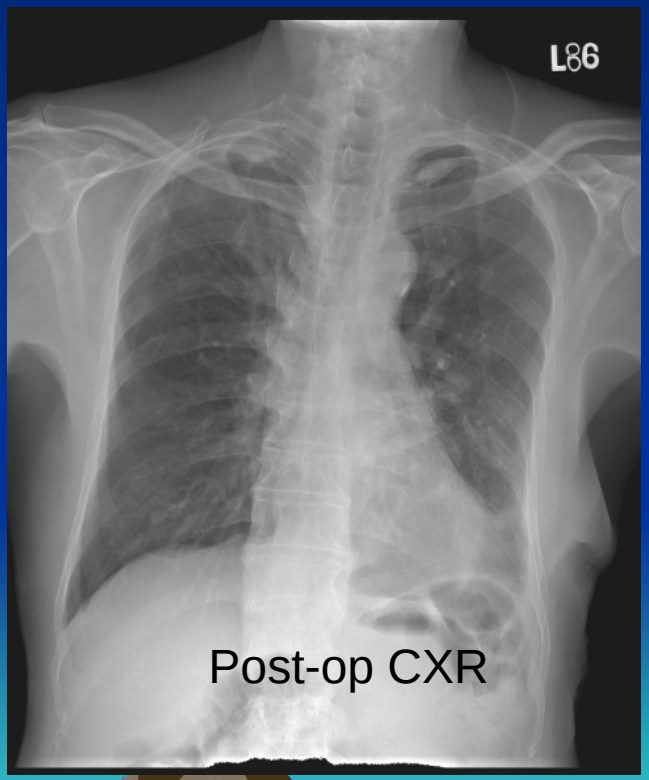
Tsai TM, et al. J Thorac Cardiovasc Surg

Non-intubated VATS segmentectomy for high risk patients:



Pre-op CXR

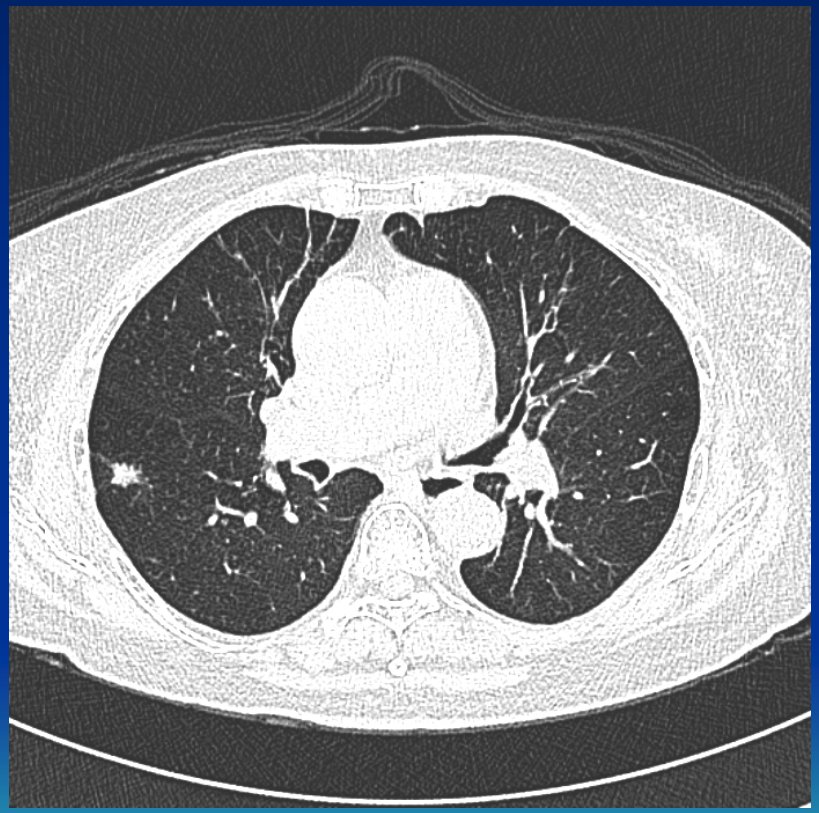
81 y/o male, COPD, LLL sq. ca
FEV1.0: 1.02L, 44.6%
% FEV1.0: 47.9%



Post-op CXR

Final pathology: T2aN0M0
Postoperative stay: 4 days

81 y/o female, RLL adenocarcinoma
FEV1.0: 0.77L, 74.5%; %FEV1.0: 58.8%



Non-intubated VATS wedge resection
Post-op stay: 5 days

Non-intubated thoracoscopic lobectomy: The NTUH experience

ORIGINAL ARTICLE

Nonintubated Thoracoscopic Lobectomy for Lung Cancer

Jin-Shing Chen, MD, PhD,† Ya-Jung Cheng, MD,‡ Ming-Hui Hung, MD,‡ Yu-Ding Tseng, MD,†*
*Ke-Cheng Chen, MD,† and Yung-Chie Lee, MD, PhD**

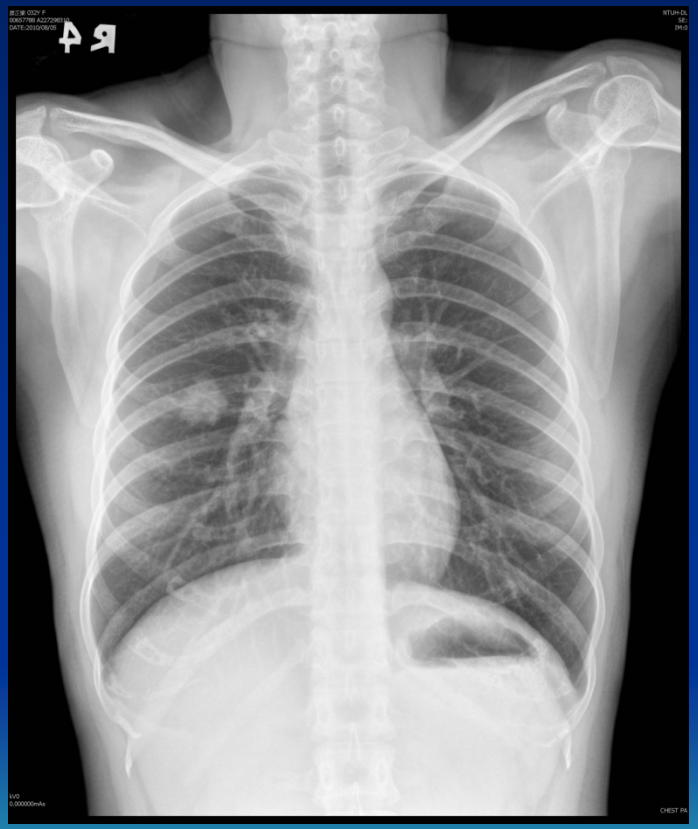
- Study design: Retrospective chart review with historical control
- Study group (2009/8-2010/6):
  - 30 lung cancer patients underwent non-intubated thoracoscopic lobectomy
- Control group (2008/8-2009/7):
  - 30 lung cancer patients with the same selection criteria underwent intubated thoracoscopic lobectomy using single-lung ventilation

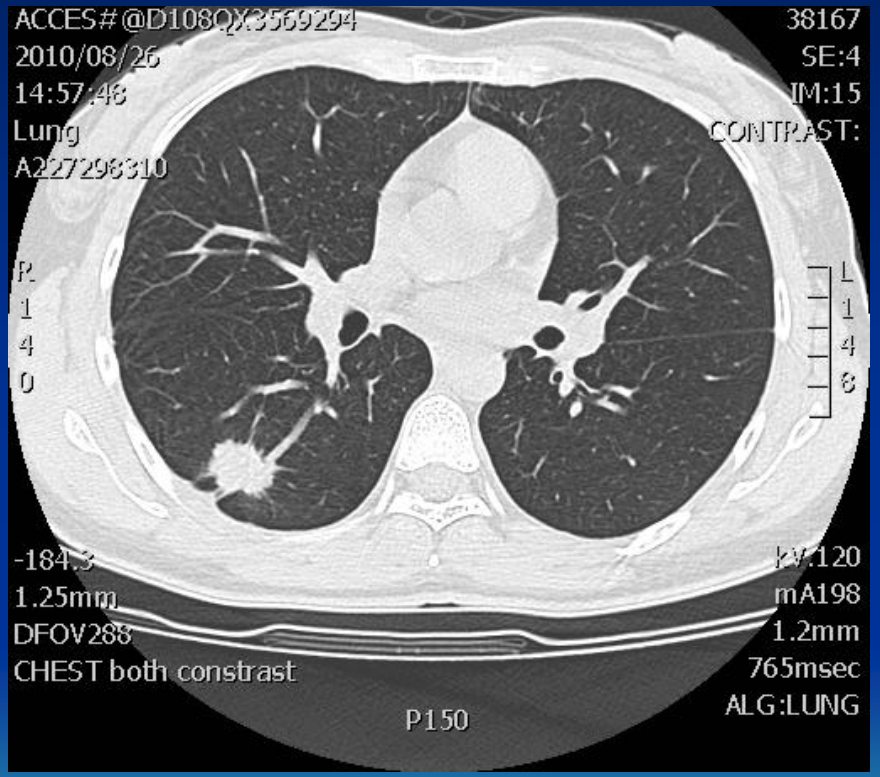
Ann Surg 2011

Anesthetic settings:

