Operative Standards For Lung Cancer
Nodal Sampling Versus Dissection: What's The Correct Choice

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Objectives

- Recognize the standards for lung cancer surgery
- Discuss the guidelines for evaluation of the patient considered for surgical resection
- Assess the data relating to intra-operative lymph node assessment
- Implement CoC Standard 5.8 for pulmonary resections

There are no disclosures

Introduction

- Lung cancer is the number one cause of cancer death, responsible for 21.7% of all cancer deaths this year
- In 2024 it is estimated that 118,270 patients will die of lung cancer in the US
- That is more than the deaths due to breast, prostate and colon cancer combined
- Lung cancer will be responsible for over one million deaths this year alone

The Good News

- The 5 year survival continues to slowly increase
- Now at 26.7%
- Many factors contributing to this welcome improvement

The Bad News

- More lung cancers will be diagnosed in woman this year 118,270 versus 116,310 in men
- Nebraska ranks 33rd in the country for lung cancer screening
- Only 3.7% of eligible patients will have a LDCT scan performed

Screening

- NSLT and Nelson trials demonstrated improved lung cancer survival in a screened population
- Compared to other cancers, prior to the increased penetrance of screening, the majority of lung cancers were detected at an advanced stage
- LDCT screening has allowed us to detect earlier stage cancers

Surgery

- Surgery remains the mainstay of treatment for early stage non-small cell cancer
- It is an integral part of the treatment of strategy for patients with Stage II-IIIA disease
- It is also appropriate treatment for stage 1 small cell lung cancers
- Increasingly more lung cancer operations are performed as minimally invasive operations

PRINCIPLES OF DIAGNOSTIC EVALUATION

- The decision to pursue preoperative biopsy of a potential stage I lung cancer should be informed by the pre-test probability of malignancy.
  - Factors that might be considered in pre-test probability assessment include risk factors, radiologic appearance (including comparison to prior chest imaging if available or FDG-PET/CT if performed), and current or prior residence in regions with prevalent endemic infectious lung disease (ie, fungal, mycobacterial), among other potential factors.
  - Patients with very high pre-test probability of stage IA lung cancer do not require a biopsy before surgery. A biopsy adds time, costs, and procedural risk and may not be needed for treatment decisions.
  - If a preoperative tissue diagnosis has not been obtained, then an intraoperative diagnosis (ie, wedge resection, needle biopsy) is necessary before lobectomy, bilobectomy, or pneumonectomy.
  - Situations in which a preoperative biopsy may be appropriate:
    - A non-lung cancer diagnosis that can be diagnosed by minimally invasive biopsy is at least moderately likely (eg, granulomatous nodule due to endemic fungus).
    - Suspected stage IB or higher lung cancer in patients who may be candidates for systemic therapy prior to surgery.
    - An intraoperative diagnosis appears difficult or very risky.[1]
    - To establish the diagnosis prior to stereotactic ablative radiotherapy (SABR).[2]

[1] Patients require tissue confirmation of non-small cell lung cancer (NSCLC) before a lobectomy, bilobectomy, or pneumonectomy. If a preoperative or intraoperative tissue diagnosis appears risky or unreliable, multidisciplinary evaluation that at least includes interventional radiology, thoracic surgery, and interventional pulmonology is recommended to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult and that the patient can proceed with anatomic resection without tissue confirmation (IJsselijk MA, et al. J Thorac Oncol 2019;14:583-595).

[2] Prior to treatment, multidisciplinary evaluation that includes treating physicians and specialists in obtaining tissue diagnosis (thoracic surgery, interventional pulmonology, and interventional radiology) is required to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult, that a clinical diagnosis of lung cancer is appropriate, and that treatment is warranted.

Note: All recommendations are category 2A unless otherwise indicated.

Diagnosis

- Not every patient has to have a tissue diagnosis prior to going to surgery
- Those with a high likelihood of having a lung cancer can proceed directly to surgery

PRINCIPLES OF DIAGNOSTIC EVALUATION

- A preoperative bronchoscopy may also be preferred for tissue diagnosis and/or mediastinal staging (endobronchial ultrasound [EBUS]).
- If a bronchoscopy has not been previously performed for diagnosis or staging, bronchoscopy should be performed during the planned surgical resection, rather than as a separate procedure.
  - Bronchoscopy is required before surgical resection (NSCL-2).
  - A separate bronchoscopy may not be needed for treatment decisions before the time of surgery and adds time, costs, and procedural risk.
  - A preoperative bronchoscopy may be appropriate if a central tumor requires pre-resection evaluation for biopsy, surgical planning (eg, potential sleeve resection), or preoperative airway preparation (eg, coring out an obstructive lesion).
  - A preoperative bronchoscopy may also be preferred for tissue diagnosis and/or mediastinal staging (EBUS).
- Invasive mediastinal staging is recommended before surgical resection for most patients with clinical stage I or II lung cancer (NSCL-2). For patients undergoing EBUS/endoscopic ultrasound (EUS) staging, this most commonly should be a separate procedure to allow for pathologic evaluation.
  - Patients having mediastinoscopy should preferably undergo invasive mediastinal staging (mediastinoscopy) as the initial step before the planned resection (during the same anesthetic procedure), rather than as a separate procedure.
  - A separate staging procedure adds time, costs, coordination of care, inconvenience, and an additional anesthetic risk.
  - Preoperative invasive mediastinal staging may be appropriate for a strong clinical suspicion of N2 or N3 nodal disease or when intraoperative cytology or frozen section analysis is not available.
- In patients with suspected non-small cell lung cancer (NSCLC), many techniques are available for tissue diagnosis.
  - Diagnostic tools that should be routinely available include:
    - Sputum cytology
    - Bronchoscopy with biopsy and transbronchial needle aspiration (TBNA)
    - Image-guided transthoracic needle core biopsy (preferred) or fine-needle aspiration (FNA)
    - Thoracentesis
    - Mediastinoscopy
    - Video-assisted thoracic surgery (VATS) and open surgical biopsy
    - Left anterior mediastinotomy/Chamberlain
  - Diagnostic tools that provide important additional strategies for biopsy include:
    - EBUS–guided biopsy
    - EUS–guided biopsy
    - Navigational bronchoscopy
    - Robotic bronchoscopy

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Evaluation

- The goal should be to try and limit the number of procedures performed on a patient during their evaluation
- For many patients a diagnostic, staging and therapeutic procedure can be performed with a single anesthetic

PRINCIPLES OF DIAGNOSTIC EVALUATION

- The preferred diagnostic strategy for an individual patient depends on the size and location of the tumor, the presence of mediastinal or distant disease, patient characteristics (such as pulmonary pathology and/or other significant comorbidities), and local experience and expertise.
  - Factors to be considered in choosing the optimal diagnostic step include:
    - Anticipated diagnostic yield (sensitivity)
    - Diagnostic accuracy including specificity and particularly the reliability of a negative diagnostic study (ie, true negative)
    - Adequate volume of tissue specimen for diagnosis and molecular testing
    - Invasiveness and risk of procedure
    - Efficiency of evaluation
      - Access and timeliness of procedure
      - Concomitant staging is beneficial, because it avoids additional biopsies or procedures. It is preferable to biopsy the pathology that would confer the highest stage (ie, to biopsy a suspected metastasis or mediastinal lymph node rather than the pulmonary lesion). Therefore, FDG-PET/CT imaging is frequently best performed before a diagnostic biopsy site is chosen in cases of high clinical suspicion for aggressive, advanced-stage tumors.
    - Technologies and expertise available
    - Tumor viability at proposed biopsy site from FDG-PET/CT imaging
  - Decisions about the optimal diagnostic steps for suspected stage I to III lung cancer should be made by thoracic radiologists, interventional radiologists, thoracic surgeons, and pulmonologists who devote a significant portion of their practice to thoracic oncology. Multidisciplinary evaluation should also include a pulmonologist or thoracic surgeon with expertise in advanced bronchoscopic techniques for diagnosis. The least invasive biopsy with the highest yield is preferred as the first diagnostic study.
    - Patients with central masses and suspected endobronchial involvement should undergo bronchoscopy.
    - Patients with pulmonary nodules may benefit from navigational bronchoscopy (including robotic), radial EBUS, or transthoracic needle aspiration (TTNA).
    - Patients with suspected nodal disease should be biopsied by EBUS, EUS, navigational bronchoscopy, or mediastinoscopy.
      - EBUS provides access to nodal stations 2R/2L, 3P, 4R/4L, 7, 10R/10L, 11–13, and other hilar nodal stations if necessary.
      - An EBUS-TBNA negative for malignancy in a clinically (FDG-PET/CT and/or CT) positive mediastinum should undergo subsequent mediastinoscopy prior to surgical resection.
      - EUS–guided biopsy provides additional access to stations 3P, 5, 7, 8, and 9 lymph nodes if these are clinically suspicious.
      - TTNA and anterior mediastinotomy (ie, Chamberlain procedure) provide additional access to anterior mediastinal (stations 5 and 6) lymph nodes if these are clinically suspicious. If TTNA is not possible due to proximity to aorta, VATS biopsy is also an option.
    - EUS also provides reliable access to the left adrenal gland.
    - Rapid on-site evaluation (ROSE), when available, helps to increase diagnostic and molecular yield.
    - Patients with lung cancer with an associated pleural effusion should undergo thoracentesis and cytology. A negative pleural cytology result does not exclude pleural involvement. Thoracoscopic evaluation of the pleura should be considered before starting curative intent therapy if pleural fluid is a lymphocytic exudate with negative pleural fluid cytology.
    - Patients suspected of having a solitary site of metastatic disease should have tissue confirmation of that site if feasible.
    - Patients suspected of having metastatic disease should have confirmation from one of the metastatic sites if feasible.
    - Patients who may have multiple sites of metastatic disease—based on a strong clinical suspicion—should have biopsy of the primary lung lesion or mediastinal lymph nodes if it is technically difficult or very risky to biopsy a metastatic site.

Note: All recommendations are category 2A unless otherwise indicated.

