Management of lung nodules
KMUH experience

高醫 胸腔外科 李憲斌

Lung nodules?

A solitary pulmonary nodule (SPN) is defined as a round opacity that is at least moderately well marginated and no larger than 3 cm in its maximum diameter. The adjective *small* has been used to describe nodules that are less than 1 cm in diameter

Radiology 1996;200(2):327–331.

GGN or GGO:GGO is a roentgenological term for lesions in the lung on thin section CT (TSCT), defined as a homogeneous hazy increase in density in the lung field that does not obscure the bronchiolovascular structure

Glossary of terms for CT of the lungs: recommendations of the Nomenclature Committee of the Fleischner Society Radiology, (1996),

LDCT for lung cancer screen program: more GGNs found, solitary/multiple, vary size

Subsolid nodule prevalence

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

How should the dimension of a solid pulmonary nodule be expressed?
For purposes of risk estimation, the dimension of small pulmonary nodules (<10 mm) should be expressed as the average of maximal long-axis and perpendicular maximal short-axis measurements in the same plane. For larger nodules and masses, both long- and short-axis measurements should be recorded (grade 2B evidence).
How should part-solid nodules be measured?
As with solid nodules, the average of the long and short dimensions of the nodule, including ground-glass and any cystic components, should be measured and recorded for smaller nodules (<10 mm). For larger nodules, both long and short dimensions should be recorded. For all part-solid nodules, the maximum diameter of the solid component should be measured if this component is >3 mm, understanding that measurements may be unreliable for small solid components. Dimensions of both solid and nonsolid components should be recorded to document change in the future (grade 2B evidence).
Which measurement unit should be used?
Measurements and averages should be expressed to the nearest whole millimeter (grade 1B evidence).
Should the dimension of every pulmonary nodule be measured?
No, small nodules <3 mm should not be measured due to accuracy limitations. Descriptors such as "micronodule" are preferable. Also, when multiple nodules are present, only the largest or morphologically most suspicious nodules need be measured. The location of each measured nodule should be explicitly referenced in the report (grade 1C evidence).
What CT section thickness should be used for measuring lung nodules?
Critical measurements for small (<10 mm) lung nodules and small solid components should be obtained by using contiguously reconstructed sections with a thickness ≤1.5 mm. Larger nodules and masses can usually be m adequately on thicker sections (grade 1B evidence).

Figure 4

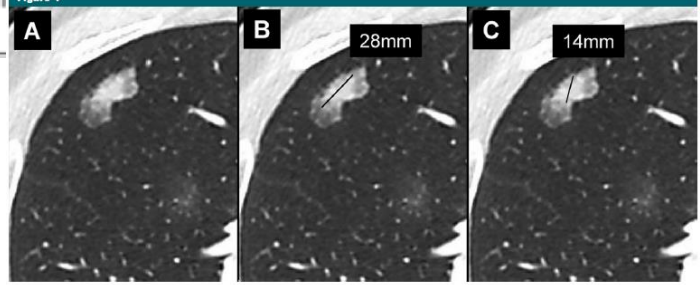


Figure 4: Transverse CT sections of a part-solid nodule in the right upper lobe. *A*, The solid component of the nodule is ill defined, resulting in variability of measurements, as performed by two radiologists. The two long-axis diameters of the solid component were, *B*, 28 mm and, *C*, 14 mm. On the basis of the clinical implications, we recommend use of the larger long-axis diameter. Only solid component measurements are shown in this figure; however, in clinical practice, nonsolid and solid components must be measured.

Figure 11

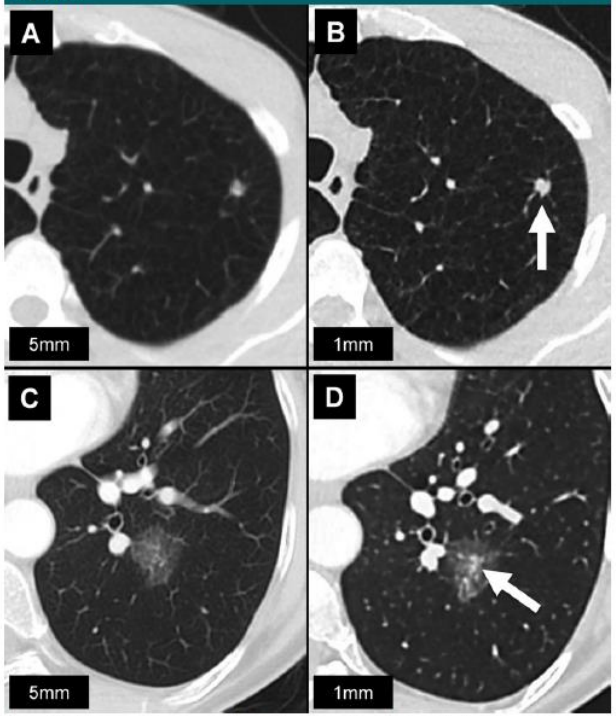


Figure 11: Transverse CT sections at the level of, *A*, *B*, a solid nodule (arrow) in the left upper lobe and, *C*, *D*, a part-solid nodule (arrow) in the left lower lobe. Solid and part-solid nodule margins are less well defined on *A* and *C* than on *B* and *D*. In addition, *D* better shows solid nodule components.

Figure 16

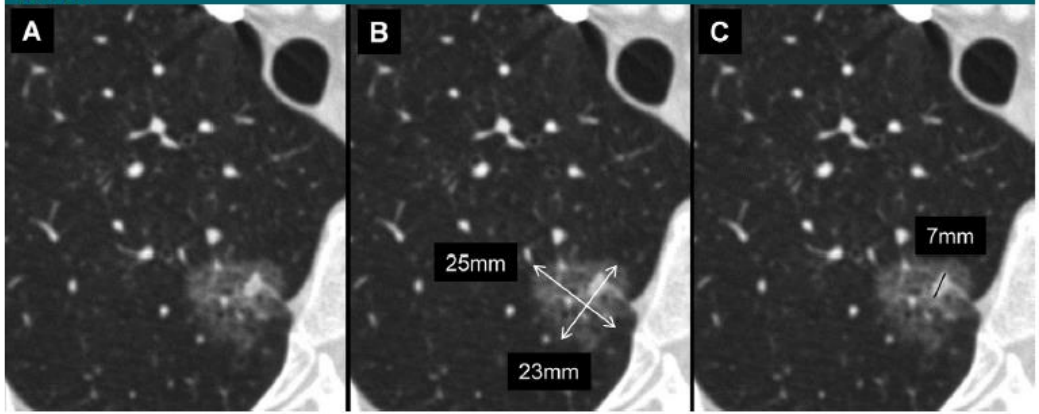
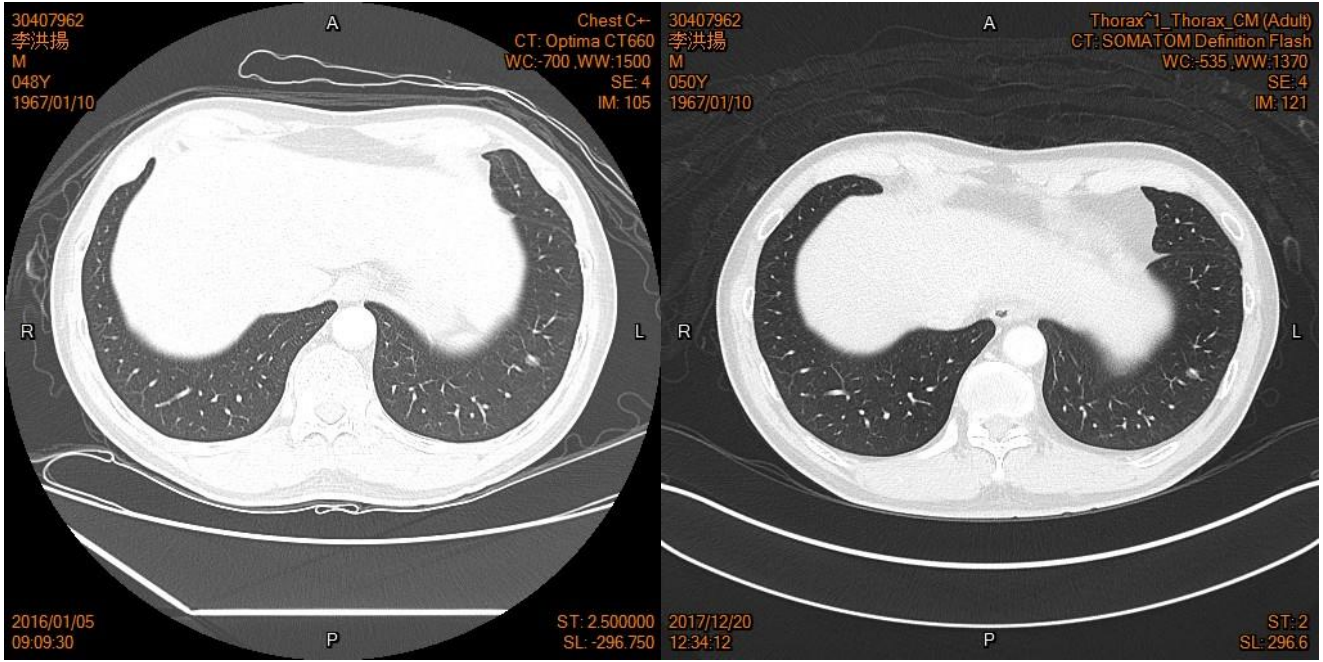
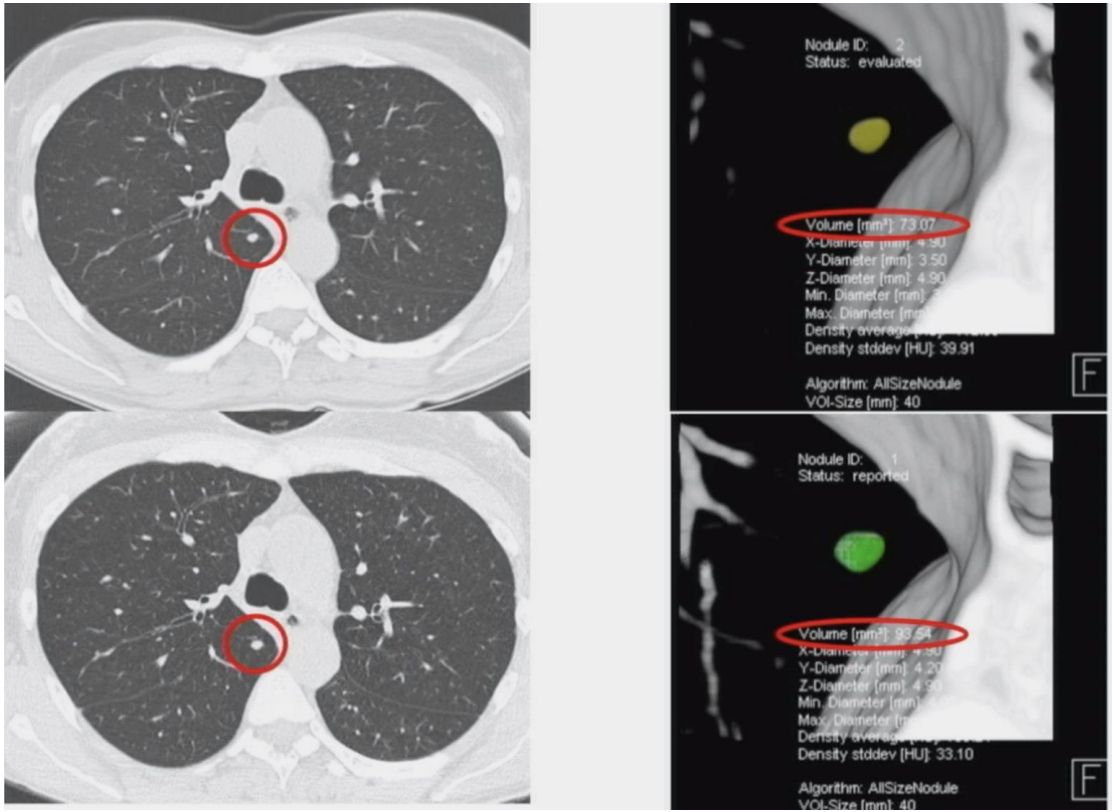


Figure 16: Transverse CT sections of a part-solid nodule in the right lower lobe. *A*, Both ground-glass and solid components are well defined. *B*, First, overall nodule dimensions are measured, resulting in an average diameter of 24 mm. *C*, Then, the long axis of the solid component is measured separately, resulting in a diameter of 7 mm.

