Which is better for the patients with PPL? - PCNA vs. Upfront surgery vs. Novel bronchoscopy

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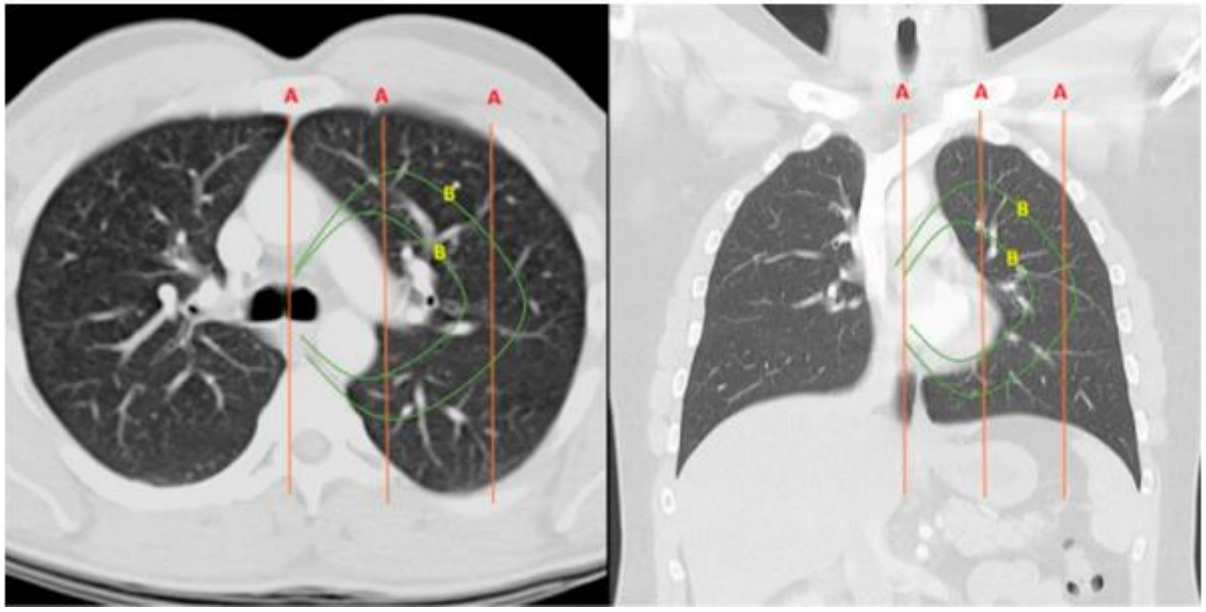
Contents

1. Background
2. Upfront surgery for PPL
3. Image-guided percutaneous biopsy for PPL
4. Bronchoscopy for PPL
5. Case Presentations
6. Conclusion

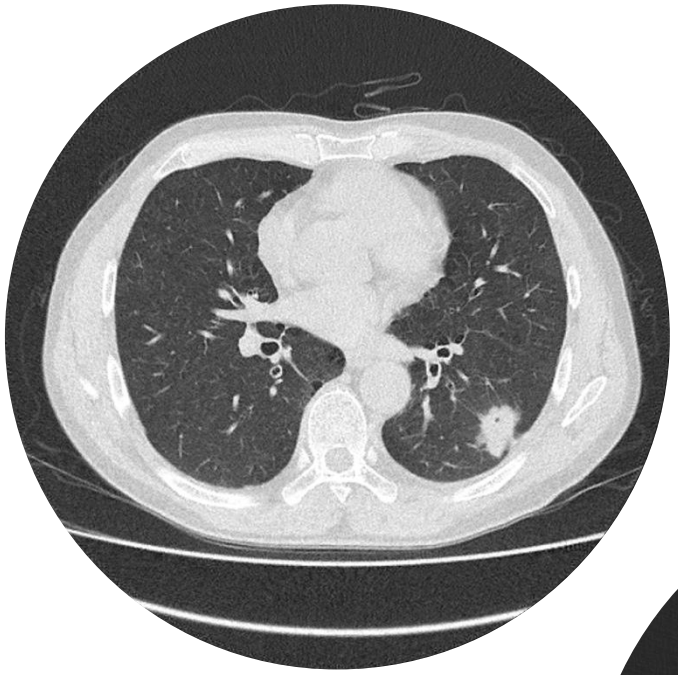
Background

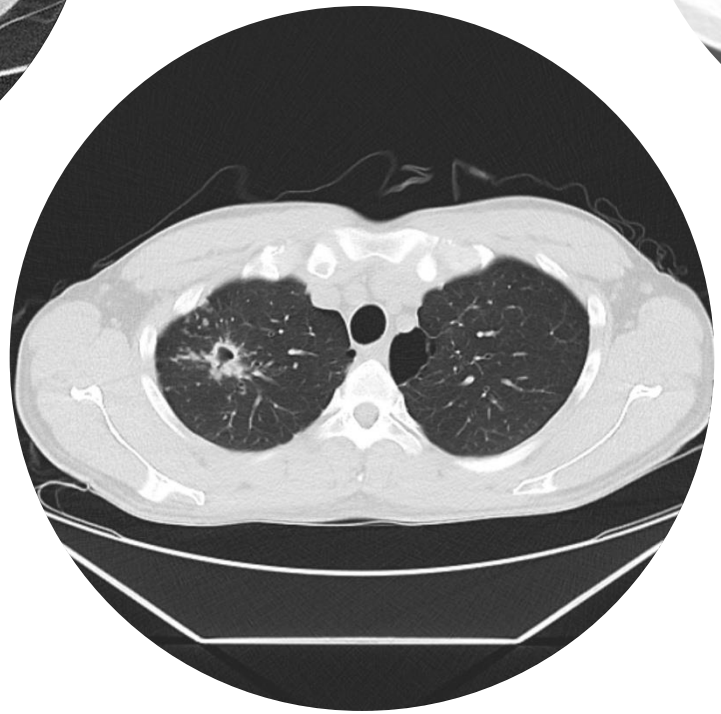
- What is PPL?
  - Generally considered as lesions in the peripheral one-third of the lung.



Ann Am Thorac Soc. 2017 Jan;14(1):118-123.

Background





Background

- Lung-RADS
  - Quality assurance tool designed to standardize lung cancer screening CT reporting
  - Reduce confusion in lung cancer screening CT interpretations

https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads

Background

- Lung-RADS

Solid nodule		
Size	**Timing/Change**	**Cat.**
<6 mm	Baseline	2
	No change	2
	Growing	4A
	New (<4 mm)	2
	New (4-6 mm)	3
6-8 mm	Baseline	3
	No change	2
	Growing	4A
	New	4A
8-15 mm	Baseline	4A
	No change	2
	Growing	4B
	New	4B
≥15 mm	Baseline	4B
	No change	2
	Growing	4B
	New	4B

Part solid nodule		
Size	**Timing/Change**	**Cat.**
<6 mm	Baseline	2
	No change	2
	Growing (solid <4 mm)	4A
	Growing(solid 4-6 mm)	4B
	New	3
≥6 mm (solid <6 mm)	Baseline	3
	No change	2
	Growing (solid <4 mm)	4A
	Growing (solid 4-6 mm)	4B
	New (solid <4 mm)	4A
	New (solid 4-6 mm)	4B
≥6 mm (solid 6-8 mm)	Baseline	4A
	No change	2
	Growing	4B
	New	4B
≥8 mm (solid ≥8 mm)	Baseline	4B
	No change	2
	Growing	4B
	New	4B

Ground glass nodule		
Size	**Timing/Change**	**Cat.**
<20 mm	Baseline	2
	No change	2
	Growing	2
	New	2
≥20 mm	Baseline	3
	No change	2
	Growing	2
	New	3

Other	Cat.
Endobronchial nodule	4A
Cat. 3,4+additional finding ; Consolidation, atelectasis, lymph node enlargement, other (spiculation, etc.)	4X
Other clinically significant findings	S
Prior lung cancer	C

Category	Description	Prob.cancer	Manage
0	Incomplete	Not evaluable	Additional LDCT images and/or comparison to prior chest CT images
1	Negative	< 1%	Continue annual screening with LDCT in 12 months
2, 2b[a]	Benign	< 1%	Continue annual screening with LDCT in 12 months
3	Probably benign	1-2%	Follow up LDCT in 6 months
4A	Suspicious	5-15%	Follow up LDCT in 3 months, PET-CT may be used when there is a solid ≥8mm
4B, X	Very suspicious	> 15%	Immediate chest CT, consider biopsy, PET-CT may be used