Diagnosis

- It is preferable to biopsy the pathology that would confer the highest stage
- Biopsy a mediastinal node or a metastasis rather than the lung lesion
- The least invasive biopsy with the highest yield is preferred as the first diagnostic study

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NCCN Guidelines Version 11.2024
Non-Small Cell Lung Cancer

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Discussion

PATHOLOGIC DIAGNOSIS OF NSCLC

NSCLC →

INITIAL EVALUATION

- 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
- Integrate palliative care[c] NCCN Guidelines for Palliative Care
- For tools to aid in the optimal assessment and management of NSCLC in older adults, see the NCCN Guidelines for Older Adult Oncology

CLINICAL STAGE[d]

Stage IA, peripheral[e] (T1abc, N0)	Pretreatment Evaluation (NSCL-2)
Stage IB, peripheral[e] (T2a, N0); Stage I, central[e] (T1abc–T2a, N0); Stage II (T1abc–T2ab, N1; T2b, N0); Stage IIB (T3, N0)[f]; Stage IIIA (T3, N1)	Pretreatment Evaluation (NSCL-3)
Stage IIB (T3 invasion, N0); Stage IIIA (T4 extension, N0–1; T3, N1; T4, N0–1)	Pretreatment Evaluation (NSCL-5)
Stage IIIA (T1–2, N2); Stage IIIB (T3, N2)	Pretreatment Evaluation (NSCL-8)
Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)	Pretreatment Evaluation (NSCL-8)
Multiple lung cancers	Treatment (NSCL-12)
Stage IIIB (T1–2, N3); Stage IIIC (T3, N3)	Pretreatment Evaluation (NSCL-13)
Stage IIIB (T4, N2); Stage IIIC (T4, N3)	Pretreatment Evaluation (NSCL-14)
Stage IVA (M1a)[c] (pleural or pericardial effusion)	Pretreatment Evaluation (NSCL-14)
Stage IVA (M1b)[c]	Pretreatment Evaluation (NSCL-15)
Stage IVB (M1c)[c] disseminated metastases	Systemic Therapy (NSCL-19)

[a] Principles of Pathologic Review (NSCL-A).
[b] Enhanced frailty or geriatric assessments may predict complications better following treatment modalities, particularly surgery. A preferred frailty assessment system has not been established.
[c] Temel JS, et al. N Engl J Med 2010;363:733-742.
[d] For patients where more than one treatment modality (surgery, radiation therapy [RT], or systemic therapy) is usually considered, a multidisciplinary evaluation should be performed.
[e] Based on the CT of the chest: Peripheral = outer third of lung; Central = inner two thirds of lung.
[f] T3, N0 related to size or satellite nodules.

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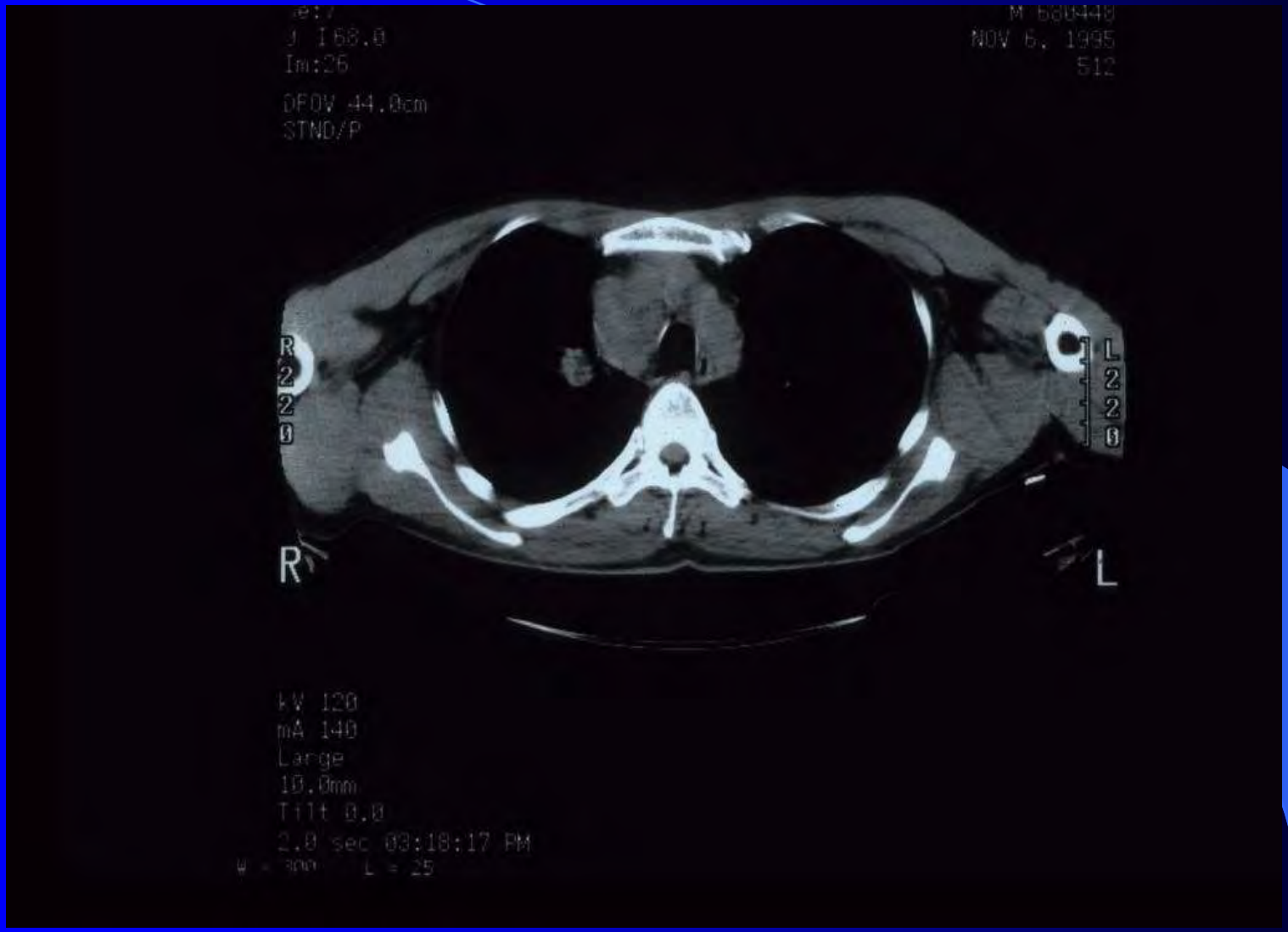
Noninvasive Staging

- CT scan- chest(including liver and adrenal glands)
- CT scan- head
- MRI
- PET scan
- Bone Scan


A
P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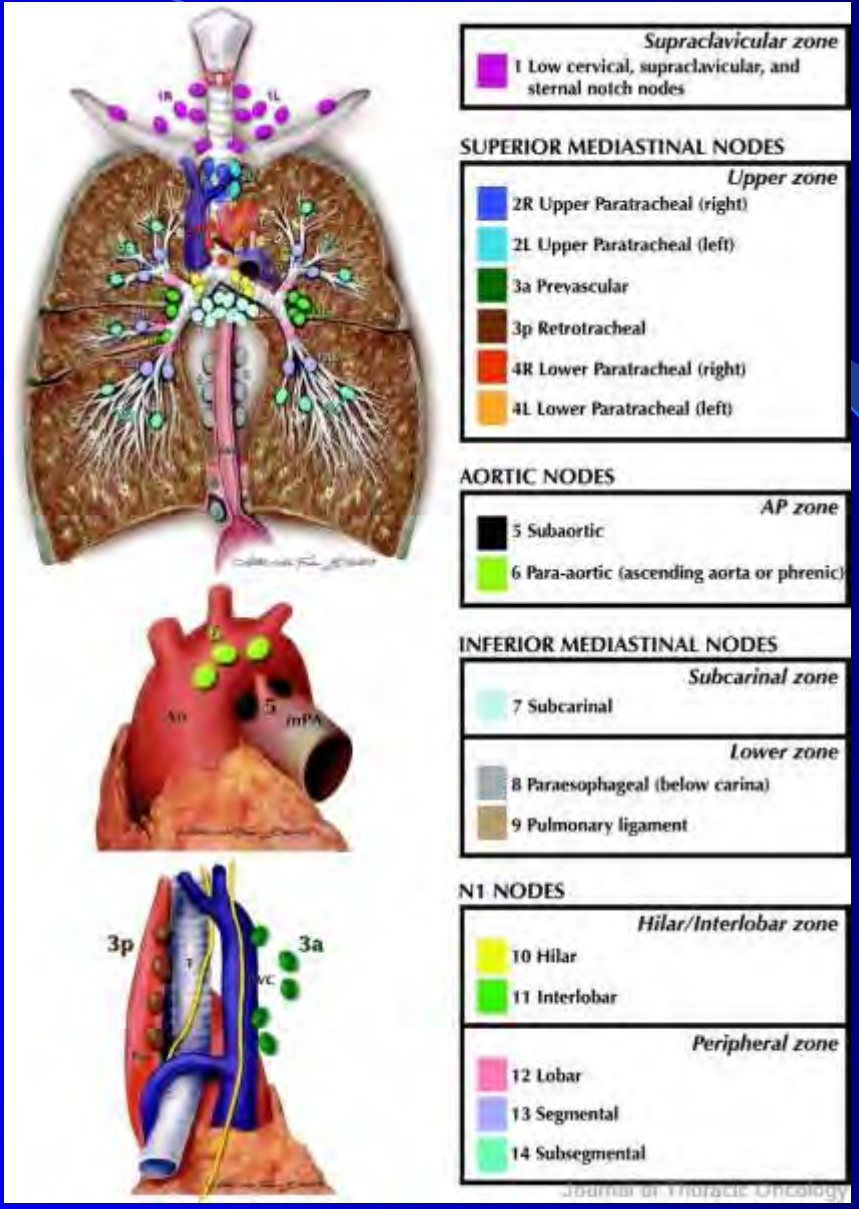
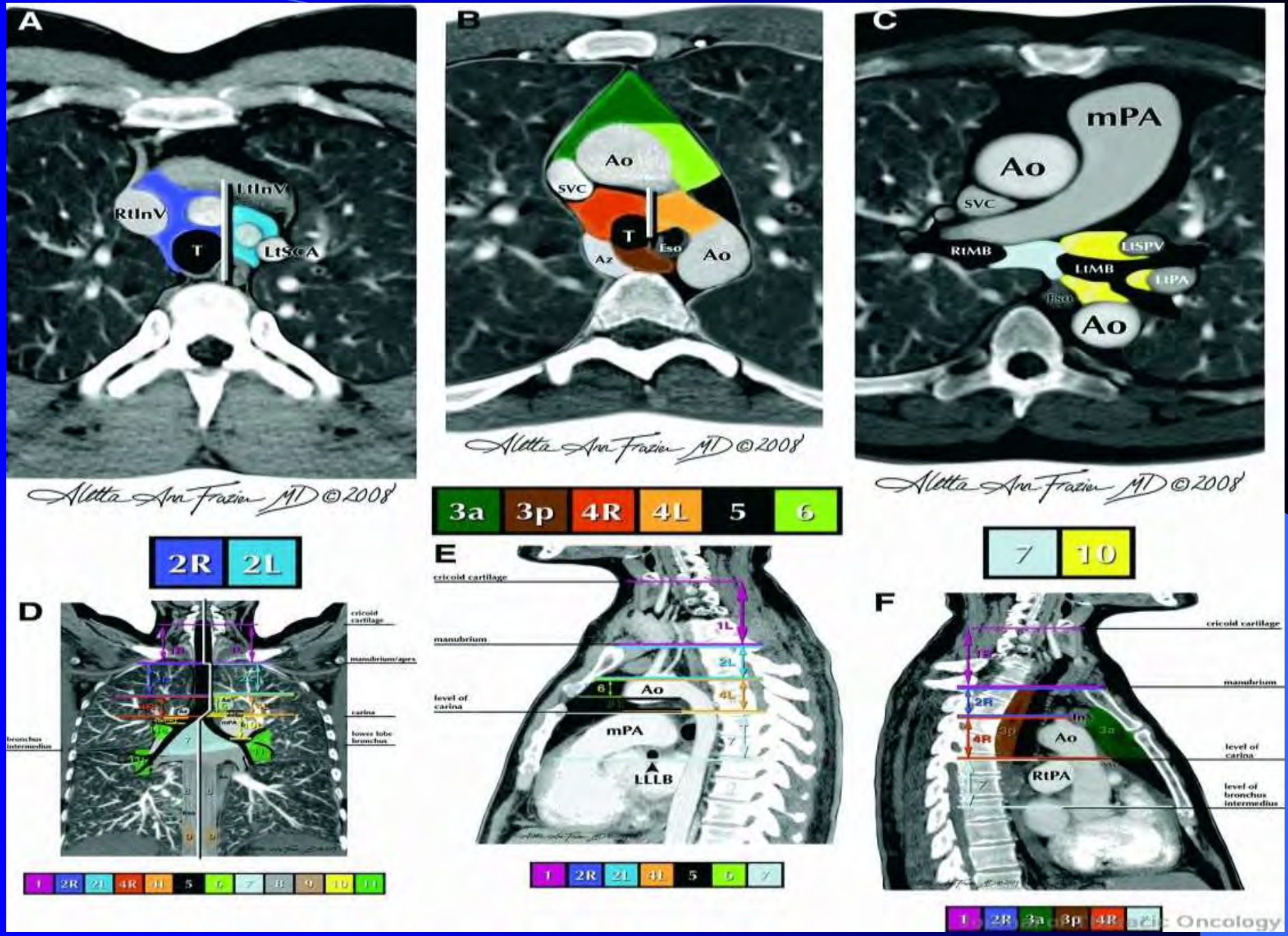

