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PERSONALIZED SURGICAL MANAGEMENT OF NSCLC

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I HAVE NO DISCLOSURES

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OBJECTIVES

- Discuss the history of surgery for lung cancer
- Review the criteria for determining a patients ability to undergo a surgical resection
- Differentiate between anatomic and non-anatomic lung resections
- Assess the current data regarding survival for lung cancer
- Review the wide variety of thoracic surgical procedures for lung cancer

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INTRODUCTION

- Lung cancer is the number one cause of cancer death
- In 2022 it is estimated that 130,740 men and women will die of lung cancer
- This represents 21.4% of all cancer deaths
- The 5 year survival for lung cancer is 22.9%
- Worldwide lung cancer will be responsible for over one million deaths

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HISTOPATHOLOGY

- Non-small cell lung cancers comprise almost 85% of all lung cancers
- The mechanisms leading to the development of the different types of tumors is still unclear
- Smoking causes all of the histologic types of cancer, but the dose-response relationship with the number of cigarettes smoked is steepest with small cell

HISTOPATHOLOGY(CONT)

- Adenocarcinoma is now the most common histology
- In women, the incidence rates of SCCA, large cell and small cell have flattened but the rate of adenocarcinoma is rising
- The change is thought to be related to increase in puff volume which deposits tobacco smoke in peripheral airways, and increase in the level of nitrates which enhances combustion. This decreases polycyclic aromatic hydrocarbons but increases tobacco specific nitrosamine NKK

STAGE I

- A Stage I lung cancer is a tumor confined to the lung <5cm in size
- Survival decreases as the tumor gets bigger
- Tumors with visceral pleural invasion also have a lower survival than tumors of the same size within the lung

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TREATMENT- STAGE I

- Pneumonectomy/bi-lobectomy/sleeve lobectomy/lobectomy with mediastinal lymph node dissection
- Anatomic segmentectomy
- Non-anatomic wedge resection
- Wedge resection with adjuvant RT
- Radiation therapy(standard versus SBRT)
- Radiofrequency ablation

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STAGE II

- A lung cancer is Stage II when the primary tumor is 5-7cm in size
- Hilar lymph nodes (N1 disease) are involved with tumor
- Increasingly diagnosed preoperatively with PET and EBUS
- A tumor is also Stage II if the primary tumor grows into the chest wall (T3 tumor)

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TREATMENT- STAGE II

- Pneumonectomy/bi-lobectomy/lobectomy/sleeve lobectomy with mediastinal node dissection
- Lobectomy with chest wall resection/reconstruction
- Segmentectomy with mediastinal node dissection
- Preoperative chemoRT followed by resection (Superior sulcus tumors only)
- ChemoRT

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STAGE III

- Most tumors are Stage IIIA when the mediastinal lymph nodes on the same side as the tumor are positive
- A patient is Stage IIIB if the lymph nodes on the opposite side of the trachea are involved or if the lymph nodes in the neck are positive
- Primary tumor >7cm (T4 tumor)
- A tumor is also Stage IIIA if it invades the heart, trachea, vertebral body, esophagus, or aorta

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TREATMENT- STAGE III

- Resection in the small group of pts with microscopic nodal involvement(detected postoperatively)
- Resection in pts with T4 tumors based on satellite lesions
- Resection in the small group of pts with T4 tumors involving carina,SVC, vertebral body
- Preoperative chemoRT followed by resection in those pts obtaining a downstaging of disease
- Definitive Chemotherapy and radiation followed by immunotherapy

STAGE IV

- The tumor has metastasized
- The most common sites are brain, bone, liver and adrenal glands
- Can also occur when the tumor spreads to the opposite lung

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Treatment- Stage IV

- Chemotherapy
- Radiation therapy
- Surgery- very limited number of patients with resectable local disease and isolated brain, adrenal, liver(?) metastases
- In the era of targeted and immunotherapies increasing use of surgery and radiotherapy in the management of oligometastatic disease

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HISTORY

- Dr. Evarts Graham performed the first successful pneumonectomy for lung cancer in1933
- It was not until the 1960's did lobectomy supplant pneumonectomy as the procedure of choice in the surgical management of lung cancer
- In the 1970's, Jensik, Faber et al, described their results in utilizing segmentectomy in selected patients
- The first VATS lobectomy was performed in 1991
- The first RATS lobectomy was done in 2003

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LUNG RESECTIONS

- Lobectomy
- Bilobectomy- either right upper and middle lobes or right middle and lower lobes
- Sleeve lobectomy- resection of a portion of the airway along with the lobe
- Pneumonectomy
- Sleeve pneumonectomy
- Carinal pneumonectomy

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EXTENDED RESECTIONS

- Lung plus chest wall
- Lung plus superior vena cava
- Lung plus vertebral body
- Lung plus atrium
- Lung plus aorta
- Lung plus esophagus

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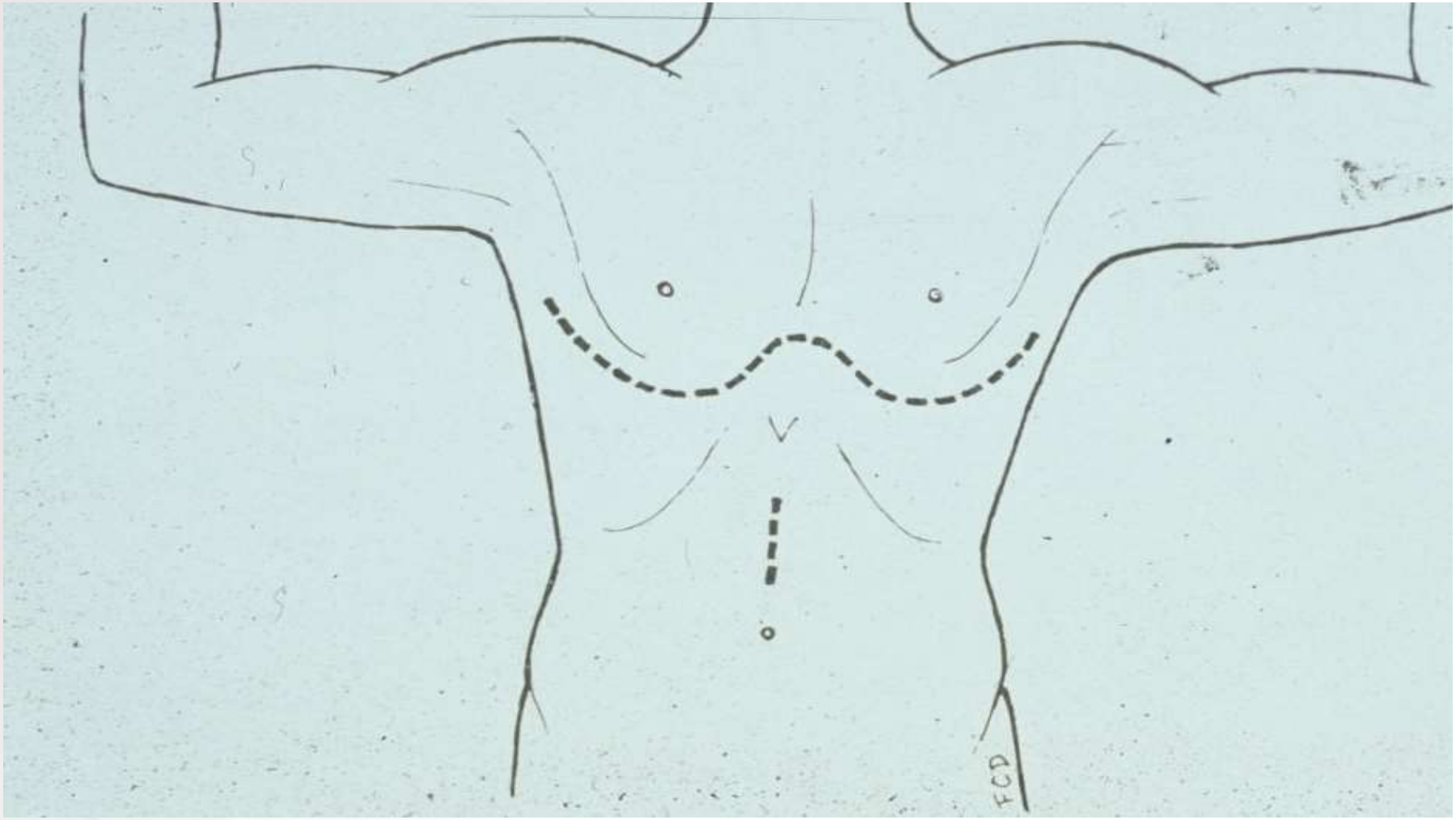