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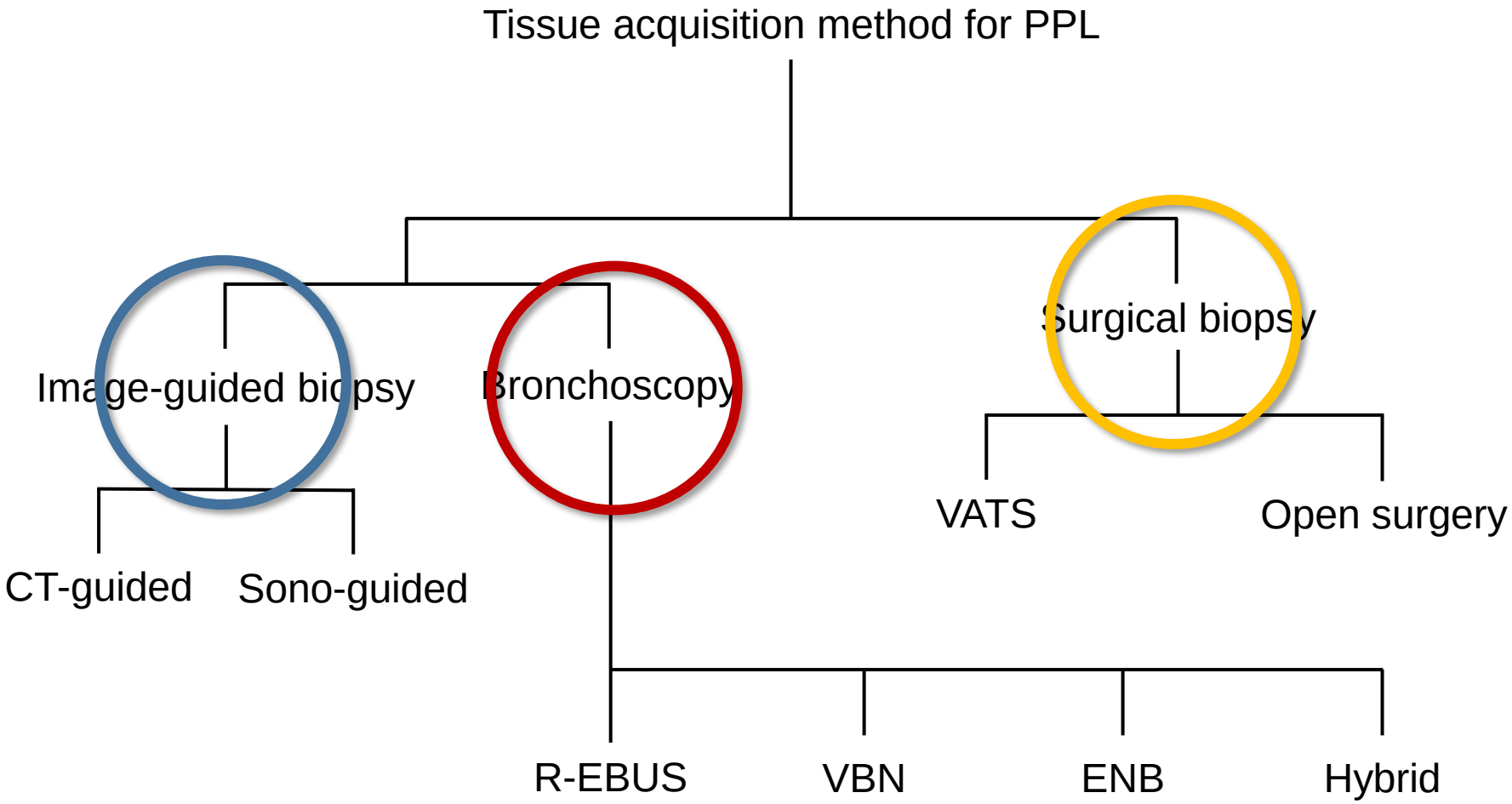
Diagnosis of PPL


Tissue acquisition method for PPL
Image-guided biopsy
Bronchoscopy
Surgical biopsy
CT-guided
Sono-guided
VATS
Open surgery
R-EBUS
VBN
ENB
Hybrid

Background

- NCCN (2018)
  - Strong clinical suspicion of stage 1 or 2 lung cancer do not require a biopsy before surgery.
  - In high-OP risk patients, try preoperative biopsy first and if no tissue is obtained, try intraoperative biopsy (wedge resection, needle bx).

Michael Young, Lung biopsy, StatPearls Publishing (USA,FL), 2022

Background

- NCCN (2018)
  - The least invasive biopsy with the highest yield is preferred as the first diagnostic study.

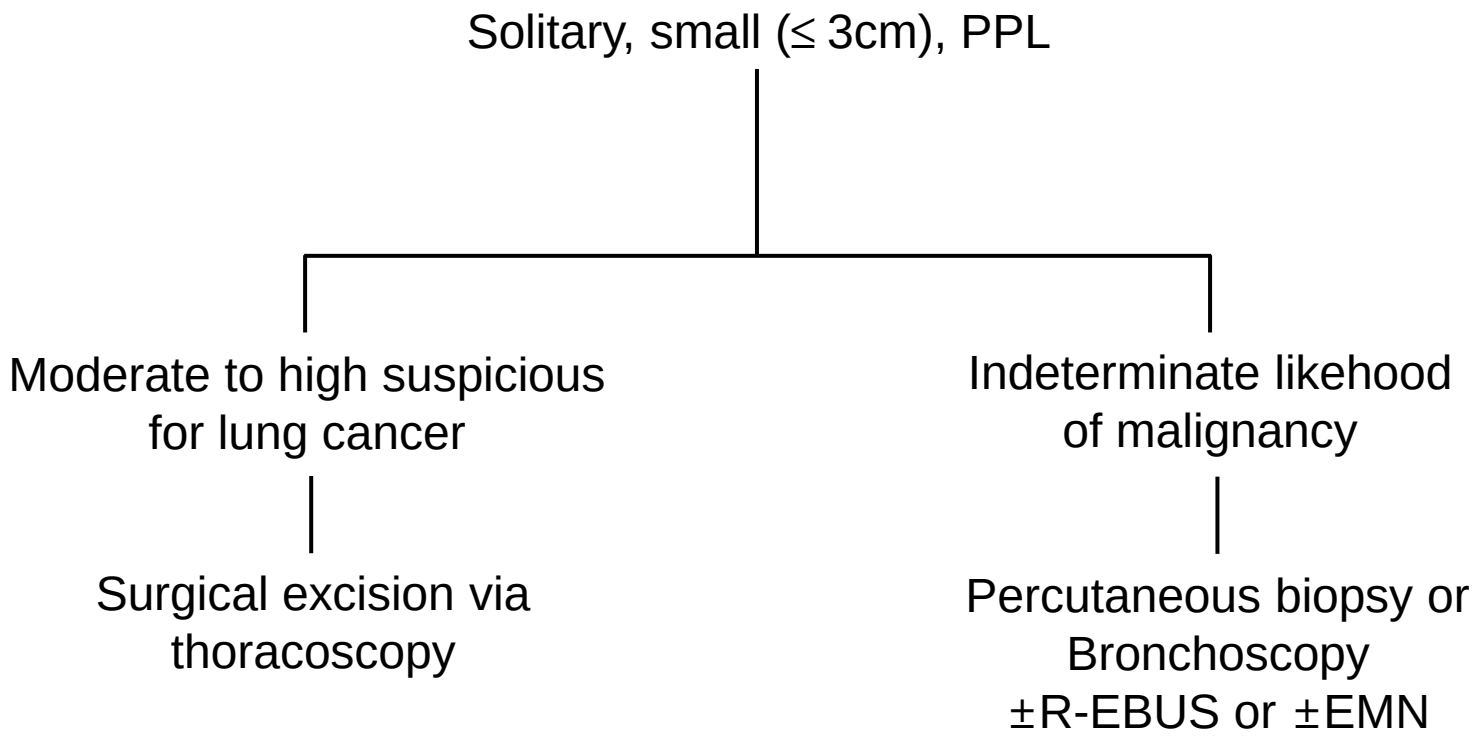
Michael Young, Lung biopsy, StatPearls Publishing (USA,FL), 2022

ACCP guideline (2013)

- Peripheral lung nodule biopsy
  1. Radial-EBUS
  2. EMN guidance bronchoscopy
  3. Percutaneous lung biopsy