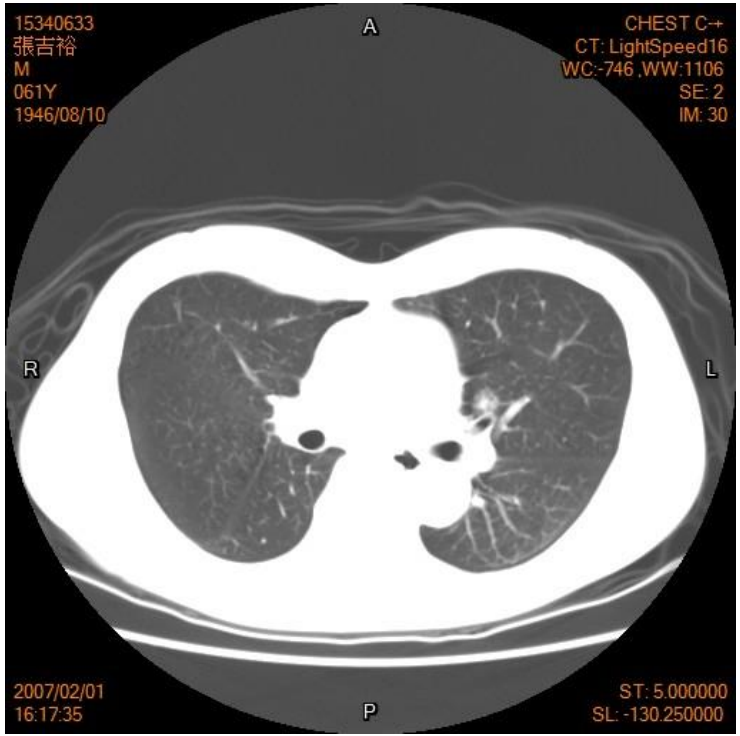
Recommendations for Measuring Pulmonary Nodules at CT: A Statement from the Fleischner Society. Radiology. 2017 Nov;285(2):584-600.

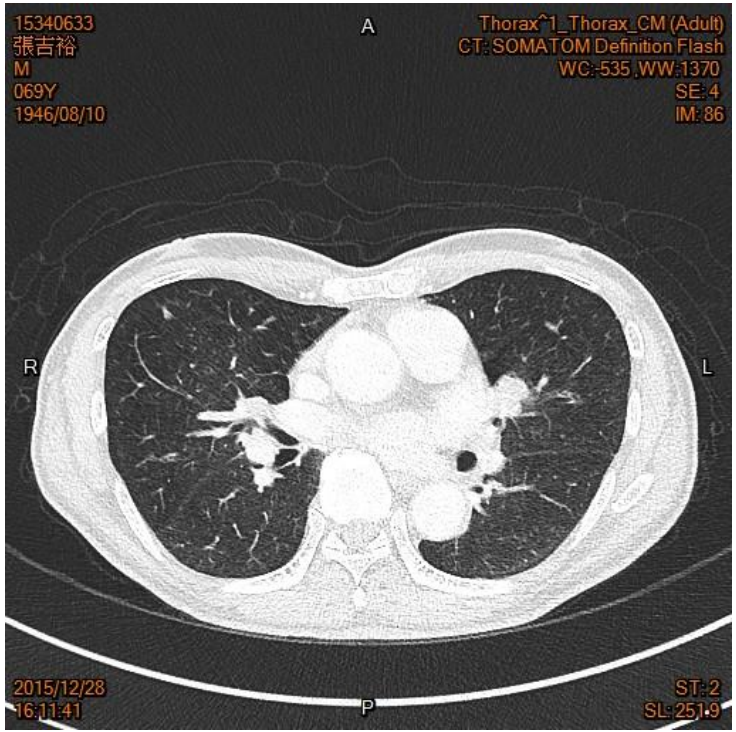


Near two-year span, no obvious change



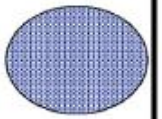
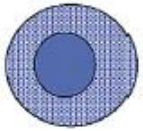
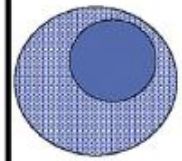
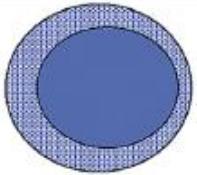
- It seems the same in dimensions but changes in total volume!!





Subsolid GGO developed in 8 years

Pathology: Pure acinar adenocarcinoma

cT*	CT image on HRCT						
	Solid part	0 cm	0 cm	≤0.5 cm†	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
	Total tumor size including GG	≤0.5 cm	0.6-3.0 cm†‡	≤3.0 cm†‡	0..6-3.0 cm††	1.1-3.0 cm††	2.1-3.0 cm††
	Pathologic Differential Diagnosis	AAH‡, AIS, MIA	AIS, MIA, LPA	MIA, LPA, AIS	LPA, Invasive AD, MIA	LPA, Invasive AD	Invasive AD
	Clinical Stage*		cTis†‡	cT1mi†‡	cT1a	cT1b	cT1c
pT	Invasive part	0 cm	0 cm	≤0.5 cm†‡	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
	Total tumor size including lepidic growth part	Usually ≤0.5 cm‡	≤3.0 cm†‡	≤3.0 cm†‡	0.6-3.0 cm††	1.1-3.0 cm††	2.1-3.0 cm††
	Pathology	AAH	AIS	MIA	Lepidic predominant AD or Invasive AD with lepidic compnent	Invasive AD with a lepidic component or lepidic predominant AD	Invasive AD with lepidic component
	Pathologic Stage		pTis†‡	pT1mi†‡	pT1a	pT1b	pT1c

Clinical decision on GGN:

The Fleshner Society guideline

NCCN guideline

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017.

B: Subsolid Nodules*

Nodule Type	Size		Comments
	<6 mm (<100 mm^3)	≥6 mm (>100 mm^3)	
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Radiology. 2017 Jul;284(1):228-243

LOW-DOSE COMPUTED TOMOGRAPHY ACQUISITION, STORAGE, INTERPRETATION, AND NODULE REPORTING (Lung-RADS)[1-4]

Acquisition	Small Patient (BMI ≤30)	Large Patient (BMI >30)
Total radiation exposure	≤3 mSv	≤5 mSv
kVp	100–120	120
mAs	≤40	≤60
	All Patients	
Gantry rotation speed	≤0.5	
Detector collimation	≤1.5 mm	
Slice width	≤2.5 mm; ≤1.0 mm preferred	
Slice interval	≤slice width; 50% overlap preferred for 3D and CAD applications	
Scan acquisition time	≤10 seconds (single breath hold)	
Breathing	Maximum inspiration	
Contrast	No oral or intravenous contrast	
CT scanner detectors	≥16	
Storage	All acquired images, including thin sections; MIPs and CAD renderings if used	
Interpretation Tools		
Platform	Computer workstation review	
Image type	Standard and MIP images	
Comparison studies	Comparison with prior chest CT images (not reports) is essential to evaluate change in size, morphology, and density of nodules; review of serial chest CT exams is important to detect slow growth	
Nodule Parameters		
Size	Largest mean diameter on a single image (mean of the longest diameter of the nodule and its perpendicular diameter, when compared to the baseline scan)	
Density	Solid, ground-glass, or mixed (mixed; otherwise referred to as part solid)	
Calcification	Present/absent; if present: solid, central vs. eccentric, concentric rings, popcorn, stippled, amorphous	
Fat	Report if present	
Shape/Margin	Round/ovoid, triangular/smooth, lobulated, spiculated	
Lung location	By lobe of the lung, preferably by segment, and if subpleural	
Location in dataset	Specify series and image number for future comparison	
Temporal comparison	If unchanged, include the longest duration of no change as directly viewed by the interpreter on the images (not by report); if changed, report current and prior size	

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Lung Cancer Screening

NCCN Guidelines
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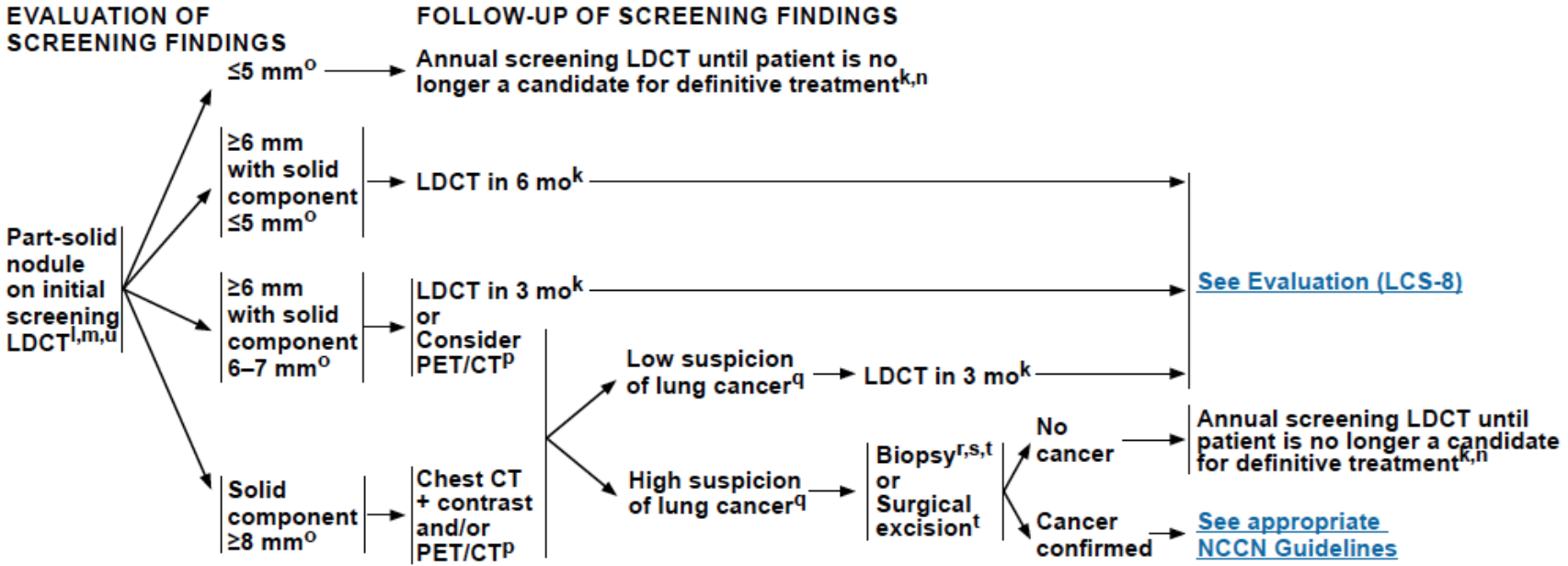

