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“Goldilocksing” Lung Resection for Early-Stage Lung Cancer: How Much is Just Right?

Current Clinical Evidence and Technical Considerations

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Thoracic Surgery

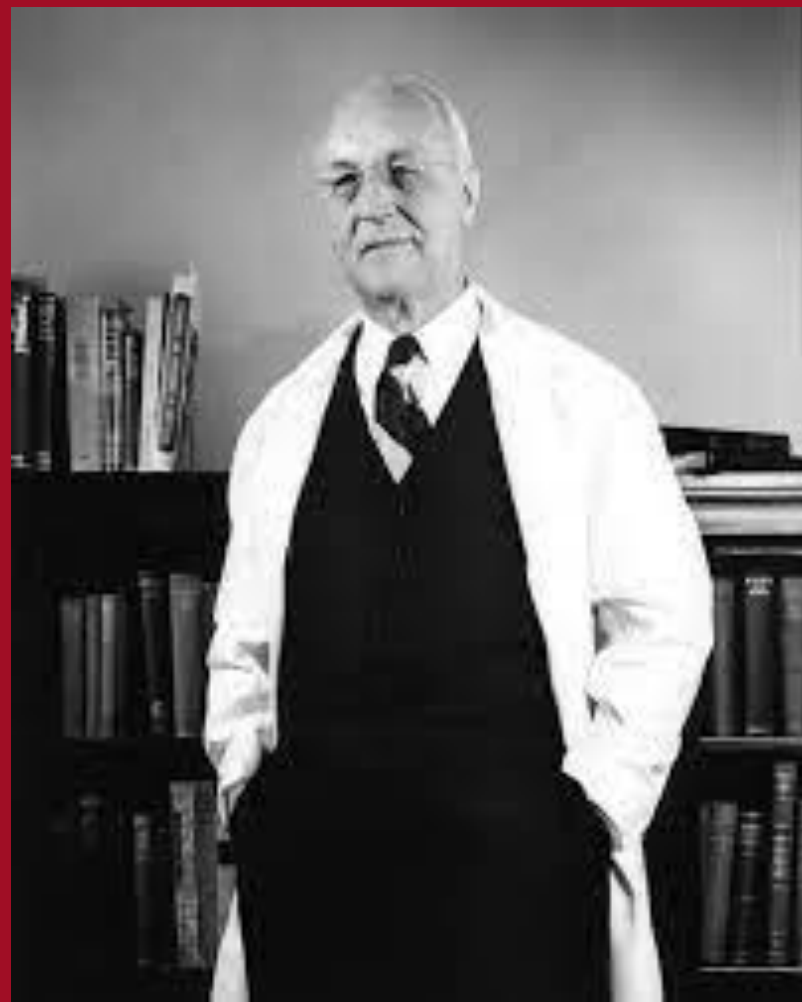
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Disclosures

None



Evarts A. Graham, M.D.



- Founded and then led the Division of Cardiothoracic Surgery at Washington University from 1933-1951
- Chairman of Surgery at Wash. U. for 32 years, from 1919 to 1951
- With Drs. Singer, Bell, and Adams, he performed first pneumonectomy for lung cancer in 1933 which became the first standard treatment
- He was instrumental in forming the American Board of Surgery in 1937 and was the first “board-certified” by the ABS.
- Collaborated with Dr. Wynder on the first large scale systematic survey on the carcinogenic effects of smoking cigarettes, which Dr. Graham himself did moderately.
- Died in 1957
- Cause of death: lung cancer (metastatic to brain and bones)

Shimpkin et al. 1962 JT CVS

- “Pneumonectomy and lobectomy in Bronchogenic Carcinoma: A comparison of end results of the Overholt and Ochsner clinics.”
- Combined the data on a total of 531 patients from Dr. Ochsner in New Orleans and Dr. Overholt in Boston
- Lobectomy equal to pneumonectomy in terms of 5 year survival and carried lower morbidity
- Established lobectomy as the new standard operation for lung cancer instead of pneumonectomy

Lung Cancer Study Group Trial 821

- 1995
- Compared sub-lobar resection with lobectomy for T1N0M0 NSCLC measuring up to 3 centimeters in size
- Better Outcomes for Lobectomy
 - Survival favored lobectomy, but didn't reach significance
 - 3x higher recurrence in sub-lobar group

1995-Present

- Lots of debate about the role of sub-lobar resection
- Lots published and presented
- Lots of imperfect data...based on series, retrospective data, database data

We do know, that a lot has changed...

