MAYO CLINIC

MODERN SURGICAL MANAGEMENT OF EARLY-STAGE NSCLC

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50th Annual Toronto Thoracic Surgery Refresher Conference
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OVERVIEW

Early stage I-II NSCLC:

- Sublobar resection as a treatment option for < 2cm, peripherally located, N0 tumors
- Treatment, but not over-treatment of GGO lesions
- Neoadjuvant vs adjuvant vs perioperative immunotherapy
- Robotic lung resection surgery:
  - Pulmonary nodule localization
  - Vascular control

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DISCLOSURES

Relevant to this talk: **Intuitive Surgical, Vergent Bioscience**

Consultant/co-development/research funds:

- Intuitive Surgical, Medtronic, Biostage, On Target, Vergent, Merck, Bristol-Myers-Squibb, Genentech, Astra Zeneca, Fujifilm

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LOBECTOMY VS SUBLOBAR RESECTION: WHERE ARE WE IN 2026?

- CALGB 140503 (Altorki et al.)
- JCOG 0802 (Saji et al.)
- Influence on practice patterns in North America

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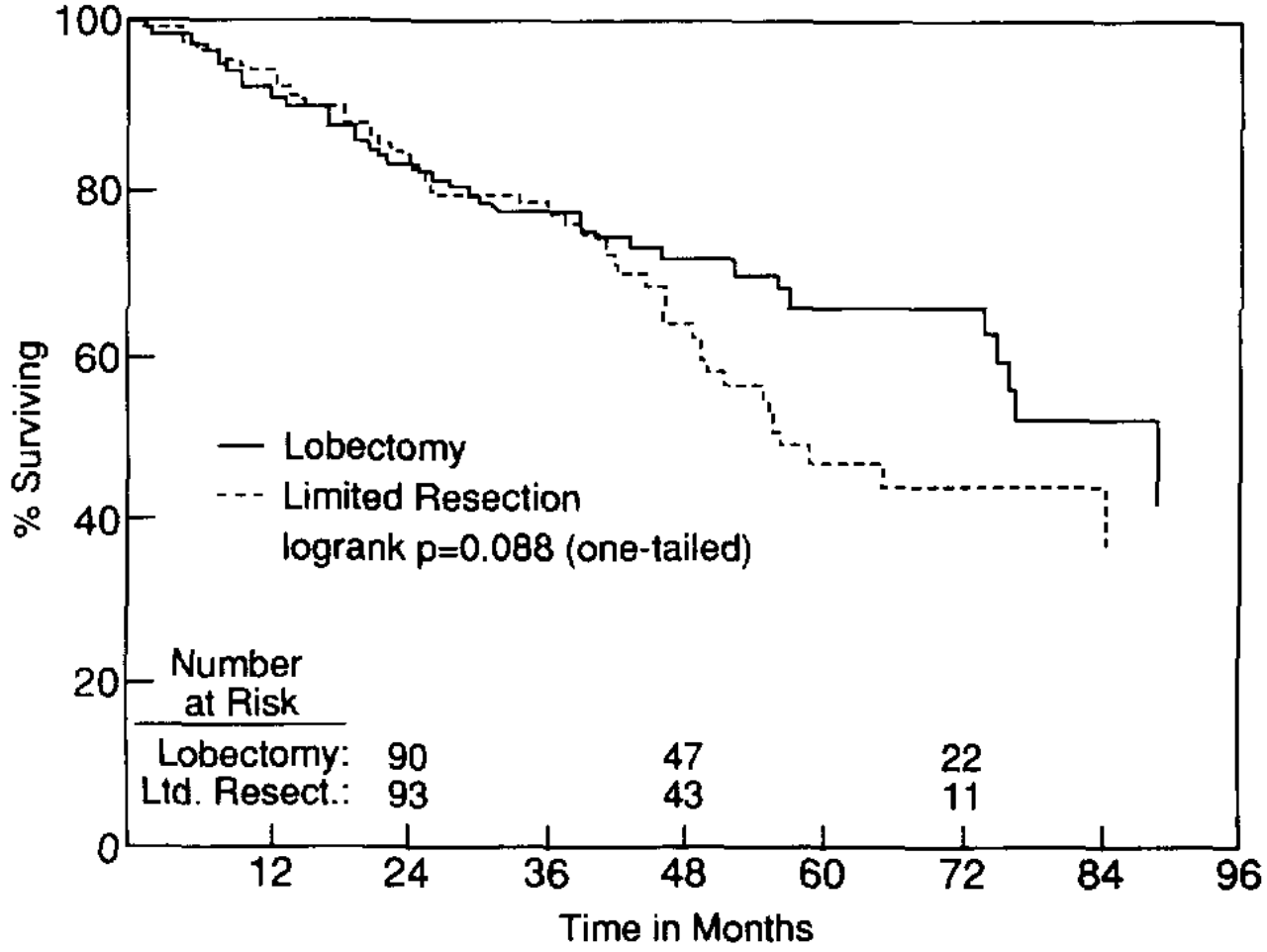
LOBECTOMY VS. LIMITED RESECTION LUNG CANCER STUDY GROUP TRIAL (1995)



Limited resection

- 30% increase in overall death rate
- 50% increase in observed rate of death with cancer

Ginsberg & Rubinstein
Ann Thorac Surg 1995;60:615-23

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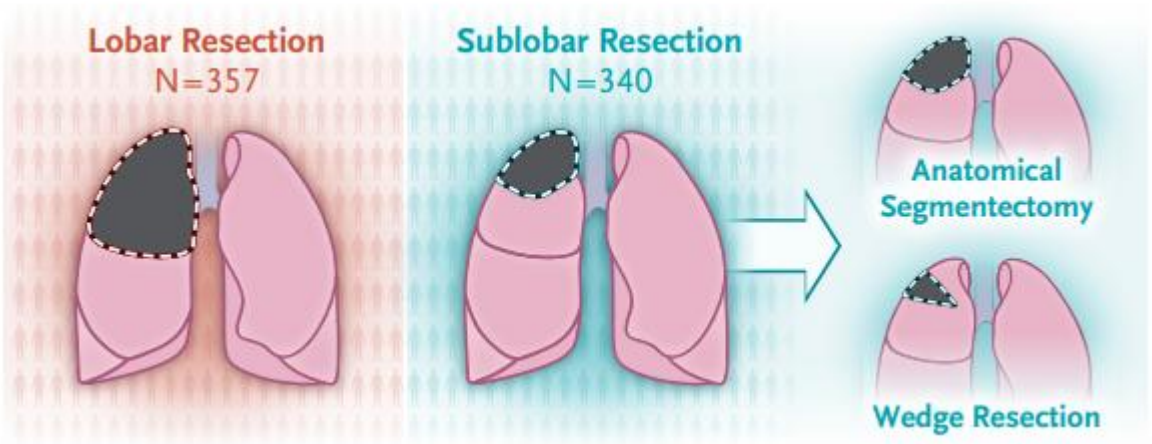
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

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

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.



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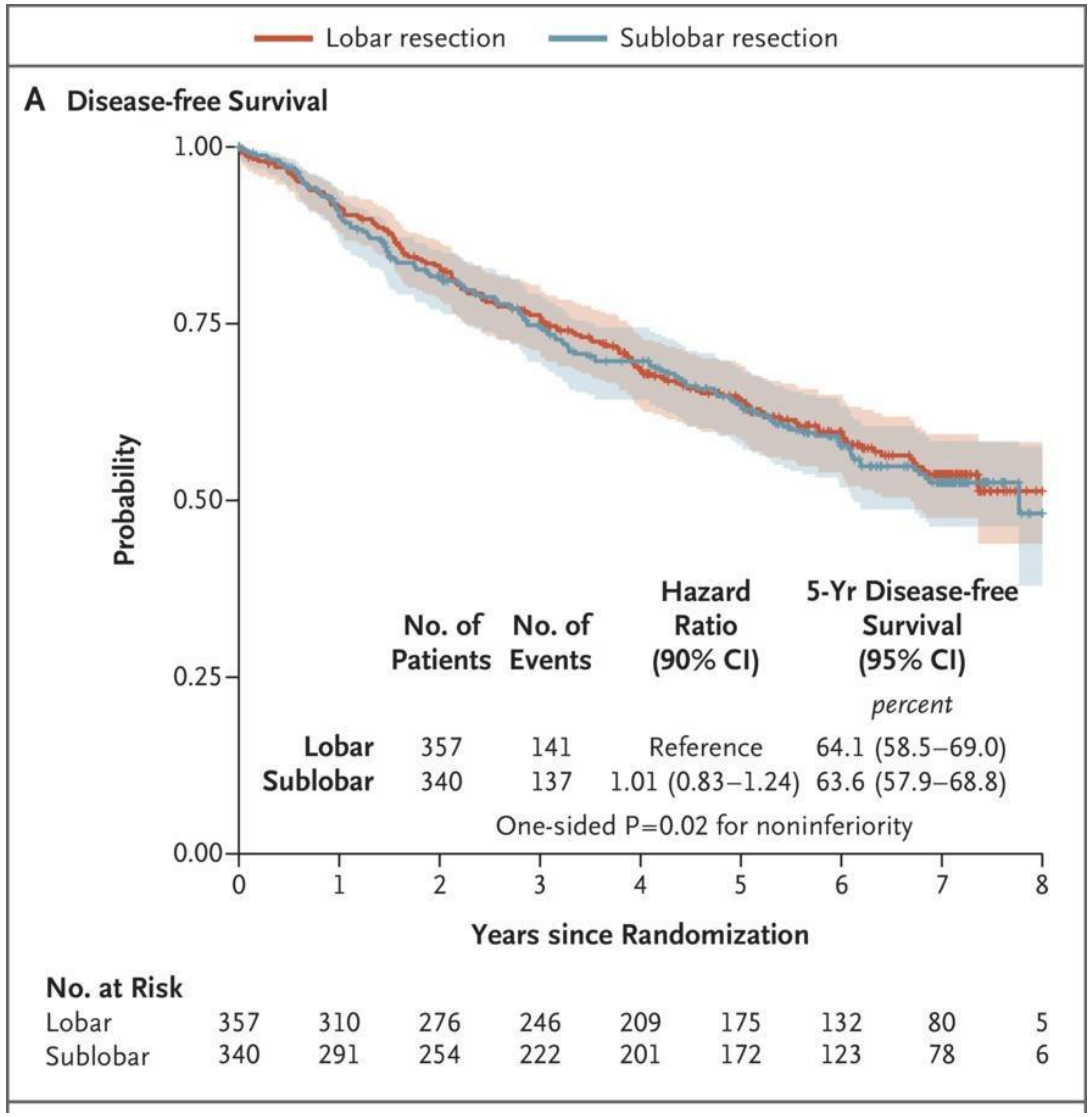