- Preparation:
  - Thoracic epidural anesthesia: T5/6 level to achieve a sensory block between T2/T9
  - Continuous monitoring: ECG, pulse oxymetry, respiratory rate, blood pressure, urine output, body temperature.
  - End-tidal CO2: monitored by a detector into one nostril
  - ABG: periodically
- Sedation:
  - Premedication: fentanyl
  - Continuous IV infusion with propofol using a target-controlled infusion (TCI) method
- No neuromuscular blockades

32 y/o female, adenocarcinoma
Clinical staging: cT1bN0-1M0

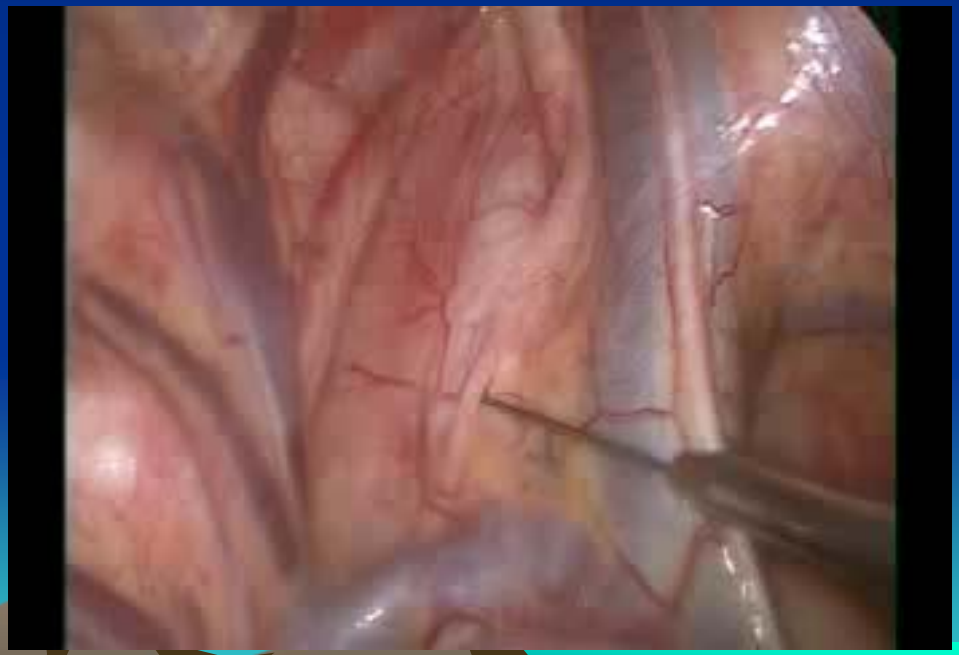




Non-intubated VATS lobectomy

Anesthesia and settings

Operation technique



Nonintubated VATS: 台大經驗 (2009-2012)

- A total of 302 patients underwent 303 VATS
  - –Needlescopic VATS wedge resection: 47 cases
  - –Conventional VATS wedge resection: 94 cases
  - –VATS segmentectomy: 20 cases
  - –VATS lobectomy: 142 cases (including benign and malignant diseases)
- Conversion to intubated general anesthesia: 14 cases (5%)
- No mortality

ORIGINAL ARTICLE

Nonintubated thoracoscopic lung resection: a 3-year experience with 285 cases in a single institution

Ke-Cheng Chen[1,3], Ya-Jung Cheng[2], Ming-Hui Hung[2], Yu-Ding Tseng[3], Jin-Shing Chen[1,3]

[1]Division of Thoracic Surgery, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [2]Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [3]Department of Surgery, National Taiwan University Hospital Yun-Lin Branch, Yun-Lin County, Taiwan

Table 1. Clinical characteristics of the patients.

Variable	N=285
Age [y][a]	59.2±12.3 [60,19-89]
Sex (male)	107 (37.5%)
Smoking (%)	75 (26.3%)
Operation methods	
Conventional VATS	237 (83.2%)
Needlescopic VATS	48 (16.8%)
Operation procedures	
Lobectomy	137 (48.1%)
Wedge resection	132 (46.3%)
Segmentectomy	16 (5.6%)
Pathological diagnosis	
Lung cancer	159 (55.8%)
Metastatic cancer	17 (6.0%)
Benign lung tumor	104 (36.5%)
Pneumothorax	5 (1.8%)

[a]Mean ± standard deviation (median, range); VATS = video-assisted thoracoscopic surgery.

Table 2. Treatment outcome of nonintubated thoracoscopic lung resection.

Variable	N=285
Anesthetic side effects (%)	
Vomiting requiring medication (%)	12 (4.2%)
Sore throat (%)	6 (2.2%)
Headache	5 (1.8%)
Operation complications (%)	
Air leaks >5 days	6 (2.1%)
Bleeding	2 (0.7%)
Pneumonia	3 (1.1%)
Conversion to tracheal intubation (%)	14 (4.9%)
Lobectomy	10/137 (7.3%)
Wedge resection	3/132 (2.3%)
Segmentectomy	1/16 (6.3%)
Conversion to thoracotomy (%)	1 (0.4%)
Mortality (%)	0 (0%)

J Thorac Dis 2012

Nonintubated VATS lobectomy in geriatric NSCLC patients

Ann Thorac Surg 2012, accepted

爭議性肺癌手術及合併標靶藥物

- Resectability?
  - Stage III and IV
    - Locally advanced lung cancer
    - Multiple lung cancers
    - Distant metastasis (liver, bone, etc)
    - Pleural seeding

標靶治療：上帝送給亞洲人的禮物？！

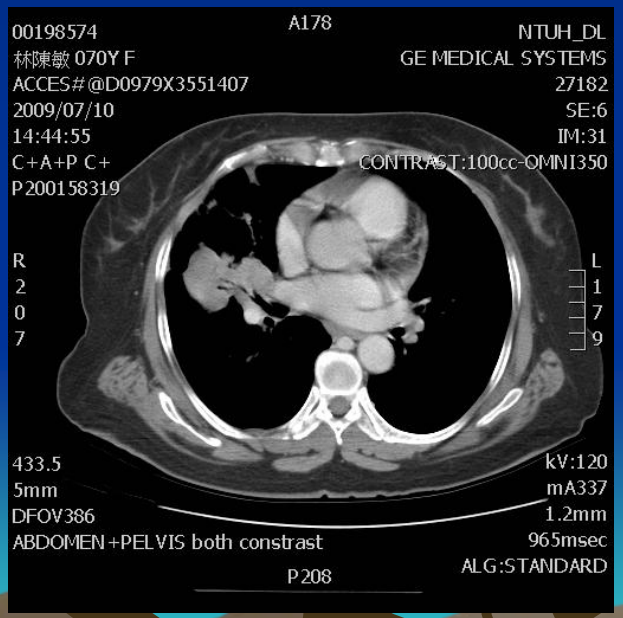
- 台灣有許多病患排斥化學治療
- 標靶藥物(EGFR TKIs)可延長晚期亞洲肺癌病患生命
- 標靶藥物治療之反應：與EGFR基因突變有關
- EGFR基因突變比例：
  - 歐美國家：<10%
  - 東亞國家：30%
  - 肺腺癌、女性、不抽菸病患之比例更高
- 比化療副作用少，理論上更適合與手術治療合併使用。

NEJM 2009; 361:947.