- Lung cancer disease profile has changed
 - Advent of LDCT
 - Significant stage shift in diagnosed lung cancer
 - Small peripheral adenocarcinomas predominate
 - GGOs and part solid tumors
 - <2cm tumors common
 - Advances in preoperative pathologic staging and pathologic classification, improving patient selection

We do know, that a lot has changed...

- So, the profile of lung cancer has dramatically changed.
- Surgery has also dramatically changed.

LCSG Operative Mortality Data (published 1983)

(These are all open operations)

30 day mortality:

- 2.9% for lobectomy
- 6.2% pneumonectomy
- 7.1% for patients >70 years if age

These numbers continue to be referred to in some literature when discussing the morbidity of surgery.

STS Database

2019 - 2021

80% minimally
invasive

Perioperative
mortality 0.5-1.1%

LOS 3D

Variable	Lobectomy (n = 40,408)	Segmentectomy (n = 7029)	Wedge Resection (n = 16,644)
Mortality			
In hospital	0.7	0.3	0.3
Operative ^b	1.1	0.5	0.6
Morbidity			
Major morbidity ^c	9.5	N/A	N/A
Unexpected return to OR	5.7	3.6	2.5
ARDS	0.4	0.2	0.2
Pneumonia	3.1	2.1	1.2
Bronchopleural fistula	0.2	0.1	0.1
Pulmonary embolus	0.5	0.3	0.2
Respiratory failure	2.0	1.1	0.8
Initial ventilator support >48 h	0.3	0.1	0.2
Tracheostomy	0.6	0.2	0.2
Myocardial infarction	0.2	0.1	0.1
New renal failure	0.5	0.2	0.3
Anastomotic leak ^d
RLN paresis	0.4	0.2	0.1
Air leak >5 days	11.7	6.7	5.1
Atrial arrhythmia ^e	8.7	4.7	2.2
Postoperative length of stay, d			
Mean	4.7	3.7	3.3
Median	3.0	3.0	2.0

We do know, that a lot has changed...

- Advances in other on-surgical and systemic therapies are further transforming the treatment landscape...as we have already heard today.

In the last year or so...

2022 in LANCET: **JCOSOG0802**: a multicenter (Japan), open-label, phase 3, randomized, controlled, non-inferiority trial, randomized to lobectomy or segmentectomy

2023 in NEJM: **CALGB 140503**: Multicenter (US, Canada, Australia), open label, phase 3, randomized, controlled, non-inferiority trial, randomized intra-op to lobectomy or sub-lobar resection

JCOSOG0802 (LANCET 2022)

- Saji et al.
- 70 institutions in Japan
- 1106 patients with IA tumors <2cm and consolidation:tumor ratio >0.5 randomized to
lobectomy vs. segmentectomy
- 5 yr OS 91.1 vs. 94.3%
- 5 year relapse free survival 88% in both groups
- Local relapse 5.4% vs. 10.5%
- Improved overall survival in segmentectomy attributed to more aggressive resection/treatment of relapses, new primaries, and other cancers, thereby overcoming the effect of the increased incidence of local recurrence

CALGB 140503 / Alliance Trial (NEJM 2023)

- Altorki et al.
- 697 pts (1080 patients pre-registered) 83 academic and community hospitals in the US, Canada, Australia
- T1a tumors <2cm
- Randomized intraoperatively, after frozen N1 and N2 lymph nodes confirmed pathologically negative, to lobectomy or sub-lobar resection
 - Reasons for failure to progress to randomization were undiagnosed benign disease (50%), intraoperative upstaging (22.6%), or malignant disease other than NSCLC (7.7%)
- Wedge vs segmentectomy not differentiated, left the discretion of surgeon and wedges could be converted to segmentectomy at the discretion of the surgeon. 60% wedge, 40% seg.
- Took a long time to accrue
- After median follow up 7 yrs
- 5 yr DFS 64.1 vs 63.6
- 5 year OS 78.9 vs 80.3
- No difference between the groups in locoregional or distant recurrence (30%!!)
- PFT difference @ 6 months, ~2%

