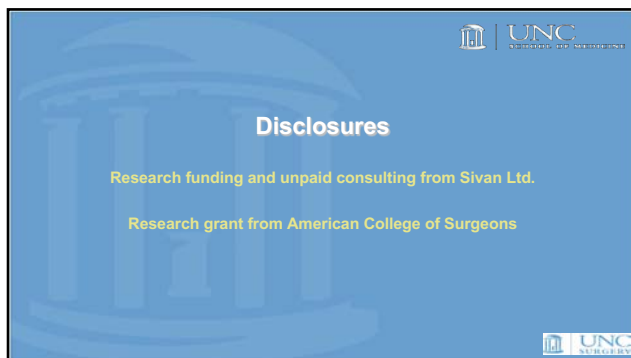
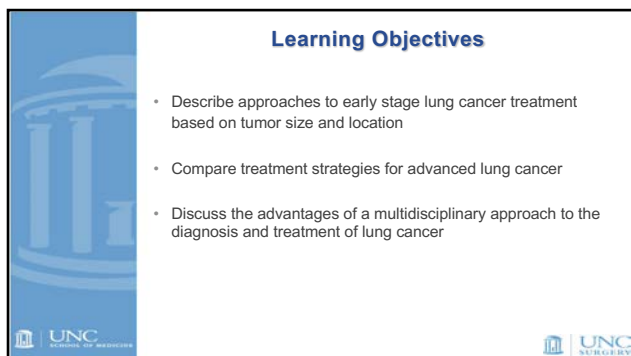



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Outline of talk

- Early stage lung cancer
 - Lobar resections
 - Sublobar resections
 - Nodule localization
 - Minimally invasive surgery
 - SBRT
- Advanced stage lung cancer
 - Defining resectability
 - Neoadjuvant regimens
 - Adjuvant regimens
- Highlights from 101st AATS and ASCO 2021




4



Common Types of Cancer	Estimated New Cases 2021	Estimated Deaths 2021
1. Breast Cancer (Female)	281,550	43,600
2. Prostate Cancer	248,530	34,130
3. Lung and Bronchus Cancer	235,760	131,880
4. Colorectal Cancer	149,500	52,980
5. Melanoma of the Skin	106,110	7,180
6. Bladder Cancer	83,730	17,200
7. Non-Hodgkin Lymphoma	81,560	20,720
8. Kidney and Renal Pelvis Cancer	76,080	13,780
9. Uterine Cancer	66,570	12,940
10. Leukemia	61,090	23,660

Lung and bronchus cancer represents 12.4% of all new cancer cases in the U.S.




12.4%



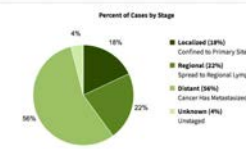
Lung and Bronchus Cancer - Cancer Stat Facts.
Available online: <https://seer.cancer.gov/statfacts/html/lungab.html>

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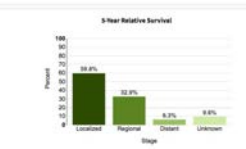
Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Lung and Bronchus Cancer


Percent of Cases by Stage



- Localized (18%)
Confined to Primary Site
- Regional (22%)
Spread to Regional Lymph Nodes
- Distant (36%)
Cancer has metastasized
- Unknown (4%)
Unstaged


5-Year Relative Survival






Lung and Bronchus Cancer - Cancer Stat Facts.
Available online: <https://seer.cancer.gov/statfacts/html/lungab.html>

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Surgery for lung cancer overview

- Stage I/II (localized)
 - » First line for medically operable
 - » Adjuvant chemotherapy for stage II (>4cm or N1)
- Stage IIIa (regional):
 - » Upfront for no mediastinal involvement (T4N0, T3-4N1)
 - » After neoadjuvant for mediastinal involvement (T1-2,N2)
- Stage IIIb/IV:
 - » Typically for diagnosis/palliation


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Outline of talk

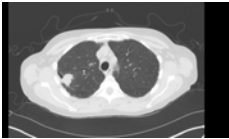
- Early stage lung cancer
 - » Lobar resections

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Lung cancer case presentation # 1



- 58yF current smoker
- Incidental RUL nodule on CT scan after MVC 3 years previously
- Enlarged to 3cm on serial CT scans

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Lung cancer case presentation # 1

- Lost to follow up
- Developed symptoms
- Staging PET showed avid hilar and mediastinal lymph nodes

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Thoracic surgery is the mainstay of curative treatment of early stage lung cancer.