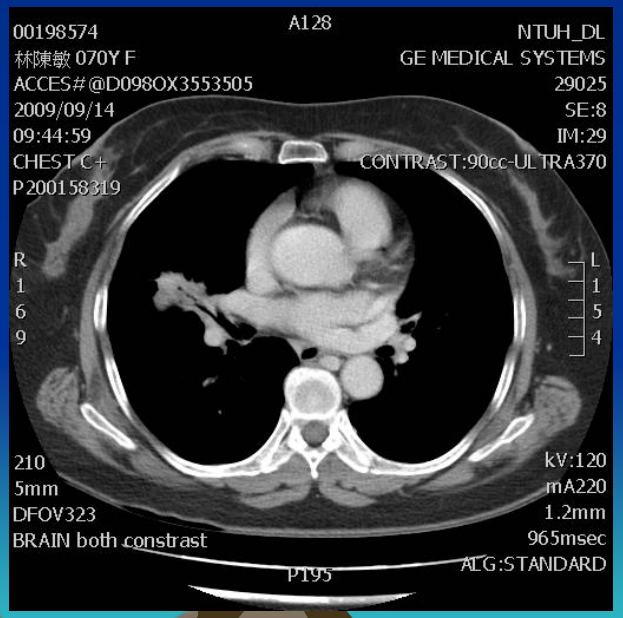
術前標靶治療對於局部嚴重肺癌之效果

70 歲女性, COPD, FEV1 = 0.96L, 55% of prediction
右中肺嚴重肺腺癌， 併右上肺葉靜脈侵犯
基因檢測：EGFR mutation analysis: Exon 21 mutation
適合使用標靶藥物

手術：由原本雙肺葉切除減小為單肺葉切除



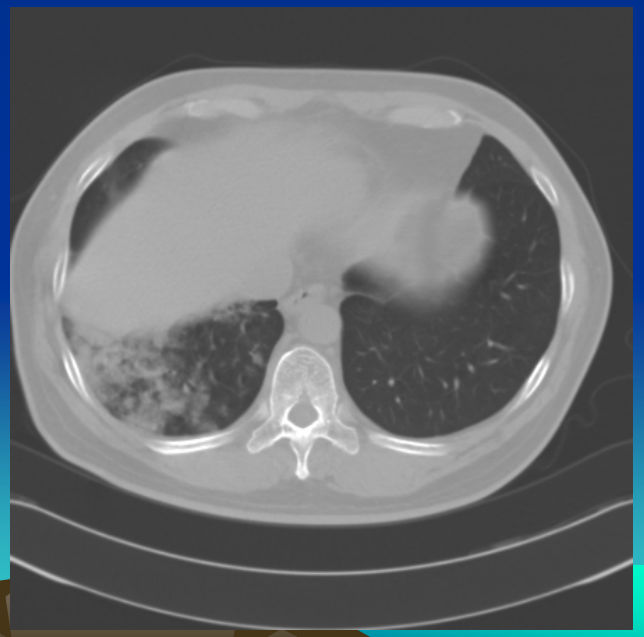
Before Gefitinib



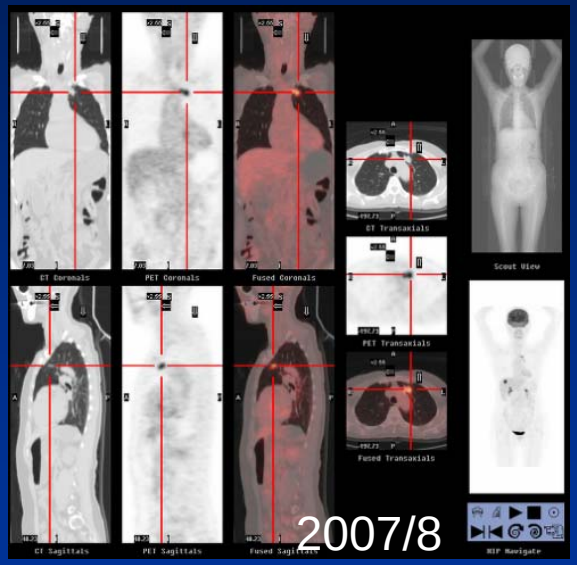
After Gefitinib

術後標靶治療對於局部嚴重肺癌之效果

- 54 歲男性, 腎臟癌切除一側腎臟
- 右中肺葉及下肺葉肺腺癌
- 手術: 右中肺楔狀切除及右下肺肺葉切除術
- 病理報告：T4N2M0, stage IIIB
- 基因檢測：EGFR Exon 21 mutation
- 術後使用標靶治療，至今42月無復發



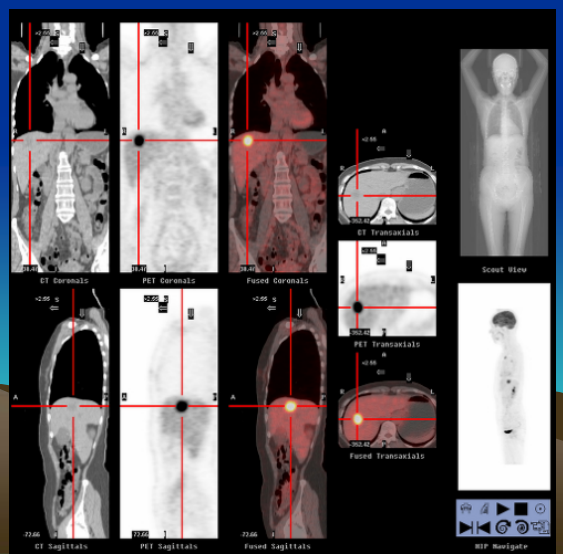
71 y/o female
LUL lung ca with liver metastasis