Post-Hoc Analysis of CALGB 140503 (JTCVS 2023)

- Lobe vs segmentectomy vs wedge
- Limitations of study, including post-hoc analysis
- “Best evidence that there are no significant differences in oncological outcomes between segmentectomy and wedge resection” in THIS SUBSET of patients with NSCLC in the clinical scenario introduced by the trial protocol.
- The protocol of the trial probably played a role...
 - i.e. not randomized, surgeon discretion about type of operation, etc

Many Risks and Challenges to Interpreting These Results

- Trials performed under stringent protocols for
 - Patient selection
 - Parenchymal margins
 - Aggressive nodal staging (N1 and N2) intra-op prior to randomization in CALGB 140503 trial
- Are all sub-2cm tumors created equal?
 - NO
 - Clinicopathologic differences, genomic differences, airway spread, etc.

So how much is just right? What's the takeaway?

- These studies were done with rigid protocols that highly selected the patient population
- In patients with marginal pulmonary function where segmentectomy spares a large volume of functional parenchyma the decision more simple
 - But...PFT differences between lobectomy and sub-lobar resection were statistically significant but clinically small in these studies
- For patients who could tolerate lobectomy, it is about PATIENT SELECTION – identifying the patients who could benefit
 - Lung preservation for aggressive intervention in the future and weighing that against the risk of local recurrence

So how much is just right? What's the takeaway?

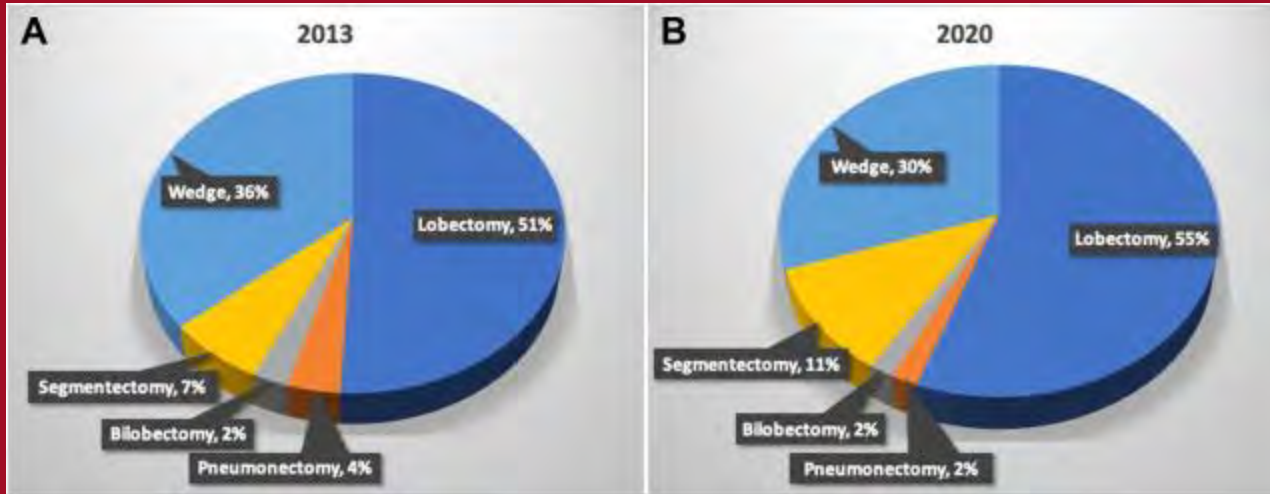
- Not a reason/excuse to compromise on optimal surgical care
- Segmentectomy is an oncologically sound operation with non-inferior overall survival to lobectomy in carefully selected patients
- Carefully applied, it represents one more tool for lung cancer treatment, carefully tailored to each patient's specific clinical situation

2023 NCCN Guidelines

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 \geq 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^a ≤ 2 cm with at least one of the following:
 - ◊ Pure AIS histology
 - ◊ Nodule has $\geq 50\%$ ground-glass appearance on CT
 - ◊ Radiologic surveillance confirms a long doubling time (≥ 400 days)
- VATS or minimally invasive surgery (including robotic-assisted approaches) should be strongly considered for patients with no anatomic or surgical contraindications, as long as there is no compromise of standard oncologic and dissection principles of thoracic surgery.
- In high-volume centers with significant VATS experience, VATS lobectomy in selected patients results in improved early outcomes (ie, decreased pain, reduced hospital length of stay, more rapid return to function, fewer complications) without compromise of cancer outcomes.