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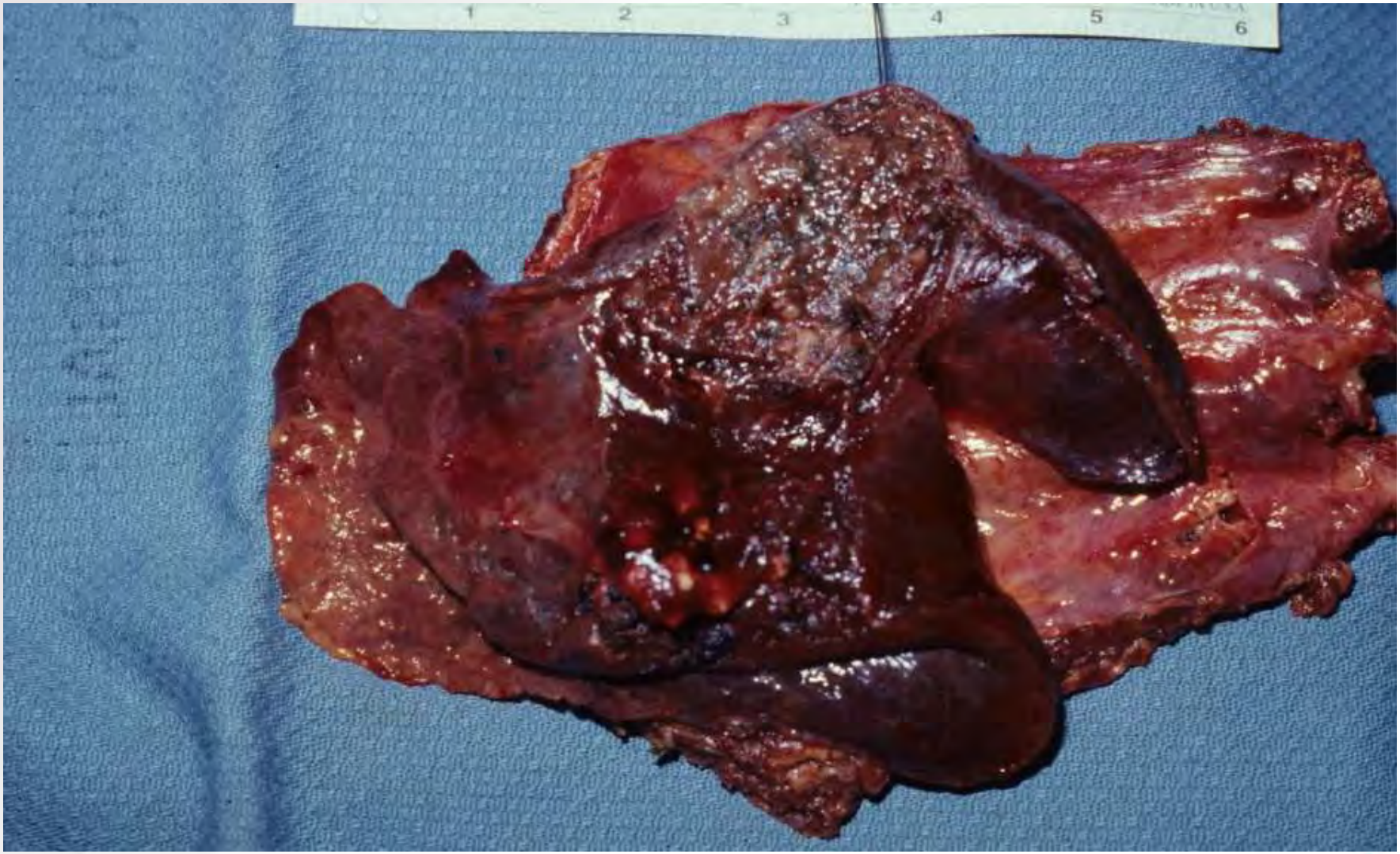

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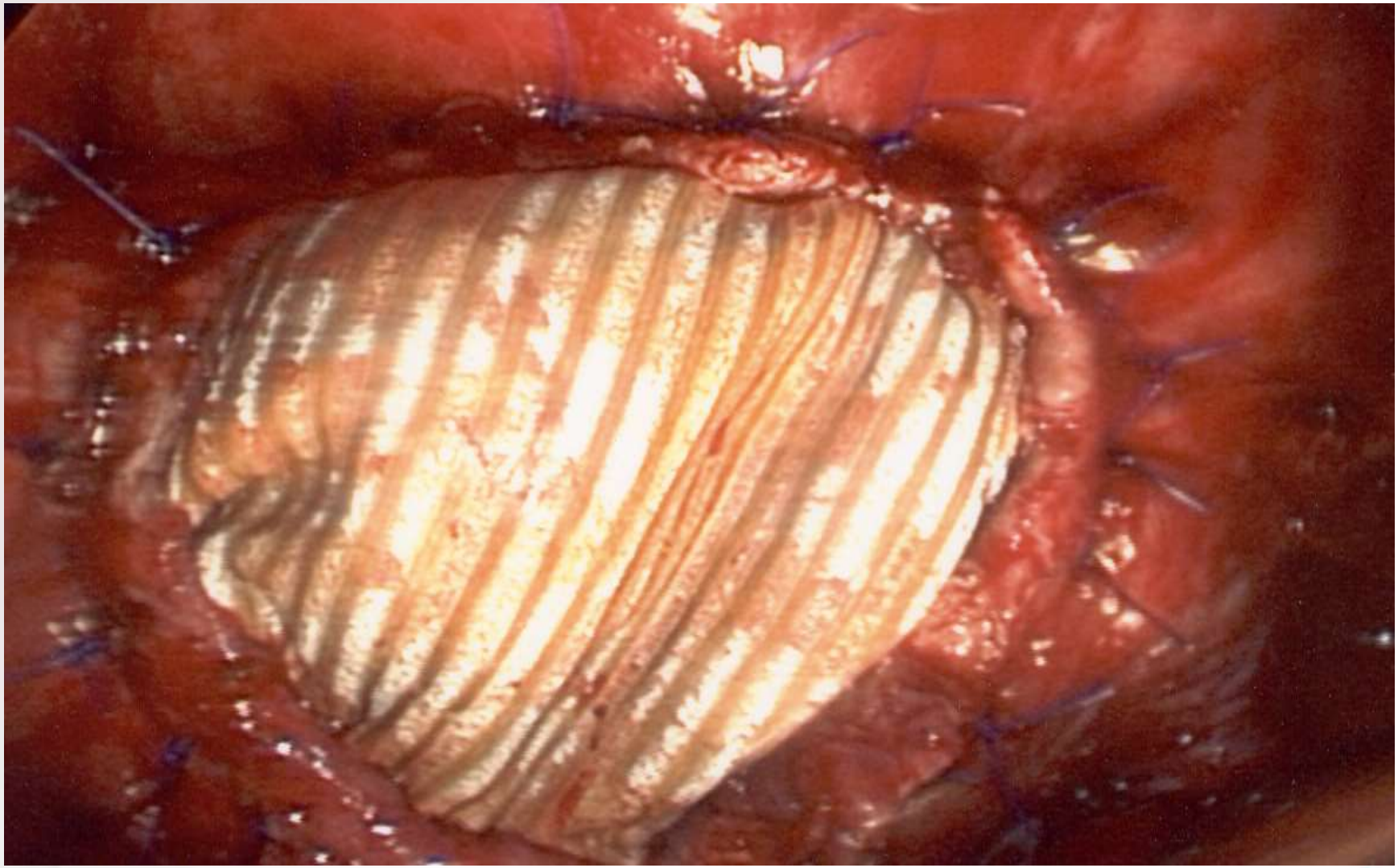

