UC San Diego Health

Lung Cancer: Multidisciplinary Approach and Systemic Treatments

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No Disclosures

New 9th Edition lung cancer staging

8th Edition TNM Categories

T/M	Label	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a Inv	IB	IIB	IIIA	IIIB
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 Inv	IIB	IIIA	IIIB	IIIC
	T3 Same Lobe Nod	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 Inv	IIIA	IIIA	IIIB	IIIC
	T4 Ipsi Nod	IIIA	IIIA	IIIB	IIIC
M1	M1a Pl Dissem	IVA	IVA	IVA	IVA
	M1a Contr Nod	IVA	IVA	IVA	IVA
	M1b Single Les	IVA	IVA	IVA	IVA
	M1c Mult Les	IVB	IVB	IVB	IVB

9th Edition TNM Categories

T/M	Description	N0	N1	N2		N3
				N2a	**N2b**	
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ≤3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 >5 to ≤7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Same lobe tumor nodule	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral tumor nodule	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Pleural/pericardial dissemination	IVA	IVA	IVA	IVA	IVA
	M1a Contralateral tumor nodule	IVA	IVA	IVA	IVA	IVA
	M1b Single extrathoracic lesion	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple lesions, 1 organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple lesions, >1 organ system	IVB	IVB	IVB	IVB	IVB

Results: N2 is subdivided into single- and multistation N2, and M1c is subdivided into single- and multiorgan system M1c, resulting in a rearrangement of T and N categories included in the stage groups IIA, IIB, IIIA, and IIIB.

Lung Cancer Screening

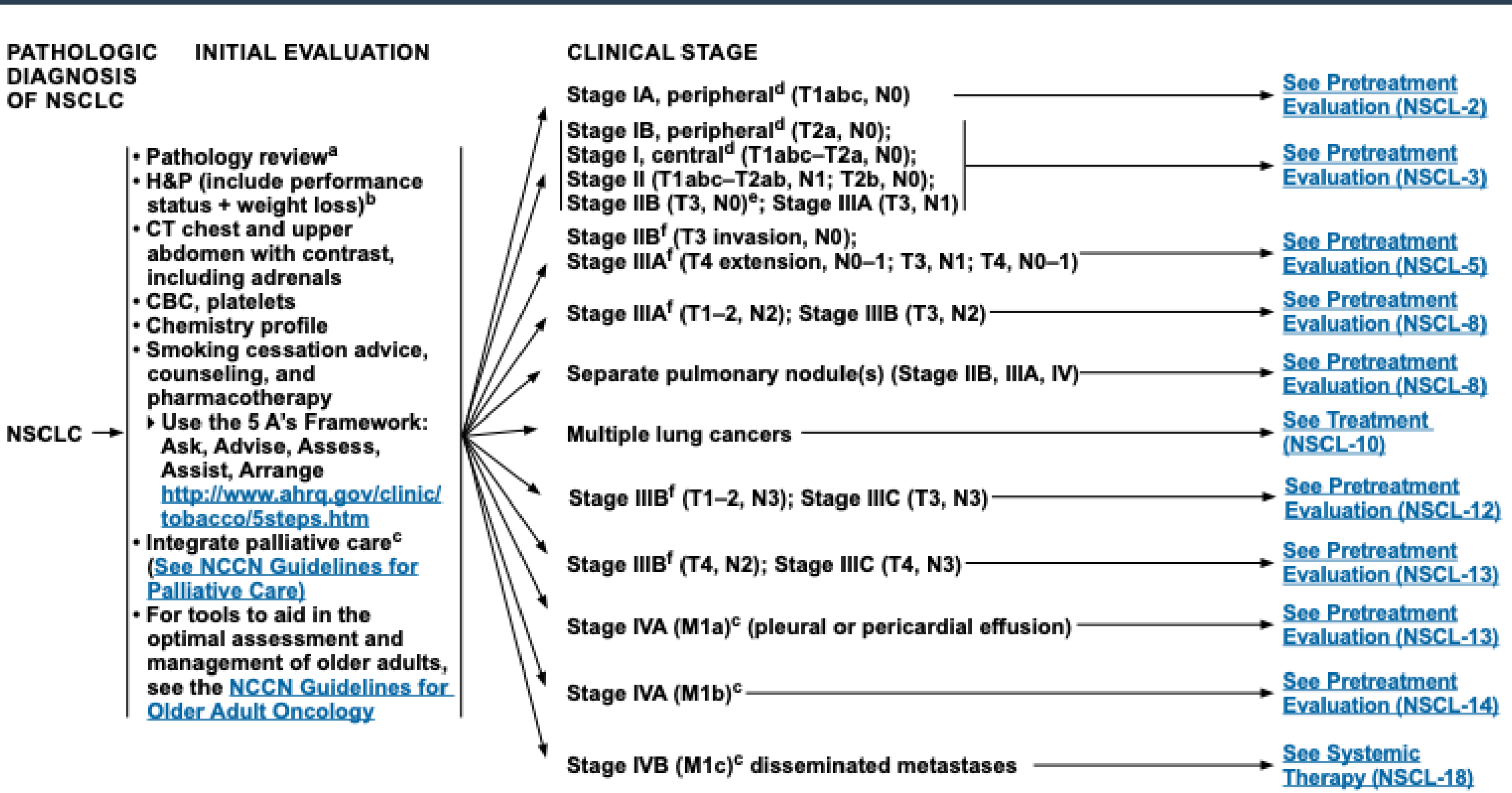
Summary Statement

Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	1. Annual screening for lung cancer with low-dose computed tomography (LDCT) 2. Adults aged 50 to 80 years 3. have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. 4. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

LDCT Reporting based on Lung Rads

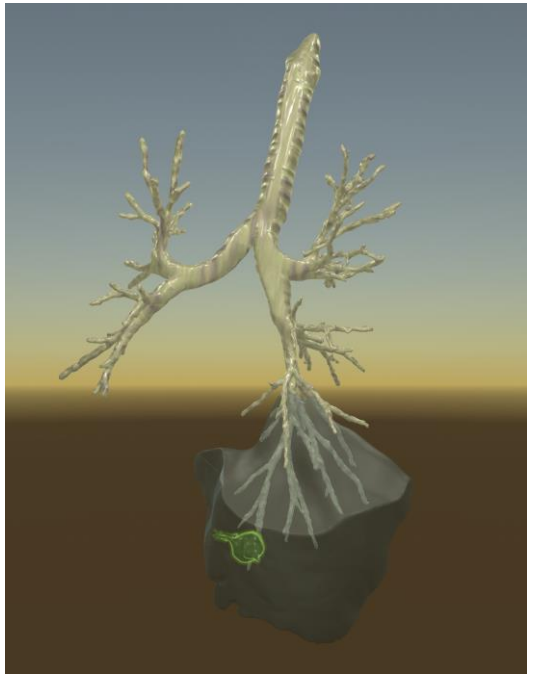
Refer at 8mm

3	**Probably Benign** Based on imaging features or behavior Estimated Population Prevalence: 9%	**Solid nodule:** • ≥ 6 to < 8 mm (≥ 113 to < 268 mm³) at baseline **OR** • New 4 mm to < 6 mm (34 to < 113 mm³)	6-month LDCT
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm³) with solid component < 6 mm (< 113 mm³) at baseline **OR** • New < 6 mm total mean diameter (< 113 mm³)	
		Non solid nodule (GGN): • ≥ 30 mm (≥ 14,137 mm³) at baseline or new	
		Atypical pulmonary cyst: (see note 12) • Growing cystic component (mean diameter) of a thick-walled cyst	
		Category 4A lesion that is stable or decreased in size at 3-month follow-up CT (excluding airway nodules)	
4A	**Suspicious** Estimated Population Prevalence: 4%	**Solid nodule:** • ≥ 8 to < 15 mm (≥ 268 to < 1,767 mm³) at baseline **OR** • Growing < 8 mm (< 268 mm³) **OR** • New 6 to < 8 mm (113 to < 268 mm³)	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm³) solid nodule or solid component
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm³) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm³) at baseline **OR** • New or growing < 4 mm (< 34 mm³) solid component	
		Airway nodule, segmental or more proximal - at baseline (see note 11)	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst **OR** • Multilocular cyst at baseline **OR** • Thin- or thick-walled cyst that becomes multilocular	
4B	**Very Suspicious** Estimated Population Prevalence: 2%	**Airway nodule,** segmental or more proximal - stable or growing (see note 11)	Referral for further clinical evaluation
		Solid nodule: • ≥ 15 mm (≥ 1767 mm³) at baseline **OR** • New or growing ≥ 8 mm (≥ 268 mm³)	Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm³) solid nodule or solid component; tissue sampling; and/or referral for further clinical evaluation Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)
		Part solid nodule: • Solid component ≥ 8 mm (≥ 268 mm³) at baseline **OR** • New or growing ≥ 4 mm (≥ 34 mm³) solid component	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst with growing wall thickness/nodularity **OR** • Growing multilocular cyst (mean diameter) **OR** • Multilocular cyst with increased loculation or new/increased opacity (nodular,ground glass, or consolidation)	
		Slow growing solid or part solid nodule that demonstrates growth over multiple screening exams (see note 8)	
4X	Estimated Population Prevalence: < 1%	Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)	