Resection breakdown 2013 to 2020





Farhood Farjah

@FarhoodFarjah



What would you recommend?

- ◆ average risk pt fit for lobectomy
- ◆ peripheral cT1N0M0 NSCLC
- ◆ LUL
- ◆ part-solid (⬆️ density & size)
- ◆ now 1.7cm (0.8cm solid)
- ◆ SUV 2
- ◆ wedge ➡️ (—) margins
- ◆ trisegmentectomy ➡️ (—) margins
- ◆ pt wants efficacy/safety/HRQOL

wedge

19.3%

segmentectomy

63.9%

lobectomy

14.5%

defer to patient

2.4%

83 votes · Final results

8:05 AM · Mar 6, 2023 · 6,511 Views

Technical Considerations for Segmental Resections

Segmentectomy techniques

- Variable anatomy: preoperative planning critical, because the anatomy is critical, and it varies!
 - Detailed reconstructions possible with new technology
 - But with axial, coronal, and sagittal cuts you can get an excellent understanding of the anatomy
- Defining the intersegmental plane: Inflation, slipknot, ICG
- Localizing small lesions below the surface (don't have access incision, away from patient is robotic, and even if have access incision lesions may not be palpable (GGOs, semisolid lesions))

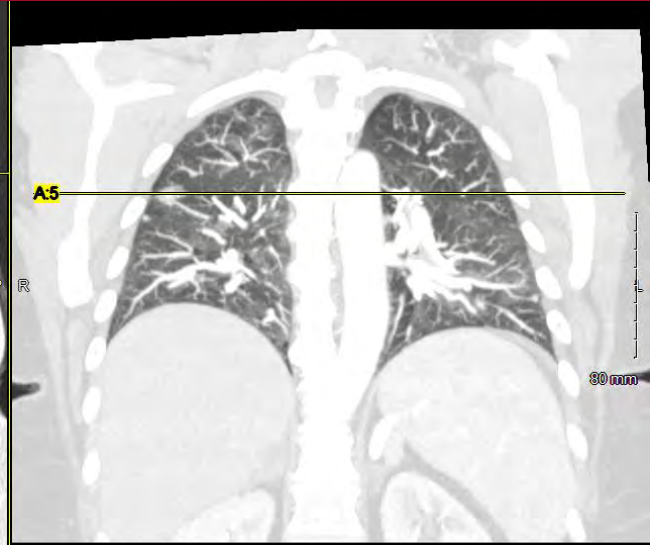
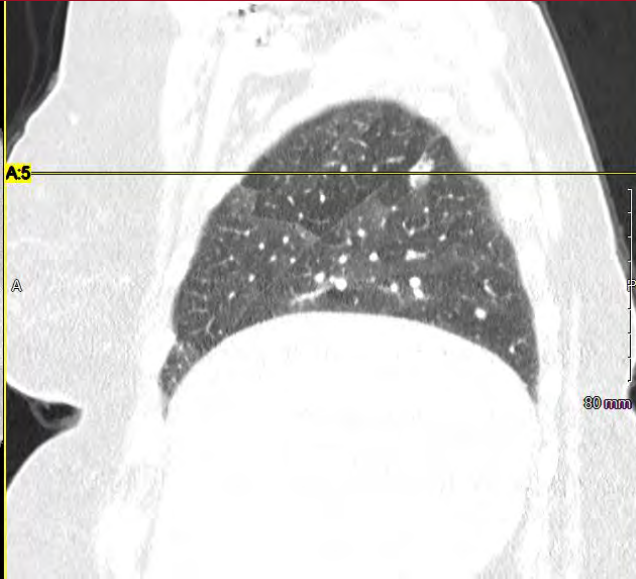
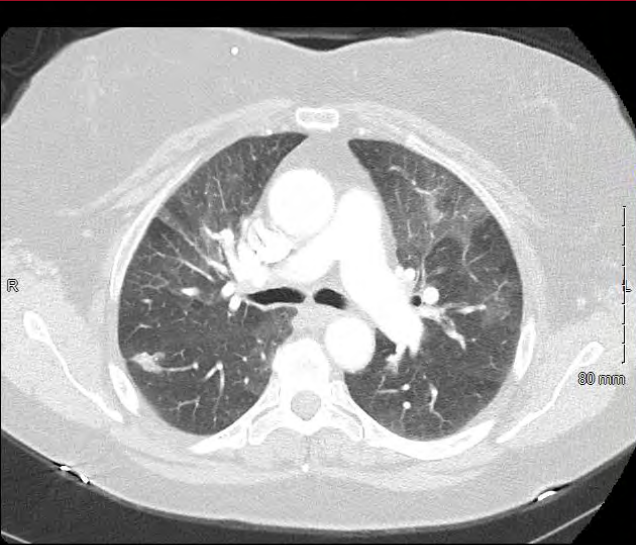
Technical Challenge #1: Defining the intersegmental plane

