Advances in Thoracic Surgical Oncology

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Learning Objectives
- Describe approaches to early stage lung cancer treatment based on tumor size and location
- Compare treatment strategies for advanced lung cancer
- Discuss the advantages of a multidisciplinary approach to the diagnosis and treatment of lung cancer
Outline of talk

- Early stage lung cancer
  - Lobectomy
  - 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

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Lung and Bronchus Cancer - Cancer Stat Facts.

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Lung and Bronchus Cancer - Cancer Stat Facts.
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

Outline of talk

- Early stage lung cancer
  - Lobar resections

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
Lung cancer case presentation # 1

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

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.
Lobectomy improves outcomes (long term survival, recurrence rates)

Lung cancer case presentation #1
• Mediastinal staging (N2 nodes negative)
• Video-assisted Thoracoscopic Surgery (VATS) right upper lobectomy
• pT2a (3.5 cm) N1
• Adjuvant chemotherapy

Outline of talk
• Early stage lung cancer
  - Lobar resections
  - Sublobar resection
  - Marginal pulmonary function
  - Multifocal disease
Segmentectomy has equivalent short-term survival to lobectomy.


Outline of talk
- Early stage lung cancer
  - Lobar resections
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  - Multifocal disease
  - Nodule localization
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

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.

New technology can be employed to simultaneously diagnose and localize nodules.
Novel approaches to localizing lesions are being developed.

- Clinically introduced in Japan in September 2019 as first in human trials
- Kyoto and Fukuoka University investigators reported initial experience:
  - 19 lesions
  - 10 wedges
  - 6 subsegments
  - 2 segments
  - 1 wedge to lobectomy
  - Margin depth mean 10 (3-14) mm
- No adverse events


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 (106)

Eligible for VIOLET (90%)

225 randomized to:

165 VATS
165 Open surgery

Phase 1 & 2 patients (102 excluded) followed up after surgery, n=484

45% followed up to primary outcome (6 weeks), 85% followed up to 1 year

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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 analgetic 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 OS (HR 0.67, 0.32 to 1.40; p=0.282)

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Robotic technology may increase access to surgery for high risk patients.


- 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 16%; p <0.001)
- Upstaging 6.2% (compared to 5.6% VATS, 8.2% Open, p = 0.049)

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  - SBRT

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. JCO 2021 abstract.

Surgery for lung cancer overview

- Stage IIA (localized)
  - First line for medically operable
  - Adjuvant chemotherapy for stage II (>4cm or N1)

- Stage IIA (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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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

Surgical technology can be used to perform increasingly extended resections.

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%


doi: 10.1016/j.athoracsur.2015.05.131. PMID: 27000584.

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Controversies in Stage IIIa (especially N2)

- SWOG 8805 (1995): established safety of induction concurrent CRT (45 Gy) in N2/N3 and/or T4
- RTOG 0229 (2012): 61.2 Gy
- 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


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 (44 Gy) + 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)


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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% IIa
  - 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.
Multidisciplinary evaluation can improve utilization of diagnostic capabilities.

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**References**

• Questions
• Thank you