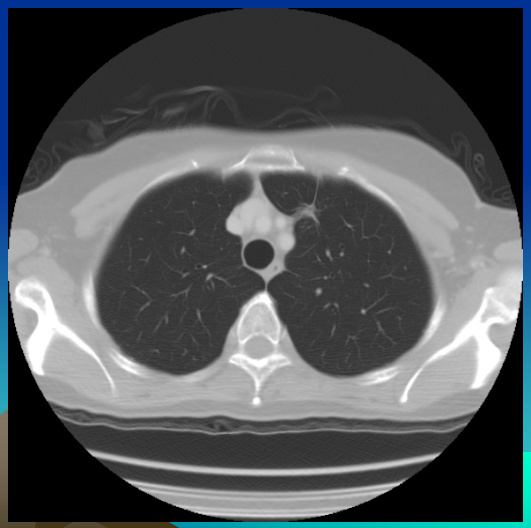


2007/8

2007/9
Hepatectomy:
metastatic lung cancer
Starting Iressa

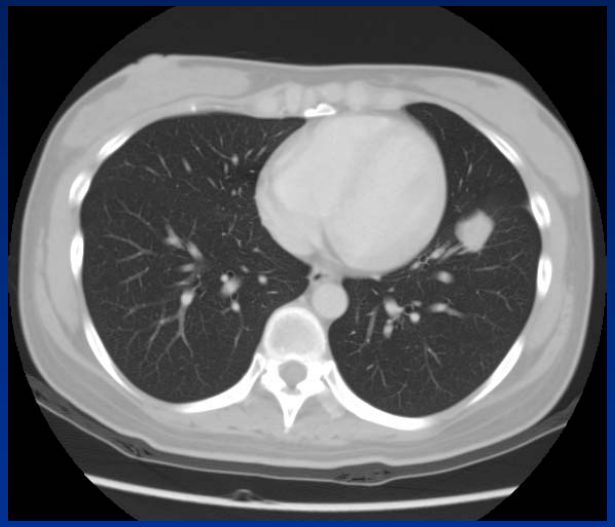
2011/3

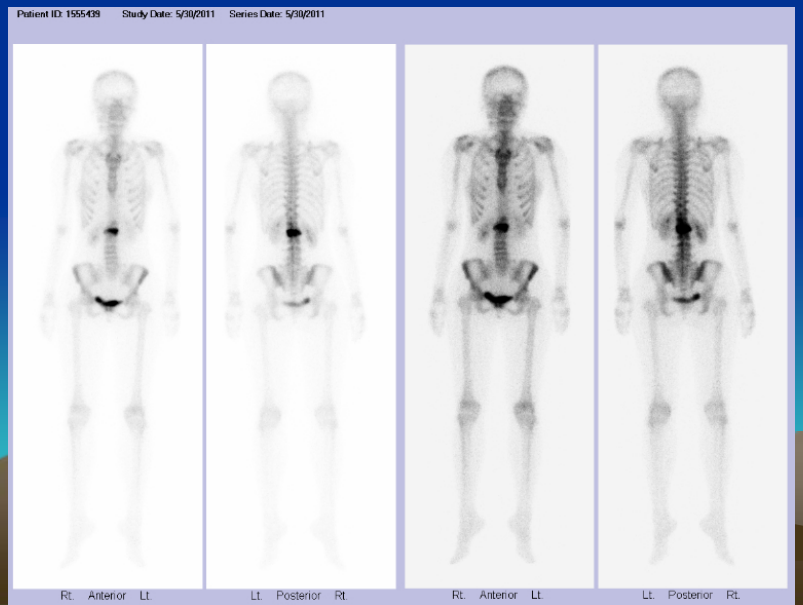


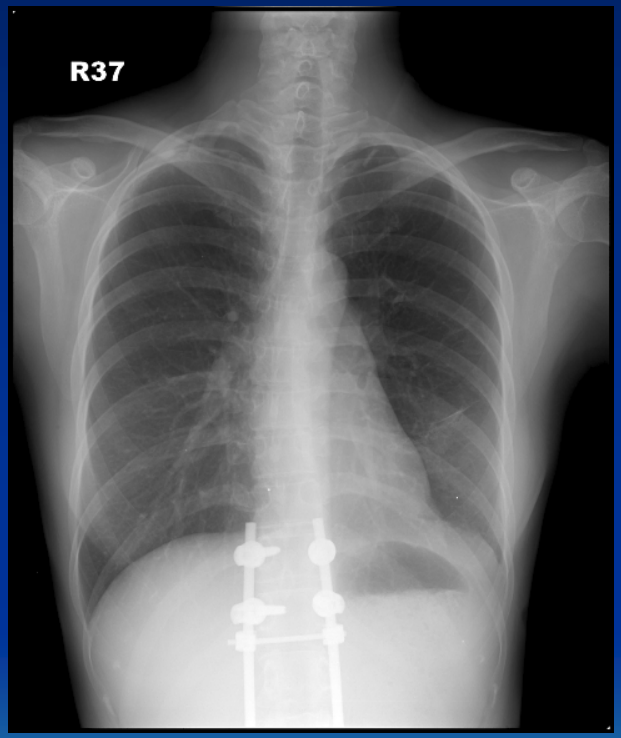


2011年接受肺腫瘤切除
至今無復發，且無使用藥品

33 y/o female
Solitary bone metastasis

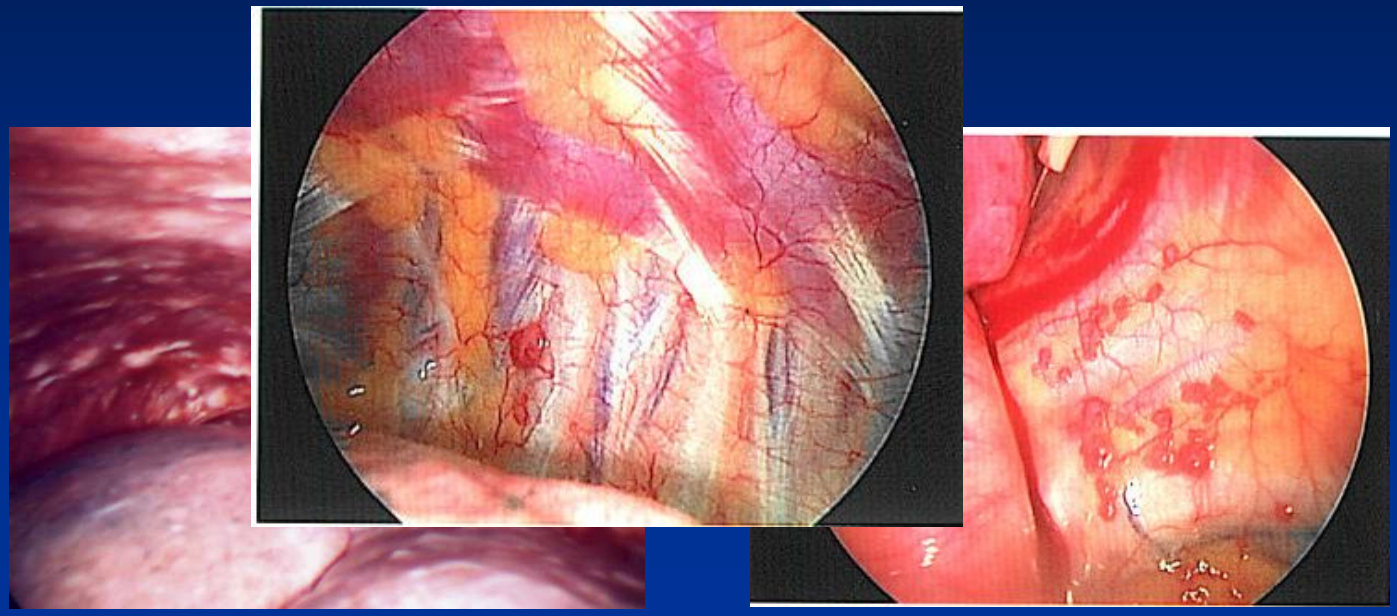






Spine: resection + radiotherapy
Lung: VATS wedge resection
Post-op: Iressa therapy

Pleural seeding during VATS



Choices:

1. Close the wound with subsequent systemic therapy
2. Reset the tumor and the seeding with subsequent systemic therapy

肺癌手術與合併治療趨勢總結

- 有效且傷害最小的手術：
  - 老年及心肺功能差的病患越來越多
  - 除了手術外還有其他有效的治療
- 廣義微創手術:
  - 減小切口(胸腔鏡)
  - 減小切除範圍(肺節切除或楔狀切除)
  - 微創麻醉(免氣管插管)
- 個人化合併治療：
  - 考量身體狀況、年齡、肺功能 (balance between radicality and life quality)
  - 基因檢測及對藥物之反應
  - 不放棄可以根治手術的機會


Thanks for your attention

Nonintubated Thoracoscopic Lobectomy for Lung Cancer

Jin-Shing Chen, MD, PhD,† Ya-Jung Cheng, MD,‡ Ming-Hui Hung, MD,‡ Yu-Ding Tseng, MD,† Ke-Cheng Chen, MD,† and Yung-Chie Lee, MD, PhD**

Objective: To evaluate the feasibility and safety of thoracoscopic lobectomy without endotracheal intubation.

Summary Background Data: General anesthesia with single-lung ventilation is considered mandatory for thoracoscopic lobectomy for non–small cell lung cancer (NSCLC). Nonintubated thoracoscopic lobectomy has not been reported previously.

Methods: From August 2009 through June 2010, some 30 consecutive patients with clinical stage I or II NSCLC were treated by nonintubated thoracoscopic lobectomy using epidural anesthesia, intrathoracic vagal blockade, and sedation. To evaluate the feasibility and safety of this novel technique, they were compared with a control group consisting of 30 consecutive patients with clinical stage I or II NSCLC who underwent thoracoscopic lobectomy using intubated general anesthesia from August 2008 through July 2009.

Results: Collapse of the operative lung and inhibition of coughing were satisfactory in the nonintubated patients, induced by spontaneous breathing, and vagal blockade. Three patients in the nonintubated group required conversion to intubated-single lung ventilation because of persistent hypoxemia, poor epidural anesthesia pain control, and bleeding. One patient in each group was converted to thoracotomy because of bleeding. The 2 groups had comparable anesthesia durations, surgical durations, blood loss, and numbers of dissected lymph nodes. Patients who underwent nonintubated surgery had lower rates of sore throat (6.7% vs 40.0%, $P = 0.002$) and earlier resumption of oral intake (mean, 4.7 hours vs 18.8 hours, $P < 0.001$). Patients undergoing nonintubated surgery also had a trend toward better noncomplication rates (90% vs 66.7%, $P = 0.057$) and shorter postoperative hospital stays (mean, 5.9 days vs 7.1 days, $P = 0.078$).

Conclusions: Nonintubated thoracoscopic lobectomy is technically feasible and is as safe as lobectomy performed with intubation in highly selected patients. It can be a valid alternative of single-lung-ventilated thoracoscopic surgery in managing early-stage NSCLC.

(*Ann Surg* 2011;00:1–6)

for managing early-stage NSCLC. In addition, it is supported by evidence-based treatment guidelines.[1–5]

Since the introduction of the double-lumen endotracheal tube, intubated general anesthesia with one-lung ventilation has been considered mandatory in both open and thoracoscopic surgery.[6] However, adverse effects of intubated general anesthesia occur after the operation and they include intubation-related complications, ventilator-induced lung injury, impaired cardiac performance, and postoperative nausea and vomiting.[7–10] To reduce the adverse effects of intubated general anesthesia, thoracoscopic surgery without endotracheal intubation has been recently employed for management of pneumothorax,[11–13] resection of pulmonary nodules,[14] resection of solitary metastases,[15] and performing lung volume reduction surgery.[16] The results achieved for these early surgeries are encouraging.

Although the feasibility of thoracoscopic surgery via nonintubated anesthesia was demonstrated in pleural and peripheral lung diseases, thoracoscopic major pulmonary resection such as lobectomy has rarely been performed via nonintubated anesthesia because of several concerns, including hypoxemia and hypercapnia induced by prolonged spontaneous one-lung breathing, uninhibited coughing induced by manipulation of the bronchial trees, and lung movement during surgical dissection.[7] These difficulties interfere with division of hilar vessels and bronchus during thoracoscopic lobectomy and cause dangerous complications, which may result in emergency conversion to tracheal intubation and thoracotomy.

