



Management of Lung Nodules (GGN)

高雄長庚經驗

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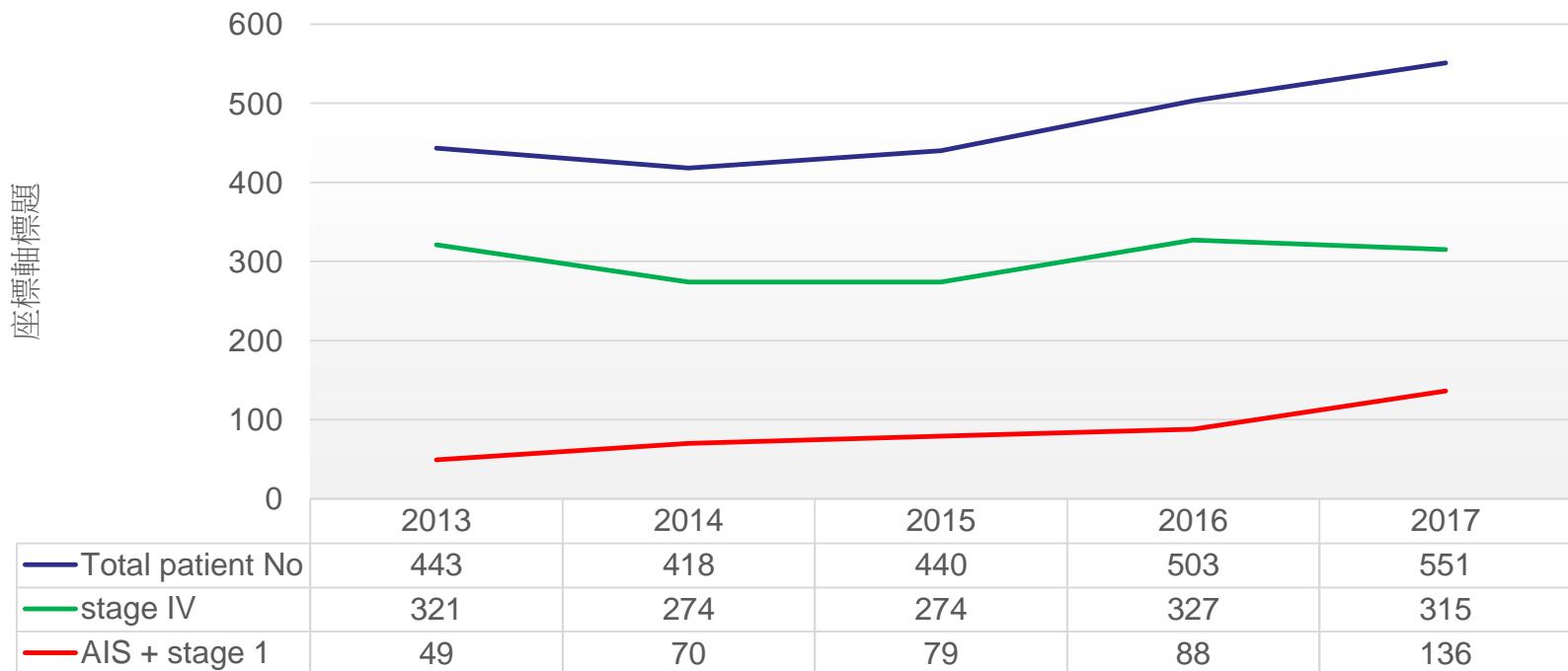
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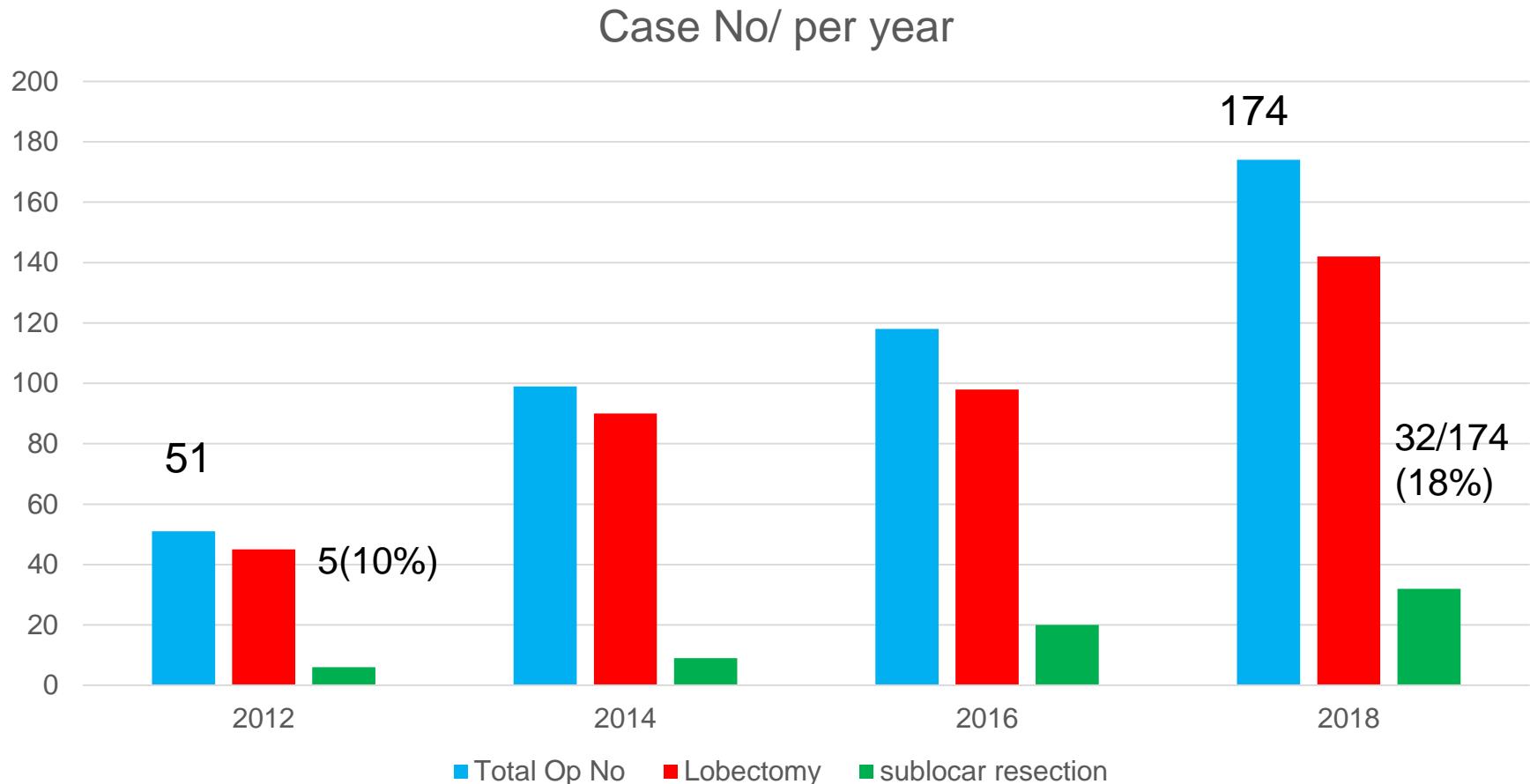
高雄長庚肺癌各期別分布的改變