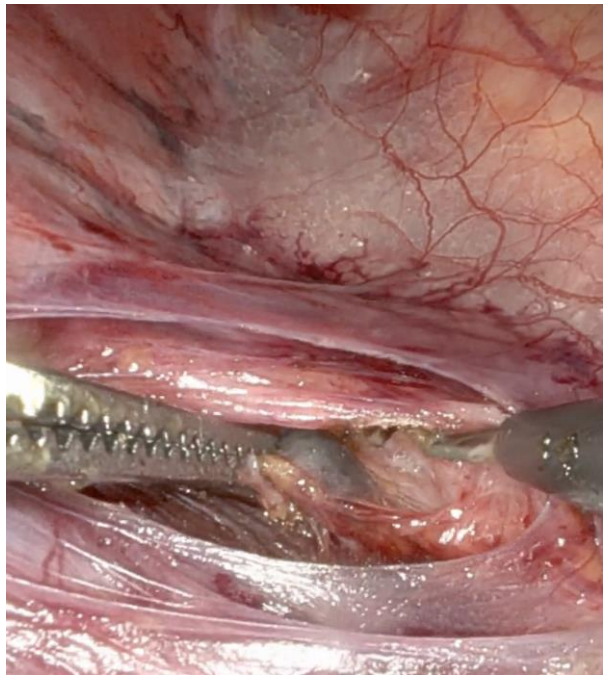

PATHOLOGIC DIAGNOSIS OF NSCLC
INITIAL EVALUATION
NSCLC
• Pathology review[a]
• H&P (include performance status + weight loss)[b]
• CT chest and upper abdomen with contrast, including adrenals
• CBC, platelets
• Chemistry profile
• Smoking cessation advice, counseling, and pharmacotherapy
‣ Use the 5 A's Framework: Ask, Advise, Assess, Assist, Arrange http://www.ahrq.gov/clinic/tobacco/5steps.htm
• Integrate palliative care[c] (See NCCN Guidelines for Palliative Care)
• For tools to aid in the optimal assessment and management of older adults, see the NCCN Guidelines for Older Adult Oncology
CLINICAL STAGE
Stage IA, peripheral[d] (T1abc, N0)
See Pretreatment Evaluation (NSCL-2)
Stage IB, peripheral[d] (T2a, N0);
Stage I, central[d] (T1abc–T2a, N0);
Stage II (T1abc–T2ab, N1; T2b, N0);
Stage IIB (T3, N0)[e]; Stage IIIA (T3, N1)
See Pretreatment Evaluation (NSCL-3)
Stage IIB[f] (T3 invasion, N0);
Stage IIIA[f] (T4 extension, N0–1; T3, N1; T4, N0–1)
See Pretreatment Evaluation (NSCL-5)
Stage IIIA[f] (T1–2, N2); Stage IIIB (T3, N2)
See Pretreatment Evaluation (NSCL-8)
Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)
See Pretreatment Evaluation (NSCL-8)
Multiple lung cancers
See Treatment (NSCL-10)
Stage IIIB[f] (T1–2, N3); Stage IIIC (T3, N3)
See Pretreatment Evaluation (NSCL-12)
Stage IIIB[f] (T4, N2); Stage IIIC (T4, N3)
See Pretreatment Evaluation (NSCL-13)
Stage IVA (M1a)[c] (pleural or pericardial effusion)
See Pretreatment Evaluation (NSCL-13)
Stage IVA (M1b)[c]
See Pretreatment Evaluation (NSCL-14)
Stage IVB (M1c)[c] disseminated metastases
See Systemic Therapy (NSCL-18)

Quality Metrics to Obtain Optimal Survival and Quality of Life

Name it

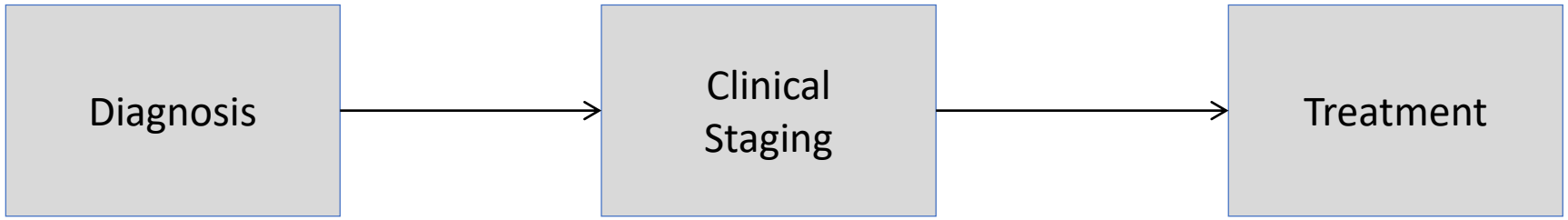


Stage it



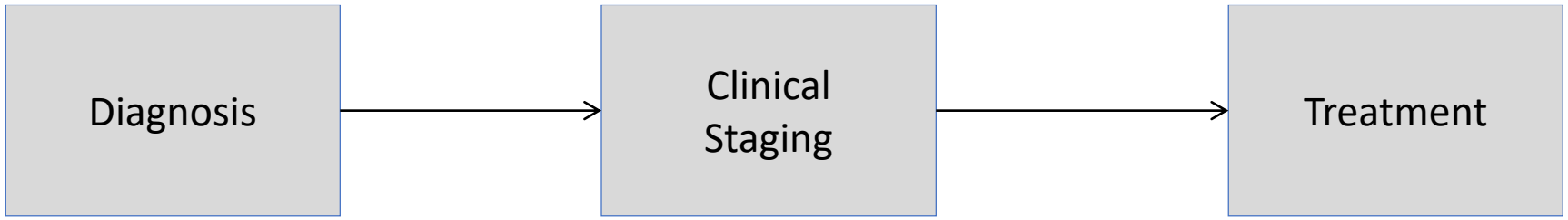
Treat it

Approach



- Transthoracic Needle Biopsy
- Bronchoscopy/EBUS - Robotic
- Surgical Biopsy (wedge resection)

Clinical Staging



Imaging

- CT Chest
- PET/CT
- Brain MRI (Stage II and greater +/- Stage Ib)

Lymph Node Assessment

- Mediastinoscopy
- Endobronchial Ultrasound (EBUS)
- EUS
- Anterior Mediastinotomy (Chamberlain)
- Navigational Bronchoscopy
- VATS

Lymph node assessment

- Z0050 trial
  - 303 patients had PET after routine staging
  - NPV of PET for mediastinal involvement: 87%
  - False positive rate: 43%

TABLE 3. Lymph node status comparing PET with final stage (all eligible patients; n = 302)*

	Final stage (No. patients)		
By PET	**N0/N1**	**N2/N3**	**Total**
N0/N1	191	29	220
N2/N3	36	46	82
Total	227	75	302

PPV, Positive predictive value; *NPV,* negative predictive value.
*Final stage equals nodal stage as determined radiographically or pathologically, including patients who did not have nodal status confirmed with biopsy, mediastinoscopy, or surgical resection. For N2/N3 disease: sensitivity = 61%; specificity = 84%; PPV = 56%; NPV = 87%.

Lymph node staging indication

- Selective approach is considered standard of care
- T2 (>3cm) or larger
- Pathologically enlarged lymph nodes > 1cm in short axis on CT
- Mediastinal or Hilar lymph nodes with PET SUV >2.5
- Centrally located tumors

Supraclavicular zone

- **1** Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes

Upper zone

- **2R** Upper Paratracheal (right)
- **2L** Upper Paratracheal (left)
- **3a** Pre-vascular
- **3p** Retrotracheal
- **4R** Lower Paratracheal (right)
- **4L** Lower Paratracheal (left)

Aortic Nodes

AP zone

- **5** Subaortic
- **6** Para-aortic (ascending aorta or phrenic)