3p
3a
Ao
5
mPA
Supraclavicular zone
1 Low cervical, supraclavicular, and sternal notch nodes
SUPERIOR MEDIASTINAL NODES
Upper zone
2R Upper Paratracheal (right)
2L Upper Paratracheal (left)
3a Prevascular
3p Retrotracheal
4R Lower Paratracheal (right)
4L Lower Paratracheal (left)
AORTIC NODES
AP zone
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
N1 NODES
Hilar/Interlobar zone
10 Hilar
11 Interlobar
Peripheral zone
12 Lobar
13 Segmental
14 Subsegmental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LtMB
LtPA
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3a
3p
4R
4L
5
6
2R
2L
D
cricoid cartilage
manubrium/apex
carina
lower lobe bronchus
bronchus intermedius
1
2R
2L
4R
4L
5
6
7
8
9
10
11
E
cricoid cartilage
manubrium
level of carina
1L
2L
4L
6
Ao
mPA
LLLB
1
2R
2L
4L
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6
7
F
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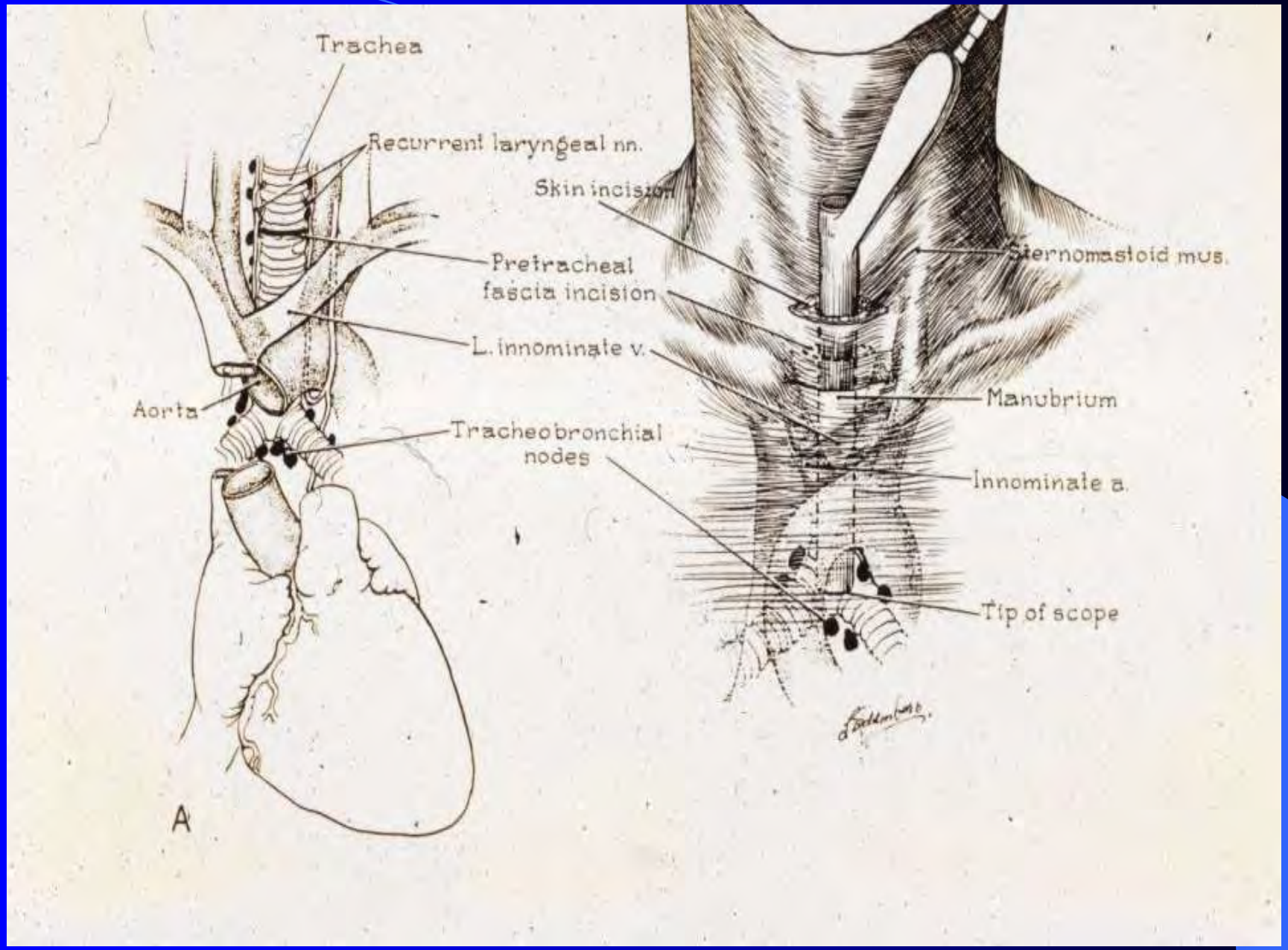
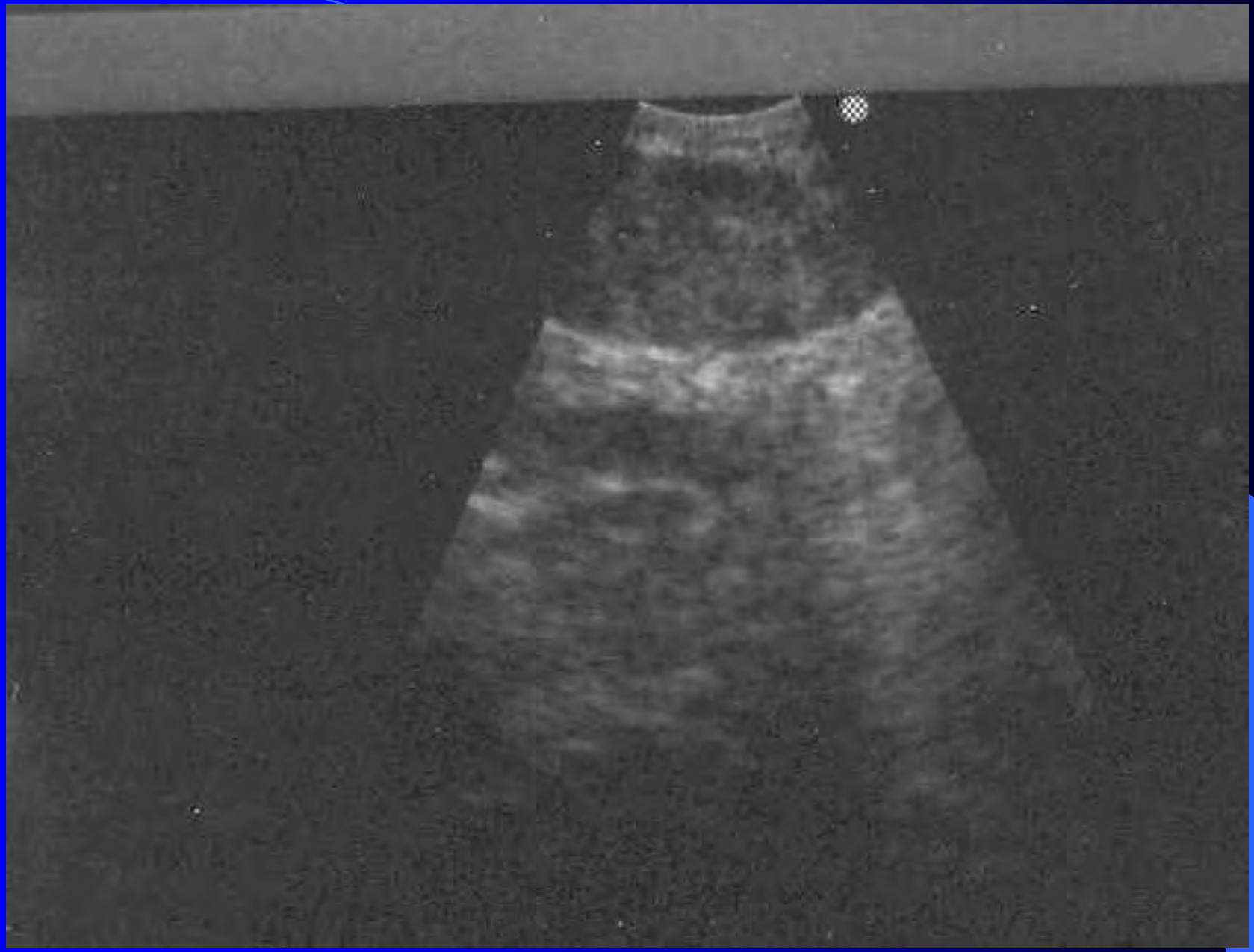
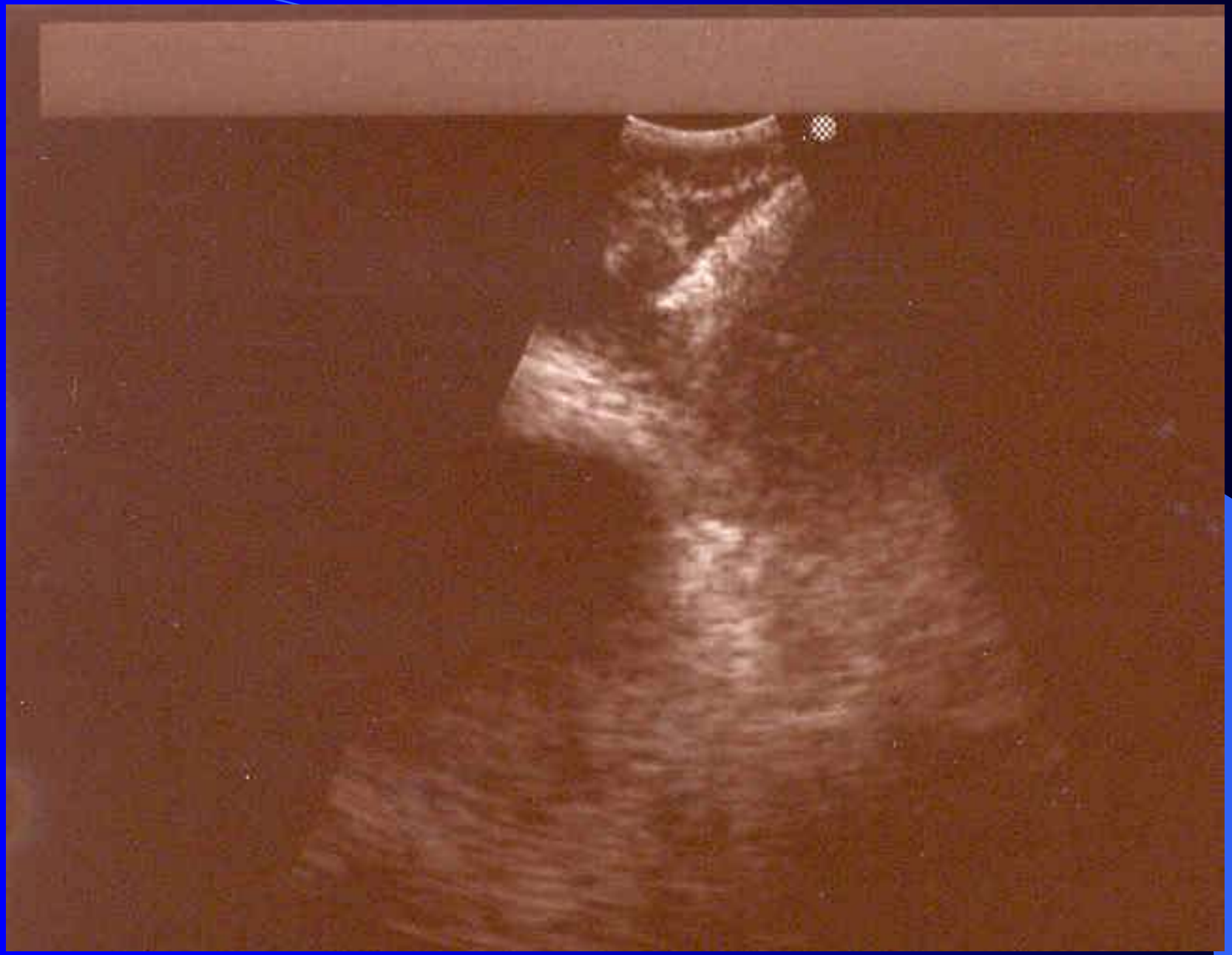
cricoid cartilage
manubrium
level of carina
level of bronchus intermedius
2R
4R
3p
3a
Ao
RtPA
1
2R
3a
3p
4R