圖表標題





Case No. of curative surgery in primary lung cancer





肺癌疾病型態及手術的改變趨勢

疾病型態的改變

- 早期癌增加
- 腫瘤微小化
- 多發性病灶

肺癌手術發展

- 微創化：單孔，不插管，無胸管
- 精準化：定位，螢光染色，3D 重組影像
- 多元化：切除，燒灼，光動力治療，微波，冷凍療法



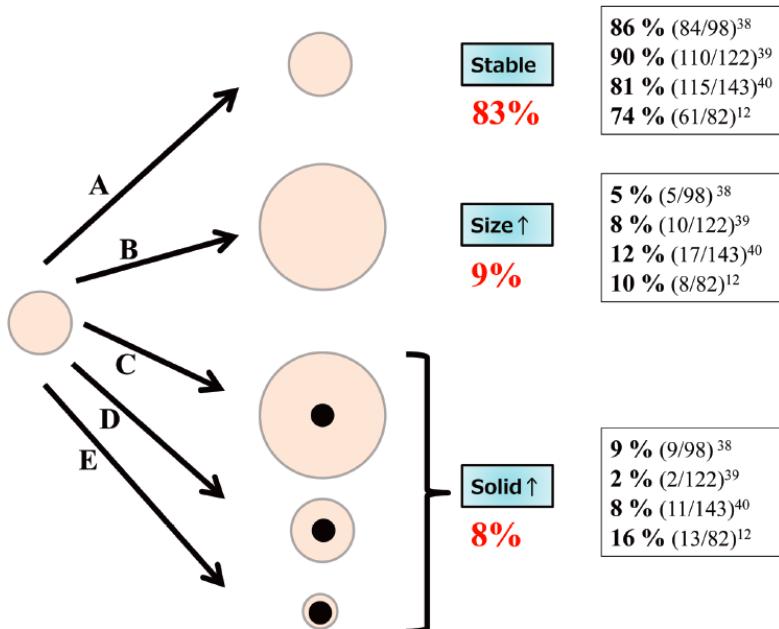
Issues for management of GGNs

- Selection criteria for surgery**
- Decision making on extent of surgical resection
- Localization method

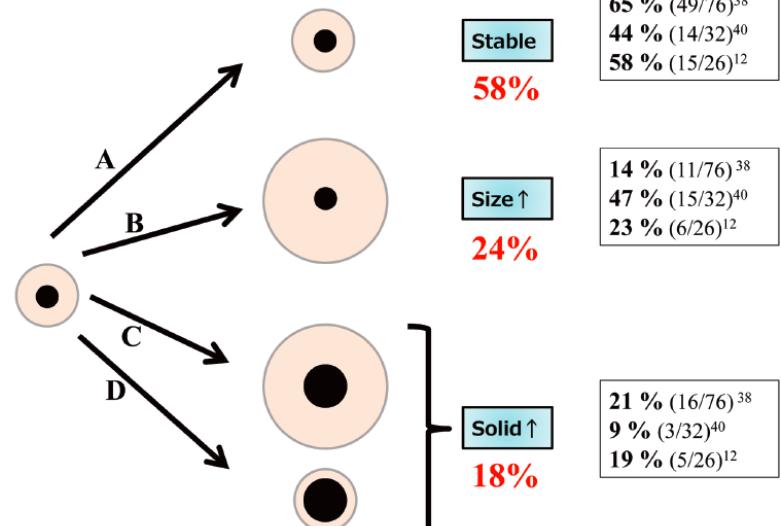
Management of ground-glass opacities: should all pulmonary lesions with ground-glass opacity be surgically resected?