Inferior Mediastinal Nodes

Subcarinal zone

- **7** Subcarinal

Lower zone

- **8** Paraesophageal (below carina)
- **9** Pulmonary ligament

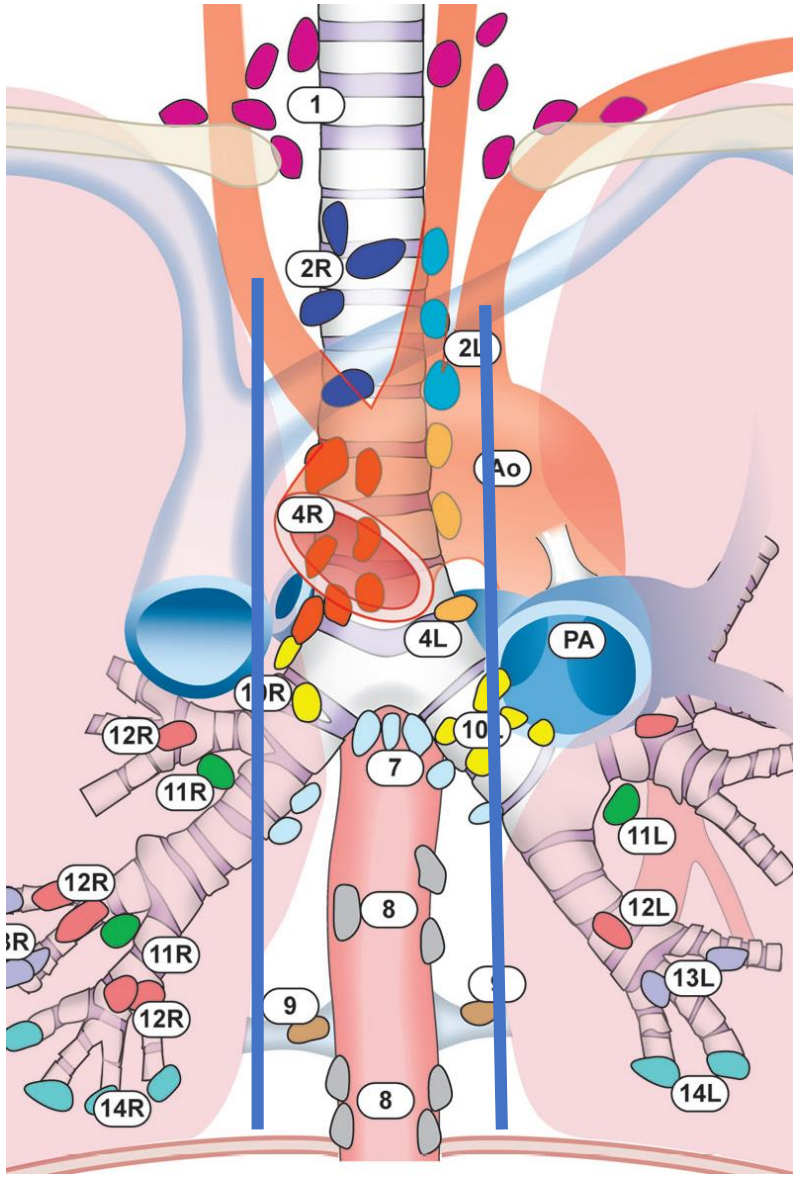
N_1 Nodes

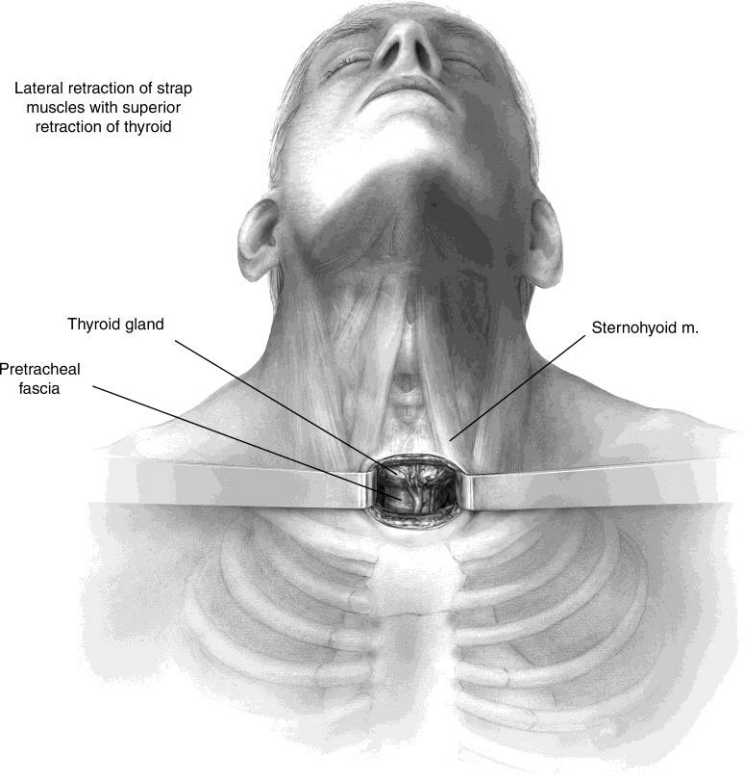
Hilar/Interlobar zone

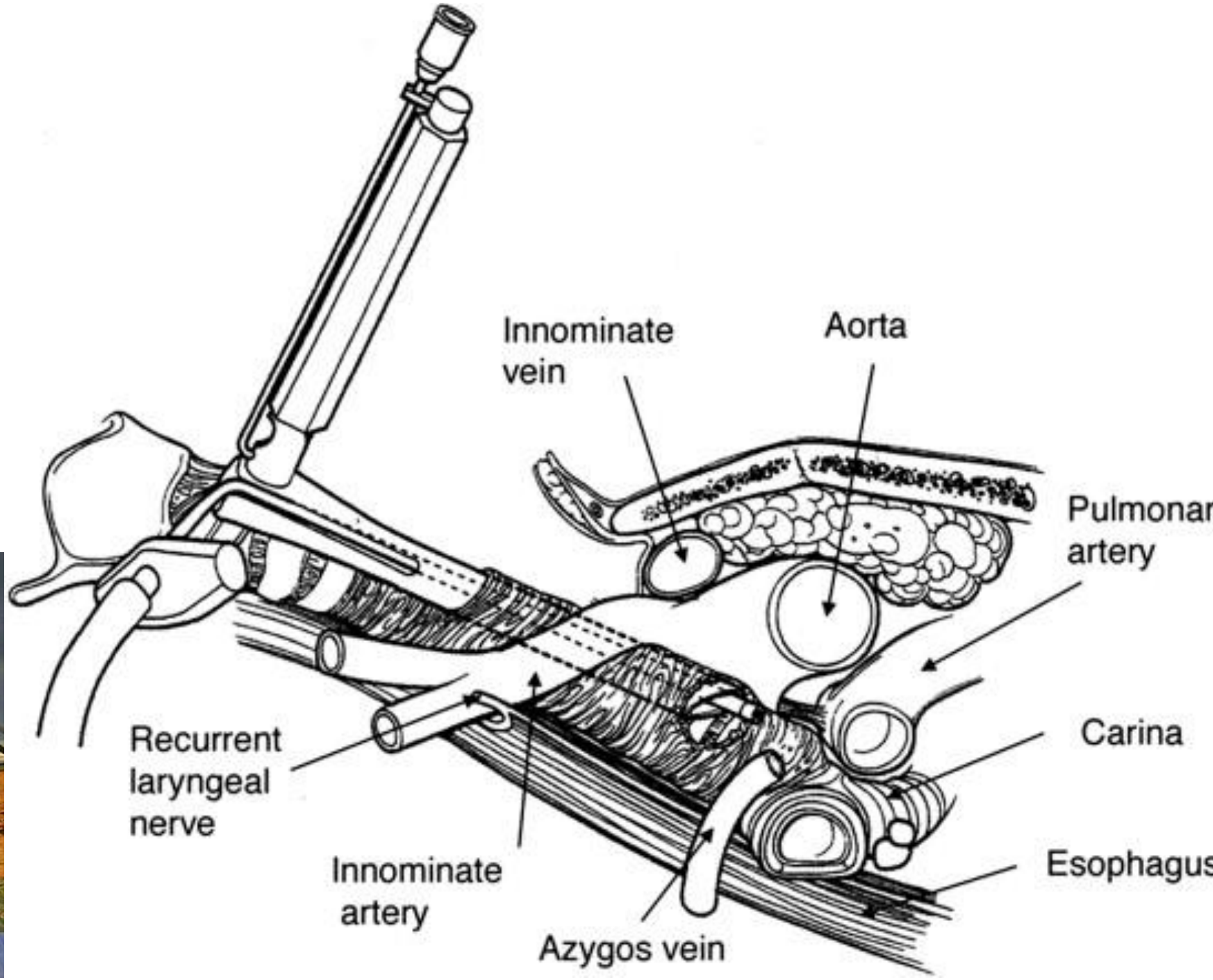
- **10** Hilar
- **11** Interlobar

Peripheral zone

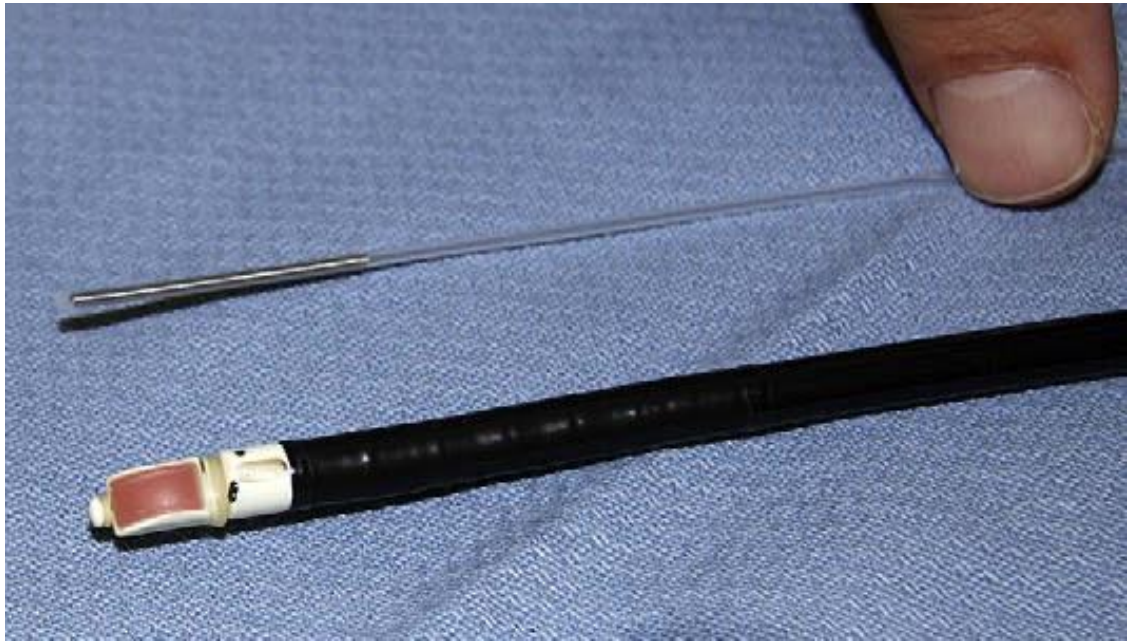
- **12** Lobar
- **13** Segmental
- **14** Subsegmental