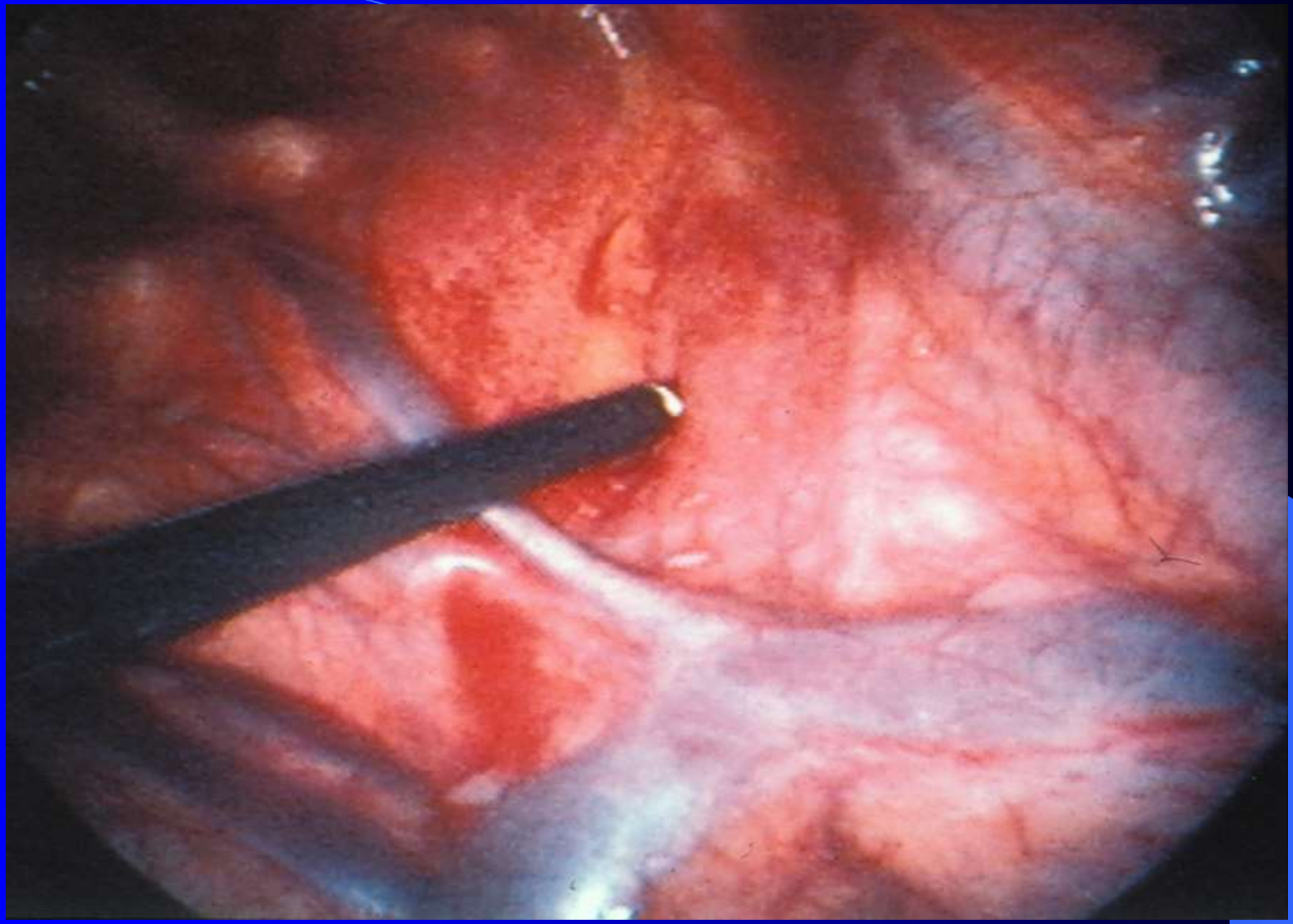
Invasive Staging

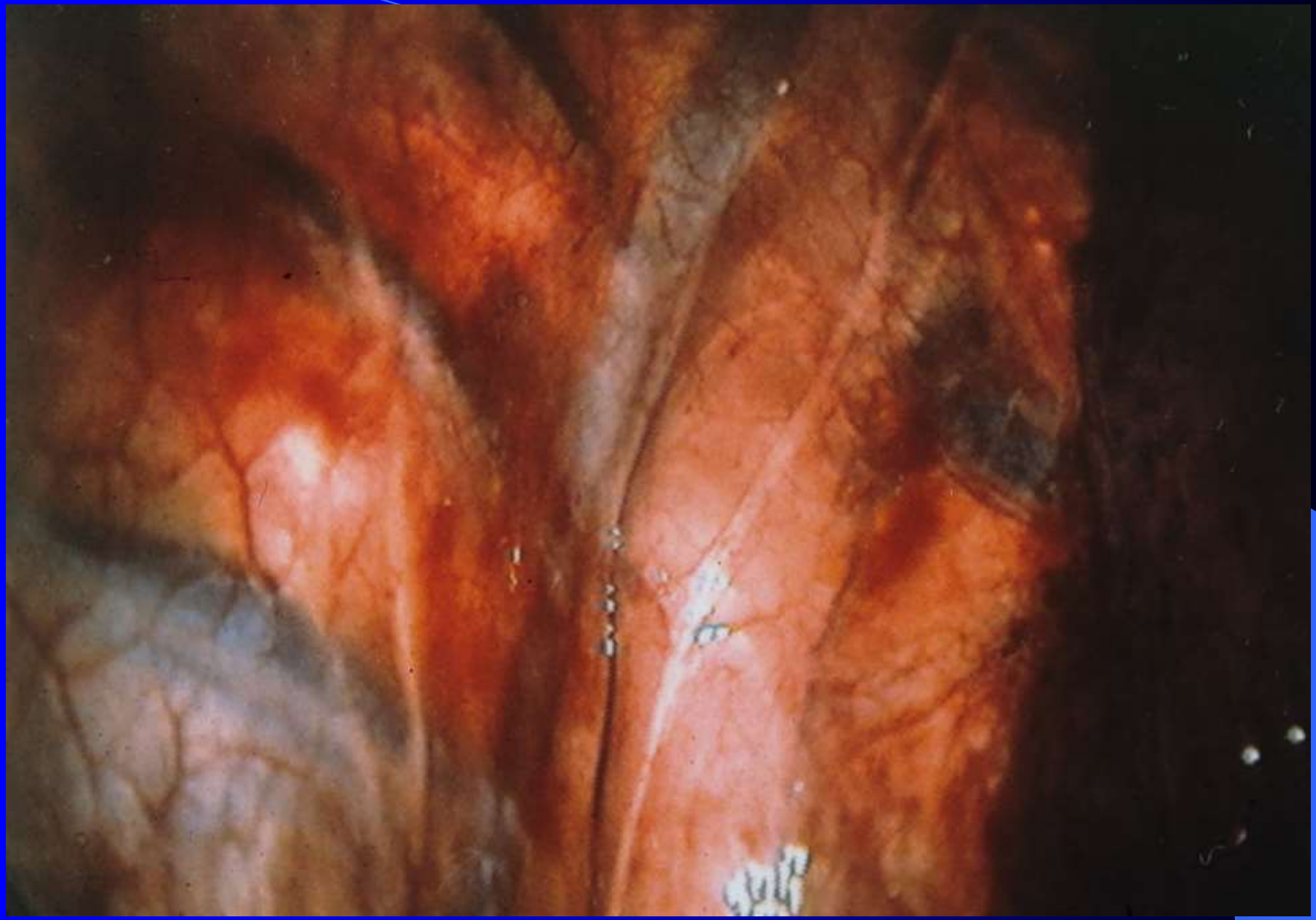
- Bronchoscopy- TBNA
- Endobronchial ultrasound(EBUS)- TBNA
- Electromagnetic Navigational Bronchoscopy
- Esophageal ultrasound(EUS)- NA
- Transthoracic needle aspiration
- Mediastinoscopy
- Mediastinotomy
- Thoracoscopy

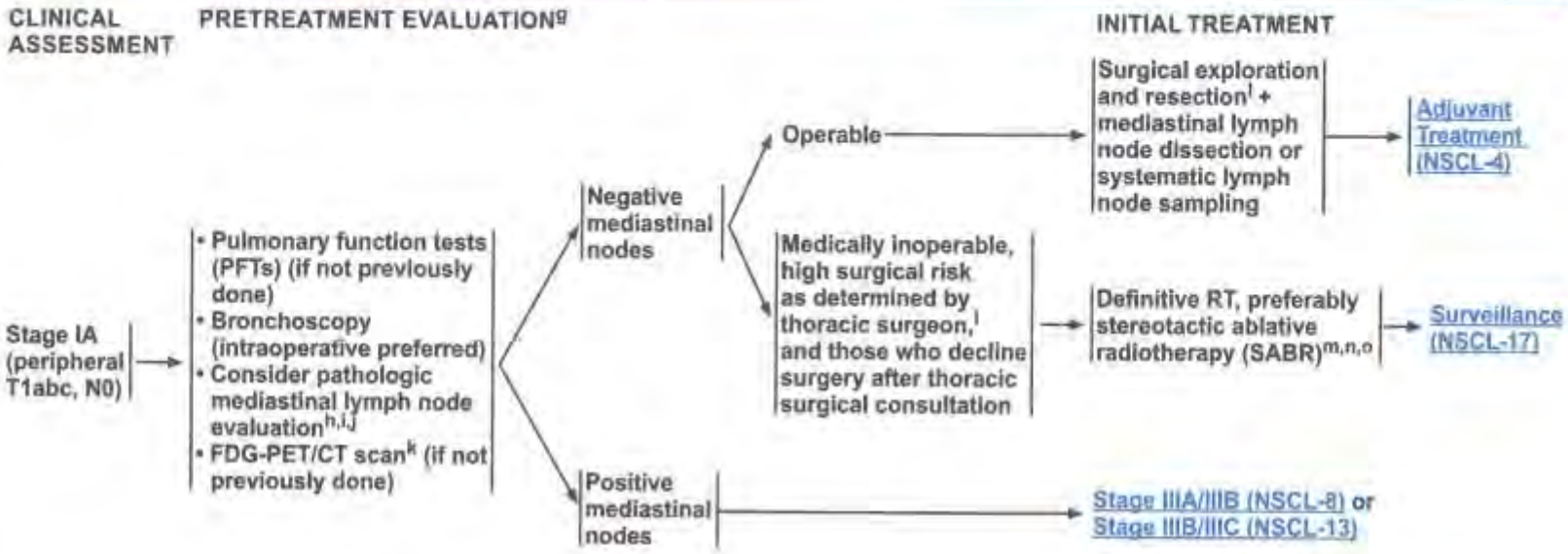

Trachea
Recurrent laryngeal nn.
Skin incision
Sternomastoid mus.
Prefracheal fascia incision
L. innominate v.
Manubrium
Aorta
Tracheobronchial nodes
Innominate a.
Tip of scope
A











[g] Testing is not listed in order of priority and is dependent on clinical circumstances, institutional processes, and judicious use of resources.

[h] Methods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy. An EBUS-TBNA negative for malignancy in a clinically (FDG-PET/CT and/or CT) positive mediastinum should undergo subsequent mediastinoscopy prior to surgical resection.

[i] There is low likelihood of positive mediastinal lymph nodes when these nodes are CT and FDG-PET/CT negative in peripheral tumors (outer third of lung) ≤3 cm. Thus, pretreatment pathologic mediastinal evaluation is optional in these settings. Invasive mediastinal staging is recommended for central tumors.

