



LUNGCANCER

Endoskopisk Utredning

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SUS

241007

Agenda

Historien om Bronkoskopi

Rigid och Flexibel Bronkoskopi

Bronkoskopi – planering, indikationer och kontraindikationer

Grundläggande bronkoskopi vid utredning av lungcancer - patientfall

EBUS

TNM

The History of Bronchoscopy

Porter 1838: "There is perhaps no disease covered by greater darkness or posing more difficulties to the practitioner than those of the larynx and the trachea."

The pre-endoscopic era:

Hipocrates (460-370 BC) - introducerde ett rör in i larynx hos patienter som kvävdes

Desault (1744-1795) - nasotracheal intubation för extraktion av främmande kropp

Czermak, fysiolog from Budapest – introducerar laryngeal spegel

Development of endoscopy:

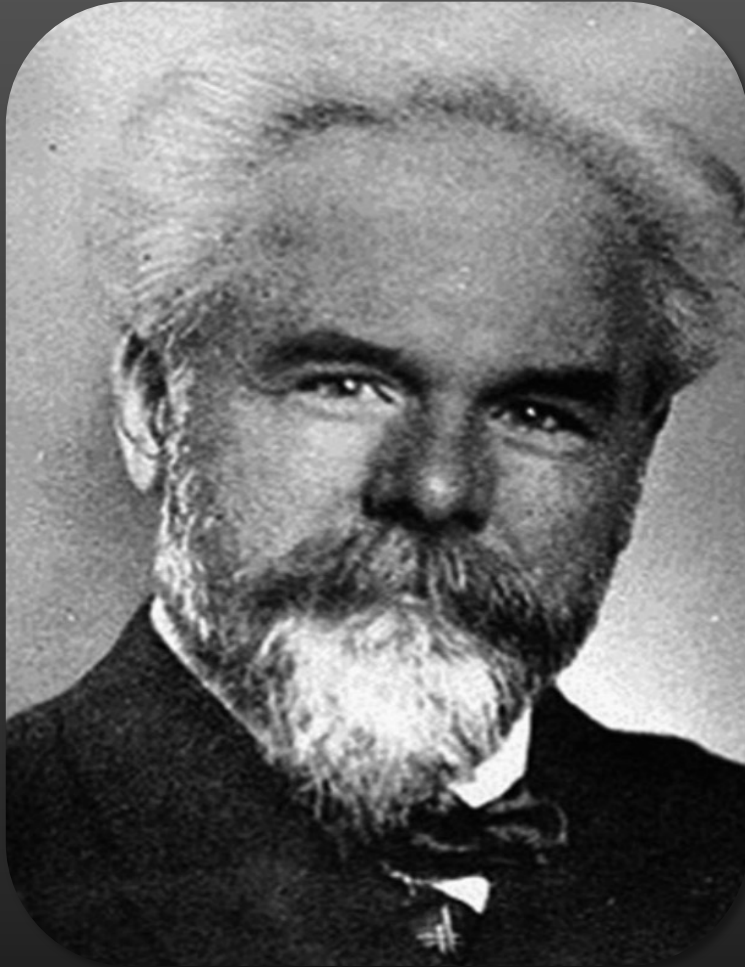
Desormeaux, urolog - **1875** - utvecklar första endoskopet - uretroskop

Alfred Kirstein, laryngolog i Berlin - **1895** modifierar esofagoskop till trakeoskop



Czermak demonstrerar laryngeal spegel, 1856

Bronchoscopy - The Pioneers



Dr. **Gustav Killian**, tysk otorhinolaryngolog och grundare av bronkoskopi



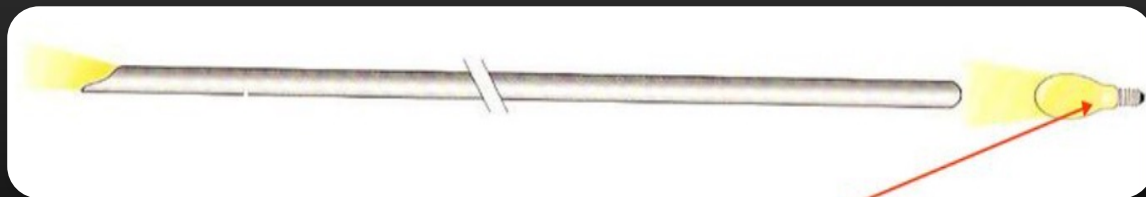
Trakea är flexibel och instrumentet kan lätt vinklas och nedföras till lobärnivå

Historien om ett fläskben

1897 Killian - ett styvt instrument (rak bronkoskop) för att ta bort främmande kropp från den högra huvudbronken utan trakeotomi

Vaken patient med kokain som lokalbedövning

703 patienter med främmande kroppar i bronkerna 1911–1921



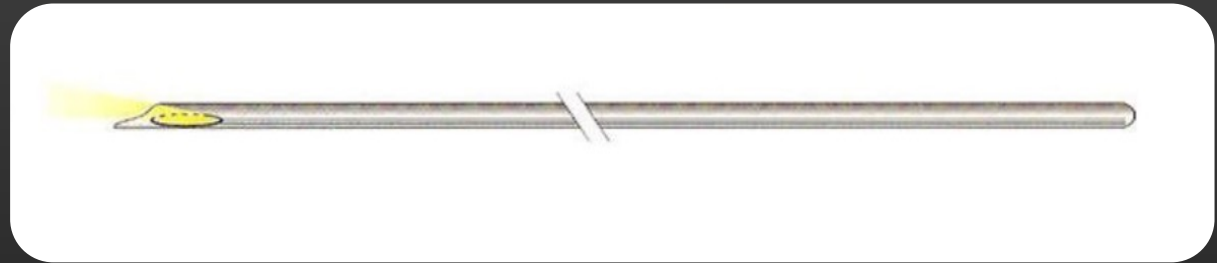
Gustav Killian's Bronchoscope , external light source



Bronchoscopy - The Pioneers



”Looking into the living lungs”
Chevalier Jackson 1928



Chevalier Jackson's Bronchoscope
with a small distal bulb & built-in suction tube

Bronchoscopy - The Pioneers

1960 - Shigeto Ikeda ersätter den lilla elektriska glödlampan med glasfibrer som kan sända starkare ljus från en extern källa

1966 - Ikeda presenterar det första flexibla bronkoskopet
International Congress on Diseases of the Chest in Copenhagen

1979 – **Ikeda** grundar WAB - World Association of Bronchology



Bronchoscopy - The Pioneers

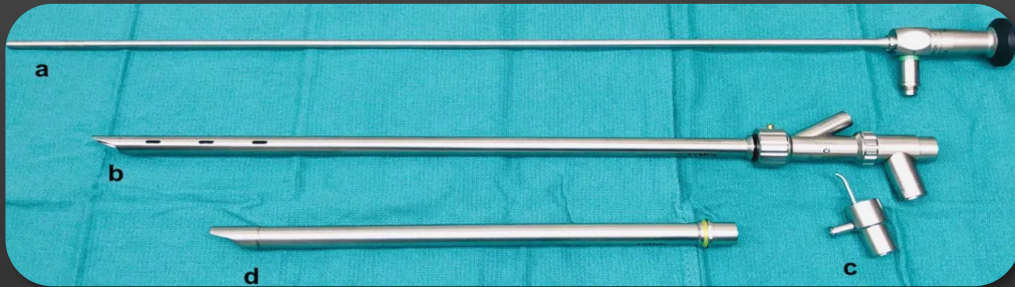


Rune Lundgren

1975 i Umeå - introducerar rigid bronkoskopi
för cancerdiagnostik och utredning
av andra lungsjukdomar

Typer av Bronkoskopier

Rigid bronkoskop: a) Teleskop, b) Bronkoskop med öppningar distalt för ventilation, d) Trakeoskop