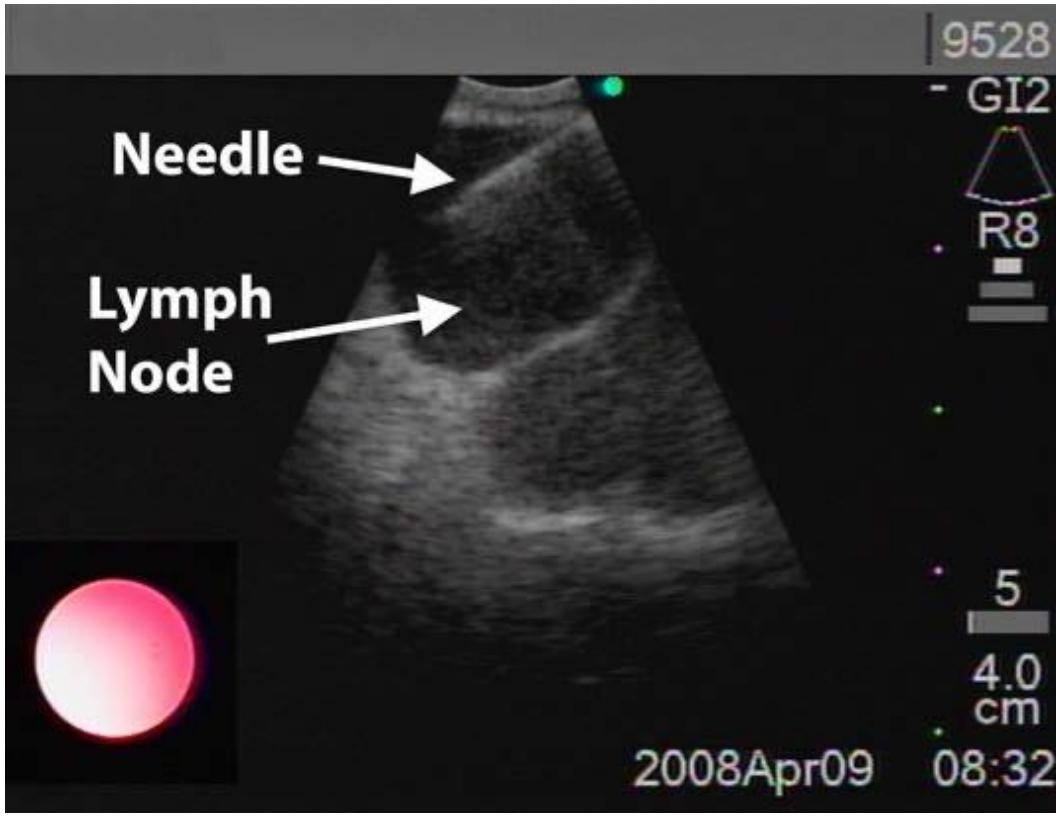



Lateral retraction of strap muscles with superior retraction of thyroid
Thyroid gland
Sternohyoid m.
Pretracheal fascia

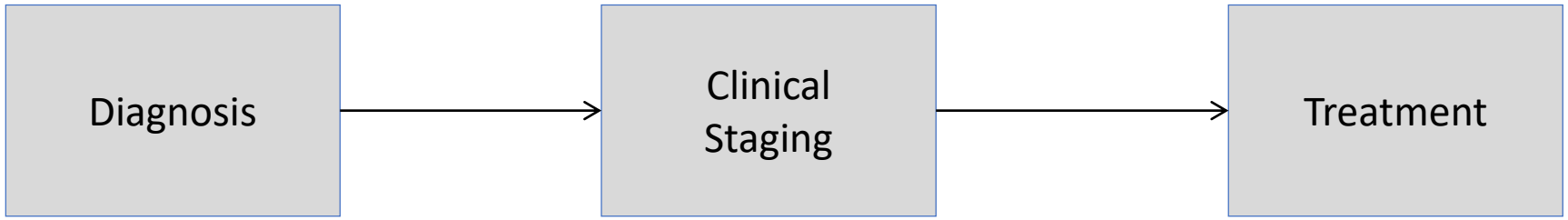

Innominate vein
Aorta
Pulmonar artery
Recurrent laryngeal nerve
Carina
Innominate artery
Esophagus
Azygos vein

Endobronchial Ultrasound (EBUS) w/ FNA





Treatment Strategy



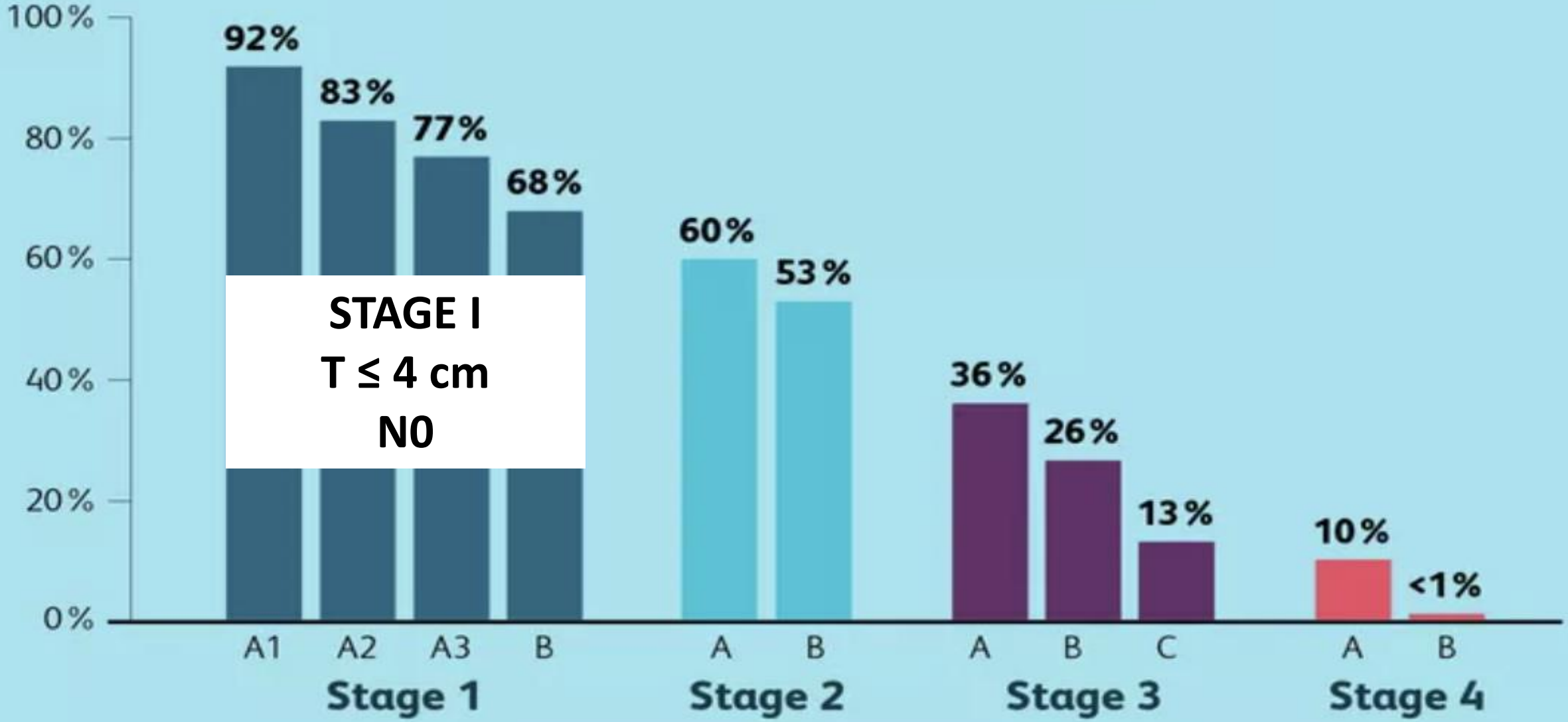
Stage I: Resection only (LACE metanalysis HR 1.4)

Stage II: Resection with adjuvant or neoadjuvant chemotherapy +/- IO
Stage IIIA (N0,N1) Resection with Neo adjuvant chemotherapy+ IO

Stage IIIA (N2) definitive chemoradiotherapy vs. neoadjuvant chemo + IO then resection (lobectomy)

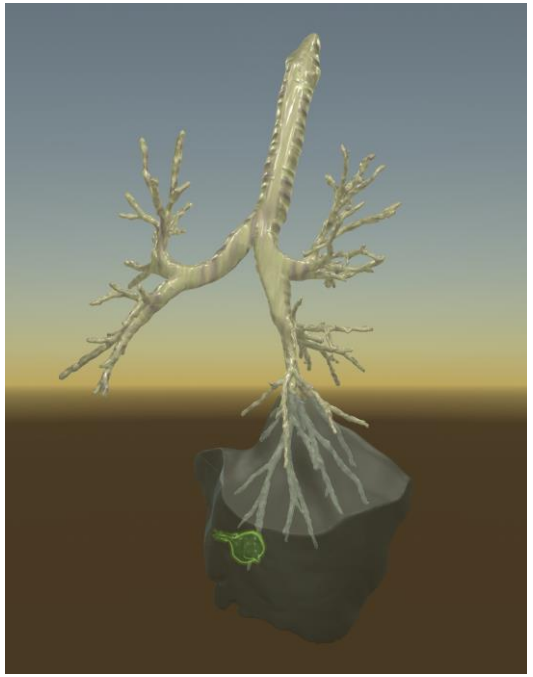
Stage IIIB+ definitive chemoradiotherapy