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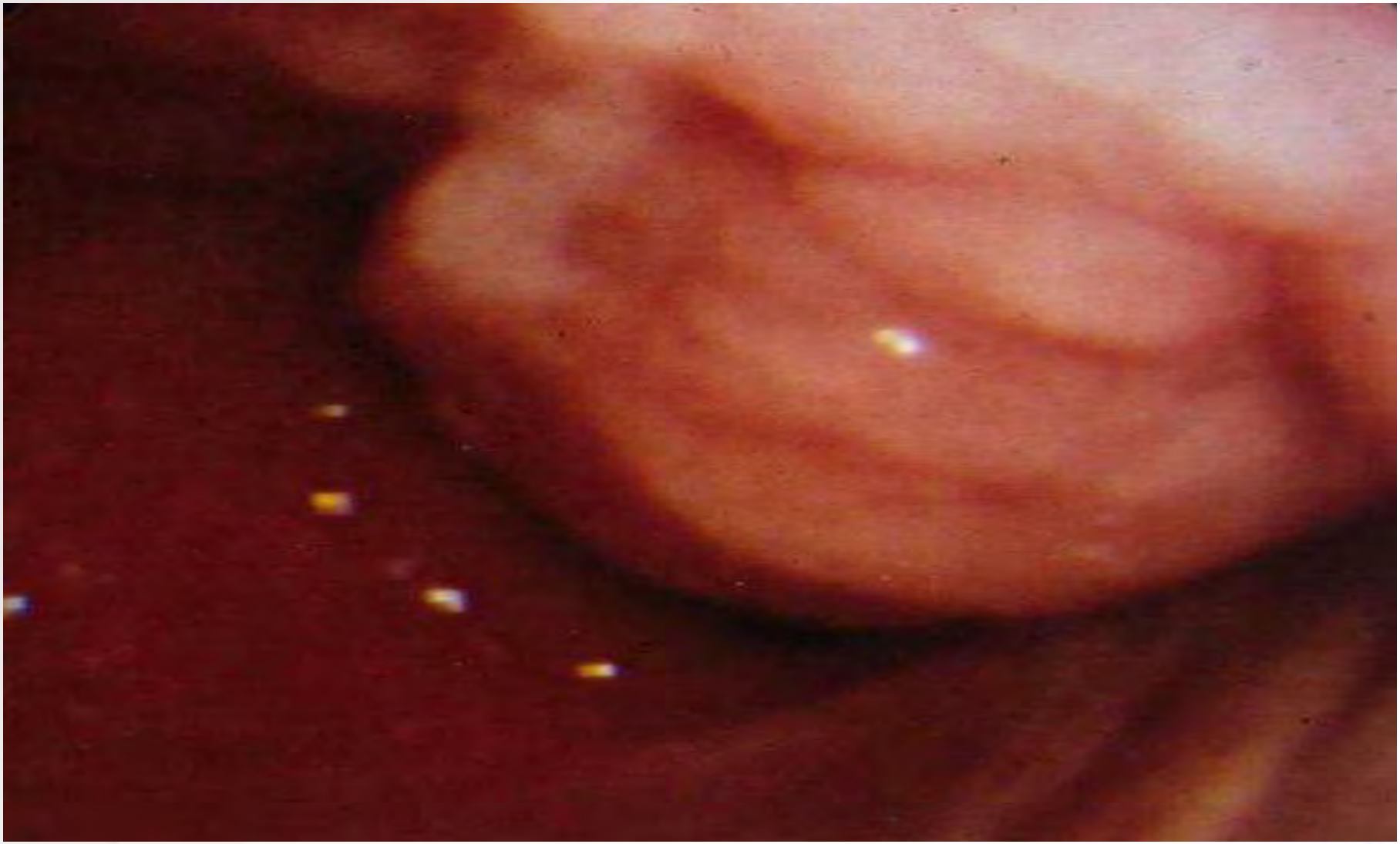

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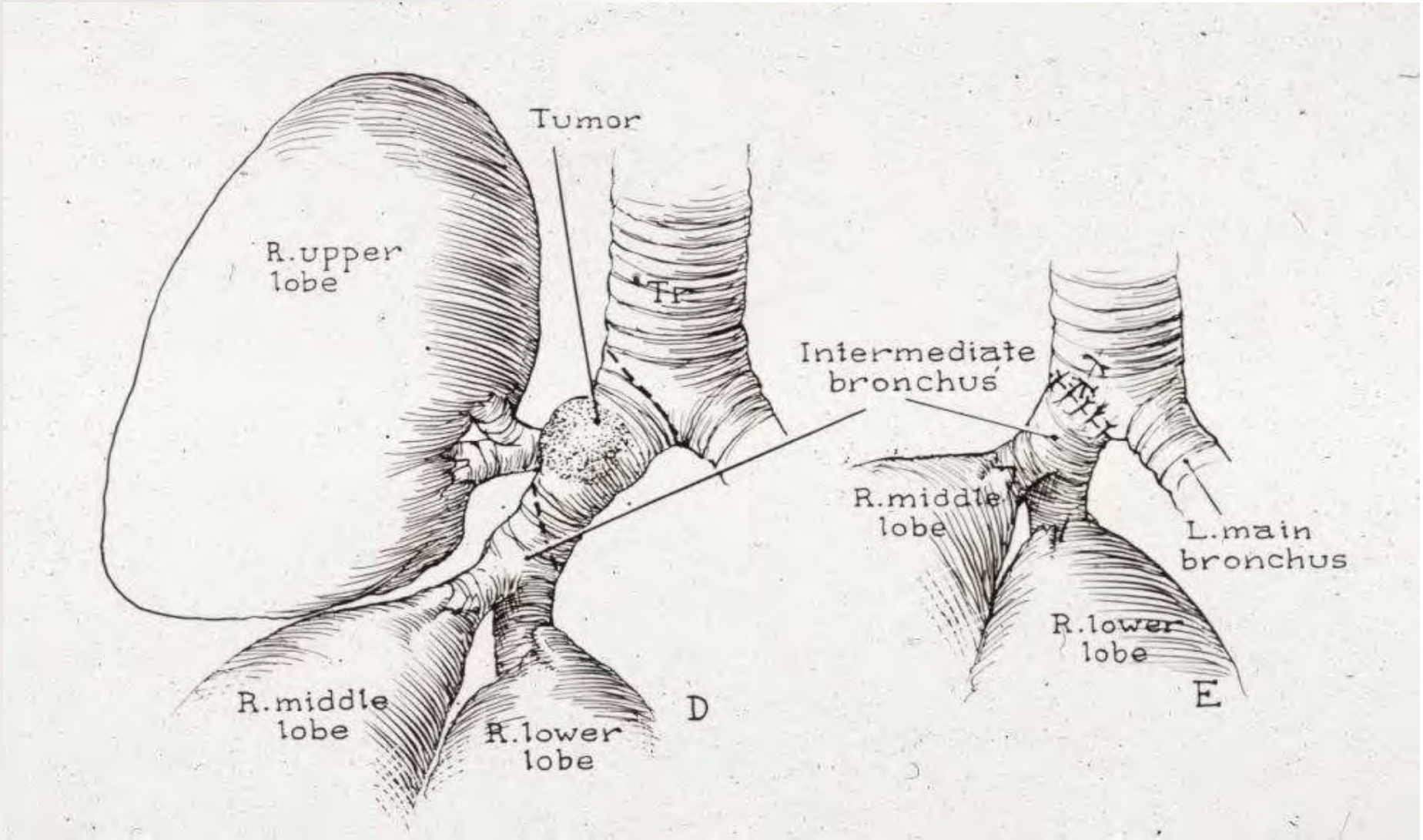