Flexibel bronkoskop



Konventionell bronkoskopi

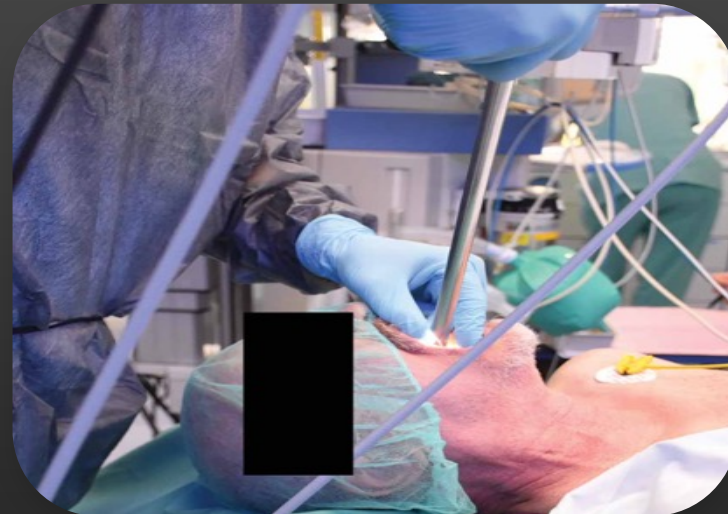
Bronkoskopi med EBUS-TBNA

Specialbronkoskopi med radiellt ultraljud och genomlysning

Elektromagnetisk navigationsbronkoskopi

Robot assisterad bronkoskopi

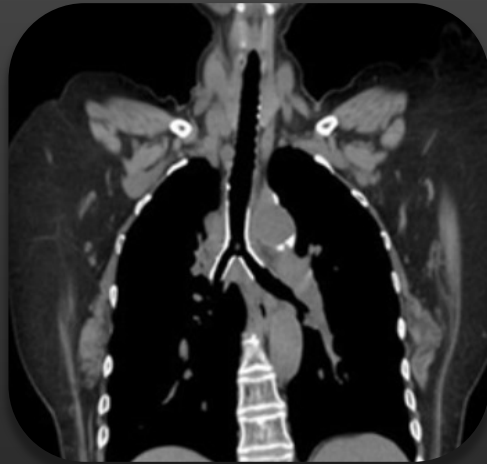
Terapeutisk bronkoskopi



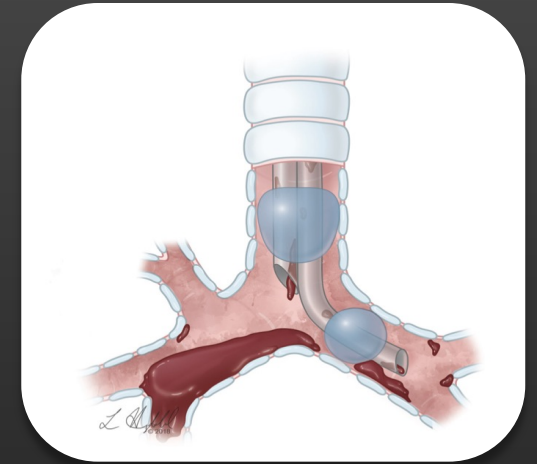
Terapeutisk Bronkoskopi - Indikationer



Endobronkiell rekanalisering av luftväg vid malign eller benign central luftvägsobstruktion
Inläggning av stent i centrala luftvägar



Extrahering av främmande kropp



Behandling av massiv hemoptys

Flexibel bronkoskopi - indikationer

Utredning av pulmonella symtom (hemoptys, prolongerad och kronisk hosta, återkommande infektioner)

Infektion (mikrobiologisk agens). Rensugning av luftvägar

Suspekt neoplasi

heshet och förflamning av stämband utan känd genes

unilateral ronki

segmentell eller lobär kollaps

lunginfiltrat och noduli

unilateral diafragmapares av oklar genes

bedömning av mediastinala förändringar

lung cancer staging

Bronkoskopisk lung volymen reduktion – heterogen emfysem – ventiler

Bronkiell termoplasti för astma

Diagnostik och behandling av bronchopleural fistel

Bronkoskopi - kontraindikationer

Grav hypoxi – inte kan korrigeras med syrgas

Instabil koronariskemi - hjärtinfarkt < 4 veckor

Patienten kan inte samtycka till ingrepp – demens

Koagulopatier

Akutvagn ska finnas tillgänglig på bronkoskopiavdelningen

Personalen ska ha kompetens och erfarenhet att utföra HLR och hantera komplikationer

(andningssvikt, hjärtarytmier, blödningar, pneumothorax)

Planera och utföra bronkoskopi

Bedöma DT thorax bilder - alla projektioner

Välja vilken **typ av bronkoskopi** ska utföras och instrument

Kontraindikationer? Antikoagulantia?

Lokal bedövning Xylokain och Lidokain 10mg/ml och 20mg/ml (maxdos ~ 8 mg/kg kroppsvikt)

Lidokain: toxiska reaktioner - VT, cardiac arrest (höga doser eller nedsatt clearance – leversvikt och hjärtsvikt)

Case rapport: 19-årig student, bronkoskopi inom ramen av en studie, går hem, får kramper och dör. Vid obduktion s-konc av Lidokain 12 mikrogram/ml – fick 1200 mg Lidokain totalt under ingreppet

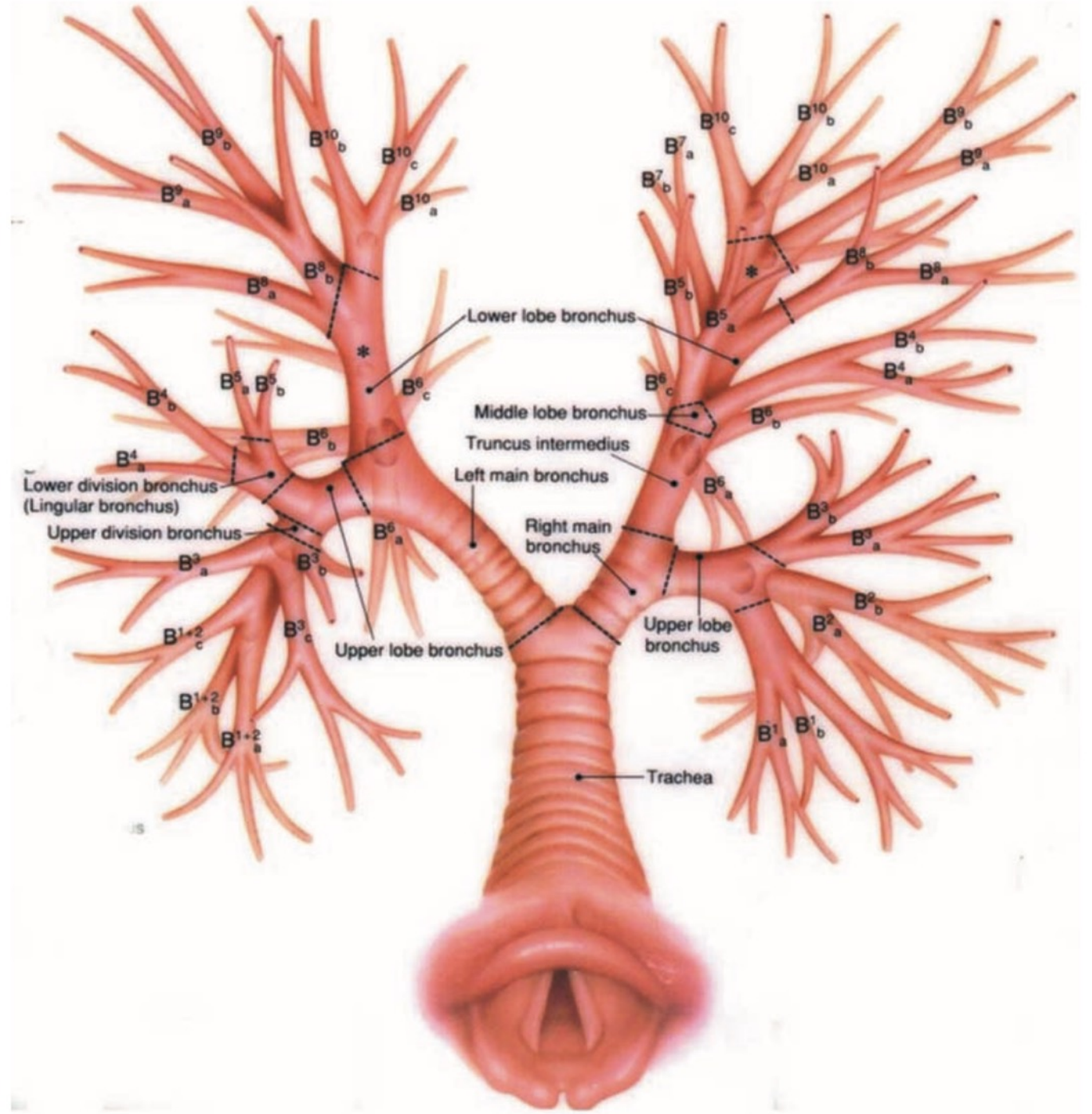
Sedering – moderate conscious sedation – Remimazolam (Byfavo) eller Midazolam och Alfentanyl