Non-Small Cell Lung Cancer: 5-Year Survival Rates

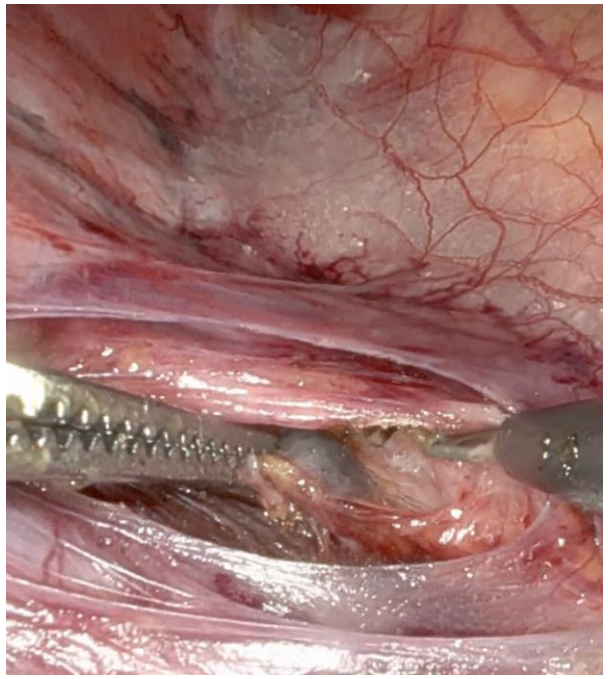


Quality Metrics to Obtain Optimal Survival and Quality of Life

Adequate Lung Resection



Adequate Lymph Node Removal



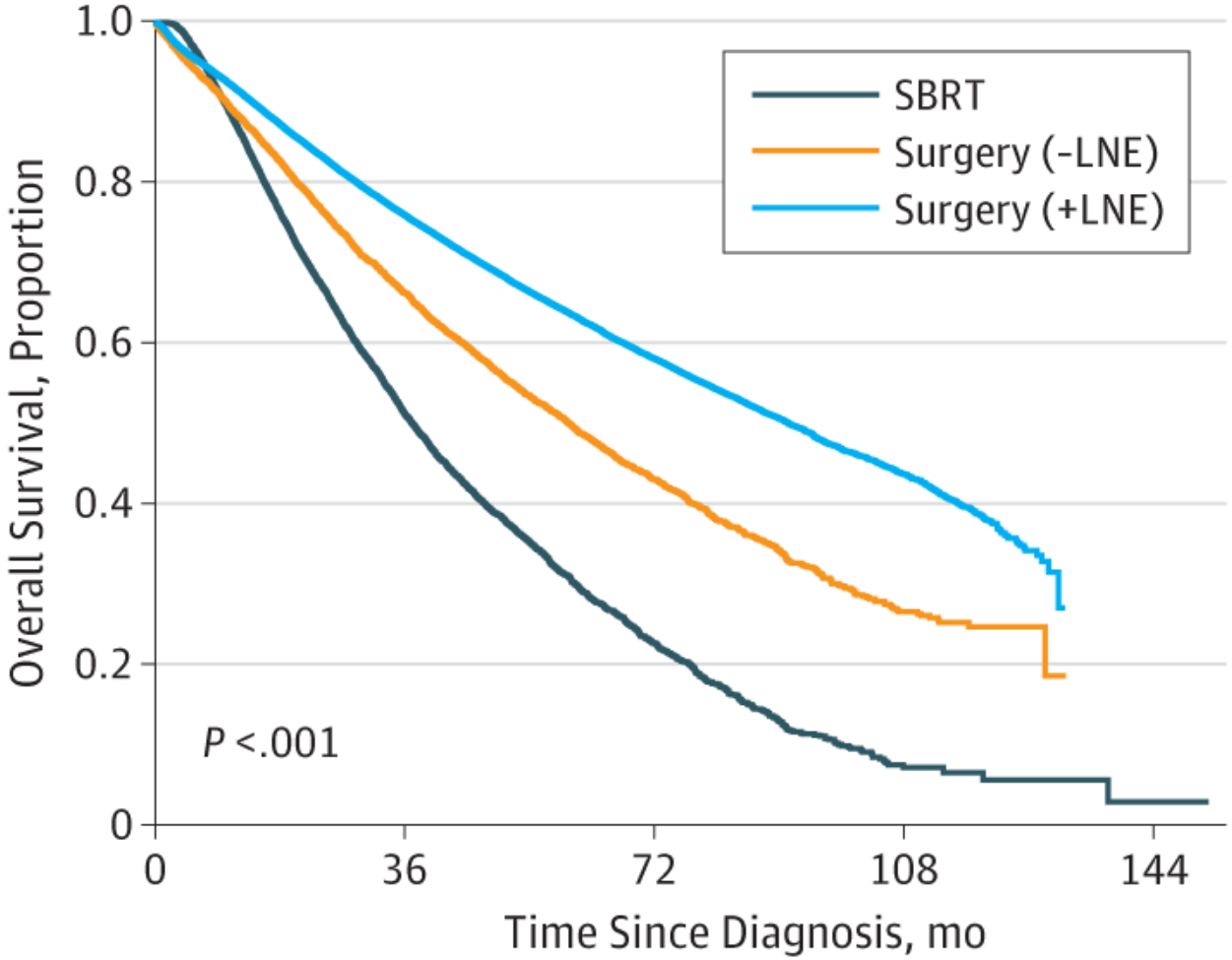
Minimally Invasive Approach

Surgery vs. Radiation for Early Stage NSCLC

- Large NCDB study n = 104K
  - Surgery with regional lymph node exam vs. SBRT
- Endpoint: Long term overall survival
- RESULTS:
  - Lobectomy with mediastinal LN dissection (>10) was associated with better long-term survival
  - Pneumonectomy was not associated with reduced mortality when:
    - No nodes were examined
    - Stage T2-3
    - When > 15 nodes taken for stage 1 disease in patients younger than 80
- Conclusion: Surgery with mediastinal lymph node excision was associated with the best long-term OS

JAMA Netw Open. 2019;2(11):e1915724. doi:10.1001/jamanetworkopen.2019.15724

B SBRT vs surgery with and without regional LNE



No. at risk

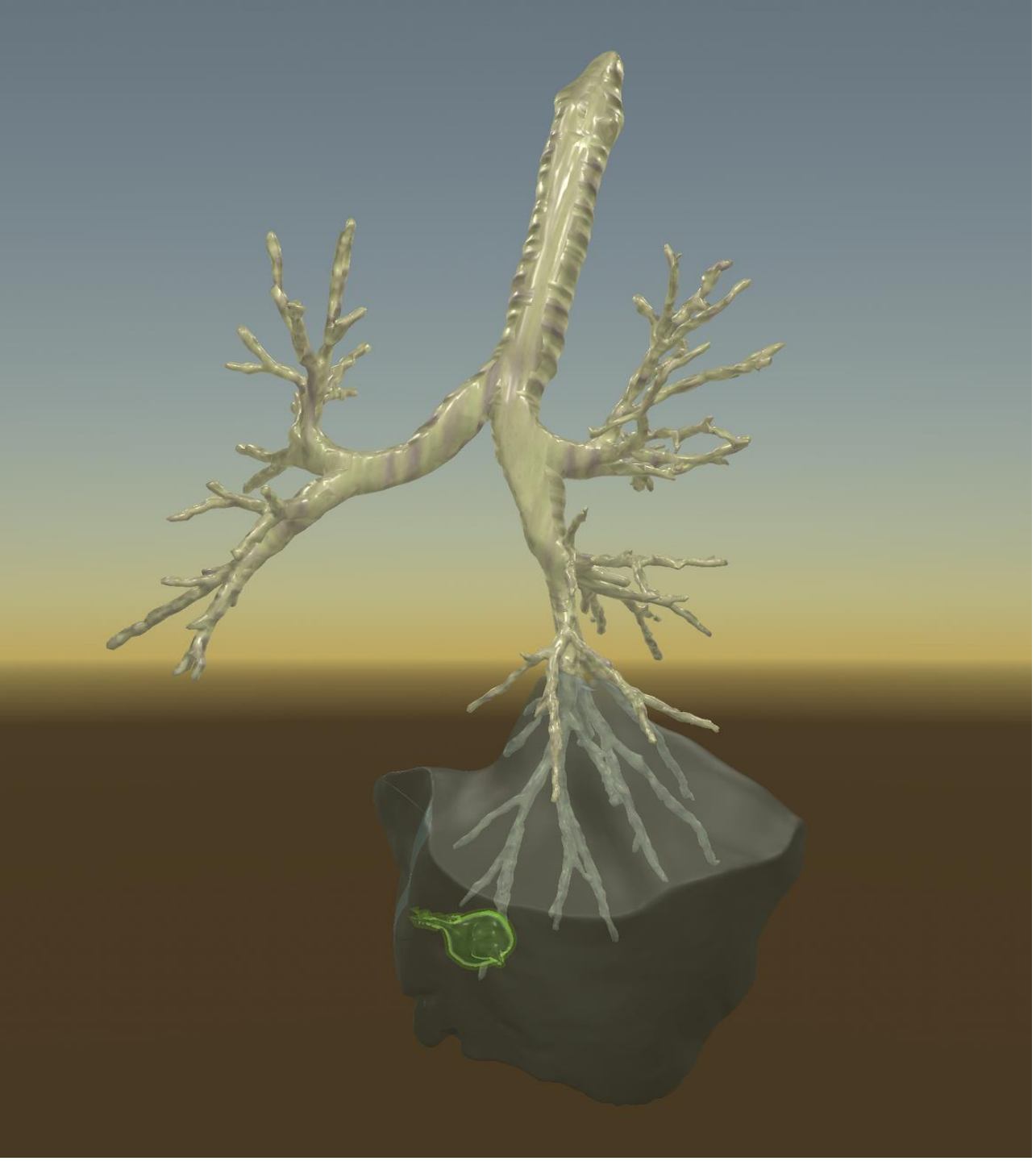
SBRT	13 379	3334	459	21	1
Surgery (-LNE)	7437	3333	1011	128	
Surgery (+LNE)	83 573	39 852	12 793	1483	

