肺癌診治之新進展 – 精準醫療

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Top 10 cancers in Hong Kong in 2016
2016年香港十大癌症統計數字

Incidence 發病率

Rank 排名	Site 部位	No. 發病數字	Rel. freq. 百分比	Crude rate* 粗發病率*
1	Colorectum 大腸	5,437	17.3%	74.1
2	Lung 肺	4,936	15.7%	67.3
3	Breast 乳腺	4,123	13.1%	56.2
4	Prostate 前列腺	1,912	6.1%	56.6
5	Liver 肝	1,810	5.8%	24.7
6	Stomach 胃	1,224	3.9%	16.7
7	Non-melanoma skin 非黑色素瘤皮膚	1,063	3.4%	14.5
8	Corpus uteri 子宮體	1,050	3.3%	26.5
9	Non-Hodgkin lymphoma 非霍奇金淋巴瘤	963	3.1%	13.1
10	Thyroid 甲狀腺	889	2.8%	12.1
	All Sites 所有部位	31,468	100.0%	428.9

Mortality 死亡率

Rank 排名	Site 部位	No. 死亡數字	Rel. freq. 百分比	Crude rate* 粗死亡率*
1	Lung 肺	3,780	26.6%	51.5
2	Colorectum 大腸	2,089	14.7%	28.5
3	Liver 肝	1,540	10.8%	21.0
4	Stomach 胃	710	5.0%	9.7
5	Breast 乳腺	704	5.0%	9.6
6	Pancreas 胰臟	678	4.8%	9.2
7	Prostate 前列腺	410	2.9%	12.1
8	Non-Hodgkin lymphoma 非霍奇金淋巴瘤	388	2.7%	5.3
9	Oesophagus 食道	335	2.4%	4.6
10	Nasopharynx 鼻咽	327	2.3%	4.5
	All Sites 所有部位	14,209	100.0%	193.7

Hong Kong Cancer Registry; 2016 [cited 2016 May 17]. Available from: http://www3.ha.org.hk/cancereg/statistics.html.

Precision medicine 精準醫療

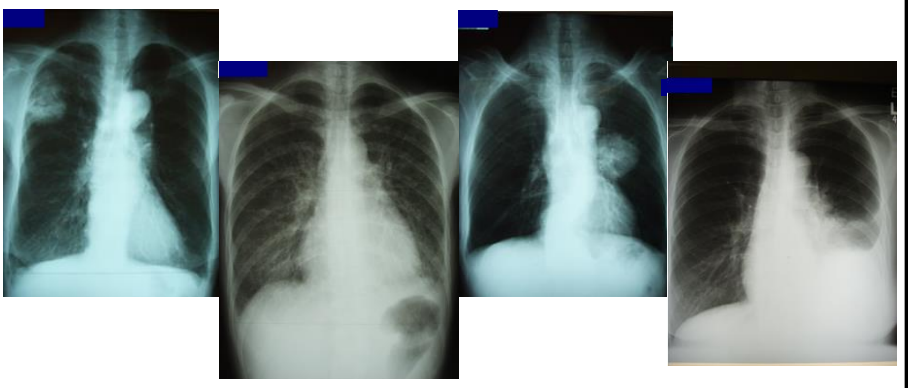
- Identification of treatment approaches that will be effective for which patients based on genetic, environmental, and lifestyle factors.

  基於遺傳，環境和生活方式因素確定對患者有效的醫療方法

- 盡量延長病患的存活期
- 症狀得以減輕
- 改善並提高生活質素

肺癌

- 每年新增病例數超過4,000例，仍然是男性和女性的首要癌症殺手。



肺癌治療個人化

- 腫瘤之分類及分期
- 癌細胞中存有的「標靶」或生物標記
- 個人的健康情況與選擇

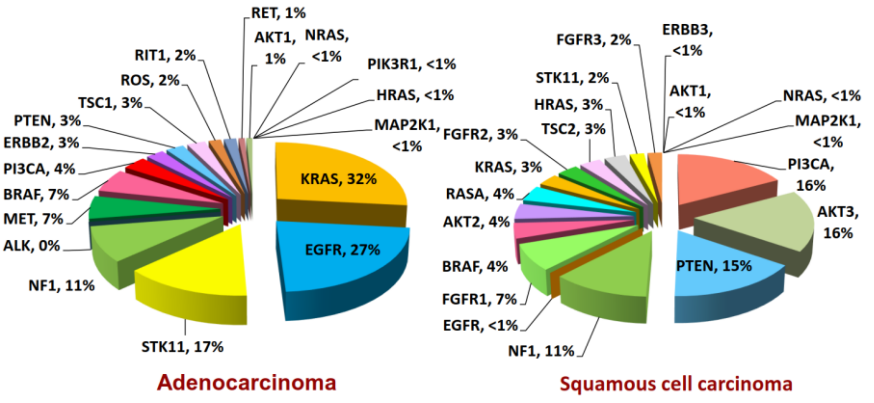
肺癌治療最理想目標

- 根除腫瘤

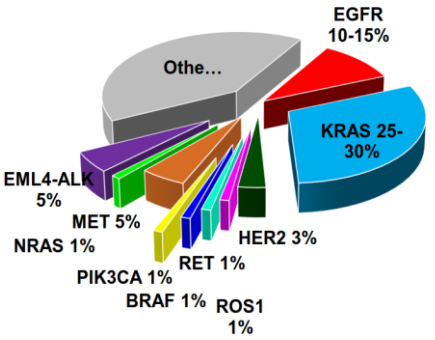
選擇最好的肺癌治療方式

- 確診
- 肺癌細胞的病理類型
- 臨床（或病理）分期
- 體能狀況

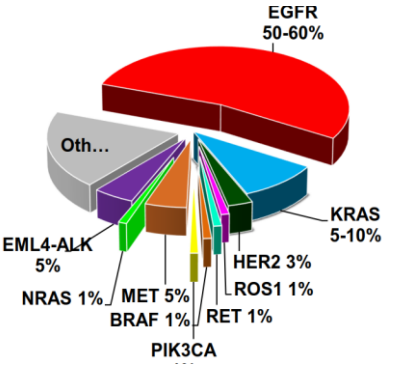
不同肺癌種類有不同的基因變化



東西方人的肺癌基因不同

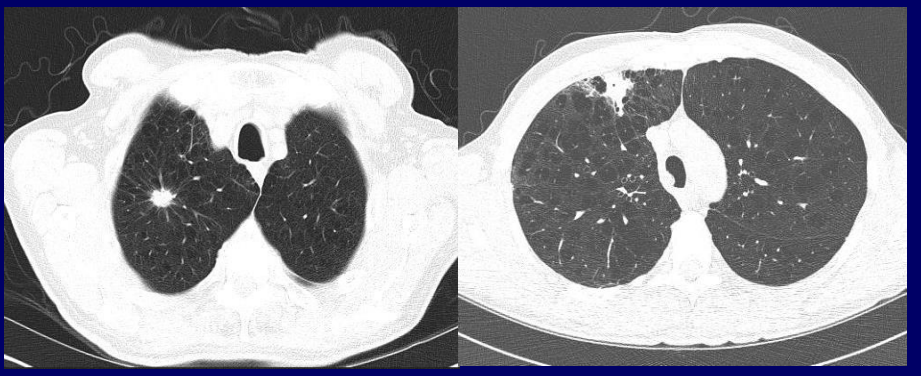


西方人



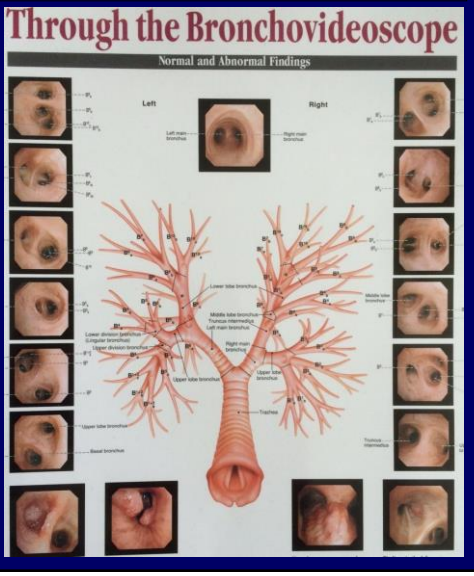
東方人

胸腔電腦掃描 CT Thorax
Lung Nodule 肺結節

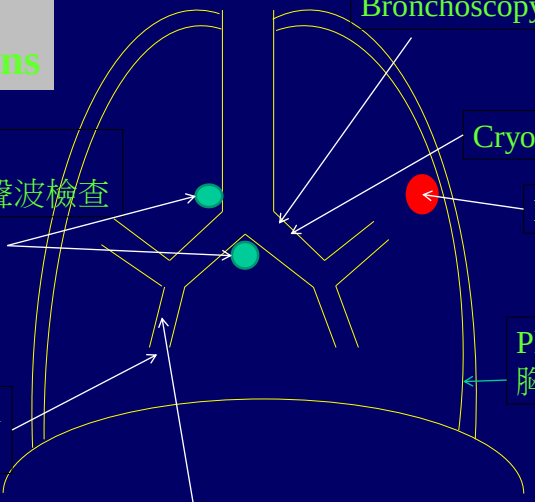


Flexible Bronchoscopy 支氣管鏡檢查

Mainly diagnostic



Pulmonary Interventions



Autofluorescent Bronchoscopy 螢光氣管鏡

EBUS-TBNA
支氣管鏡內超聲波檢查

Cryoprobe /APC

Miniprobe

Pleuroscopy
胸膜鏡

Endobronchial Valves

Bronchial Thermoplasty

Mechanisms of AFI 螢光氣管鏡

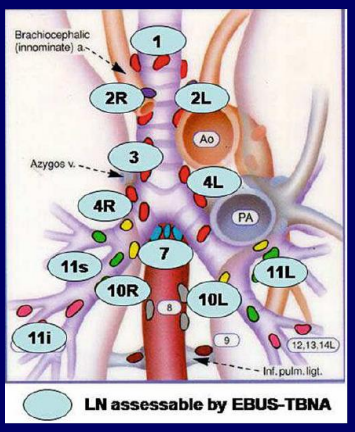
Yasufuku K. Clin Chest Med 2010

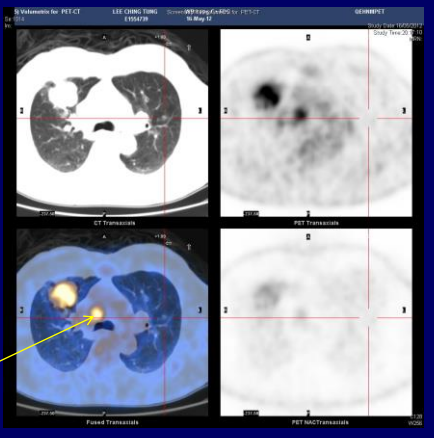
Mechanisms of AFI

Yasufuku K. Clin Chest Med 2010

支氣管鏡內超聲波檢查 (EBUS)

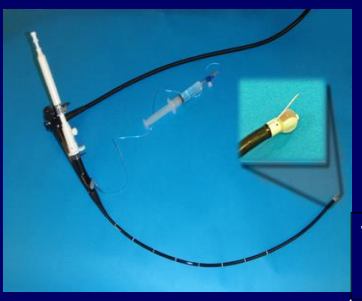
Access beyond airway walls



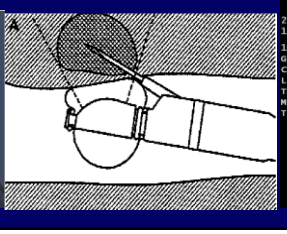


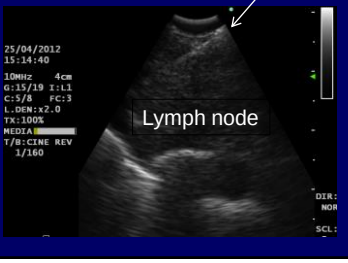
The Equipment

- 6.9mm scope with 2mm instrument channel
- Hybrid: USG/Doppler + video-bronchoscope
- Real-time USG-guided sampling with 22G needle



TBNA needle





肺癌TNM分期

T	Primary Tumor	腫瘤	腫瘤本身的大小和入侵鄰近器官的情形
N	Regional Lymph Node	淋巴結	擴散到區域淋巴的情形
M	Distant Metastasis	轉移	擴散到肺部以外的器官

肺癌治療方式

手術切除　適用於初期肺癌患者

放射治療　區域性的局部治療方式

局部症狀控制，包括腫瘤造成咳血或是局部肺葉塌陷，以及手術後的預防局部復發及控制

可與化學治療合併使用提升局部晚期肺癌的治療，或為晚期肺癌患者緩解治療之用

化學治療　對小細胞肺癌治療之效果顯著

在非小細胞肺癌方面，可單獨使用或與放射線治療合用

生物治療　標靶治療

免疫療法

標靶治療

- 針對癌細胞中存有的「標靶」，用專一性的藥物攻擊這些「標靶」來殺死癌細胞，但對正常細胞則不造成或只有很低的傷害
- 應用於第一線或第二線化學治療後有再度惡化的非小細胞肺癌病患
- 當肺癌細胞存有EGFR基因突變時，更可採用EGFR-TKI作為第一線治療

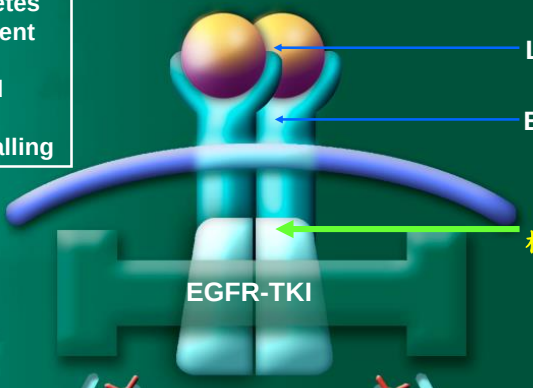
標靶治療

類別	標靶或生物標記測試	藥物	
EGFR-TKI	表皮生長因子受體(*EGFR*)基因第十八至二十一段存有基因突變	Gefitinib Erlotinib Afatinib Dacomitinib	
EGFR T790M inhibitor	*EGFR* T790M mutation	Osimertinib	
EML4-ALK inhibitor	*EML4-ALK* 移動融合基因	Crizotinib Ceritinib, Brigatinib Lorlatinib	
ROS1 inhibitor	*ROS1* 移動融合基因	Crizotinib	
RET	*RET-KIF5b* 移動融合基因	?Carbozantinib	

EGFR 基因突變

EGFR inhibition

EGFR-TKI competes with ATP to prevent activation of the EGFR and initiation of downstream signalling



Proliferation

Inhibition of apoptosis

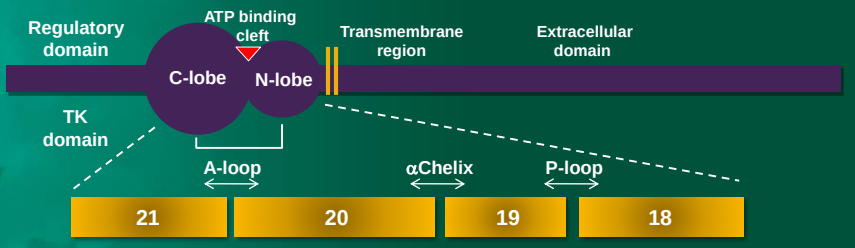
Invasion

Angiogenesis

Metastasis

Heerbst et al 2002

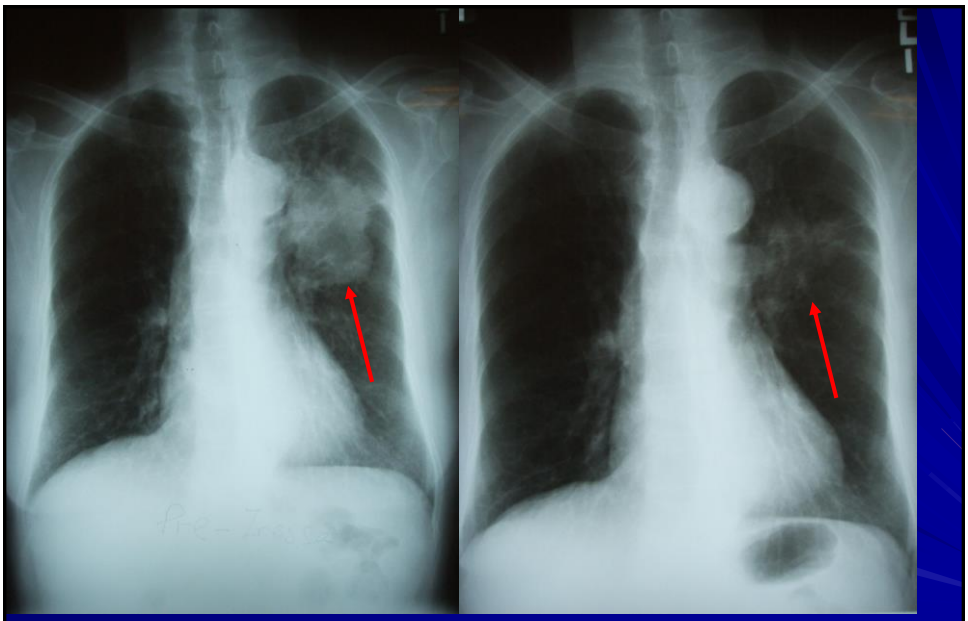
EGFR 基因突變



Distribution of mutation types (% of mutations)		
Literature review	Asian studies	Non-Asian studies
Most prevalent mutation types	Literature (n=1523)	Literature (n=583)
Exon 19 deletion	51%	58%
Exon 21 point mutation L858R	42%	32%
Exon 20	2%	6%
Exon 18 G719A/C	3%	2%
Exon 21 L861Q	1%	1%

Some patients had more than one mutation type

AstraZeneca data on file 2009



標靶治療前　　標靶治療六週後

標靶治療

常見

- 皮膚紅疹及異常
- 腹瀉

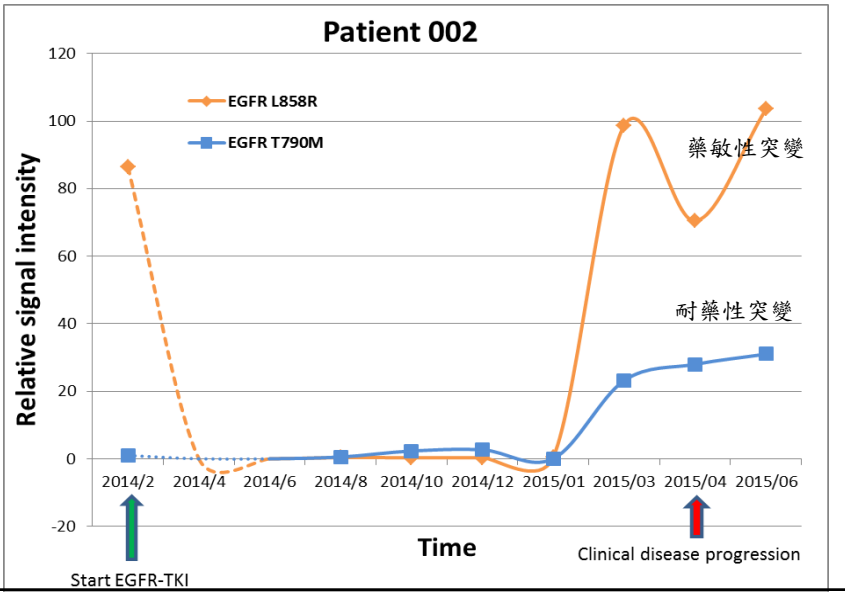
個別標靶治療可引起之罕見副作用

- 間質性肺炎
- 出血，血栓塞，穿腸
- 影響視力

WHO Grade III Stomatitis/Mucositis (can only tolerate fluid diet) 口腔炎

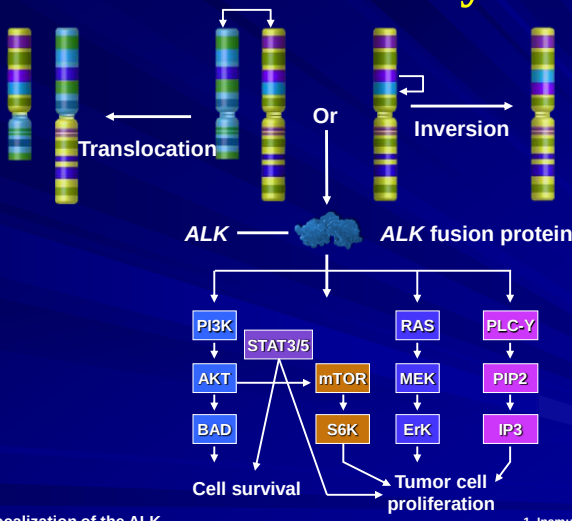
Paronchyia with ingrown toe nail
甲溝炎

血液檢測*EGFR*基因突變



ALK 融合基因 and *ROS1* 融合基因

ALK Pathway



* Subcellular localization of the ALK fusion gene, while likely to occur in the cytoplasm, is not confirmed.[1,2]

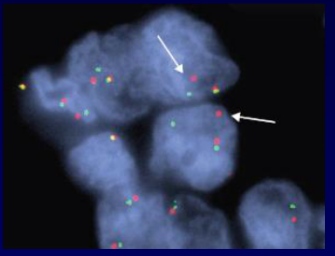
1. Inamura K et al. *J Thorac Oncol* 2008;3:13–17.
2. Soda M et al. *Proc Natl Acad Sci* USA 2008;105:19893–19897.
Figure based on: Chiarle R et al. *Nat Rev Cancer* 2008;8(1):11–23; Mossé YP et al. *Clin Cancer Res* 2009;15(18):5609–5614.