- >80,000 lung resection procedures are performed annually in the United States.
- Surgeries are increasing by 1.7% per year.

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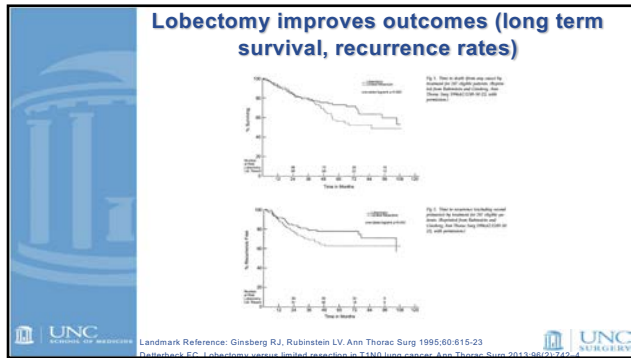
Fingar KR et al. Statistical Brief #186: Most Frequent Operating Room Procedures Performed in U.S. Hospitals, 2003-2012. PMID: 25695123
Images from <https://www.mskcc.org/cancer-care/patient-education/about-your-thoracic-surgery>

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Lung cancer case presentation # 1


- Mediastinal staging (N2 nodes negative)
- Video Assisted Thoracoscopic Surgery (VATS) right upper lobectomy
- pT2a (3.5cm) N1
- Adjuvant chemotherapy

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Outline of talk

- Early stage lung cancer
 - » Lobar resections
 - » Sublobar resection
 - Marginal pulmonary function
 - Multifocal disease


15




Segmentectomy has equivalent short-term survival to lobectomy.

	90-day mortality		P-value	90-day mortality		P-value
	Lobar resection	Sublobar resection		Lobar resection	Sublobar resection	
Overall	4/357 (1.1%)	4/346 (1.2%)	0.556 (-4.3 to 2.5)	4/357 (1.1%)	4/346 (1.2%)	0.556 (-4.3 to 2.5)
≤65 years	1/87 (1.1%)	0/81 (0%)	→	1/87 (1.1%)	0/81 (0%)	→
66-75 years	1/142 (0.7%)	0/141 (0%)	→	1/142 (0.7%)	0/141 (0%)	→
≥76 years	1/111 (0.9%)	1/103 (1.0%)	→	1/111 (0.9%)	1/103 (1.0%)	→
≤65 years	1/117 (0.9%)	0/111 (0%)	→	1/117 (0.9%)	0/111 (0%)	→


Altorki NK, Wang X, Wigle D, et al. Perioperative mortality and morbidity after sublobar versus lobar resection for early-stage non-small-cell lung cancer: post-hoc analysis of an international, randomised, phase 3 trial (CALGB/Alliance 140503). Lancet Respir Med. 2018 Dec;6(12):915-924.




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Technique to perform segmentectomy.






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Outline of talk

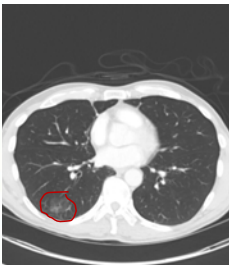
- Early stage lung cancer
 - » Lobar resections
 - » Sublobar resection
 - Marginal pulmonary function
 - Multifocal disease
 - » Nodule localization




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Lung cancer case presentation # 2



- 63yM w former smoking history
- Scan for restaging of lymphoma
- Increasing 2.5cm ground glass opacity in right lower lobe



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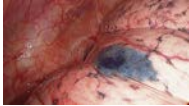
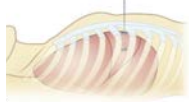


Non-solid/small/central nodules may need intraoperative localization.

Preop CT Scan data is used to map nodule location during intraoperative bronchoscopy using electromagnetic sensors in pads on chest, bronchoscope tip.

Dye (blue, fluorescent) is injected at the mapped site.

Surgeon visualizes dye(s) intraoperatively.