JAMA Netw Open. 2019;2(11):e1915724. doi:10.1001/jamanetworkopen.2019.15724

Basic surgical evaluation

Can the patient

1. Walk up 2 flights of stairs without stopping to catch their breath
2. or without chest pain



Lung Resection

1. Lobar vs. Sublobar
2. Post neoadjuvant therapy IB

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Altorki et al. N Engl J Med 2023;388:489-98. DOI: 10.1056/NEJMoa2212083

Method

- International multicenter RCT phase 3 trial
- Patients with clinical stage T1aN0 (Peripheral < 2.0cm)
    - Randomized to lobectomy or sublobar (wedge (59%) or segmentectomy)
    - Choice of surgical approach (open, vats or robotic) per surgeon
    - No mandate on LN dissection beyond sampling of major hilar and 2 mediastinal LN stations
- End points
    - Primary: Disease Free survival
    - Secondary: Overall Survival, recurrrence and expiratory flow at 6 months
- Aim: Determine if sublobar is non-inferior to lobectomy

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

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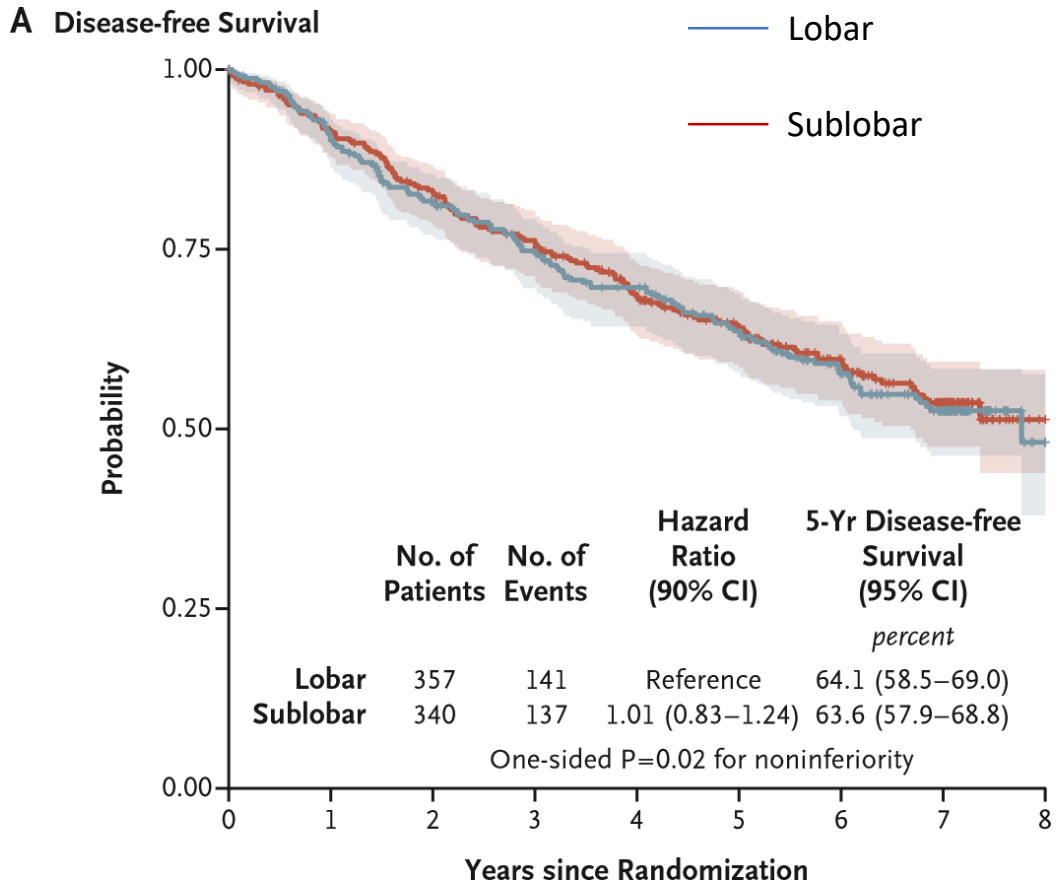

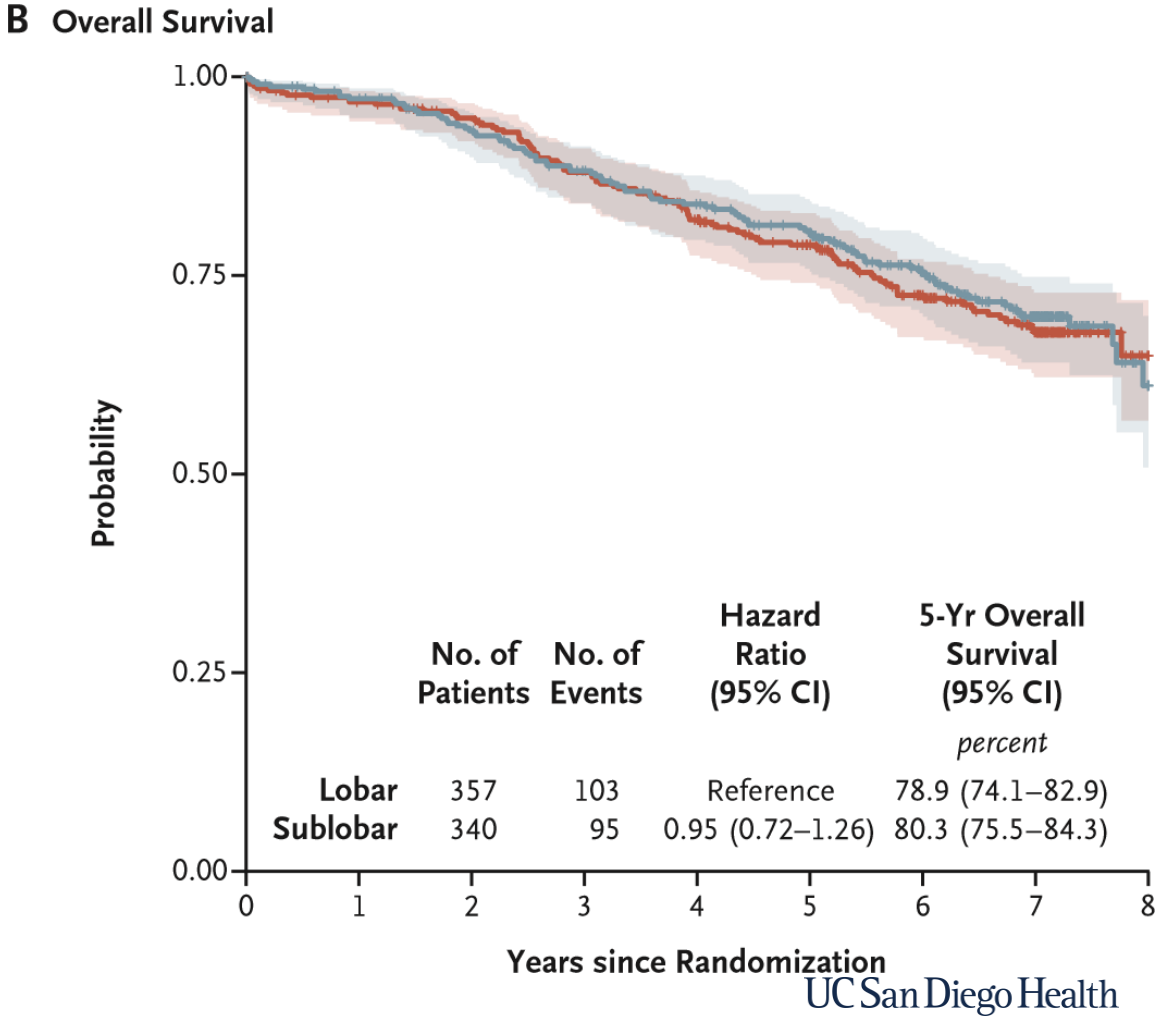

3D Modeling to Improve Definition of the Sublobar Anatomy

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Updates on Surgical Approaches to Late-stage Lung Cancer

Checkmate 816

ORIGINAL ARTICLE

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylors, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*

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Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