Yoshihisa Kobayashi¹, Tetsuya Mitsudomi²

Pure GGO : 17%



Subsolid GGO : 42%



Natural history of pure GGO

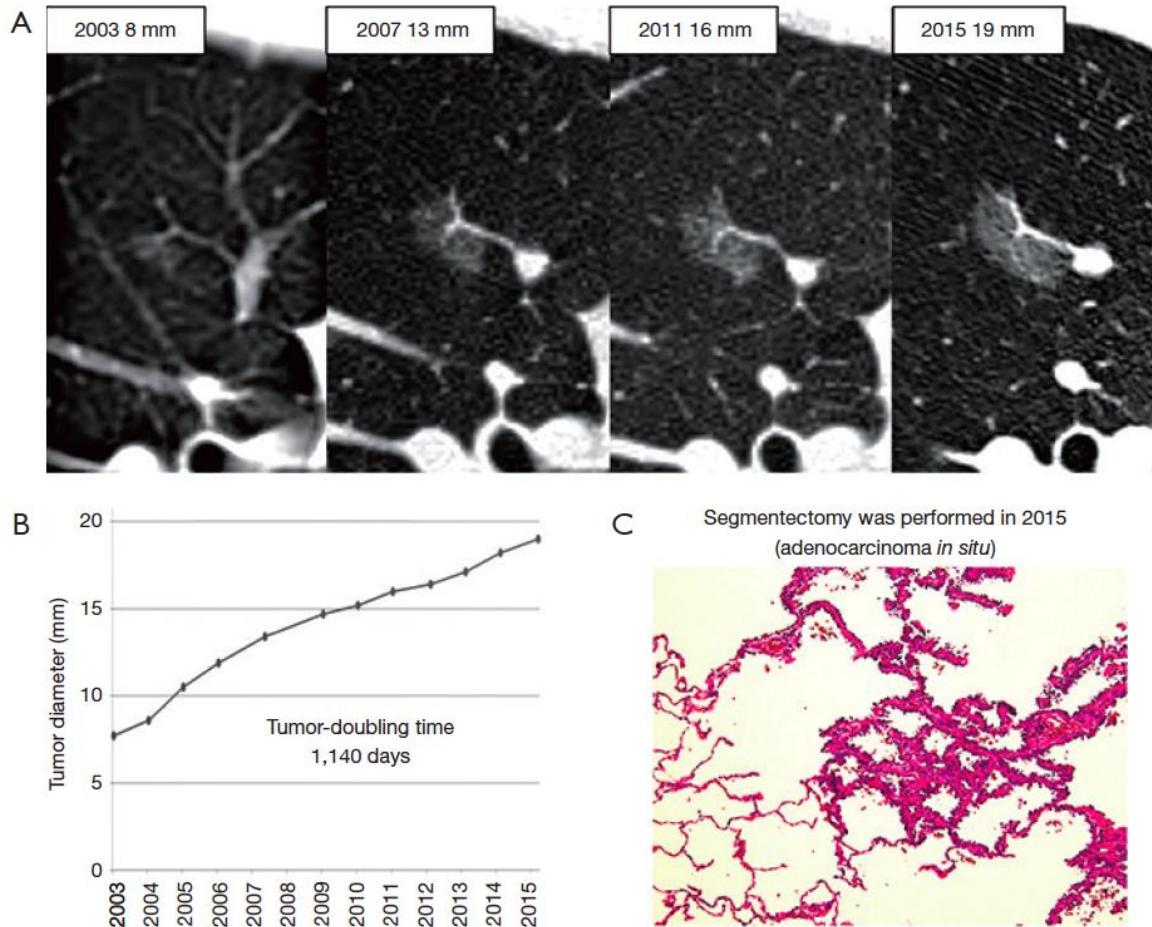


Figure 5 Computed tomography images and pathological features of representative pure GGN. (A) Pure GGN was detected in a 49-year-old male with previous smoking history of 4 pack years; This GGN slowly increased in diameter without appearance of solid components; (B) tumor-doubling time was 1,140 days; (C) segmentectomy was performed in 2015 after 12-years of follow-up. This tumor was diagnosed as adenocarcinoma *in situ* (hematoxylin-eosin staining, $\times 40$). GGN, ground-glass nodule.