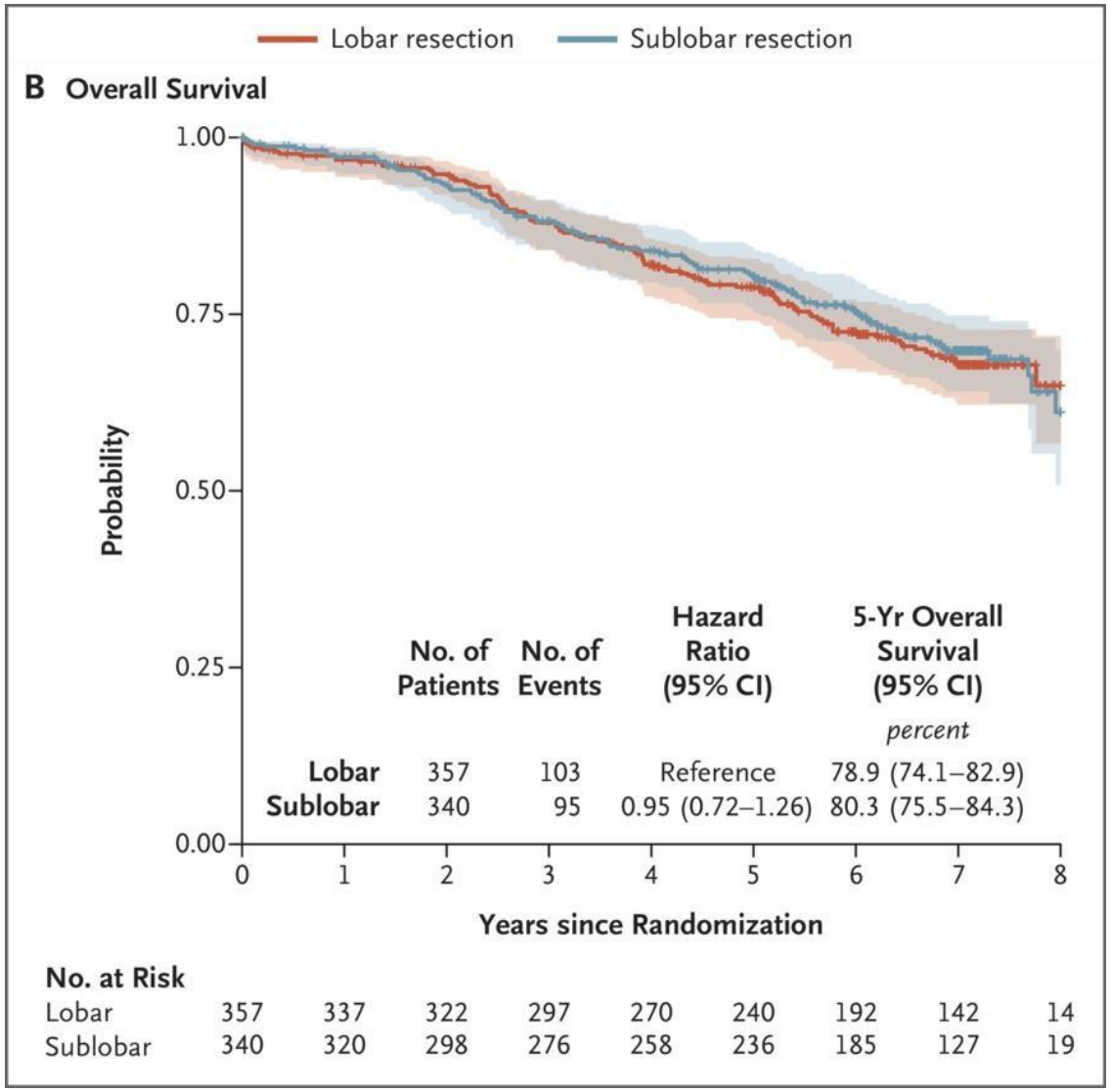

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Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial

*Hisashi Saji, Morihito Okada, Masahiro Tsuboi, Ryu Nakajima, Kenji Suzuki, Keiju Aokage, Tadashi Aoki, Jiro Okami, Ichiro Yoshino, Hiroyuki Ito, Norihito Okumura, Masafumi Yamaguchi, Norihiko Ikeda, Masashi Wakabayashi, Kenichi Nakamura, Haruhiko Fukuda, Shinichiro Nakamura, Tetsuya Mitsudomi, Shun-Ichi Watanabe, Hisao Asamura, on behalf of the West Japan Oncology Group and Japan Clinical Oncology Group**

Lancet 2022; 399: pp. 1607-1617.

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Randomized Trial of segmentectomy Compared to Lobectomy in Small-Sized Peripheral Non-Small Cell Lung Cancer (JCOG0802/WJOG4607L)

PHASE 3, MULTICENTER, RANDOMIZED CONTROLLED TRIAL

1100 Stage IA peripheral NSCLC ≤2cm C/T ration > 0.5	Lobectomy N=554 	Segmentectomy N=552 
5-year overall survival	**91.1%**	**94.3%** HR: 0663; 95% CI, 0.47-0.93; P<0.0001 for non-inferiority; P=0.0082 for superiority
Post-op FEV1 at 1 year Median Range	N=526 **-12.0%** -57.1% to 49.6%	N=528 **-8.5%** -37.0% to 30.0% P<0.0001
Local recurrence	**30 (5.4%)**	**58 (10.5%)** P=0.0018

CALGB 140503 - CONCLUSIONS

- In patients with peripheral cT1a N0 NSCLC (≤ 2 cm) without lymph node metastases, sublobar resection was not inferior to lobectomy for the primary endpoint of DFS or the secondary endpoint of overall survival

- The results of this trial and JCOG 0802 establish sublobar resection as the standard of care for this subset of patients

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SUBSEQUENT FOLLOW UP PAPERS…

- Visceral pleural invasion = worse DFS and RFS; higher rate of local and distant disease recurrence, independent of the extent of parenchymal resection (JAMA Oncol. 2024;10(9):1179-1186)

- Wedge resection outcomes **no different** than segmentectomy (*J Thorac Cardiovasc Surg 2024;167:338-47*)

- Others pending…

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HOT TAKE:

- A properly done wedge resection for a <2 cm, peripherally located, node negative NSCLC is an acceptable oncologic approach with **no difference** in clinical outcome versus segmentectomy

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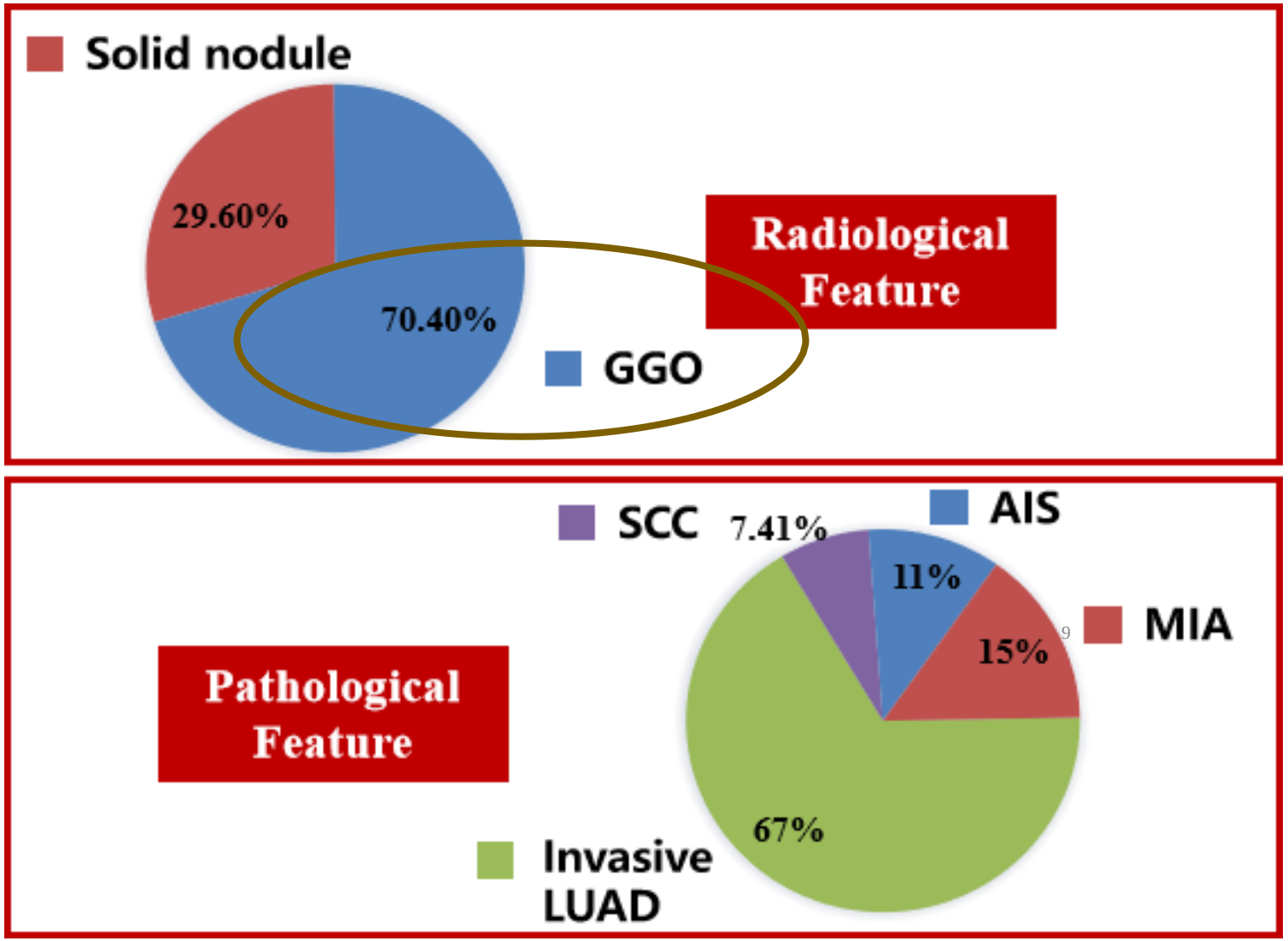
LUNG CANCER SCREENING IN SHANGHAI, CHINA



Slides from
Dr. Haiquan Chen
Fudan University/
Shanghai Cancer
Center

Luo X et al. Translational Oncol. 2017, 10(4):485-490

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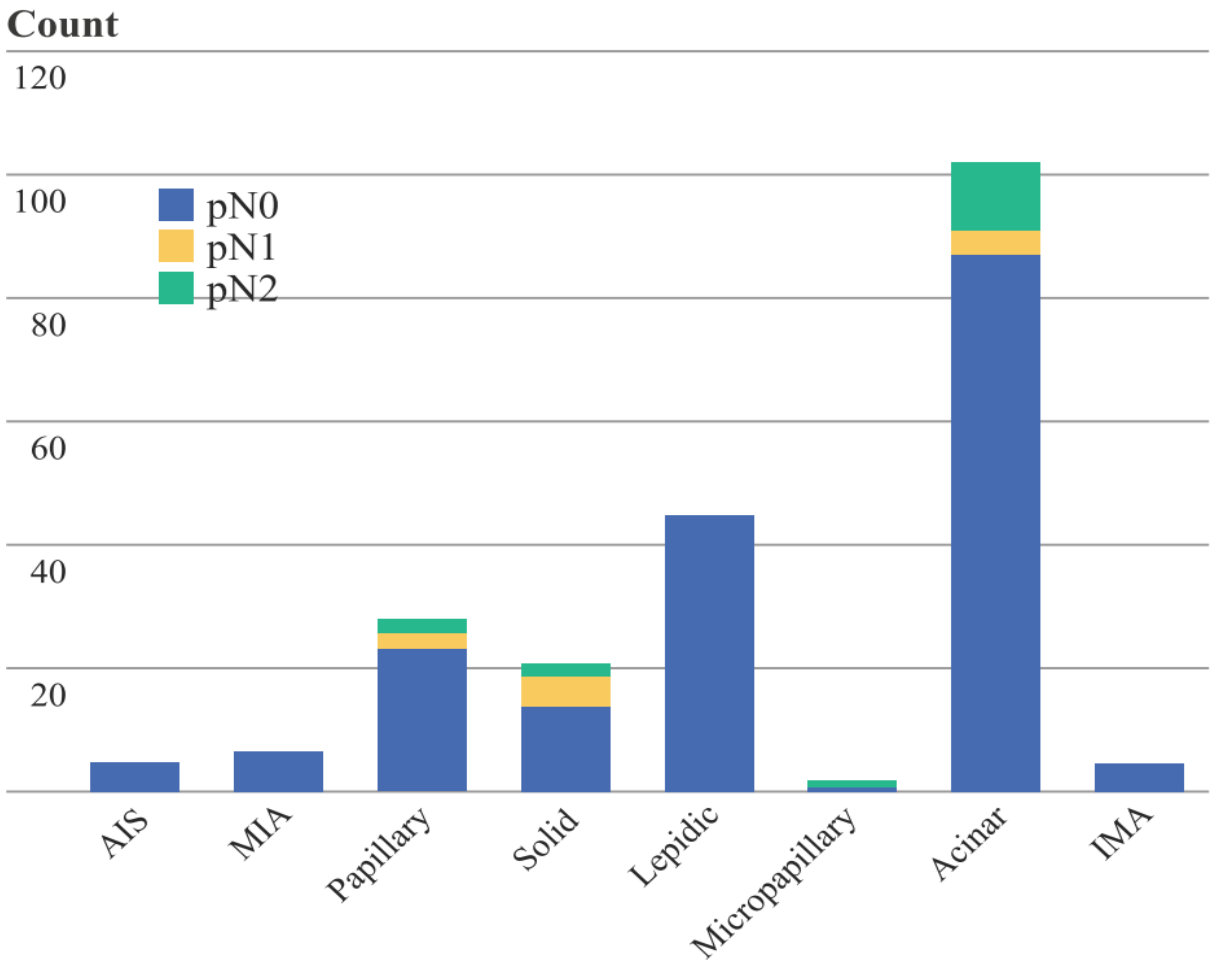
LYMPH NODE DISSECTION FOR GGO