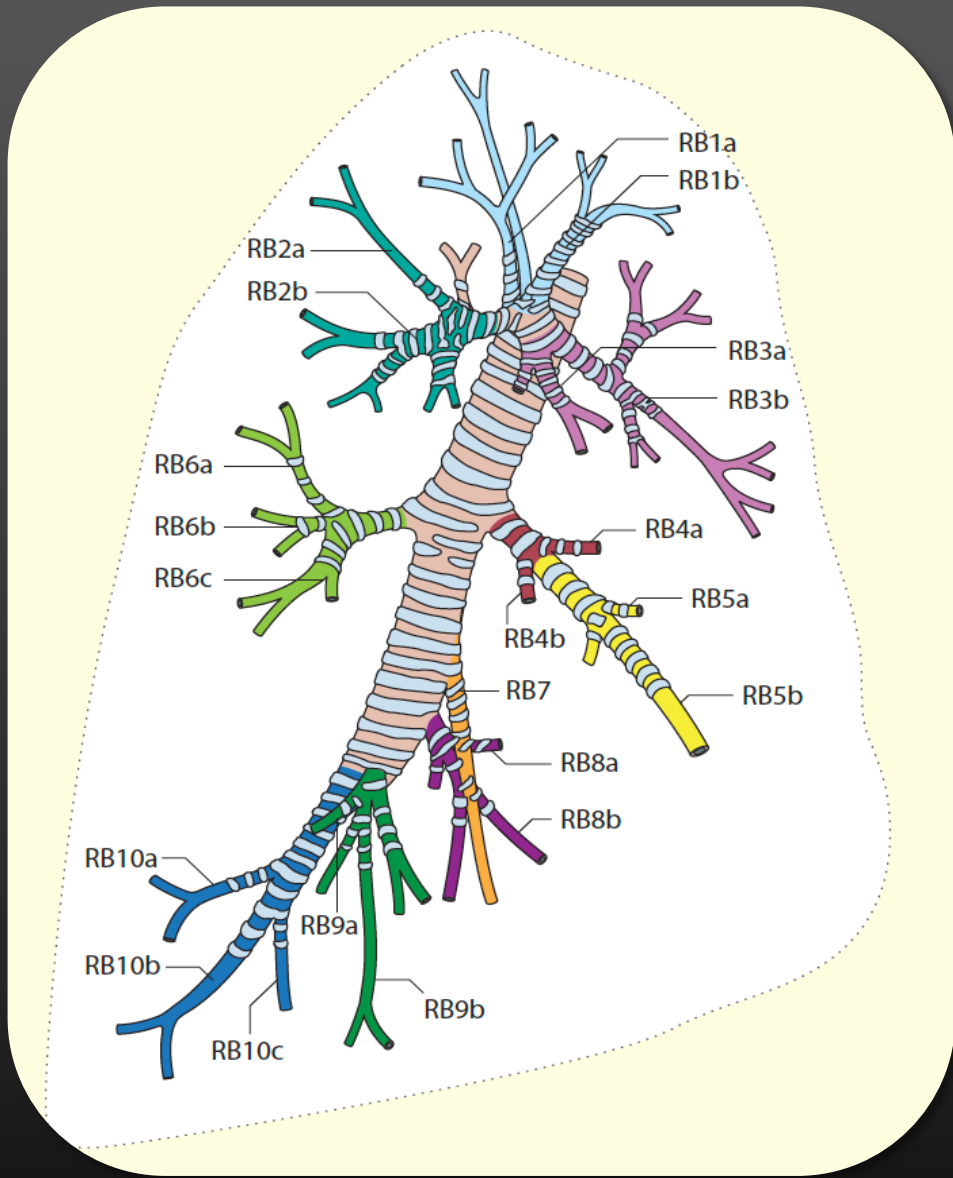
Propofol – propofol kurs

Generell anestesi?

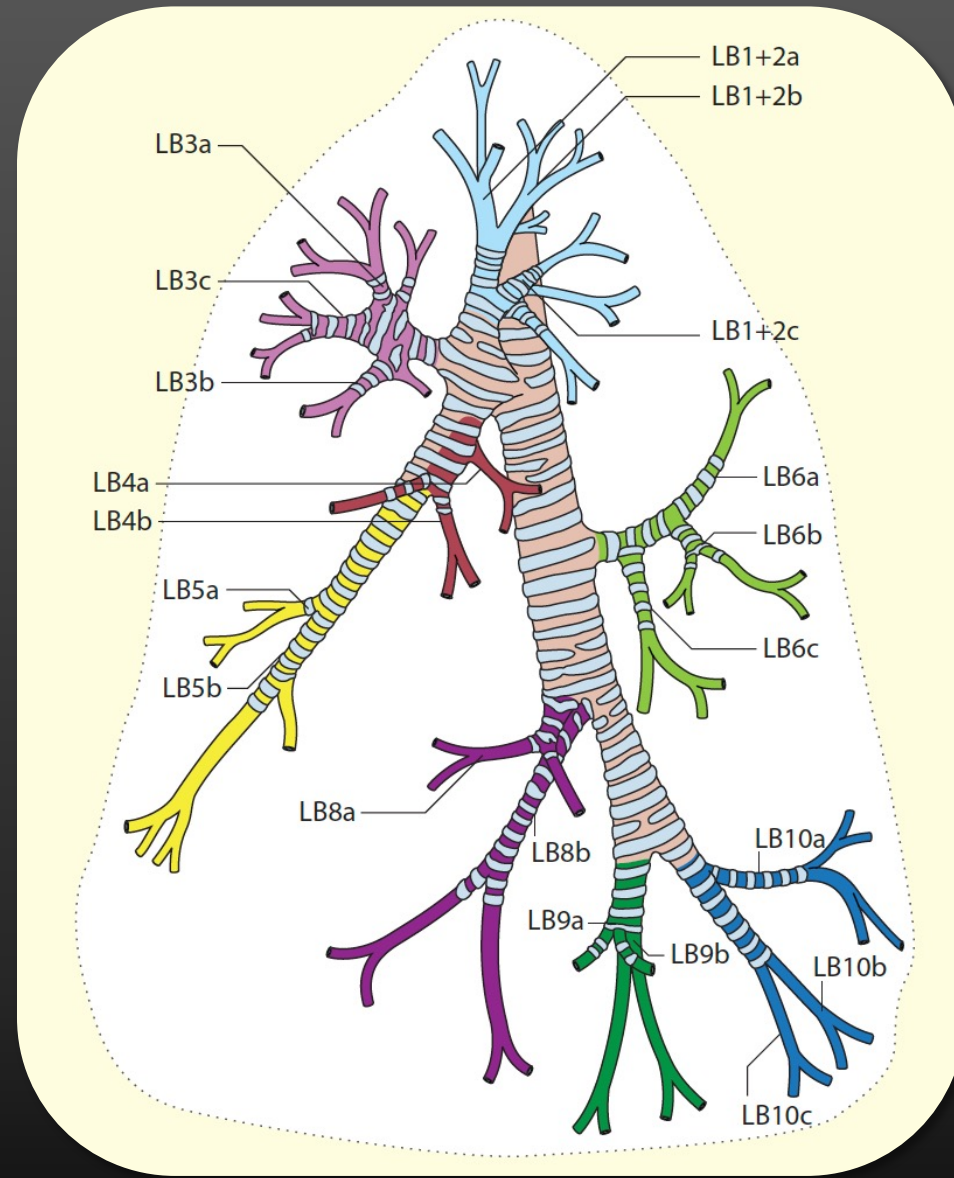
Airway anatomy for the bronchoscopist

Atlas of Flexible Bronchoscopy, Shah 2012
Introduction to Bronchoscopy, Ernst 2009
Atlas of Fiberoptic bronchoscopy, Prasad 2014





Höger bronkträd



Vänster bronkträd

Bronchial nomenclature

För the bronkoskopist:

Bronkialsegment – arabiska siffror - tex RB2

Bronkialsubsegment - a, b, c i sekvens - tex RB2a

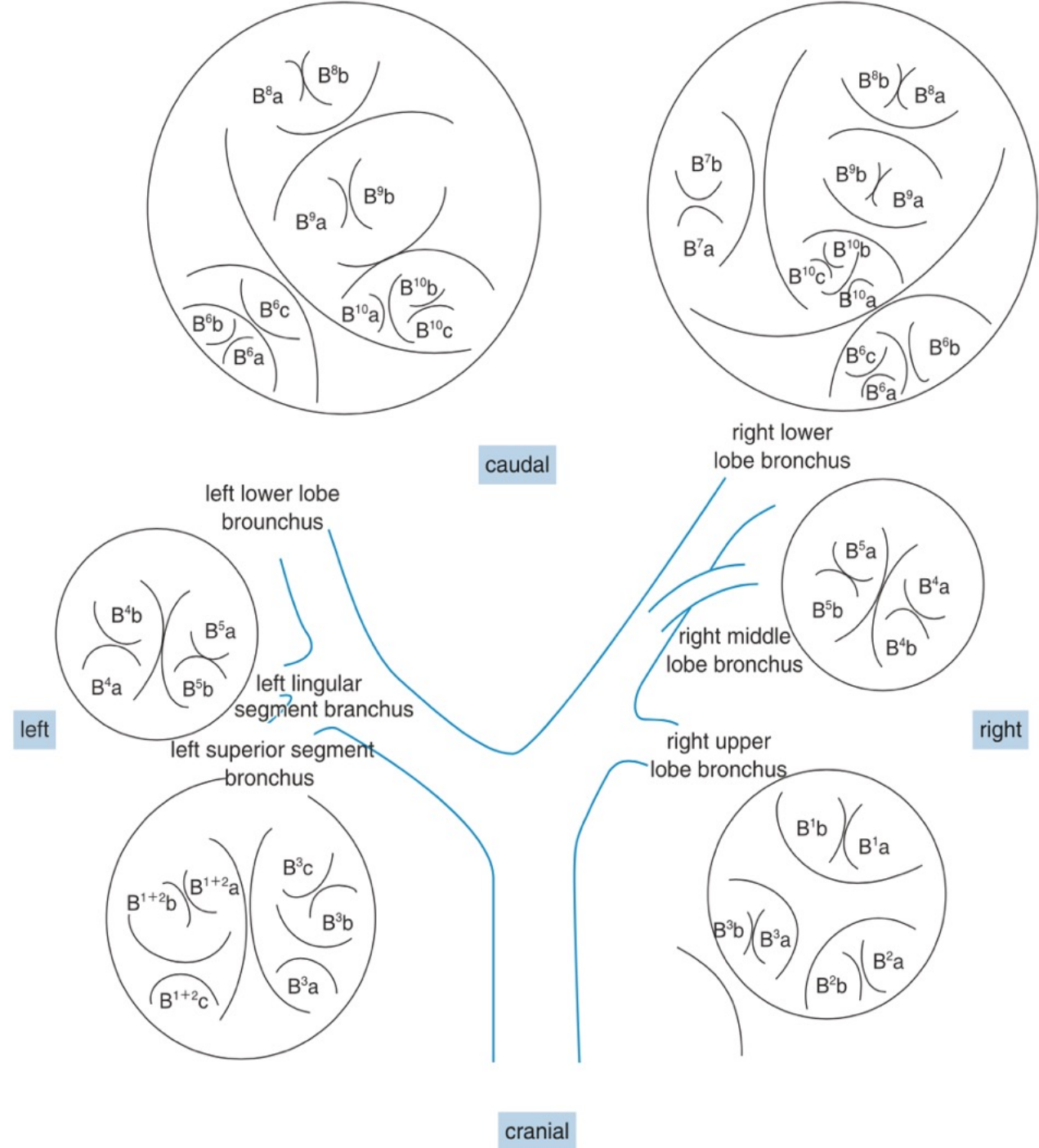
Bronkial sub-subsegment i, ii, iii - tex RB2ai