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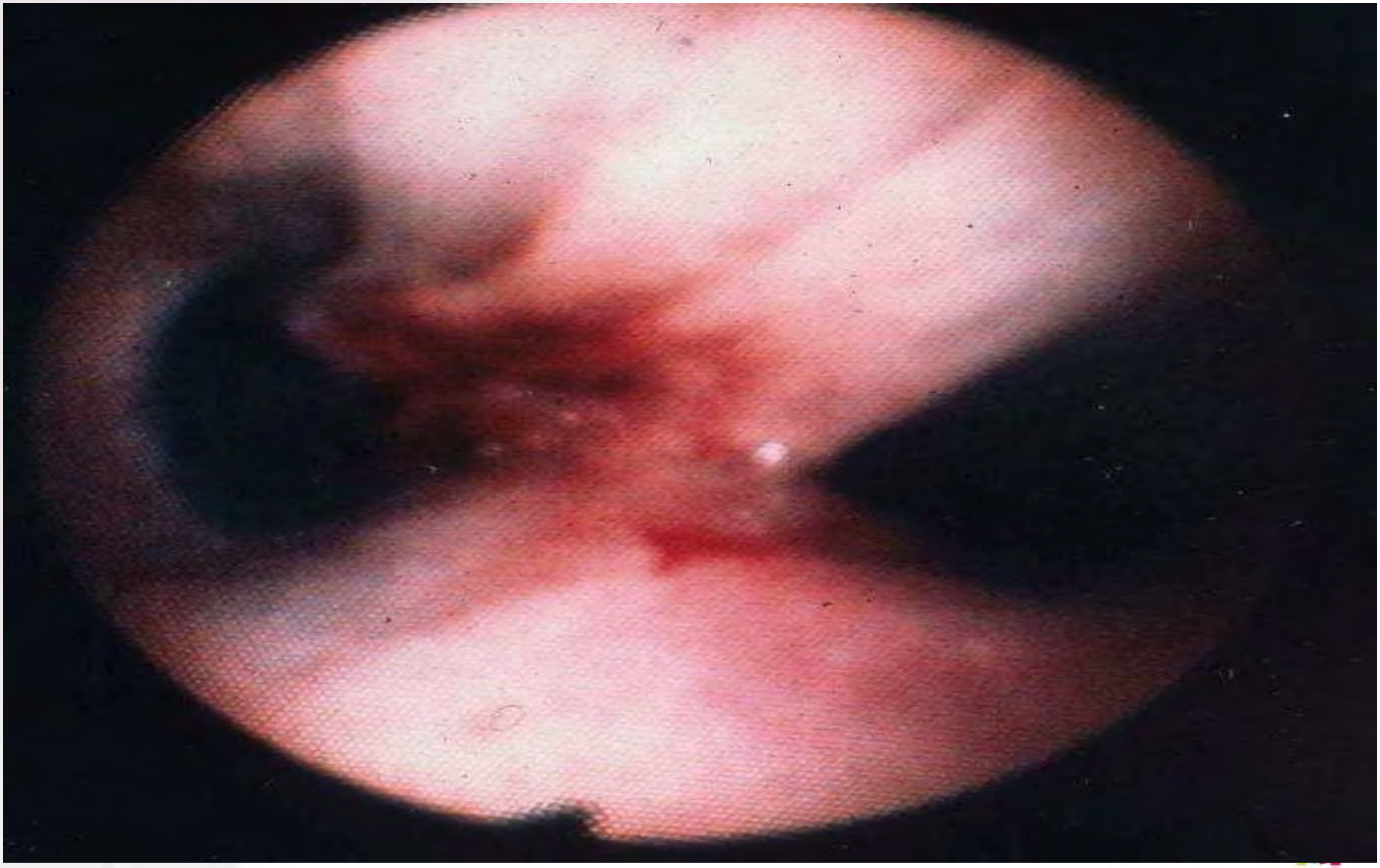

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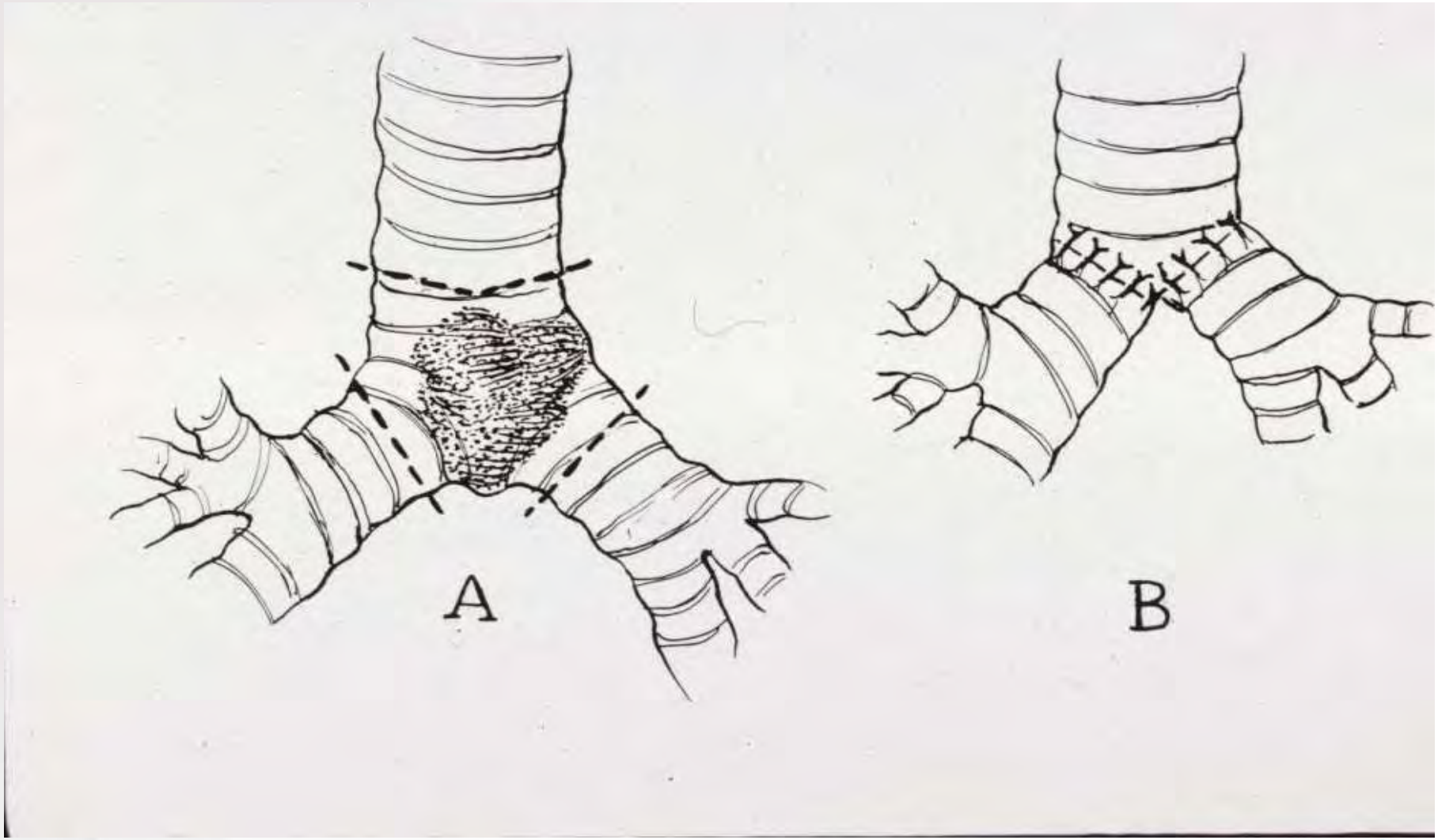