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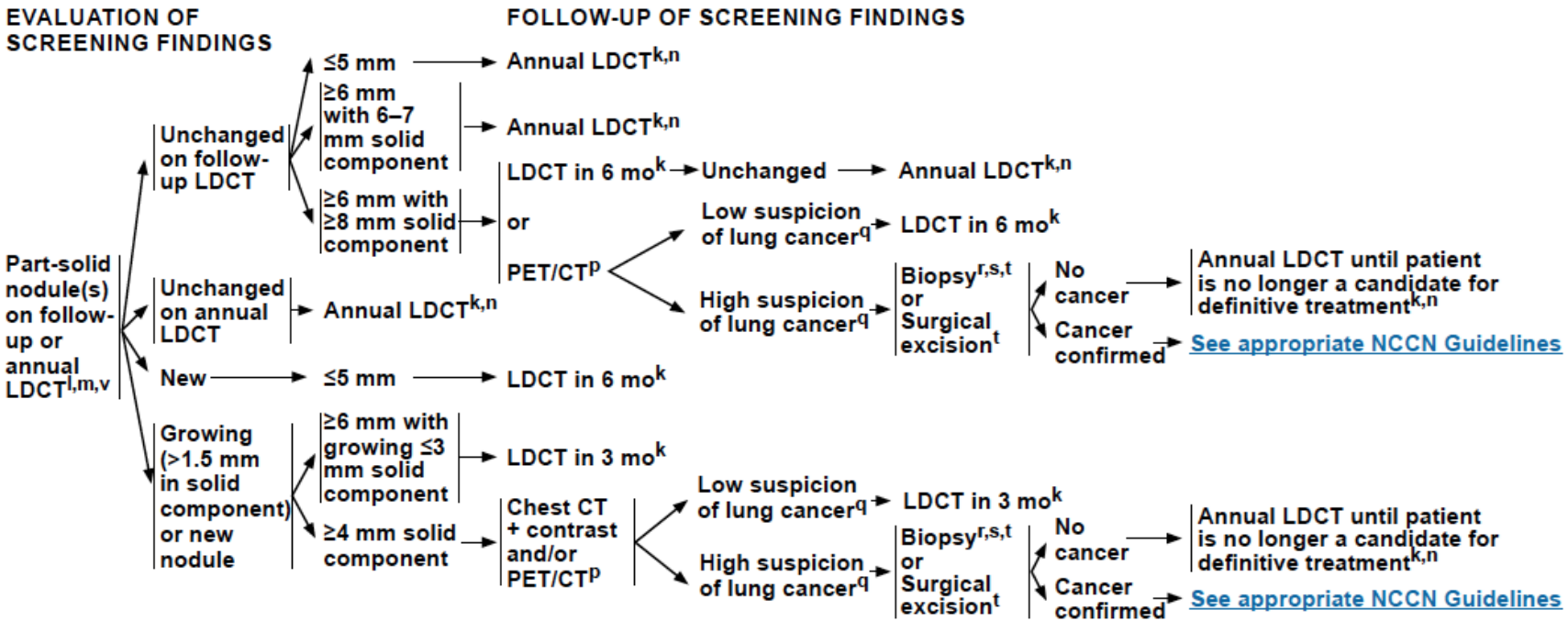
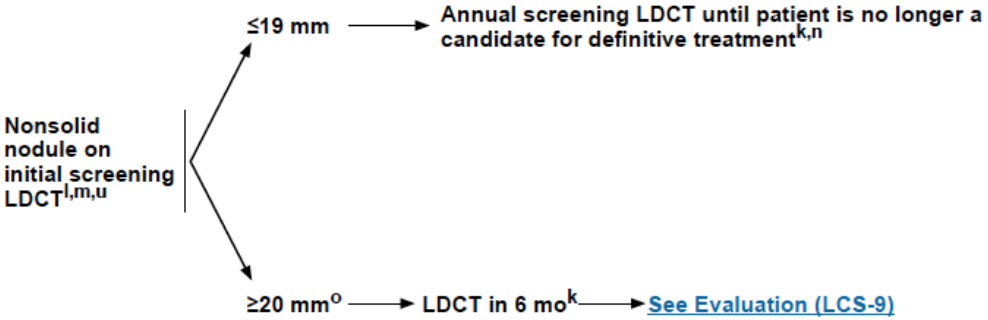


EVALUATION OF SCREENING FINDINGS

FOLLOW-UP OF SCREENING FINDINGS



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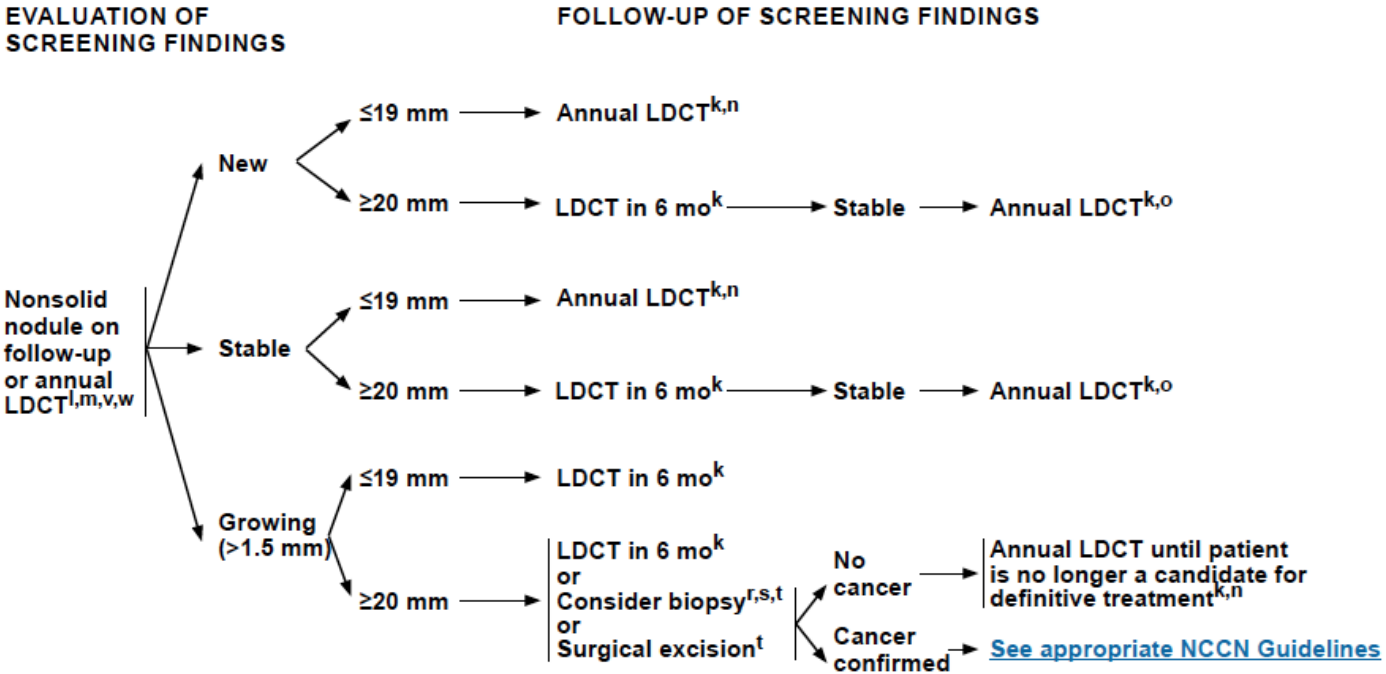
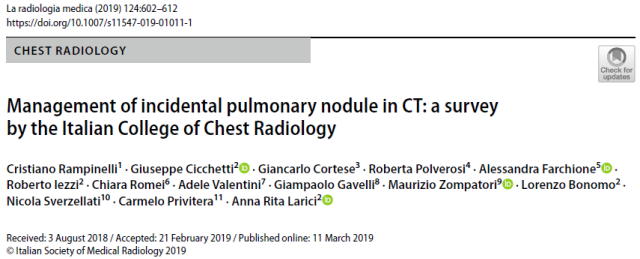


In the real- world, how do we approach?

- Only 57.7% of participants adhere to the Fleischner Society guidelines for the management of incidental pulmonary nodules.
- However, 56.6% and 75.6% of respondents have a more cautious approach than that recommended by the guidelines and tend to use a shorter follow-up for both solid and ground-glass nodules
- Sixty-four percent of respondents did not organize lung nodule multidisciplinary meetings in their institution, while 27.9% and 7.9%, respectively, attended a weekly or monthly discussion



La radiologia medica (2019) 124:602–612
https://doi.org/10.1007/s11547-019-01011-1

CHEST RADIOLOGY

Check for updates

Management of incidental pulmonary nodule in CT: a survey by the Italian College of Chest Radiology

Cristiano Rampinelli[1] · Giuseppe Cicchetti[2] · Giancarlo Cortese[3] · Roberta Polverosi[4] · Alessandra Farchione[5] · Roberto Iezzi[2] · Chiara Romei[6] · Adele Valentini[7] · Giampaolo Gavelli[8] · Maurizio Zompatori[9] · Lorenzo Bonomo[2] · Nicola Sverzellati[10] · Carmelo Privitera[11] · Anna Rita Larici[2]

Received: 3 August 2018 / Accepted: 21 February 2019 / Published online: 11 March 2019

What we learned after years

- Invasive adenocarcinomas only seen in pGGN that developed a solid component
  - Median time to progression= **3.8 years**
- International Early Lung Cancer Action Project (I-ELCAP)
  - pGGNs lung cancer specific survival = **100%**
  - regardless of time to treatment (median 19 months, IQR 6-41 months)
- National Lung Screening Trial (NLST)
  - 18 patients with lung cancer as PSN (all resected, stage I)
  - Average volume doubling time = **4276 days**
  - Number of patients with PSN dying from lung cancer (D_x/R_x) = **0**

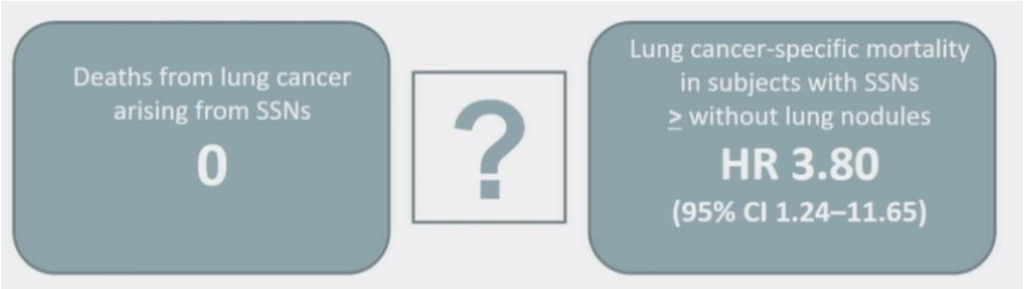
Kakinuma R, et al. J Thorac Oncol 2016;11:1012-28.