Bronkial sub-sub-subsegment α, β, γ - tex RB2aia

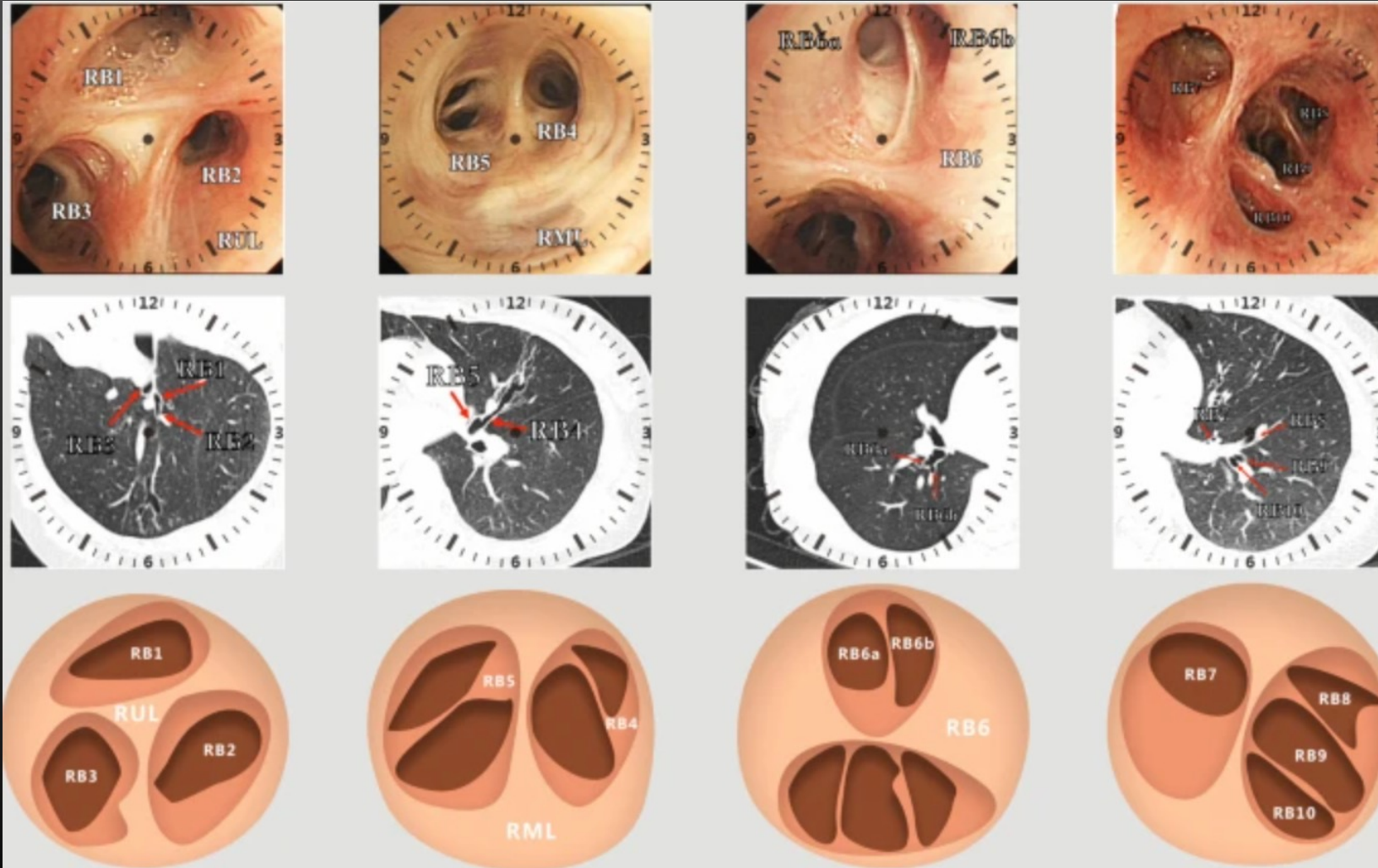
Bronkial sub-sub-subsegment x, y - tex RB2aiax