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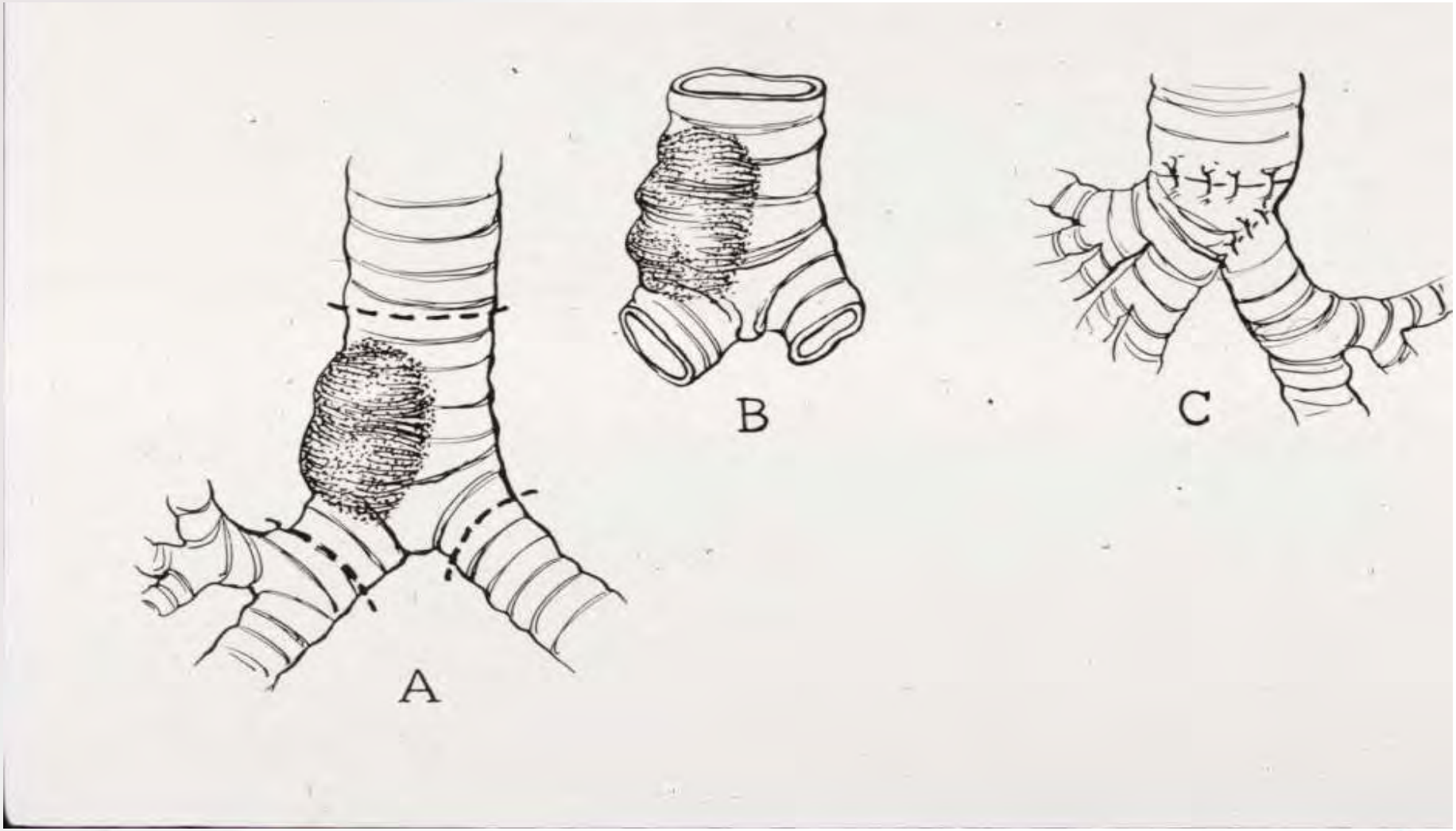

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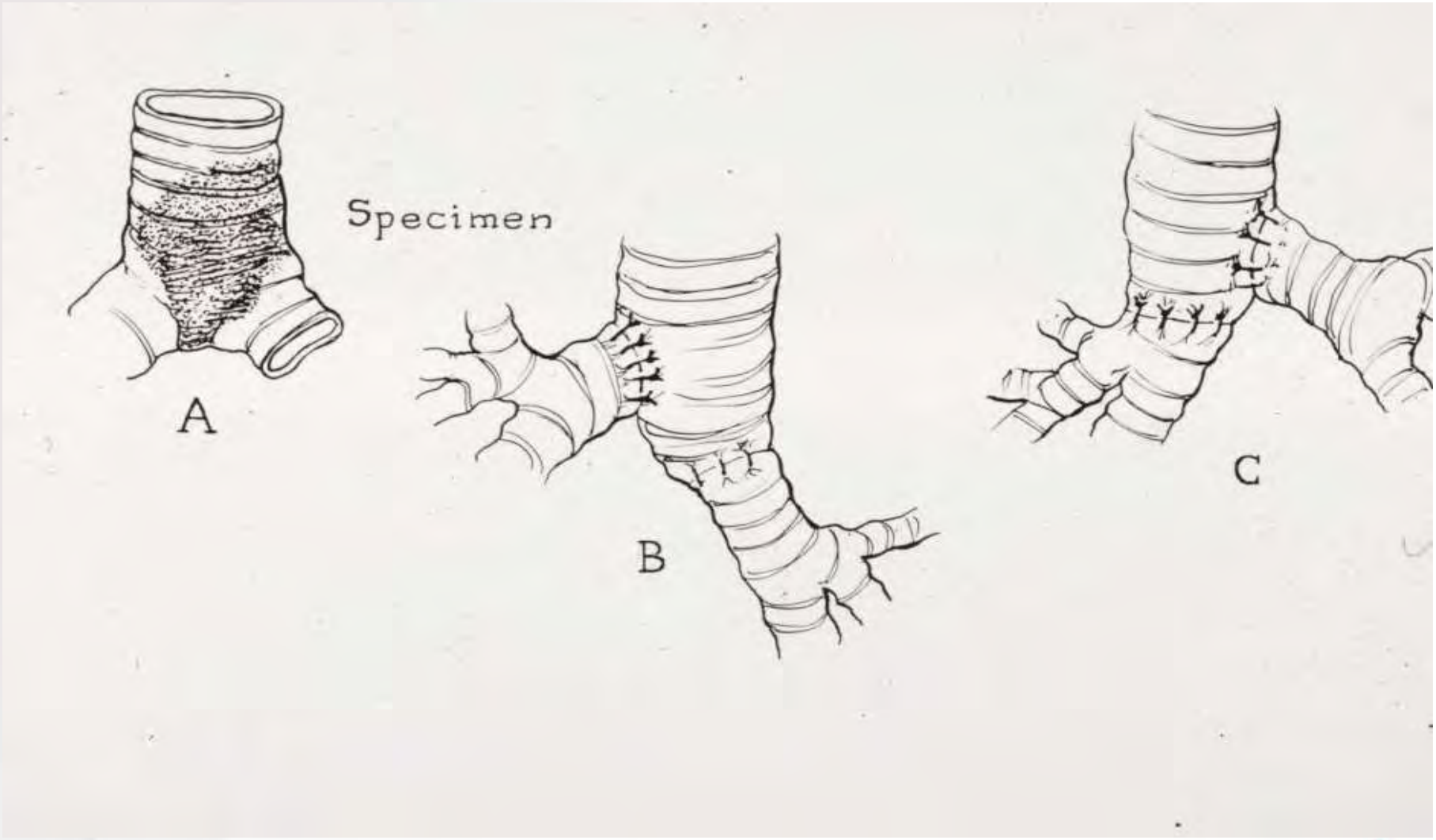

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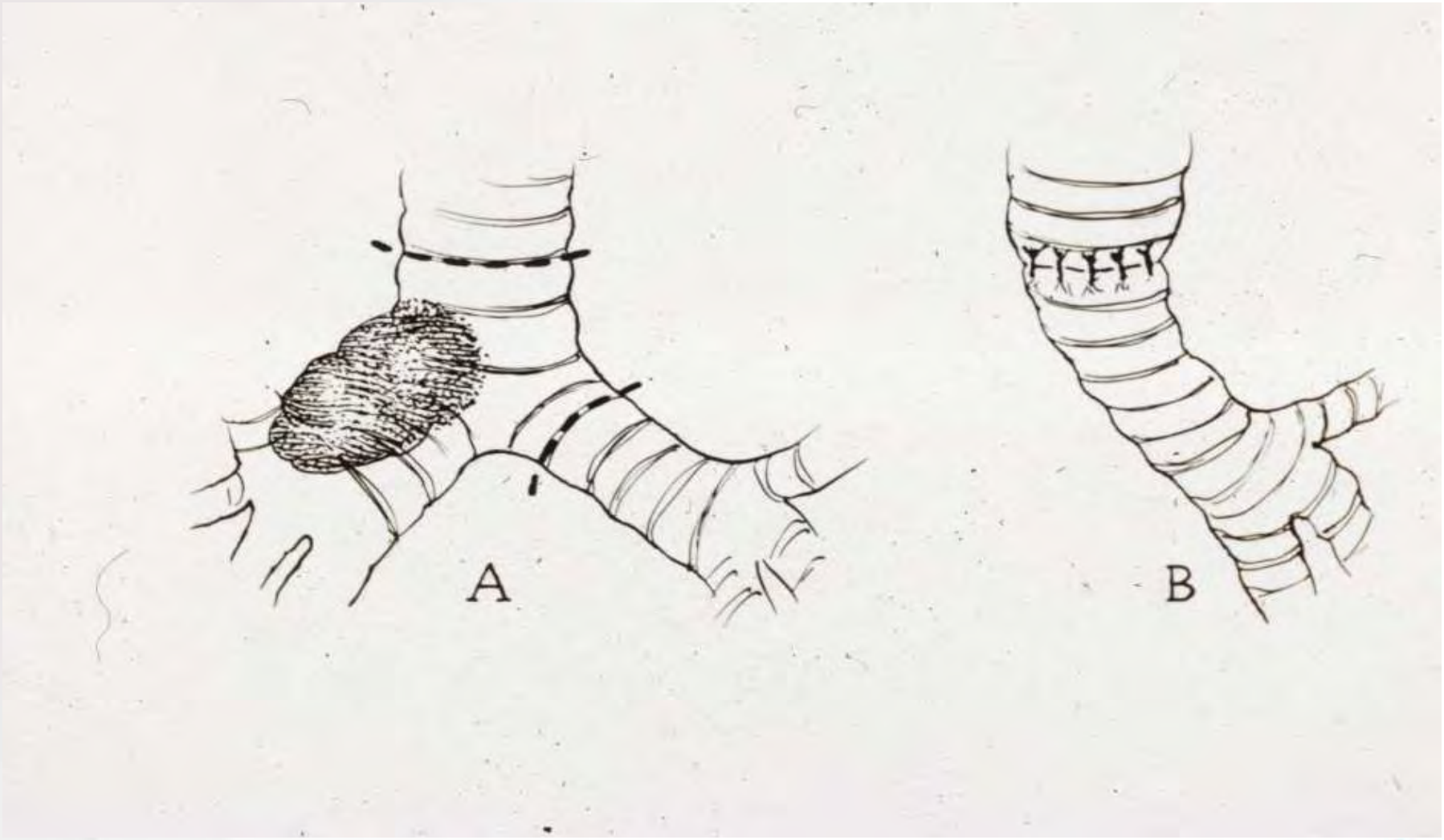