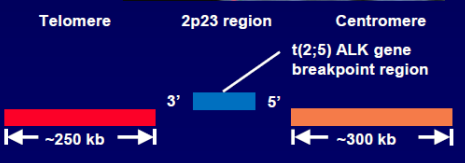
ALK-Positive NSCLC

ALK translocation in NSCLC →oncogenic activation

- Adenocarcinomas
- Never or light smokers
- Median age 50 years
- No sex differences

Break-apart FISH assay for *ALK*-fusion genes

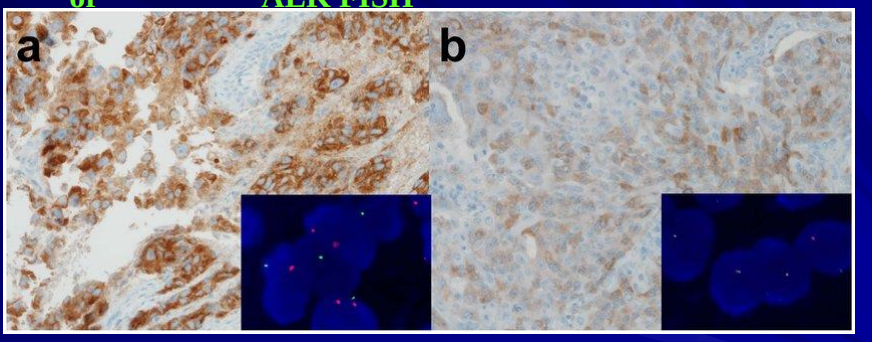




Shaw AT, et al. *Lancet Oncol.* 2011;12(11):1004-1012. Camidge DR, et al. *Lancet Oncol.* 2012;13(10):1011-1019. Wellstein A, et al. *Nat Med.* 2011;17(3):290-291.

Anaplastic Lymphoma Kinase (*ALK*) rearrangement

- **Biomarkers:** ALK immunohistochemical staining
  or ALK FISH

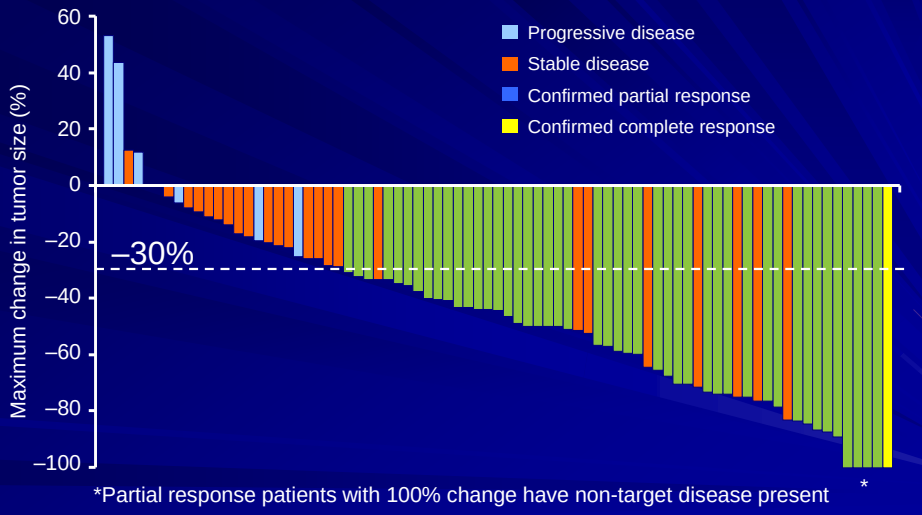


Clinical indications: ***ALK*** **re-arranged or IHC +ve tumor**

First line: Crizotinib

Second line or beyond: Ceritinib/Alectinib/Lorlatinib
or systemic chemo/immunotherapy

Tumor Responses to Crizotinib for Patients with *ALK*-positive NSCLC



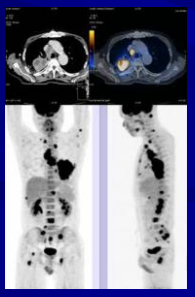
*Partial response patients with 100% change have non-target disease present

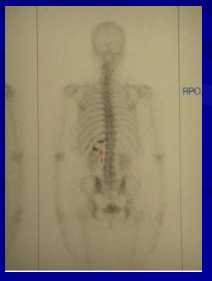
肺癌治療效果評估及跟進

平片X光

纖維支氣管
內視鏡檢查

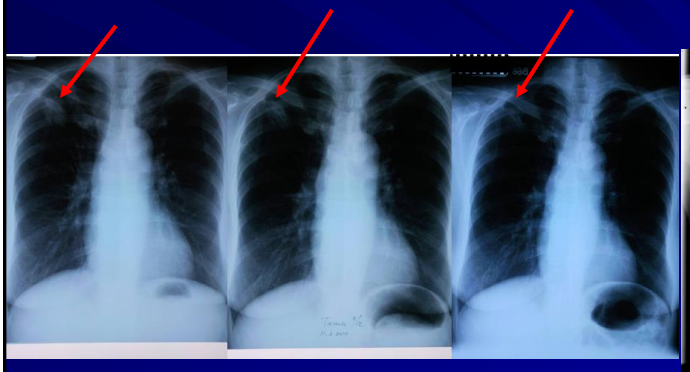
電腦掃描或
正電子-電腦
雙容掃描





放射同位素骨掃描

Interval radiological improvement



Baseline (12.2009) 3 months (3.2010) 6 months (6.2010) 14 months (2.2011)

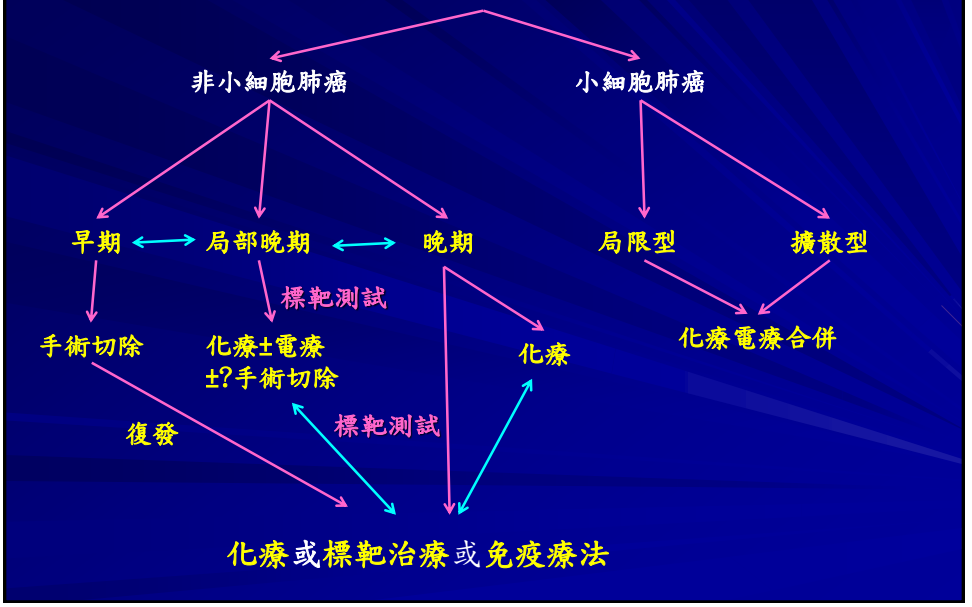
As documented on CT Thorax

Erlotinib
6 months

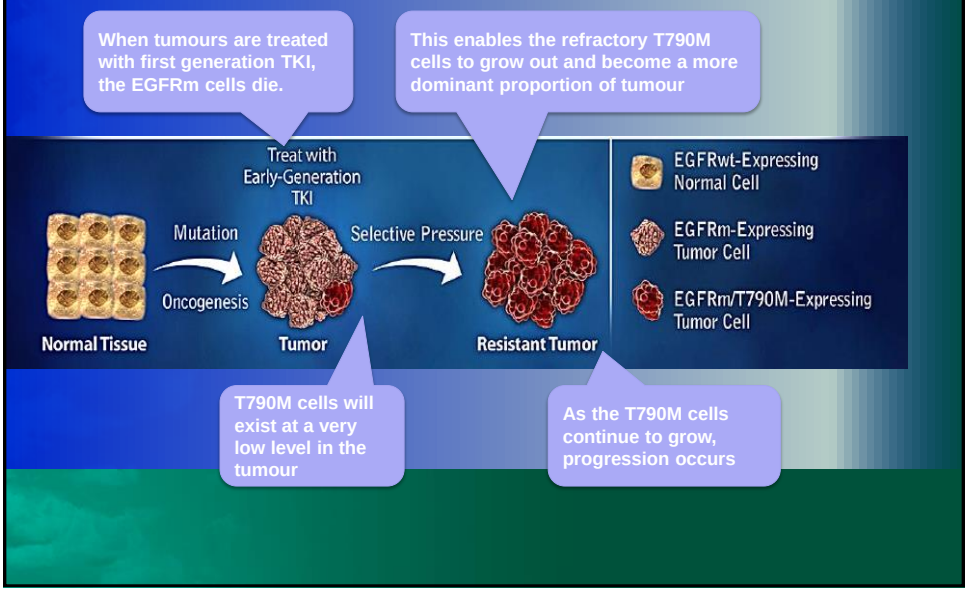
RUL mass with air bronchogram, spiculated borders and ground glass opacity, 4.2 x 2.5 x 3.5 cm (SUVmax 2.5)
Precarinal LN 1.6 x 1.0 x 2.0 cm (SUVmax 2.7)
Small R hilar LN 0.5 cm (no metabolic activity)

RUL mass, 3.3 x 2.0 x 2.6 cm (SUVmax 1.1)
Precarinal LN 0.5 x 0.6 cm (SUVmax 1.3)
No enlarged hilar LN seen

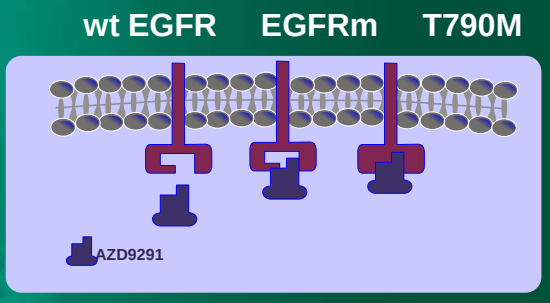
肺癌治療方式



EGFR-TKIs 抗藥性
EGFR T790M mutation



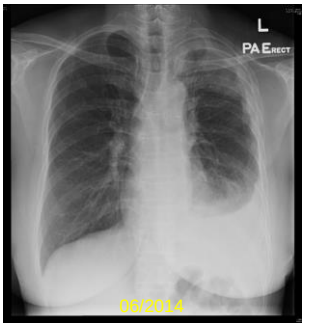
第三代 *EGFR* 標靶藥 and T790M 基因突變



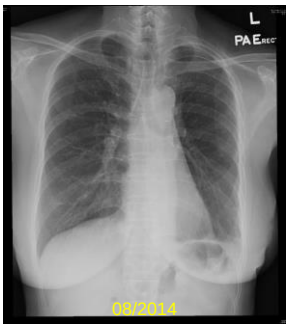
Potent inhibition of T790M	Delay/stop T790M resistance
Potent inhibition of EGFRm	Similar to gefitinib, erlotinib, afatinib
Low activity on wt EGFR	Lower rash, diarrhoea

Patient 1, LYP, F/67, non-smoker

LUL lobectomy, pIII AdenoCa, adjMIP x 4
10/1997

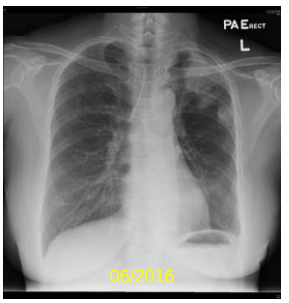


Back and chest pain !
Pleural Bx: AdenoCa, Del 19



Gefitinib x 6/52

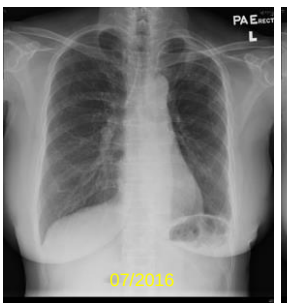
Patient 1, LYP, F/67, non-smoker



Gefitinib x 2 years

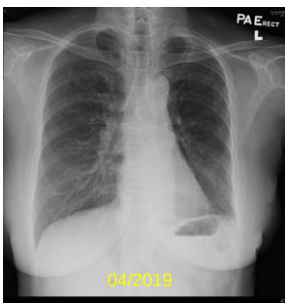
L shoulder pain

Re-biopsy: AdenoCa
Del 19 + T790M



Osimertinib x 2 weeks

↓ L shoulder pain



Osimertinib x 2.5 years

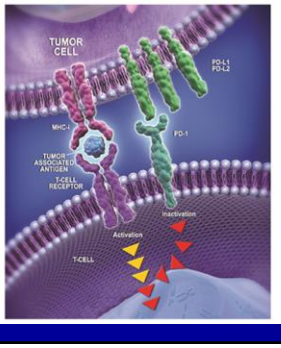
No more L shoulder pain

Immunotherapy 免疫療法

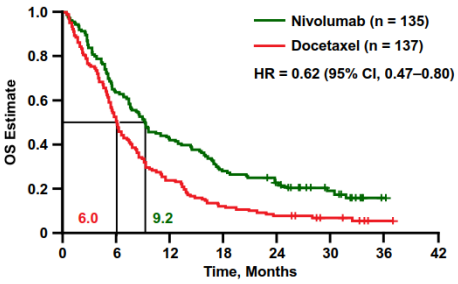
Immunotherapy: Immune-checkpoint inhibitor

- PDL1/PD1 axis
- Monoclonal antibodies that target either
  1. Programmed Death-ligand 1 expression on tumor cells, or
  2. Programmed Death 1 expression on cytotoxic T cells
- E.g: Pembrolizumab, Nivolumab, Atezolizumab

- Potent, humanized monoclonal antibody against PD-1 that prevents PD-1 from binding to its ligands, PD-L1 and PD-L2
- Robust antitumor activity and manageable toxicity in multiple tumor types
- As monotherapy for previously treated and treatment-naive advanced NSCLC in KEYNOTE-001 (n = 495)[1]
  - 19.4% ORR, 3.7-month median PFS, 12.0-month median OS
  - 45.2% ORR in patients with PD-L1 expression in ≥50% of tumor cells

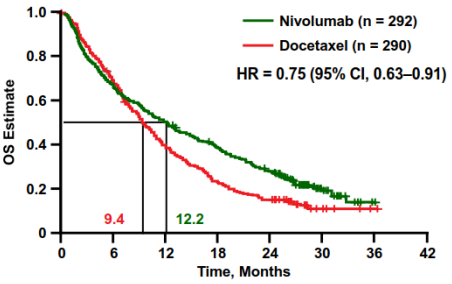


CheckMate 017 (squamous NSCLC)



	Nivolumab n = 135	Docetaxel n = 137
12-month OS rate, %	42	24
24-month OS rate, %	23	8

CheckMate 057 (nonsquamous NSCLC)

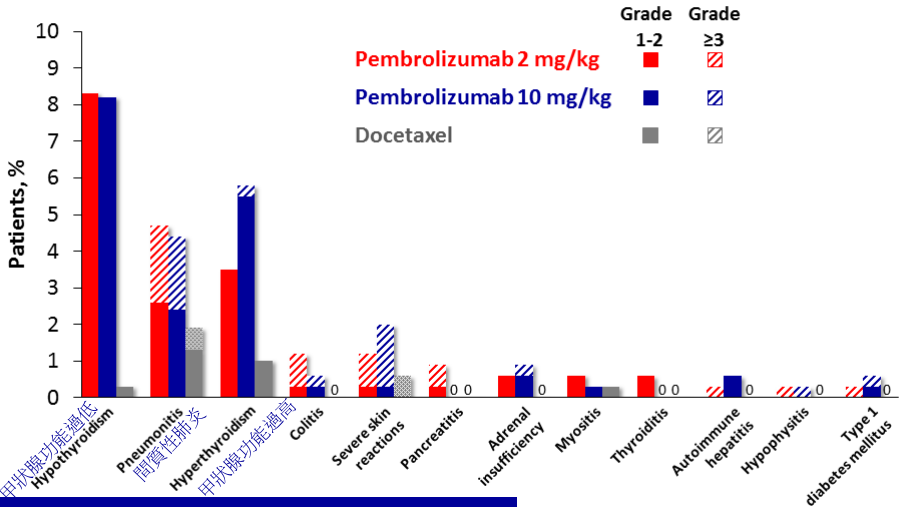


	Nivolumab n = 292	Docetaxel n = 290
12-month OS rate, %	51	39
24-month OS rate, %	29	16

Borghaei H, et al. *J Clin Oncol.* 2016;34(suppl): Abstract 9025.

RS Herbst. Presented December 20, 2015.

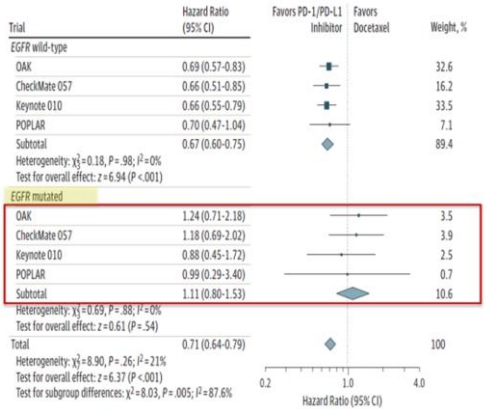
Immune-Mediated AEs Occurring in ≥2 Patients in the Pembrolizumab Arms



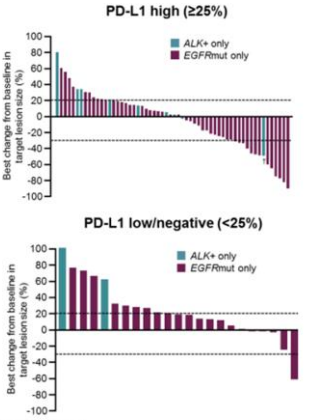
RS Herbst, WCLC 2015

Anti-PD1 in *EGFR/ALK* +ve tumor

Meta-Analysis: Survival Benefit of Anti-PD-1/PD-L1 vs Chemotherapy According to *EGFR* Status[1]



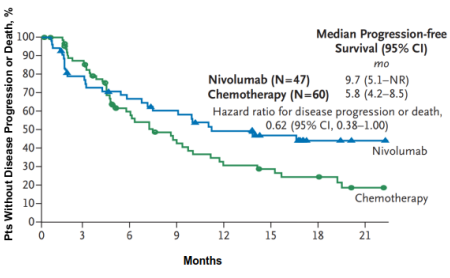
ATLANTIC Trial: Response With Durvalumab in *EGFR*mut/*ALK*+ According to PD-L1 Status[2]



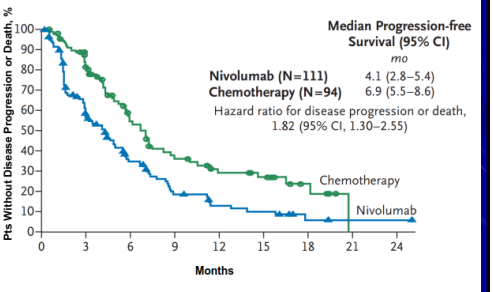
1. Lee CK, et al. *JAMA Oncol.* 2018;4(2):210-216. 2. Garassino M, et al. *Lancet Oncol.* 2018;19(4):521-536.

Tumor mutation burden

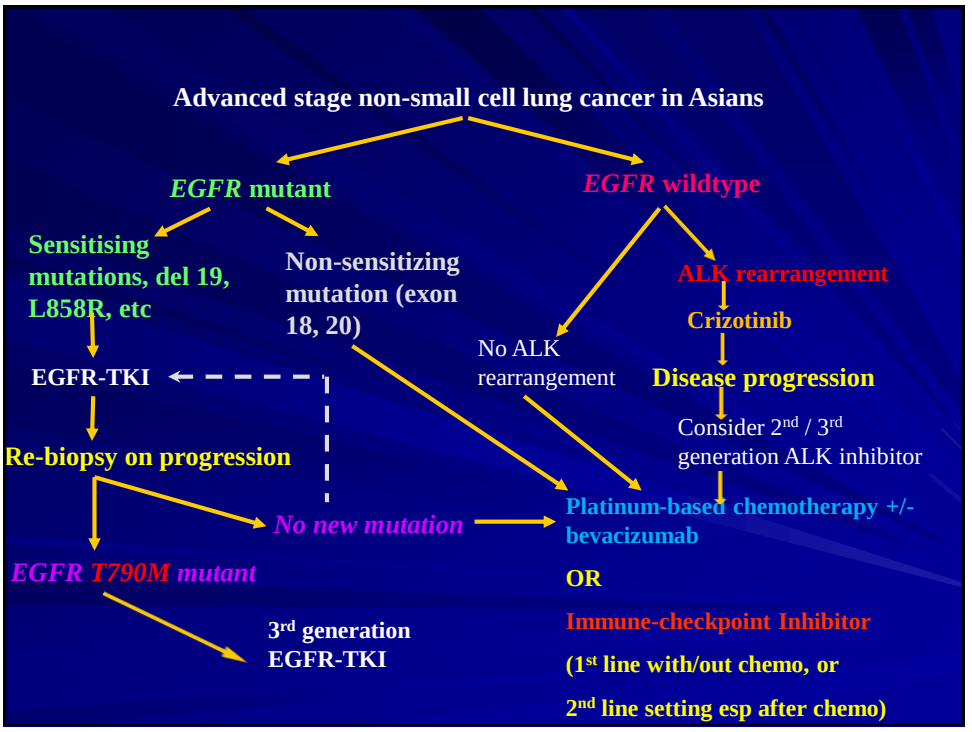
PFS Among Patients With High TMB



PFS Among Patients With Low/Medium TMB



Carbone DP, et al. *N Engl J Med.* 2017;376(25):2415-2426.