Predictive Factors of Lymph Node Status in Small Peripheral Non-small Cell Lung Cancers: Tumor Histology is More Reliable

Yang Zhang, MD[1,2], Yihua Sun, MD[1,2], Lei Shen, MD[2,3], Yuan Li, MD[2,3], Jiaqing Xiang, MD[1,2], Yawei Zhang, MD[1,2], Hong Hu, MD[1,2], and Haiquan Chen, MD[1,2]

ANNALS OF SURGICAL ONCOLOGY

- **Predict N0 based on pathological subtypes**



- No LN metastasis for peripheral ≤2cm **AIS, MIA and lepidic predominant LUADs.**

Ann Surg Oncol 2013 20(6):1949-54; J Thorac Cardiovasc Surg 2012,144(6):1360-4.

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Selective LN Dissection Strategy

Journal of Clinical Oncology

Original Reports

Check for updates

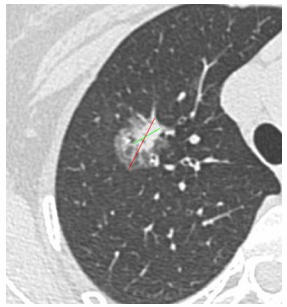
Phase III study of mediastinal lymph node dissection for ground glass opacity-dominant lung adenocarcinoma

Yang Zhang, MD[1,2,3]; Bin Qian, MD[4]; Qingping Song, MD[5]; Junjie Ma, MD[6]; Hang Cao, MD[1,2,3]; Chaoqiang Deng, MD[1,2,3]; Shengping Wang, MD[3,7]; Ting Ye, MD[1,2,3]; Jiaqing Xiang, MD[1,2,3]; Yawei Zhang, MD[1,2,3]; Yihua Sun, MD[1,2,3]; Yueren Yan, MD[1,2,3]; Shanbo Zheng, MD[1,2,3]; Haoxuan Wu, MD[1,2,3]; Qingyuan Huang, MD[1,2,3]; Hong Hu, MD[1,2,3]; Yuan Li, MD, PhD[3,8]; Fangqiu Fu, MD[1,2,3]; Haiquan Chen, MD, PhD[1,2,3]

★ **ECTOP-1009： The world's first multicenter, phase III RCT on LN dissection for GGO-dominant lung cancer**

Key inclusion criteria

- Clinical stage T1N0M0, resectable patients
- Solitary GGN-predominant tumor on CT (CTR ≤0.5)
- **Invasive lung adenocarcinoma**
- Receiving segmentectomy or lobectomy



N=638 → R 1:1

- SEG/LOB + No LN Dissection
- SEG/LOB + Systematic LN Dissection

→ Follow-up

- 2R, 4R, 7, and 8 LNs of right lung tumors
- 4L, 5, 6, 7, and 8 LNs of left lung tumors
- For lower lobe lung tumors, 9 LN dissection are necessary

Zhang Y et al. J Clin Oncol. 2025, 2500610.

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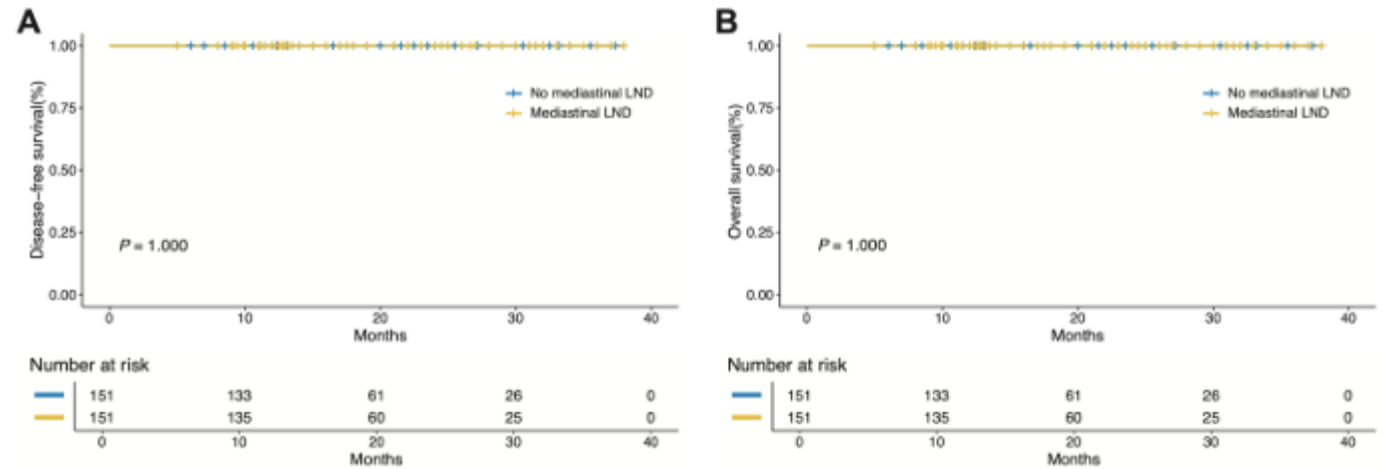
Selective LN Dissection Strategy

Table 2. Outcomes related to surgery and pathology.

Variables	No LND (N=151)	Systematic LND (N=151)	*P* values
Resected LN counts, median (IQR)	3 (1, 6)	10 (8, 15)	<0.001
Resected LN stations, median (IQR)	2 (1, 3)	6 (5, 7)	<0.001
Operative procedure, n (%)			0.246
Segmentectomy	114 (75.5)	105 (69.5)	
Lobectomy	37 (24.5)	46 (30.5)	
Duration of surgery, mins, mean	73	109	<0.001
Blood loss, ml, mean	45	89	<0.001
Duration of chest tube, days, mean	2.7	3.0	0·037
Length of postoperative stay, days, mean	3.7	4.4	0.002
Predominant histologic pattern, n (%)			0.786
LPA	60 (39.7)	57 (37.7)	
APA	70 (46.4)	72 (47.7)	
PPA	19 (12.6)	19 (12.6)	
IMA	1 (0.7)	0 (0)	
SPA	1 (0.7)	2 (1.3)	
MPA	0 (0)	1 (0.7)	
pT			0.283
1a	23 (15.3)	13 (8.6)	
1b	100 (66.7)	104 (68.9)	
1c	26 (17.3)	32 (21.2)	
2a	1 (0.7)	2 (1.3)	
pN			1.000
N0	151 (100)	151 (100)	



- **Regardless of whether it was the SLND or the no LND group, all patients had no lymph node metastasis (pN0).**
- **Less surgery duration, blood loss, and length of postoperative stay were observed in the no LND group.**
- **The disease-free survival rate and overall survival rate of both groups were 100%.**

Zhang Y,… Chen H, J Clin Oncol. 2025, 2500610.

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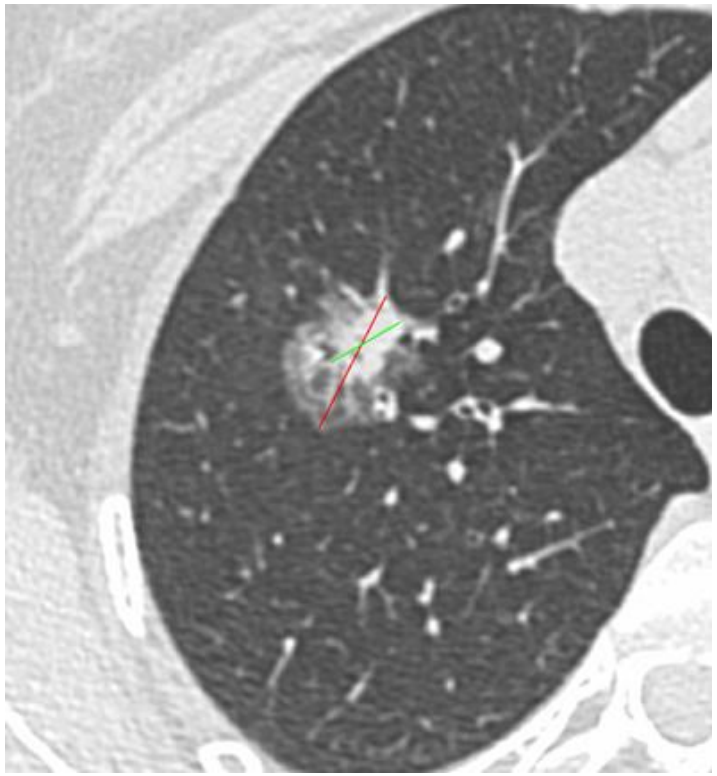
HOT TAKE:

- Lymph node sampling/dissection can be safely omitted for invasive clinical stage T1N0M0 lung adenocarcinoma with solitary GGO-predominant tumor on CT (CTR ≤0.5)



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PERIOPERATIVE IMMUNOTHERAPY FOR EARLY STAGE I-II DISEASE

- Measurable neoadjuvant benefit for Stage IB, II; modest vs effect for Stage IIIA
- No data comparing adjuvant vs neoadjuvant vs perioperative (sandwich) regimens
- How do we best treat Stage IB, II disease? Does it matter?
  - (Neoadjuvant vs adjuvant vs perioperative?)