Yankelevitz DF et al. Radiology 2015;277:555-64.

Yip R et al. AJR Am J Roentgenol 2017;208:1011-21.

Multicenter Italian Lung Detection (MILD) screening trial

- SSNs prevalence: 16.9%.
- During 9.3 ± 1.2 years of follow-up, HR of lung cancer diagnosis 6.77
- 73% of cancers not arising from SSN (median time to diagnosis 52 months from SSN).



- **Lung cancer arising from SSN did not lead to death within the follow-up period**.

Journal of Thoracic Oncology Vol. 13 No. 10: 1454-1463

MILD: New cancers in areas away from SSNs

- High risk of developing lung cancer elsewhere in the lung, with only a minority of cases arising from SSN, and never representing the cause of death.

- Biomarker of lung cancer risk!

Journal of Thoracic Oncology Vol. 13 No. 10: 1454-1463

KMUH experience of GGN screen

- Low dose CT screen: Not only high risk group but also normal people if they strongly concerned about health
- Subsequent CT schedule if GGN or solid nodule found : 4-6months for first follow-up
- Regular CT (6-12 months)without contrast for nodule/GGN follow-up

- Slice thickness on lung window evolution: 5mm-> 2.5mm-> 2mm->1.5mm

- CTA with contrast if segmentectomy is planned

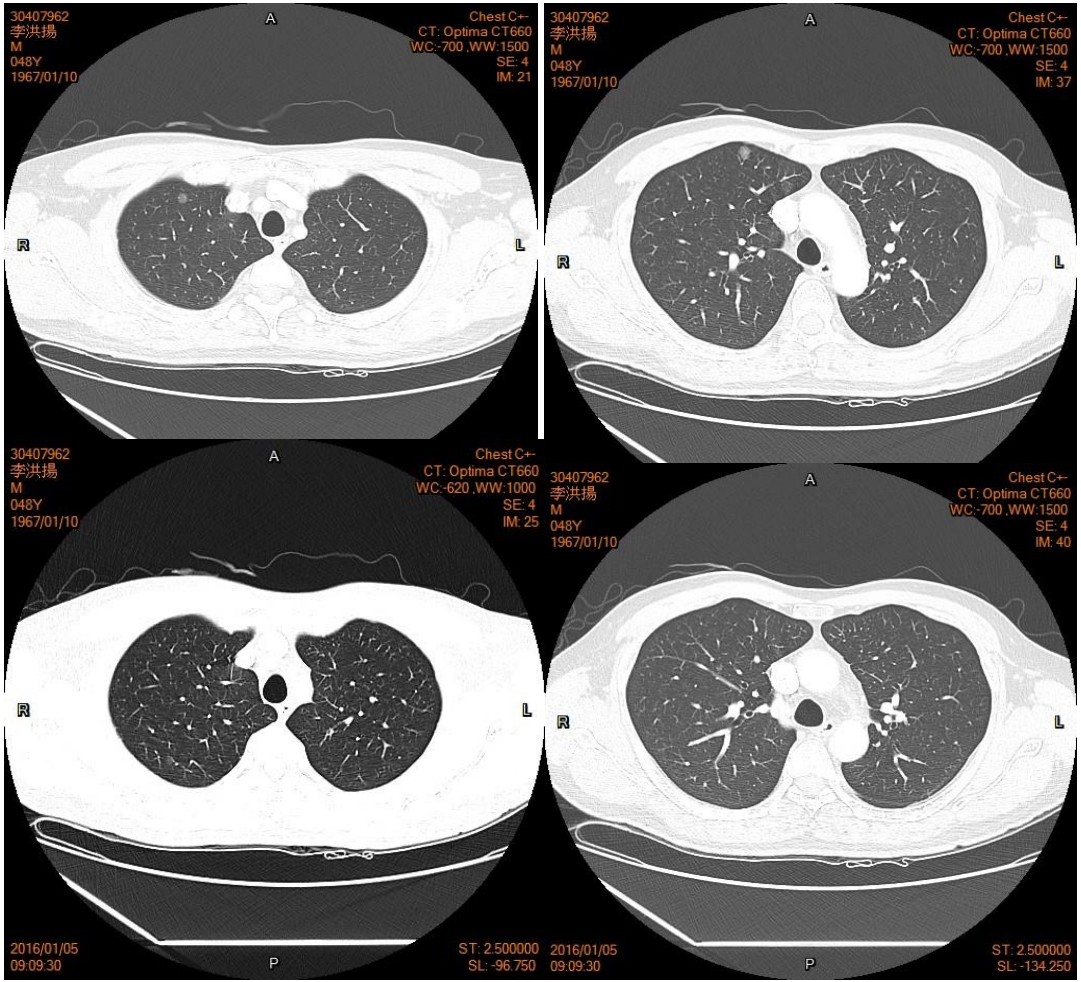
How do thoracic surgeons think?

- Nodular size and morphology
- Nodular location
- Nodular multiplicity
- Nodular growth rate
- Emphysema and fibrosis
- Patient characteristics, mental status
- Tobacco and other inhaled carcinogens

From Surgeon’s Point of View

- Invasive surgery: VATS or thoracotomy
- Biopsy: CT-guided or bronchoscopic-guided
- Follow-up on regular basis

- Surgical challenge of GGNs and solid nodules
- Technique:
- From Radical resection(Lobectomy/sleeve lobectomy /Pneumonectomy)
- To Limited resection (Wedge resection/Segmentectomy)
- However...

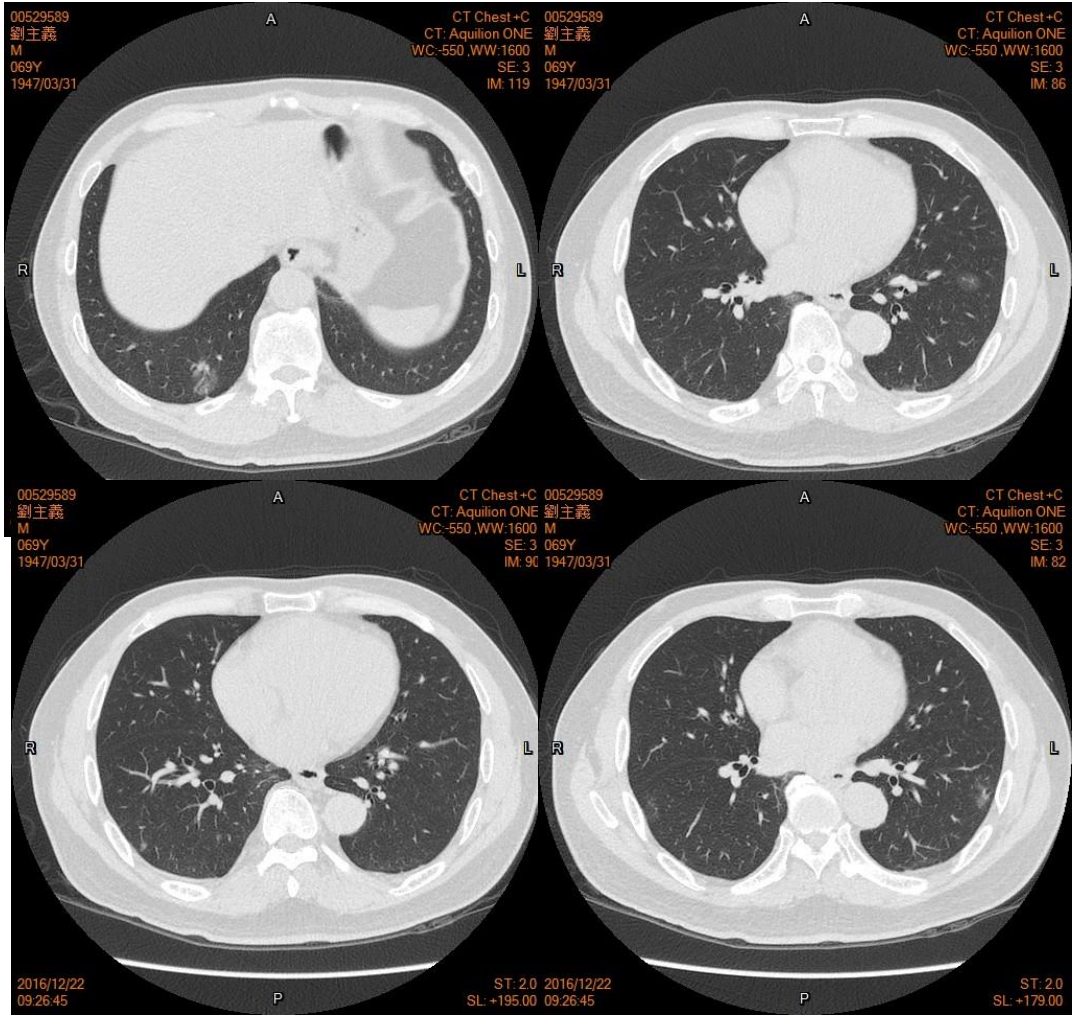


RUL Lobectomy?

RS1+3
Segmentectomy!

if there is another lesion in RS2?

Path: pure lepedic



Bilateral basilar segmentectomy?

Bilateral lobectomy?

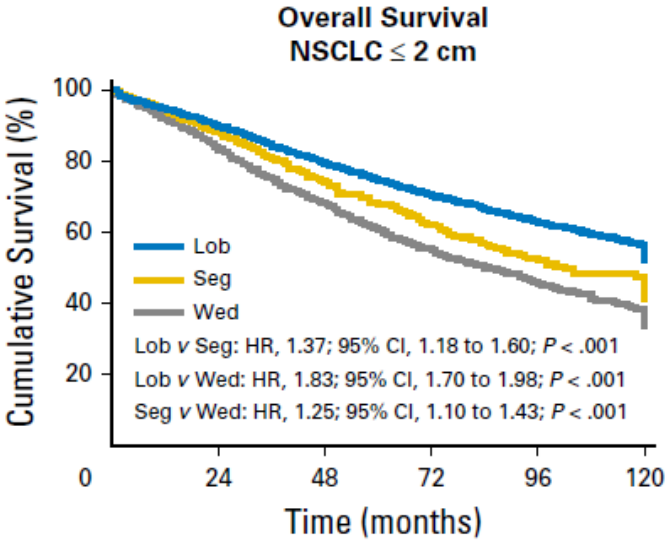
Right extend S9+10 segmentectomy(acinar adenocarcinoma (mixed with papillary and lepidic patterns)

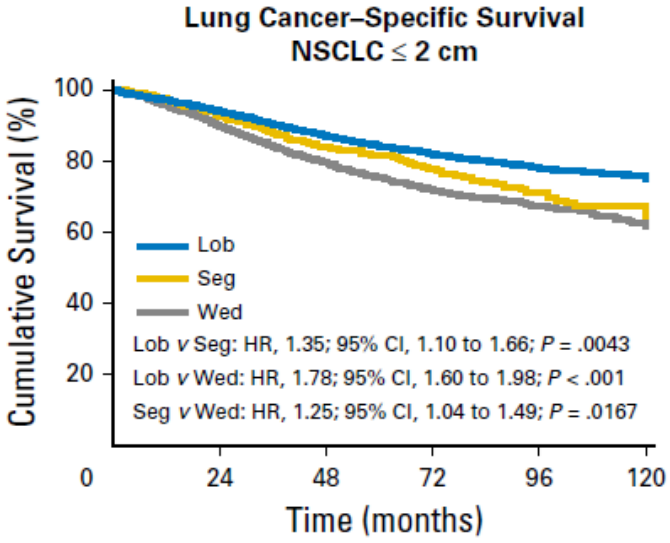
Left S7+8 segmentectomy

once or equentially?