THE UNIVERSITY OF HONG KONG
DEPARTMENT OF MEDICINE

胸腔電腦掃描及肺癌篩查研究

(IRB Ref. no.: UW17-192)

研究題目：
以低劑量胸腔斷層掃描和標準化管理系統進行條件性肺癌篩查 - 國際研究

本研究的目的：
本研究旨在透過胸腔低劑量電腦斷層掃描作為篩選肺腫瘤的方法。我們亦透過此研究，希望有機會了解戶外和家庭空氣污染如何影響肺癌風險，並且發展血液檢查以提高肺癌風險預測工具的準確性。

肺癌篩查計劃：
將於 2018 年 4 月開始

合資格人士：
1) 年齡在 55 至 80 歲之間
2) 是現在或前吸煙者，有 30 年的吸煙史
3) 從沒有被診斷有肺癌

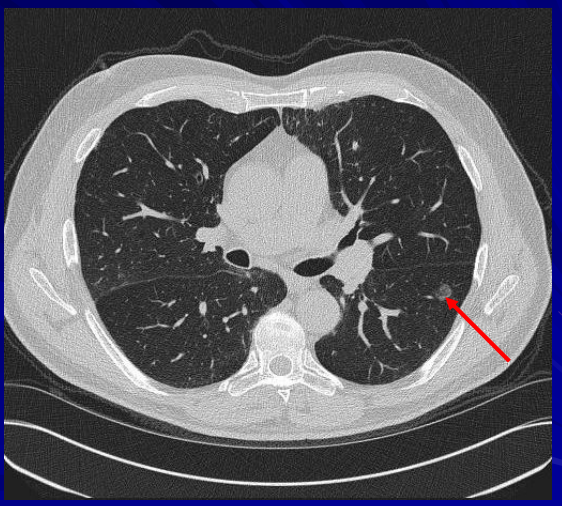
參加辦法：
請致電： 2255-4767 (黎姑娘) 或 2255-5886 (莊姑娘) 或 2255-5464 (劉姑娘)

研究階段：
第一階段：電話訪問
第二階段：進行問卷調查及胸腔低劑量電腦斷層掃描(LDCT)

收費：
研究相關的檢查都是免費的。

低劑量胸腔電腦掃描及肺癌篩查研究

1) 年齡在55至80歲之間
2) 是現在或前吸煙者，有30年的吸煙史
3) 從沒有被診斷有肺癌



Clinical features
臨床信息

Gender, smoking, staging
histology, lung co-morbidities
(emphysema, fibrosis, TB)

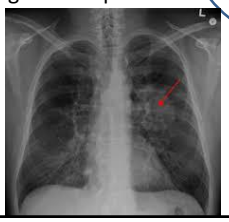
INTEGRATION

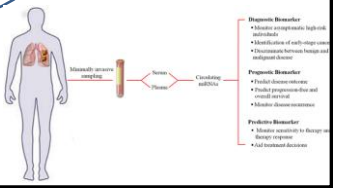
Size, border, segmentation,
Textures, calcification,
ground-glass component

Radiomics
放射學信息

Genomics
基因組信息

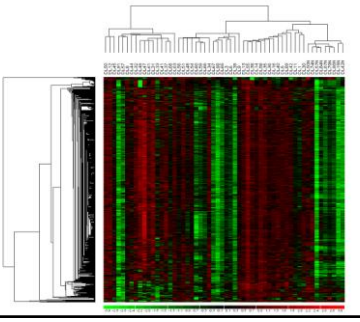
肺腫瘤Tumor: targets or profiling
血液中肺癌DNA突變
Blood: targets or profiling
致癌基因突變
EGFR, ALK.....





研究肺癌的：
1. 臨床特徵
2. CT掃描特徵和
3. 肺癌腫瘤和血液中肺癌DNA基因組變化與突變的關係

=>大數據庫=>人工智能=>診斷預測



Thank you

Lung Cancer: How to Reduce its Mortality

肺癌：如何降低其死亡率

Alan D. L. Sihoe 司徒達麟 醫生

MBBChir, MA(Cantab), FRCSEd(CTh), FCSHK, FHKAM, FCCP, FACS

Specialist in Cardiothoracic Surgery
Honorary Associate Professor, The University of Hong Kong

低劑量電腦掃描及早確診肺癌

司徒達麟醫生
香港大學李嘉誠醫學院
生物醫學學院名譽副教授

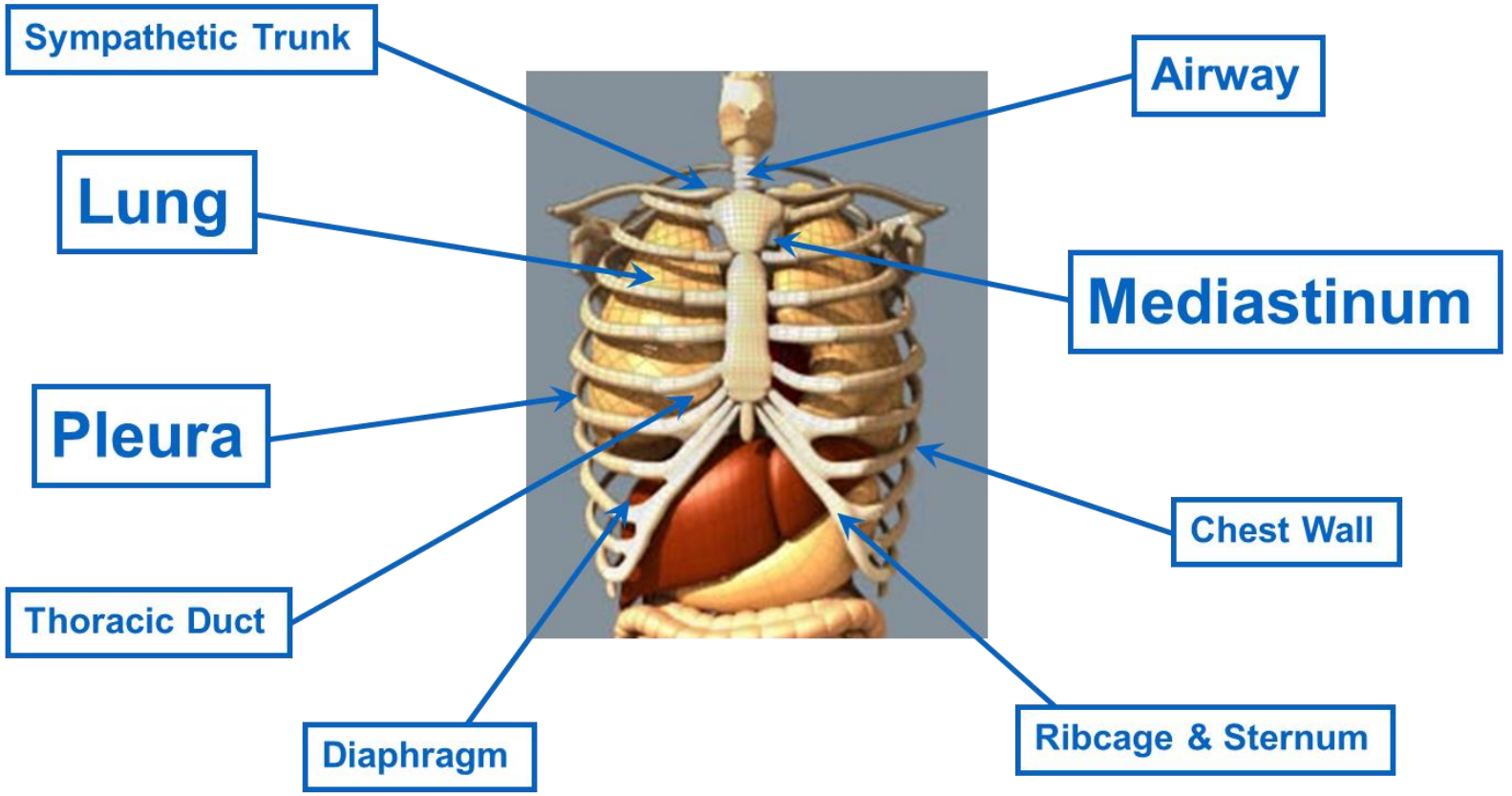
肺癌在香港是殺傷力最強、死亡率最高的頭號癌症殺手，全港市民平均每十二人便有一人死於肺癌。最新的放化療、標靶藥及免疫治療等只能控制病情，不能完全治愈。其實，有效根治肺癌的方法一直存在：就是手術切除；但關鍵是手術只適合早期肺癌，而肺癌的初期病徵不明顯，當病人發現身體不適時才去求診，大部分病情已經延至後期。此外，昔日的肺癌手術創傷比較大，所以也有部分早期患者因為年紀大或體質不好，未能接受手術。

幸好，近年已有新方案解決「未能及時診斷」及「手術創傷大」這兩大問題。前者是使用低劑量電腦掃描（LDCT）進行肺癌篩檢，輻射量較少，收費也較相宜。最近，分別在美國和歐洲的大型臨床研究發現，利用LDCT可以大大增加早期發現肺癌的機會，從而顯著降低死亡率。

當篩查發現有早期肺癌時，今天的患者也毋須如以往的病人般那麼擔心。香港大學的教授團隊已經累積經驗，把肺癌外科治療精益求精，達至世界水平。現時使用的微創技術，會先利用熟練的單孔胸腔鏡手術，減少手術創傷，之後再為合適的患者進行新式的亞肺葉切除（段切除）以保留更多肺功能，最後配合改良版臨床路徑綜合治療，加速康復及減少併發症。最終目標是令以前不可或不願接受手術的肺癌病人，提供根治性治療的希望！

<刊載於《東方日報》，2019年4月6日>

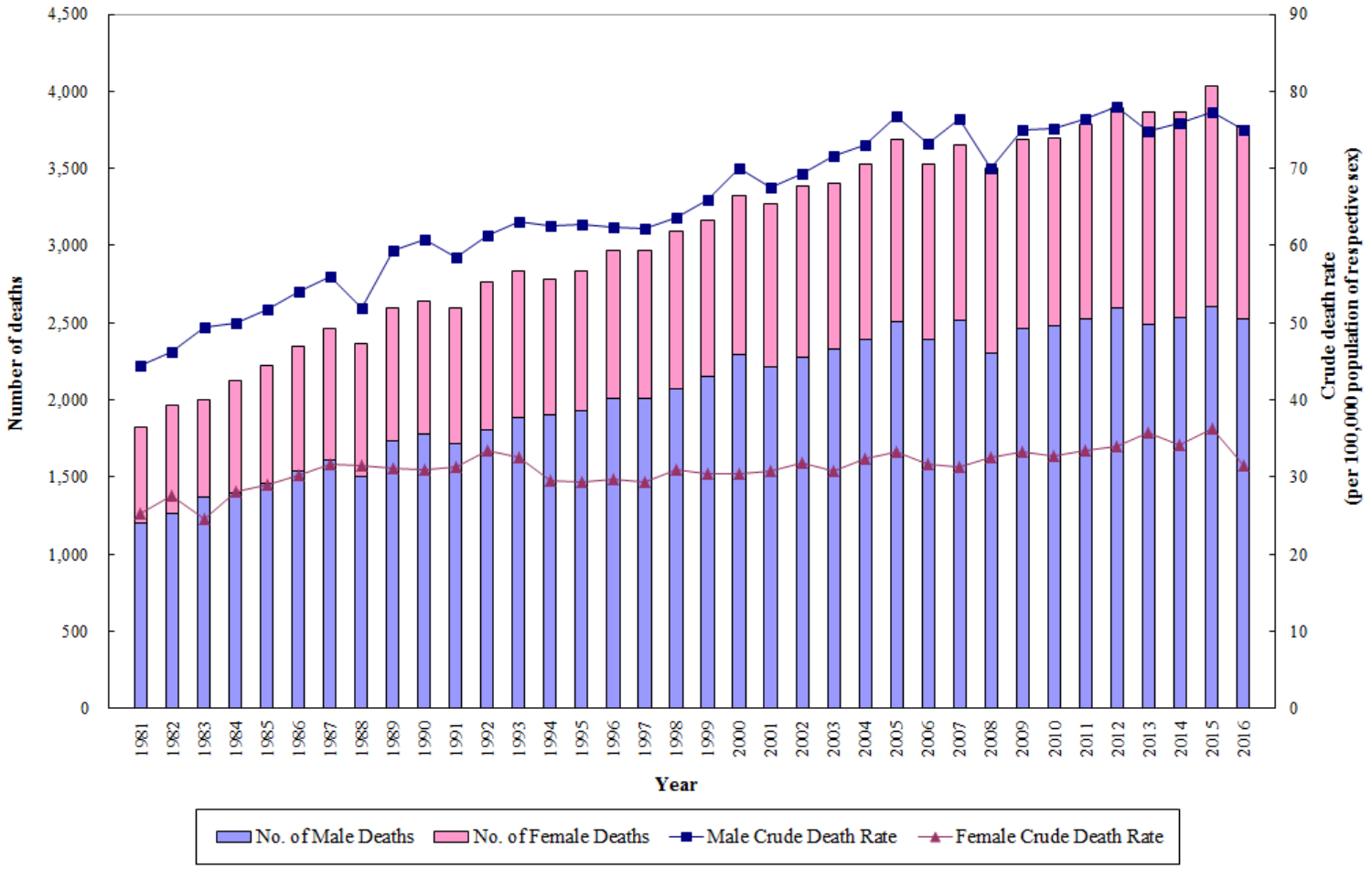
Thoracic Surgery 胸外科



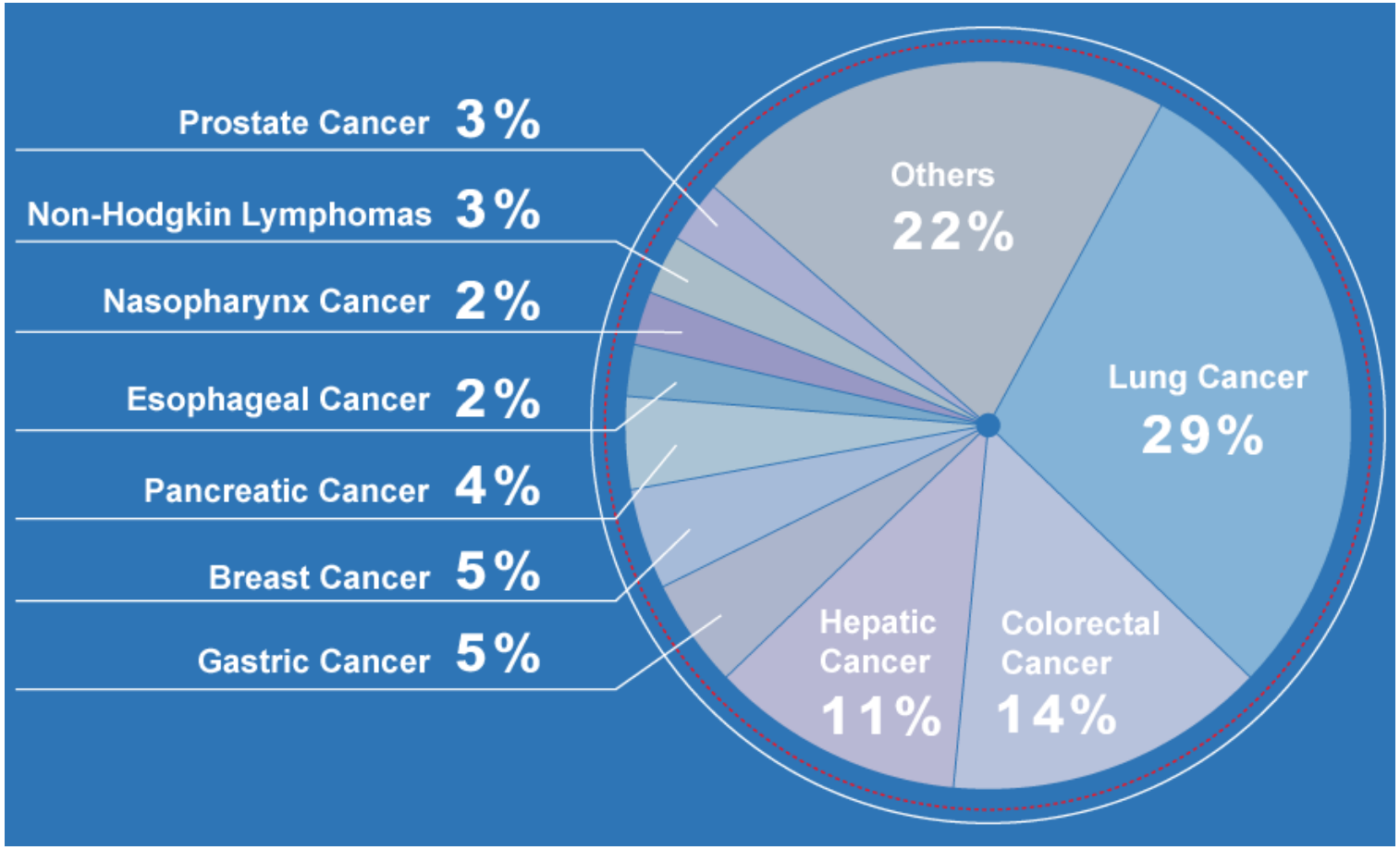
Cause of Death	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1. Malignant neoplasms (ICD10: C00-C97)	11406	11658	11510	11791	12310	12093	12316	12456	12839	13076	13241	13336	13589	13803	14316	14209	14354
2. Pneumonia (ICD10: J12-J18)	3026	3194	3877	3676	4291	4201	4978	5486	5312	5814	6211	6960	6830	7502	8004	8292	8032
3. Diseases of heart (ICD10: I00-I09, I11, I13, I20-I51)	4703	4969	5311	5866	5868	5619	6372	6777	6414	6636	6334	6283	5834	6405	6190	6201	6138
4. Cerebrovascular diseases (ICD10: I60-I69)	3130	3218	3462	3416	3434	3302	3513	3691	3443	3423	3339	3276	3252	3336	3259	3224	3124
5. External causes of morbidity and mortality† (ICD10: V01-Y89)	1844	2068	2044	2243	2150	1961	1854	1766	1938	1864	1567	1655	1860	1834	1993	1813	1697
6. Nephritis, nephrotic syndrome and nephrosis (ICD10: N00-N07, N17-N19, N25-N27)	1053	1055	1184	1182	1261	1287	1347	1419	1448	1493	1545	1629	1589	1684	1655	1706	1659
7. Chronic lower respiratory diseases (ICD10: J40-J47)	2114	2075	2102	2123	2261	1924	2096	2103	1912	2093	1965	1981	1743	1742	1660	1639	1505
8. Dementia (ICD10: F01-F03)	252	289	256	276	283	288	317	495	638	767	753	904	999	1112	1145	1371	1455
9. Septicaemia (ICD10: A40-A41)	424	467	572	615	701	676	737	797	736	826	767	837	852	884	891	970	971
10. Diabetes mellitus (ICD10: E10-E14)	676	574	783	728	602	511	506	548	492	522	457	398	360	390	492	498	400
All other causes	4677	4749	5322	5405	5522	5553	5927	5992	5875	6185	6009	6413	6491	7018	7152	6739	6548
All causes	33305	34316	36423	37321	38683	37415	39963	41530	41047	42699	42188	43672	43399	45710	46757	46662	45883

HealthyHK, Department of Health
The Government of the Hong Kong Special Administrative Region