Predictors for the growth of GGNs

Author, year (ref.)	Number of GGNs	Univariate analysis	Multivariate Cox for time to growth	Multivariate logistic for growth incidence
Hiramatsu, 2008 (7)	125 ^{*1}		Size	Size PH of lung cancer
Chang, 2013 (8)	122 pure	Size	NE	NE
Matsuguma, 2013 (11)	98 pure		Size PH of lung cancer	NE
	76 part-solid		NE factor	NE
Kobayashi, 2014 (17)	120 ^{*1}		Size Smoking	Size Smoking
Kobayashi, 2015 (18)	120 ^{*1}	EGFR	NE	NE
Kakinuma, 2016 (13)	1053 pure		Size Male Size ^{*2} Smoking ^{*2}	NE
	81 hetero		Size	NE
	106 part-solid		Size	NE

Figure 2 Summary of predictors for the growth of GGNs (7,8,11,13,17,18). *1: pure GGNs and part-solid GGNs; *2: changes in the appearance of the solid component is defined as the outcome. NE, not evaluated; PH, past history; GGN, ground-glass nodule.



Indication for resection

156 patients (M:60, F:96), 173 GGNs (2015–
17)

	Pure GGN (N=96)	Subsolid GGN (N=77)
Tumor size > 8mm	76(80%)	73(95%)
Tumor growth	17	8
Radiologic morphology	43	65
Family history	6	5
Patient concern	8	1



Incidence of positive pathology : 88.4%

	Benign		Malignancy			Incidence of IA
Histology/ size (cm)	Benign	AAH	AIS	MIA	Invasive adeno.	
< 0.6	5	3	2	2	0	0%
0.6 – 0.8	5	5	10	1	5	2.9%
0.8 – 2.0	10	5	13	13	71	41%
> 2.0	0	0	0	1	22	12.7%
Total			25(15%)	17(10%)	98(56%)	



Radiology findings of pure GGNs

	Pre-invasive lesion (n=51)	IA (n=35)
Tumor size		
< 1cm	28	3
\geq 1cm	23	32 *
Radiology findings		
spiculated	9	18
Pleural indentation	6	11
Vessel convergence	10	13



Radiology findings of subsolid GGNs

	Pre-invasive lesion (n=8)	IA (n=63)
Tumor size		
< 1cm	3	2
≥ 1cm	5	61 *
Solid part		
< 0.5cm	3	13
≥ 0.5cm	5	50 *
CT ratio		
< 0.5	5	27
≥ 0.5	3	37 *
Radiology findings		
spiculated	5	45
Pleural indentation	2	18
Vessel convergence	2	8



Selective criteria for surgery in KSCGMH

Size & growth

- Pure GGN : $\geq 8\text{mm}$, growth or persistence with high suspicion of lung cancer
- Sub-solid nodule : $\geq 6\text{mm}$, growth or persistence with high suspicion of lung cancer

Suspicion of lung cancer

- Presence of solid component in pure GGO
- Morphology : spiculation, pleural indentation, well-defined margin, vessel convergence, pseudo-cavity, round to oval shape
- Family history of lung cancer
- Past history of cancer



Issues for management of GGNs

- Selection criteria for surgery
- **Decision making on extent of surgical resection**
- Localization method



Decision making on extent of resection

- C/T ratio (consolidation/tumor)

- Radiographic staging

- PET-scan : biological aggressiveness

- Safe margin

- Frozen diagnosis (histological invasiveness)



Radiology staging in GGN lesions

	CT image on HRCT						
cT*	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 component	Invasive AD with a lepidic component or lepidic predominant AD	Invasive AD with lepidic component
	Pathologic Stage		pTis‡‡	pT1mi‡‡	pT1a	pT1b	pT1c