- There are clear strengths of the robot particularly for dissecting segmental anatomy and defining the intersegmental plane
- Also, a forgiving platform in terms of set up, particularly for early career surgeons
- Importance and quality of the lymph node dissection
- Use of navigational bronchoscopy to localize the lesion

Segmentectomy Patient

- 59 year old woman, current smoker.
- BMI 36.
- On chronic immunosuppression, has LGL leukemia.
- 1.1cm tumor at the top of the superior segment of the right lower lobe, biopsy proven well differentiated adenocarcinoma
- PFTs only mildly diminished, with mild restrictive disease, and definitely adequate for lobectomy

CT



S6 (Right) Robotic Assisted Superior Segmentectomy



ROBOTIC
THORACIC
SURGERY



Times: 340, 610, 650, 830, 924, 945, 1050, 1142, 1211, 1300, 1448, 1534, 1725, 1800, 1843, 1922, 2048. (Console time for our patient, not one in video, 120 mins)

Credit: Daryl Pearlstein, MD

Back to our patient

- Chest tube out POD #1.
- Discharged home POD #2.
- Doing well in follow up 6 months out.
- Still smoking.



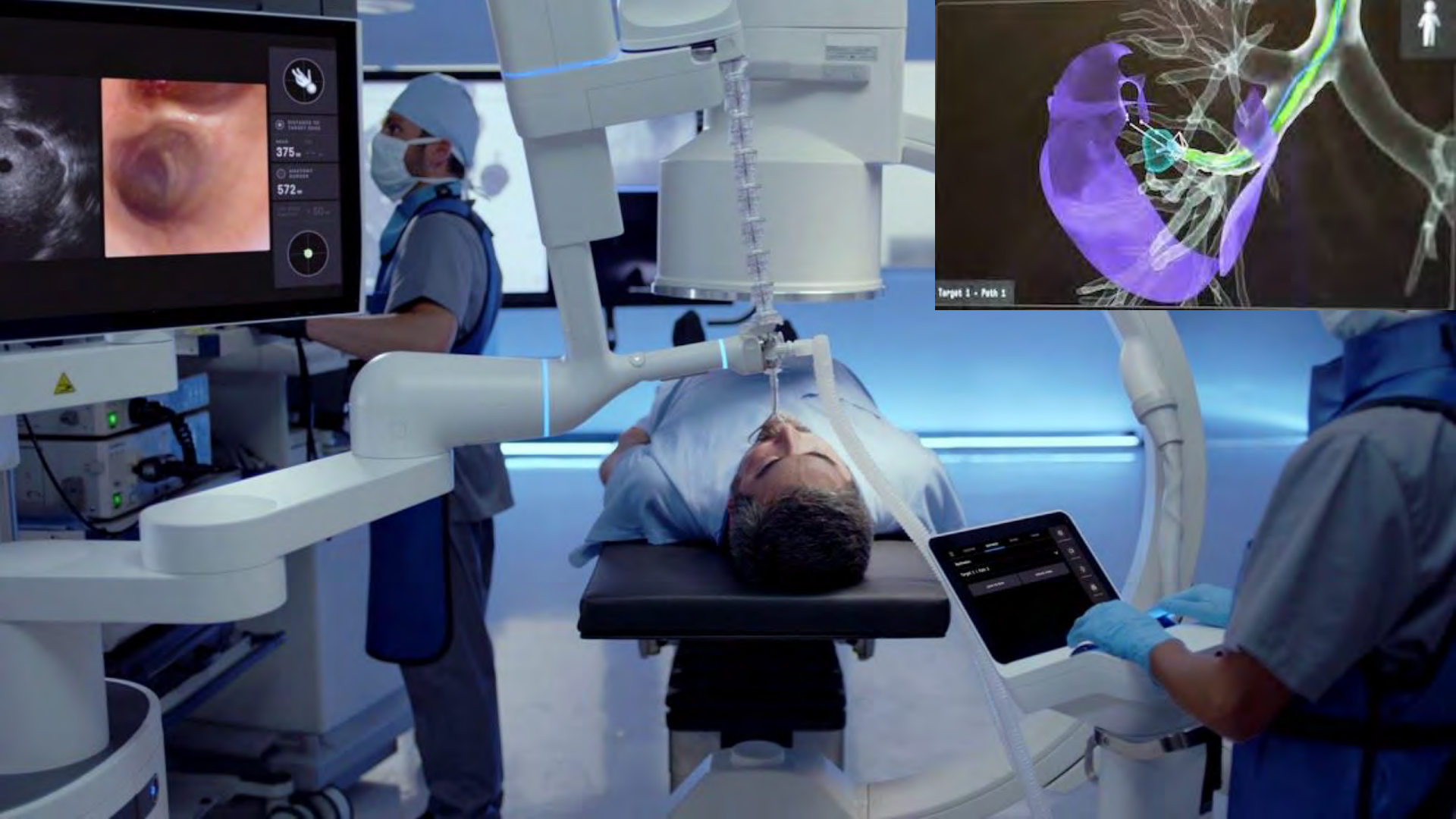
Path: Level 2R, 4R, 9R, 7, 11R, 12R (0/11) lymph nodes negative, 1.1cm well to moderately differentiated adenocarcinoma, no pleural or lymphovascular invasion, negative surgical margins (closest approach 1.5cm from staple line).

Technical Challenge #2: How to best localizing Small Lesions For Sub-lobar Resection, particularly if not palpable or using the robot

- GGOs/small tumors that are below the surface may be difficult to find/may not be palpable and the robot does not have tactile feedback anyway and typically no access incision.
- Marking – many techniques out there.....