(Minimally invasive adenocarcinoma, nonmucinous adenocarcinoma.)

Lobectomy VS sublobar resection in early stage lung cancer





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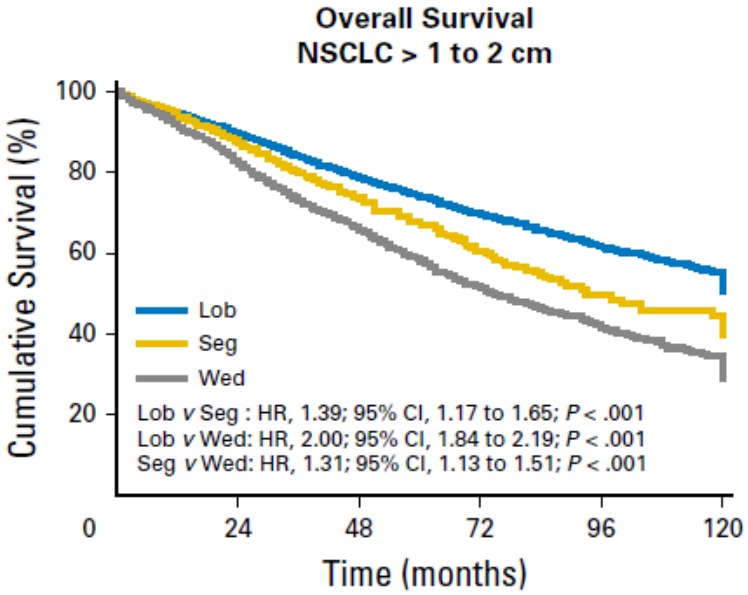

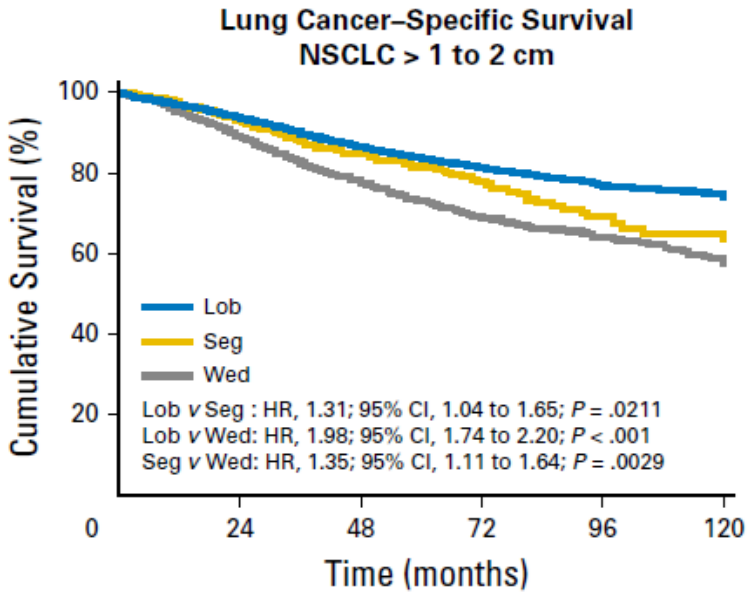

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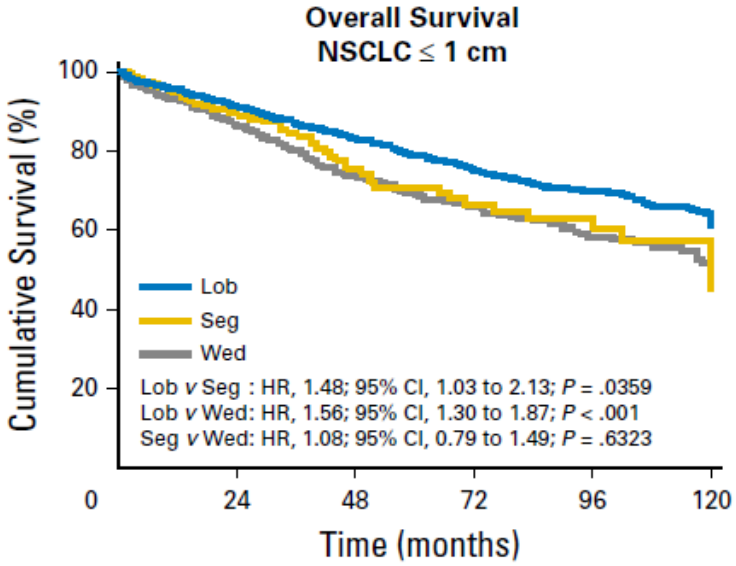

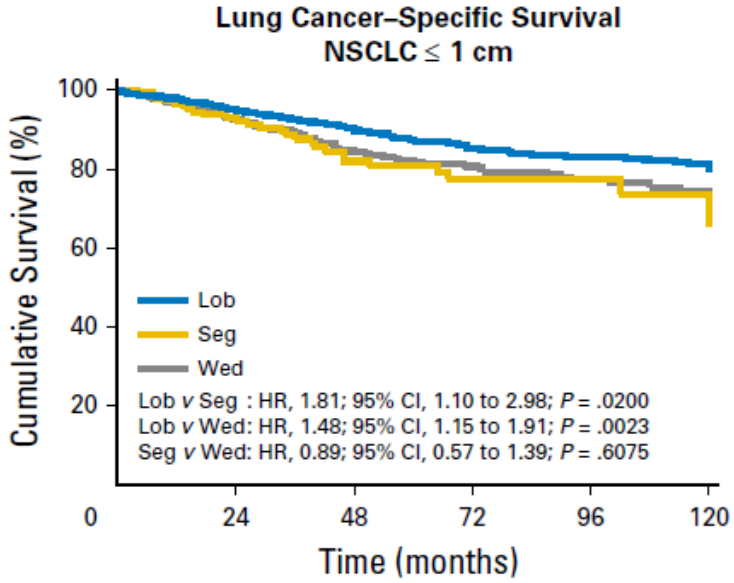

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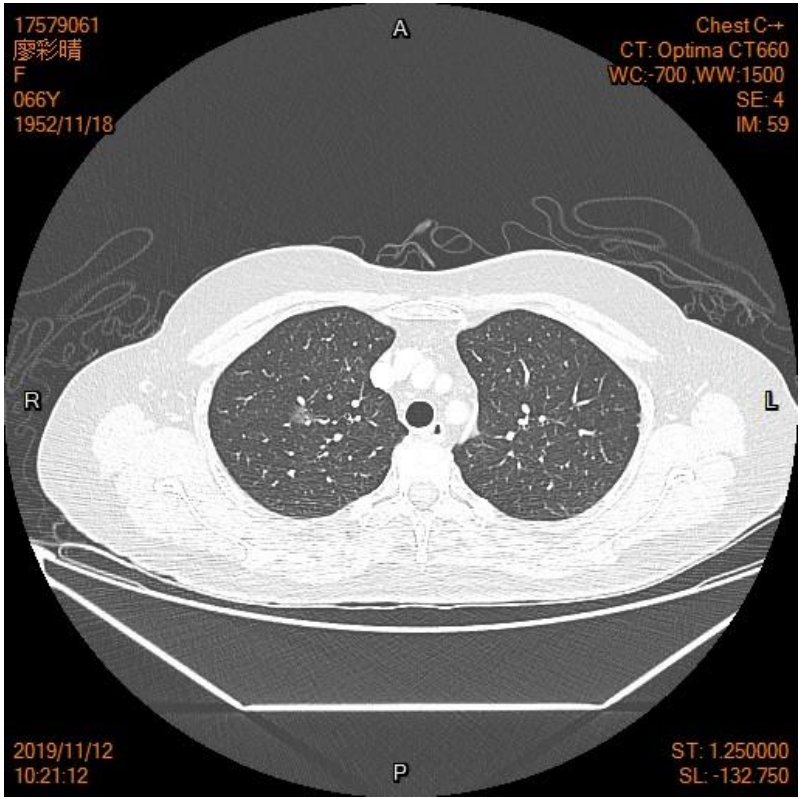
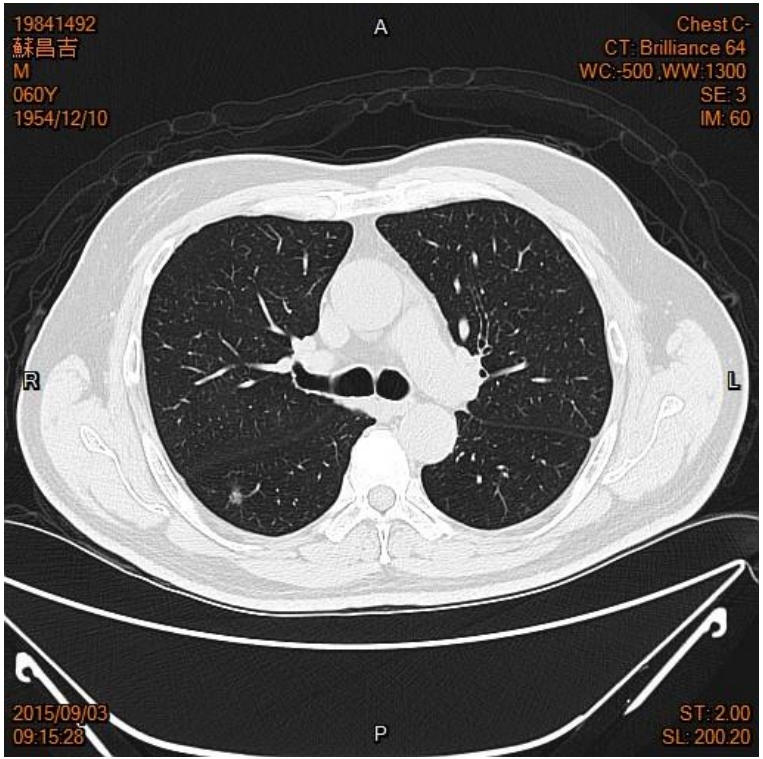
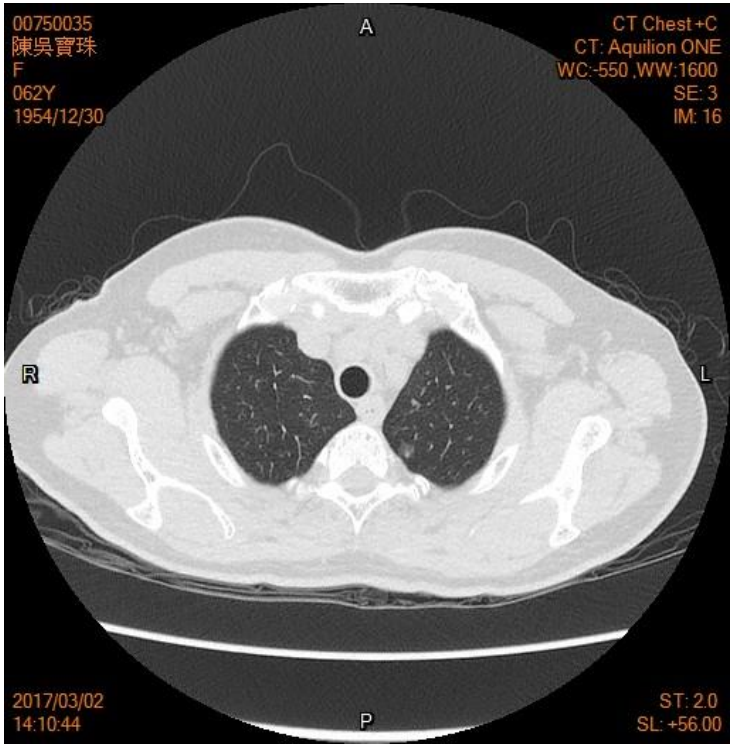
Lobectomy or not?