Number of Deaths and Crude Death Rate due to Lung Cancer, 1981-2016



Lung Cancer in Hong Kong

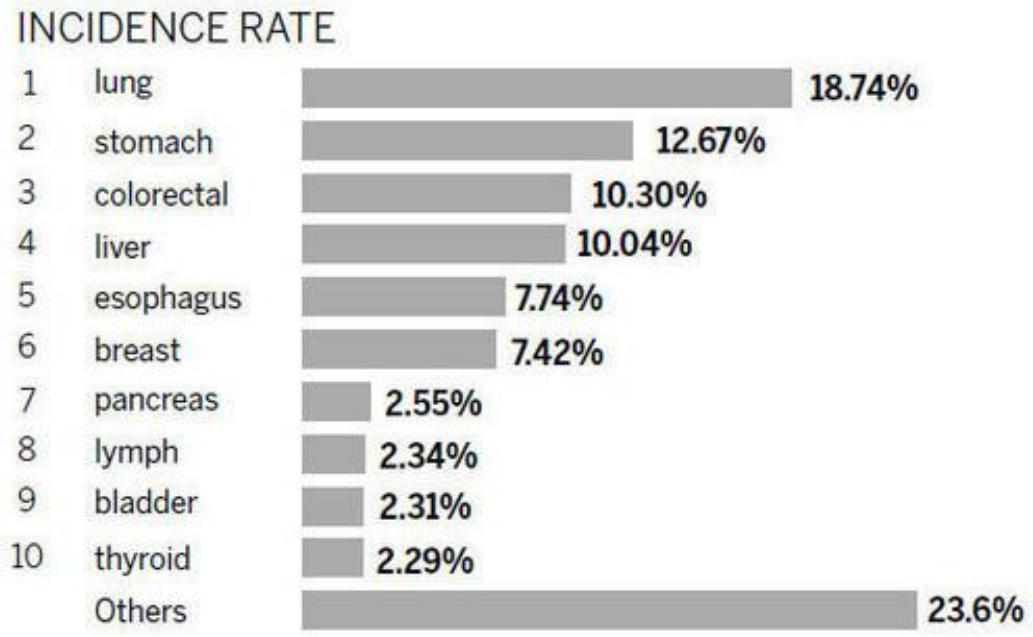


TOP TYPES OF CANCER IN TERMS OF INCIDENCE RATE AND DEATH RATE AMONG CHINESE

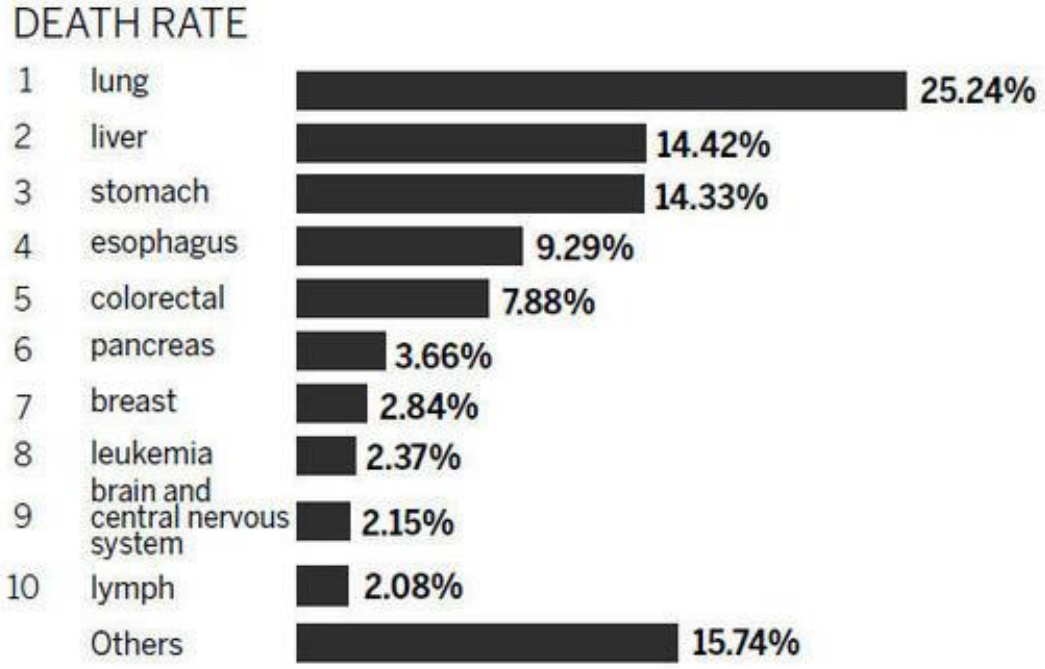
Source: The National Central Cancer Registry under the Ministry of Health

FENG XIUXIA / CHINA DAILY

發病率



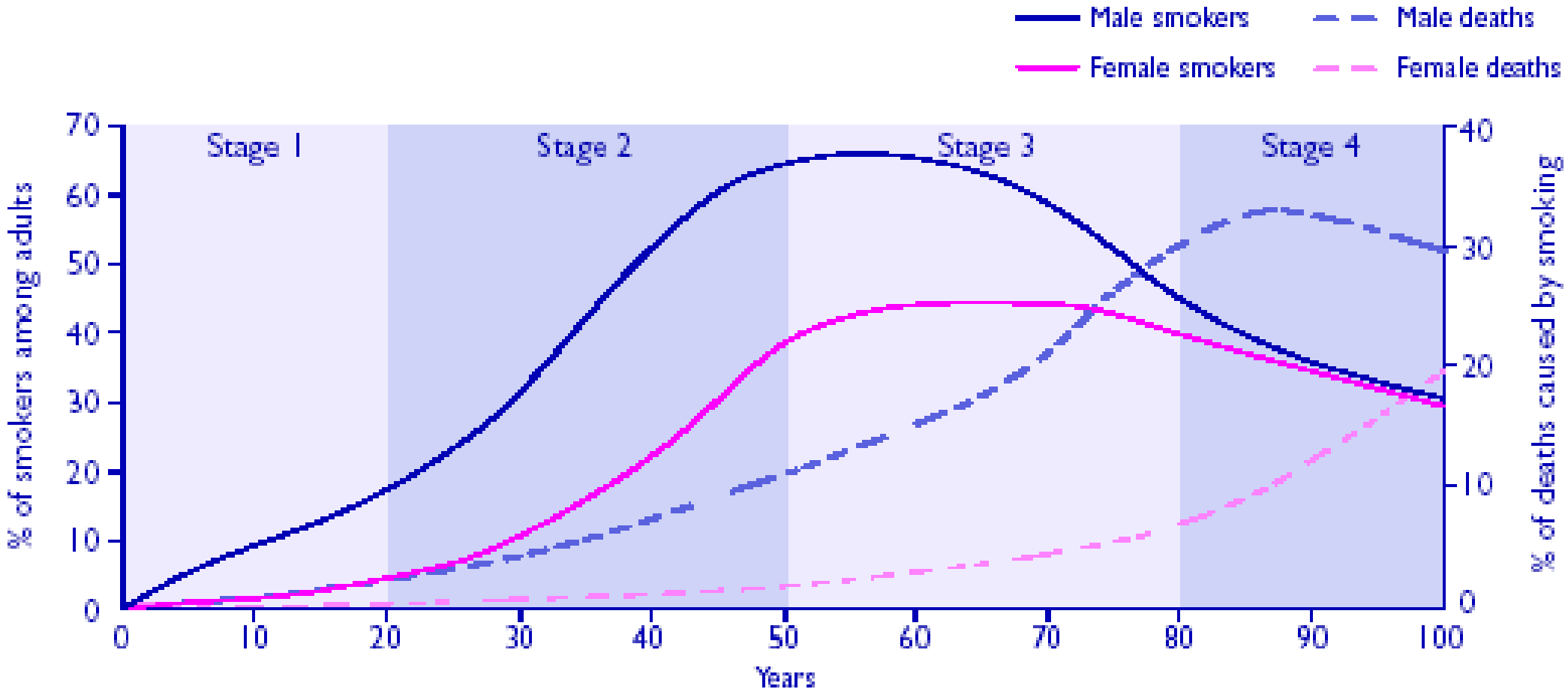
死亡率



Aetiology 病因

- Tobacco smoke: >90% cases 抽煙
  - Passive smoking
  - >10 yrs cessation for risk to start decreasing
- Others:

Asbestos	Atmospheric pollution
Radiation	Metals (nickel, silver?)
Chemicals	***Genetic***



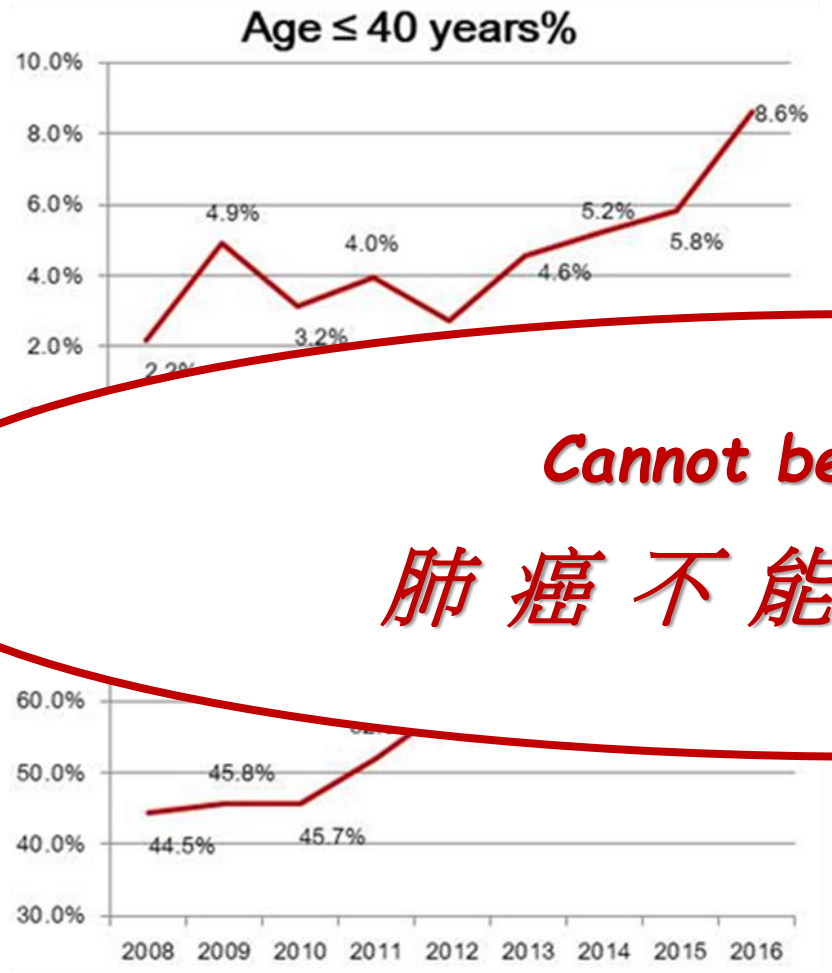
Stage 1
Sub-Saharan Africa

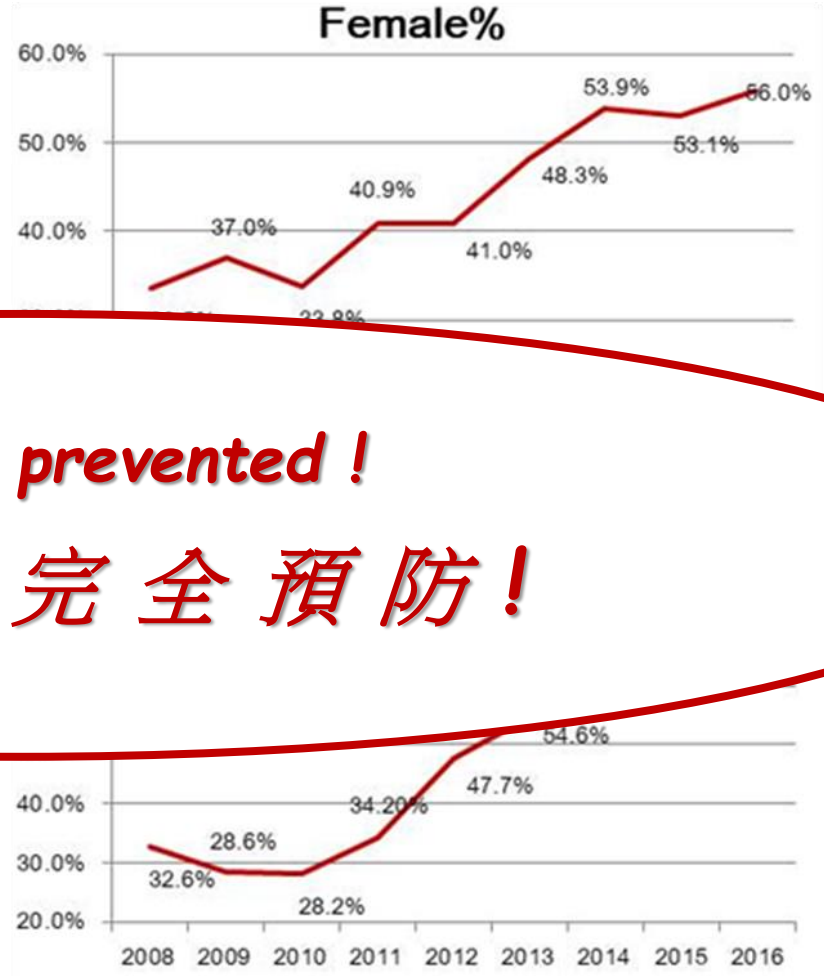
Stage 2
China, Japan, South East Asia, Latin America, North Africa

Stage 3
Eastern Europe, Southern Europe, Latin America

Stage 4
Western Europe, North America, Australia

2008 - 2016: 7524 primary lung cancer patients



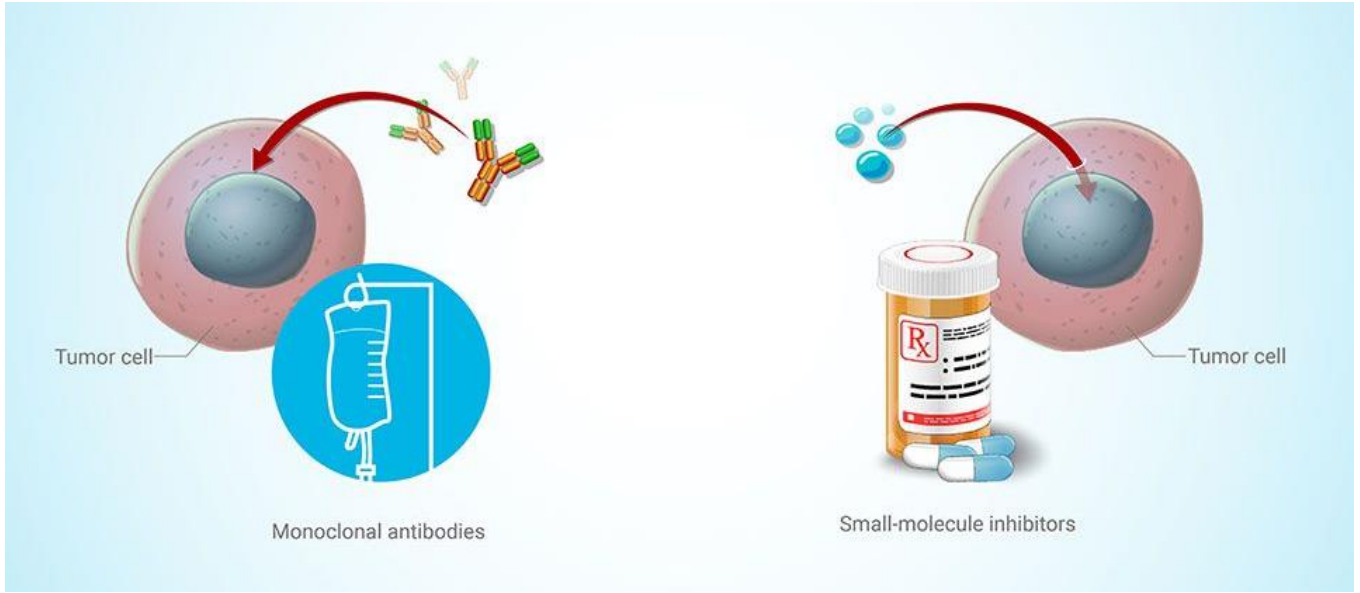


Cannot be prevented !

肺癌不能完全預防！

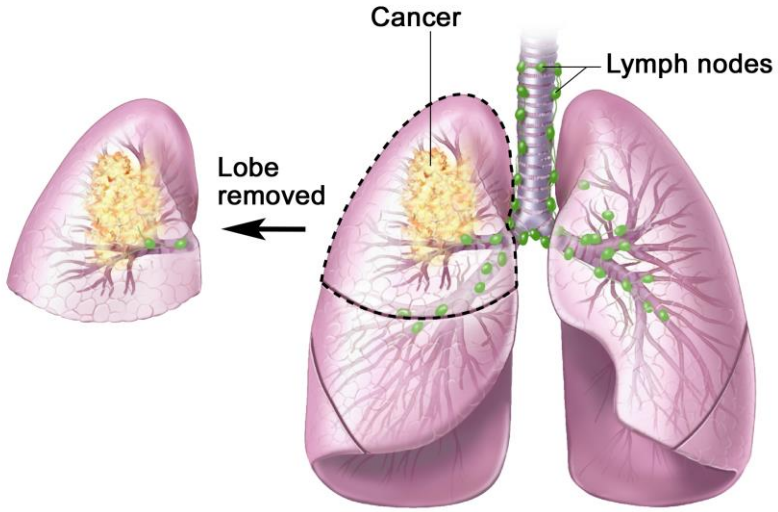
Images courtesy of: Dr Chen Haiquan (Fudan University Cancer Hospital, Shanghai)

Cure exists！ 肺癌可以根治！



Immunotherapy
免疫治療

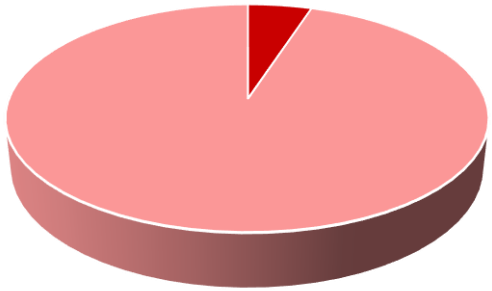
Target therapy
標靶治療



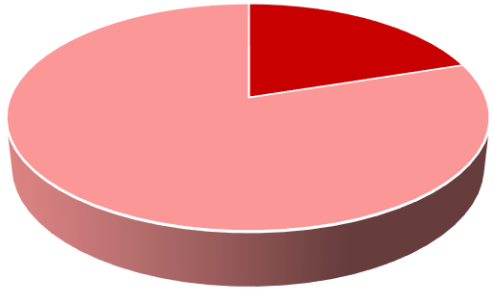
Surgery
手術切除

Resection rates 肺癌切除率

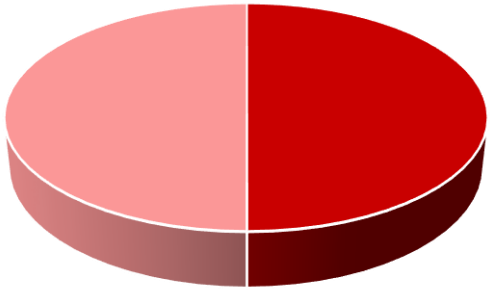
馬來西亞
5%



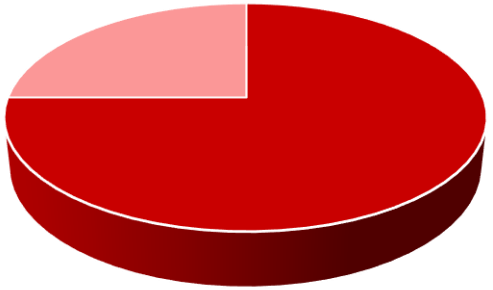
美國, 香港
20%



韓國
50%



日本
75%



Symptoms 徵狀

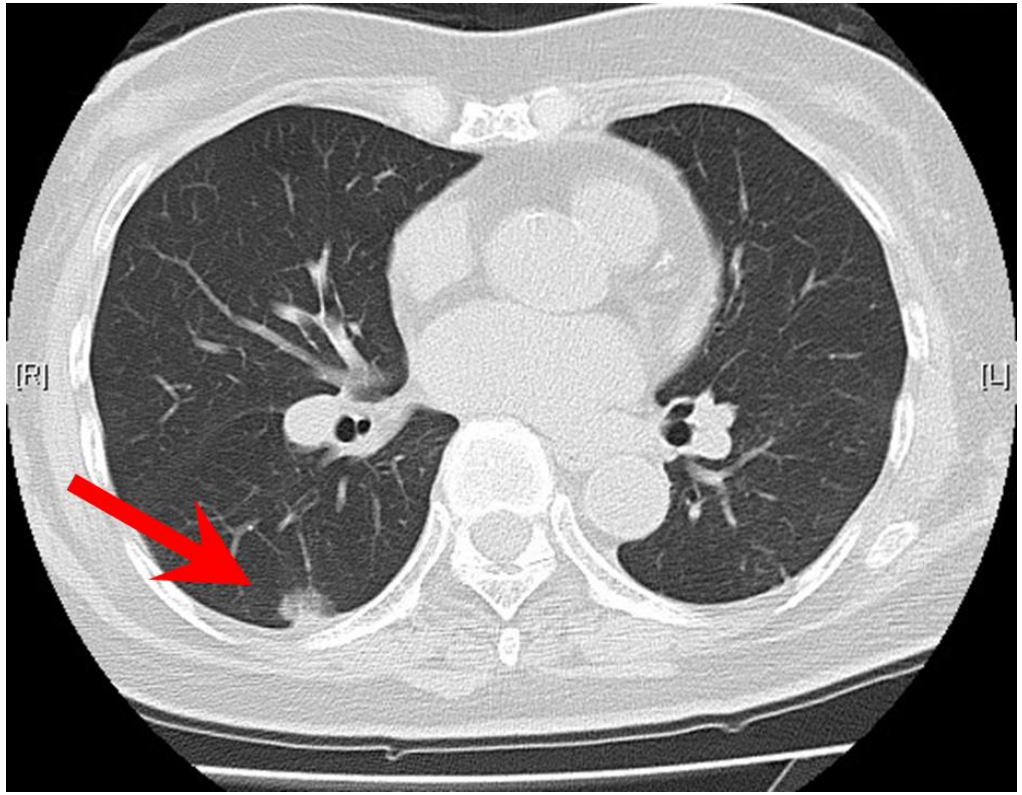
1. Bronchopulmonary 呼吸氣道
   - cough, hemoptysis, dyspnoea, chest pain, wheeze, pneumonia

Most patients are *asymptomatic* !