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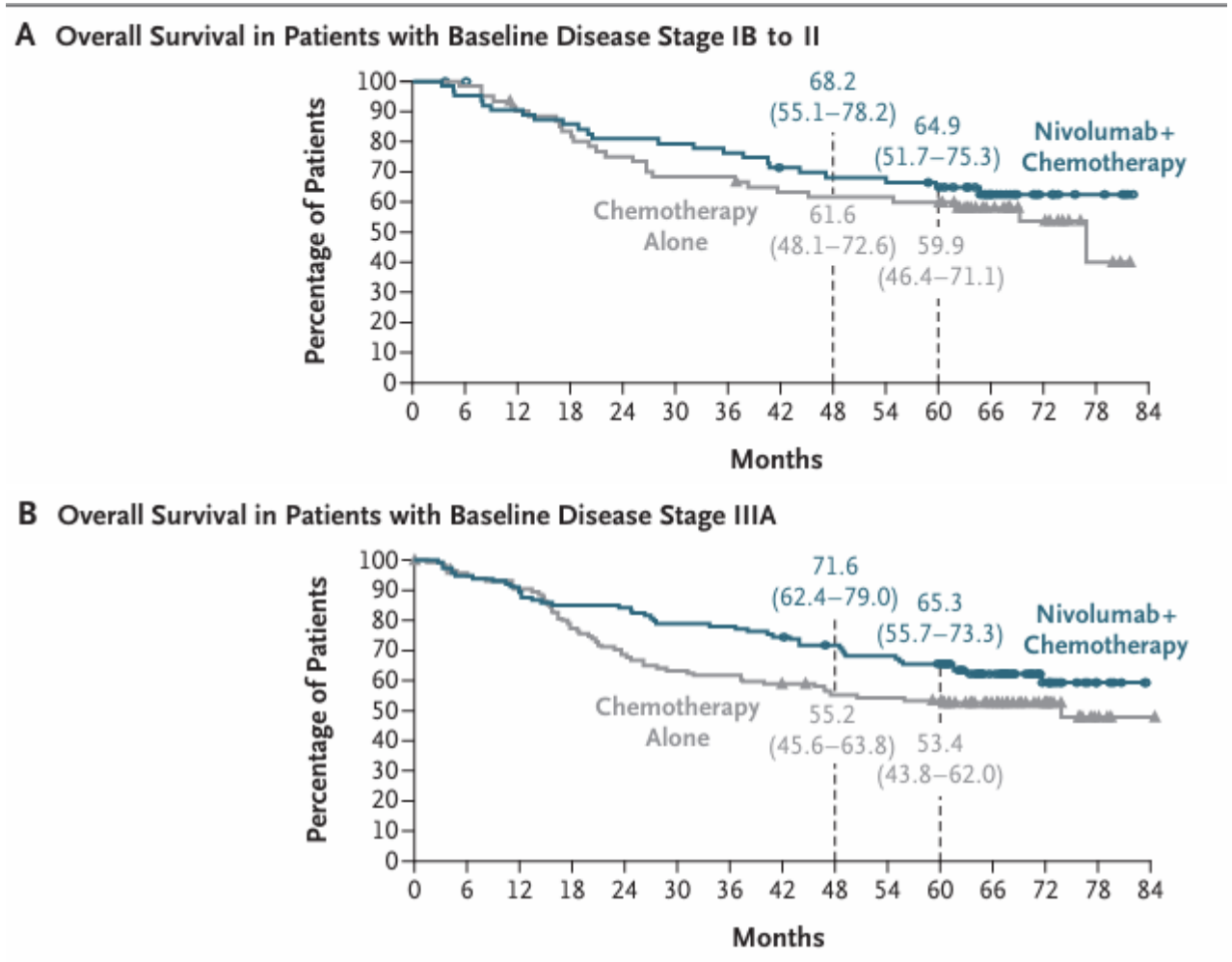
NEOADJUVANT IMMUNOTHERAPY FOR EARLY STAGE I-II DISEASE



- 5 yr survival for Checkmate 816 trial (neoadjuvant nivo + chemo x 3 cycles)

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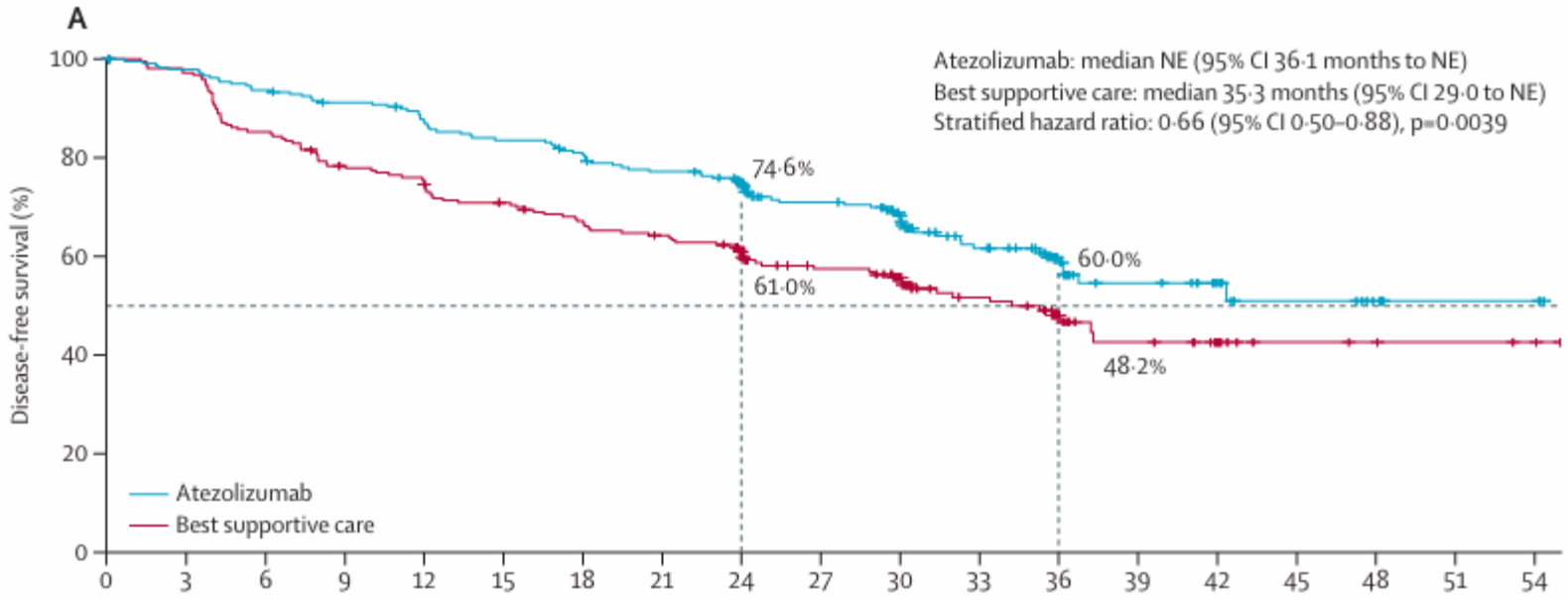
ADJUVANT IMMUNOTHERAPY

- FDA approval based on IMpower010 and Keynote 091
- Benefit for 12 monthly doses after completing adjuvant platinum-based chemo
- Approval based on 24 and 36 month DFS



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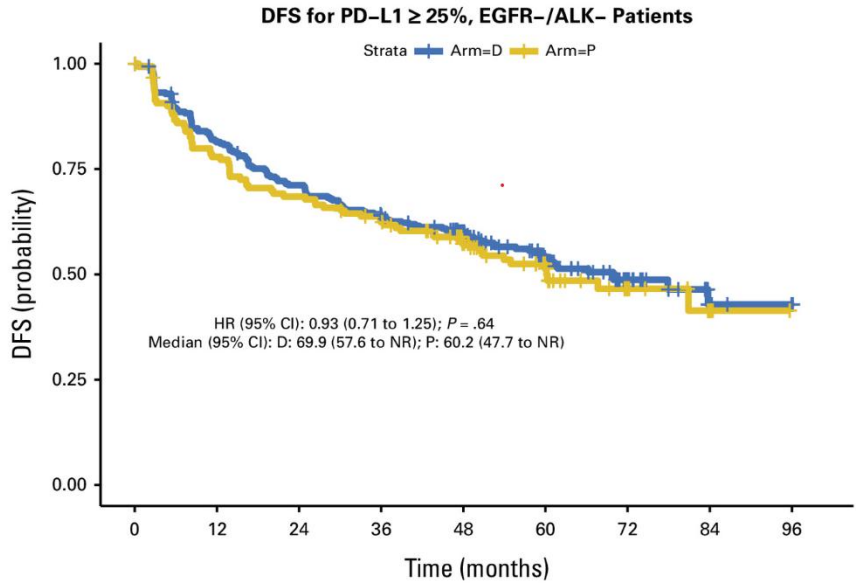
ADJUVANT IMMUNOTHERAPY

- ANVIL - Adjuvant Nivolumab vs Observation in Resected Non–Small Cell Lung Cancer. *JAMA* (Published Online: June 1, 2026)
- BR.31 - Adjuvant Durvalumab in Completely Resected Early-Stage Non–Small Cell Lung Cancer. *J Clin Oncol* 44, 553-564(2026)
  - NO benefit in the adjuvant setting!



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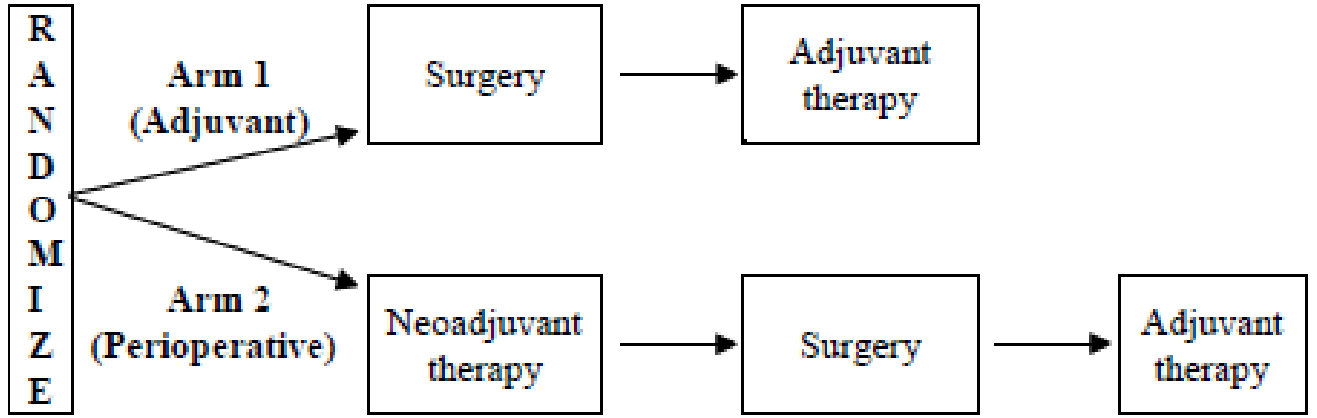
Perioperative versus adjuvant systemic therapy in patients with resectable NSCLC – PROSPECT LUNG (USA NCI)

Eligibility Criteria

- Histologic or cytologic confirmation of surgically resectable stage IIA to IIIB NSCLC (per AJCC 9th edition) or stage IIA to IIIB NSCLC (per AJCC 8th edition) up to single station N2
- Age ≥ 18 years
- ECOG PS ≤ 2 (or Karnofsky ≥ 60%)
- No prior treatment for NSCLC or administration within 5 years
- No previous malignancy within 3 years

Schema



Patients will be followed for 10 years or until death, whichever comes first.

PROSPECT LUNG

- IIA to IIIB NSCLC
- No prior Rx
- Up to single station N2

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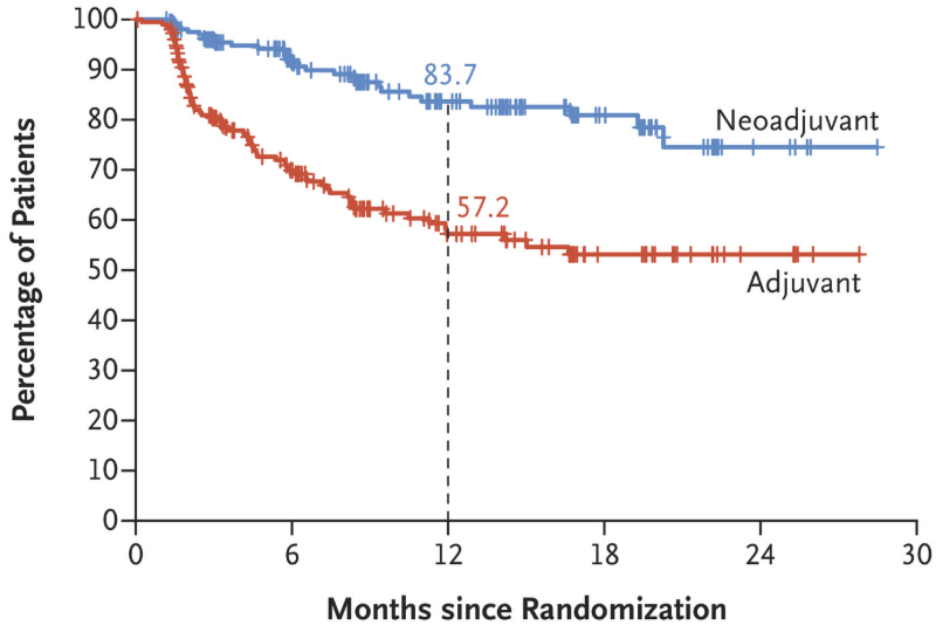
HOT TAKE:

Main benefit from immunotherapy is up front in the neoadjuvant setting; greater effect the higher the stage

- Pre-treat as much as you can rather than trying to make up for it in the adjuvant setting

Neoadjuvant Nivolumab and Ipilimumab in Resectable Stage III Melanoma.