I vänster lunga clockwise

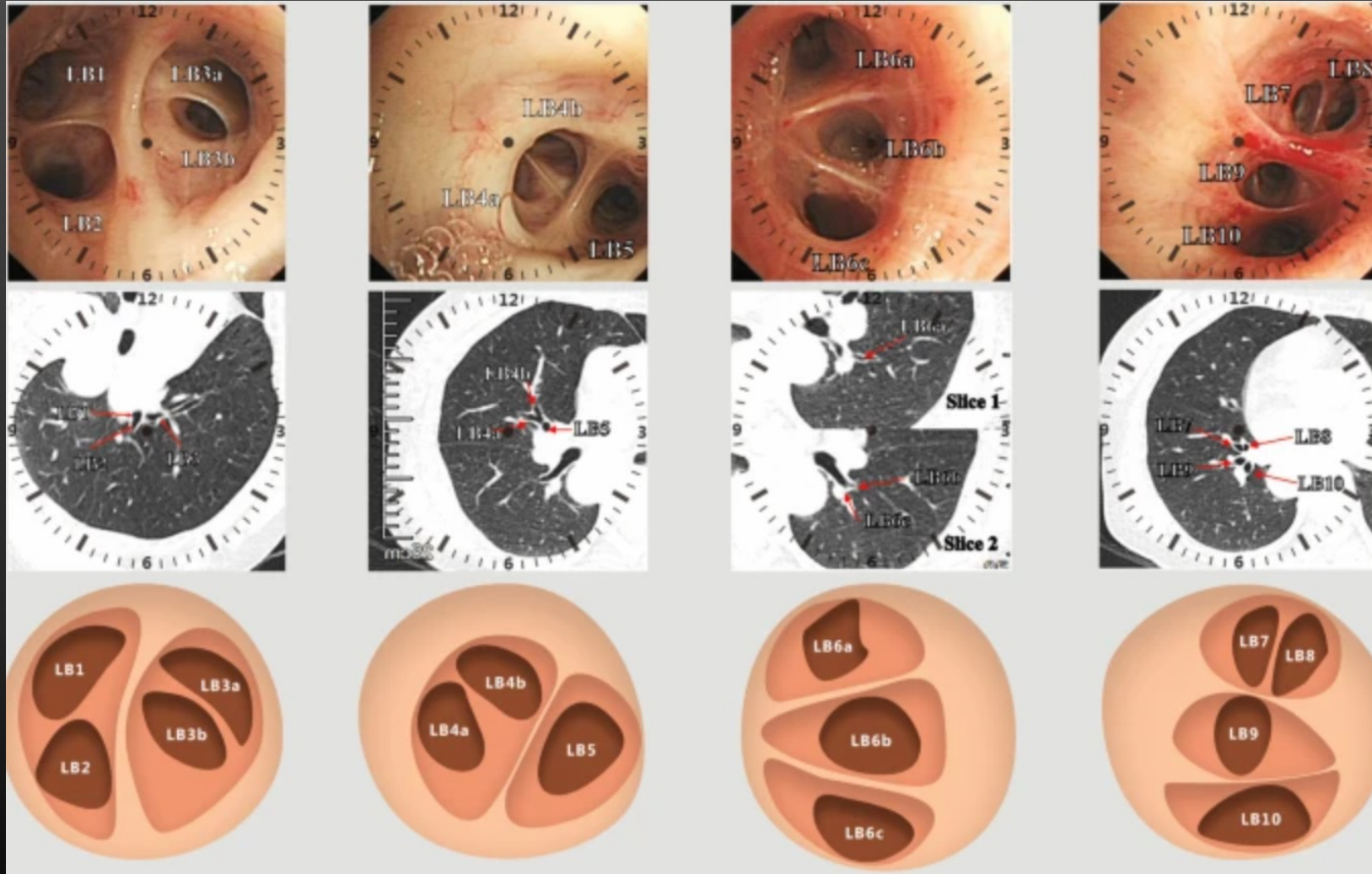
I hö lunga anticlockwise



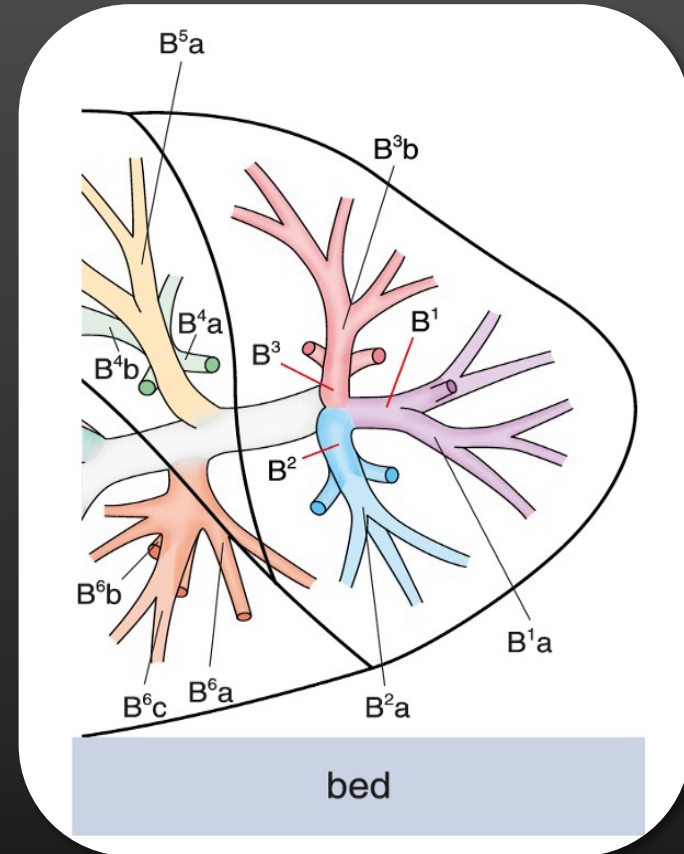
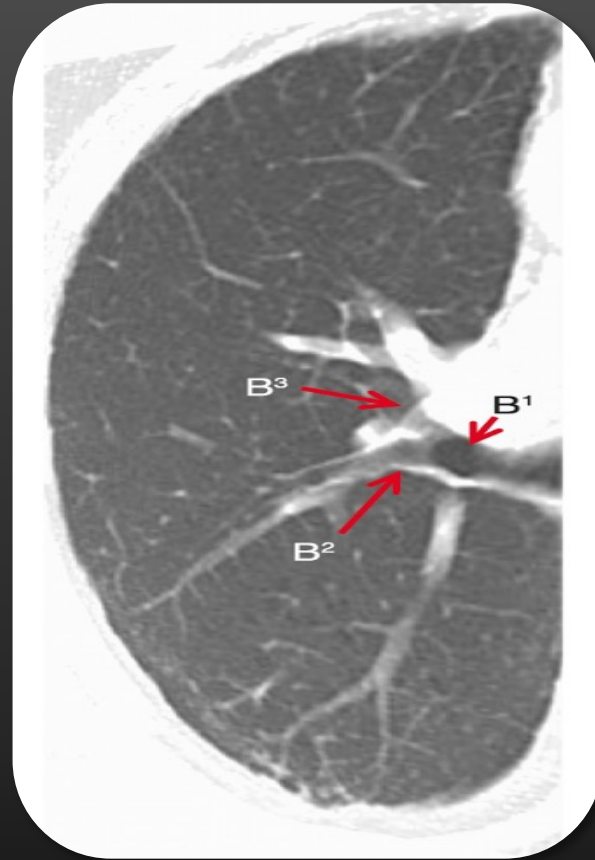
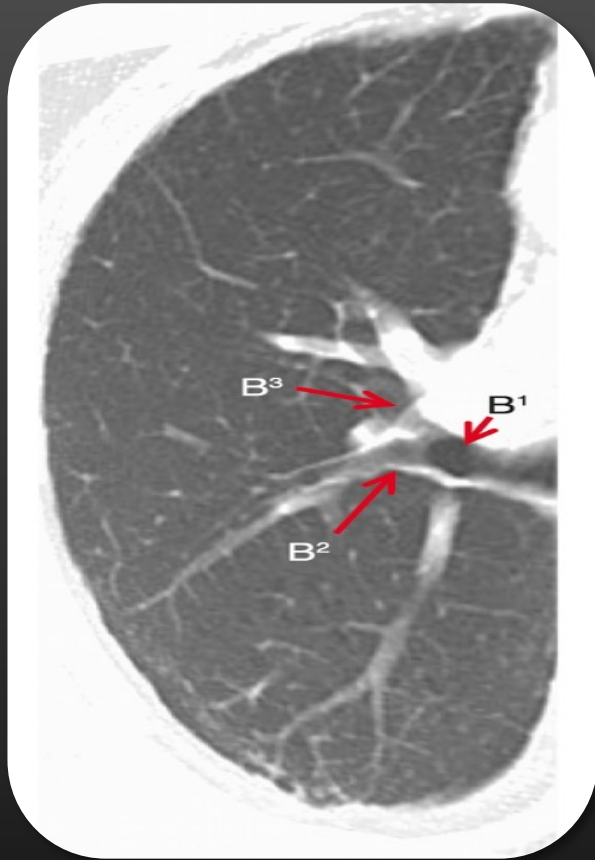
Bronchial nomenclature



Bronchial nomenclature



Bronchial branch tracing, Kurimoto, 2015



Patfall 1

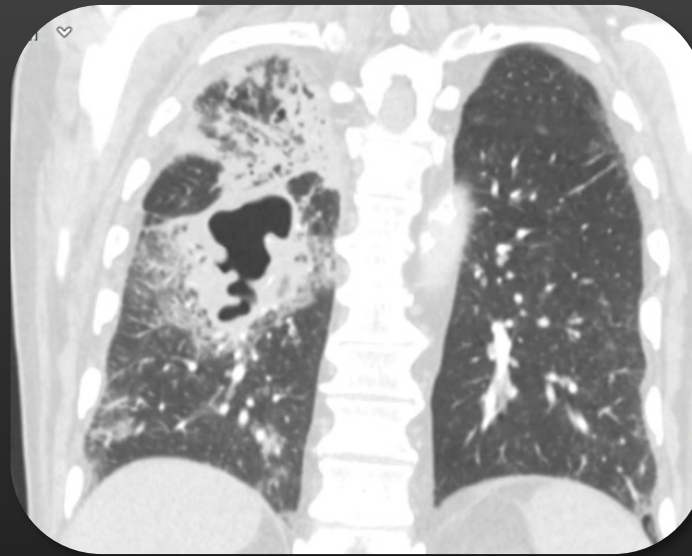
80 år, rökare

Hö kolektomi 2019 pga kolorektal ca. Recidiv i paraaortala lymfkörtlar 2022 – fick radioterapi.

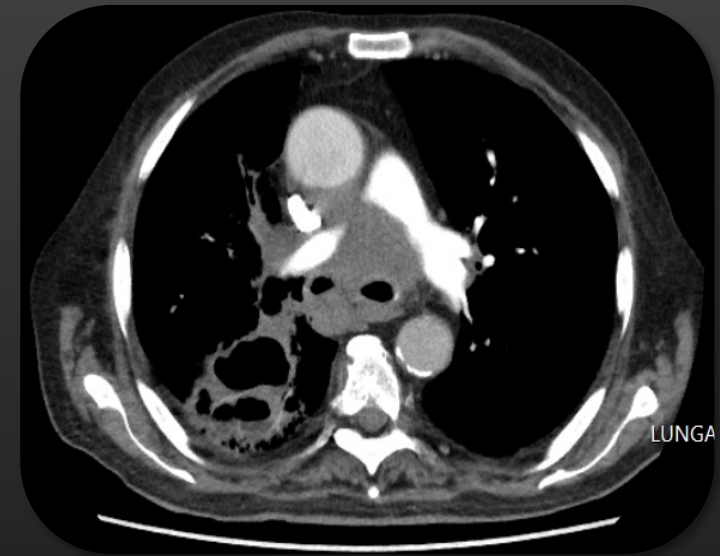
Mkt andfådd, 1L syrgas/min. Nyttillkomna bilaterala lungförändringar – recidiv av kolorektal cancer?



Vidare utredning?



Vilken typ av bronkoskopi?



Hur många biopsier?