Slide courtesy of Dr. Jason Akulian

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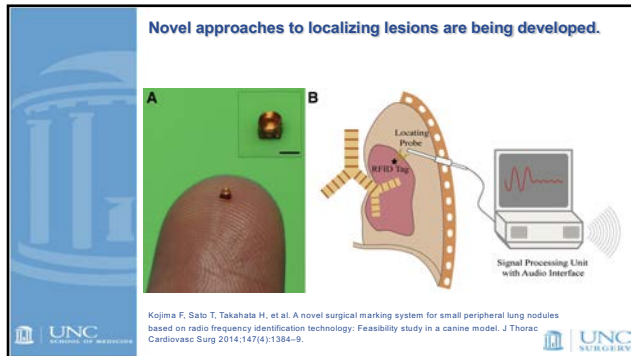
New technology can be employed to simultaneously diagnose and localize nodules.



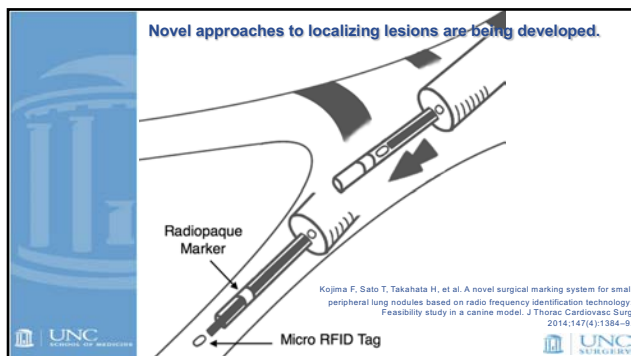

Agrawal A, et al. Robotic bronchoscopy for pulmonary lesions: a review of existing technologies and clinical data. J Thorac Dis. 2020 Jun;12(6):3279-3286. doi: 10.21037/jtd.2020.03.35. PMID: 32642251; PMCID: PMC7330790.



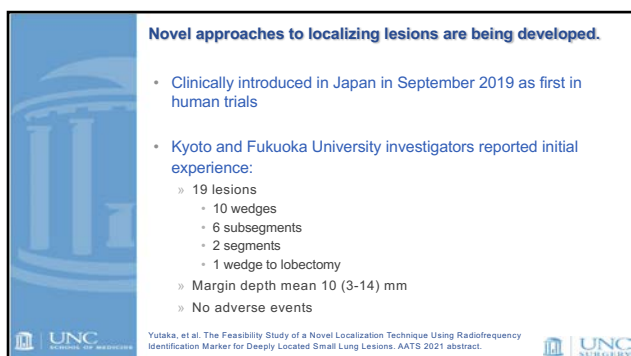
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Outline of talk


- Early stage lung cancer
 - » Lobar resections
 - » Sublobar resections
 - » Nodule localization
 - » Minimally invasive surgery
 - Video Assisted Thoracoscopic Surgery
 - Robotic Assisted Thoracoscopic Surgery



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VIOLET establishes minimally invasive for early stage lung cancer resection.





Phase 2, in 9 centres (24 months recruitment)

All patients referred for lobectomy for lung cancer (100%) n=1312

Eligible for VIOLET (60%)

Not eligible, 40%, n= 525

Not recruited, 50% in phase 1 centres, 70% phase 2 centres in first 6 months, 50% thereafter, n= 411

336 randomised to:

168 VATS


168 Open surgery

Phase 1 & 2 patients (162+336) followed up after surgery, n=498

>95% followed to primary outcome (5 weeks), 80% followed to 1 year

Lim E; VIOLET Trialists. Study protocol for Video assisted thoracoscopic lobectomy versus conventional Open Lobectomy for lung cancer, a UK multicentre randomised controlled trial with an internal pilot (the VIOLET study). BMJ Open. 2019 Oct 14;9(10):e029507. doi: 10.1136/bmjopen-2019-029507. PMID: 31615795; PMCID: PMC6797374.

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VIOLET establishes minimally invasive for early stage lung cancer resection.

- Study design
 - » cT1-3, N0-1 and M0 lung cancer
 - » 56 months, 503 participants
- Results favor VATS:
 - » less pain on VAS
 - » less analgesic consumption
 - » better physical function (EORTC QLQ-C30)

- » improved global health status
- » fewer complications
- » no difference in serious adverse events
- » hospital stay was shorter (4 vs 5 days)
- » lower 1 year readmission rates (29.0% vs. 35.9%)
- » Similar PFS (HR 0.74, 0.43 to 1.27; p=0.27)
- » Similar OS (HR 0.67, 0.32 to 1.40; p=0.282)