- Central lesion
- Lesion more than 2cm
- Dominant by solid components
- For adequate margin if frozen revealed close to staple line
- Young or good pulmonary reserve

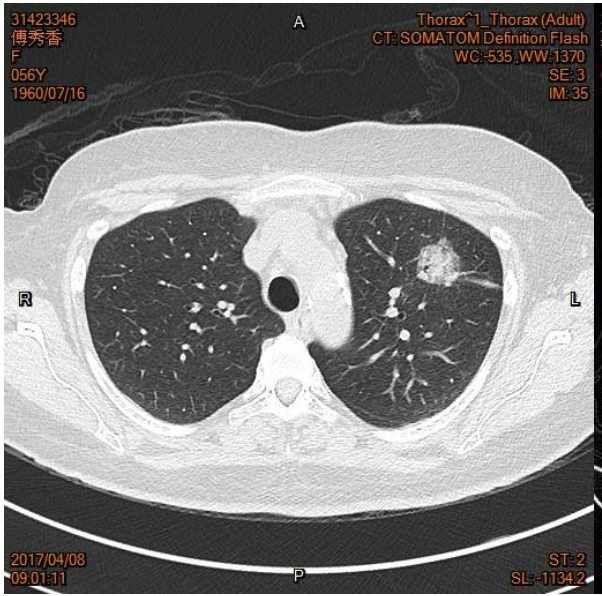




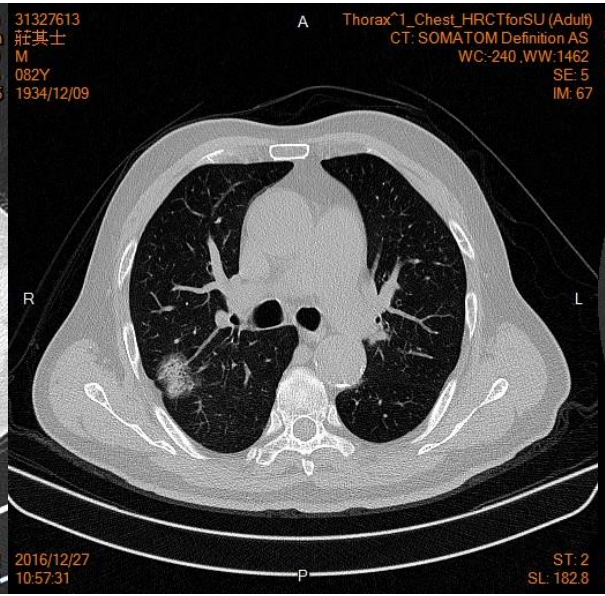
Subsolid GGO small size 0.6cm
Pathology:1.0 cm
Lepidic (70 %), acinar (30 %)
Segmentectomy, RS6 margin 2.5 cm



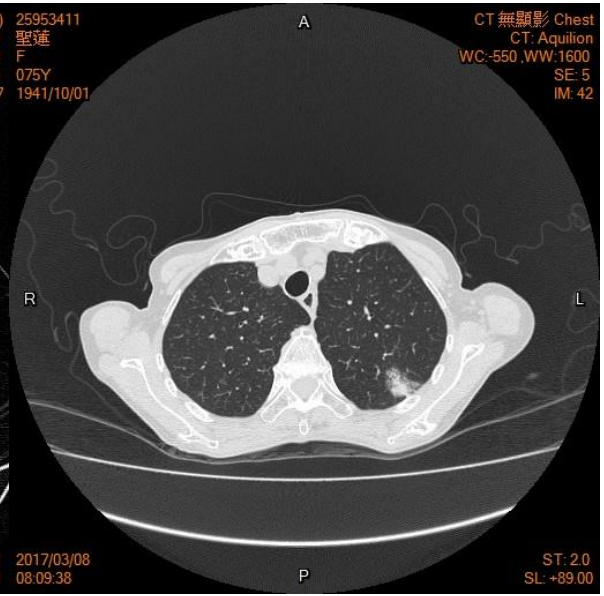
small GGO with point solid 0.3cm
pathology size: 0.8cm
AIS, lepidic (100 %)
Wedge resection Margin 0.5cm



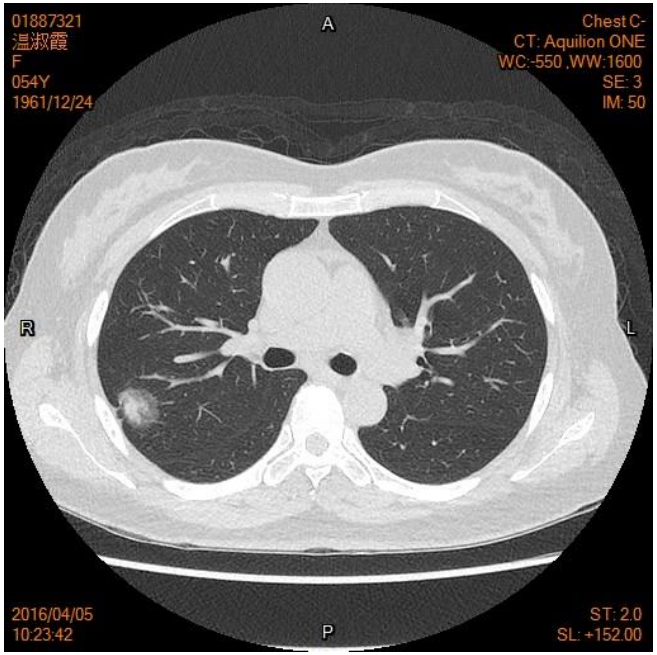
Part solid GGO CT: 2.4cm
Pathology:3.5cm
Lepidic (15 %), acinar (80 %), papillary (5 %)
Lobectomy margin 2cm



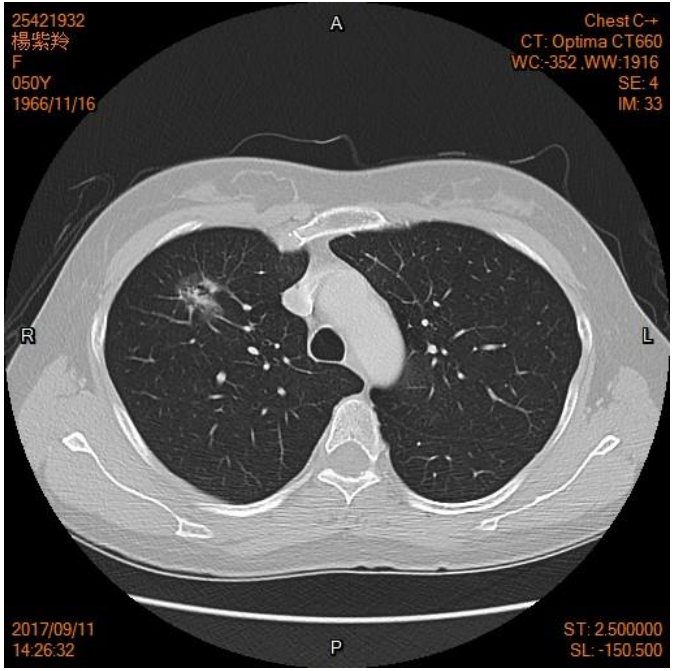
Part solid GGO CT: 3.1cm
Pathology: 2.7cm
Lepidic (5 %), acinar (80 %), papillary (15 %)
Lobectomy , margin 0.9cm



Part solid GGO CT: 2.2cm
Pathology: 2.5cm
Lepidic (40 %), acinar (55 %), papillary (5 %)
Segmentectomy LS1+2+3, margin 0.2cm



Part solid GGO CT: 2.5cm
Pathology:2.5cm
Lepidic (35 %), acinar (65 %)
Lobectomy



Part solid GGO CT: 2.7cm
Pathology:2.3cm
Lepidic (30 %), acinar (20 %), solid (50 %)
Lobectomy

KMUH Experience on Operation

●Wedge resection vs segmentectomy vs Lobectomy

●Pre-op CT guide localization is preferred if wedge resection is planned or margin is worried

●Intra-operative frozen section routinely if no pre-op diagnosis or PET/CT

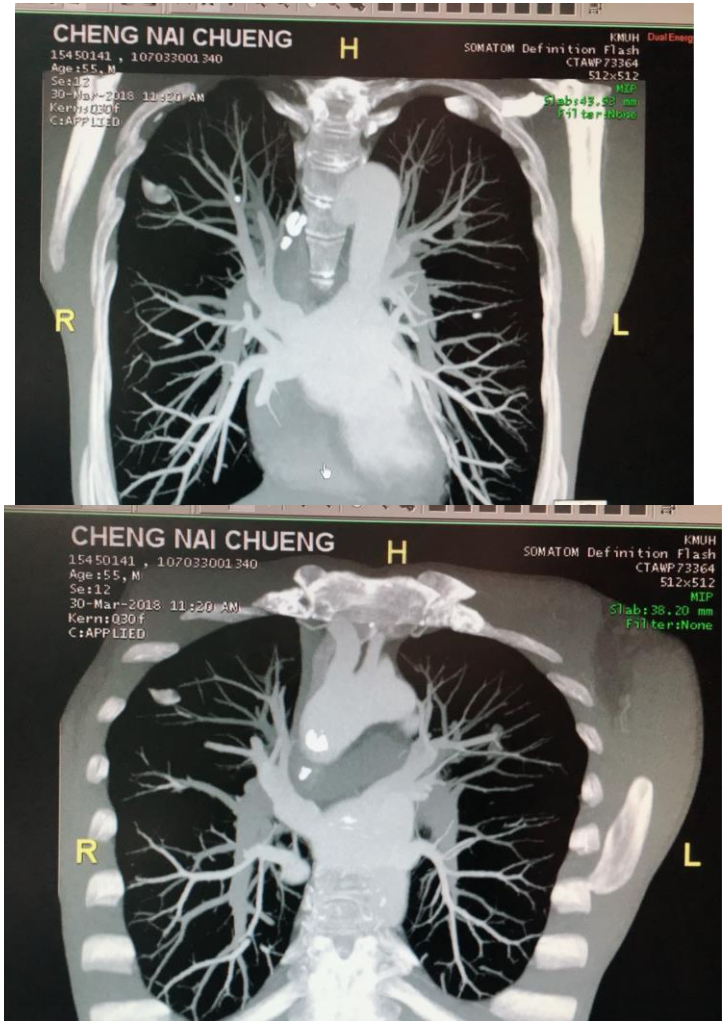
●Segmentectomy or Lobectomy: if no adequate margin on wedge resection told by pathologist(Frozen section: margin positive or VERY CLOSE!)