[j] In patients who are medically inoperable, while mediastinal biopsy is generally preferred, the risks in selected patients may outweigh the benefits.

[k] FDG-PET/CT performed skull base to mid-thigh. Positive FDG-PET/CT scan findings for distant disease need pathologic or other radiologic confirmation. If FDG-PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

[l] Principles of Surgical Therapy (NSCL-B).

[m] Principles of Radiation Therapy (NSCL-C).

[n] Image-guided thermal ablation (IGTA) therapy (eg, cryotherapy, microwave, radiofrequency) may be an option for select patients. Principles of Image-Guided Thermal Ablation Therapy (NSCL-D).

[o] Prior to treatment, multidisciplinary evaluation that includes treating physicians and specialists in obtaining tissue diagnosis (thoracic surgery, interventional pulmonology, and interventional radiology) is required to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult, that a clinical diagnosis of lung cancer is appropriate, and that treatment is warranted.

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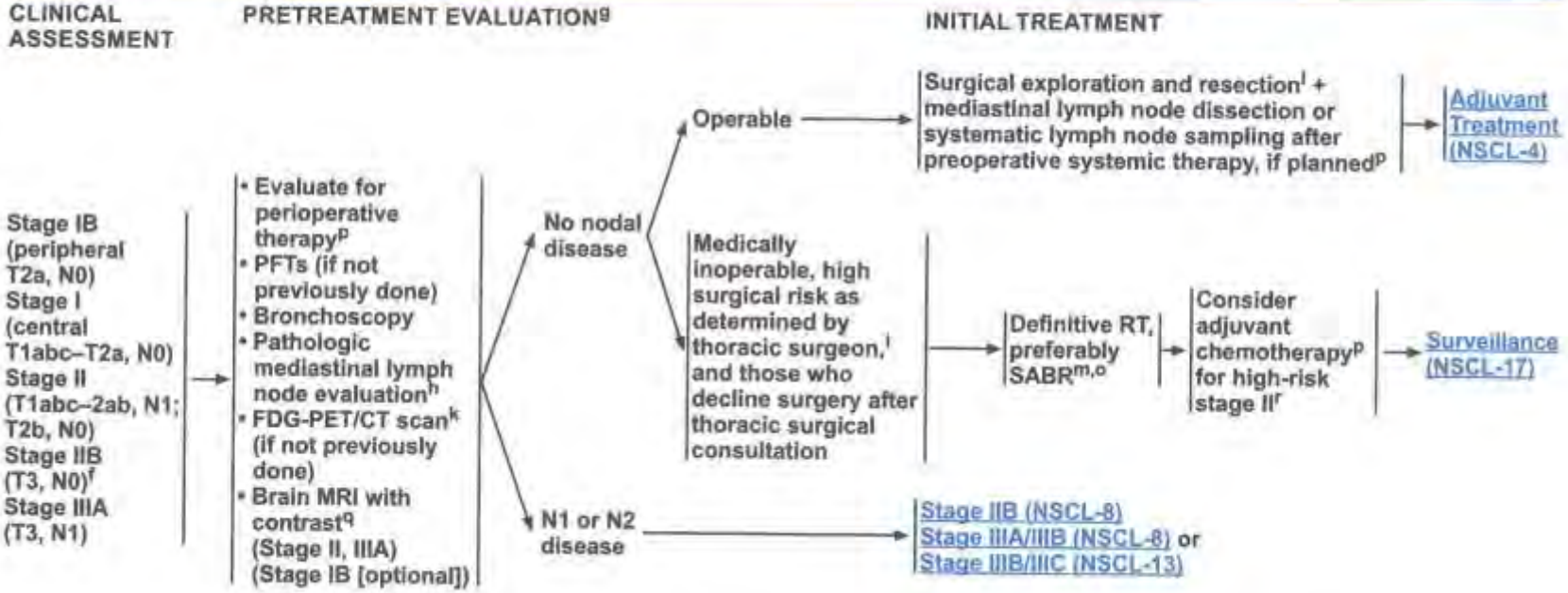