Michael Young, Lung biopsy, StatPearls Publishing (USA,FL), 2022

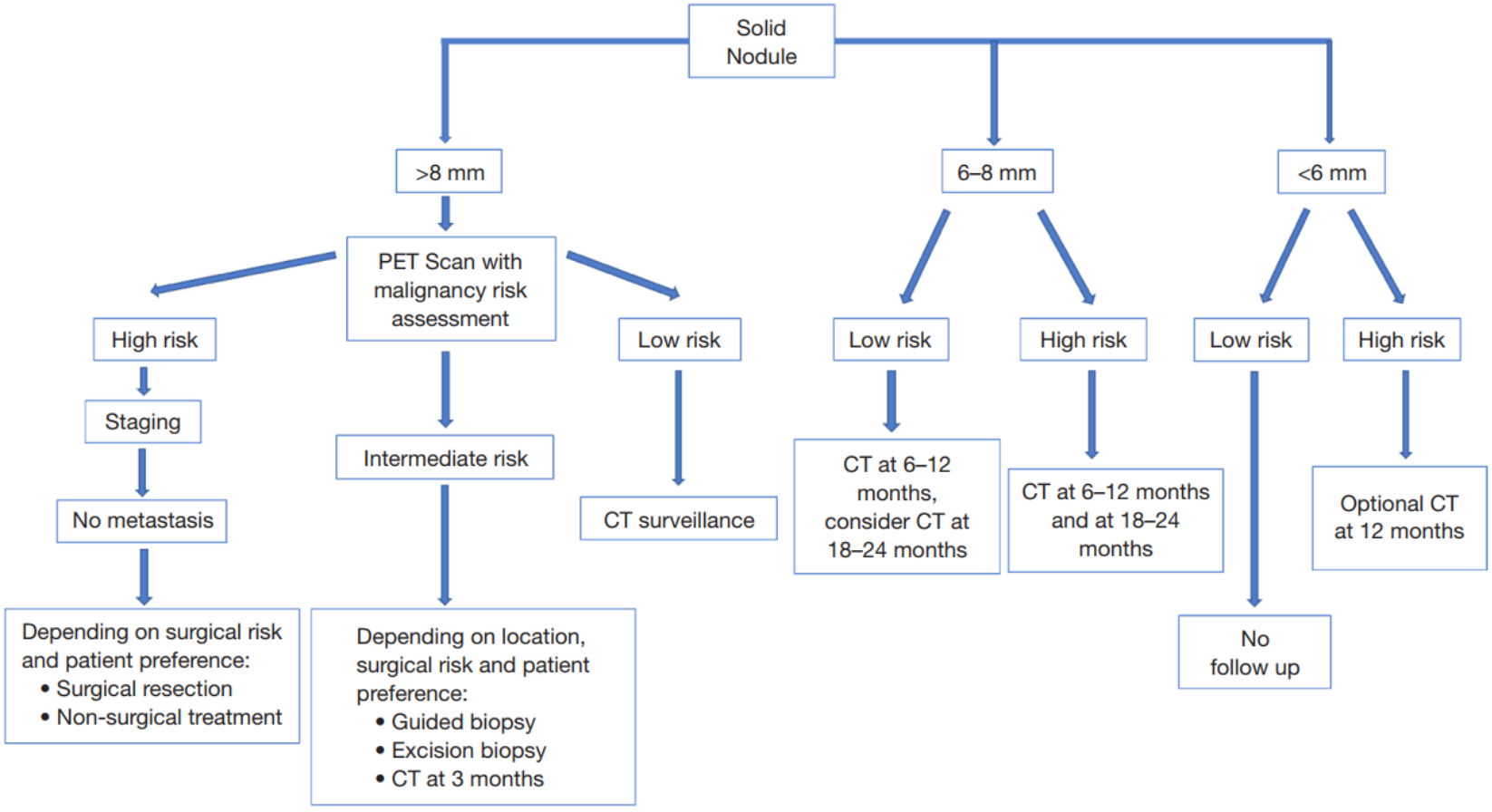
ACCP guideline (2013)



Michael Young, Lung biopsy, StatPearls Publishing (USA,FL), 2022

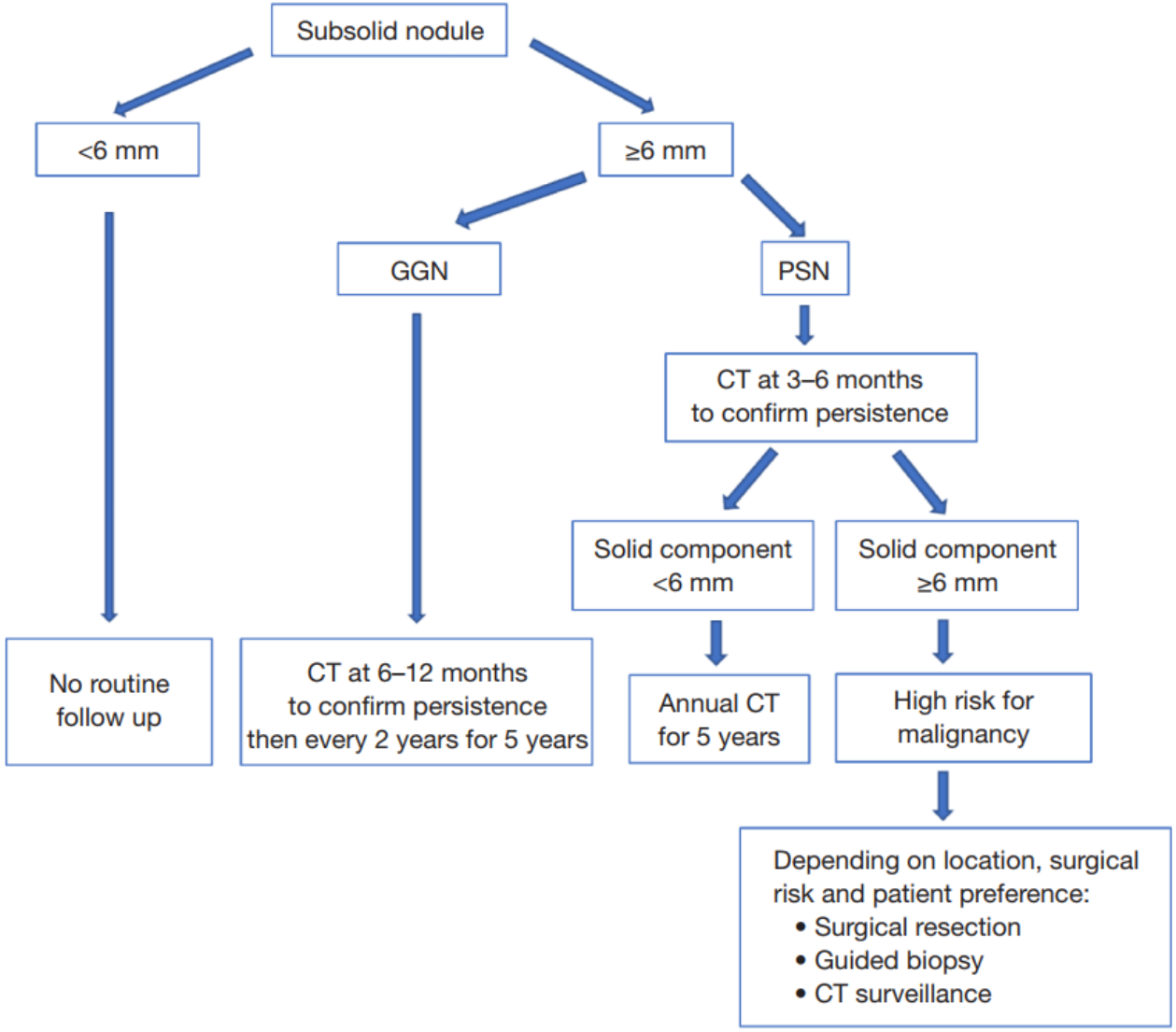
Algorithm for diagnosis of PPL

Solid nodule



Ann Transl Med. 2019 Aug;7(15):348

Part-solid nodule



Ann Transl Med. 2019 Aug;7(15):348

Upfront surgery for PPL

Indications

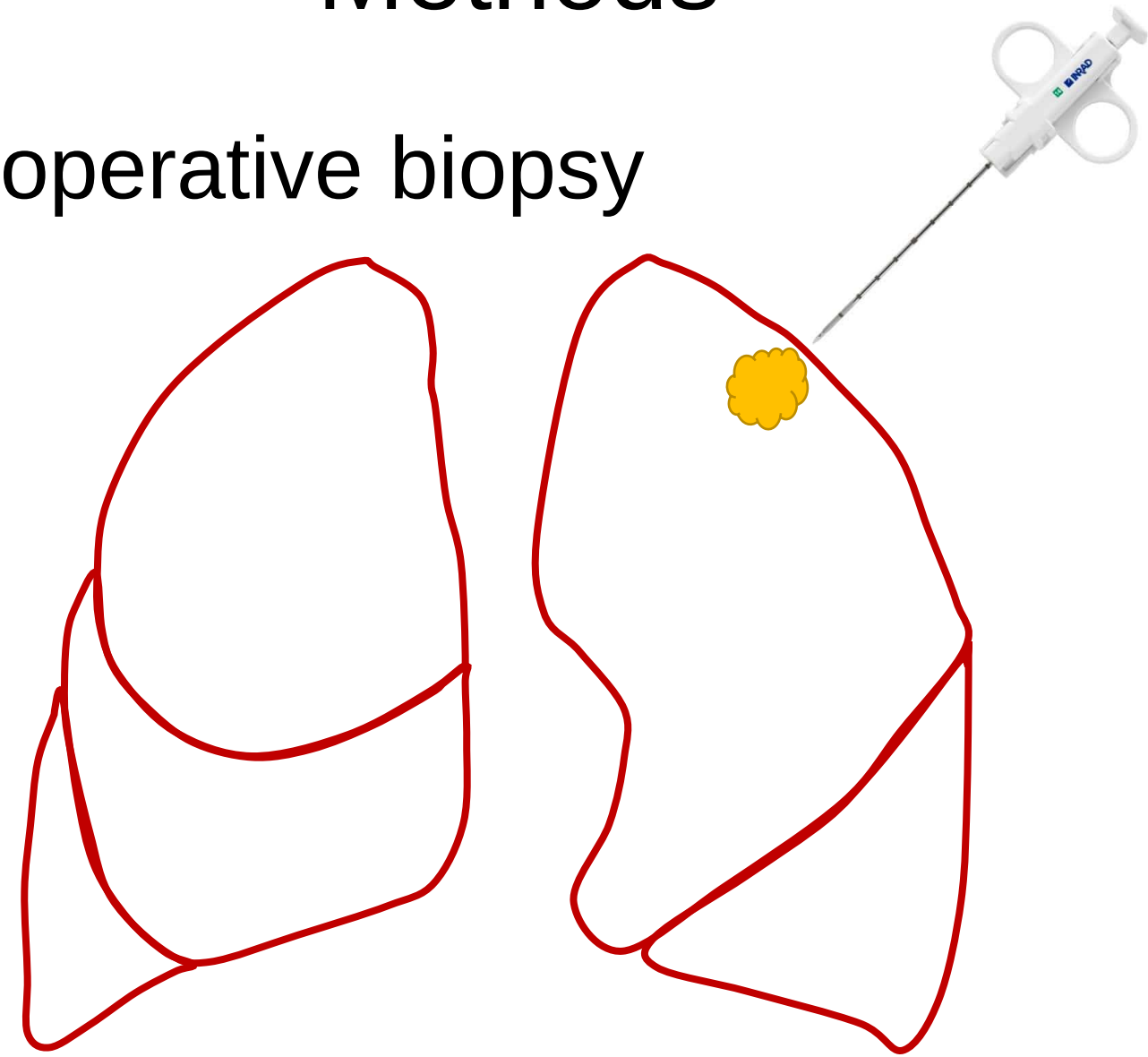
- Small nodules with malignant findings on imaging that require biopsy.
- The patient's general condition is adequate for surgery under general anesthesia.
- Lung resection is possible based on pulmonary function tests.
- The patient wants surgery.