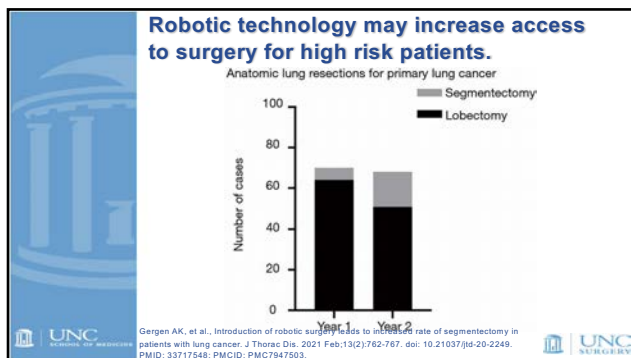
Lim E., et al. Video-assisted thoracoscopic versus open lobectomy in patients with early-stage lung cancer: One-year results from a randomized controlled trial (VIOLET). ASCO 2021 abstract

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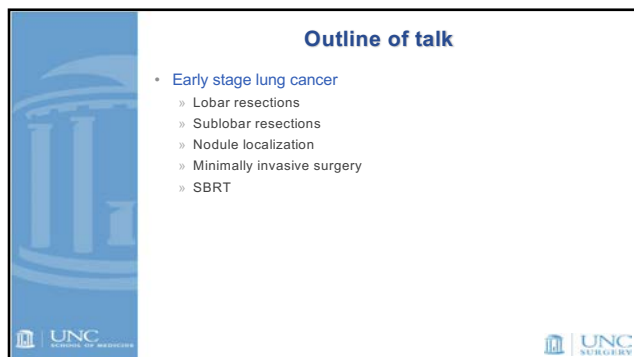
Robotic technology may improve lymph node sampling for NSCLC.

- Society of Thoracic Surgery (STS) database analysis
- 634 Robotic, 2,200 VATS, and 562 open segments
- Robotic segments removed ≥ 6 lymph nodes more commonly (34% vs. 14% vs 18%; $p < 0.001$)
- Upstaging 6.2% (compared to 5.6% VATS, 8.2% Open, $p = 0.049$)

Kneueritz, P., et al. Lymph Node Assessment During Segmentectomy for Stage I Non-Small Cell Lung Cancer in the National Society of Thoracic Surgery Database: A Propensity Score Adjusted Comparison of the Robotic, Vats and Open Approach. AATS 2021 abstract.

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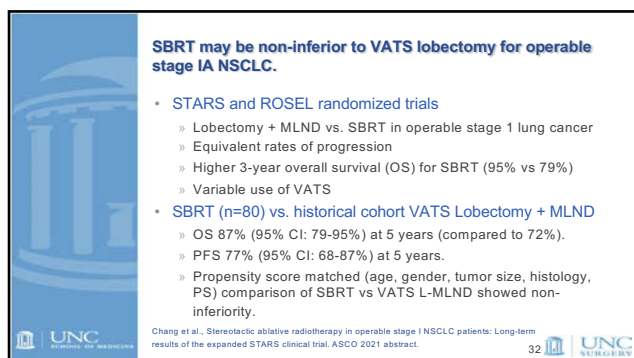
Outline of talk

- Early stage lung cancer
 - » Lobar resections
 - » Sublobar resections
 - » Nodule localization
 - » Minimally invasive surgery
 - » SBRT

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SBRT may be non-inferior to VATS lobectomy for operable stage IA NSCLC.

- STARS and ROSEL randomized trials
 - » Lobectomy + MLND vs. SBRT in operable stage I lung cancer
 - » Equivalent rates of progression
 - » Higher 3-year overall survival (OS) for SBRT (95% vs 79%)
 - » Variable use of VATS
- SBRT (n=80) vs. historical cohort VATS Lobectomy + MLND
 - » OS 87% (95% CI: 79-95%) at 5 years (compared to 72%).
 - » PFS 77% (95% CI: 68-87%) at 5 years.
 - » Propensity score matched (age, gender, tumor size, histology, PS) comparison of SBRT vs VATS L-MLND showed non-inferiority.