[f] T3, N0 related to size or satellite nodules.
[g] Testing is not listed in order of priority and is dependent on clinical circumstances, institutional processes, and judicious use of resources.
[h] Methods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy. An EBUS-TBNA negative for malignancy in a clinically (FDG-PET/CT and/or CT) positive mediastinum should undergo subsequent mediastinoscopy prior to surgical resection.
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[m] Principles of Radiation Therapy (NSCL-C).
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[p] Perioperative Systemic Therapy (NSCL-E).
[q] If MRI is not possible, CT of head with contrast.
[r] Examples of high-risk factors may include poorly differentiated tumors (including lung neuroendocrine tumors [excluding well-differentiated neuroendocrine tumors]). These factors independently may not be an indication and may be considered when determining treatment with adjuvant chemotherapy.

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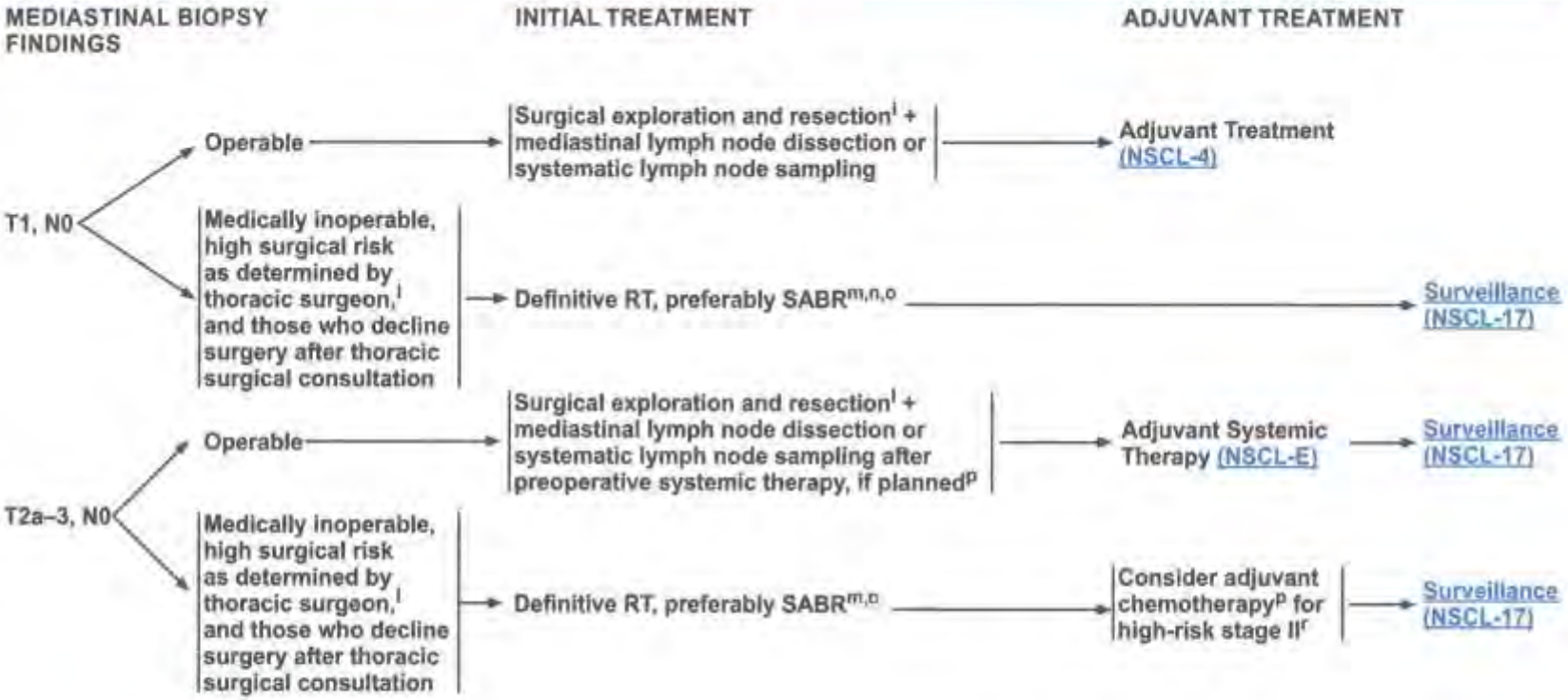

[l] Principles of Surgical Therapy (NSCL-B).
[m] Principles of Radiation Therapy (NSCL-C).
[n] Image-guided thermal ablation (IGTA) therapy (eg, cryotherapy, microwave, radiofrequency) may be an option for select patients. Principles of Image-Guided Thermal Ablation Therapy (NSCL-D).
[o] Prior to treatment, multidisciplinary evaluation that includes treating physicians and specialists in obtaining tissue diagnosis (thoracic surgery, interventional pulmonology, and interventional radiology) is required to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult, that a clinical diagnosis of lung cancer is appropriate, and that treatment is warranted.
[p] Perioperative Systemic Therapy (NSCL-E).
[r] Examples of high-risk factors may include poorly differentiated tumors (including lung neuroendocrine tumors [excluding well-differentiated neuroendocrine tumors]). These factors independently may not be an indication and may be considered when determining treatment with adjuvant chemotherapy.

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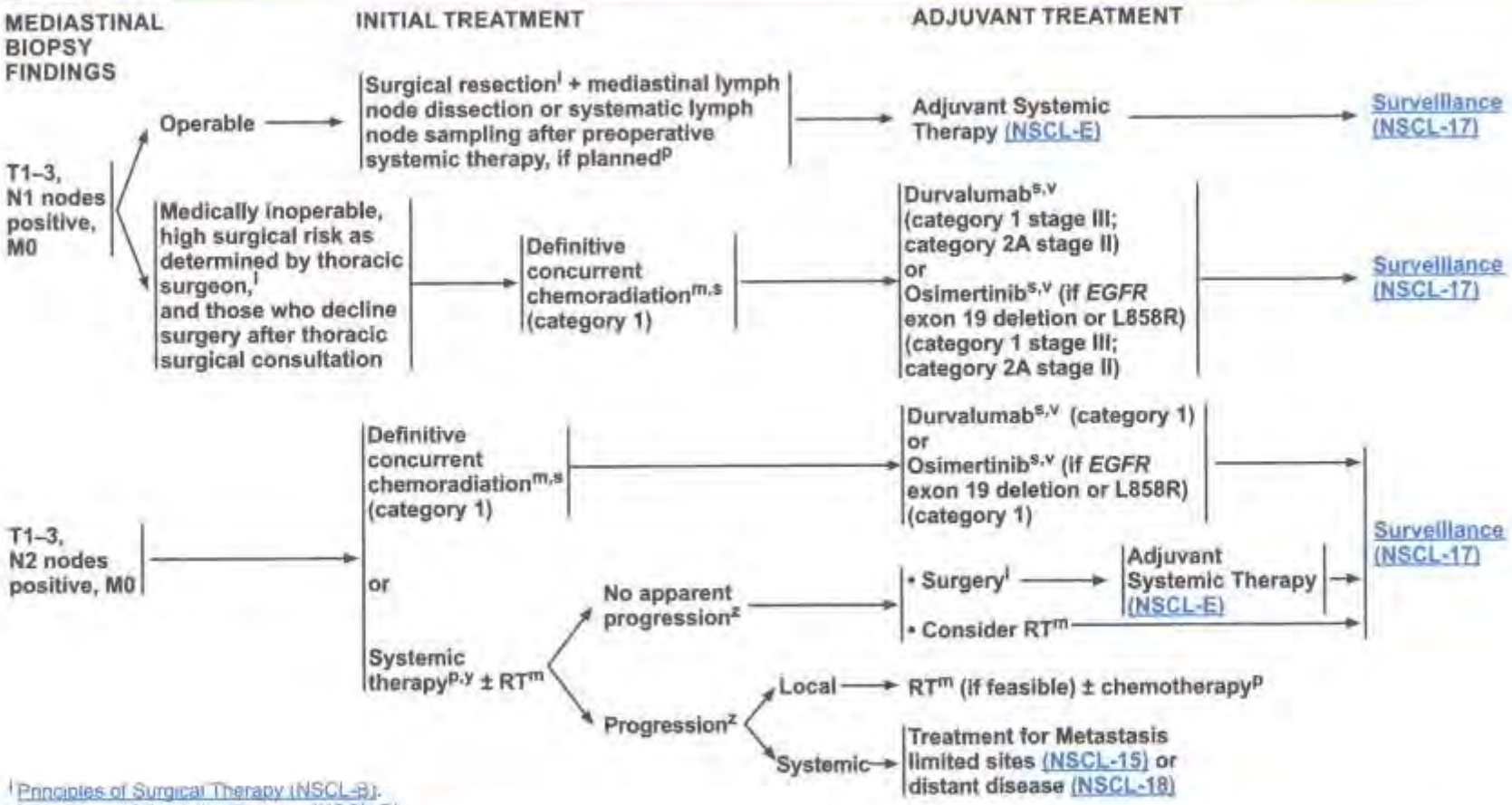

[l] Principles of Surgical Therapy (NSCL-B).
[m] Principles of Radiation Therapy (NSCL-C).
[p] Perioperative Systemic Therapy (NSCL-E).
[s] Concurrent Chemoradiation Regimens (NSCL-F).
[v] For patients who have received sequential chemoradiation, durvalumab can be considered as consolidation immunotherapy or, if *EGFR* exon 19 deletion or L858R, osimertinib is recommended.
[y] Selected patients with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.
[z] Chest CT with contrast and/or FDG-PET/CT to evaluate progression.