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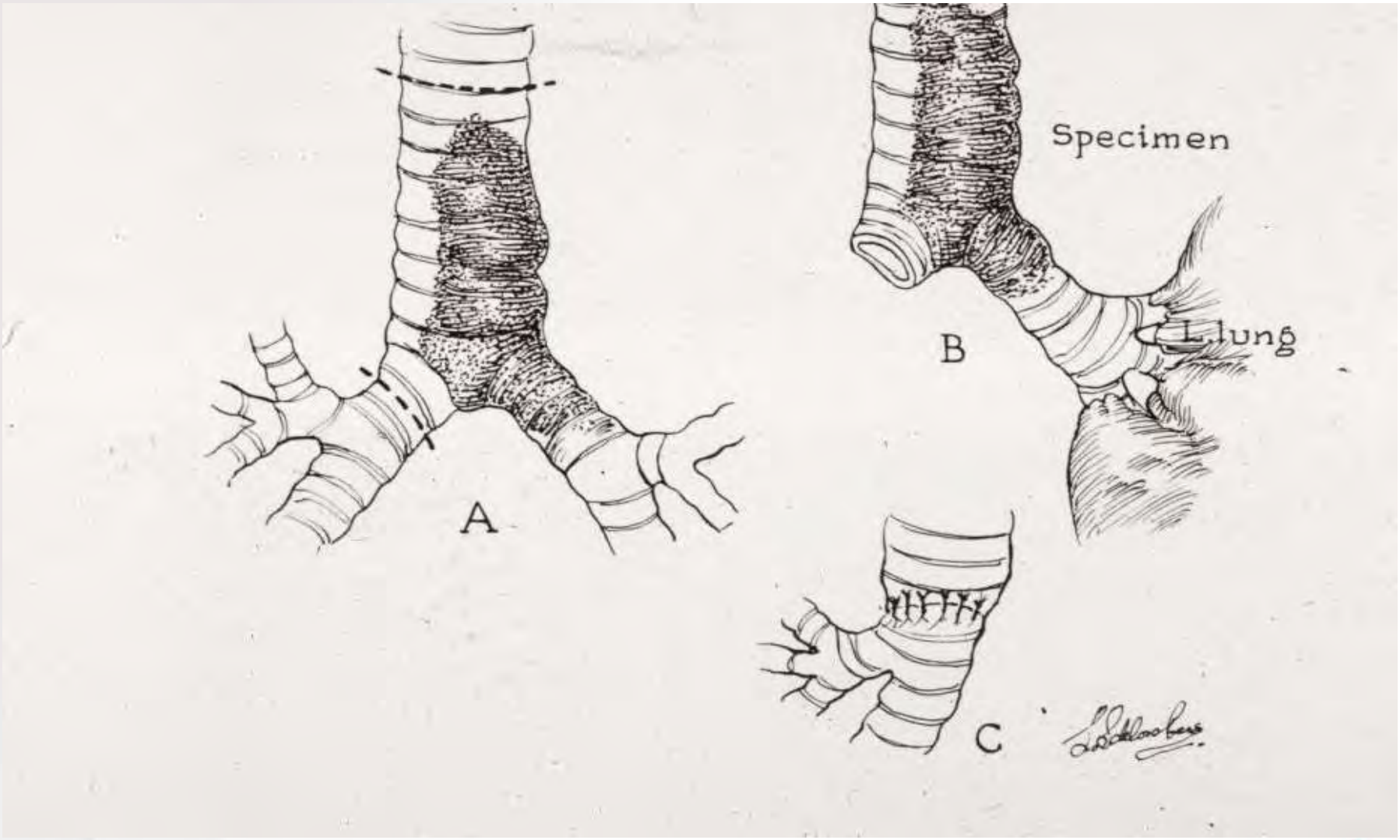

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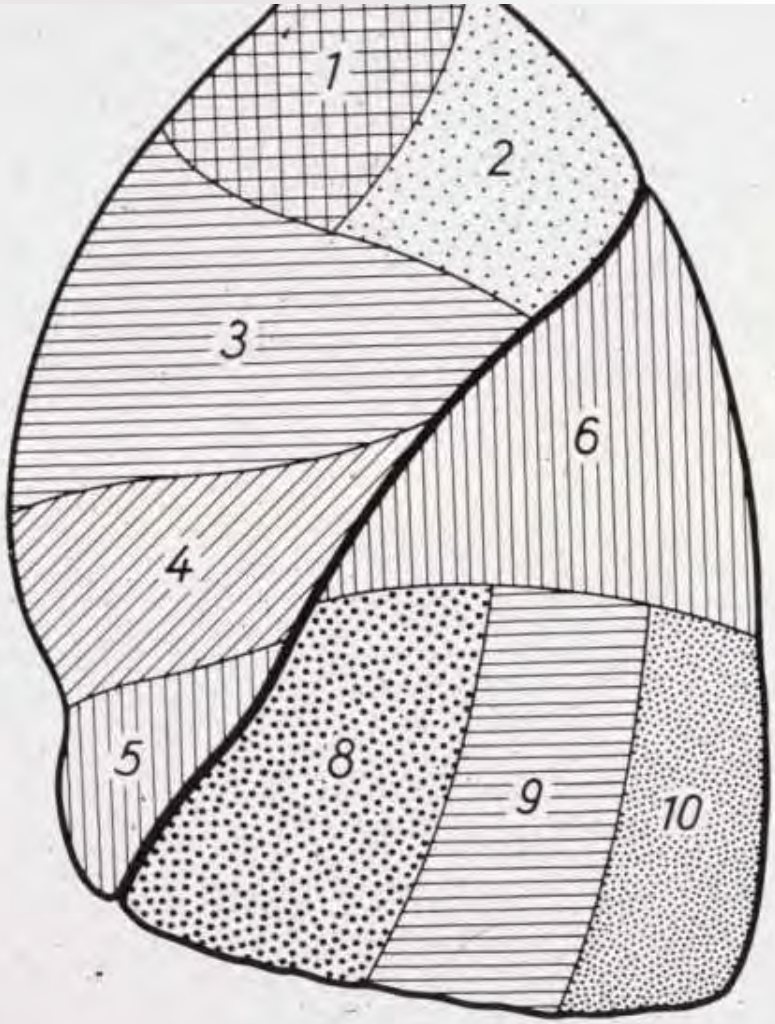

NOTE: 1) bronchopulmonary segments are anatom
subdivisions of the lung, each of which is supplied by its
segmental tertiary bronchus and artery, and drained by int
segmental veins.