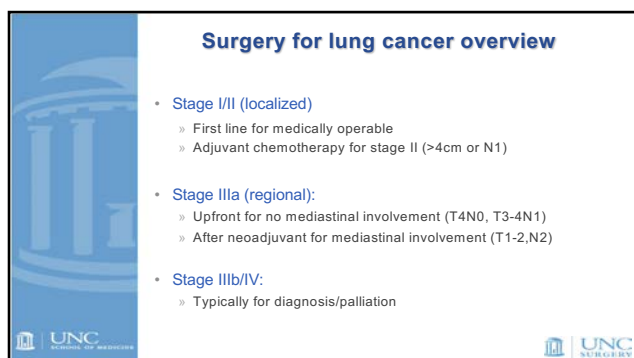
Chang et al., Stereotactic ablative radiotherapy in operable stage I NSCLC patients: Long-term results of the expanded STARS clinical trial. ASCO 2021 abstract.

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Surgery for lung cancer overview

- Stage I/II (localized)
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 - » Adjuvant chemotherapy for stage II (>4cm or N1)
- Stage IIIa (regional):
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 - » After neoadjuvant for mediastinal involvement (T1-2,N2)
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Outline of talk

- Early stage lung cancer
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- Advanced stage lung cancer
 - » Defining resectability




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Role of Surgery in stage III disease

Stage IIIa (T3N1, T4N0-N1)



- Location dependent and "resectable"
 - Tumors of chest wall (T3), proximal airway and mediastinum (T4) = surgical resection
 - T3 superior sulcus tumors : pre-operative chemoradiation followed by surgery
 - T4 superior sulcus tumors : definitive chemoradiation followed by immunotherapy




35



Surgical technology can be used to perform increasingly extended resections.



Mody GN, Jaklitsch MT, et al. Early Surgical Outcomes of En Bloc Resection Requiring Vertebrectomy for Malignancy Invading the Thoracic Spine. Ann Thorac Surg. 2016 Jan;101(1):231-6.



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Surgical technology can be used to perform increasingly extended resections.

- 32 patients/12 years
- 56% major morbidity
- 3% 30 day mortality
- 1 year survival 73.6%
- 5 year survival 40.3%


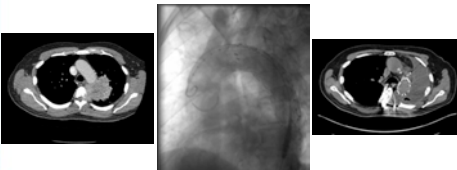


Fig 4. (A) and (B) Pre-operative reconstruction. The ipsilateral thoracotomy is placed if not already there. Cage and plate are placed as necessary through the thoracotomy. Note that the thoracotomy is not always a wedge or an en bloc.

Mody GN, Jakitsch MT, et al. Early Surgical Outcomes of En Bloc Resection Requiring Vertebroplasty for Malignancy Involving the Thoracic Spine. Ann Thorac Surg. 2016 Jan;101(1):231-6.

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Surgical technology can be used to perform increasingly extended resections.




Mody GN, Swanson S, et al. Thoracic Endovascular Aortic Stent Graft to Facilitate Aortic Resection During Pneumonectomy and Vertebroplasty for Locally Invasive Lung Cancer. Ann Thorac Surg. 2016 Apr;101(4):1587-9. doi: 10.1016/j.athoracsur.2015.05.131. PMID: 27000584.

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- Early stage lung cancer
 - » Lobar resections
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 - » Defining resectability
 - » Neoadjuvant regimens


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Controversies in Stage IIIa (especially N2)

- SWOG 8805 (1995): established safety of induction concurrent CRT (45 Gy) in N2/NS and/or T4
- RTOG 0229 (2012): 61.2Gy
- Intergroup 0139 (2009)
 - » Induction chemoradiation -> if no progression, 1: surgery 2: continued radiotherapy
 - » No overall survival advantage between two groups; Progression free survival better in surgery arm
 - » Subgroup analysis: improved overall survival in patients receiving lobectomy, rather than pneumonectomy
- ESPATUE (2015)
 - » Induction chemoradiation -> if tumors deemed resectable, 1: surgery 2: chemoradiation boost
 - » No difference in 5 year overall survival
- Mediastinal clearance improves OS
- Surgical resection may be best indicated for large tumors with sterilized mediastinum

Sher DJ. Neoadjuvant Chemoradiotherapy for Stage III Non-Small Cell Lung Cancer. Front Oncol. 2017 Dec 4;7:281. doi: 10.3389/fonc.2017.00281. PMID: 29255697; PMCID: PMC5722852.




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Surgery is increasingly considered in patients with advanced NSCLC.