Sublobar resection or lobectomy

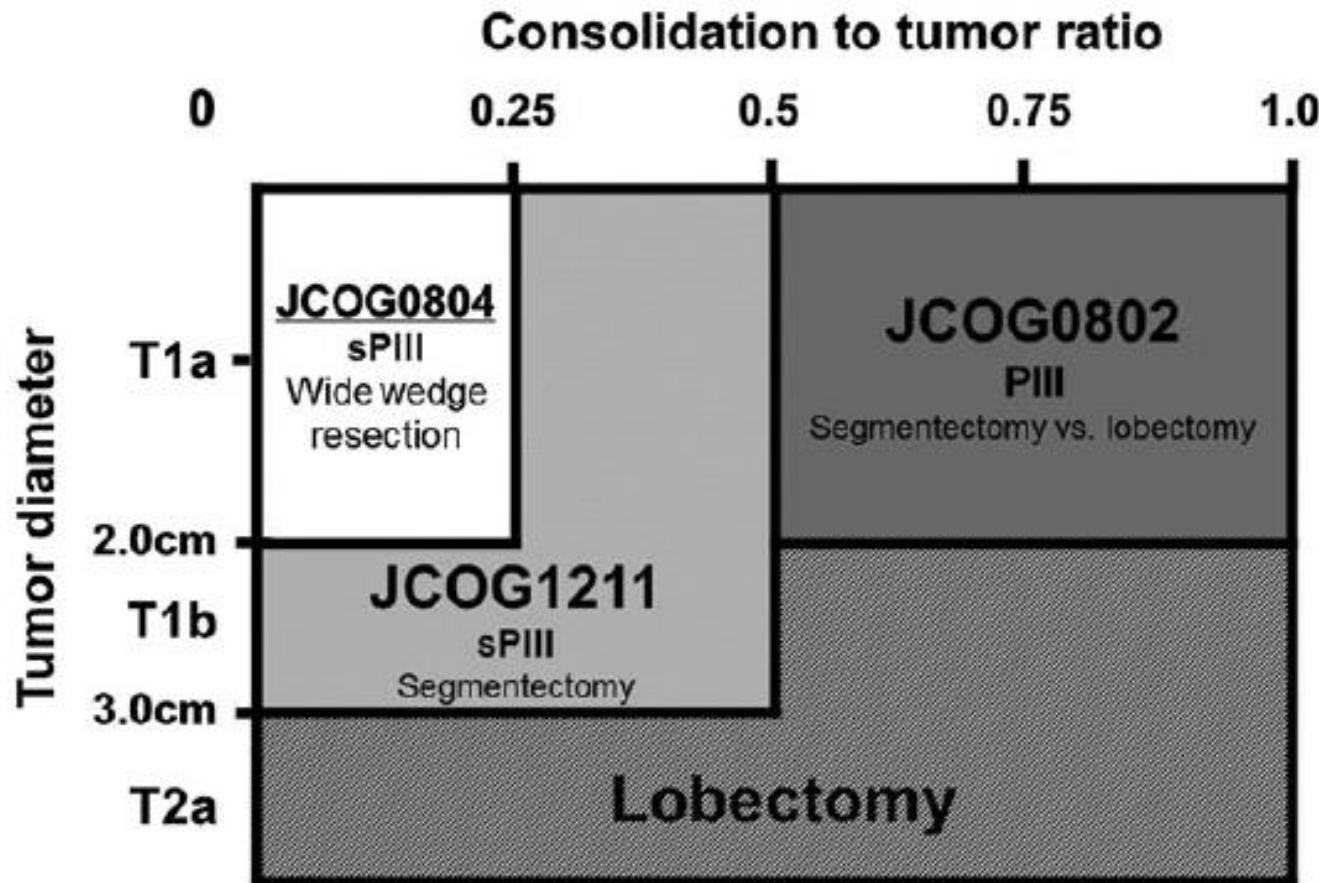


Figure 5. Study populations classified according to the maximum tumour diameter and C/T ratio.



Lobectomy v. s sublobar resection

	Lobectomy (n=76)	Sublobar resection(n=97)	P value
Tumor size			< 0.001
< 1cm	3	44	
≥ 1cm	73 (58%)	53	
Solid part			< 0.001
< 0.5cm	53	82	
≥ 0.5cm	23(60%)	15	
CT ratio			< 0.001
< 0.5	30	80	
≥ 0.5	46(73%)	17	
Frozen diagnosis			< 0.001 *
Non-IA	12 (AIS :2, MIA:10)	76	
IA	64(75%)	21	
Final pathology			
Non-IA	5 (all MIA)	70	
IA	71	27	



Correlation rate between frozen and permanent diagnosis

		Final pathology (N=160)			
Frozen Dx	Benign	AAH	AIS	MIA	IA
Benign	12	1	3	1	1
AAH		9	0	1	0
AIS			20	5	4
MIA				9	12
IA		1	1	0	80



Correlation rate between frozen and permanent diagnosis

Under diagnosis n =28				
Permanent diagnosis		Wedge	Segmentectomy	Lobectomy
AAH	1		1	
AIS	3	2	1	
MIA	7	4	1	2
IA	17		8	9

Over diagnosis n = 3				
Permanent diagnosis		Wedge	Segmentectomy	Lobectomy
AAH	1	1		
AIS	1		1	
MIA	1			1



The Influence of Clinical T Factor on Predicting Pathologic N Factor in Resected Lung Cancer

Check for updates

- 825 cN0M0 patients
- Tumor size or consolidation size < 1cm => No pN+
- Tumor 1-3cm : 13.4% pN+
- Frequency of pN+ : tumor without GGO was 5.5 times higher than with GGO

Size, cm	Pathologic Lymph Node Metastasis		
	GGO+ (n = 388)		GGO- (n = 437)
	Total Size	Consolidation Size	Total Size
<1	0/24 (0)	0/170 (0)	0/16 (0)
1 to <2	3/140 (2.1)	7/129 (5.4)	16/131 (12.2)
2 to <3	7/134 (5.2)	7/61 (11.5)	27/112 (24.1)
3 to <4	3/65 (4.6)	2/19 (10.5)	22/79 (27.8)
4 to <5	4/12 (33.3)	1/5 (25.0)	10/54 (18.5)
5 to <6	1/9 (11.1)	2/3 (33.3)	5/22 (22.7)
6 to <7	1/3 (33.3)	0/0 (0)	3/10 (30)
≥7	0/1 (0)	0/1 (0)	4/13 (30.8)
Total	19/388	19/388	87/437

GGO+, with ground-glass opacity; GGO-, without ground-glass opacity.