●Sometimes add another wedge resection/segmentectomy to gain adequate margin

●LN dissection routinely: N1 and N2 stations

CTA in KMUH

Axial/coronal/saggital sections



Equipment And Approach-1

●Thoracoscopic based operation: Single port or two port
●Thoracotomy: rare, only in multiple and faint nodules or need finger palpation
●Robot-assisted approach
●Energy device: Hamonics Ace Shears or Ligasure/Maryland for vessels dissection and LN dissection
●Suction: always in very low pressure
●Laparoscopic 5mm or 3mm grasper/clamps
●Dissector: Scanlan Dennis or **SCANLAN® Gonzalez-Rivas Dissector** Fine Tip DeBakey
●Stapler: Metronics Endo-GIA and Tri-staple(gold load and black load) or Endo-Cutter; Hemolock

Equipment And Approach-2

●Neoveil/Hemopatch cover for staple line/ parenchymal raw surface exclusively

●Wound protector: Alexis wound protector

●Air-leak test after resection complete:
●Always repair obvious air leak if there is discontinuity on pleural surface, direct or tension free with bovine pericardium

●Selectively ignore staple line air leakage, cover with Neoveil/Hemopatch or Surgicel

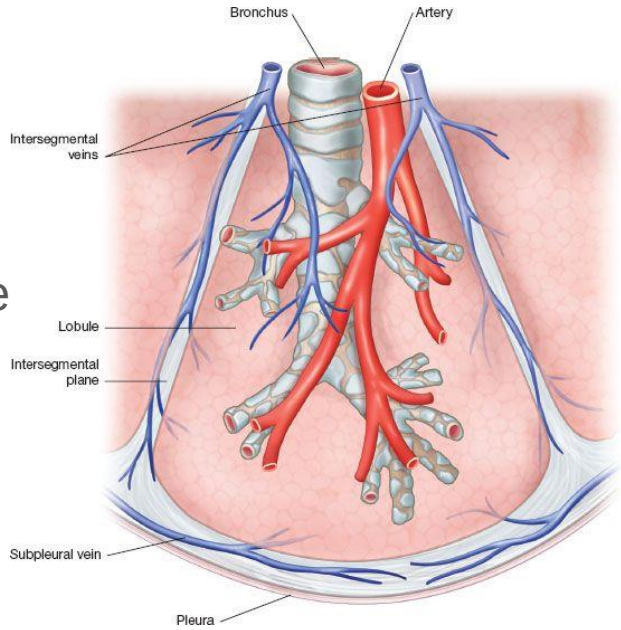
Some Thinking About Segmentectomy

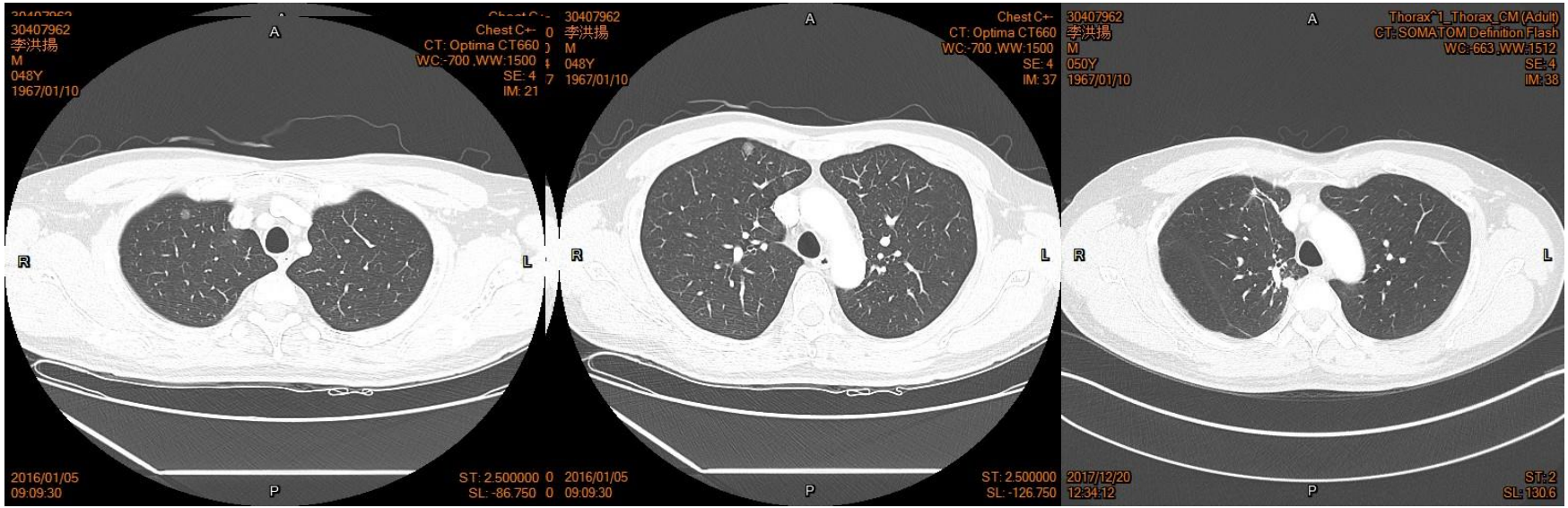
●Is segmental vein isolation and transection necessary ?

●Is it important to dissect along Intersegmental plane if stapler-based segmentectomy is planned ?

●Resection margin vs intersegmental plane which is more important ?

●Single segmentectomy in basilar segment of lower lobe necessary? For basilar segments in lower lobe, bisegmentectomy(7+8, 9+10) is my preferred choice

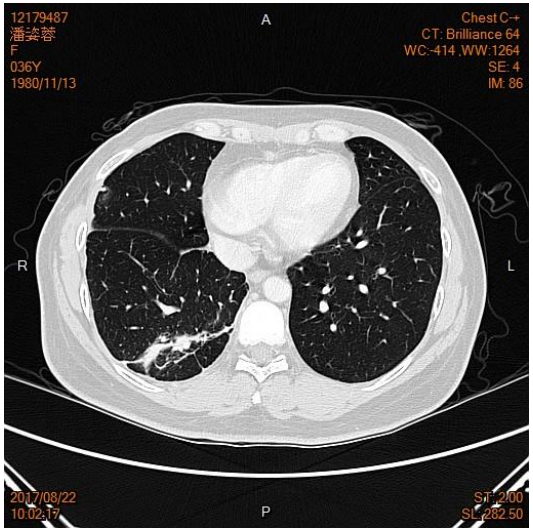


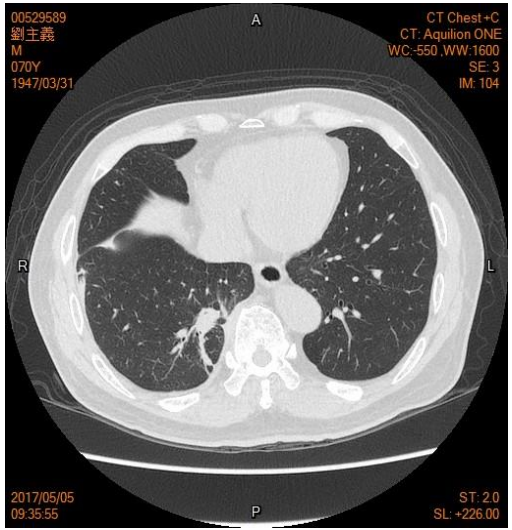


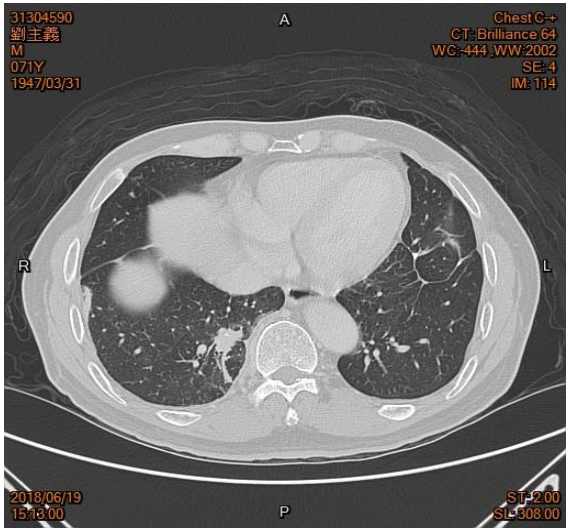
Granulation along staple line or local recurrence?

If local recurrence suspected, how to confirm? Which subtype of recurrence?

Challenges in follow-up after segmentectomy







Granulation along staple line or local recurrence?

Pathology: characterized by mixed larged-sized, thick-walled vessels and small-sized capillary channels located in the lung-pleura junction. The features suggest **hemangioma**.

IRONY in Limited Resection

Limited resection is preferred for single small GGO lesion.

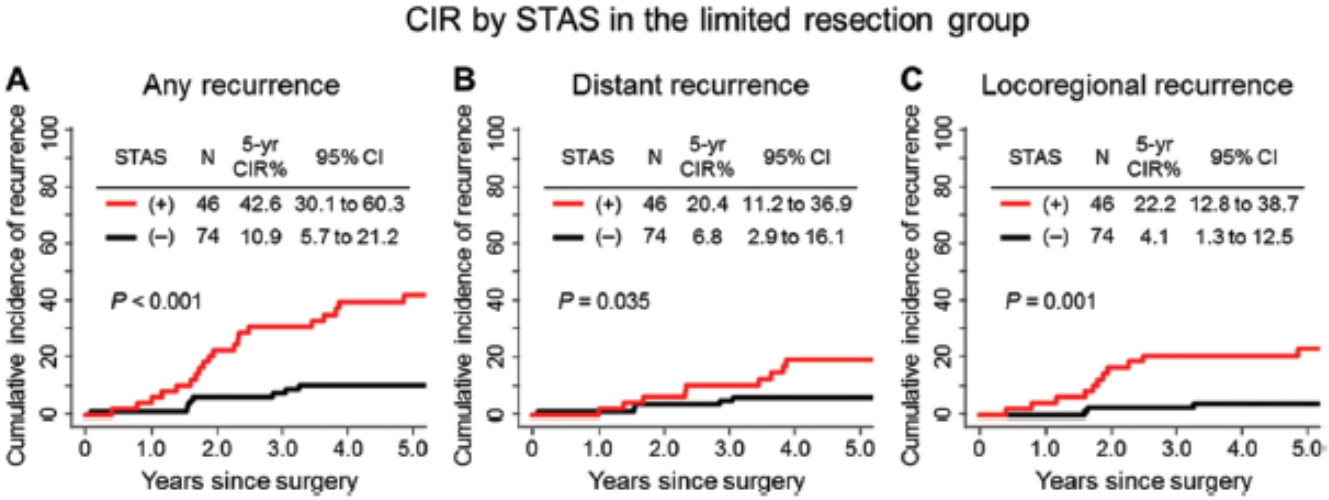
Margin? LN dissection?