Using combination of epidural anesthesia, intrathoracic vagal blockade, and appropriate sedation, we found that nonintubated thoracoscopic lobectomy is technically feasible although the safety and efficacy were unclear. In addition, comparison between nonintubated and intubated thoracoscopic lobectomy has never been performed. We hypothesized that nonintubated thoracoscopic lobectomy was associated with a prompt recovery of gastrointestinal function, fewer

Chen JS et al. Ann Surg 2011

並非沒有風險
Conversion to general anesthesia

- Timing:
  - Severe and dense adhesions
  - Poor oxygenation
  - Significant mediastinal movement
  - Uncontrollable bleeding (Emergent)
- Method:
  - Seal the wound with a chest tube to re-expand the lung
  - Rotate the operation table
  - Single lumen endo-tube insertion +/- bronchoscopy, followed by blocker.

困難手術 VS. 容易手術

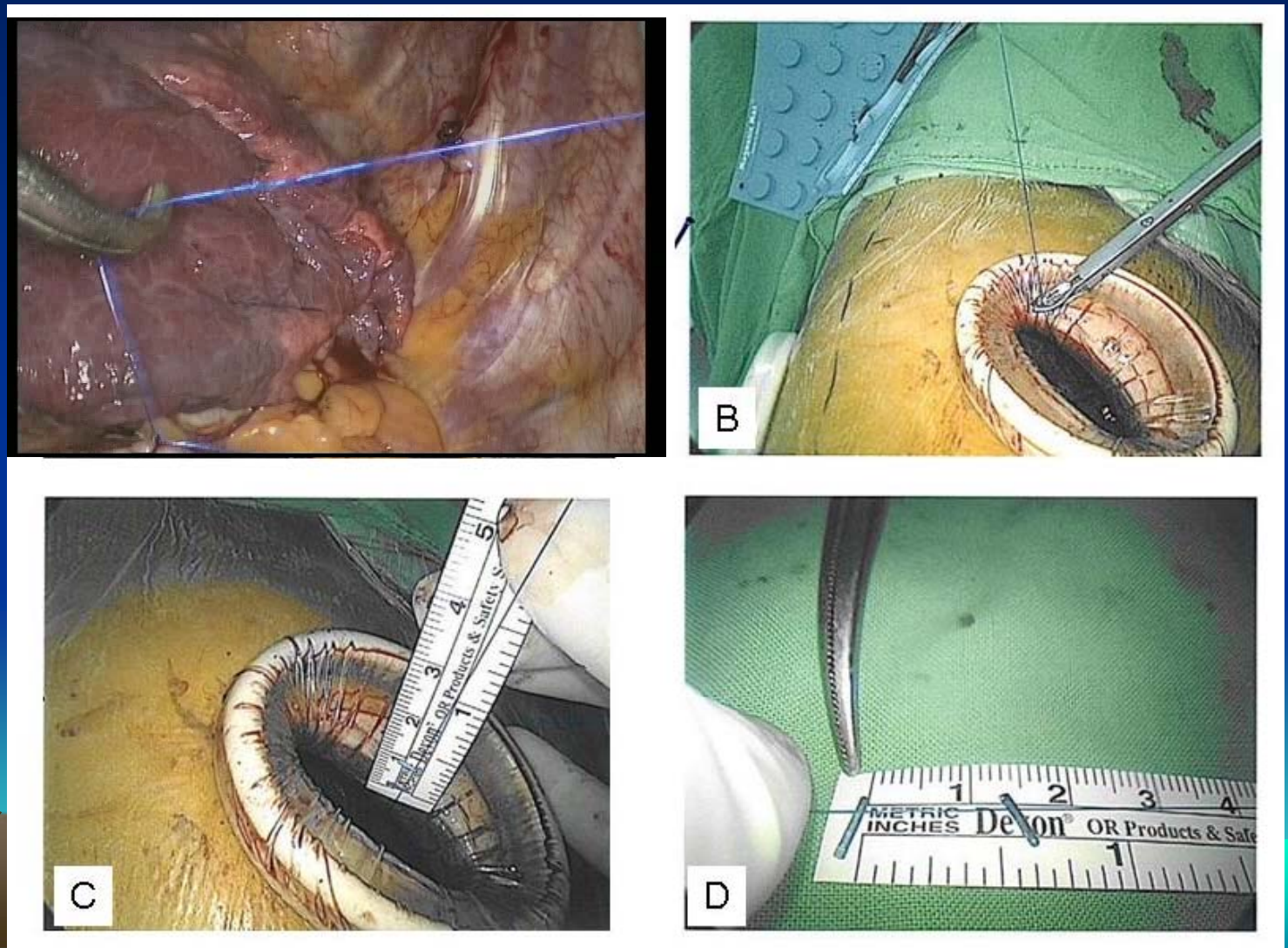
高困難度手術(呼吸快，位移大)

中困難度手術(呼吸慢，位移大)

低困難度手術
(呼吸慢，位移小)

是否可以客觀評估手術之困難度？

呼吸速率、縱隔及橫膈位移測量



初步成果

20例免插管肺葉切除術之手術困難度比較

	Easy group N = 13	Difficult group N = 7	P Value
Respiration rate, /min	14.9 ± 2.8	17.9 ± 3.7	0.096
Mediastinal movement, mm	5.8 ± 3.1	12.5 ± 6.6	0.037
Diaphragm movement, mm	15.3 ± 9.4	20.7 ± 6.0	0.187

縱隔位移(呼吸速率?)會影響手術困難度

位移> 10 mm: 困難

未來研究重點：使用藥物減少呼吸速率及縱隔位移

Non-Intubated Thoracoscopic Lobectomy for Lung Cancer:
A Prospective, Randomized trial

ClinicalTrial.gov ID: NCT01533233

陳晉興 鄭雅蓉 陳榮楷 楊泮池

台大醫院 外科部 麻醉部 內科部 臨床試驗中心

Patients and methods

- A total of 100 patients were enrolled between 2010 to 2011
  - **Non-intubated group**: 50 lung cancer patients underwent non-intubated thoracoscopic lobectomy + LN dissection
  - **Intubated group:** 50 lung cancer patients with the same selection criteria underwent single-lung intubated thoracoscopic lobectomy + LN dissection

Selection criteria for thoracoscopic lobectomy

- Inclusion criteria:
  - Clinical stage I or II peripheral NSCLC; thoracoscopic lobectomy is feasible
  - Age between 25 to 80 years
  - Tumor size $\leq$ 5 cm without evidence of chest wall, diaphragm or main bronchus involvement
  - Predicted FEV1.0 > 60% or FEV1.0 > 1.5L
  - Adequate hematological function
    - (ANC > 1.5 x 109/L, platelets > 100 x 109/L)
    - PT, PTT<1.5X
- Exclusion criteria:
  - Failed epidural catheter insertion
  - ASA score > 3
  - Unfavorable airway or spinal anatomy
  - Preoperative chemotherapy or radiotherapy
  - Pregnant or lactation female

Outcome variables

- Primary outcome:
  - Safety: Complication rate in each group
- Secondary outcomes:
  - Short-term outcome: Postoperative hospital stay, conversion rate to GA, anesthesia and operating time, period of ventilator use and chest tube drainage, blood loss, pain score, time to oral intake, hoarseness, sore throat, rate of vomiting require medicine.