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PRINCIPLES OF SURGICAL THERAPY

Evaluation

- Determination of resectability, surgical staging, and *pulmonary resection should be performed by thoracic surgeons who perform lung cancer surgery as a prominent part of their practice*.
- CT and FDG-PET/CT used for staging should be within 60 days before proceeding with surgical evaluation.
- For medically operable disease, resection is the preferred local treatment modality (other modalities include SABR, thermal ablation such as radiofrequency ablation, and cryotherapy). Thoracic surgical oncology consultation should be part of the evaluation of any patient being considered for curative local therapy. In cases where SABR is considered for high-risk or borderline operable patients, a multidisciplinary evaluation including a radiation oncologist is recommended.
- The overall plan of treatment as well as needed imaging studies should be determined before any non-emergency treatment is initiated.
- Thoracic surgeons should actively participate in multidisciplinary discussions and meetings regarding patients with lung cancer (eg, multidisciplinary clinic and/or tumor board).
- Patients who actively smoke should be provided counseling and smoking cessation support (NCCN Guidelines for Smoking Cessation). While patients who actively smoke have a mildly increased incidence of postoperative pulmonary complications, these should not be considered a prohibitive risk for surgery. Surgeons should not deny surgery to patients solely due to smoking status, as surgery provides the predominant therapy for patients with early-stage lung cancer.

Resection (NSCL-B 2 of 6)
Margins and Nodal Assessment (NSCL-B 3 of 6)

The Role of Surgery in Patients with N2 NSCLC (NSCL-B 3 of 6 through NSCL-B 5 of 6)

[a] Peripheral is defined as the outer one third of the lung parenchyma.

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PRINCIPLES OF SURGICAL THERAPY

Resection

- Anatomic pulmonary resection is preferred for the majority of patients with NSCLC.
- Sublobar resection - Segmentectomy and wedge resection should be strongly considered for peripheral T1ab, N0 tumors.[1]
- Sublobar resection should achieve parenchymal resection margins ≥2 cm or ≥ 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 with poor pulmonary reserve or other major comorbidity that contraindicates lobectomy.
- Minimally invasive surgery (VATS or 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. Robotic surgery should only be initiated by surgeons who have completed and maintained proficiency in the technique.
- 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.
- Studies of robotic-assisted pulmonary resection show non-inferiority to traditional VATS approaches when performed by experienced robotic surgeons.[2,3]
- Lung-sparing anatomic resection (sleeve lobectomy) is preferred over pneumonectomy, if anatomically appropriate and margin-negative resection is achieved.
- T3 (invasion) and T4 local extension tumors require en-bloc resection of the involved structure with negative margins. If a surgeon or center is uncertain about potential complete resection, consider obtaining an additional surgical opinion from a high-volume specialized center.

Evaluation (NSCL-B 1 of 6)
Margins and Nodal Assessment (NSCL-B 3 of 6)

The Role of Surgery in Patients with N2 NSCLC (NSCL-B 3 of 6 through NSCL-B 5 of 6)

References

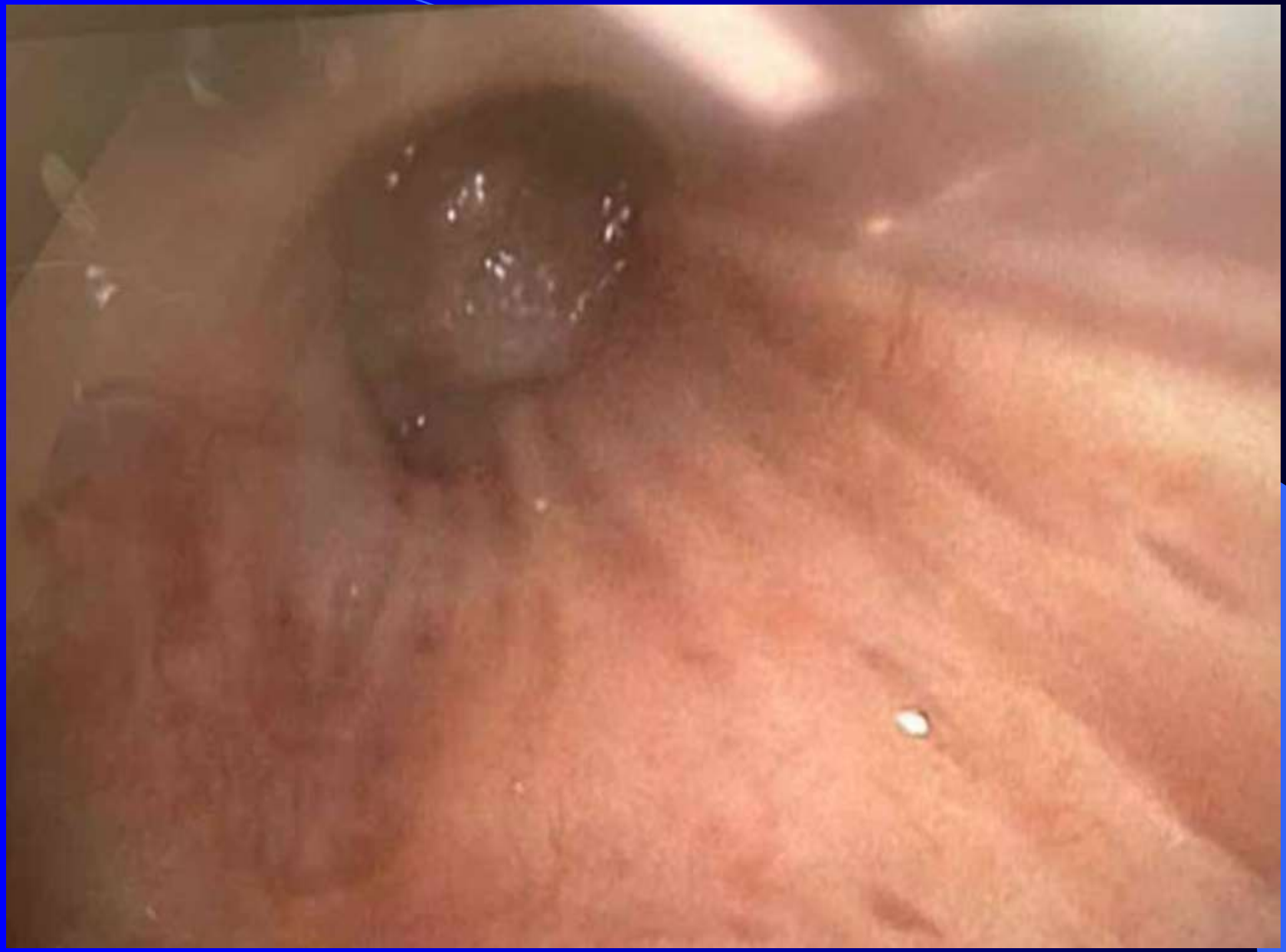
Note: All recommendations are category 2A unless otherwise indicated.