S. Shimamatsu. etc, Ann Thorac Surg 2019



Is lymph nodes dissection necessary in cT1a(<2cm) GGN dominant patients ?

Patients receiving lymph nodes dissection : 127

- Invasive adenocarcinoma : 93 patients
- AIS + MIA : 34 patients
- N1 : 6.8
- N2: 11
- Only two patients have positive LN (N1- 1, N2- 1)
- Two distant recurrence (size : 2.3cm, MIP => contralateral meta. ; 1.5cm, limited resection, mixed type)
- No loco-regional failure



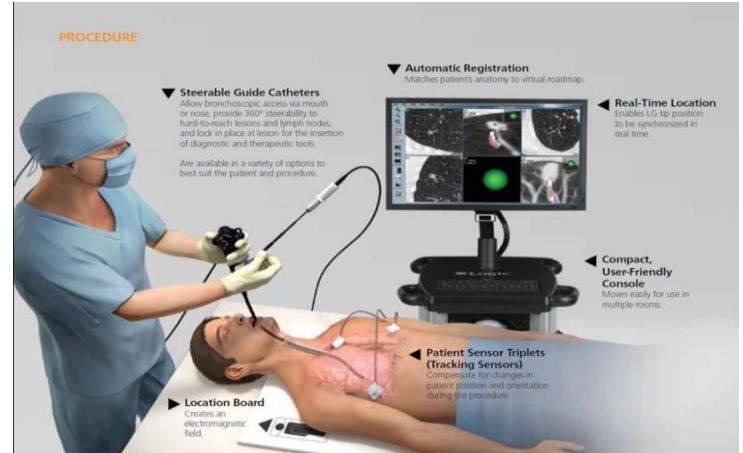
Issues for management of GGNs

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- **Localization method**

早期肺癌及微小肺結節精準定位及全方位治療模式 (iVATS, ENB)

Hybrid room 精準定位, 治療

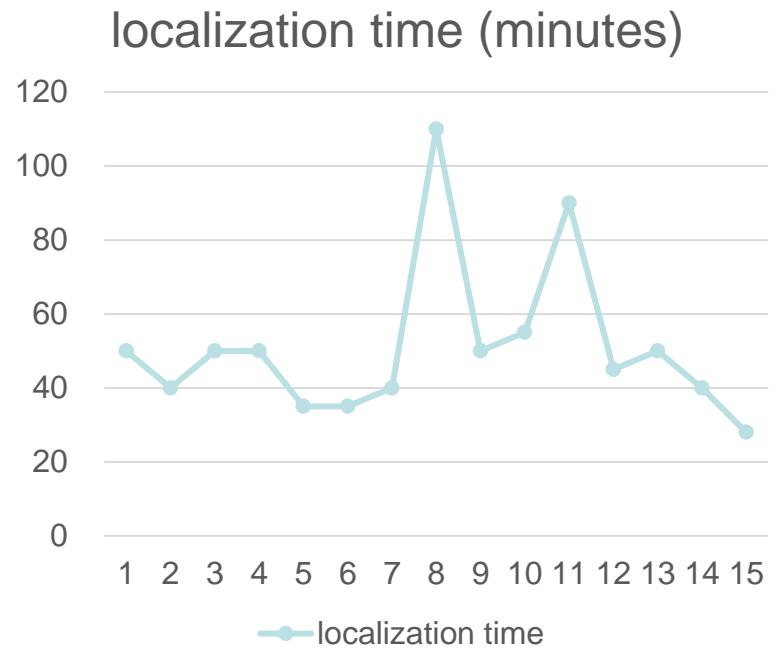
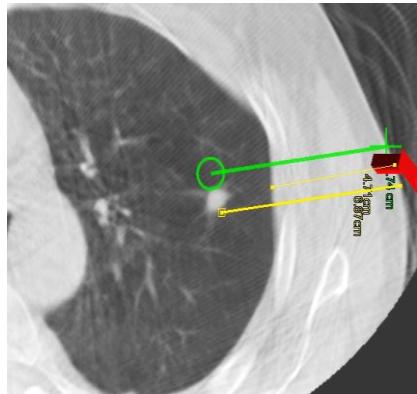
- Zeego-assist laser-guide localization
- ENB (endoscopic navigation bronchoscopy)
- Transbronchial or transthoracic lung tumor surgery



Intra-operative localization at hybrid OR using Zeego

Preliminary result :

- Small pGGN ($< 0.8\text{cm}$) : 8/25
- Deep or centrally located : 17/25
- Complication : dislodge(2), minor bleeding(1), pneumothorax(2)
- Success rate : 92%
- Unpredictable air embolism



早期肺癌精準切除的要件

- 術前影像判讀,決定需切除的分葉或次分葉血管氣管以及腫瘤安全切除範圍
- 術中需精確辨識 intersegmental plane 或 resection margin