大多數患者沒有徵狀！

5. Nonspecific/constitutional symptoms
   - weight loss, weakness, anorexia, lassitude, malaise

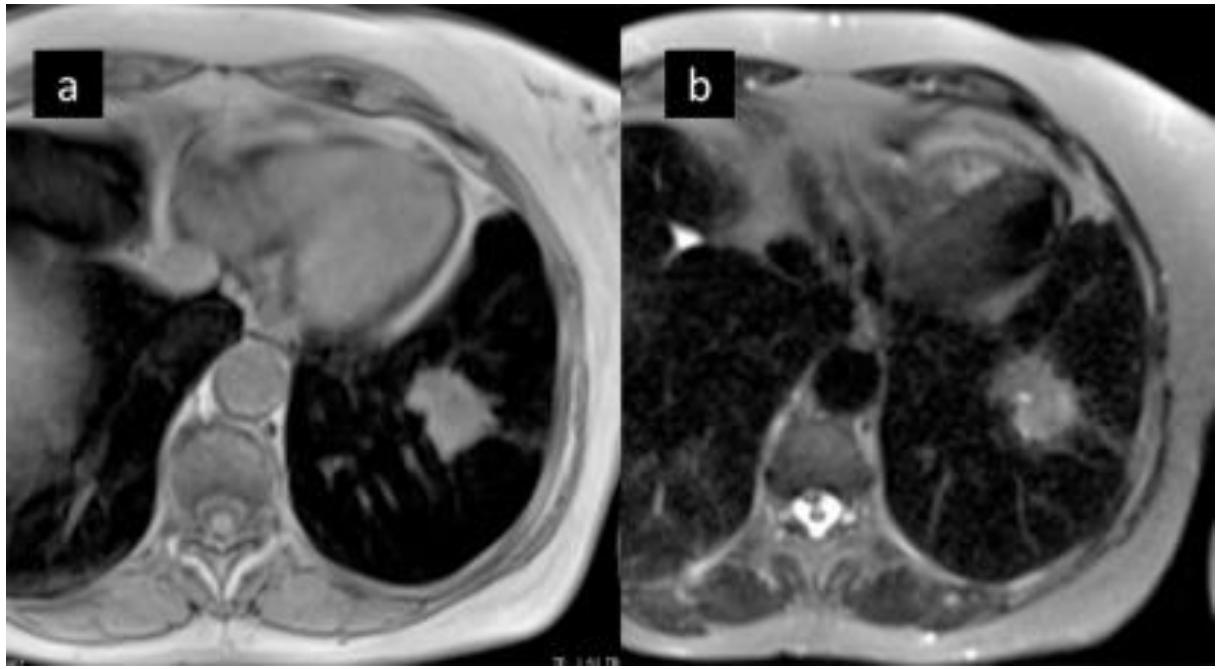
Presentation 最初求醫



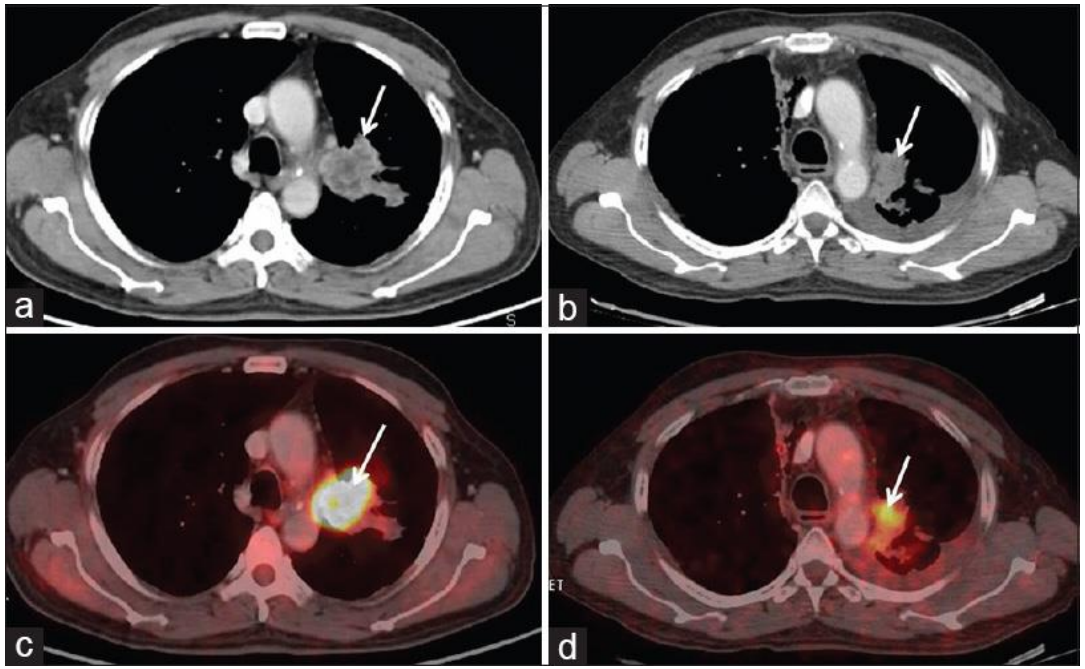
Demographics ?

高危一族？

Imaging ?　　更好，更貴的掃描？



MRI



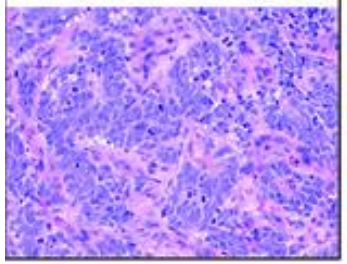
PET-CT

Lung cancer histology

Small cell carcinoma

Pure small cell lung carcinoma

Combined small cell/ non-small cell lung carcinoma



Non-small cell carcinoma

Carcinoid tumor

Typical carcinoid

Atypical carcinoid

Carcinomas of salivary gland type

Mucoepidermoid carcinoma

Adenoid cystic carcinoma

Carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements

Sarcomas with spindle and/or giant cells

Spindle cell carcinoma

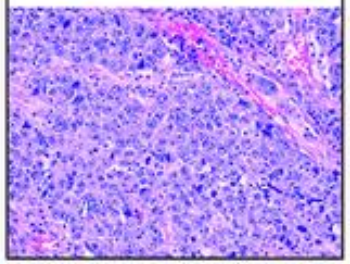
Giant cell carcinoma

Carcinocarcinoma

Pulmonary blastoma

Large cell carcinoma

Several variants



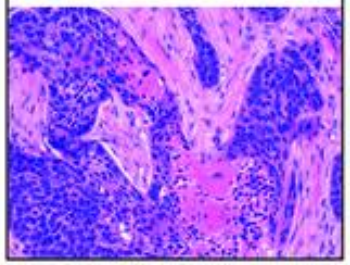
Squamous cell carcinoma

Papillary

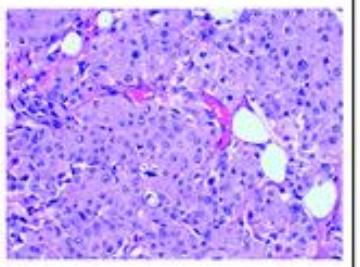
Clear cell

Basaloid

Small cell



Adenocarcinoma

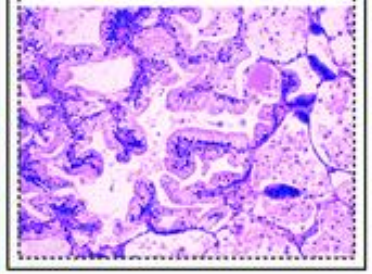


Acinar

Papillary

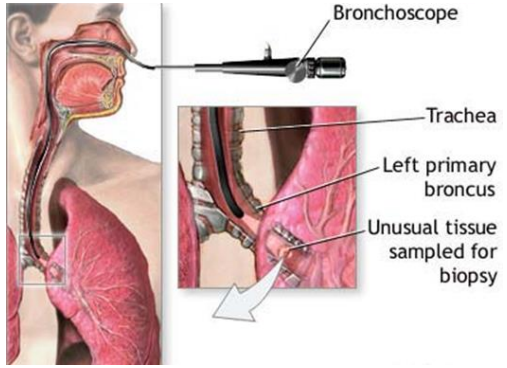
Solid adenocarcinoma with mucin

Bronchioalveolar

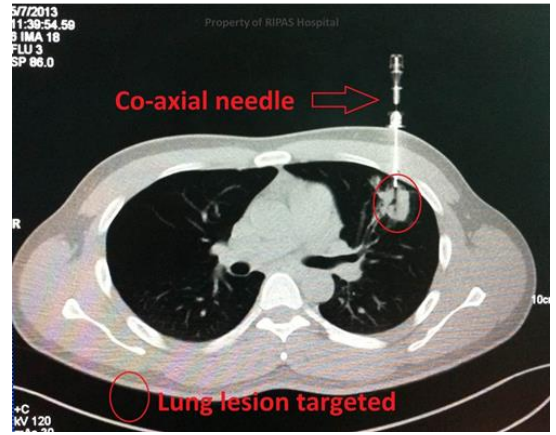


Non-surgical biopsy 活檢診斷

Bronchoscopy
支氣管鏡



CT-FNAC
針穿刺活檢



Percutaneous CT-guided fine needle aspiration for lung cancer smaller than 2 cm and revealed by ground-glass opacity at CT

Katsuhiko Shimizu*, Norihiko Ikeda, Masahiro Tsuboi, Takashi Hirano, Harubumi Kato

Lung Cancer (2006) 51, 173–179

Table 3 Characteristics between GGO-dominant lesion and solid-dominant lesion

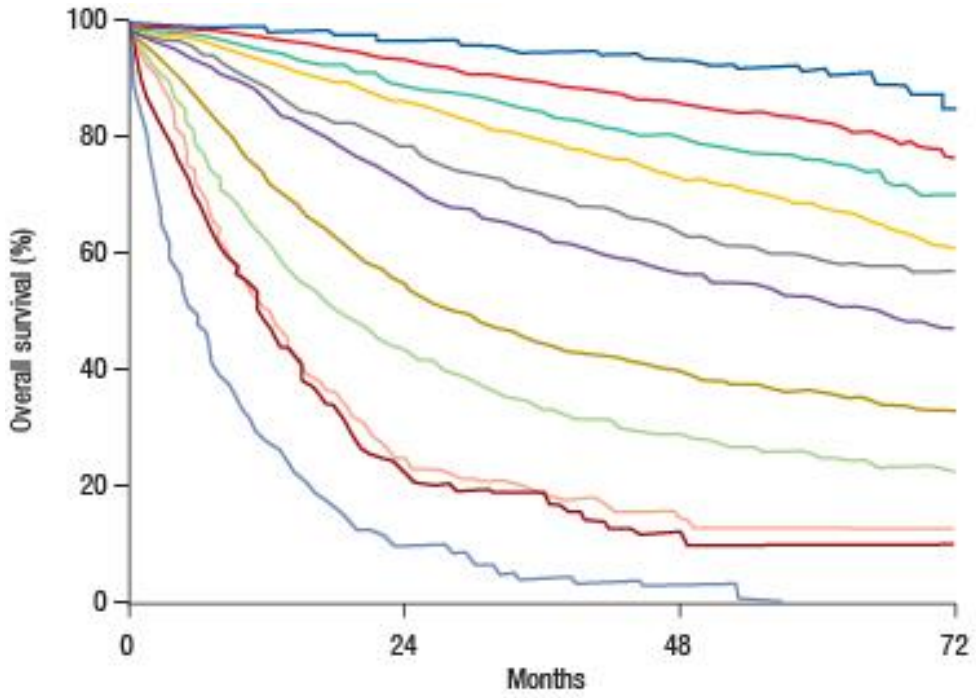
	GGO lesion	Solid lesion	*p*-value
Diagnostic yield (%)	51.2 (22/43)	75.6 (40/53)	0.018
Diagnostic yield of lesion size (%)			
<10 (mm)	35.2 (6/17)	62.5 (10/16)	0.170
11–15 (mm)	50.0 (8/16)	75.0 (12/16)	0.273
16–20 (mm)	80.0 (8/10)	85.7 (18/21)	0.999
Lesion size (mm)	12.88 ± 4.04	14.51 ± 4.51	0.069
Lesion depth (mm)	47.98 ± 15.34	50.10 ± 17.62	0.544
Pleura-lesion depth (mm)	15.63 ± 11.78	16.87 ± 15.20	0.670
Pneumothorax	32.6 (14/43)	30.2 (16/53)	0.978
Pneumothorax with chest tube placement	11.6 (5/43)	13.2 (7/53)	0.999

TNM Staging 8th edition 分期

	TNM 8th - Primary tumor characteristics
T_x	Tumor in sputum/bronchial washings but not be assessed in imaging or bronchoscopy
T_0	No evidence of tumor
T_{is}	Carcinoma in situ
T_1	≤ 3 cm surrounded by lung/visceral pleura, not involving main bronchus
$T_{1a(mi)}$	Minimally invasive carcinoma
T_{1a}	≤ 1 cm
T_{1b}	> 1 to ≤ 2 cm
T_{1c}	> 2 to ≤ 3 cm
T_2	> 3 to ≤ 5 cm *or* involvement of main bronchus without carina, regardless of distance from carina or invasion visceral pleural *or* atelectasis or post obstructive pneumonitis extending to hilum
T_{2a}	>3 to ≤4cm
T_{2b}	>4 to ≤5cm
T_3	>5 to ≤7cm in greatest dimension *or* tumor of any size that involves chest wall, pericardium, phrenic nerve *or* satellite nodules in the same lobe
T_4	> 7cm in greatest dimension *or* any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, spine *or* separate tumor in different lobe of ipsilateral lung
N_1	Ipsilateral peribronchial and/or hilar nodes and intrapulmonary nodes
2	Ipsilateral mediastinal and/or subcarinal nodes
3	Contralateral mediastinal or hilar; ipsilateral/contralateral scalene/ supraclavicular
M_1	Distant metastasis
M_{1a}	Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion
M_{1b}	Single extrathoracic metastasis, including single non-regional lymphnode
M_{1c}	Multiple extrathoracic metastases in one or more organs

	N0	N1	N2	N3
T1	IA	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB
T2b	IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a	IVA	IVA	IVA	IVA
M1b	IVA	IVA	IVA	IVA
M1c	IVB	IVB	IVB	IVB

Importance of Staging 為何分期?



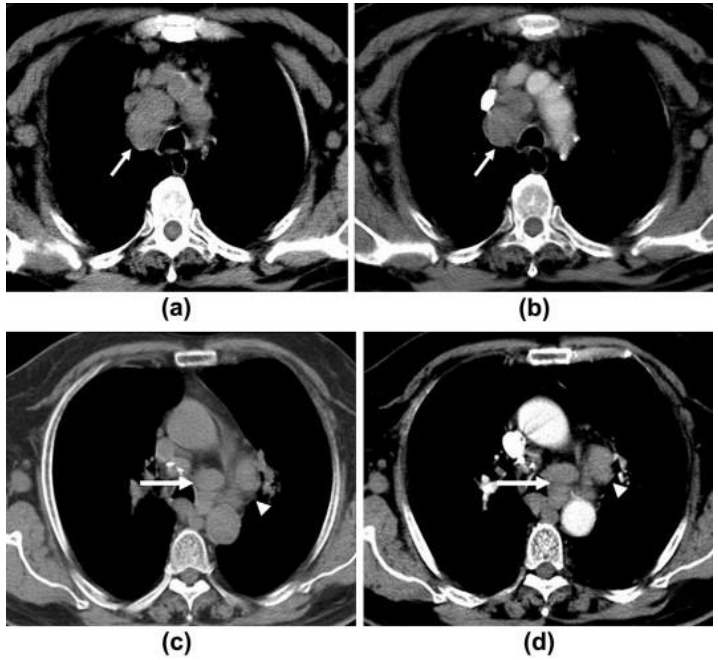
Staging	60-month overall survival (%)
IA1	92
IA2	83
IA3	77
IB	68
IIA	60
IIB	53
IIIA	36
IIIB	26
IIIC	13
IVA	10
ICB	0