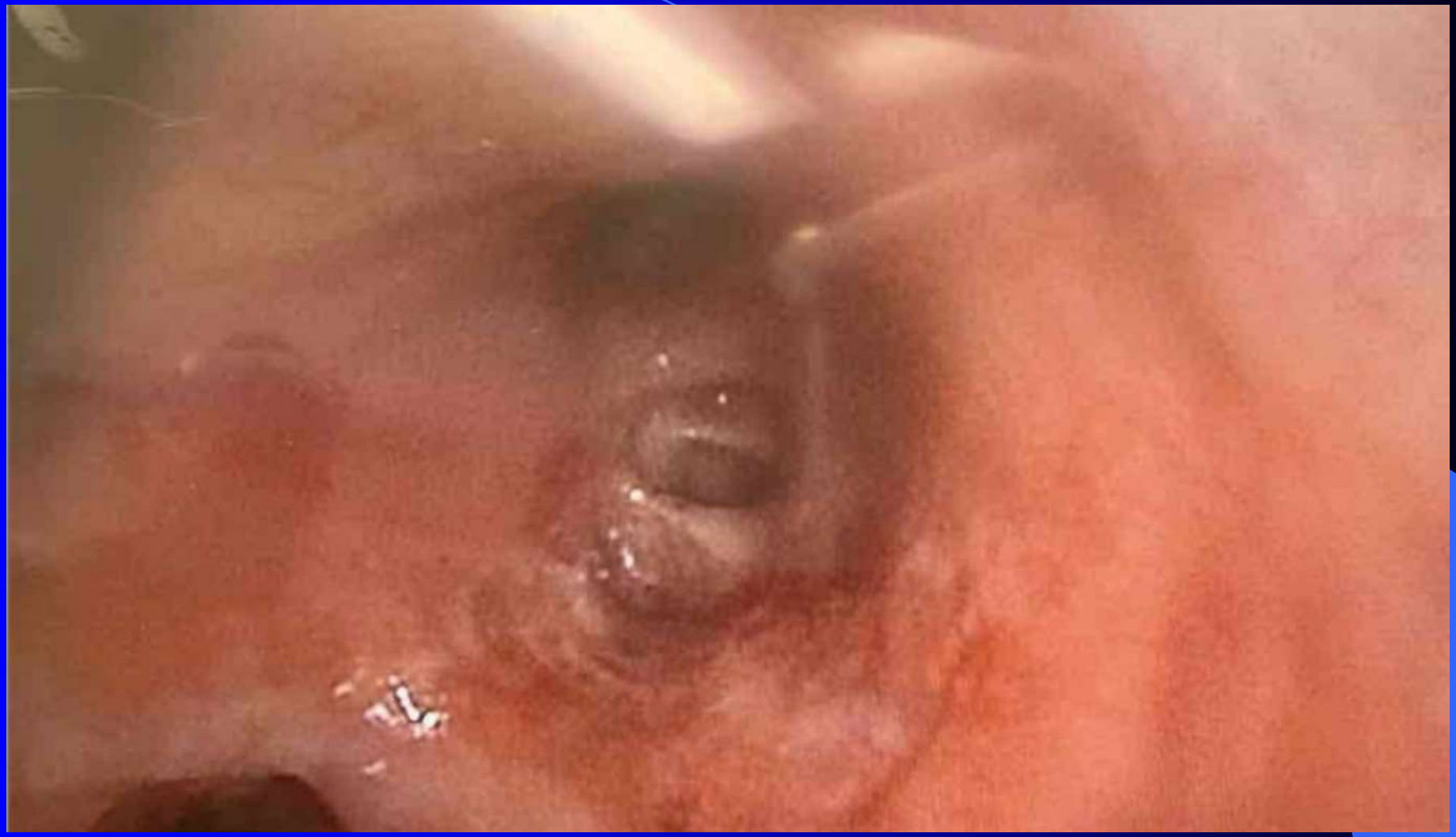
Surgical Resection

- Wedge resection
- Segmentectomy
- Lobectomy/Bi-lobectomy
- Sleeve lobectomy
- Pneumonectomy
- Extended resections

Operative Standards

- Bronchoscopy
- Diagnostic thoracoscopy
- Lung resection- goal to achieve an R0 resection
- Evaluation of mediastinal nodes





PRINCIPLES OF SURGICAL THERAPY

Margins and Nodal Assessment

- Surgical pathologic correlation is critical to assess apparent close or positive margins, as these may not represent true margins or may not truly represent areas of risk for local recurrence (eg, medial surface of mainstem or bronchus intermedius when separate subcarinal lymph node dissection has been performed; pleural margin adjacent to aorta when no attachment to aorta is present).
- N1 and N2 node resection and mapping should be a routine component of lung cancer resections—a minimum of one N1 and three N2 stations sampled or complete lymph node dissection.
- Formal ipsilateral mediastinal lymph node dissection is indicated for patients undergoing resection for N2 disease.
- Complete resection requires free resection margins, systematic node dissection or sampling, and the highest mediastinal node negative for tumor. The resection is defined as incomplete whenever there is involvement of resection margins, unremoved positive lymph nodes, or positive pleural or pericardial effusions. A complete resection is referred to as R0, microscopically positive resection as R1, and macroscopic residual tumor as R2.
- Patients with clinical stage IB or greater, or high-risk factors, should be referred to medical oncology for evaluation.
- Consider referral to a radiation oncologist for N2 disease.

The Role of Surgery in Patients with N2 NSCLC

The role of surgery in patients with pathologically documented N2 disease remains controversial.[4] Two randomized trials evaluated the role of surgery in this population, but neither showed an overall survival benefit with the use of surgery.[5,6] However, this population is heterogeneous and the panel believes that these trials did not sufficiently evaluate the nuances present with the heterogeneity of N2 disease and the likely oncologic benefit of surgery in specific clinical situations.

- The presence or absence of N2 disease should be vigorously determined by both radiologic and invasive staging prior to the initiation of therapy since the presence of mediastinal nodal disease has a profound impact on prognosis and treatment decisions. (NSCL-1, NSCL-2, and NSCL-6)
- Patients with occult-positive N2 nodes discovered at the time of pulmonary resection should continue with the planned resection along with formal mediastinal lymph node dissection. If N2 disease is noted in patients undergoing VATS, the surgeon may consider stopping the procedure so that induction therapy can be administered before surgery; however, continuing the procedure is also an option.
- The determination of the role of surgery in a patient with N2-positive lymph nodes should be made prior to the initiation of any therapy by a multidisciplinary team, including a thoracic surgeon who has a major part of his/her practice dedicated to thoracic oncology.[7]
- The presence of N2-positive lymph nodes substantially increases the likelihood of positive N3 lymph nodes. Pathologic evaluation of the mediastinum must include evaluation of the subcarinal station and contralateral lymph nodes. EBUS ± EUS are additional techniques for minimally invasive pathologic mediastinal staging that are complementary to mediastinoscopy. Even when these modalities are employed it is important to have an adequate evaluation of the number of stations involved and biopsy and documentation of negative contralateral lymph node involvement prior to a final treatment decision.

The Role of Surgery in Patients with N2 NSCLC is continued on NSCL-B 4 of 6 through NSCL-B 5 of 6

References

Note: All recommendations are category 2A unless otherwise indicated.

Sampling v Dissection

- Systematic lymph node sampling is defined as an exploration of each nodal station with biopsy of at least one representative node
- Mediastinal lymph node dissection is the en-bloc resection of all midline and ipsilateral lymph node basins
- MLND yields 17-18 nodes vs MLNS 7-8 nodes

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- MLND did not improve survival in T1-2N0 patients
- MLND is recommended for patients with N1
- MLND should be performed in patients with Stage IIIA disease

CoC Standard 5.8 Pulmonary Resection

- Audits of surgeons op notes and path reports showed poor concordance regarding procedure performed and extent of lymph node sampling
- ANY curative intent lung resection
- One hilar node and 3 mediastinal nodes
- Site visits starting in 2023 need >80% compliance

PRINCIPLES OF SURGICAL THERAPY

The Role of Surgery in Patients with N2 NSCLC

- Repeat mediastinoscopy, while possible, is technically difficult and has a lower accuracy compared to primary mediastinoscopy. One possible strategy is to perform EBUS (± EUS) in the initial pretreatment evaluation and reserve mediastinoscopy for nodal restaging after neoadjuvant therapy.[8]
- Patients with a single lymph node smaller than 3 cm can be considered for a multimodality approach that includes surgical resection.[4,9,10]
- Restaging after induction therapy is difficult to interpret, but CT ± FDG-PET/CT should be performed to exclude disease progression or interval development of metastatic disease.
- Patients with negative mediastinum after neoadjuvant therapy have a better prognosis.[10,11]
- Neoadjuvant chemoradiotherapy is used in one-third of the NCCN Member Institutions, while neoadjuvant chemotherapy is used in the other two-thirds. Overall survival appears similar provided RT is given postoperatively, if not given preoperatively.[5,12] Neoadjuvant chemoradiotherapy is associated with higher rates of pathologic complete response and negative mediastinal lymph nodes.[13] However, that is achieved at the expense of higher rates of acute toxicity and increased cost.
- When neoadjuvant chemoradiotherapy is used with doses lower than those used for standard definitive therapy, all efforts should be made to minimize any possible breaks in radiotherapy for surgical evaluation. Treatment breaks of more than 1 week are considered unacceptable.
- When timely surgical evaluation is not available, the strategy of neoadjuvant chemoradiotherapy should not be used. Another option in individual cases, and with the agreement of the thoracic surgeon, is to complete definitive chemoradiotherapy prior to re-evaluation and consideration for surgery.[14,15] If a surgeon or center is uncertain about the feasibility or safety of resection after definitive doses of radiation, consider obtaining an additional surgical opinion from a high-volume specialized center. These operations may also benefit from additional considerations of soft tissue flap coverage in the radiation field at the time of resection.
- Data from a large multi-institutional trial indicate that pneumonectomy after neoadjuvant chemoradiotherapy has unacceptable morbidity and mortality.[5] However, it is not clear if this is also true with neoadjuvant chemotherapy alone. Further, many groups have challenged that cooperative group finding with single-institution experiences demonstrating safety of pneumonectomy after induction therapy.[16-19] In addition, there is no evidence that adding RT to induction regimens for patients with operable stage IIIA (N2) disease improves outcomes compared to induction chemotherapy.[20]

References

Note: All recommendations are category 2A unless otherwise indicated.

N2 Disease

- Mediastinal nodes >1cm and/or PET positive require tissue confirmation
- EBUS as initial step in mediastinal staging
- Negative EBUS in the setting of highly suspicious nodes should be confirmed by mediastinoscopy

PRINCIPLES OF SURGICAL THERAPY

The Role of Surgery in Patients with N2 NSCLC

A questionnaire was submitted to the NCCN Member Institutions in 2021 regarding their approach to patients with N2 disease. Their responses indicate the patterns of practice when approaching this difficult clinical problem.

- All NCCN Member Institutions treat select N2 patients with multimodality therapy that includes surgery.
- The majority of NCCN Member Institutions prefer EBUS for initial mediastinal staging, reserving mediastinoscopy for possible restaging.
- The majority of NCCN Member Institutions do not pathologically restage mediastinal lymph nodes after induction therapy and prior to surgery.
- All NCCN Member Institutions consider surgery for single-station non-bulky N2 disease.
- Approximately half of the institutions consider surgery for single-station bulky disease, 39% for multi-station non-bulky disease, and 21% for multi-station bulky disease.
- Two-thirds of NCCN Member Institutions prefer induction chemotherapy; one-third prefer chemoradiation.
- The majority require at least stable disease after induction, but do not require radiologic or pathologic response prior to surgery.
- Roughly a half would consider pneumonectomy after induction chemotherapy, but less than a quarter would consider pneumonectomy after chemoradiation.
- Approximately three-fourths would give adjuvant RT for positive residual N2 disease, but only approximately one-fourth would give RT for N2 pathologic complete response.

Note: All recommendations are category 2A unless otherwise indicated.

Conclusions

- We need to significantly increase screening in Nebraska
- Surgery remains the preferred option for medically operable patients with early stage disease
- Long term survival is improved when patients receive their surgical care from dedicated thoracic surgical oncologists

Conclusions(cont)

- At the time of any lung resection performed with curative intent either MLND or MLNS should be performed
- For CoC accredited facilities >80% of resections should have at least one hilar and 3 mediastinal nodes sampled

The Role of Surgery in Patients with N2 NSCLC – References

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