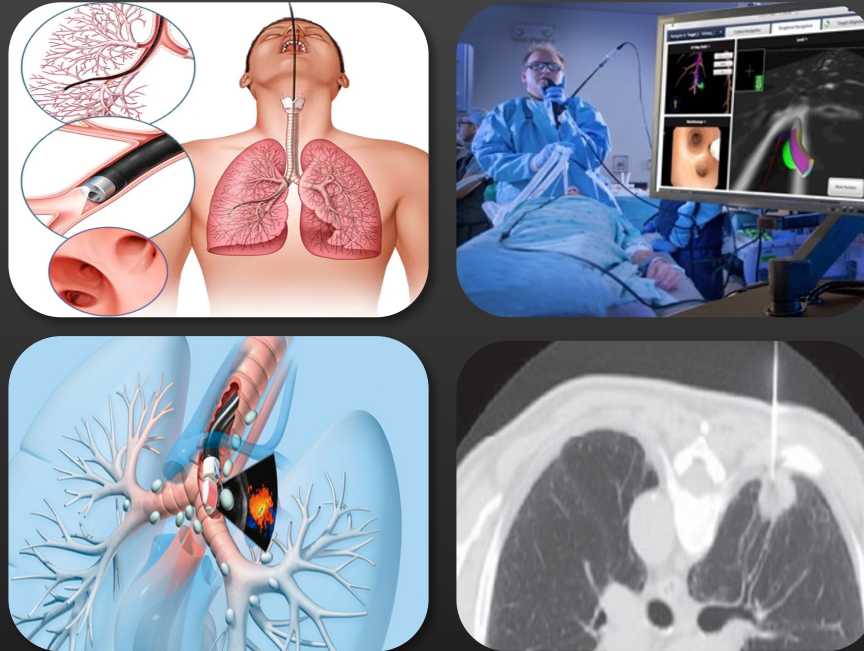
Lungcancer - utredning

Parallel diagnosis, stadiindelning och molekylär testing

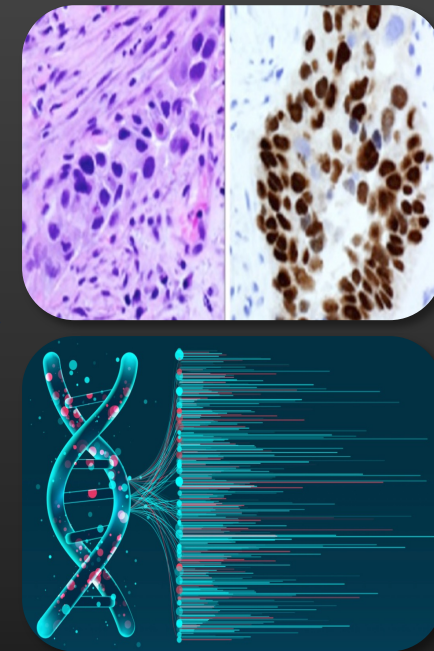
SUSPICION



INVESTIGATION



DIAGNOSIS

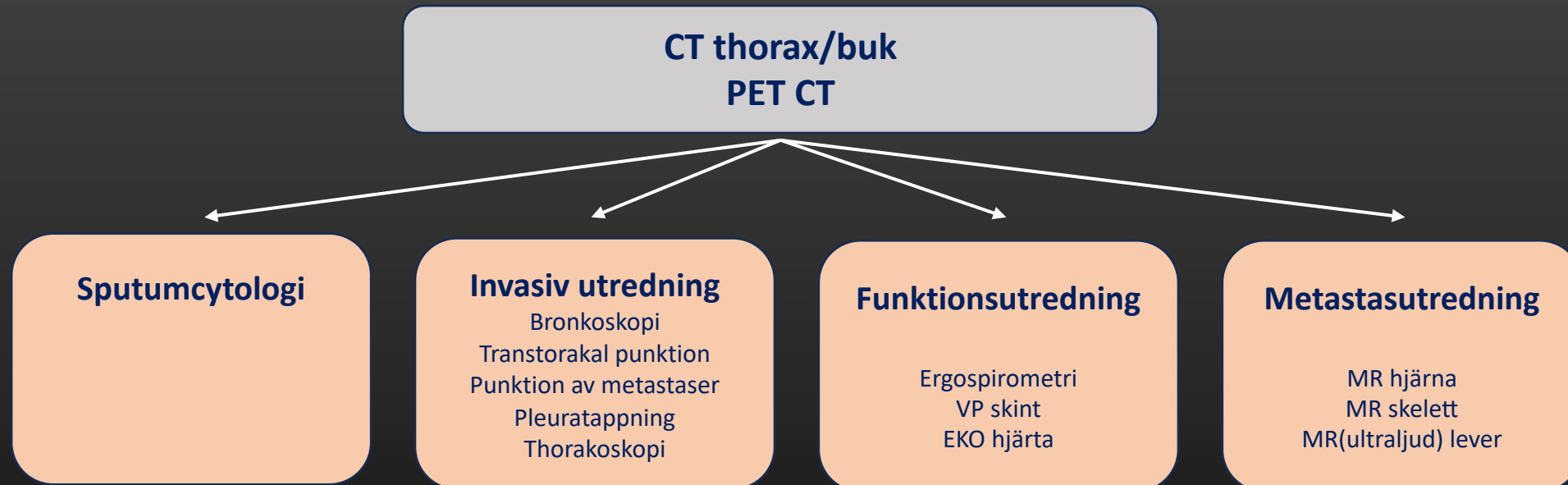


Lungcancer - utredning

Anamnes - rökning, exponering, tidigare sjukdomar, annan cancer

Status - allmäntillstånd PS (WHO), hjärt- och lungstatus, LN

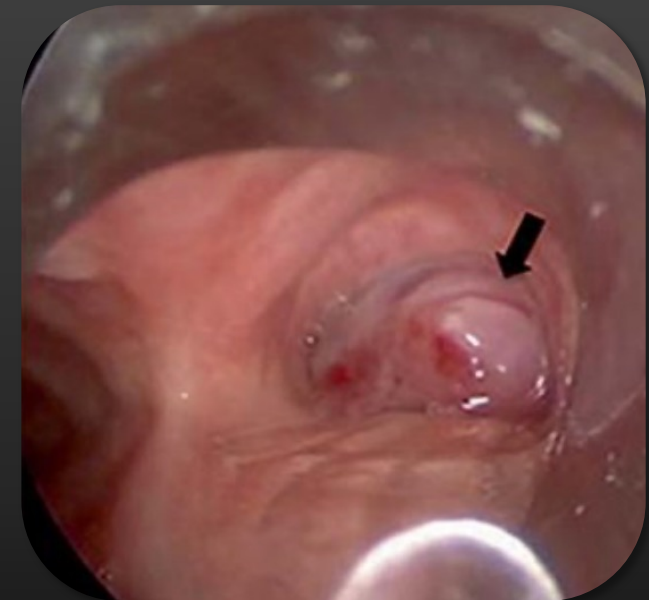
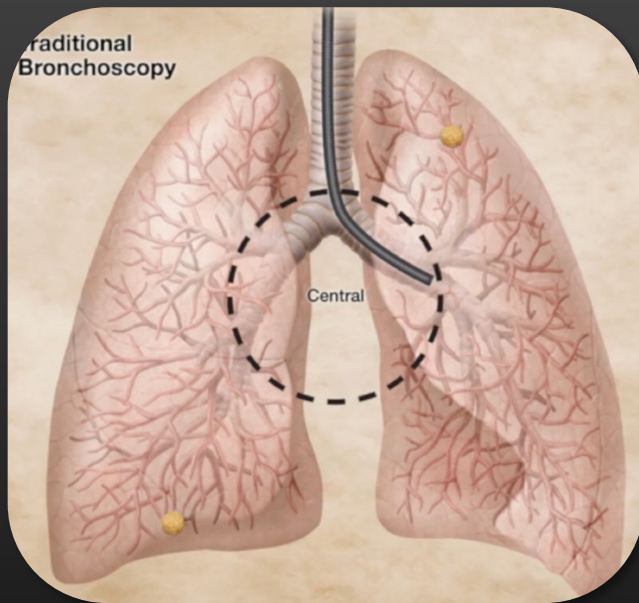
Lungfunktion - spirometri med DLCO



Konventionell bronkoskopi

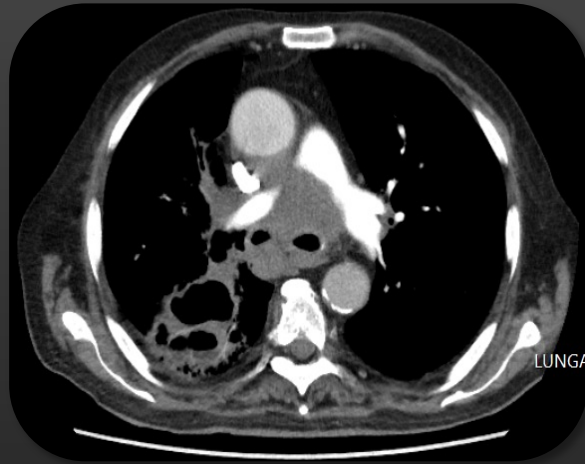
Direkt biopsiering av synliga förändringar, hög sensitivitet

Meta-analys, 35 studier mellan 1971 och 2004, sensitivitet 88%

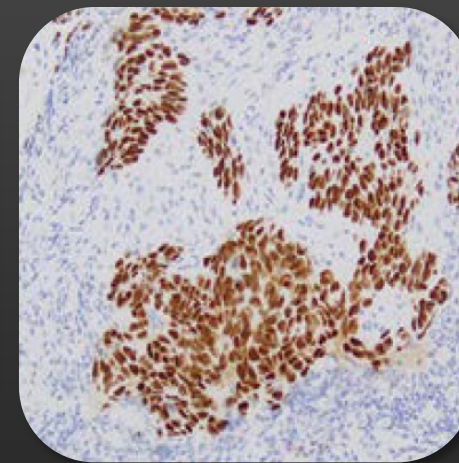
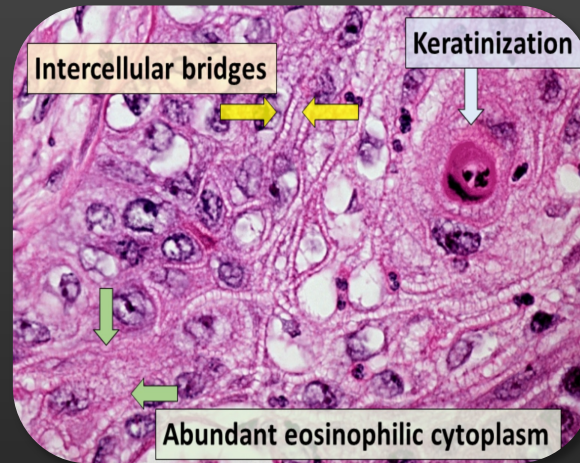


Rivera MP et al, Chest 2013 Establishing the diagnosis of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of chest physicians evidence-based clinical practice guidelines