NEJM 2024;391:1696-1708



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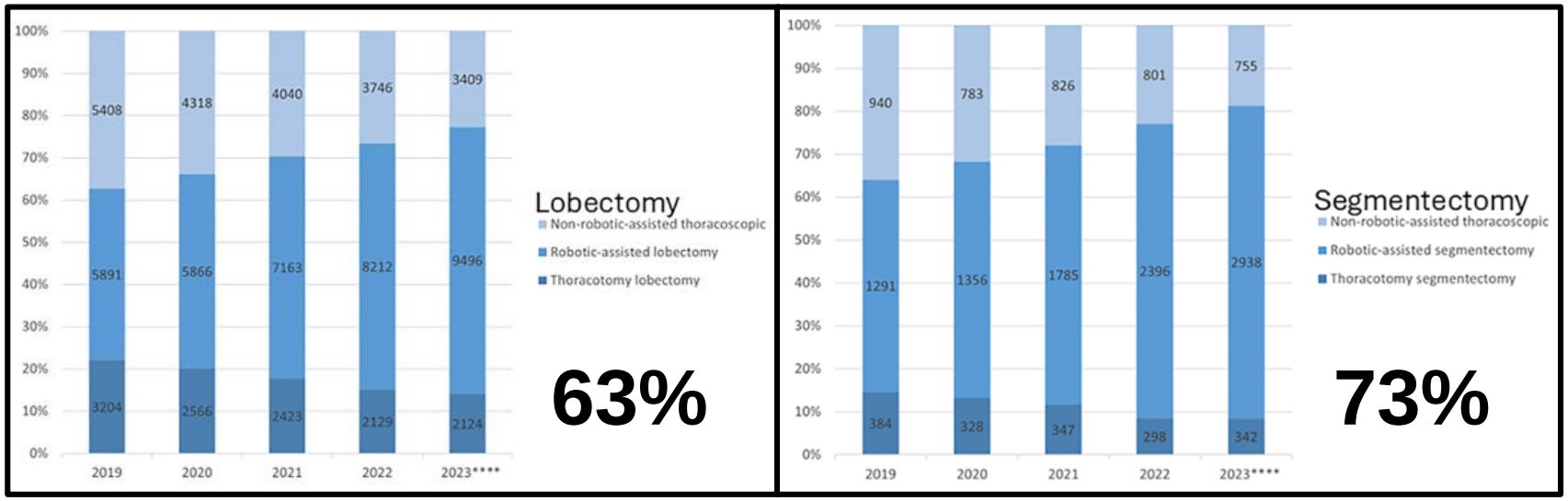
ROBOTIC THORACIC SURGERY

THE REALITY OF TODAY



Society of Thoracic Surgeons – General Thoracic Surgery Database



…performed robotically in 2023

Towe CW et al. ***Ann Thorac Surg*** 2025;119(4):733-743

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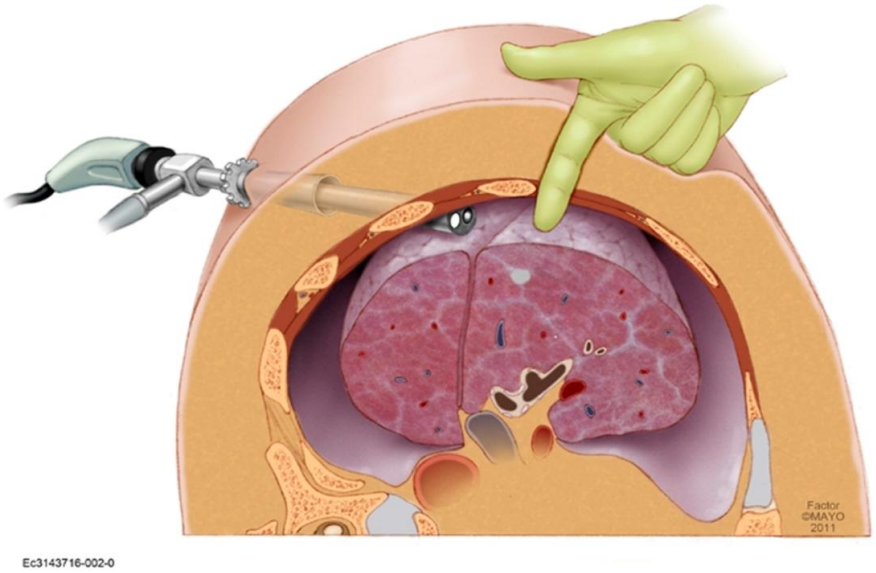
ROBOTIC THORACIC SURGERY

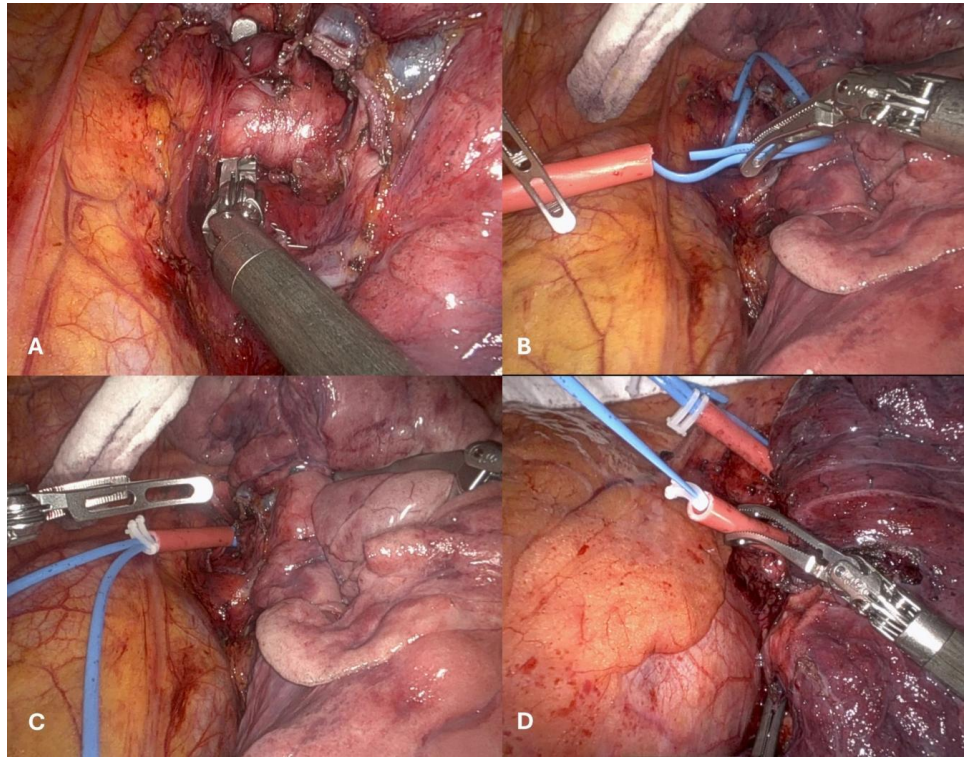
THE REALITY OF TODAY



2 practical issues:

- Vascular control
- Nodule localization





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HOT TAKE:

- Taking time to learn and implement robotic vascular control is worth it - DO IT; you will not regret it

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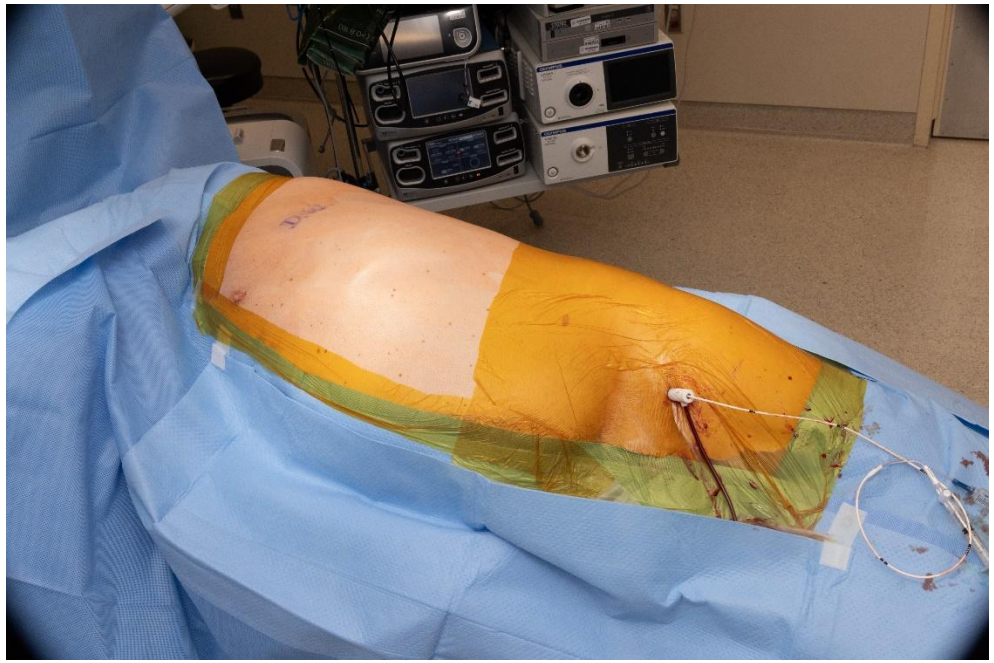
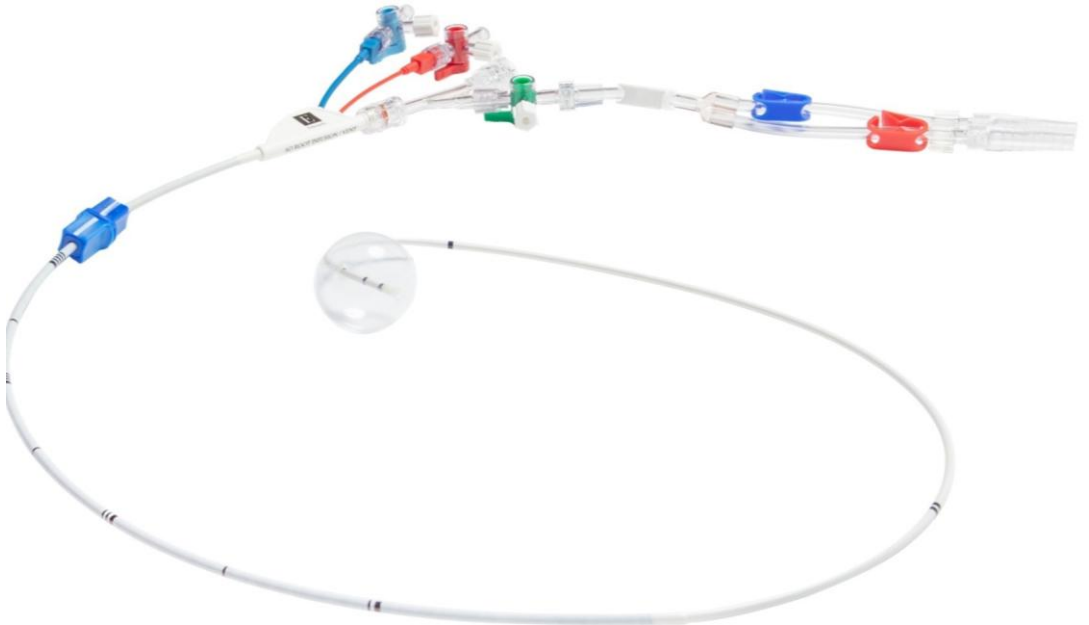
I. PULMONARY ARTERY ENDOBALLOON OCCLUSION PROCEDURE

Endovascular control of the pulmonary artery can be achieved with an IntraClude Endoballoon into the left main pulmonary artery using TEE and Fluoroscopy confirmation.