Resection

- **Anatomic pulmonary resection is preferred for the majority of patients with NSCLC.**
- **Sublobar resection - Segmentectomy and wedge resection should achieve parenchymal resection margins ≥2 cm or ≥ the size of the nodule.**
- **Sublobar resection should also sample appropriate N1 and N2 lymph node stations unless not technically feasible without substantially increasing the surgical risk.**
- **Segmentectomy (preferred) or wedge resection is appropriate in selected patients for the following reasons:**
  - **Poor pulmonary reserve or other major comorbidity that contraindicates lobectomy**
  - **Peripheral nodule[1] ≤2 cm with at least one of the following:** Peripheral is defined as the outer one third of the lung parenchyma.
    - **Pure AIS histology**
    - **Nodule has ≥50% ground-glass appearance on CT**
    - **Radiologic surveillance confirms a long doubling time (≥400 days)**

Histopathologic subtype unknown before and during resection!
consolidation/tumor ratio>50% means higher acinar/solid subtype!
Resection margin> 2cm
only 48.48%(16/33) in segmentectomy KMUH 2015-2018
only 13.95%(6/43) in wedge resection KMUH 2015-2018

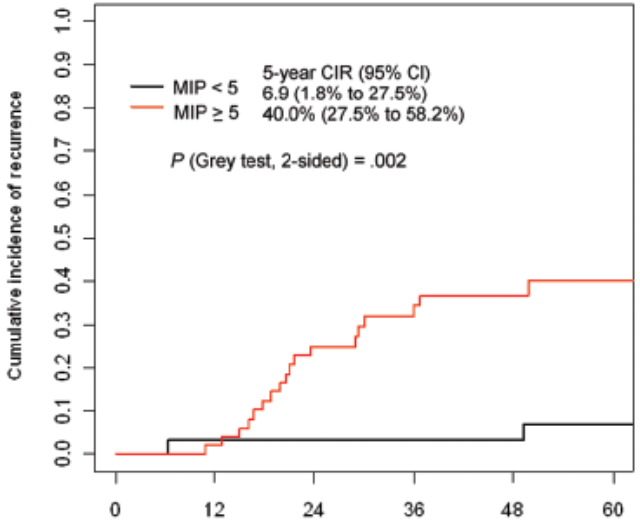
Tumor spread through air spaces (STAS)/recurrence

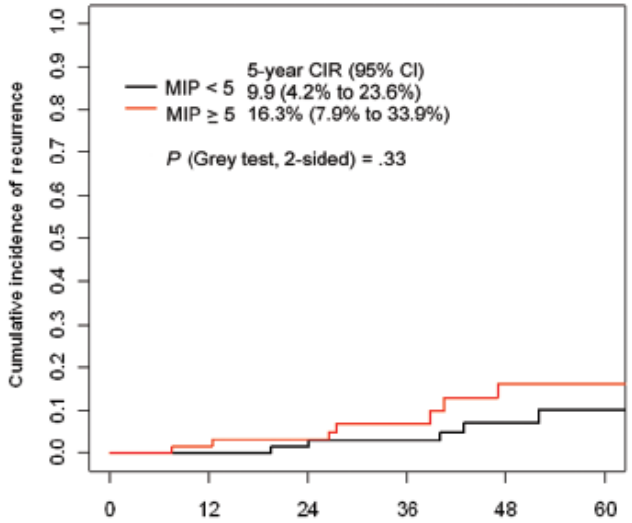


STAS pattern is a significant risk factor of disease recurrence in small (less than or equal to 2 cm) stage I lung adenocarcinoma

Journal of Thoracic Oncology® • Volume 10, Number 5, May 2015

Subtype matters: micropapillary imposed locoregional recurrence





- In MIP component of 5% or greater patients, recurrences were mainly locoregional; there was a reduced probability of recurrence in cases with a surgical margin of 1 cm or greater.

J Natl Cancer Inst;2013;105:1212–1220

Accuracy of frozen section, you should trust more

Table 3. Accuracy of frozen section for predicting predominant histological subtype and the presence or absence of histological patterns in permanent sections

Parameter	Accuracy, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	κ
Predominant histological subtype				
Overall	68 (63–73)	NA	NA	0.565
Lepidic	90 (86–92)	75 (64–84)	93 (90–96)	0.681
Acinar	76 (71–80)	70 (61–77)	79 (73–84)	0.481
Papillary	85 (81–88)	62 (50–72)	91 (87–94)	0.527
Micropapillary	94 (91–96)	21 (9–40)	99 (97–100)	0.277
Solid	91 (88–94)	79 (67–87)	94 (90–96)	0.700
Presence or absence of histological pattern				
Lepidic	80 (76–84)	75 (69–80)	91 (84–96)	0.588
Acinar	89 (85–92)	90 (86–93)	67 (35–90)	0.252
Papillary	72 (67–77)	70 (64–75)	79 (69–87)	0.397
Micropapillary	67 (62–72)	37 (30–45)	94 (89–97)	0.321
Solid	84 (80–88)	69 (61–76)	96 (92–98)	0.670

NA, not applicable.

Histopathology 2015, 66, 922–938. DOI: 10.1111/his.12468

Using frozen section to identify histological patterns in stage I lung adenocarcinoma of ≤3 cm: accuracy and interobserver agreement

Yi-Chen Yeh,[1,2,3] Jun-ichi Nitadori,[1,4] Kyuichi Kadota,[1] Akihiko Yoshizawa,[1] Natasha Rekhtman,[5] Andre L Moreira,[5] Camelia S Sima,[6] Valerie W Rusch,[1] Prasad S Adusumilli[1,7] & William D Travis[5]

Intra-operative Frozen Section

- From 2015 to 2018, 201 patients with Stage I lung cancer(T1a to T2a N0M0)
- Intra-op frozen section done in 103 patients(51.2%) with total 110 sections
- Purpose of frozen section:
    - Primary lung tumor: 97
    - Other nodules in the same side: 5
    - Pleural lesion in the same side: 2
    - Resection margin:6

Result of intra-op frozen section

- Frozen section = final report: 99 /110(90%)
- Negative(No malignancy seen) -> positive on permanent: 3 cases(2.7%)
    - Inflammation and fibrosis-> adenocarcinoma in 2 cases
    - Negative parietal pleura seeding-> positive in one
- Changes in diagnosis: 3 cases
    - AIS-> MIA in one
    - AIS -> adeno in 2

- Rough frozen section reports
    - Malignancy/carcinoma-> adenocarcinoma in 3 cases
    - Indeterminate -> adenocarcinoma in one
    - Carcinoma -> AIS in one

- Frozen section is a relative reliable tool in pulmonary nodules
- But we need further descriptions: Spread through air space, micropapillary or solid subtypes for clinical decisions!

Non-surgical options?

- Overall survival rates were comparable between TA and SRT (1 year, 85.4% vs 86.3%, respectively, *P = .76; 2 years, 65.2% vs 64.5%, respectively, P = .43; 3 years,* 47.8% vs 45.9%, respectively, *P = .32; 5 years, 24.6% vs 26.1%, respectively, P = .81).*

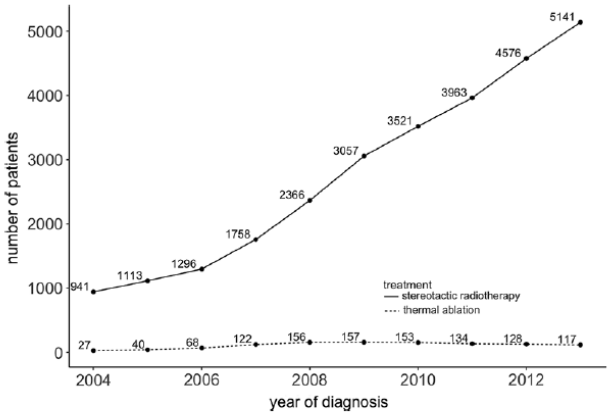


Figure 2: Graph of absolute number of patients with stage 1 non–small cell lung cancer treated by thermal ablation and stereotactic radiation therapy between 2004 and 2013 in the National Cancer Database.

ORIGINAL RESEARCH • VASCULAR AND INTERVENTIONAL RADIOLOGY

Radiology

Survival Rates after Thermal Ablation versus Stereotactic Radiation Therapy for Stage 1 Non–Small Cell Lung Cancer: A National Cancer Database Study

Johannes Uhlig, MD, MPH • Johannes M. Ludwig, MD • Sarah B. Goldberg, MD, MPH • Anne Chiang, MD, PhD • Justin D. Blasberg, MD • Hyun S. Kim, MD

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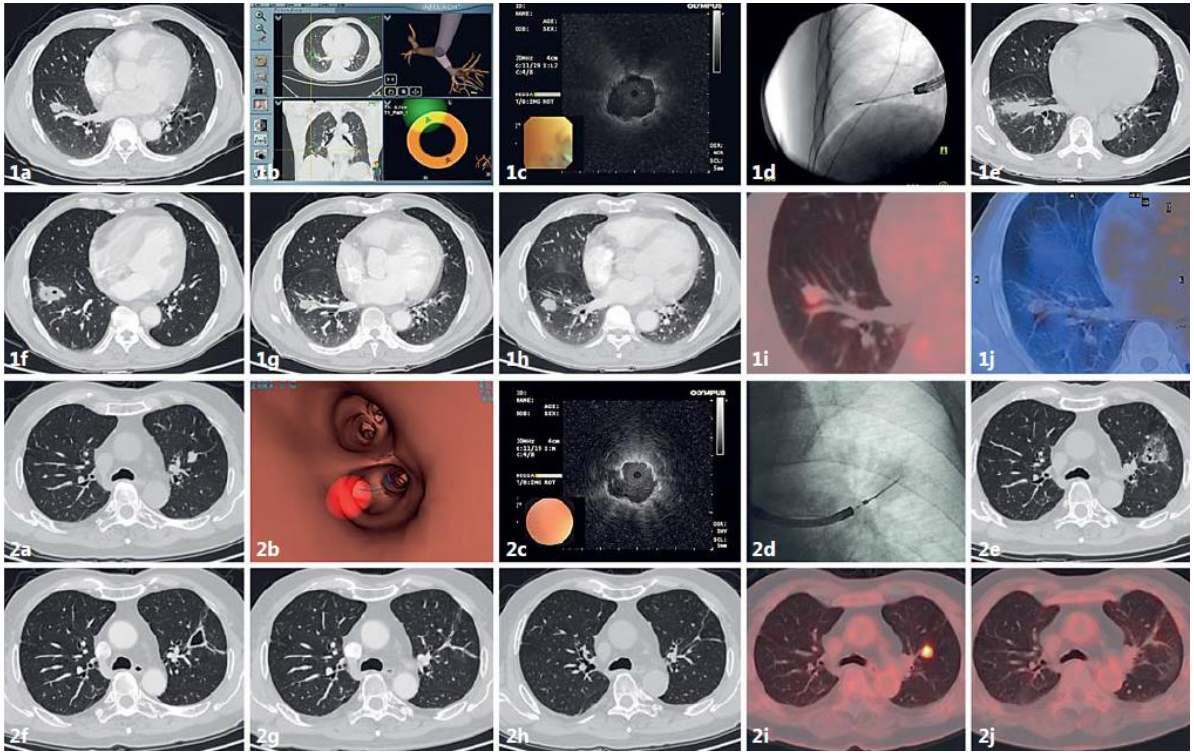

Navigation Bronchoscopy-Guided Radiofrequency Ablation for Nonsurgical Peripheral Pulmonary Tumors

Fangfang Xie[a, b] Xiaoxuan Zheng[a] Bo Xiao[c] Baohui Han[b] Felix J.F. Herth[d] Jiayuan Sun[a, b]

Personal thinking about GGN

- CT scan follow-up within 6 months for lesion existence
- Non-surgical approach is not a bad idea but need CT follow-up on a regular schedule
- Regular CT follow-up even GGN resected, maybe life-long, new lesions may arise in normal lung
- Resection margin is critical, more than 2cm is favored, frozen section is essential
- Lobectomy gets favorable outcome and should list on surgical options
- Bronchoscopic interventions is inevitable in the future but long-term results in doubts

- Thank you!!