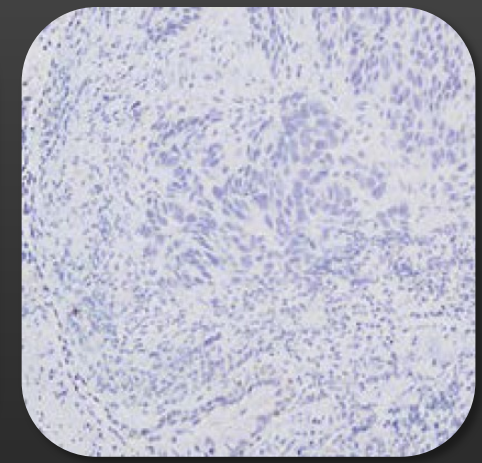
Patfall 1



SqC



p40 +



TTF1 -

Patfall 2

66 år, exrökare, KOL, hjärtsvikt, pacemaker

Icke produktiv hosta sedan dec 2020. Kompenserad. Normalt NT pro BNP

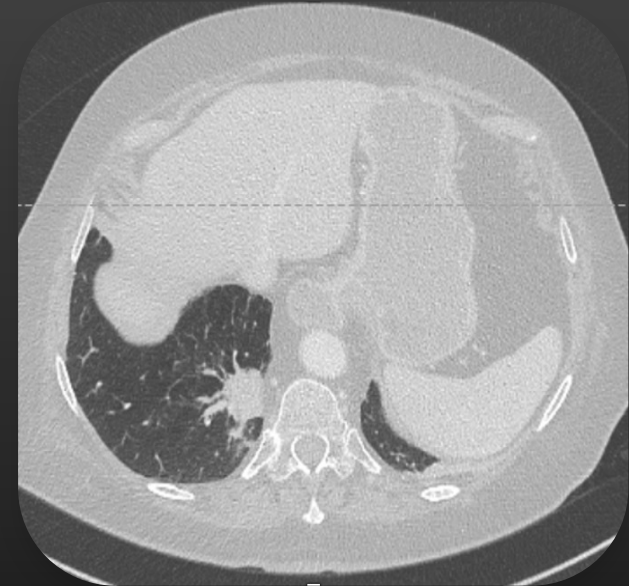
Rtg pulm feb 2021. CT thorax aug 2021



Februari 2021



Augusti 2021



Peripheral Pulmonary Lesion

Patfall 2



**Konventionell bronkoskopi
för perifera
lungförändringar -
sensitivitet för malignitet
< 20 %**

Bronkoskopi för perifera lungförändringar

| | | Generation | Diameter, cm | Length, cm | |
|------------------------------------|-------------------------|----------------|--------------|------------|------|
| conducting zone | trachea | 0 | 1.80 | 12.0 | |
| | bronchi | 1 | 1.22 | 4.8 | |
| | | 2 | 0.83 | 1.9 | |
| | | 3 | 0.56 | 0.8 | |
| | bronchioles | 4 | 0.45 | 1.3 | |
| | | 5 | 0.35 | 1.07 | |
| terminal bronchioles | | 16 | 0.06 | 0.17 | |
| transitional and respiratory zones | respiratory bronchioles | 17 | ↓ | ↓ | |
| | | 18 | ↓ | ↓ | |
| | | 19 | 0.05 | 0.10 | |
| | alveolar ducts | T ₃ | 20 | ↓ | ↓ |
| | | T ₂ | 21 | ↓ | ↓ |
| | | T ₁ | 22 | ↓ | ↓ |
| | alveolar sacs | T | 23 | 0.04 | 0.05 |

Standard bronkoskop (6mm) till 4:e bronkgenerationen (tex LB9)

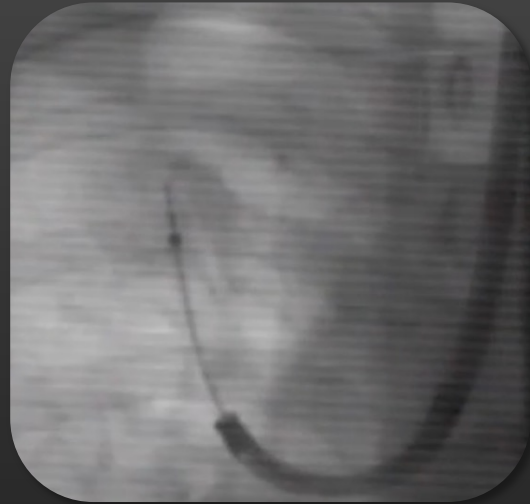


Ultratunn (3 mm) till 6:e bronkgenerationen (tex LB9aiα)

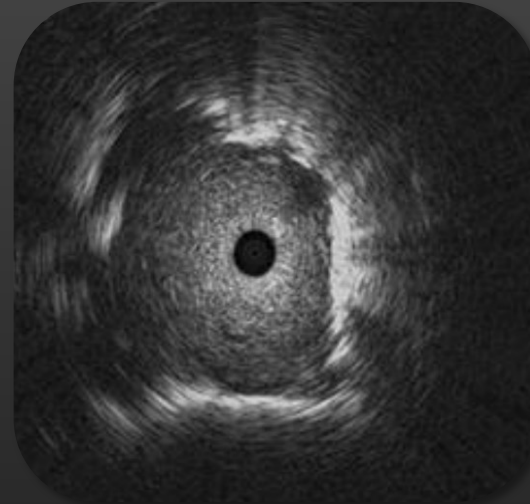
Bronkoskopi av perifera lungförändringar



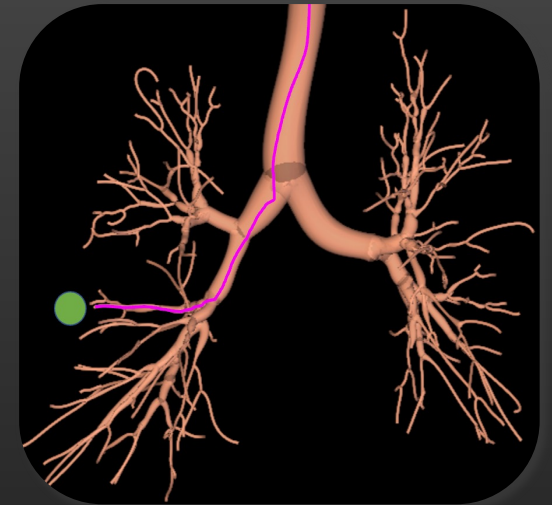
Bronchus sign?



Genomlysning



Radiellt ultraljud

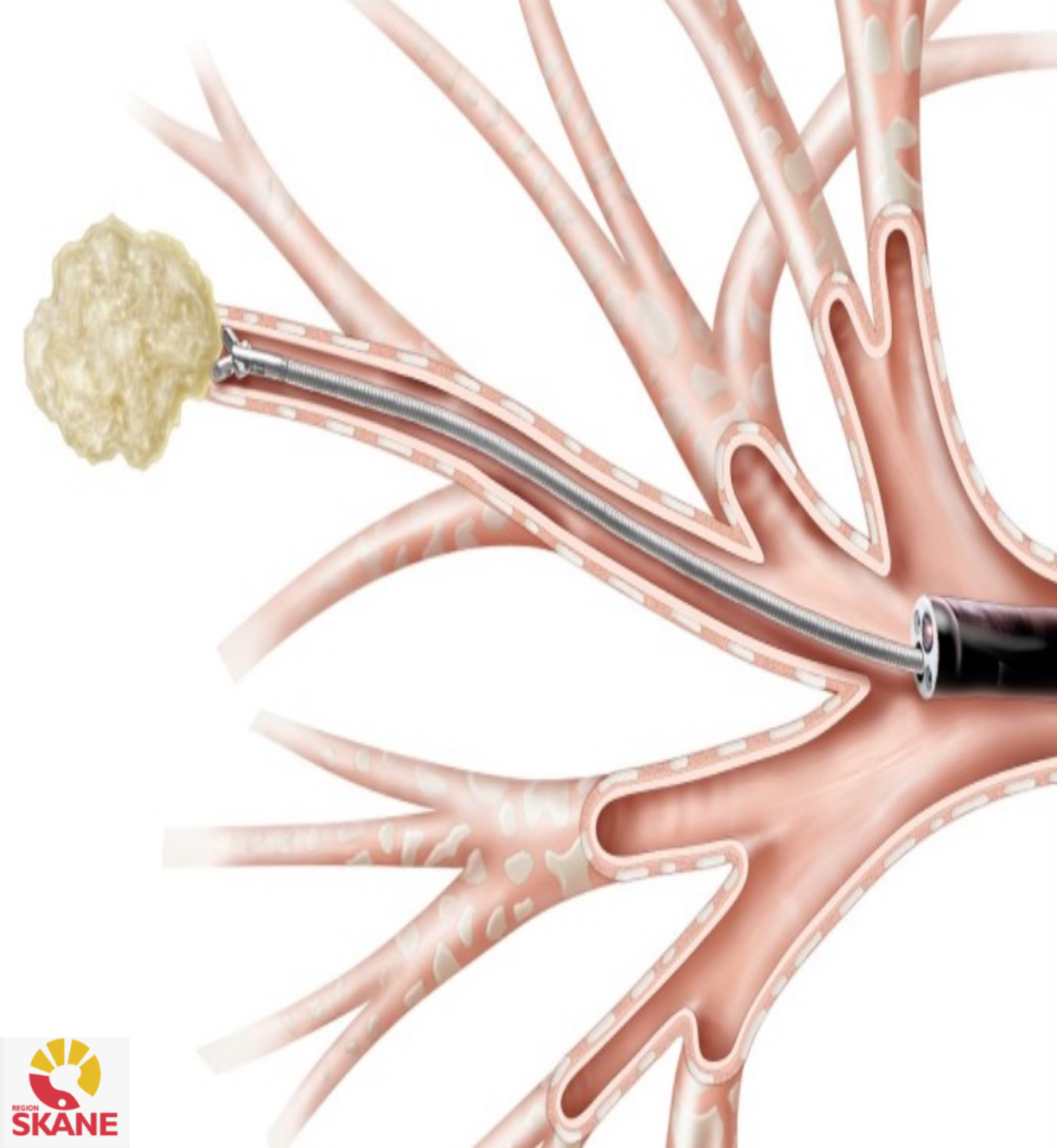


Navigationsbronkoskopi

Bronkoskopi av perifera lungförändringar

A **guide sheath catheter** with a radial **ultrasound mini probe** is inserted via the working channel of the bronchoscope into the **right subsegment** where the lesion is located





Specialbronkoskopier

Bronchoscopy with radial EBUS and fluoroscopy

EMN – electromagnetic navigational bronchoscopy

Robotic-assisted bronchoscopy

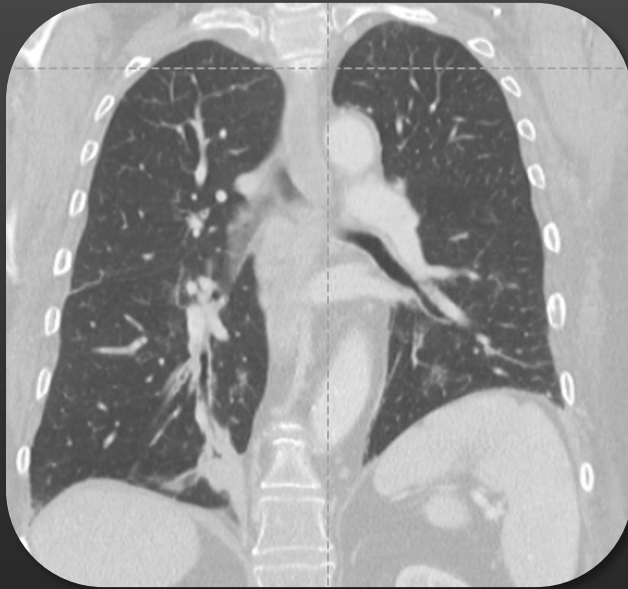
> [Chest](#). 2020 Apr;157(4):994-1011. doi: 10.1016/j.chest.2019.10.042. Epub 2019 Nov 15.