2) the trachea divides into two primary bronchi, each
which supplies an entire lung. Each primary bronchus divi
into secondary or lobar bronchi. There are two lobar bron
on the left and three on the right, each supplying a sin
lobe. The secondary bronchi divide into the segmental
tertiary bronchi, which are distributed to the bronch
pulmonary segments. Usual descriptions of the bronch
pulmonary segments enumerate 8 to 10 segments in the
lung.

3) the bronchopulmonary segments of the left lung
numbered and named as follows:

Upper lobe

1 Apical
2 Posterior } Frequently considered as a single segment
3 Anterior
4 Superior } Lingular
5 Inferior

Lower lobe

6 Superior
7 Medial basal } Usually considered as a single segment.
8 Anterior basal } Medial basal cannot be seen from lateral view.
9 Lateral basal
10 Posterior basal

4) in the left lower lobe the medial basal bronchus aris
separate from the anterior basal in only about 13 %
humans studied. Thus, in most instances the medial basal an
anterior basal segments combine as an anteromedial bas
segment.

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Fig. 138: Right Lung, Bronchopulmonary Segments, Lateral View

NOTE: 1) the concept of subdividing the lungs into functional bronchopulmonary segments allows the surgeon to determine whether segments of lung might be resected in operations in preference to entire lobes.

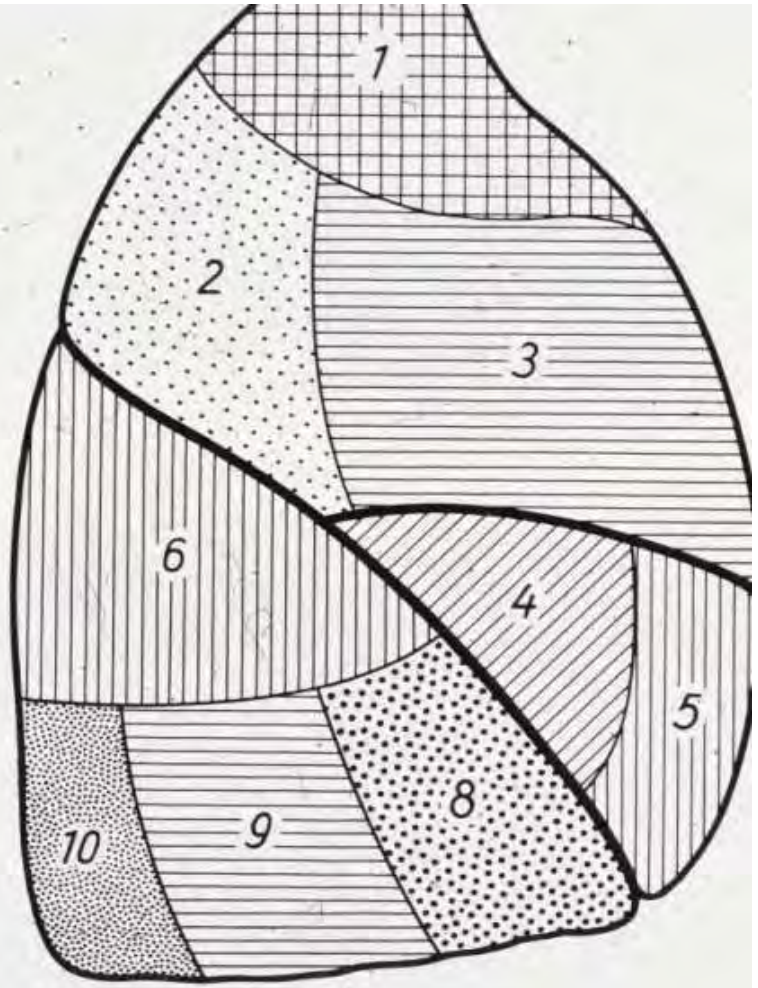
2) although minor variations exist in the division of the bronchial tree, a significant consistency has become recognized in the bronchopulmonary segmentation. The nomenclature utilized here was offered by Jackson and Huber in 1943 (Dis. of Chest **9:** 319–326) and has now become generally accepted because it is the simplest and most straightforward of the many suggested.

3) the bronchopulmonary segments of the right lung are numbered and named as follows:

Upper lobe
1 Apical
2 Posterior
3 Anterior

Middle lobe
4 Lateral
5 Medial

Lower lobe
6 Superior
7 Medial basal (cannot be seen from lateral view)
8 Anterior basal
9 Lateral basal
10 Posterior basal



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SUB-LOBAR RESECTION

- Wedge resection- is a non-anatomic resection of a pulmonary nodule/mass
- Segmentectomy- entails the division of the segmental pulmonary artery, vein and bronchus supplying the anatomic segment

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CLINICAL ADVANTAGES

- Decreasing the extent of resection lowers the operative mortality
- In a study of 2200 lung resections mortality following pneumonectomy was 6.2%, lobectomy 2.9% and sublobar resections 1.4%
- Sublobar resection preserves pulmonary function which improves morbidity and mortality

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Ginsberg et al. J Thorac Cardiovasc Surg

EARLY EXPERIENCE

- In 1973 Jensik et al reported on a series of 119 patients
- They included three groups: pts with prior resections n=16; palliative resections n=37; curative resections n=69.
- 5 year survival was 56.4% which was comparable to lobectomy at the time

Jensik et al J Thorac Cardiovasc Surg 1973;66:563-72.

RED FLAG

- The same group presented a subsequent study in 1994
- 173 pts with Stage I NSCLC- pts underwent a segmentectomy n=68 or a lobectomy n=105
- Pts undergoing a lobectomy had a survival advantage which disappeared in tumors <3cm
- Significantly the locoregional recurrence rate was 22.7% after segmentectomy vs 4.9% for lobectomy

Warren et al. J Thorac Cardiovasc Surg 1994;107:1087-94.

LUNG CANCER STUDY GROUP

- Randomized, controlled trial sublobar resection vs lobectomy
- Required 2cm margin and intraoperative frozen sections on lymph nodes
- 276 pts were entered in this study with a minimum of 4.5 years of follow-up
- 495 additional pts were registered but excluded due to: benign disease (40%), larger resections (25%), advanced stage (25%), other than NSCLC histology (15%)

Ginsberg et al. Ann Thorac Surg 1995;60:615-23.

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LUNG CANCER STUDY GROUP RESULTS

- 247 pts- sub-lobar resection n=122, lobectomy n=125
- Total recurrence and locoregional recurrence was significantly higher after limited resection
- Limited resection was associated with a 30% increase in overall death rate and a 50% increase in the observed death with cancer rate

CRITICISMS

- One criticism of the study was the substantial use of wedge resection (32.8%) rather than segmentectomy
- The other concern was the inclusion of tumors up to 3cm in size

CURRENT ERA

- In 1987, the Japanese implemented a national lung cancer screening program
- This resulted in the detection of smaller, earlier stage lung cancers
- Enthusiasm for more limited resections resurfaced in the setting of these more favorable tumors

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MODIFICATIONS

- Focused more on anatomic resections than wedge resections
- Included the use of extended segmentectomies
- Systematic lymph node evaluation
- Histologic examination of stapled margins

RESULTS

- Okada et al reported their results of extended segmentectomy vs lobectomy for tumors <2cm
- There were no local recurrences in either group
- 5 year survival was 87.1% for segmentectomies vs 87.8% for lobectomy

Okada et al. Ann Thorac Surg 2001; 71:956-60.

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RESULTS (CONT.)

- Bando et al reported their results performing segmentectomies for tumors <2cm
- The 5 year survival was 82% and the local recurrence rate was 1.9%
- In 2005, Martin-Ucar et al compared segmentectomy vs lobectomy in a group of patients with impaired pulmonary function (FEV1 <40%)
- No difference in 5 year survival and local recurrence rate was similar at 18%

Bando et al. Eur J Cardiothorac Surg 2002;21:894-99.