→ **Operable** 可以手術

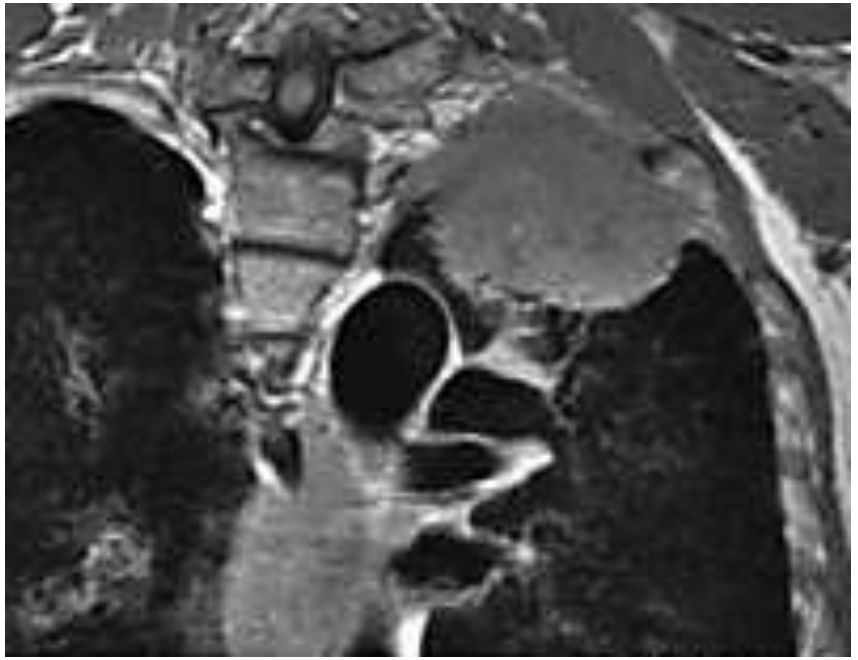
→ **Inoperable** 手術無效

TNM 8th Edition

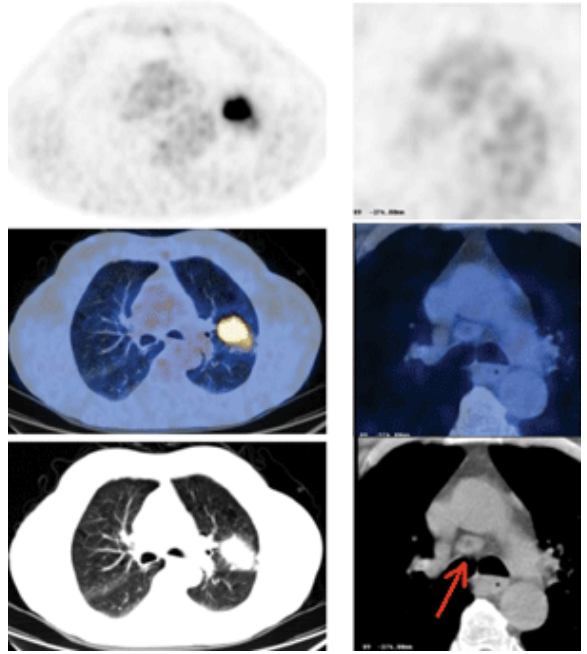
Non-invasive 非侵入性檢查



CT + contrast
（增强 CT）

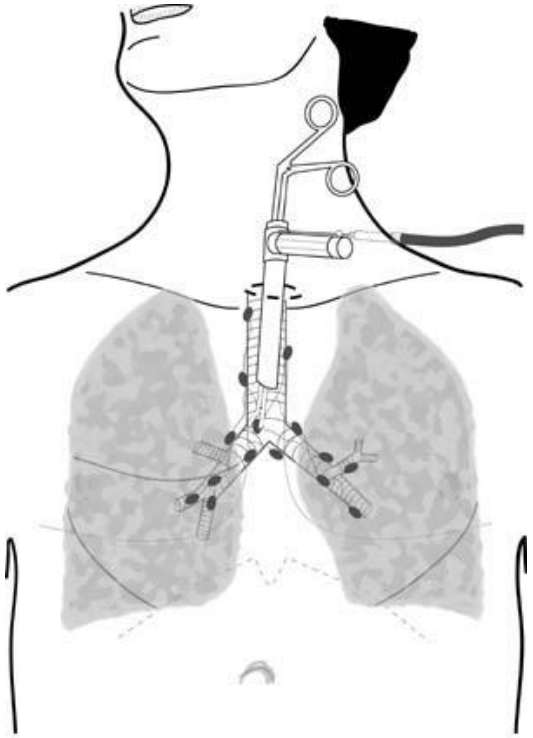


MRI



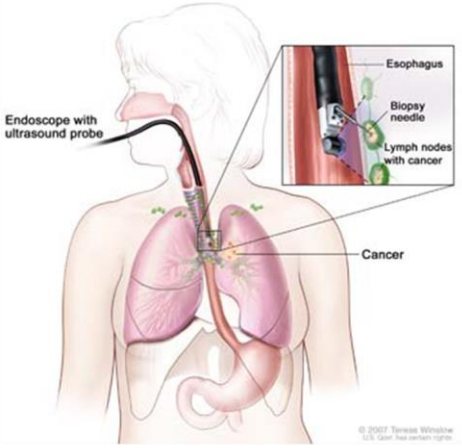
PET-CT

Invasive 侵入性檢查



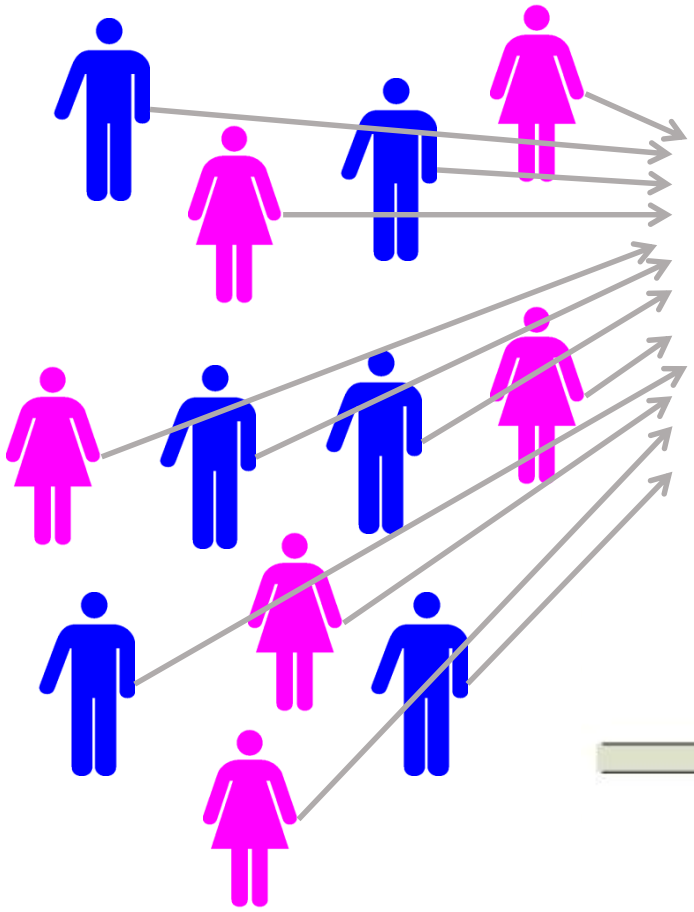
Pleural aspiration
抽胸水

Mediastinoscopy
縱隔鏡手術

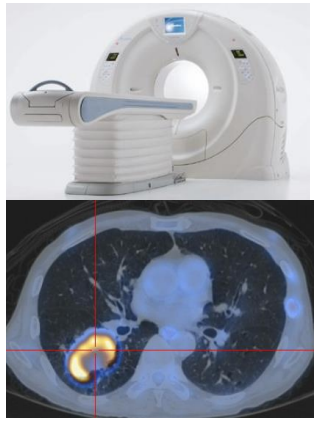


Endobronchial Ultrasound (EBUS)
氣管鏡超聲波

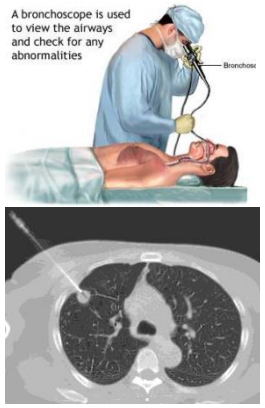
Bottle Neck 樽頸位



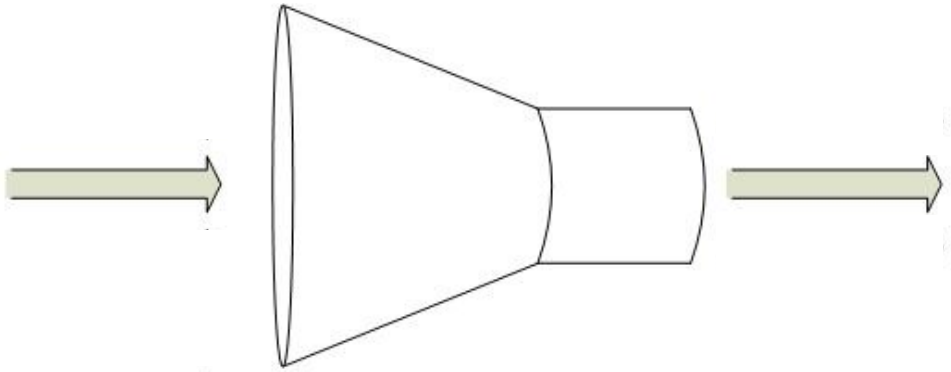
發現結節



活檢



手術治療



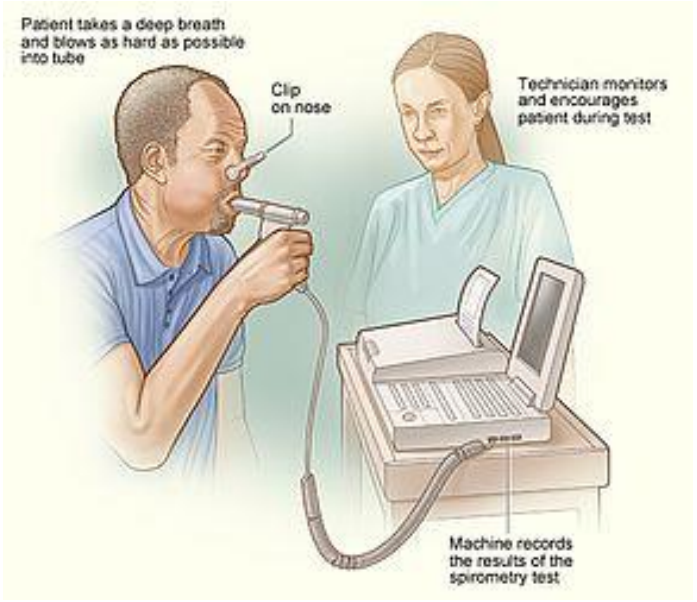
Options for treatment 治療方案

1. Surgery 手術
2. Radiotherapy + SBRT 放射治療
3. Chemotherapy + Targeted Tx 化療
4. Others
   - Ablation (MW, RF) 消融
   - Immunotherapy 免疫治療

Candidacy for Surgery 適合手術嗎？

1. Staging (stage I-II) 分期
2. Patient factors 病人因素
   a) Medical co-morbidities 共存疾病
      - Often elderly smokers
      - ↑↑ risk for Respiratory & Cardiac complications
   b) Pulmonary function 肺功能

Pulmonary function 肺功能



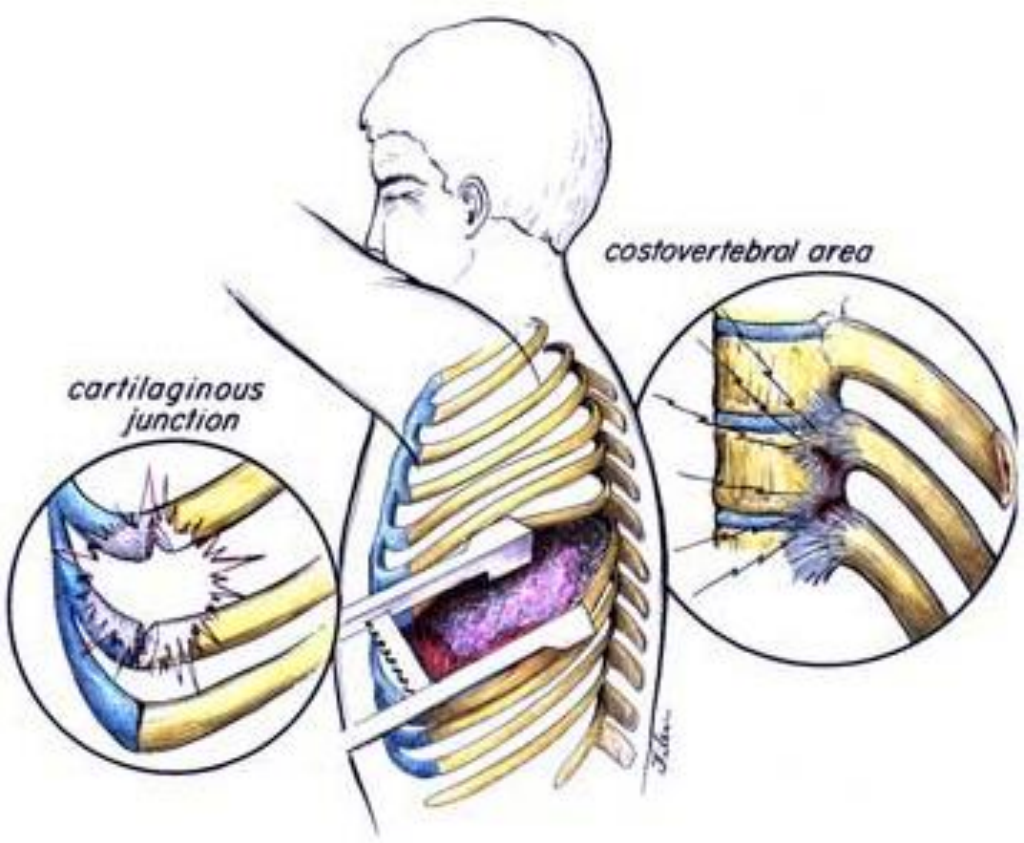
Spirometry
肺功能測定

6 Minute Walk Test
6分鐘步行測試

Oxygen Uptake testing
氧氣吸收測試

Operating Theatre 手術室

Open Thoracotomy 傳統開胸手術



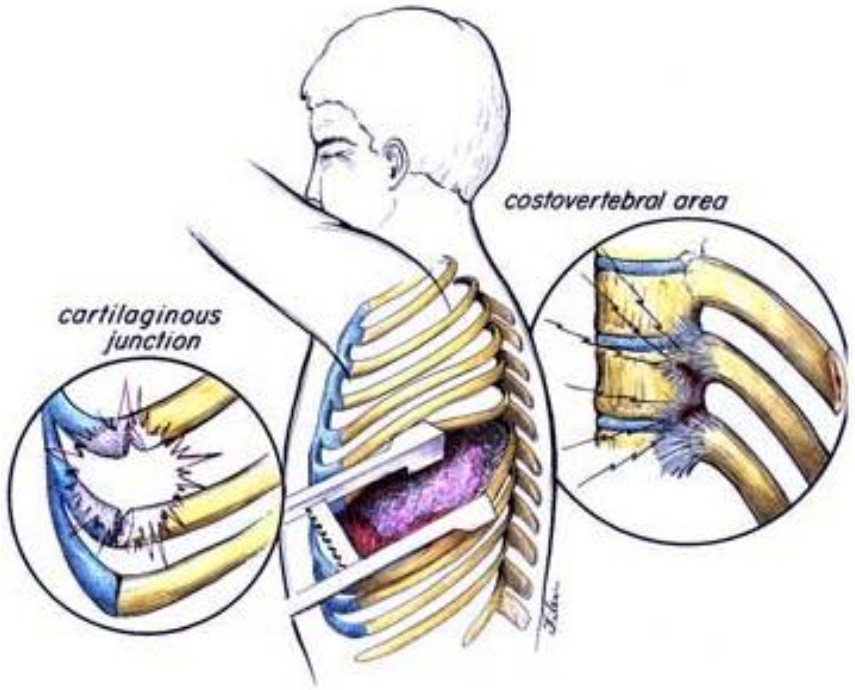
Video-Assisted Thoracic Surgery 胸腔鏡手術

Complications 併發症

- Non-specific: e.g. bleeding, infection etc.
- Specific:
  - Sputum retention → atelectasis
  - Air leak (alveolar / bronchial)
  - Cardiac (esp. arrhythmia)
  - Others: e.g. chylothorax, nerve palsy etc.

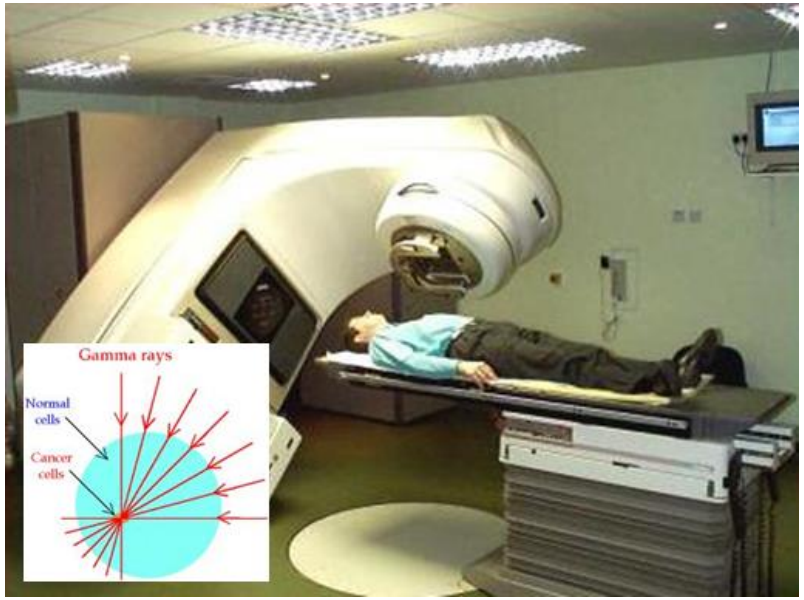
Sequelae 後遺症

1. Reduced pulmonary reserve
2. Pain / Paresthesia
    - Prevalent
    - Debilitating
    - Chronic
    - Refractory

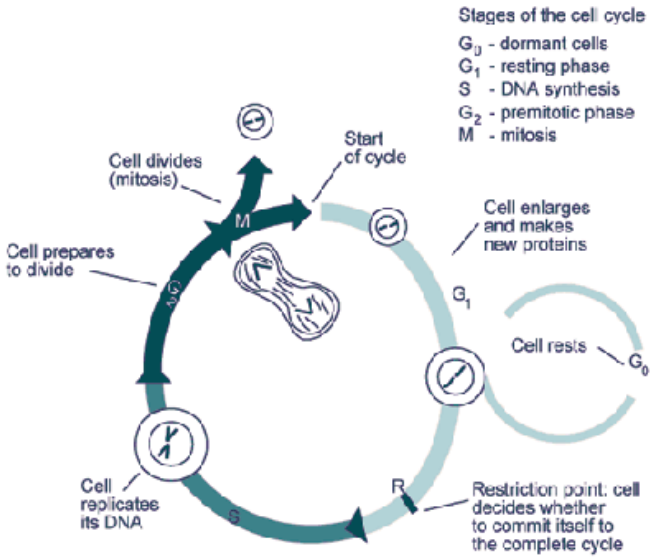


Adjuvant Therapy 輔助治療

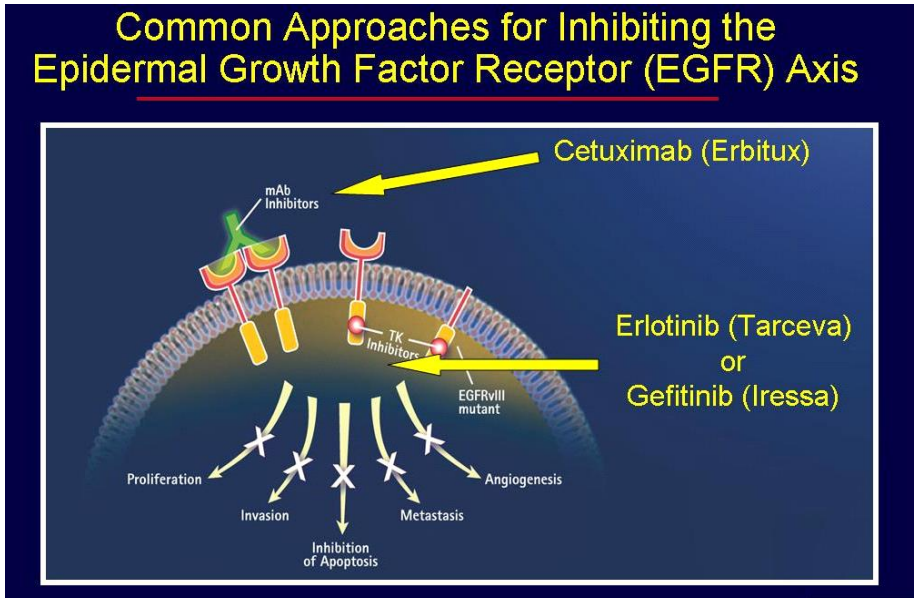
Radiotherapy



Chemotherapy



Targeted therapy



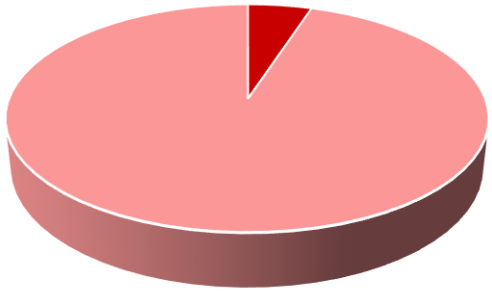
The Goal of MIS 微創手術終極目標

- **Thoracotomy:** ☹☹☹☹☹☹☹☹😐😐
- **VATS (Today):** ☹☹☹☹☹☹☹☹☺☺
- **VATS (Goal):** ☹☹☹☹☹☹☺☺☺☺

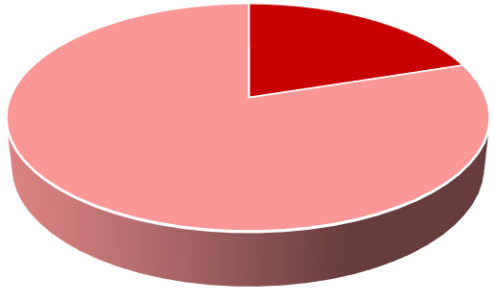
Uniportal VATS
RUL Lobectomy
(Post-op day 2)

Resection rates 肺癌切除率

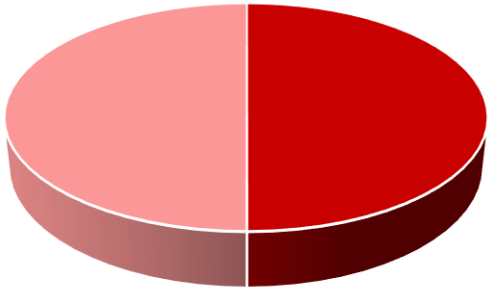
馬來西亞
5%



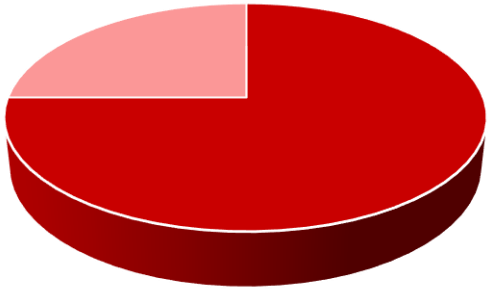
美國, 香港
20%



韓國
50%



日本
75%

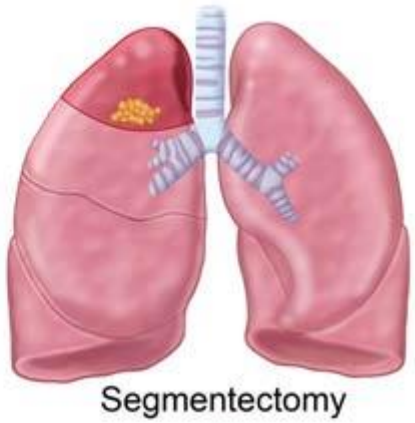


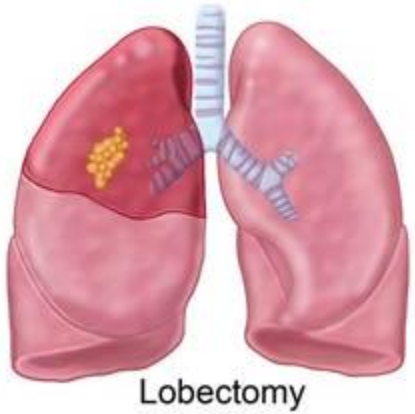
VATS Evolution 胸腔鏡手術的進化

傳統3孔 針孔 雙孔 單孔

Lung Cancer Resections 肺癌切除


Wedge Resection


Segmentectomy

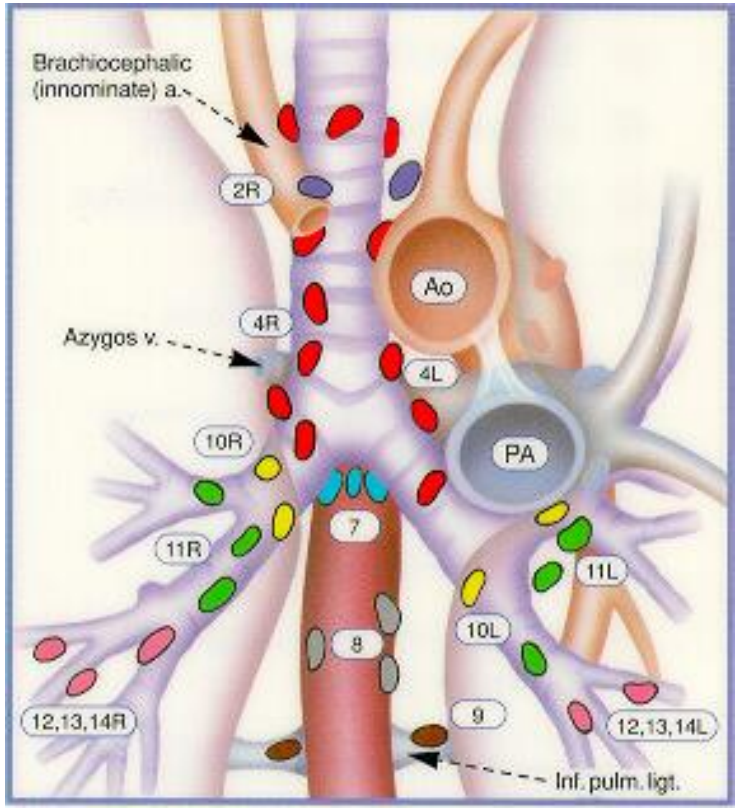

Lobectomy


Pneumonectomy

Sublobar Resection

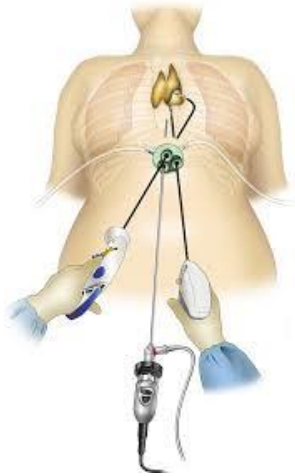
Lymph Nodes 淋巴結

- ***LN Sampling*** 淋巴結取樣
  - ↓ morbidity / complications
  - ↓ immune response disruption
- ***LN Clearance*** 淋巴結清掃
  - ↑ accurate staging
  - ↓ local recurrence