Enrollment and randomization

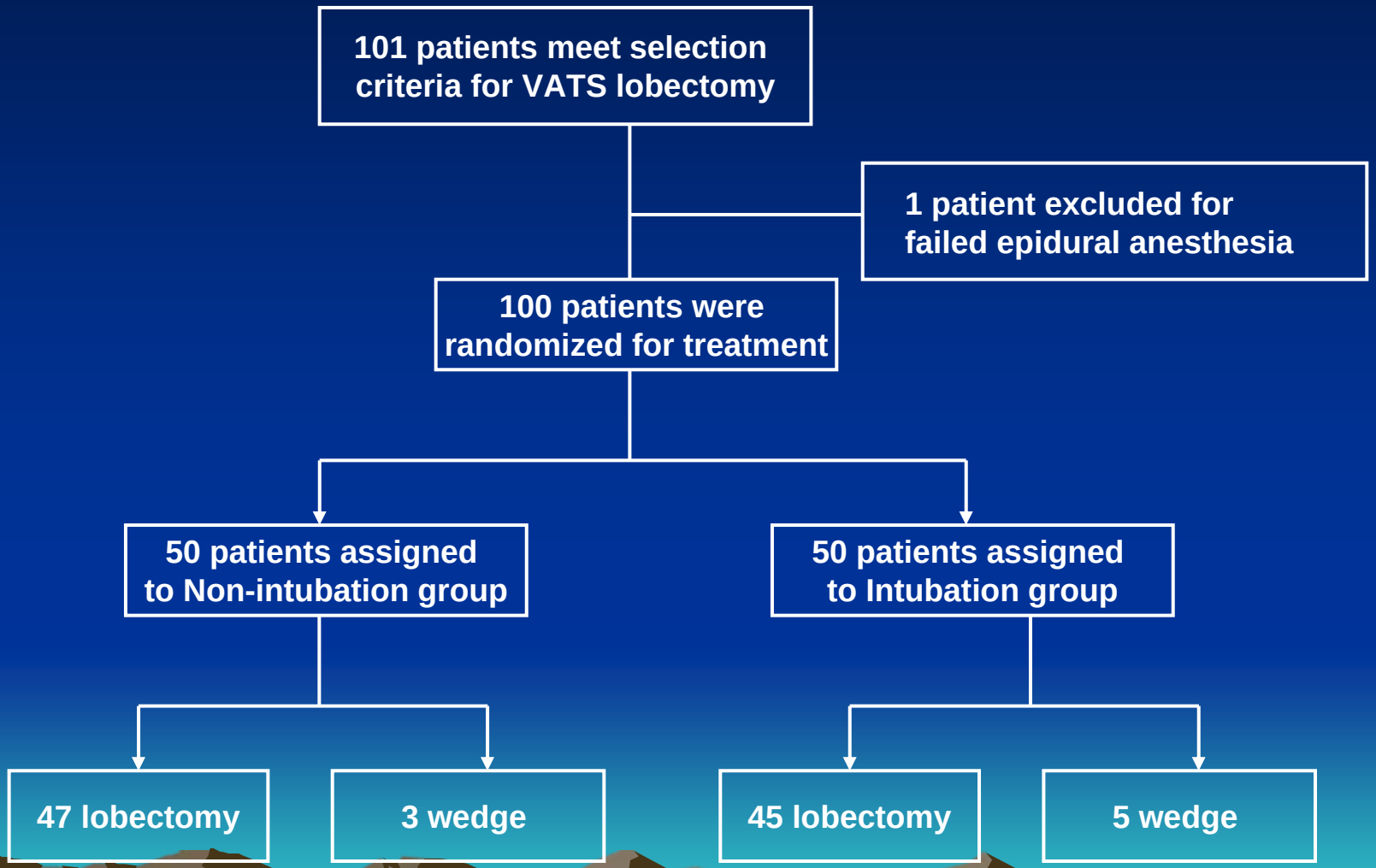


Table 1. Demographics and Baseline Characteristics

	Non-intubated group (n = 50)	Intubated group (n = 50)	*p* -value
Age (year)	56.4 ± 12.7	60.8 ± 11.3	0.086
Male (%)	23 (46%)	20 (40.0%)	0.632
Height (cm)	161.2 ± 9.1	157.9 ± 6.9	0.067
Weight (kg)	59.5 ± 9.2	59.6 ± 9.8	0.953
Smoking (%)	8 (16%)	9 (18%)	0.920
Tumor size (cm)	2.34 ± 1.2	2.26 ± 1.3	0.755
FVC (% prediction)	110.4 ± 15.7	106.4 ± 13.3	0.248
FEV1.0 (% prediction)	111.0 ± 19.9	105.8 ± 14.5	0.197
Lobe, %			0.585
RUL	18 (36%)	13 (26%)	
RML	3 (6%)	5 (10%)	
RLL	12 (24%)	10 (20%)	
LUL	12 (24%)	15 (30%)	
LLL	5 (10%)	7 (14%)	
Cell type (%)			0.231
Adenocarcinoma	45 (90%)	39 (78%)	
Squamous cell ca	1 (2%)	4 (8%)	
BAC	2 (4%)	5 (10%)	
Others (non-lung ca)	2 (4%)	2 (4%)	
Lobectomy	47 (94%)	45 (90%)	0.814
ASA class (%)			0.694
I	5 (11.9%)	7 (17.5%)	
II	20 (47.6%)	16 (40.0%)	
III	17 (40.5%)	17 (42.5%)	

Table 2. Operative And Anesthetic Results

	Non-intubated lobectomy (n = 50)	Intubated lobectomy (n = 50)	*p* -value
Anesthesia induction time (min)	26.0 ± 12.5	32.4 ± 19.9	0.102
Operating time (min)	192.5 ± 39.4	186.9 ± 48.9	0.589
Global in-operating room time (min)	252.5 ± 46.8	228.5 ± 50.8	0.052
Conversion to intubation (%)	2 (4%) *	NA	
Conversion to thoracotomy (%)	0 (0%)	0 (0%)	1.000
Peak ETCO2 (mmHg)	43.3 ± 6.3	39.2 ± 6.0	0.026
Lowest SaO2 (%)	95.7 ± 3.9	97.8 ± 3.8	0.027
Blood loss (ml)	94.5 ± 88.1	110.0 ± 145.6	0.621

* Caused by tachypnea (1) and severe mediastinal movement (1)

Table 3. Postoperative Results

	Non-intubated lobectomy (n = 50)	Intubated lobectomy (n = 50)	*p* -value
Pathological stage, %			0.579
IA	32 (64%)	28 (56%)	
IB	8 (16%)	6 (12%)	
IIA	3 (6%)	8 (16%)	
IIB	0	1 (2%)	
IIIA	5 (10%)	5 (10%)	
Non-lung cancer	2 (4%)	2 (4%)	
Dissected lymph node (no)	13.1 ± 6.1	14.4 ± 6.7	0.384
Hoarseness (%)	0	5 (10.0%)	0.036
Postoperative pain (VAS)			
Day 1	3.3 ± 3.0	2.9 ± 2.3	0.590
Day 2	2.3 ± 1.6	2.1 ± 1.4	0.373
Day 3	1.8 ± 1.0	1.7 ± 0.8	0.333
Postoperative chest drainage (d)	2.6 ± 0.8	3.4 ± 2.3	0.094
Postoperative hospital stay (d)	5.5 ± 1.9	6.8 ± 3.0	0.032
Complications (%)			
Air leaks > 5 days	3 (6%)	5 (10%)	0.604
Arrhythmia	1 (2%)	2 (4%)	1.000
Mortality	0	0	1.000

Summary of non-intubated VATS lobectomy :

- Safe with comparable short-term results for early lung cancer patients as intubated VATS
- Complication rates were comparable, only 2 patient (4%) require conversion to intubation
- Comparable anesthetic induction time, operating time, global OR time, and blood loss
- Non-intubated VATS lobectomy:
  - Higher peak ETCO2, lower lowest SaO2
  - A shorter postoperative hospital stay
- Comparable p-staging and number of dissected lymph nodes
- Mid-term results (pulmonary function, residual neuralgia) and long-term survival: to be decided

Table 5. Difference in Anesthesia methods Between Published data

Study group	NTUH,2011	Pompeo 2004, 2008, 2010	Rocco 2010**	Katlic 2010	Elia 2005
Anesthesia	Epidural IV sedation + Vagal block	Epidural + IV sedation	Epidural + Local IV sedation	Local + IV sedation	Intercostal block
Pleural	+	+	+*	+	+*
Bullectomy or bulloplasty	+	+	-	-	-
Wedge resection	+	+	+	+	-
Mediastinal manipulation	+	±	-	±	-
Lobectomy	+	-	-	-	-

*Theoretically feasible
**Confined to case report

肺癌手術的未來：

- 未來的世界是老年人的世界
  - 體力不好、心臟不好、呼吸功能不好、手術併發症比例高
- 不僅開刀方式要微創，麻醉方式也要微創
  - 縮小傷口：Needlescopic VATS
  - 減少切除範圍：Lobectomy to segmentectomy
  - 微創麻醉：Non-intubated VATS
- General anesthesia with endotracheal intubation 決不是每一台胸腔手術的必然選擇