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I. PULMONARY ARTERY ENDOBALLOON OCCLUSION PROCEDURE





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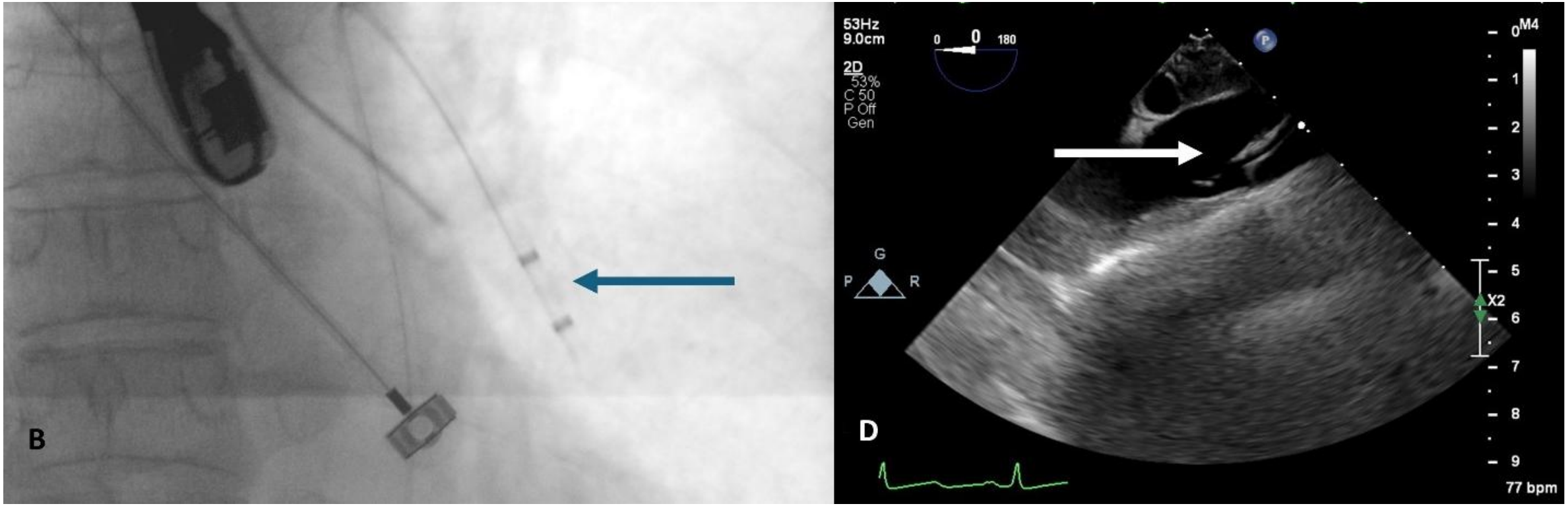
I. PULMONARY ARTERY ENDOBALLOON OCCLUSION PROCEDURE



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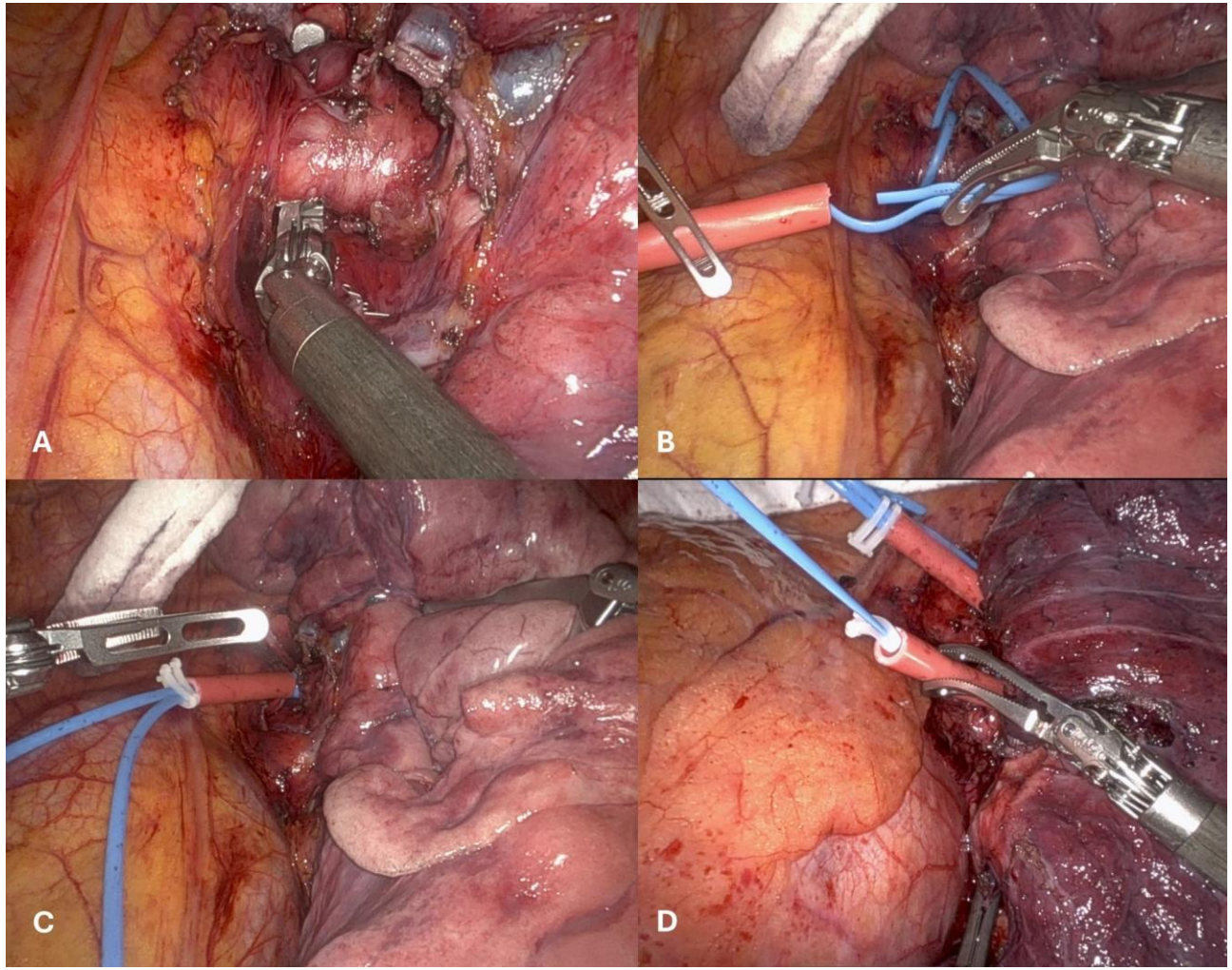
II. INTRA-OPERATIVE PA CONTROL WITH RUMMEL TOURNIQUET



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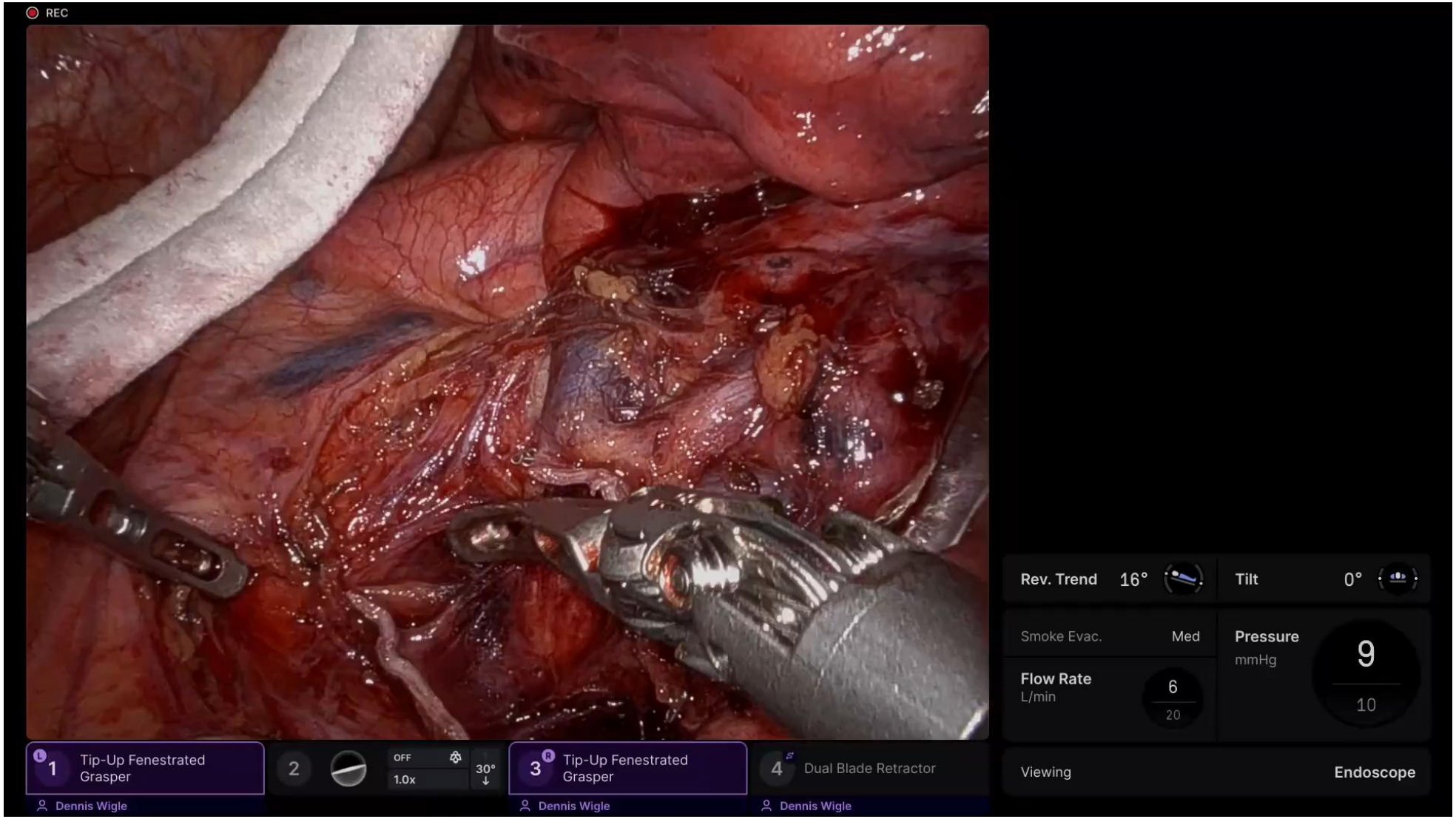
II. INTRA-OPERATIVE PA CONTROL WITH RUMMEL TOURNIQUET