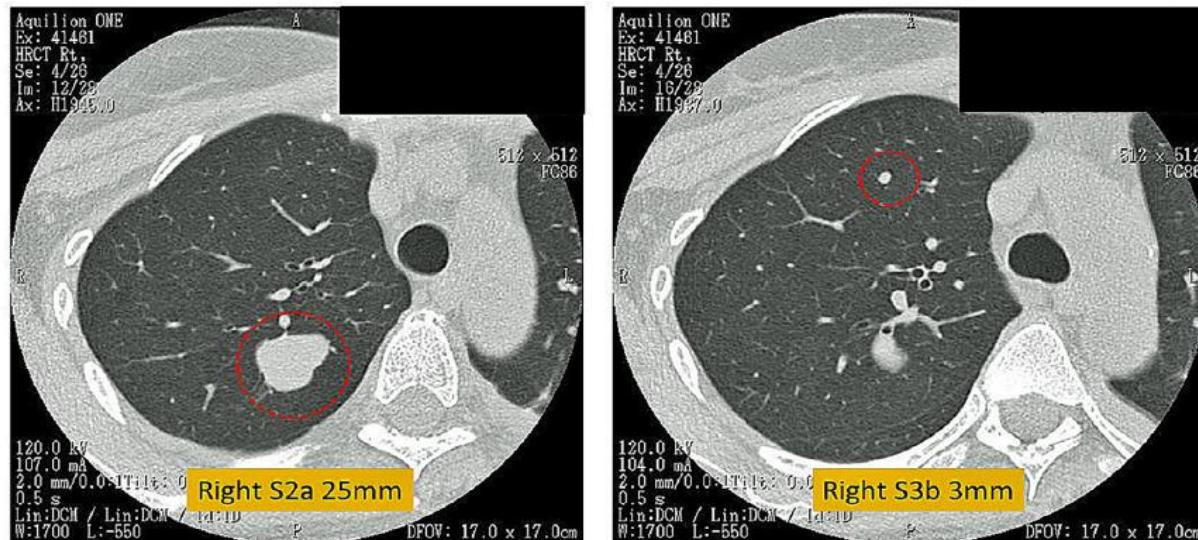


Figure 1. Right metastatic lung tumor from renal leiomyosarcoma in a 42-year-old female. She had already undergone left S10b+c subsegmentectomy. There are 2 nodules in the right upper lobe at S2a and S3b.