Double lumen endotracheal tube-
長又粗，不適合東方女性

Carlens tube,
Since 1949

Vagal blockade: to inhibit coughing reflex during hilar manipulation

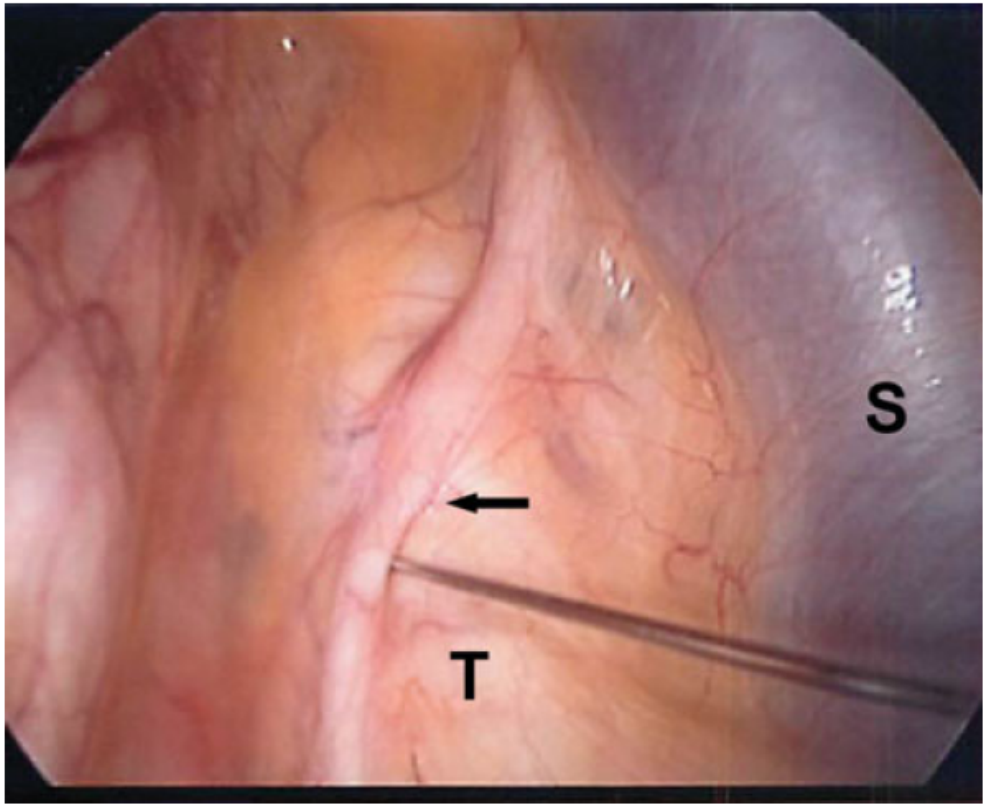
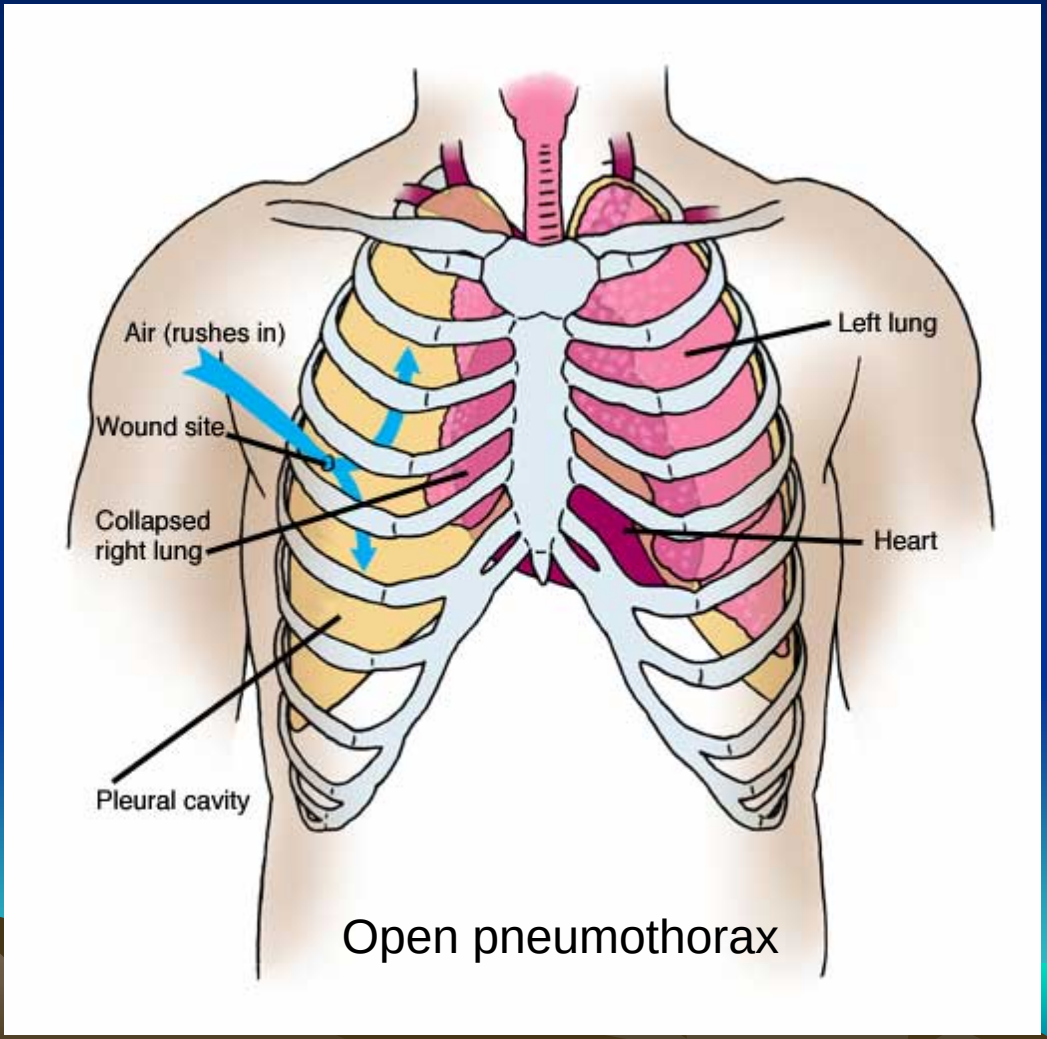


FIGURE 1. Local infiltration of bupivacaine adjacent to the vagus nerve (arrow) to produce intrathoracic vagal blockade in patients with right-sided lung cancer. S indicates superior vena cava; T, trachea.

Chen JS, Ann Surg, 2011

病患自主呼吸，如何讓手術之肺臟塌陷？

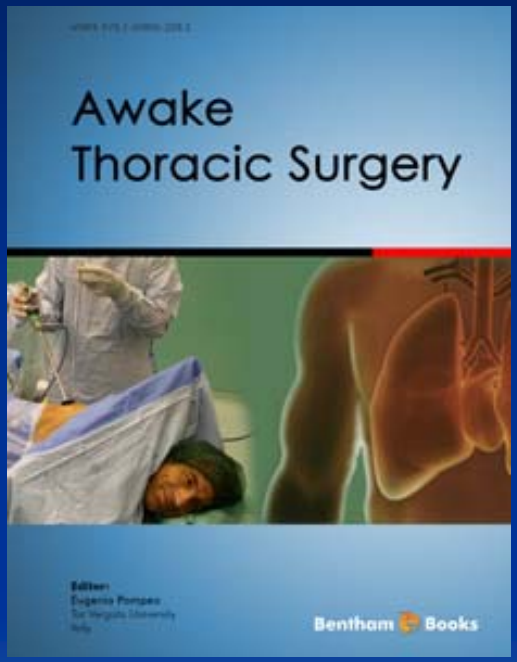


近代Nonintubated thoracic surgery之創始：针灸传奇【尼克松参观针灸麻醉开胸术】

- **原美国总统尼克松参观针灸麻醉开胸手术：**
- 据著名的胸外科专家辛育龄讲“上世纪70年代，中美关系出现了缓和，1972年尼克松访华，在访问期间，他们特意提出要参观针灸麻醉，因为他觉得这实在不可思议的魔术。

Nonintubated VATS手術現況:

- 肋膜腔疾病之診斷及治療：
  - Pleural biopsy (199?)
  - Spontaneous pneumothorax, empyema (1998)
- 周邊楔型肺臟切除：
  - Resection of pulmonary nodules (2004)
  - Resection of solitary metastasis (2007)
  - Lung volume reduction surgery (2006)
- 肺葉切除：目前只有本團隊研究報告 (2011)



Mineo TC. Eur J Cardiothorac Surg. 2007

Nonintubated VATS需克服之困難：

- 肺功能不良病患，使用單肺自主呼吸可能引發血中二氧化碳濃度過高，甚至呼吸衰竭
- 手術時肺臟及縱隔腔位移
- 支氣管受刺激，引發咳嗽反應
- 側躺開刀姿勢， 要再插double lumen tube困難

Mineo TC. Eur J Cardiothorac Surg. 2007

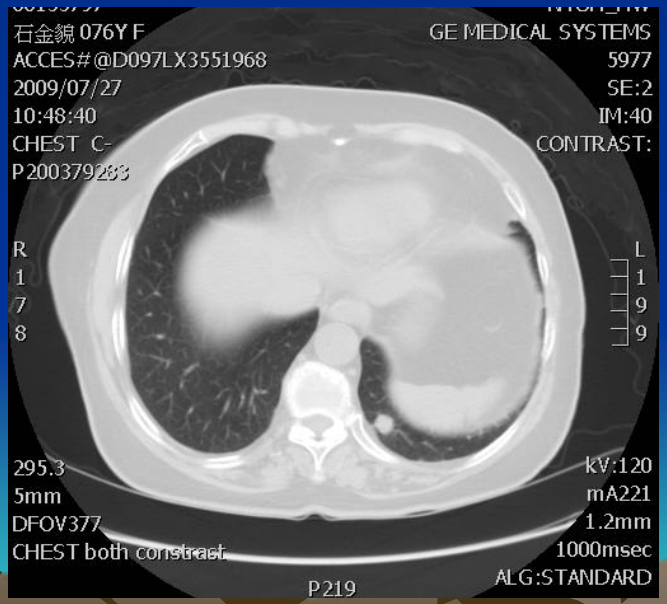
Nonintubated VATS在台灣或台大醫院是否可行？

- 台灣手術室麻醉現況：
  - 麻醉醫師只有在插管及拔管時會出現
  - 一位麻醉科醫師須同時照顧數位病患
- 麻醉安全第一守則：建立安全及穩固的呼吸道
- 放倒病患及氣管插管是最好的選擇