Contraindications

- The patient's general condition is not suitable for surgery under general anesthesia.
- Pulmonary function tests indicate that resection of the lung is inappropriate.
- The patient does not want surgery.

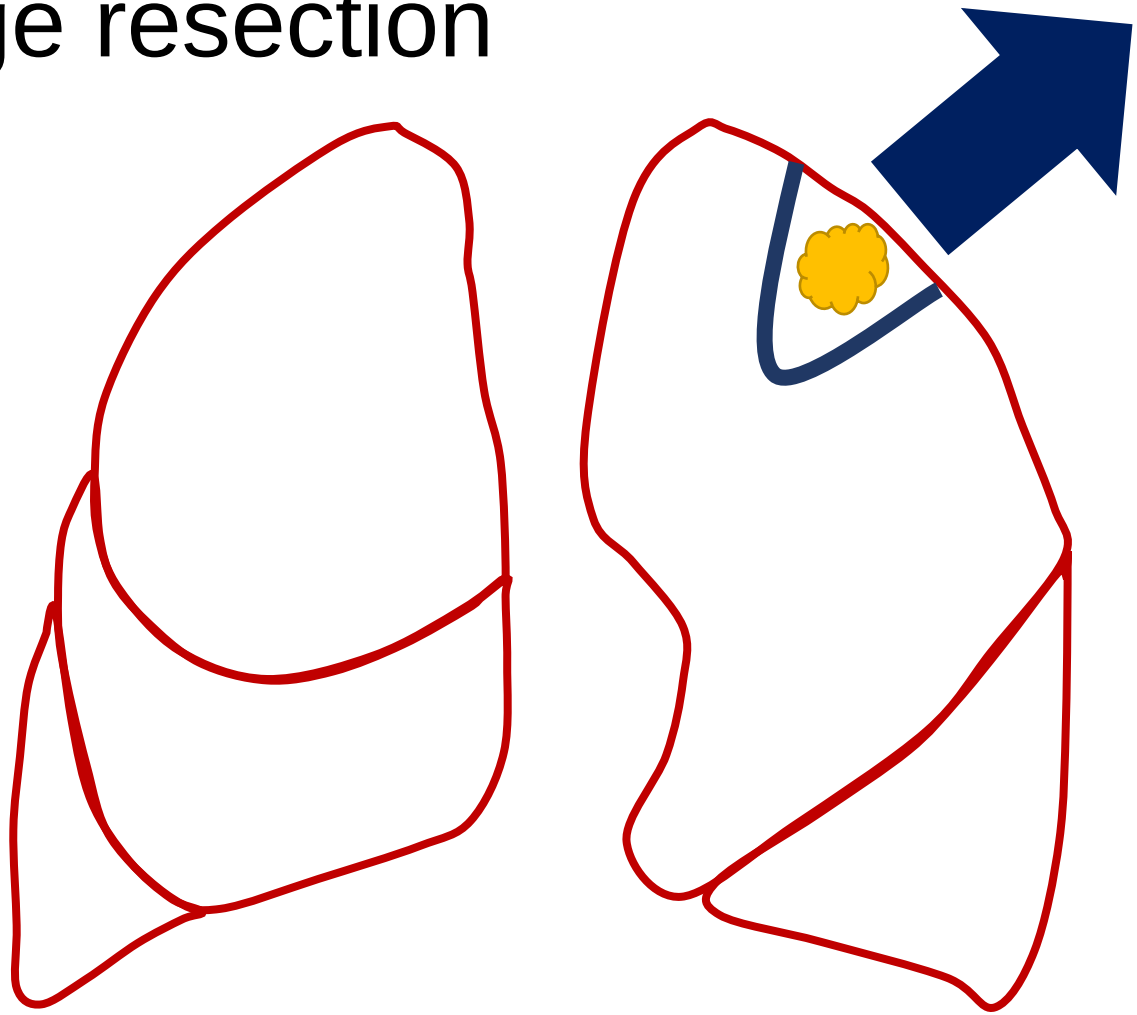
Methods

- Intra-operative biopsy



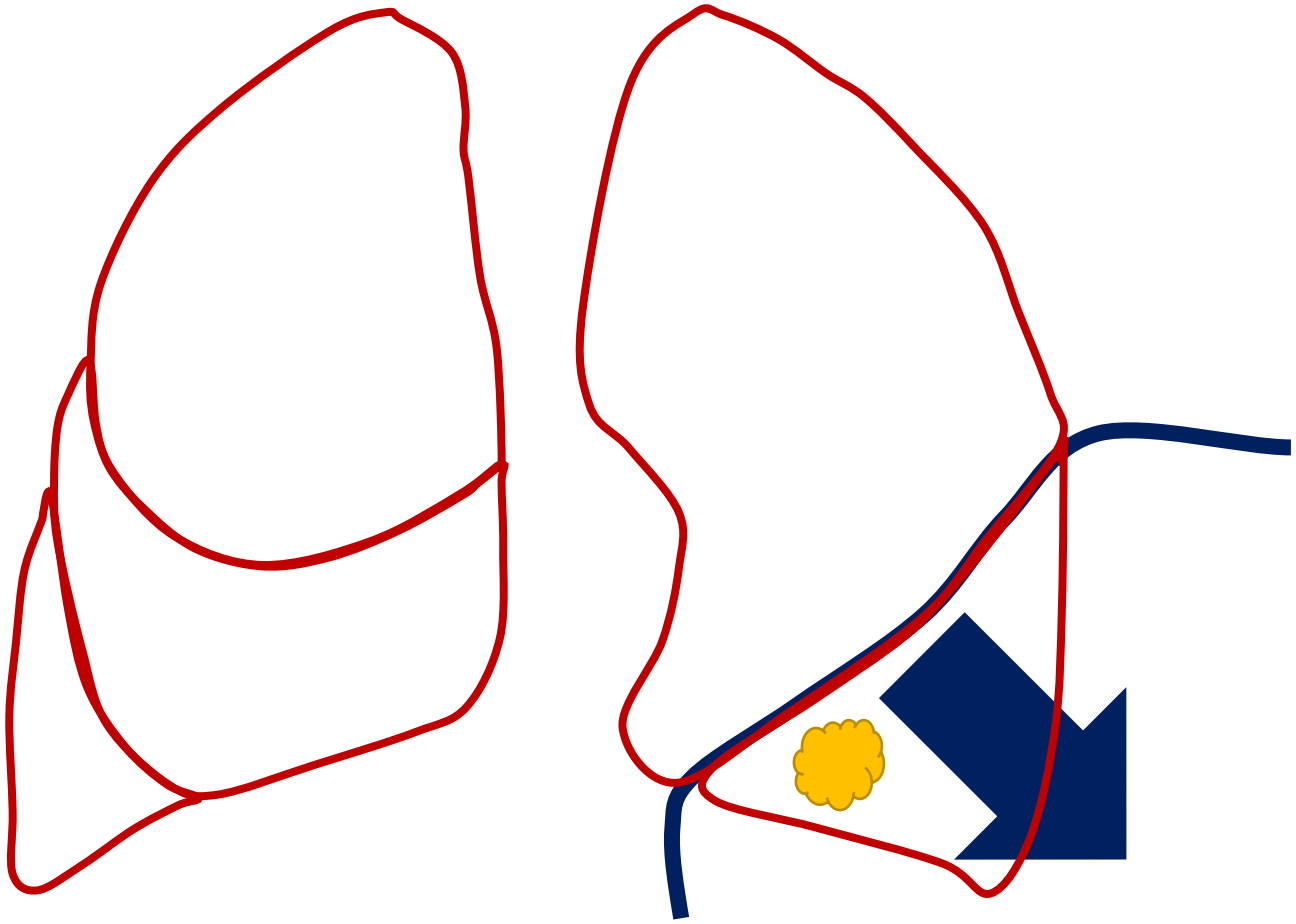
Methods

- Wedge resection



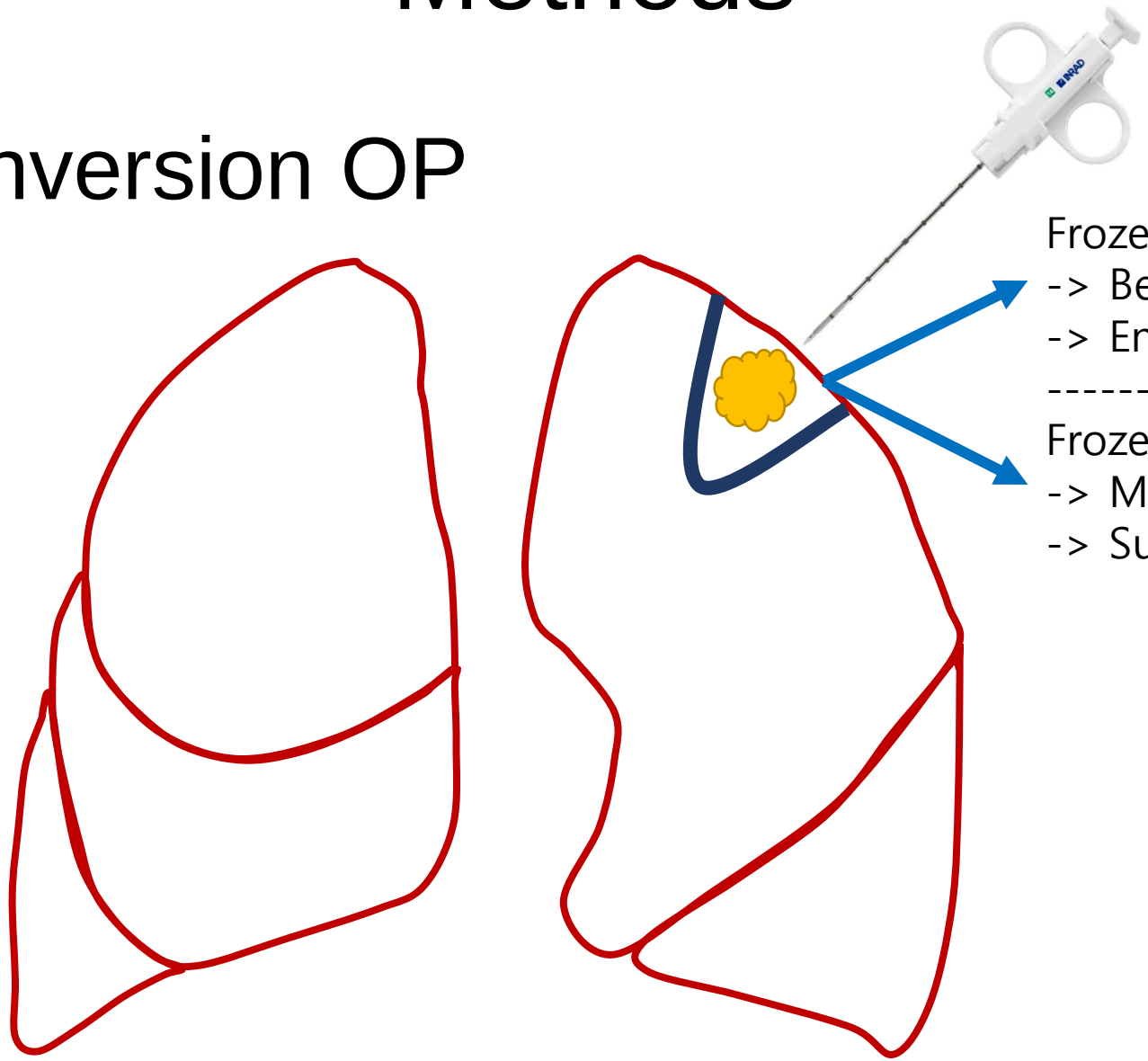
Methods

- Lobectomy



Methods

- Conversion OP



Data

- Madariaga and colleague
- 2012.10~2018.5
- Diagnostic or therapeutic resection was performed in 129 (17.2%) patients.

J Thorac Cardiovasc Surg. 2020 Apr;159(4):1558-1566.

Data

- Direct surgical resection is safe and effective in carefully selected patient.
- We only consider nodules categorized as lung-RADS 4.
- Resection of lung-RADS 4 nodules, only 4% (1/25) had benign pathology.
- Re-review of interpreted CT.
- Specific non-neoplastic diagnosis often conveys benefit.

J Thorac Cardiovasc Surg. 2020 Apr;159(4):1558-1566.

Image-guided percutaneous biopsy for PPL

Background

- PerCutaneous Needle Aspiration (PCNA)
- Percutaneous Thoracic Needle Biopsy (PTNB)
- Trans Thoracic Needle Biopsy (TTNB)

Radiol Clin N Am 56 (2018) 377–390

Indications

- Suspicious pulmonary nodules or masses seen on imaging tests.
- For patients with lesions adjacent to the lung parenchyma or pleura.
- Able to lie for more than 1 hour.

Radiol Clin N Am 56 (2018) 377–390

Contraindications

- Unresponsive to the operator's demands, such as respiratory hold.
- Reduce a patient’s suitability for PTNB include underlying acute and chronic medical conditions.
- Severe emphysema.
- Lesions adjacent to blood vessels.

Korean J Radiol 2021;22(2):263-280

Complications

- Pneumothorax
  - Incidence: about 20% (0-60%)
  - Small chest tube insertion: 1-14.2%