- Design
 - » Pooled analysis of 3 Swiss trials
 - » IIIa (including single-multistation N2) and IIIb
 - » Chemo (3 cycles cisplatin/docetaxel + surgery vs. chemo + sequential RT (44Gy) + surgery
- Results
 - » 81% of 197 patients resected
 - » 80% R0 including 30/36 extended resection (mostly chest wall)
 - » OS 45% at 5 years and 28% at 10 years (similar in extended resection)

Furrer K., et al. Extended Resections for Advanced Stages T3/T4 NSCLC Including N2 Disease After Neoadjuvant Treatment: Results and Conclusions of SAKK Pooled Analysis (16/06, 16/00, 16/01). 19th AATS abstract 2021, <https://annualmeeting.aats.org/>




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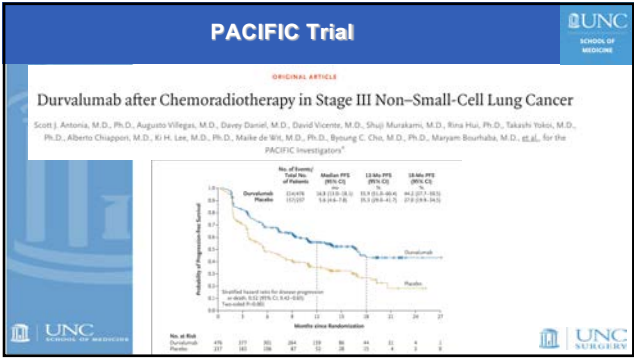


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- Advanced stage lung cancer
 - » Defining resectability
 - » Neoadjuvant regimens
 - » Adjuvant regimens



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Immunotherapy improves pathologic response and retains surgical feasibility: CheckMate 816 (NCT02998528)

- **Study design**
 - » 358 adults with resectable stage Ib–IIIA (AJCC 7th) NSCLC, ECOG PS 0–1, and no known *EGFR/ALK* alterations.
 - 64% IIIa
 - » randomized to preoperative immunotherapy + chemo (nivolumab 360 mg + platinum-doublet chemo Q3W 3 cycles) or chemo only
- **Results**
 - » improved pathological complete response (pCR) and depth of pathologic response for all stages with neoadjuvant NIVO + chemo

Spicer, et al. Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). ASCO 2021 abstract.

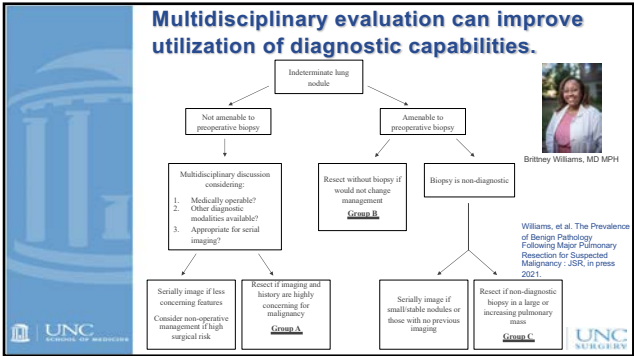
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Immunotherapy improves pathologic response and retains surgical feasibility: CheckMate 816 (NCT02998528)

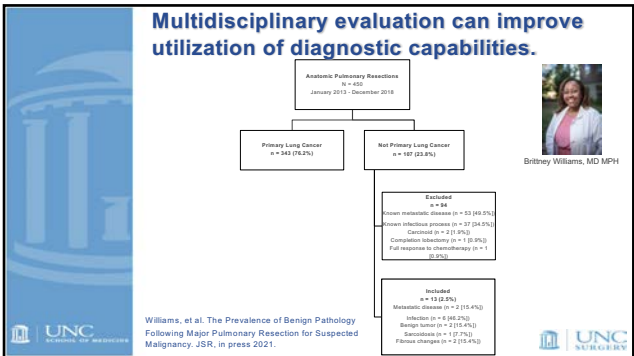
	NIVO + chemo	chemo
Definitive surgery	83%	75%
Minimally invasive	30%	22%
Conversion	11%	16%
Lobectomy	77%	61%
Pneumonectomy	17%	25%
R0 resection	83%	78%
Viable tumor	10%	74%
Duration of surgery	184 min	217 min
LOS	10 days	10 days
Surgical AEs	41%	47%

Spicer, et al. Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). ASCO 2021 abstract.

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- Questions
- Thank you



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