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TUMOR SIZE

- Okada et al analyzed 1272 consecutive lung resections to help further stratify suitability for sublobar resection
- Four groups with primary tumor size ≤10mm, 11-20mm,21-30mm and ≥31mm
- Cancer specific survival was 100, 83.5, 76.5, and 57.9%
- Sublobar resection was performed in 52% of tumors <20mm and 16% of tumors >20mm

SURVIVAL

- 5 year cancer specific survival for pts with Stage I disease having tumors <20mm and 21-30mm was 92.4 and 87.4% after lobectomy
- After segmentectomy 96.7 and 84.6%
- After wedge resection 85.7 and 39.4%
- When tumors were >30mm survival was 81.3, 62.9 and 0% respectively

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Okada et al. J Thorac Cardiovasc Surg 2005;129:87-93

CONCERNS

- The studies highlight the differences in results between segmentectomy and lobectomy pertaining to rates of local recurrence in the Western and Japanese literature

STRATEGIES TO REDUCE LOCAL RECURRENCE

- It has been known since the late 1980's that external beam radiation decreases local recurrence
- A small Phase II CALGB study of sublobar resection followed by RT (56 Gy) in 58 pts failed to show a benefit
- Even though no benefit was seen in this study, the use of adjuvant therapy was deemed promising

Miller et al. Ann Thorac Surg 1987;44:340-43.
Shenib et al. J Thorac Cardiovasc Surg 2005;129:81

INTRAOPERATIVE BRACHYTHERAPY

- In 1998, D'Amato et al described the use of ^{125}I impregnated vicryl mesh applied to the staple line
- This was done in a group of 14 high risk patients and showed no adverse effects
- In a group of 101 pts undergoing sublobar resection with ^{125}I seeds embedded in the staple line, Santos et al reduced local recurrence to 2% compared to18.6% for historical controls

D'Amato et al. Chest 1998;114:1112-5.
Santos et al. Surgery 2003;134:691-7.

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RECOMMENDATIONS

- Clinical Stage I <2cm
- FEV1 <60%
- DLCO <60%
- PA systolic pressure >40 mm Hg
- Oxygen requirement
- Congestive heart failure
- LV ejection fraction <40%
- Resection should be a segmentectomy

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ACOSOG Z4032

FAVORABLE CRITERIA

- Peripheral tumors
- Tumors <2cm
- At least a 1cm margin
- No endobronchial tumor
- Age >75
- Absence of nodal disease
- Ground glass opacity
- BAC histology

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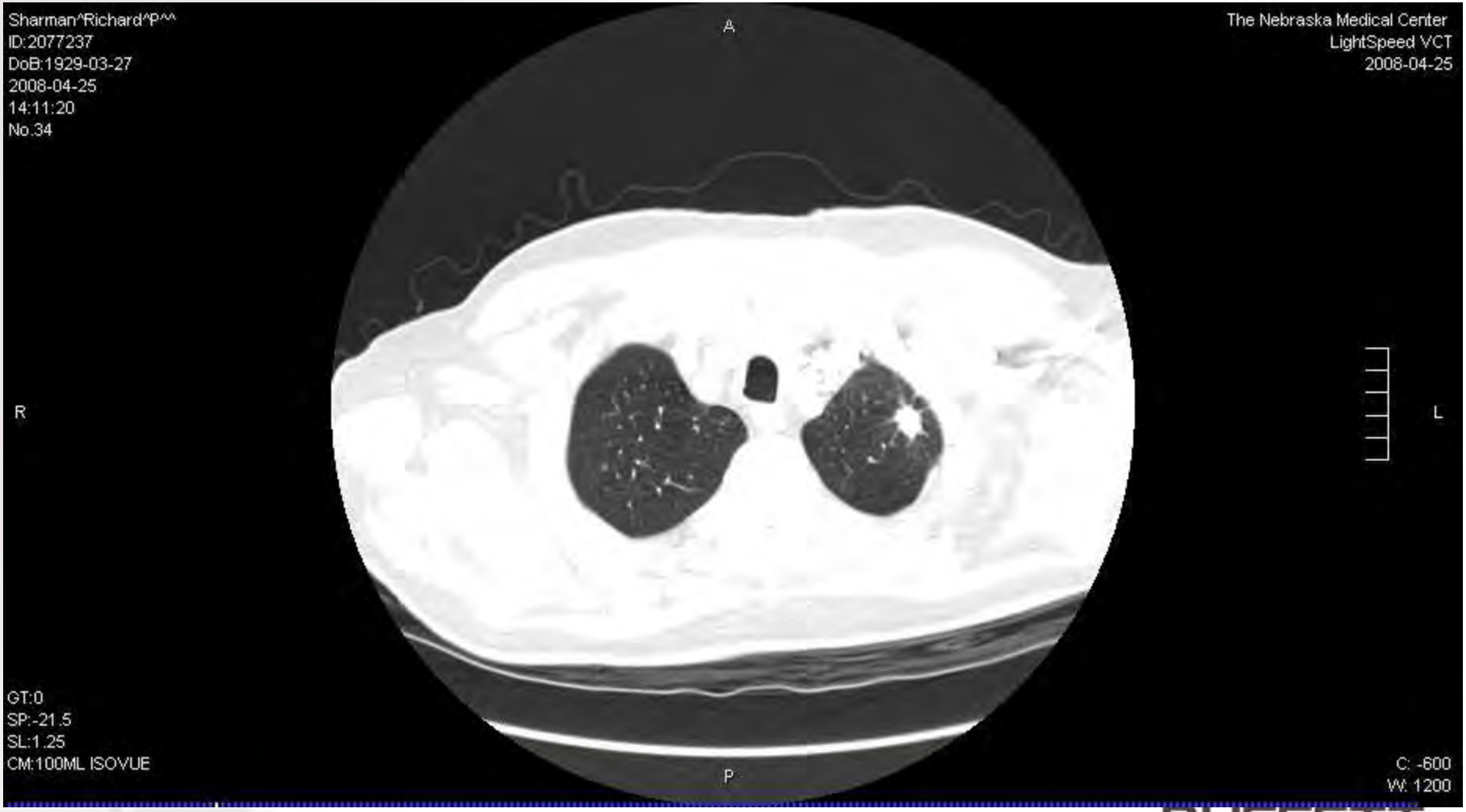

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SURGICAL APPROACH

- Segmentectomy can be performed open or by VATS
- Atkins et al reviewed 77 consecutive segmentectomies, 48 VATS and 29 open
- Operative times, blood loss and chest tube duration was similar
- Shorter lengths of stay were observed after VATS
- Mortality was 6.9% open vs 0% VATS

Atkins et al. Ann Thorac Surg 2007;84:1107-13.

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MORBIDITY AND MORTALITY

- The operative mortality was 1.8%
- Complications include- pneumonia, prolonged air leak, MI, port site infections, atrial dysrhythmias
- In the larger series of VATS lobectomy the complication rate has ranged from 10-21.9%
- This compares to historic data for open lobectomies of approx. 40%

ADVANTAGES

- Less postoperative pain
- Shorter hospital stay
- Decreased morbidity and mortality
- Improved survival in patients undergoing resection for lung cancer
- Increased immunologic benefit- decreased CRP and IL-6
- Decreased cost

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VATS VS OPEN LOBECTOMY

- Very few prospective randomized studies comparing VATS vs open lobectomy
- Kirby et al 1995- 30 open/25 VATS- found no statistical difference in operating time, intraperative blood loss, duration of chest tube drainage or length of stay
- There were significantly more complications in the open group, but these were mainly prolonged air leaks

ONCOLOGIC OUTCOMES

- Retrospective study of 963 pts with clinical stage I disease undergoing lobectomy from 2002-2011
- VATS lobectomy in 307(32%) and open in 656 (68%)
- Fewer pT2 and SCCA in VL group (39% vs 48% and 26% vs 18%)
- 30 day mortality 0.3 vs 1.4%
- 5 year survival 78% vs 73%

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Stephens N, et al. Eur J Cardio Thorac Surg 46(2014):607-13

CURRENT STATUS

- Most lung resections are not performed by thoracic oncologists
- Estimated that only 30% of lobectomies are currently performed with VATS techniques
- There have been no prospective, randomized studies evaluating VATS vs open lobectomy from an oncologic perspective, so we do not know if long term survival is compromised or superior as a few studies have suggested

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CONCLUSIONS

- Surgery remains the best option for patients diagnosed with early stage lung cancer
- Whenever possible the surgical resection should be performed in a minimally invasive fashion (VATS/RATS)
- The surgical procedure should be tailored to the individual patient
- A methodical approach should be utilized in the evaluation of the patient diagnosed with lung cancer
- Whenever possible this should be discussed in a multi-disciplinary fashion

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