 - ICG (Indocyanine green)
 - Methylene Blue
 - Omnipaque?
 - Some add blood to prior to injection?
 - ICG soaked coil?

Navigational bronchoscopy and localizing small lesions

1. Combining diagnosis and pathologic staging of suspicious nodules into one procedure
2. Biopsy multiple nodules in different lobes or different lungs in one procedure
3. Facilitating the marking or fiducial placement in small tumors



375

572



Target 1 - Path 1



Localizing Small Lesions

Marking Nodule

Source: Bawaadam H, Benn BS, Colwell EM, Oka T, Krishna G. Lung Nodule Marking With ICG Dye–Soaked Coil Facilitates Localization and Delayed Surgical Resection. *Annals of Thoracic Surgery Short Reports*. 2023 Feb 27.

Localizing Small Lesions

- Intraoperative View with Firefly

Source: Bawaadam H, Benn BS, Colwell EM, Oka T, Krishna G. Lung Nodule Marking With ICG Dye–Soaked Coil Facilitates Localization and Delayed Surgical Resection. *Annals of Thoracic Surgery Short Reports*. 2023 Feb 27 .

Localizing Small Lesions

Resected Tissue with Marked Nodule in Specimen

Source: Bawaadam H, Benn BS, Colwell EM, Oka T, Krishna G. Lung Nodule Marking With ICG Dye–Soaked Coil Facilitates Localization and Delayed Surgical Resection. *Annals of Thoracic Surgery Short Reports*. 2023 Feb 27.

Takeaway

- With correct patient selection (beyond the basic radiographic and pathologic data to include tumor genomics and more detailed clinicopathologic data), sublobar resection will continue to play an increasingly important role in optimal surgical treatment for lung cancer patients.

Future Question

What Will Be the Role for Single Anesthetic Events in the Treatment of Early Stage Lung Cancer?