- Hemorrhage and hemoptysis
  - Incidence: about 11%

J Thorac Dis 2015;7(S4):S292-S299

Complications

- Air embolism
  - Air embolism in TTNA is extremely rare but can be very fatal.
    1. Placement of the needle tip in a pulmonary vein and removal of the inner stylet.
    2. Placement of the needle through both a bronchus and adjacent pulmonary vein, followed by creation of a fistula

J Thorac Dis 2015;7(S4):S292-S299

Complications

- Tumor seeding
  - Tumor seeding is an extremely rare complication.
  - Incidence: 0.012-0.061%
  - Mean time of biopsy to development of metastasis: 2.6 mo.
  - No definitive risk factors.
  - Treatment: wide en bloc resection

J Thorac Dis 2015;7(S4):S292-S299

Data

- Rivera MP. and colleague
- Meta-analysis
  - Sensitivity: 90% [CI:88-91%]
  - Specificity: 97% [CI:96-98%]
  - False positive rate: 1%
  - False negative rate: 22%
  - Non-diagnostic result should not be used to rule out malignancy.

Chest. 2013 May;143(5 Suppl):e142S-e165S.

Data

- Liu XL. and colleague
- CT-guided TTNB
- 2010.3 ~ 2015.6
- Single-centre retrospective study
- Inclusion criteria
  - Small (≤ 20mm) lung nodules
- Exclusion criteria
  - Nodule size of ≤ 5mm

J Int Med Res. 2020 Feb;48(2):300060519879006

Data

- The technical success rate: 100%.
- Sensitivity: 90% [CI:88-91%]
- Specificity: 100% [CI:96-98%]
- Positive predict value: 100%
- Negative prediec value: 78.9%
- Overall diagnostic accuracy: 92.7%

J Int Med Res. 2020 Feb;48(2):300060519879006

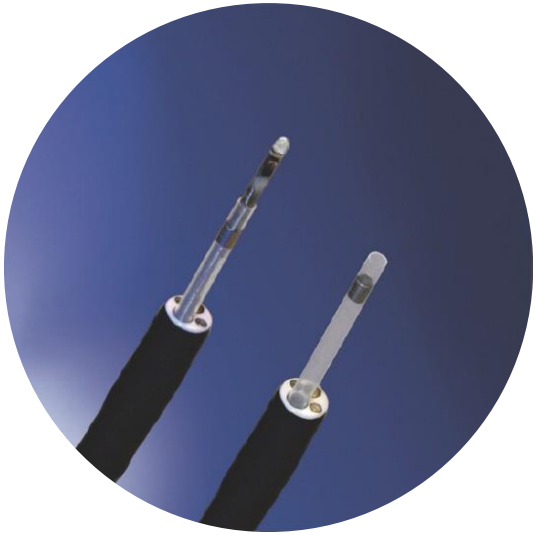
Bronchoscopy for PPL

Methods

- Radial probe endobronchial ultrasound (RP-EBUS)
- Ultrathin bronchoscopy
- Virtual bronchoscopic navigation (VBN)
- Electromagnetic navigation (EMN)

Methods

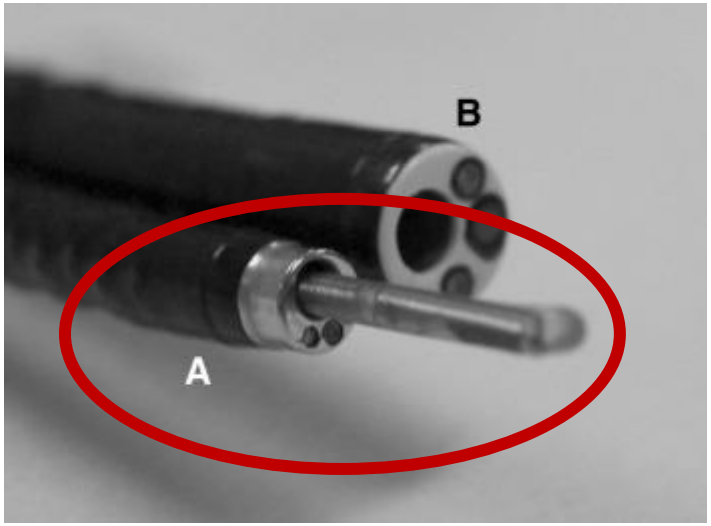
- Radial probe endobronchial ultrasound (RP-EBUS)