Uniportal VATS

Uniportal Segmentectomy

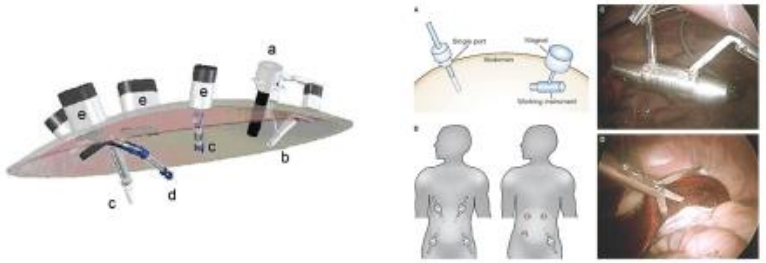


Non-intubated VATS

Subxiphoid VATS

Technology 注入新技術

Magnetic Anchoring

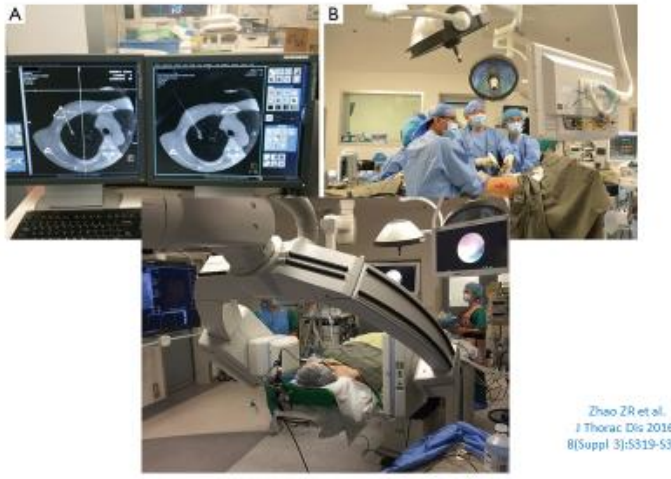


Next Generation Robots

Insertable Robotic Effector Platform (IREP)

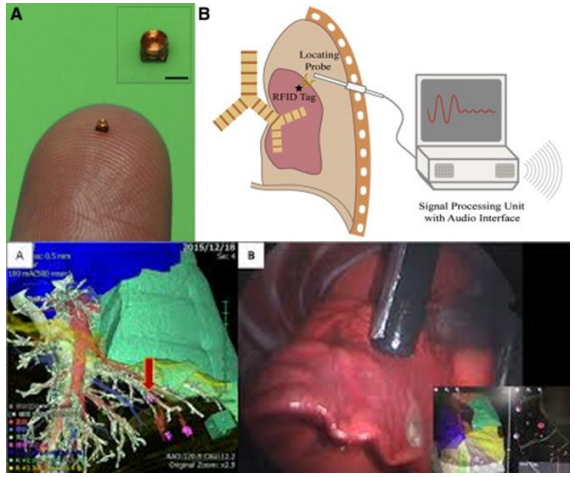
3D Printing

Localization: Hybrid OR

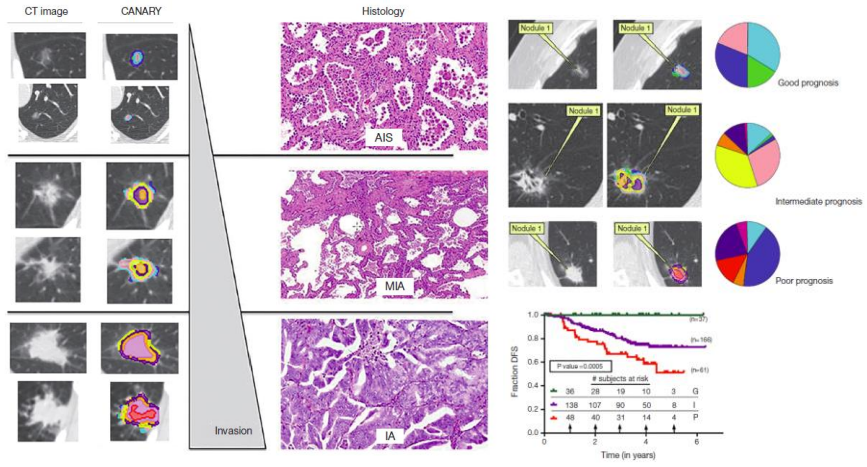


Zhao ZR et al.
J Thorac Dis 2016;
8(Suppl 3):S319-S327

Radio-Frequency ID Tag



Artificial Intelligence



Enhanced Recovery After Surgery (ERAS)

手術後增強恢復

	Pre-operation	Day 0	Day 1	Day 2	Day 3	Day 4 / 5	Day 6 and after *(if not yet discharged)*
Goal	*Ensure pt prepared for OT* *Anticipate post-op needs*	*Intensive monitoring for post-op complications*	*Ensure safety & comfort* *Ensure early mobilization*	*Ensure safety & comfort* *Remove chest drain*	*Ensure safety & comfort* *Facilitate elimination*	*Discharge if pt safe & home/family ready*	*Manage any cause of prolonged stay*
Monitoring	Height & Weight Baseline BPP / RR / T / SpO_2	BPP / SpO_2 / RR Q1H x6h - then BPP/T Q4h; SpO_2 / RR Q1h till PCA off CD chart Q1H until stable - then Q4H	BPP / RR / T / SpO_2 Q4H CD chart TDS	BPP / RR / T / SpO_2 Q4H CD chart TDS	BPP / RR / T / SpO_2 QID	BPP / RR / T / SpO_2 QID	BPP / RR / T / SpO_2 BD until discharge If CD in situ: CD chart TDS
Investigation	Sputum x C/ST, AFB Ensure available: - CXR (within 4/52) - latest CT films - CBP (within 4/52) - FEV1 (within 4/52)	CXR on suction Blood tests only if ordered	CXR after off suction	CXR after off CD	CXR	CXR	If CD in situ: daily CXR If CD removed: CXR alternate days
Patient Activity	Activity as tolerated Purchase & practice Triflow SFI payment if applicable	Sit up in bed as tolerated Begin Triflow use as tolerated	Sit out all day Mobilize as tolerated Encourage Triflow use - 10x per 30 mins	Sit out all day Encourage mobilization Encourage Triflow use - 10x per 30 mins	Sit out all day Encourage mobilization Encourage Triflow use - 10x per 30 mins	Sit out all day Encourage mobilization Encourage Triflow use - 10x per 30 mins	Sit out all day Encourage mobilization Encourage Triflow use - 10x per 30 mins
Treatment	Prescribe pre-admission meds by resident - except Aspirin/Plavix Chest physio training	Follow surgeon's post-op orders: - CD to suction - IV fluids - IV antibiotics - IV PCA overnight - Oral analgesia on DAT	Off O_2 Off CD suction Off PCA Off IV Fluids Resume Aspirin/Plavix Ensure adequate regular & prn analgesia Post-op chest physio	Off CD if: - if no air leak - output ≤200ml/day Wound review by surgeon Change all dressings Ensure adequate regular & prn analgesia Post-op chest physio	Ensure adequate regular & prn analgesia Post-op chest physio	Ensure adequate regular & prn analgesia Post-op chest physio Change all dressings pre-discharge (on D4/D5)	If CD not yet removed: - chemical pleurodesis by surgeon if air leak Change CD box every 7 days Change wound dressings every 3-4 days Post-op chest physio
Nutrition & Elimination	DAT NPO after MN or per anesthetist's order	NPO for 4-6hrs then DAT Bed pan / Foley prn	DAT Pt self-mobilizing to toilet	DAT Pt self-mobilizing to toilet	DAT Pt self-mobilizing to toilet Dulcolox supp. if no BO	DAT Pt self-mobilizing to toilet	DAT Pt self-mobilizing to toilet
Communication	Surgeon to see patient and family pre-op - arrange mutually convenient time - consent for OT, studies, SFI	Surgeon to see patient and family - explain OT findings	Ensure pt understands: - need for mobilization - need to use Triflow - how to ask for prn analgesia	Remind patient & family of planned discharge POD4/5	Remind patient & family of planned discharge POD4/5	Ensure patient & family have all post-discharge needs met	Surgeon to see patient and family - explain prolonged stay & management plan
Discharge Plan	Evaluate & manage: - pt emotional needs - post-discharge needs Advise patient & family of planned discharge POD4/5			Manage post-discharge needs: - home environment - family situation	Manage post-discharge needs: - home environment - family situation	HOME if patient mobile & independent - discharge summary - discharge drugs - sick leave f/u SOPD 1/52 + CXR Refer other depts prn	HOME if patient mobile & independent - plan as POD4

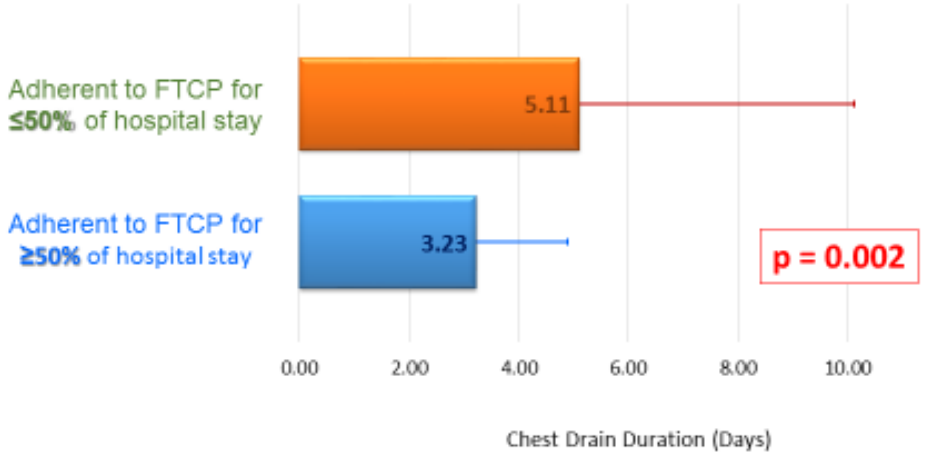
Adherence to a Clinical Pathway for Video-Assisted Thoracic Surgery

Predictors and Clinical Importance

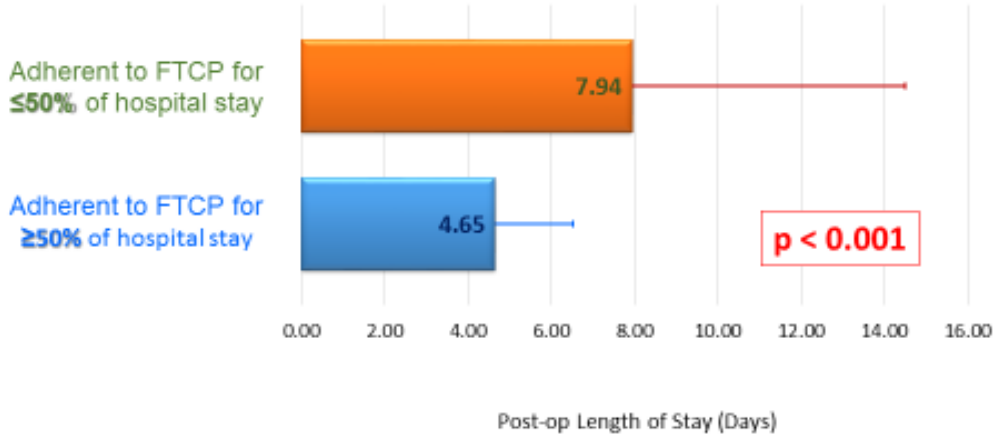
Alan D. L. Sihoe, FRCSEd (CTh), Peter S. Y. Yu, MRCS, Timothy H. Kam, MBBS, S. Y. Lee, MBBS, and Xuyuan Liu, MBBS

(*Innovations* 2016;11: 179–186)

Chest Drain Duration



Length of Stay



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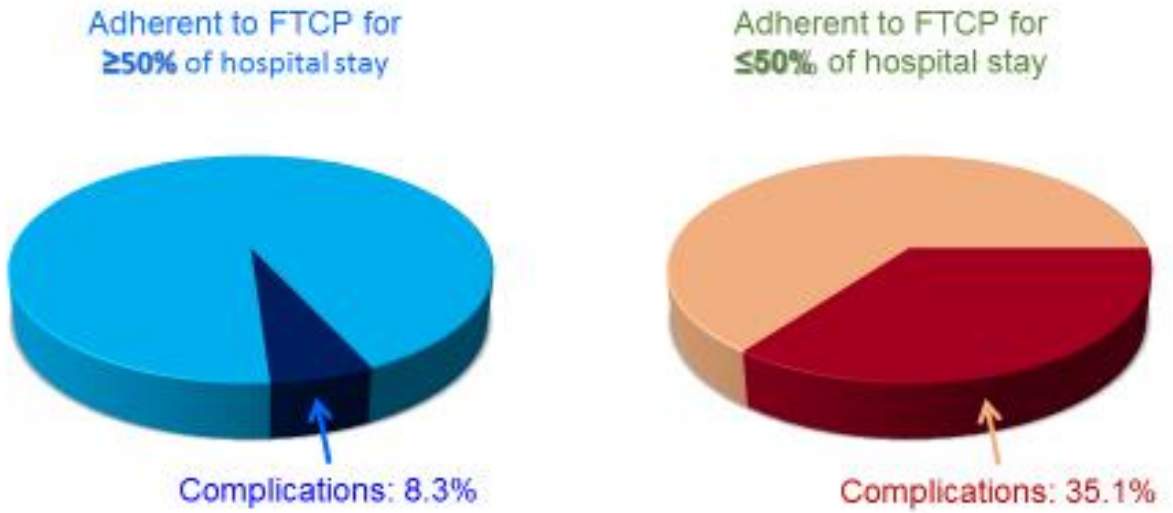
(*Innovations* 2016;11: 179–186)

Smokers: Complications



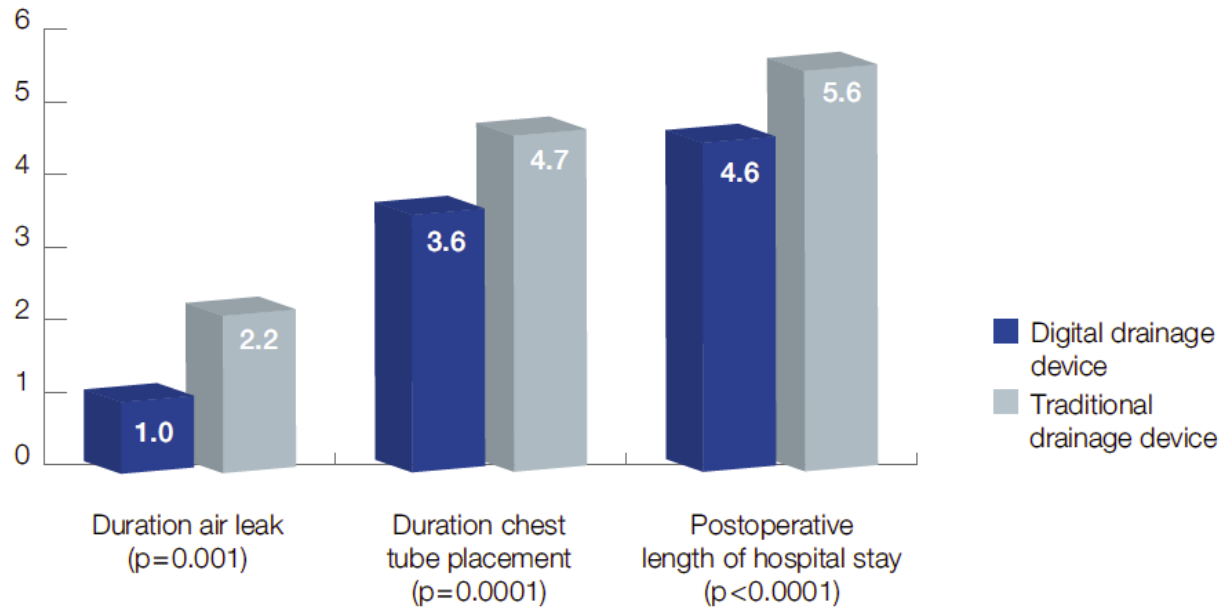
p = 0.023

Multicenter International Randomized Comparison of Objective and Subjective Outcomes Between Electronic and Traditional Chest Drainage Systems

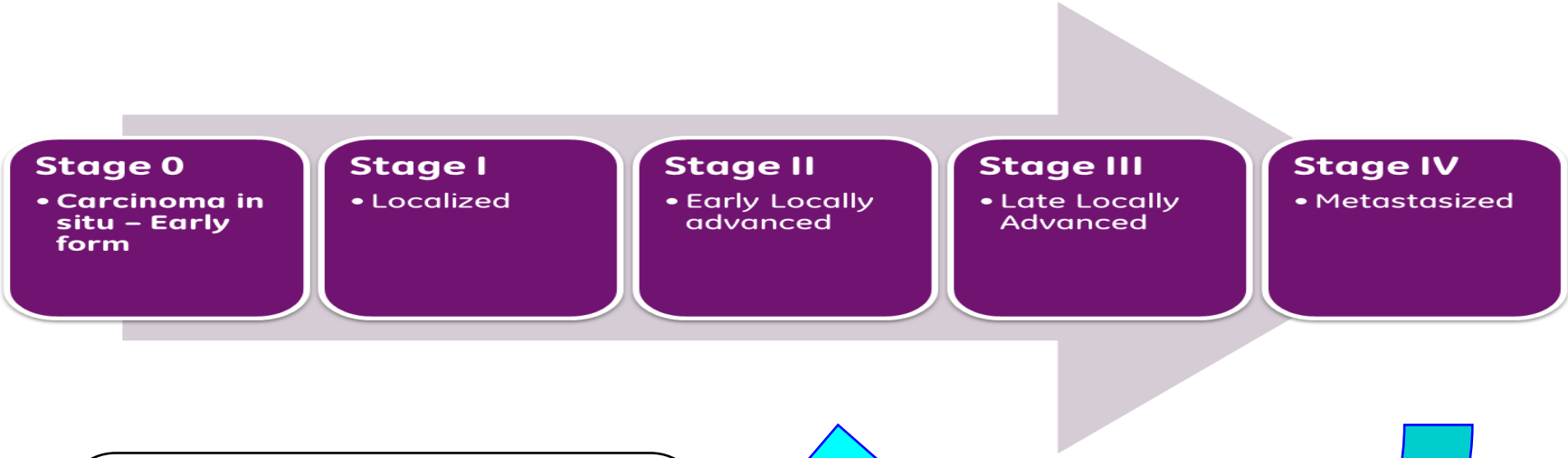
Cecilia Pompili, MD, Frank Detterbeck, MD, Kostas Papagiannopoulos, MD, Alan Sihoe, MB BChir, FRCSEd(CTh), Kostas Vachlas, MD, Mark W. Maxfield, MD, Henry C. Lim, MD, and Alessandro Brunelli, MD

Department of Thoracic Surgery, Ospedali Riuniti Ancona, Ancona, Italy; Department of Thoracic Surgery, Yale-New Haven Hospital, Yale University, New Haven, Connecticut; Division of Thoracic Surgery, St. James's University Hospital, Leeds, United Kingdom; and Department of Thoracic Surgery, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China