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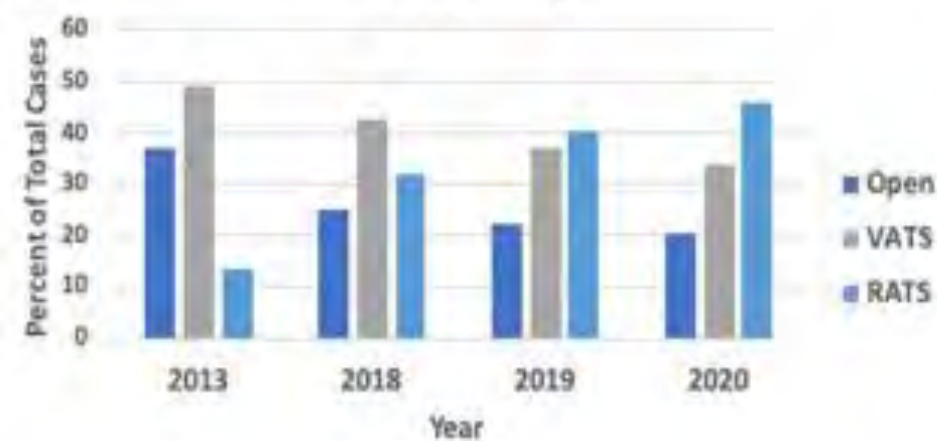
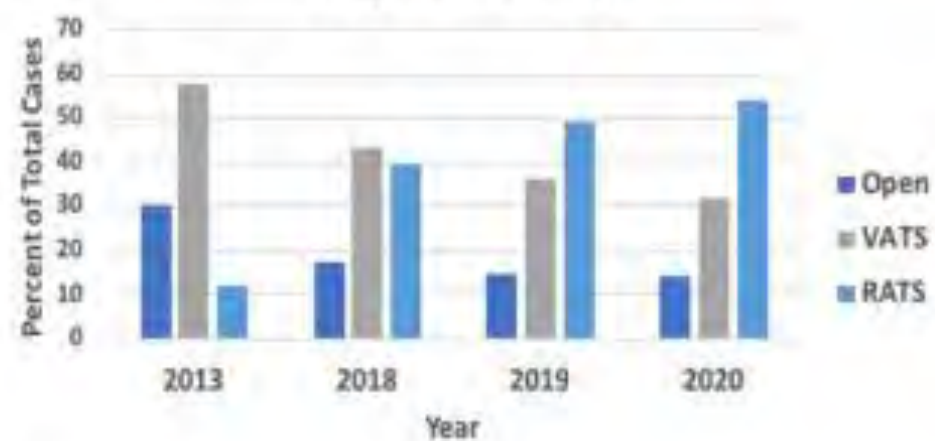
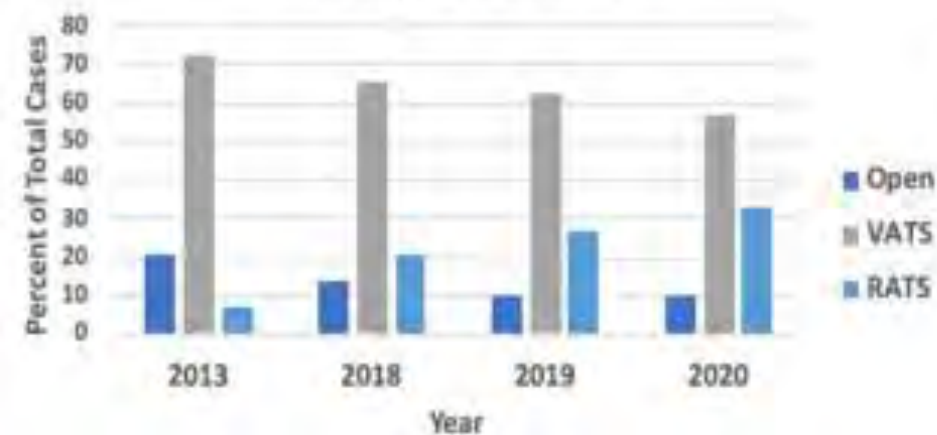
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A**Lobectomy****B****Segmentectomy****C****Wedge Resection****D****Esophagectomy**