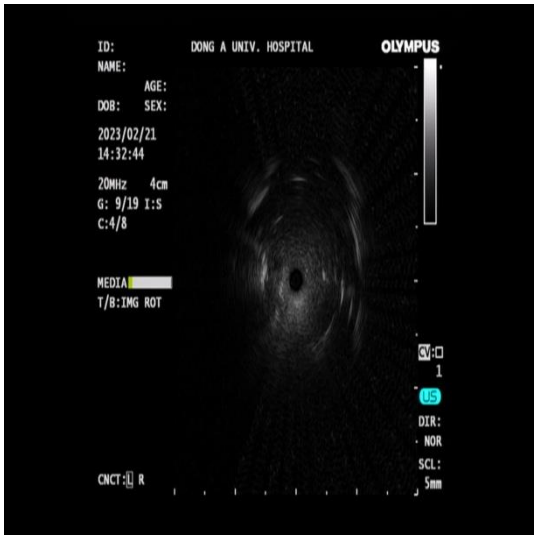


https://medical.olympuscanada.com/products/radial-ebus

Methods

- Ultrathin bronchoscopy



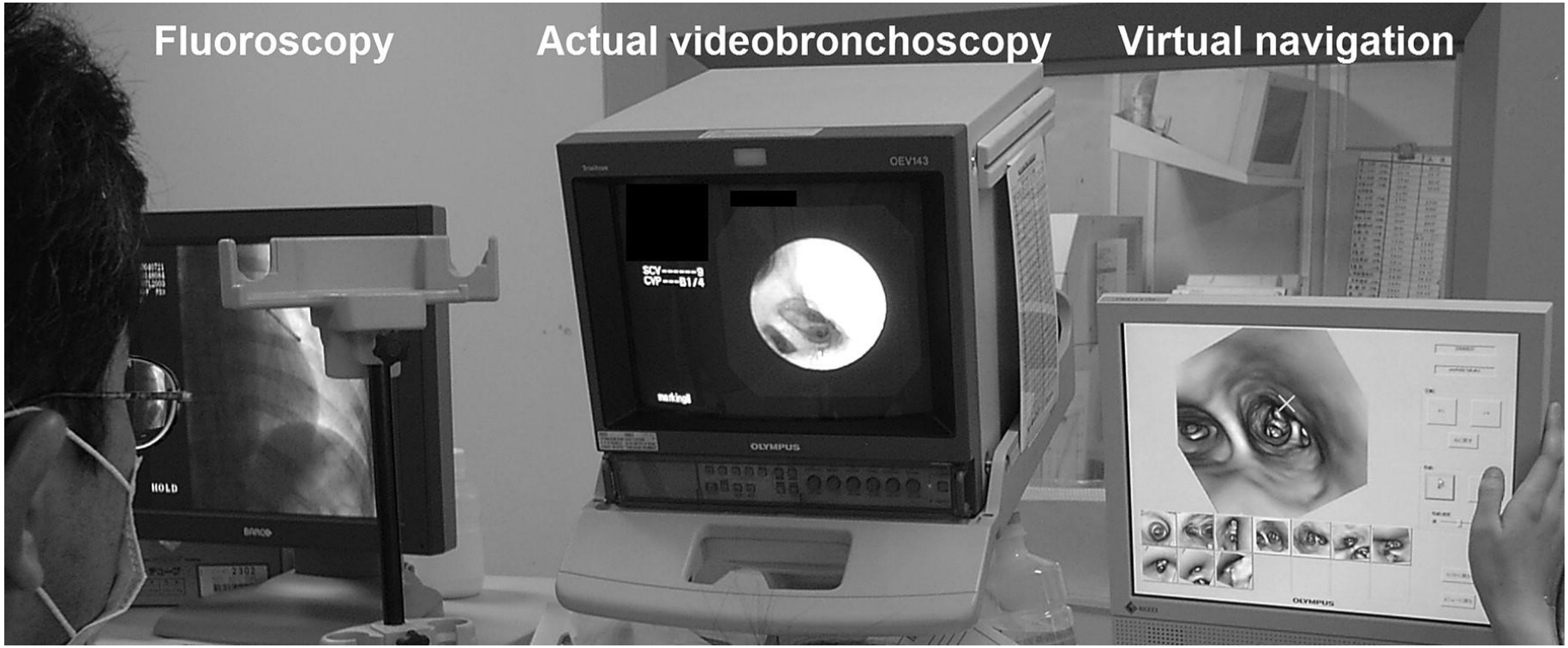


J Thorac Oncol. 2009 Oct;4(10):1274-7.

https://medical.olympuscanada.com/products/radial-ebus

Methods

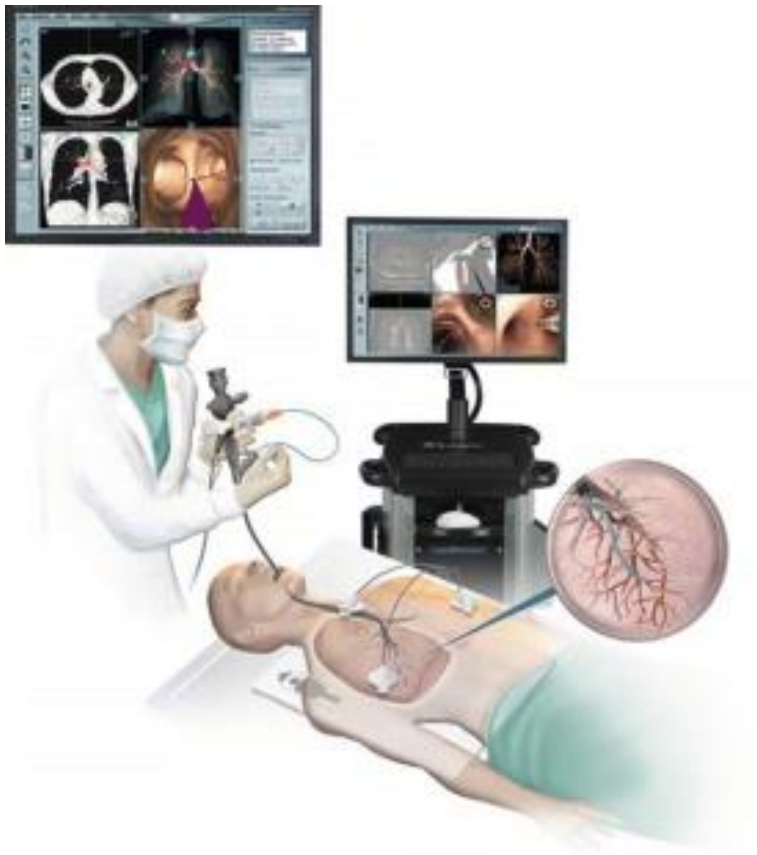
- Virtual bronchoscopic navigation (VBN)



Thorax 2011;66:1072e1077

Methods

- Electromagnetic navigation (EMN)



Interventions in Pulmonary Medicine pp 281–297

Data (EBUS-TBLB vs PCNA)

	EBUS-TBLB	PCNA
Sensitivity (%) [95% CI]	69 [67-71]	94 [94-95]
Complication rate (Severe bleeding,%)	0.087	0.32
Complication rate (Pneumothorax,%)	0.48	1.09

Transl Lung Cancer Res 2017;6(1):23-34

Data (TBLB ± VBN)

- Kato A. and colleague
- 2011.11~2014.11
- Single center, prospective
- 100 patients
- Patients with small PPL (<20 mm in diameter)

Respirology. 2018 Nov;23(11):1049-1054.

Data (TBLB ± VBN)

	VBN+	VBN-	*P* value
Diagnostic yield (%)	84	58	0.013
Biopsy number (n)	3.54 ± 1.07	2.98 ± 1.06	0.01

Respirology. 2018 Nov;23(11):1049-1054.

Data (ENB)

- Folch EE. and colleague
- 2011.11~2014.11
- Meta-analysis
- Forty studies with a total of 3,342 participants.

Chest. 2020 Oct;158(4):1753-1769.

Data (ENB)

	EMN
Sensitivity (%,[95% CI])	76 [74 - 78]
Specificity (%,[95% CI])	100 [99 – 100]

Chest. 2020 Oct;158(4):1753-1769.

Data (ENB)

- Although different navigation systems were used, similar sensitivities were reported.
- ENB is very safe with good sensitivity for diagnosing malignancy in patients with PPLs.

Chest. 2020 Oct;158(4):1753-1769.

Data (VBN assist)

- Giri M. and colleague
- ~2020.8
- Meta-analysis
- Six RCTs with 1626 patients were included.

Ther Adv Respir Dis. 2021 Jan-Dec;15:17534666211017048.

Data (VBN assist)

	VBNA	NVBNA	*P* value
Pooled diagnostic yield (%,[95% CI])	74.17 [77.4 – 82.0]	69.51 [67.5-79.9]	0.13

Ther Adv Respir Dis. 2021 Jan-Dec;15:17534666211017048.

Data (VBN assist)

- VBNA group, the total examination time was significantly shorter (MD=−3.94min, p=0.003)

- VBNA had superior diagnostic yield than NVBNA for PPLs ≤ 20mm (RR=1.18, 95% CI: 1.05–1.32).

Ther Adv Respir Dis. 2021 Jan-Dec;15:17534666211017048.

Data (EBUS-GS±ENB)

- Zheng X. and colleague
- 2018.7~2019.10
- Prospective, multicenter, randomized controlled clinical trial
- 385 patients
- Presence of PPNs suspicious for malignancy (8≤ PPN ≤30 mm in diameter)

Ann Am Thorac Soc. 2022 Oct;19(10):1730-1739.