Forde et al. N Engl J Med 2022;386:1973-85. DOI: 10.1056/NEJMoa2202170

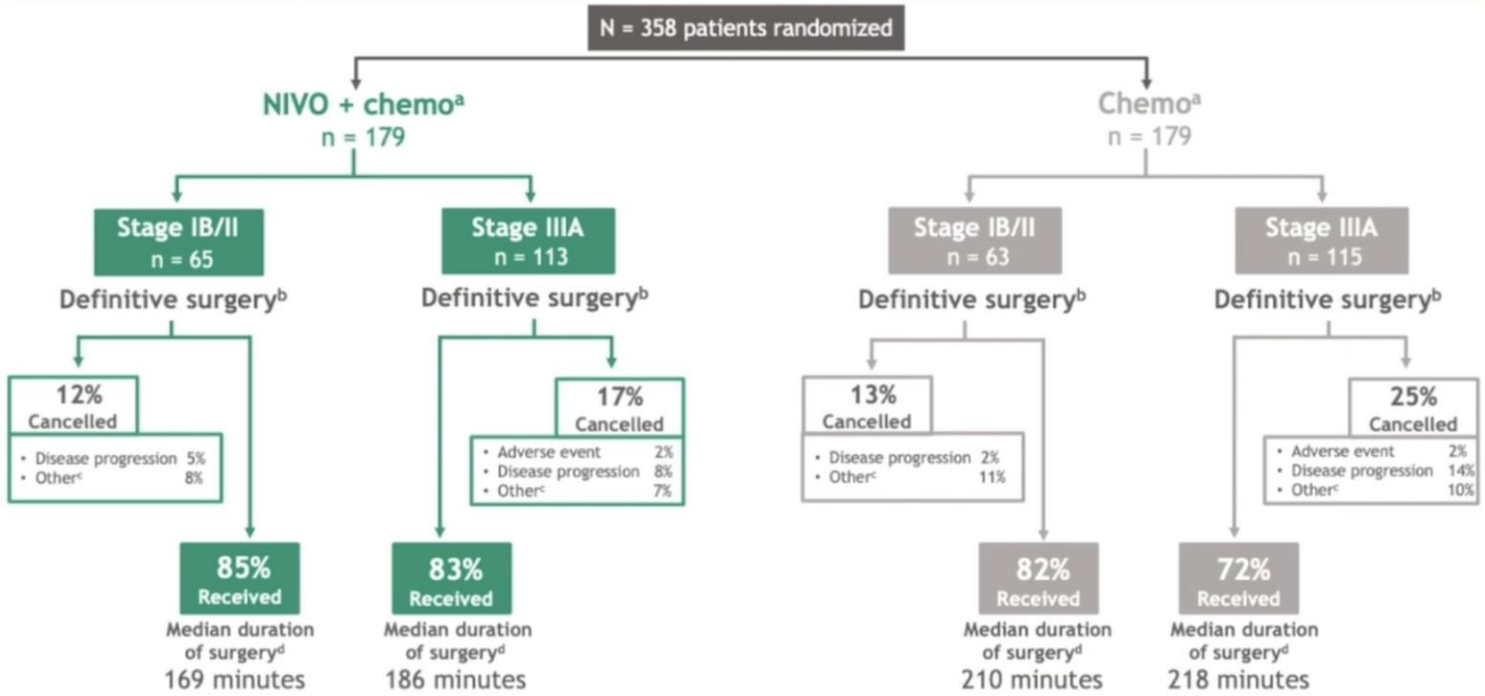
- Phase III RCT
  - NSCLC IB-IIIA
    - Nivolumab+platinum based chemo vs. Chemo alone followed by surgery
  - How did this change our surgery?

What does that mean for us?
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Surgery summary: by baseline stage of disease



[a]1 patient with stage IV in each arm; [b]Patients with definitive surgery not reported: NIVO + chemo, 3% (stage IB/II), 0 (stage IIIA); chemo, 5% (stage IB/II), 3% (stage IIIA); [c]Other reasons included patient refusal, unresectability, and poor lung function; [d]Patients (n) with reported duration of surgery: NIVO + chemo, 46 (stage IB/II), 76 (stage IIIA); chemo, 47 (stage IB/II), 74 (stage IIIA); IQR for median duration of surgery: NIVO + chemo, 126.0-275.0 (stage IB/II) and 134.5-245.5 (stage IIIA); chemo, 150.0-267.0 (stage IB/II) and 147.0-290.0 (stage IIIA).

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2021 ASCO ANNUAL MEETING

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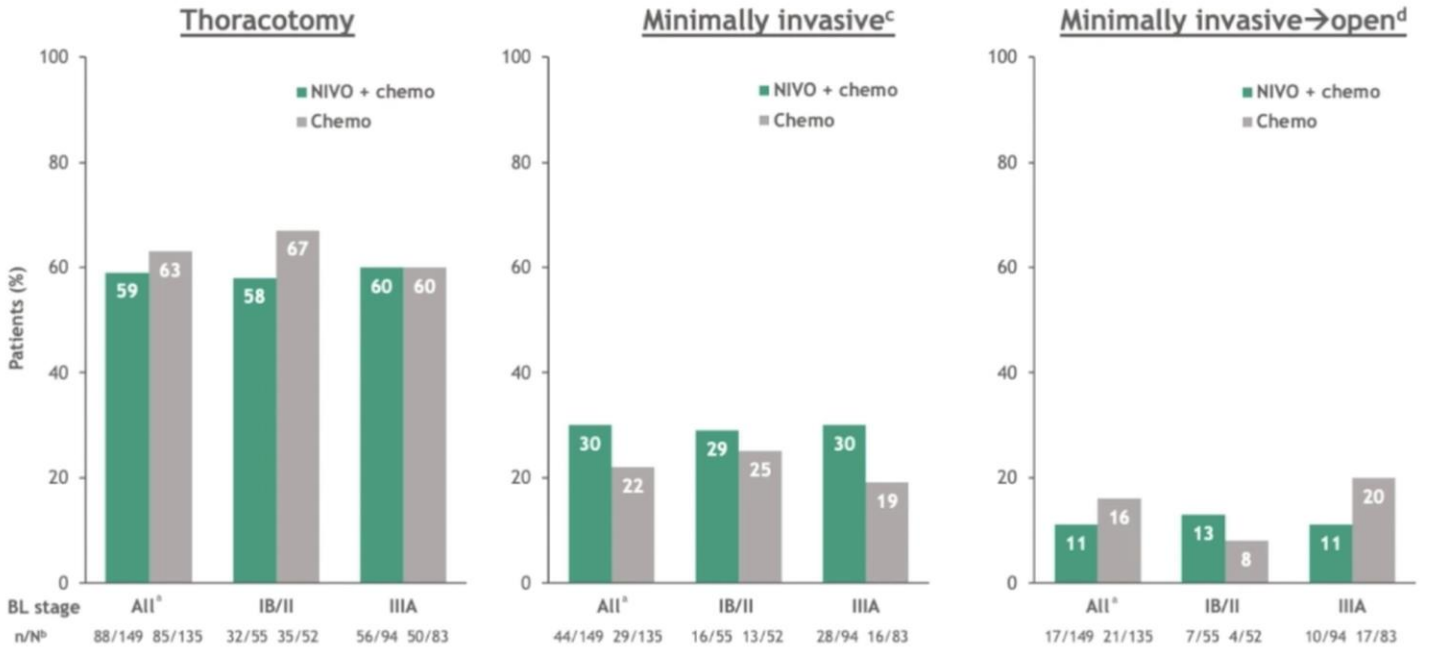
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Surgical approach by baseline stage of disease



[a]Patients with all baseline stages of disease and definitive surgery; [b]Denominator based on patients with definitive surgery; [c]Thoracoscopic/robotic; [d]Minimally invasive to thoracotomy.

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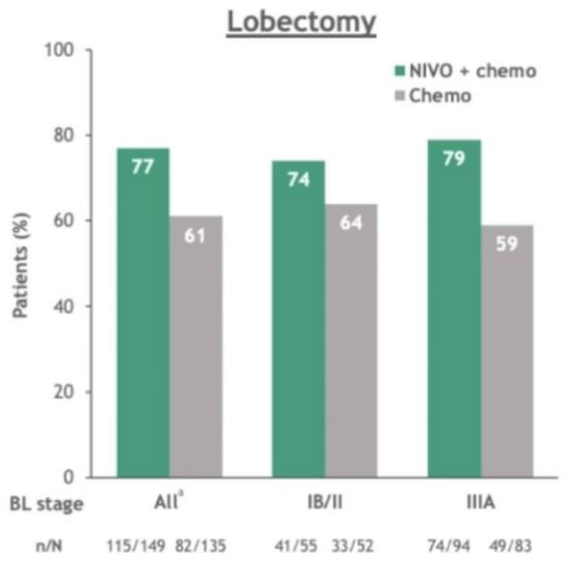
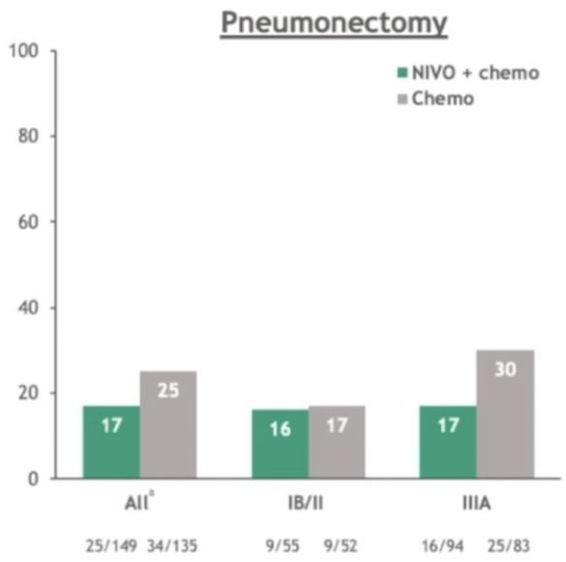
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Type of surgery by baseline stage of disease





Patients may have had > 1 surgery type. Patient numbers (n/N) for stage IB/II and stage IIIA, respectively, for bilobectomy (NIVO + chemo: 1/55, 2/94; chemo: 2/52, 2/83), sleeve lobectomy (NIVO + chemo: 2/55, 0/94; chemo: 5/52, 5/83), and other (NIVO + chemo: 13/55, 11/94; chemo: 12/52, 9/83). [a]Patients with all baseline stages of disease with surgery.