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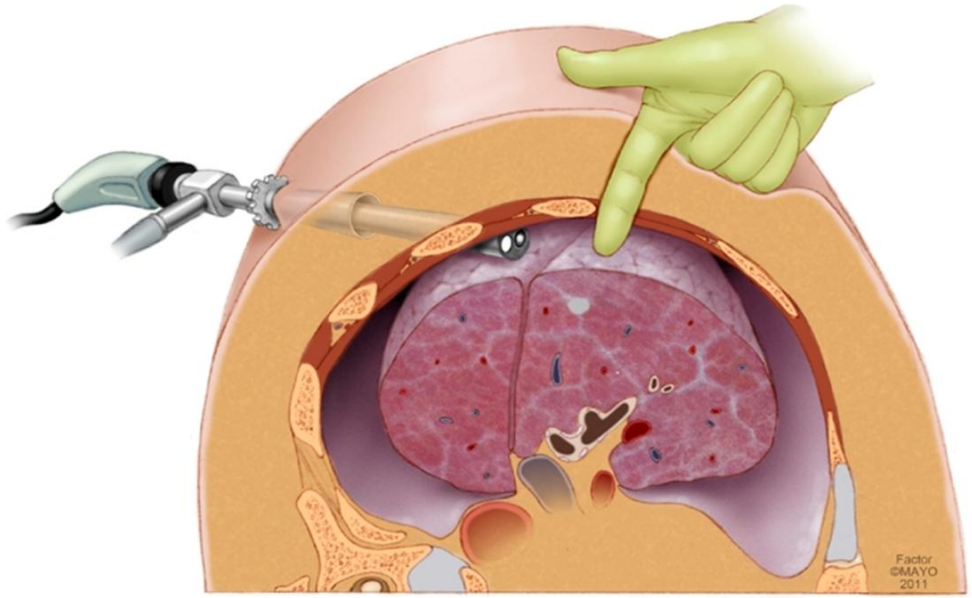
NODULE LOCALIZATION: AN ONGOING CLINICAL PROBLEM

Hot take:

Despite advances to date, nodule localization is under appreciated and continues to be a field ripe for innovation

(Particularly in a closed port robotic system)



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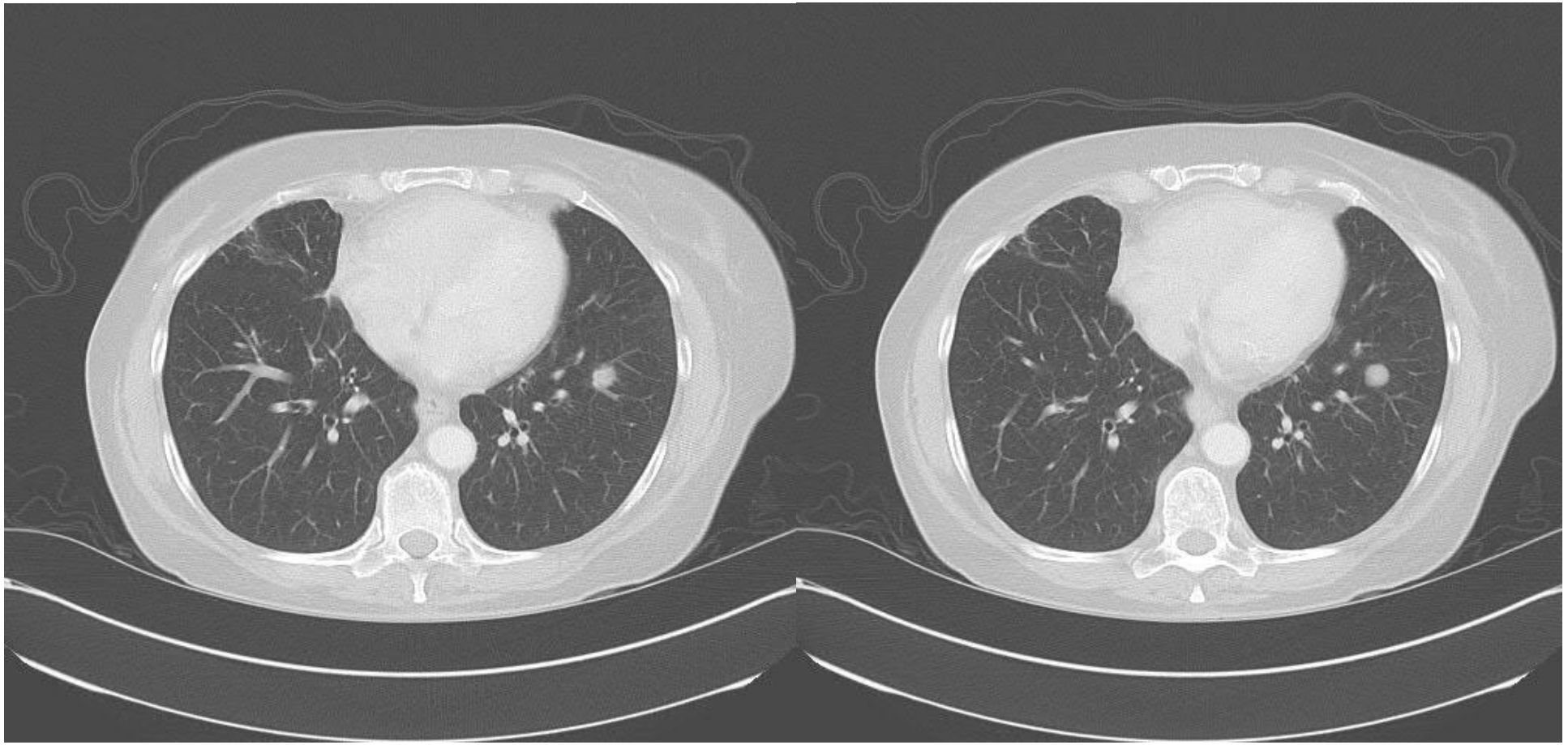
TOO DEEP



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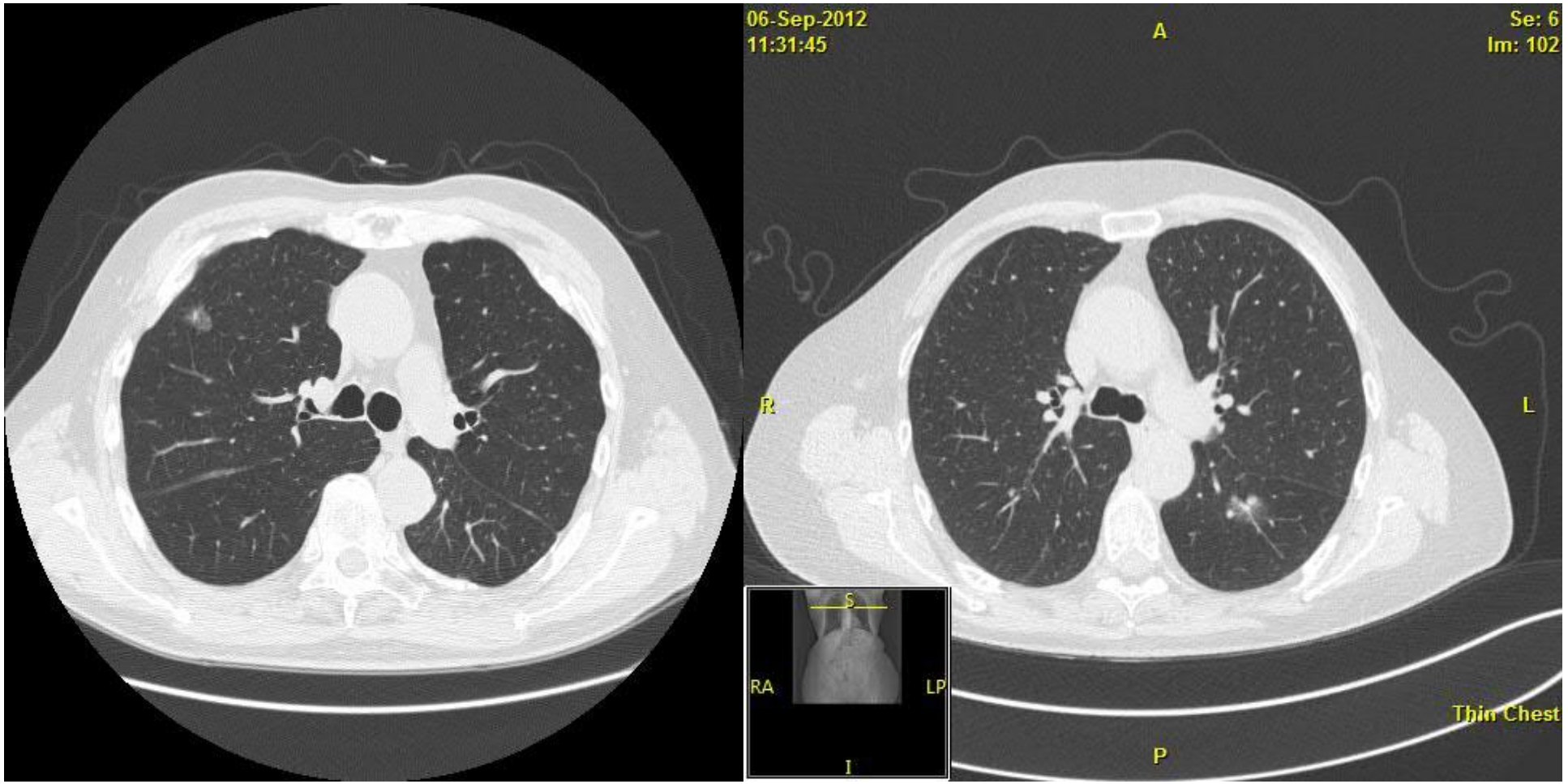
GROUND GLASS OPACITY – TOO SOFT



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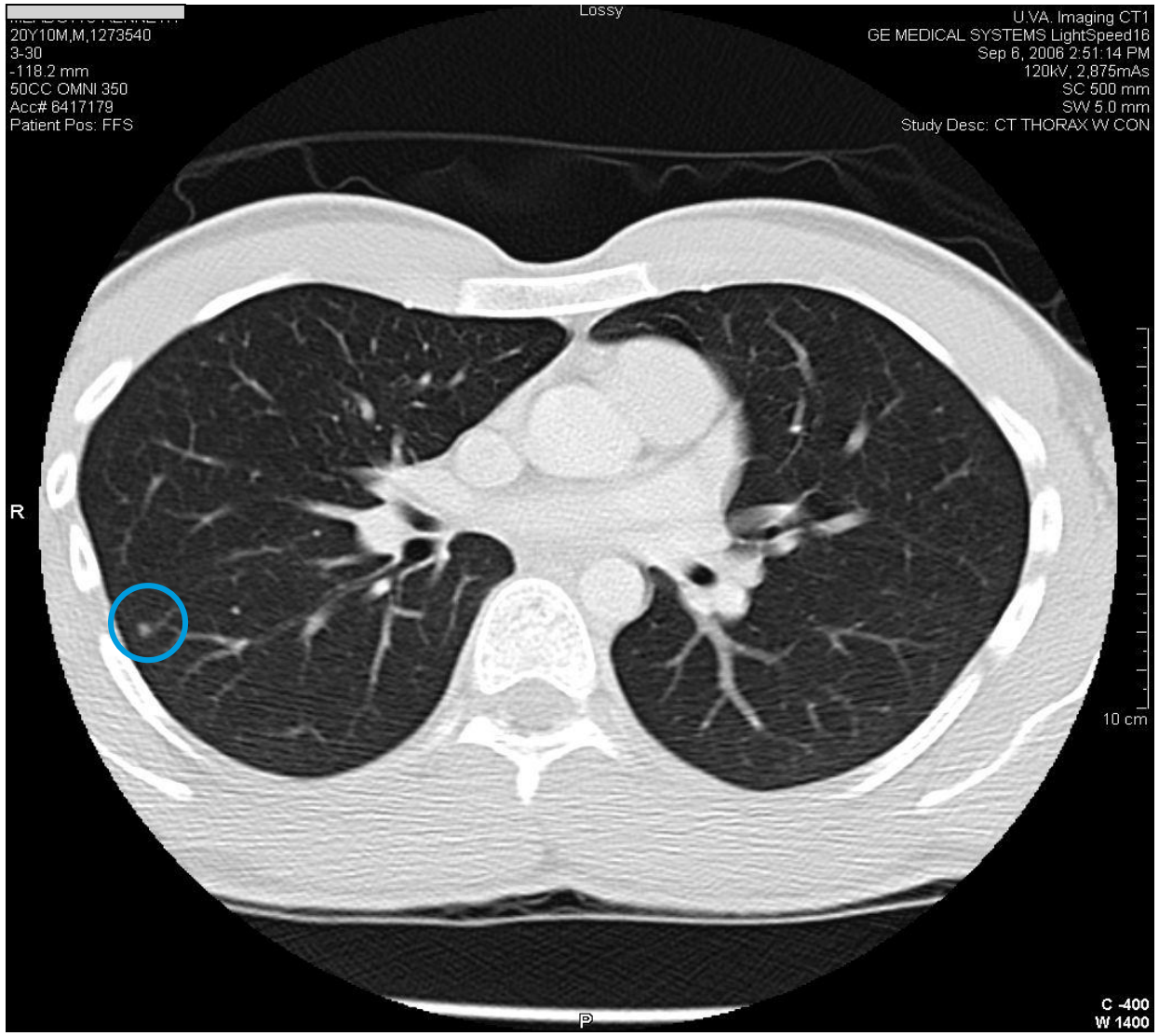
TOO SMALL