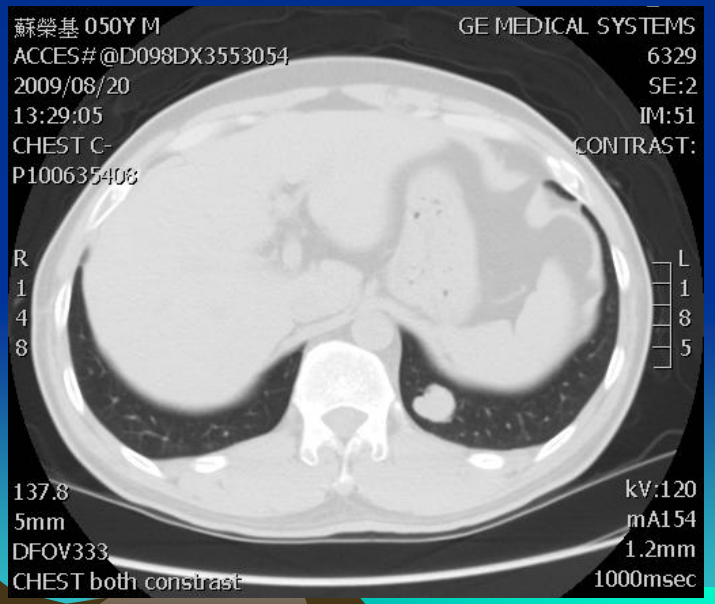
胸腔手術不插氣管內管：
自找麻煩！
發神經了？

前兩例Nonintubated needlescopic VATS 切除肺節結

76歲女性，大腸癌術後
左下肺1公分腫瘤



59歲男性, 胸腺癌術後
復發



Nonintubated needlescopic VATS

- Safe and feasible
- 100% diagnostic rate, satisfactory scars and less wound pain
- Easy conversion to standard VATS if major pulmonary resection is required
- An attractive method for diagnosis of small peripheral lung nodules.

Selection criteria for thoracoscopic lobectomy

- Inclusion criteria:
  - Stage I or II peripheral NSCLC
  - Tumor size < 6 cm
  - Without evidence of chest wall, diaphragm or main bronchus involvement
- Exclusion criteria:
  - ASA score > 3
  - Bleeding disorders
  - Unfavorable airway or spinal anatomy

Take home message for non-intubated VATS:

1. Cooperation between surgeons and anesthesiologists
2. Risk/benefit analysis before the operation

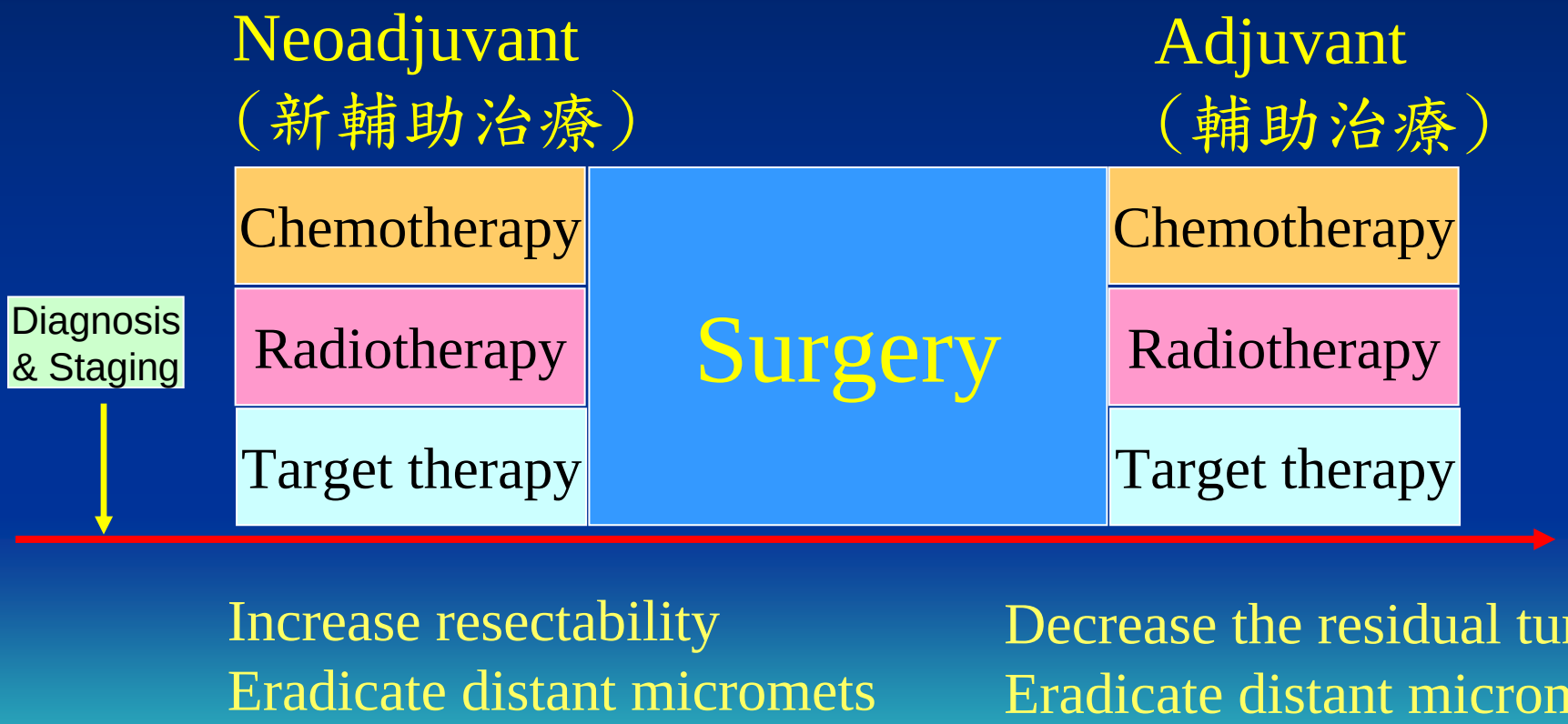
	Intubated Lobectomy	Nonintubated Lobectomy
Benefits	A secured airway	Avoid use of ventilator and muscle relaxants
	Quiet operation field	Selective intubation and one-lung ventilation is not required
		Earlier oral intake and ambulation
Risks	Intubation-related complications	Conversion to endotracheal intubation:
	Ventilator-associated complications	Nonemergent
		Emergent
		Increased difficulty in operation

Chen JS, Ann Surg 2011

免氣管插管之胸腔鏡手術結論

- 可使用於診斷及治療良性及惡性肺疾病
- 可進行楔狀切除術、肺節切除術、肺葉切除術
- 可雙側手術
- 免氣管插管之胸腔鏡肺葉切除術手術成果類似插管麻醉之肺葉切除術
  - 安全性
  - 腫瘤考量
- 需與麻醉醫師充分溝通配合

中晚期可切除肺癌之合併治療



Randomized Trials of Neoadjuvant Therapy in IIIA NSCLC

	Stage	No. of patients	Regimen	MS (months)	5-yr SR (%)	Hazard *P* value
Pass et al. (1992)	IIIA	14	Surgery	16	12	0.80
		13	CT+surgery	29	30	NS
Roth et al. (1994)	IIIA	32	Surgery	11	14	0.78
		28	CT+surgery	64	36	<0.05
Rosell et al. (1994)	IIIA	30	Surgery	8	0	0.75
		29	CT+surgery	26	25	<0.05
Depeirre et al. (2002)	IB-IIIA	119	Surgery	26	NA	0.82
		101	CT+surgery	37	NA	0.15

Concerns: 1. Positive results: only small patient numbers

2. Most trials stop earlier because positive results of adjuvant C/T

第三期中晚期可切除肺癌:

- 單純手術預後不佳：
  - 5-15%五年存活率
  - 80% 病患會發生遠處轉移
- 必須於術前或術後追加全身性治療
  - 化學治療
  - 標靶治療

Andre F, JCO 2000;18:2981