Data (EBUS-GS±ENB)

	ENB+GS	GS only	*P* value
Diagnostic yield (%,[95% CI])	82.7 [77.4 – 82.0]	73.7 [67.5-79.9]	0.03
Malignant nodule diagnostic yields (%)	90.3	78.7	0.009
Time to find lesions (sec)	213.2 ± 145.6	264.8 ± 189.5	0.003

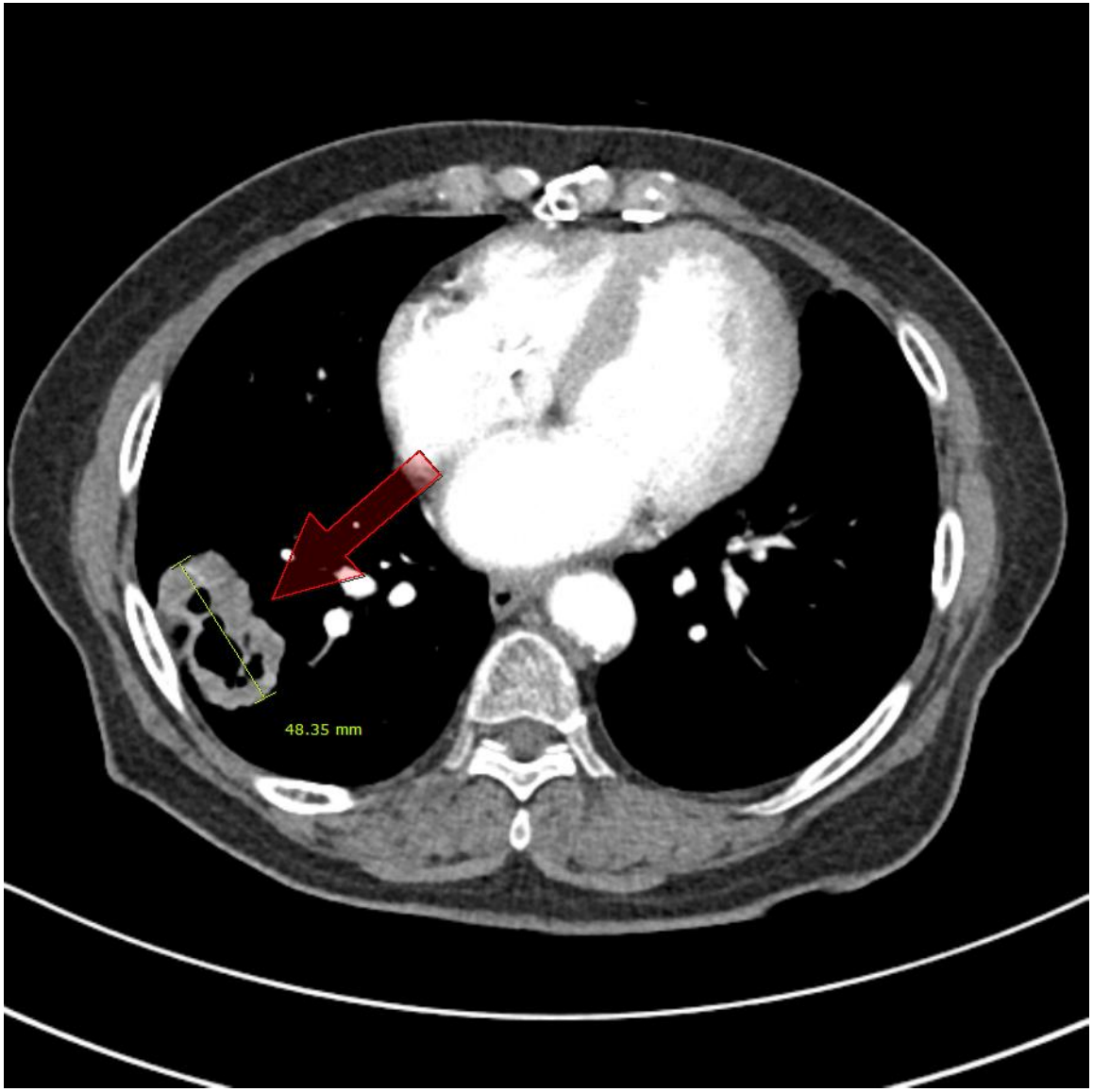
Ann Am Thorac Soc. 2022 Oct;19(10):1730-1739.

Case Presentations

Case presentation (1)

- Female
- 80 years old
- Current smoker 1PPD for 60yrs
- Incidental lung nodule
- s/p CABG d/t CAOD
- s/p Pacemaker implantation d/t complete AV block

Case presentation (1)



Case presentation (1)

- Which diagnostic method did you choose?
  1. PET-CT
  2. Radial probe EBUS
  3. Image guided needle biopsy
  4. VATS wedge resection
  5. Image f/u

Background

- Lung-RADS

Solid nodule		
Size	**Timing/Change**	**Cat.**
<6 mm	Baseline	2
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6-8 mm	Baseline	3
	No change	2
	Growing	4A
	New	4A
8-15 mm	Baseline	4A
	No change	2
	Growing	4B
	New	4B
≥15 mm	Baseline	4B
	No change	2
	Growing	4B
	New	4B

Part solid nodule		
Size	**Timing/Change**	**Cat.**
<6 mm	Baseline	2
	No change	2
	Growing (solid <4 mm)	4A
	Growing(solid 4-6 mm)	4B
	New	3
≥6 mm (solid <6 mm)	Baseline	3
	No change	2
	Growing (solid <4 mm)	4A
	Growing (solid 4-6 mm)	4B
	New (solid <4 mm)	4A
	New (solid 4-6 mm)	4B
≥6 mm (solid 6-8 mm)	Baseline	4A
	No change	2
	Growing	4B
	New	4B
≥8 mm (solid ≥8 mm)	Baseline	4B
	No change	2
	Growing	4B
	New	4B

Ground glass nodule		
Size	**Timing/Change**	**Cat.**
<20 mm	Baseline	2
	No change	2
	Growing	2
	New	2
≥20 mm	Baseline	3
	No change	2
	Growing	2
	New	3

Other	**Cat.**
Endobronchial nodule	4A
Cat. 3,4+additional finding ; Consolidation, atelectasis, lymph node enlargement, other (spiculation, etc.)	4X
Other clinically significant findings	S
Prior lung cancer	C

Category	**Description**	**Prob.cancer**	**Manage**
0	Incomplete	Not evaluable	Additional LDCT images and/or comparison to prior chest CT images
1	Negative	< 1%	Continue annual screening with LDCT in 12 months
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3	Probably benign	1-2%	Follow up LDCT in 6 months
4A	Suspicious	5-15%	Follow up LDCT in 3 months, PET-CT may be used when there is a solid ≥8mm
4B, X	Very suspicious	> 15%	Immediate chest CT, consider biopsy, PET-CT may be used

대한내과학회지: 제 95 권 제 2 호 2020

Case presentation (1)

- The patient's disadvantage
  - Poor physical performance
  - Not so good pulmonary function test result
  - Many concomitant disease

⇒ Diagnosis with radial probe EBUS

Case presentation (1)

- Radial probe-EBUS

PATHOLOGICAL DIAGNOSIS

Lung, lower lobe, right, EBUS-guided transbronchial lung biopsy:

SQUAMOUS CELL CARCINOMA

(Immunohistochemical stain)

Block A	p63	Positive
Block A	CD56	Negative
Block A	TTF-1	Negative

Case presentation (1)

- PET-CT

Case presentation (1)

- Expected clinical stage
  - T3N0M0, Stage IIB
  - VATS RLLobectomy/c MLND

Case presentation (1)