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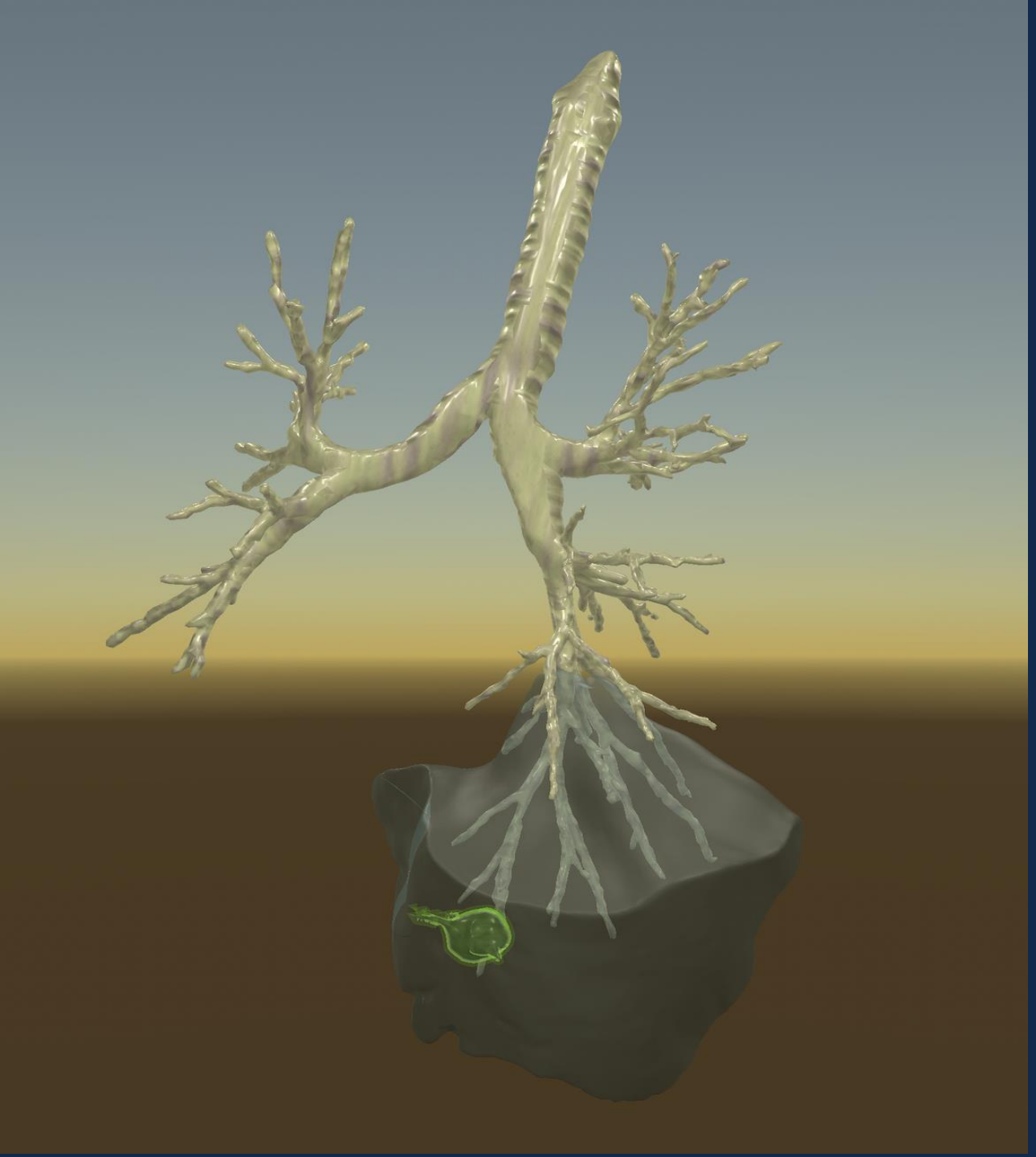
2021 ASCO ANNUAL MEETING

UC San Diego Health



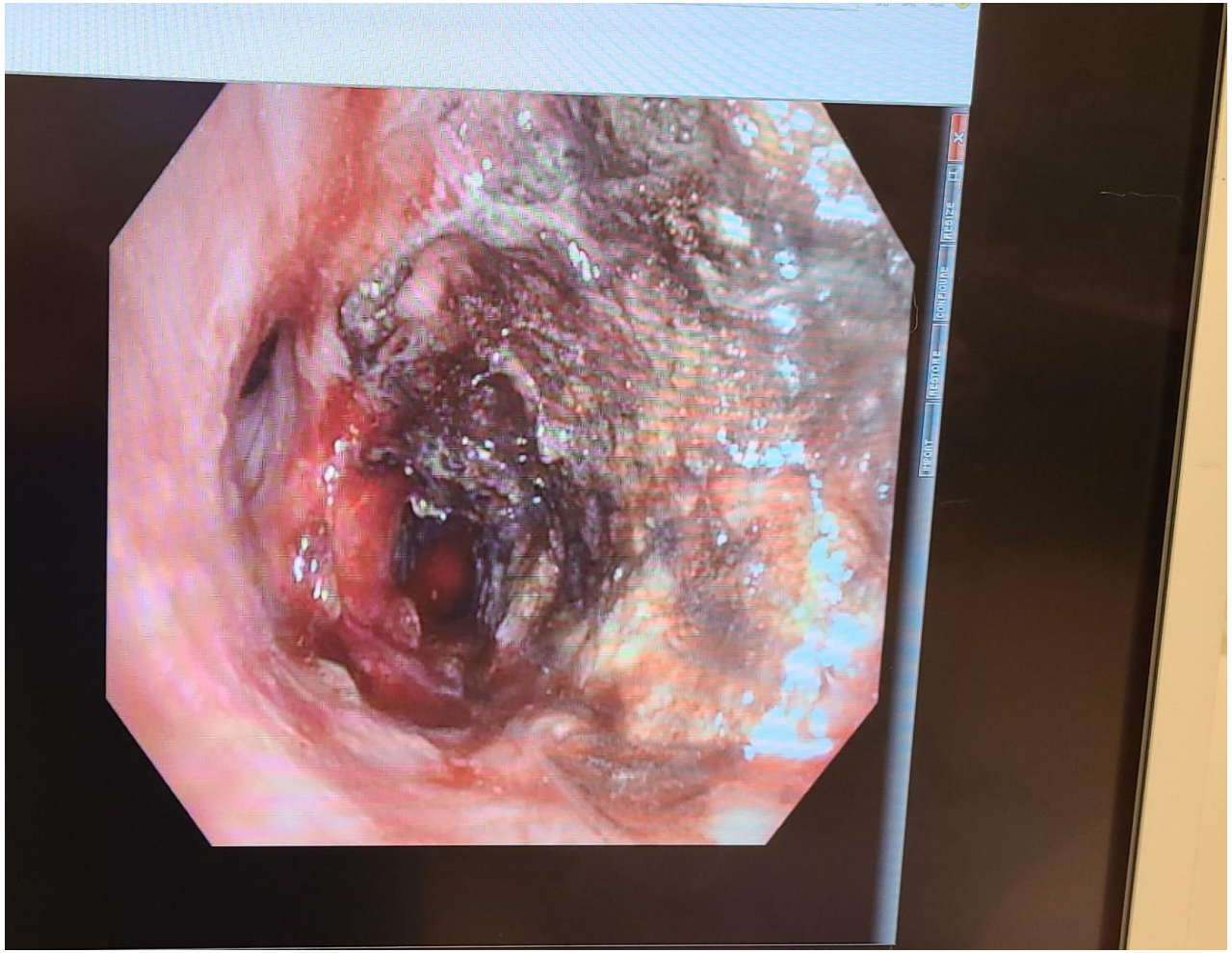
Post neoadjuvant therapy

1. No difference in delay or cancellation
2. More minimally invasive cases
3. Fewer pneumonectomies

PART III
The role of surgery in stage IV NSCLC
Diagnosis, Staging and Management

Stage IV bronchoscope management

- Flexible or Rigid broncoscpy
  - Nd:yag laser
  - Stent
  - Cryo



Thoracoscopy

40% of patients with cytologically negative pleural effusions were proven non-malignant by VATS

Routine VATS finds unsuspected pleural studding in 4% of cases

Thoracoscopy interventions

Pleural biopsy for confirmation of Stage IV disease

Pleurodesis

Tunneled catheter placement

Pericardial effusion drainage

Thank You

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