Ann Thorac Surg 2014;98:490–7

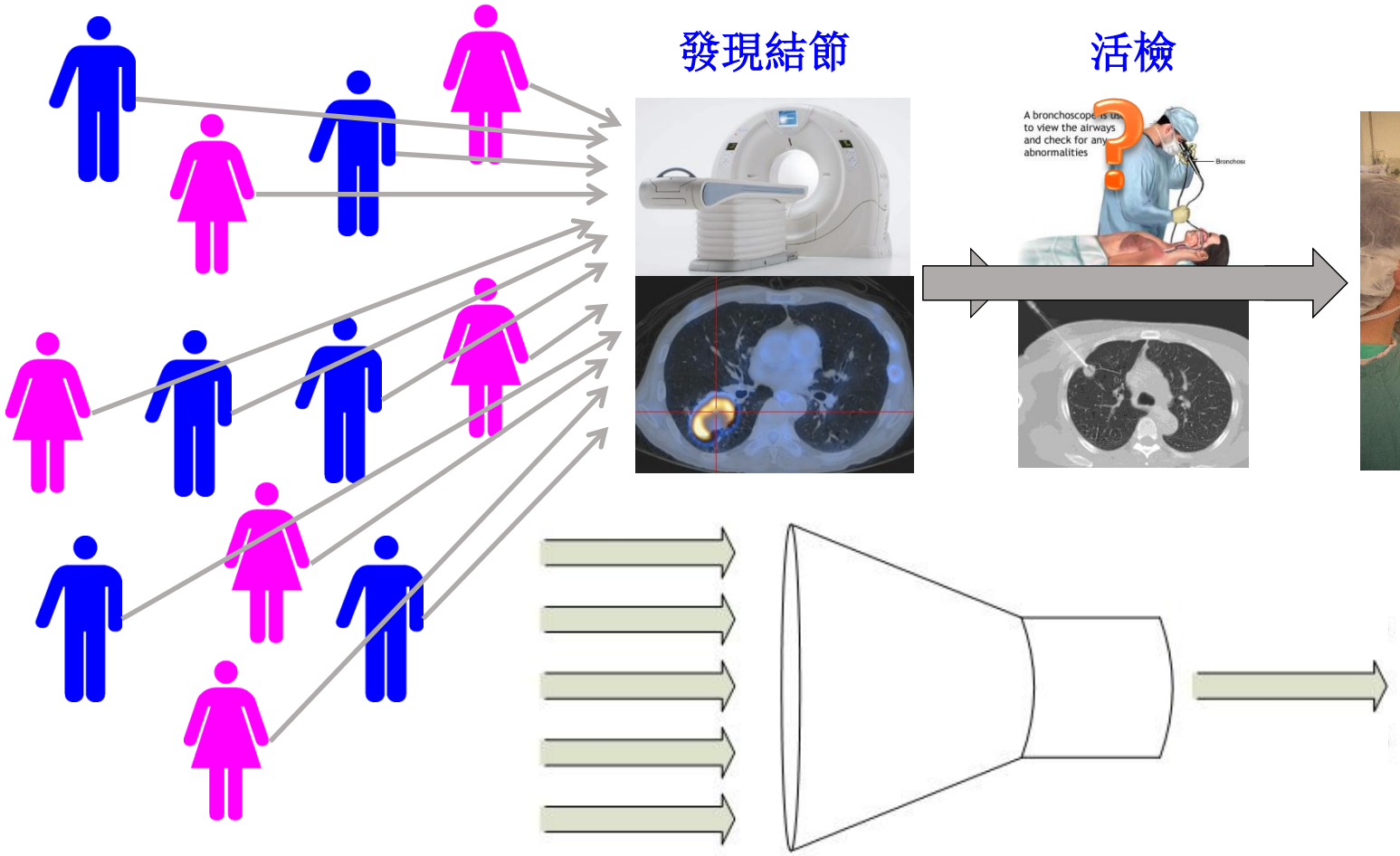


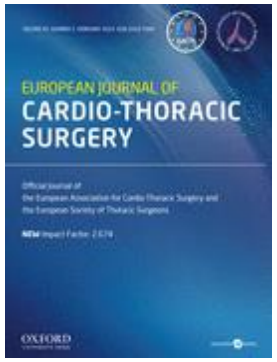
‘Inoperable’ disease ?　晚期都可以手術？



- Oligometastatic disease
- Targeted Therapy
- Immunotherapy

Bottle Neck 樽頸位





Operating on a suspicious lung mass without a preoperative tissue diagnosis: pros and cons†

Alan D.L. Sihoe*, Raj Hiranandani, Henry Wong and Enoch S.L. Yeung

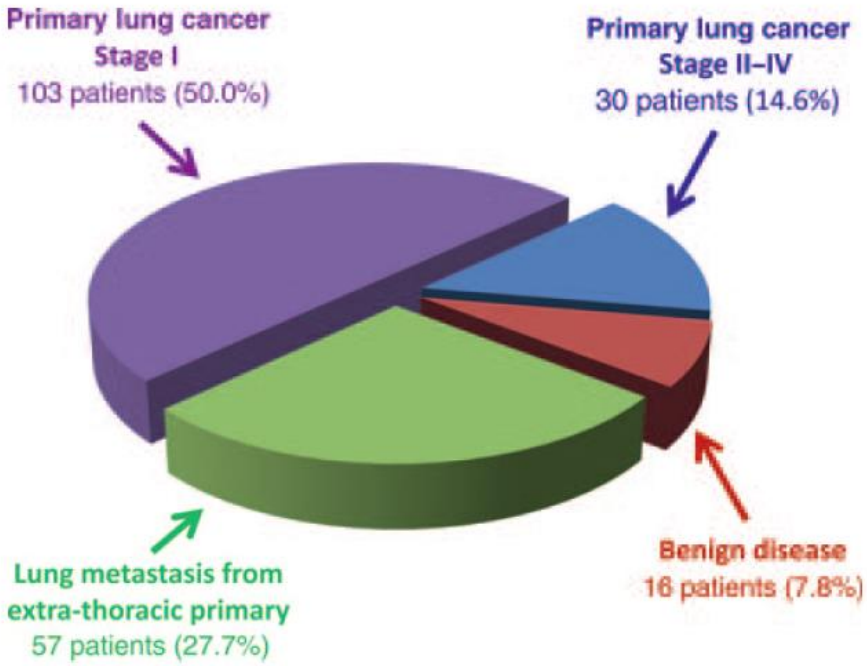
Division of Cardiothoracic Surgery, Department of Surgery, Li Ka Sing Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China

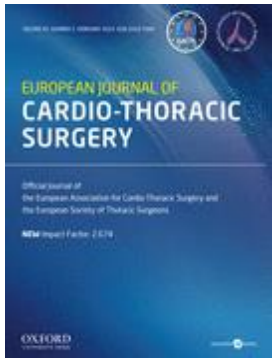
European Journal of Cardio-Thoracic Surgery 44 (2013) 231–237

Table 2: Interval between first presentation and acceptance for thoracic surgery

Interval	POTD (n = 237)	No POTD (n = 206)	P-value
>14 days	191 (81%)	151 (73%)	0.07
>28 days	130 (55%)	87 (42%)	<0.01

POTD: preoperative tissue diagnosis.





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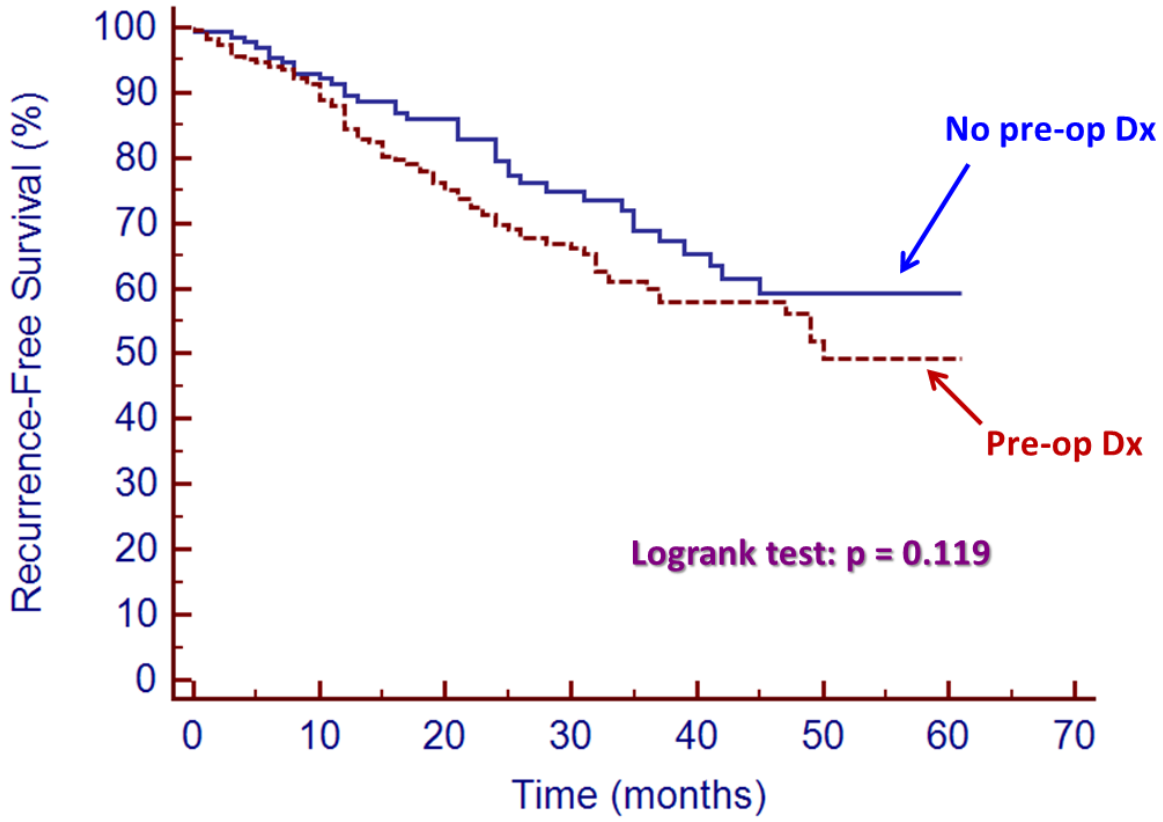
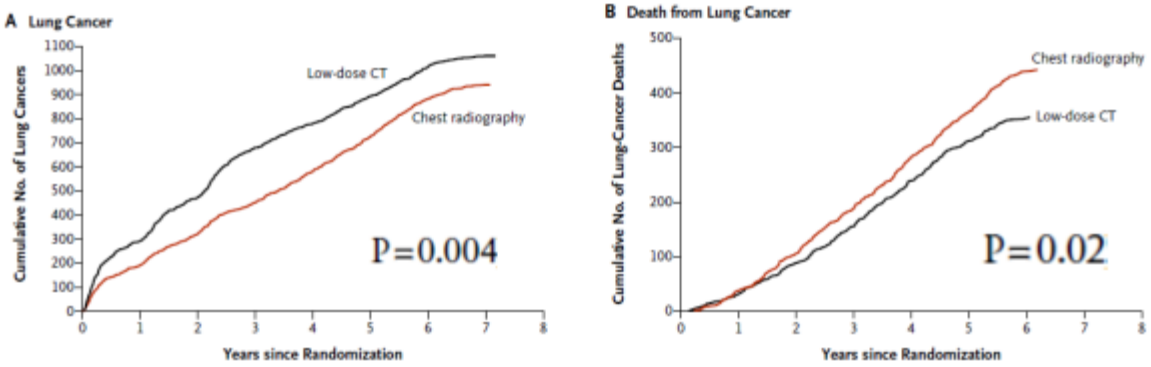


Lung Cancer Screening 肺癌篩查

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

N Engl J Med 2011;365:395-409.



National Lung Screening Trial

IASLC 19th World Conference on Lung Cancer
September 23-26, 2018 Toronto, Canada
#WCLC2018
WWW.IASLC.ORG

NELSON Study Shows CT Screening for Nodule Volume Management Reduces Lung Cancer Mortality by 26 Percent in Men

Toronto, Canada – September 25, 2018 – Findings from a recent study demonstrate that the use of computed tomography (CT) screening among asymptomatic men at high risk for lung cancer led to a 26 percent (9-41%, 95% CI) reduction in lung cancer deaths at 10 years of study follow-up (at 86% compliance). In the smaller subset of women, the rate-ratio of dying from lung cancer varied between 0.39 and 0.61 in different years of follow-up, indicating an even significant and larger reduction in lung cancer mortality than in men.

NELSON Trial

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

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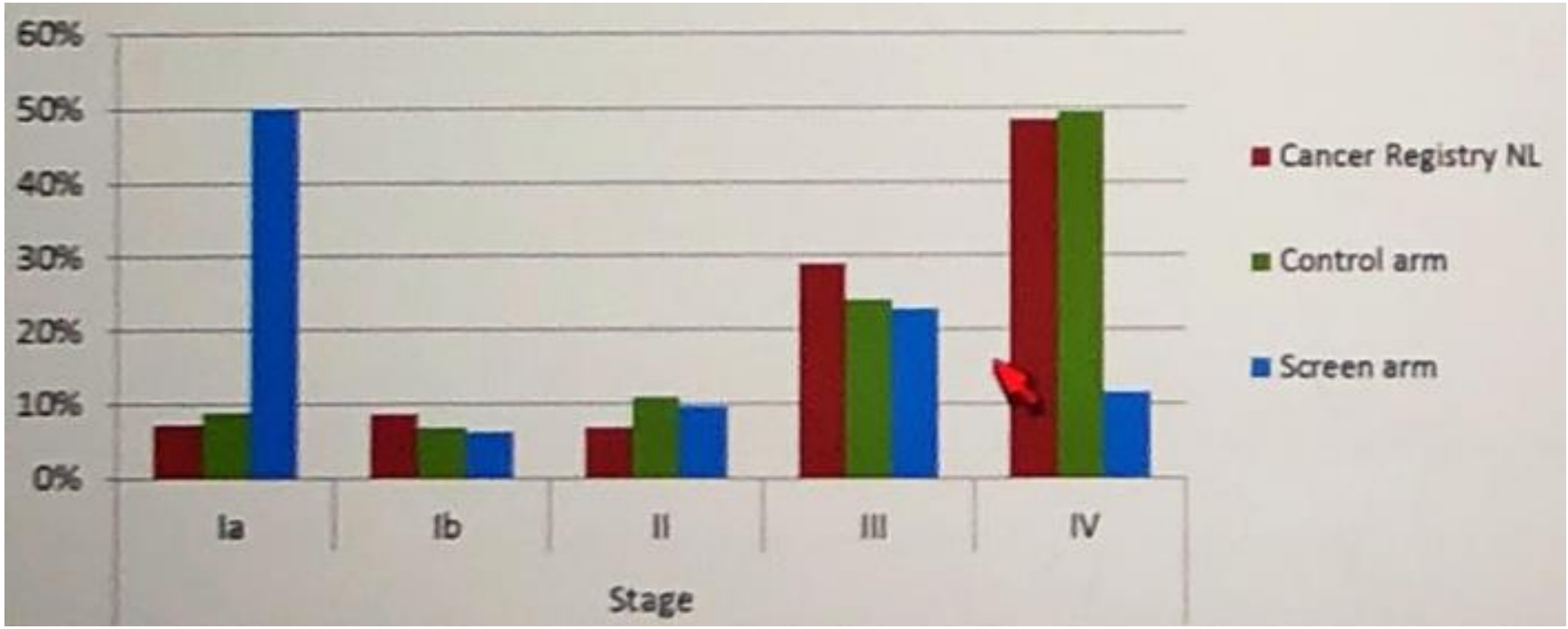
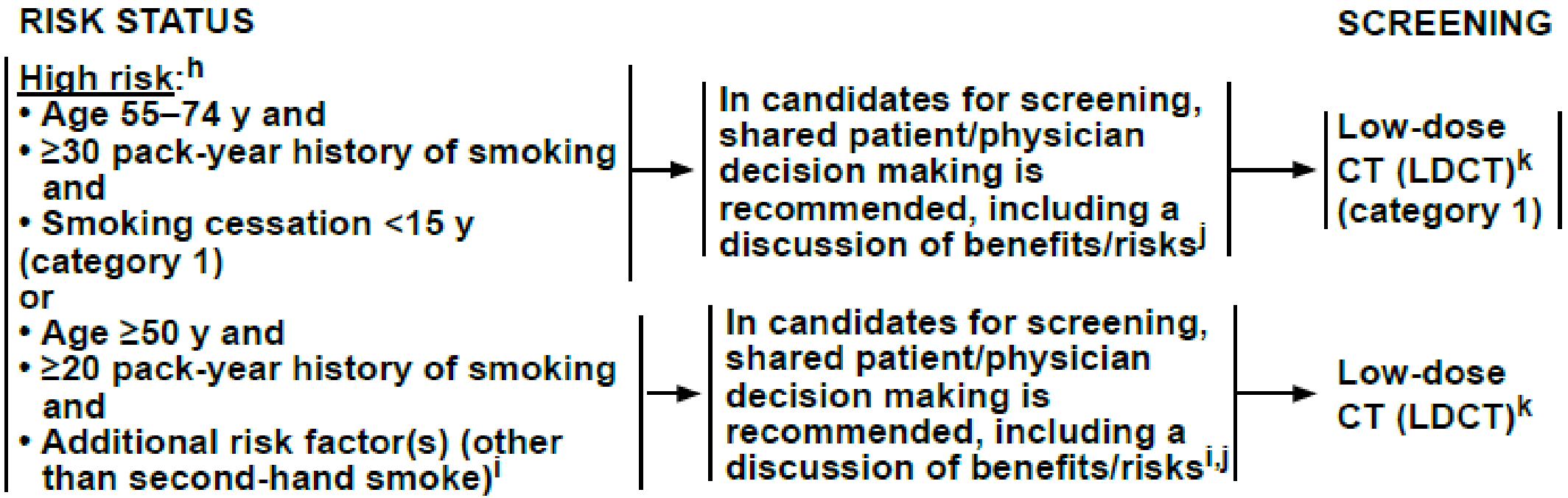


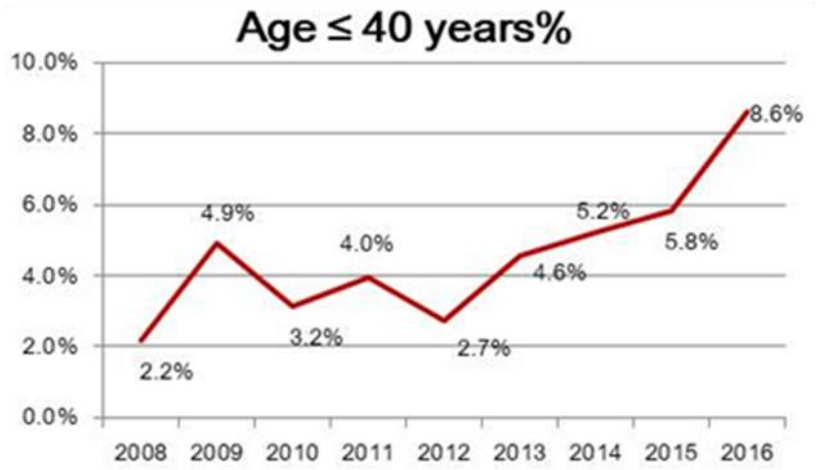
Shanghai Pulmonary Hospital

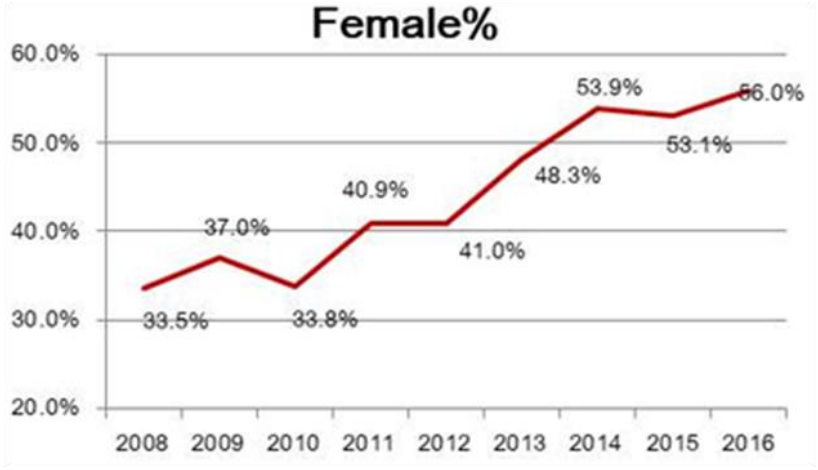
National Comprehensive Cancer Network®

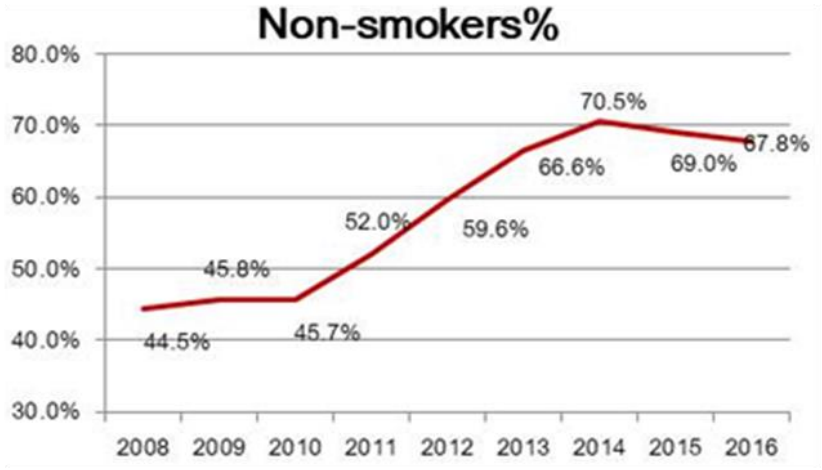
NCCN Guidelines Version 2.2014
Lung Cancer Screening

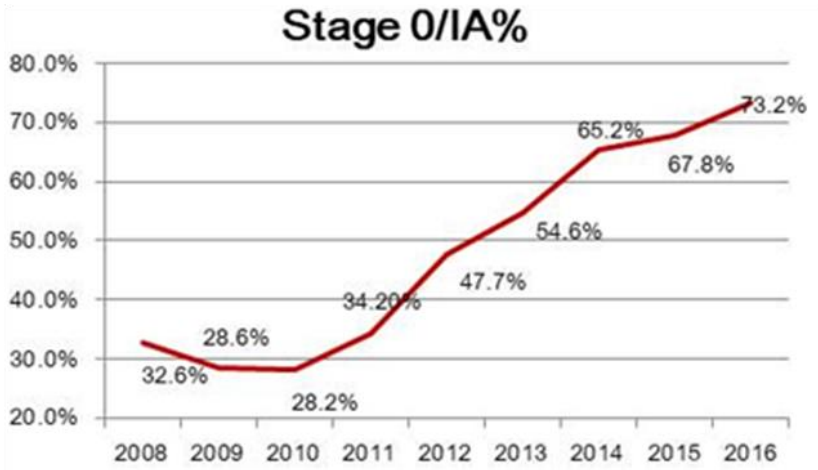


2008 - 2016: 7524 primary lung cancer patients









Images courtesy of: Dr Chen Haiquan (Fudan University Cancer Hospital, Shanghai)

Lung Cancer 肺癌

- High Mortality due to:
  - High incidence 發病率高
  - Low cure (resection) rate 治愈率低
- Barriers to cure:
  - Late presentation 遲發現
  - Long investigation 檢查慢
  - Ineligible for surgery 不合適

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