- VATS RLLobectomy/c MLND

PATHOLOGICAL DIAGNOSIS

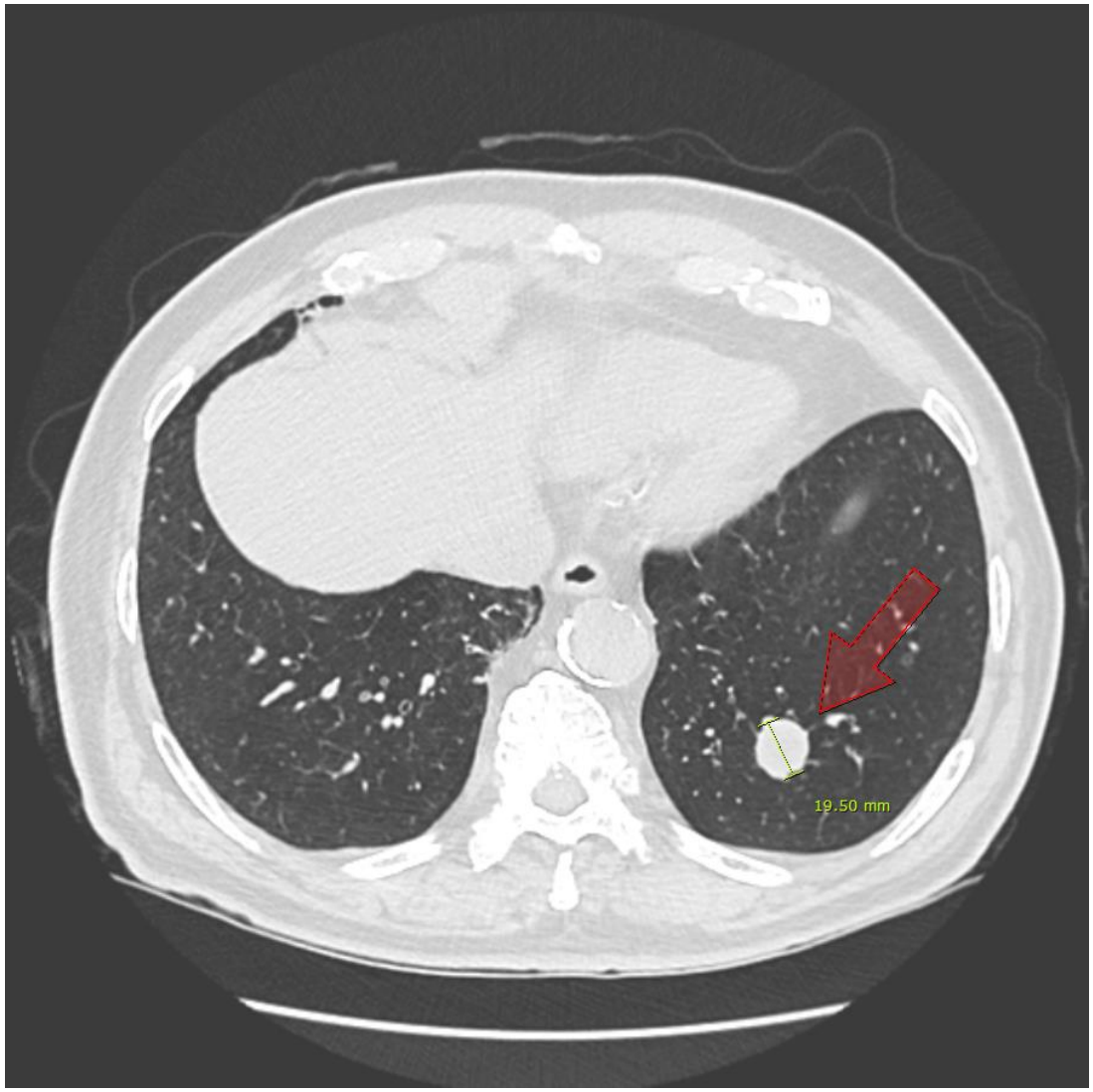
Lung, lower lobe, right, VATS lobectomy:
1. Location: RLL
2. Histologic type:
   SQUAMOUS CELL CARCINOMA, non-keratinizing type
3. pT stage: pT3 (by 8th AJCC staging system)
   1) Tumor size: 5.4x4.7cm
   2) Involvement of pleura:
      No involvement of visceral pleura (PL0)
   3) Involvement of main bronchus (-)
   4) Tumor focality: Unifocal
   5) Direct invasion of adjacent structure (-)
   6) Tumor-associated findings: Not identified
4. pN stage (Lymph node metastasis)
   No tumor (0/30) (pN0)
   1) Peribronchial (0/1)
   2) LN No.2R (0/8)
   3) LN No.4R (0/4)
   4) LN No.7 (0/8)
   5) LN No.8 (0/1)
   6) LN No.10 (0/4)
   7) LN No.11I (0/1)
   8) LN No.11S (0/1)
   9) LN No.12M (0/1)
   10) LN No.12U (0/1)
5. Resection margin:
   Free from carcinoma
   (safety margin: bronchial 4.3cm)
6. Lymphatic invasion: Not identified
7. Venous invasion: Not identified

T3N0M0 (stage IIB)

Case presentation (2)

- Male
- 73 years old
- Current smoker 1PPD for 60yrs
- Incidental lung nodule
- No previous medical history

Case presentation (2)



Case presentation (2)

- Which diagnostic method did you choose?
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- Lung-RADS

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Part solid nodule		
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	New	3
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	No change	2
	Growing (solid <4 mm)	4A
	Growing (solid 4-6 mm)	4B
	New (solid <4 mm)	4A
	New (solid 4-6 mm)	4B
≥6 mm (solid 6-8 mm)	Baseline	4A
	No change	2
	Growing	4B
	New	4B
≥8 mm (solid ≥8 mm)	Baseline	4B
	No change	2
	Growing	4B
	New	4B

Ground glass nodule		
Size	**Timing/Change**	**Cat.**
<20 mm	Baseline	2
	No change	2
	Growing	2
	New	2
≥20 mm	Baseline	3
	No change	2
	Growing	2
	New	3

Other	Cat.
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0	Incomplete	Not evaluable	Additional LDCT images and/or comparison to prior chest CT images
1	Negative	< 1%	Continue annual screening with LDCT in 12 months
2, 2b[a]	Benign	< 1%	Continue annual screening with LDCT in 12 months
3	Probably benign	1-2%	Follow up LDCT in 6 months
4A	Suspicious	5-15%	Follow up LDCT in 3 months, PET-CT may be used when there is a solid ≥8mm
4B, X	Very suspicious	> 15%	Immediate chest CT, consider biopsy, PET-CT may be used

대한내과학회지: 제 95 권 제 2 호 2020

Case presentation (2)

- The patient strongly desires surgery
- The patient's advantage
  - Good physical performance
  - Good pulmonary function test result
  - No concomitant disease
  - Expected to be low stage

⇒ Diagnosis and treatment with surgery

Case presentation (2)

- VATS wedge resection convert to lobectomy/c MLND

PATHOLOGICAL DIAGNOSIS

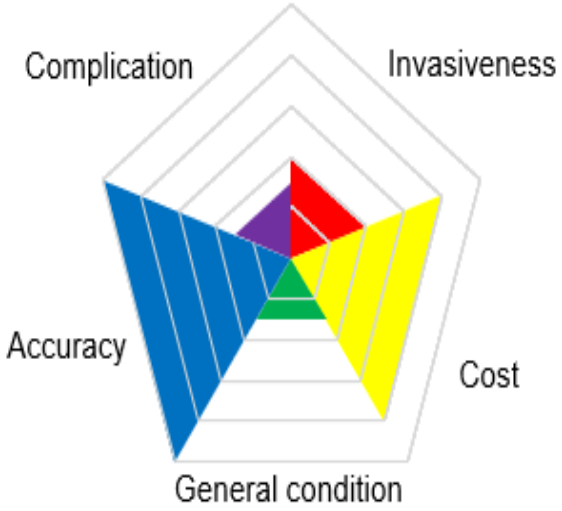
Lung, lower lobe, left, VATS lobectomy:
1. Location: LLL
2. Histologic type: SQUAMOUS CELL CARCINOMA, keratinizing type
3. pT stage: pT1c (by 8th AJCC staging system)
   1) Tumor size: 2.6x2cm
   2) Involvement of pleura:
      No involvement of visceral pleura (PL0)
   3) Involvement of main bronchus (-)
   4) Tumor focality: Unifocal
   5) Direct invasion of adjacent structure (-)
   6) Tumor-associated findings: Not identified
4. pN stage (Lymph node metastasis)
   No tumor (0/9) (pN0)
   1) Hilar (frozen) (0/1)
   2) Peribronchial (0/1)
   3) Hilar (0/1)
   4) Paraaortic (0/2)
   5) Subcarinal (0/3)
   6) Subaortic (0/1)
5. Resection margin:
   Free from carcinoma
   (safety margin: bronchial 7.5cm)
6. Lymphatic invasion: Not identified
7. Venous invasion: Not identified
8. Perineural invasion: Not identified
9. Spread through air spaces: Not identified
10. Distant metastasis: Not applicable
11. Separate lesion: Not identified

T1cN0M0 (stage IA3)

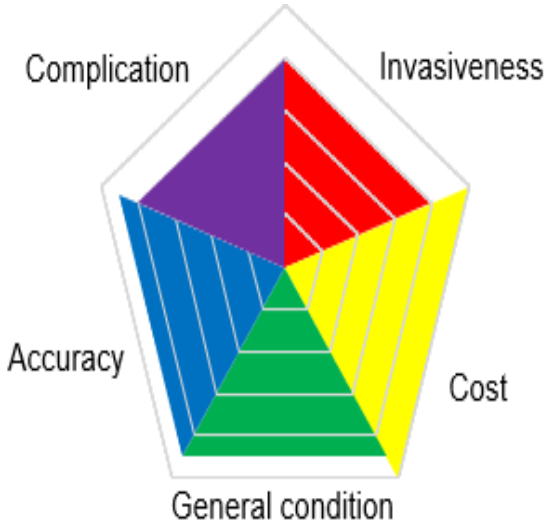
Conclusion

Conclusion

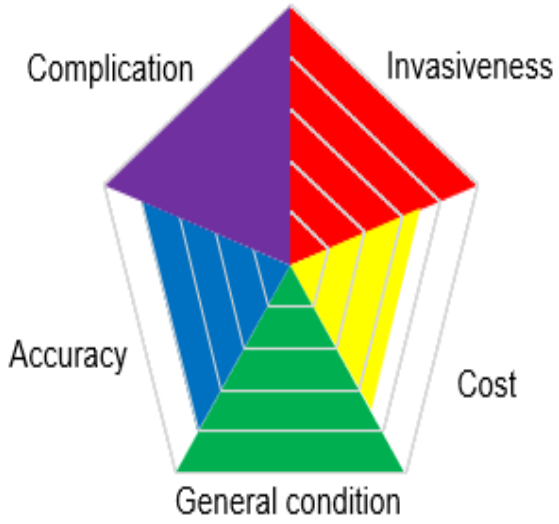
Upfront surgery



PCNA



Bronchoscopic modality



경청해주셔서 감사합니다.