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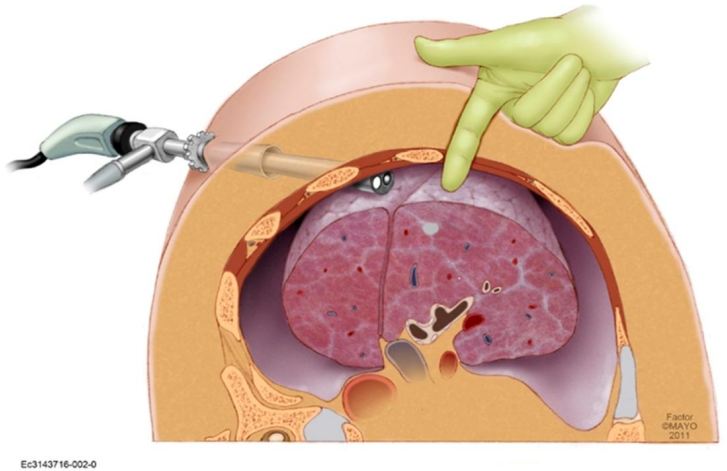
LUNG NODULE LOCALIZATION USING TC 99M MAA

Many approaches:

- Fiducial placement (CT or bronchoscopy)
- IV dye injection – folate analogues (Pafolacianine, OTL38), cathepsin-activated fluorophores (Abenacianine VGT-309), and others
- Tc 99m macroaggregated albumin (MAA)



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LUNG NODULE LOCALIZATION USING TC 99M MAA





- CT - guided placement of 22 gauge needle using CT fluoroscopy

- Injection of Tc 99m MAA
  - 0.3 millicuries
  - 0.1 ml volume
  - Flush with 0.3 ml of saline



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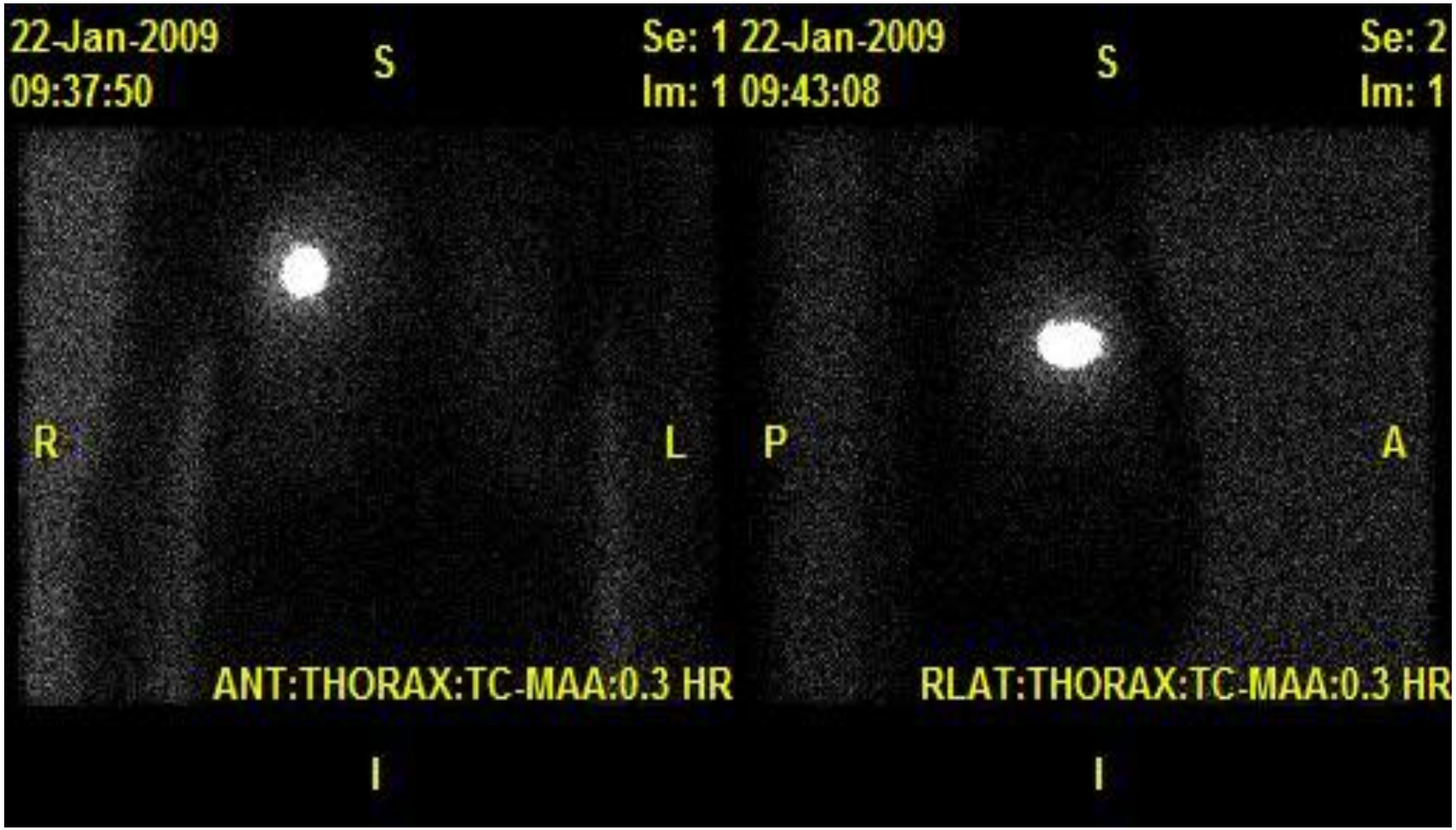
SCINTIGRAM TO VERIFY INTRAPARENCHYMAL PLACEMENT



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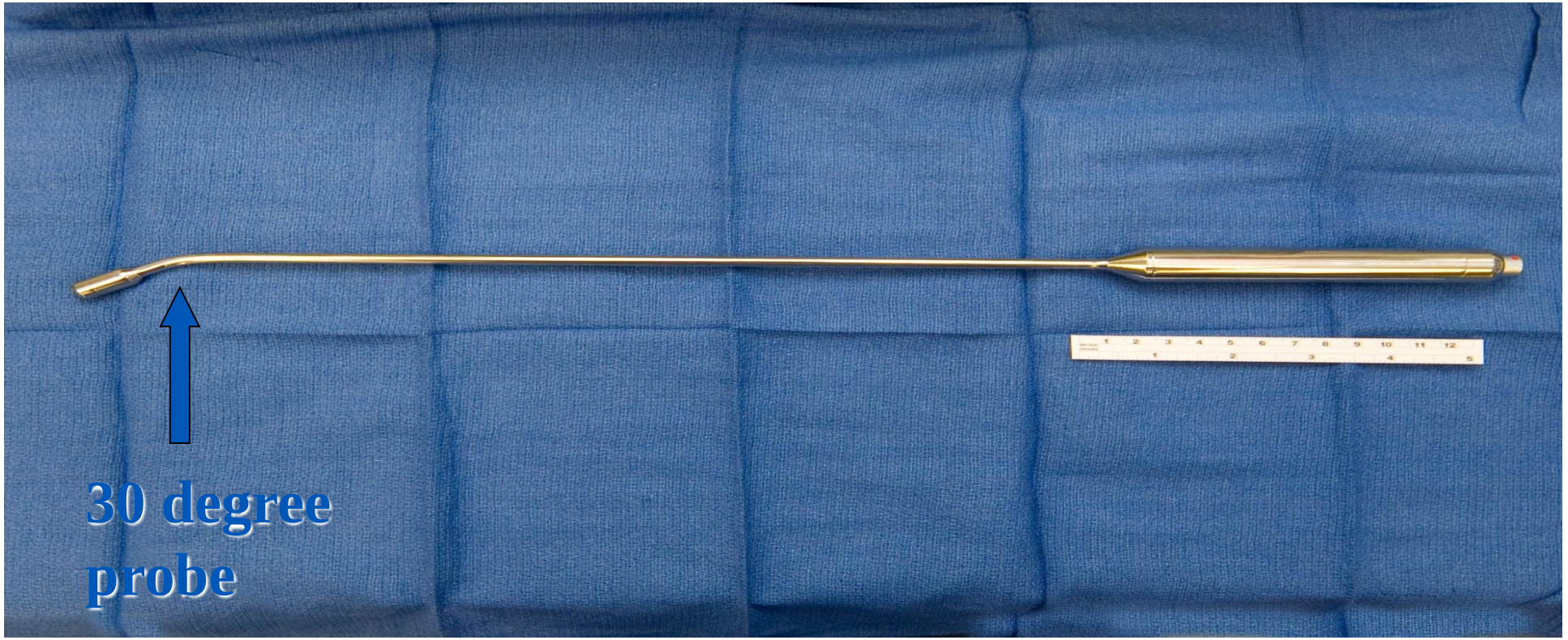
DANIEL PROBE



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NAVIGATOR GPS CONTROL UNIT



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LUNG NODULE LOCALIZATION USING TC 99M MAA

Advantages:

- 1000+ cases to date at Mayo Clinic
- Ready availability of tracer, CT technology, radiology expertise, and gamma radio-probe in most hospitals
- Stability as nodule marker for up to 12 hours; up to 19 hours (with increased tracer dose) if placed preceding afternoon
- No known hazard to patient or hospital personnel
- Can mark nodules located in any region of the lung

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Questions &
Discussion
THANK YOU!!



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HOT TAKES FOR TALK

- A properly done wedge resection for a 2 cm or less lesion in a node-negative patient has no different clinical outcome than the most elegant of segmentectomies
- GGO lesions may not need MLND
- most of the benefit people get from immunotherapy is up front in the neoadjuvant setting - pre-treat as much as you can rather than trying to make up for it in the adjuvant setting
- despite advances to date, nodule localization is under appreciated and continues to be a field ripe for innovation
- Taking time to learn and implement robotic vascular control is worth it - do it; you will not regret it
- in the next 10 years, bronchoscopic based therapeutics are the biggest threat to surgical resection as a treatment modality for early stage lung cancer

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