術前 3D 模擬

精準確認腫瘤所在位置及安全切除範圍

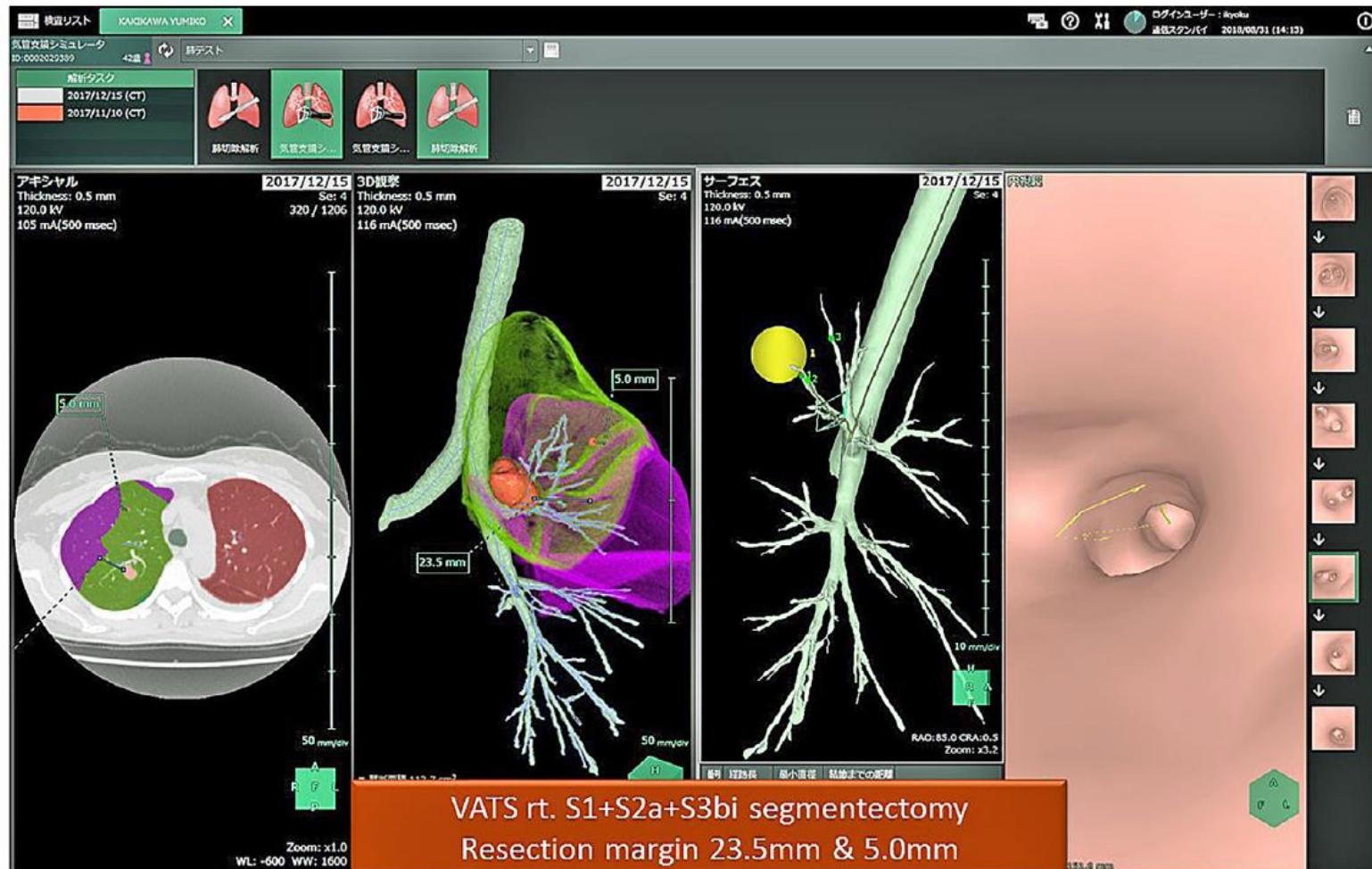


Figure 2. Virtual segmentectomy and bronchoscopy of patient in [Figure 1](#). After creating several virtual segmentectomies, the most appropriate resection area was selected based on the surgical margin. Right S1 (segment) + S2a (subsegment) + S3bi (subsubsegment) resection were selected.

術中透過導航氣管鏡定位染色 精準標示切除範圍

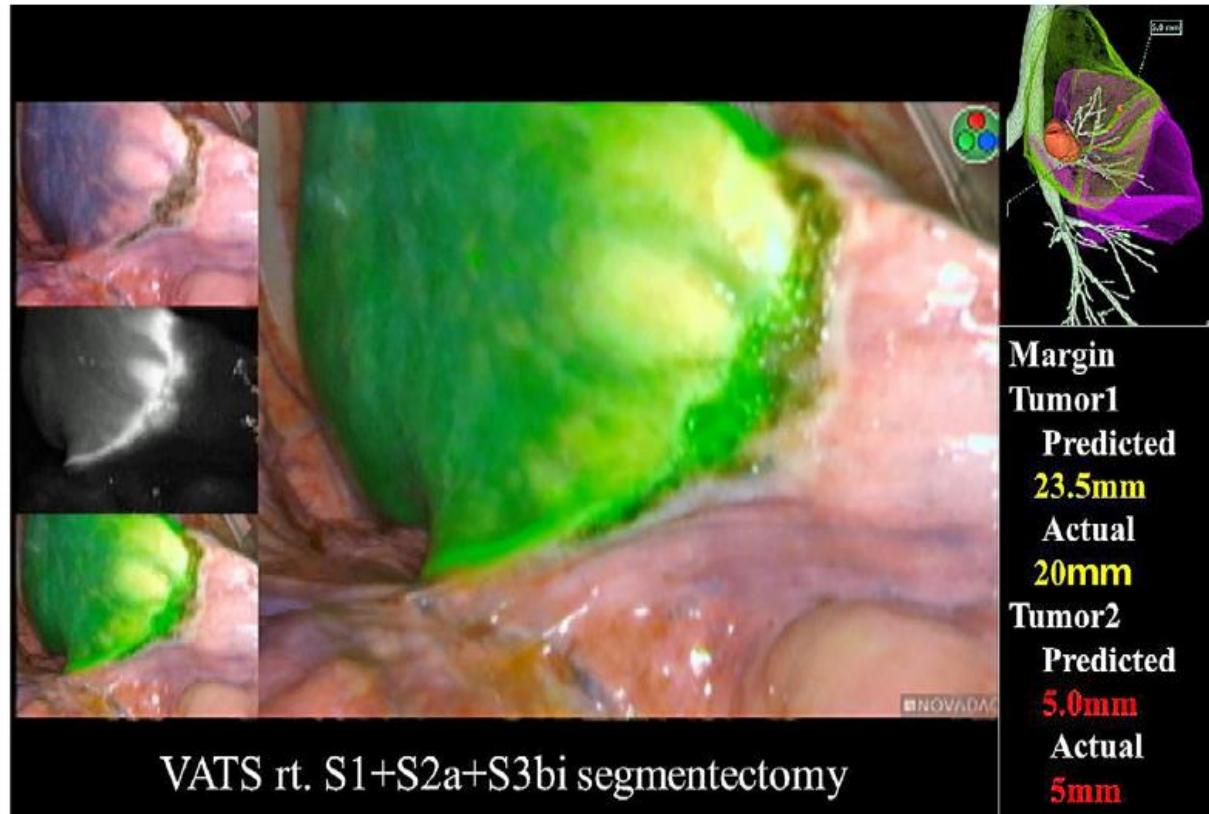


Figure 3. ICG fluorescence of the patient in Figure 1 is clearly visualized at the initial time of operation. The real image was completely matched with a virtual image.



Summary

Selective criteria for GGNs resection

- Size
- Tumor growth rate
- Radiologic findings, family history of lung cancer, previous cancer history, smoking

Extent of curative resection in GGNs

- C/T ratio
- Size
- Biologic aggressiveness
- Margin

Localization of small lung nodules : simple, safe, precise localization



感謝聆聽，請指教