Sensitivity of Radial Endobronchial Ultrasound-Guided Bronchoscopy for Lung Cancer in Patients With Peripheral Pulmonary Lesions: An Updated Meta-analysis

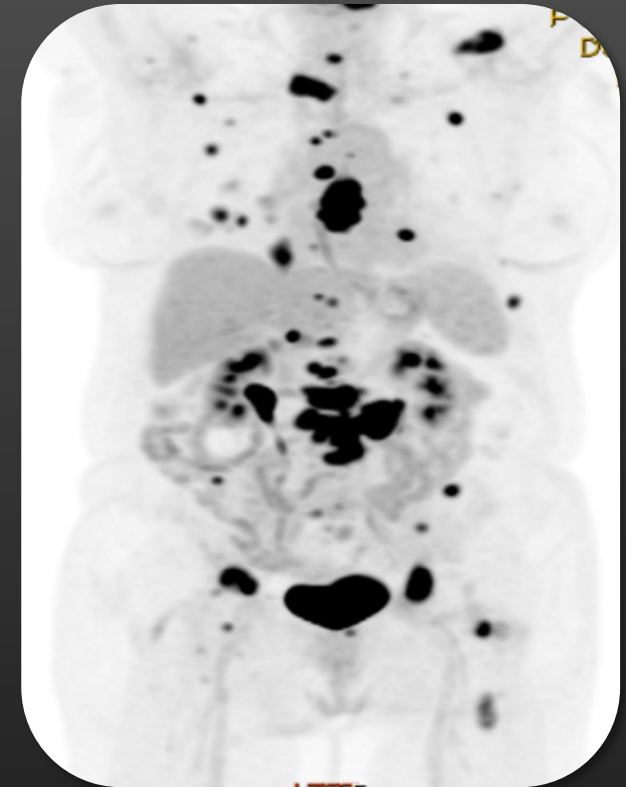
Paula V Sainz Zuñiga ¹, Erik Vakil ², Sofia Molina ¹, Roland L Bassett Jr ³, David E Ost ⁴

- 51 study, total of 7601 pat
- Pooled radial EBUS sensitivity of 0,72 (95% CI, 0,70-0,75)
- Failed to demonstrate an association between **sensitivity** and **air bronchus sign**, **average nodule size**, **use of guide sheet**, use of fluoroscopy, virtual bronchoscopy.
- **ROSE** was associated with increased sensitivity (p 0.01)
- Pooled **pneumothorax** rate 0,7% - excellent safety profile
- Significant between-study heterogeneity

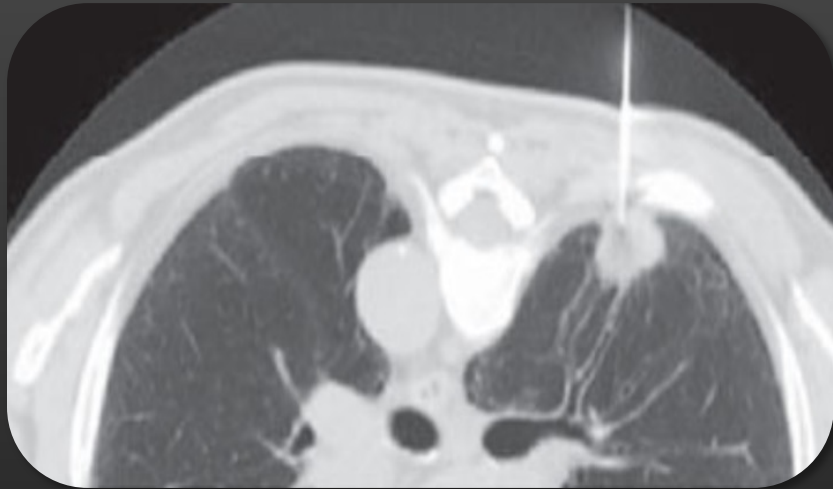
Patfall 2



Vad är nästa steget i utredningen?



Transtorakal punktion

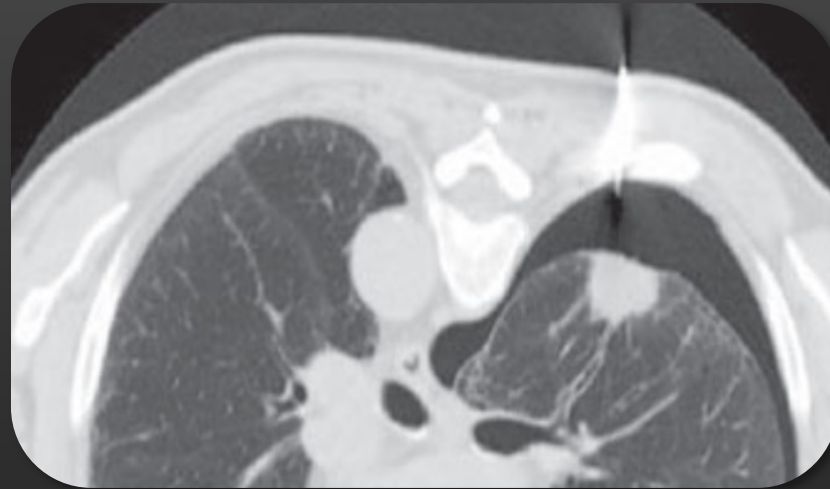


Komplikationer from transtorakal lungbiopsi

Pneumothorax hos 11%

Hemoptys 2%

Hematom 1%



Kontraindikationer - Inga absoluta!

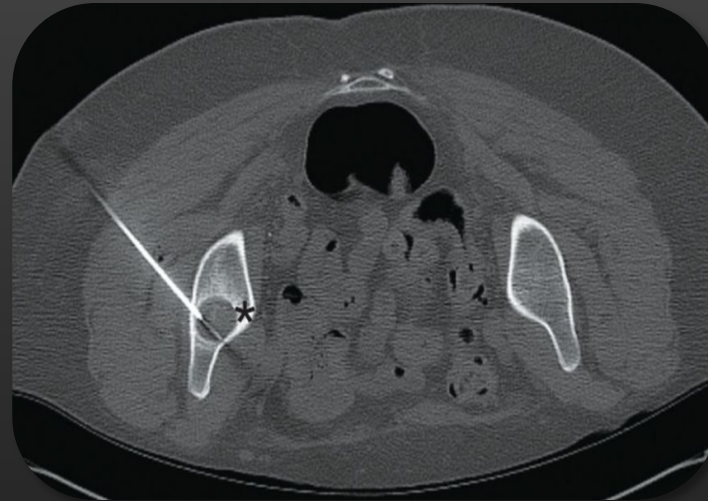
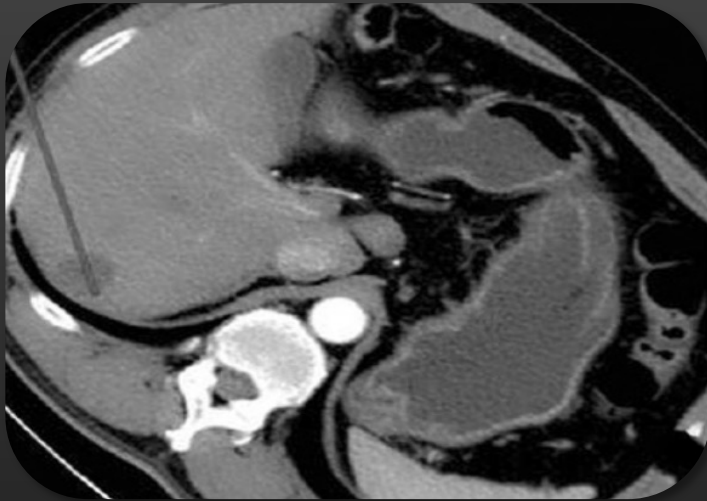
Kan ej ligga stilla eller samarbeta med operatören

Emfysem och låg FEV 1 hos KOL patienter

Trombocytopeni och antikoagulantia

Lungcancer - diagnostik

Biopsi from annat organ: lever, binjure, skelett, hudmetastas, ytlig lymfkörtel



Practice Guideline > Chest. 2013 May;143(5 Suppl):e142S-e165S.

doi: 10.1378/chest.12-2353.

Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines

M Patricia Rivera ¹, Atul C Mehta ², Momen M Wahidi ³

Låg sensitivitet för PPL < 2 cm

TTNA har mkt bra sensitivitet för malignitet (pooled sensitivity 90%) med högre risk för pneumothorax

R-EBUS and EMN ökar dg utbytet vid PPL

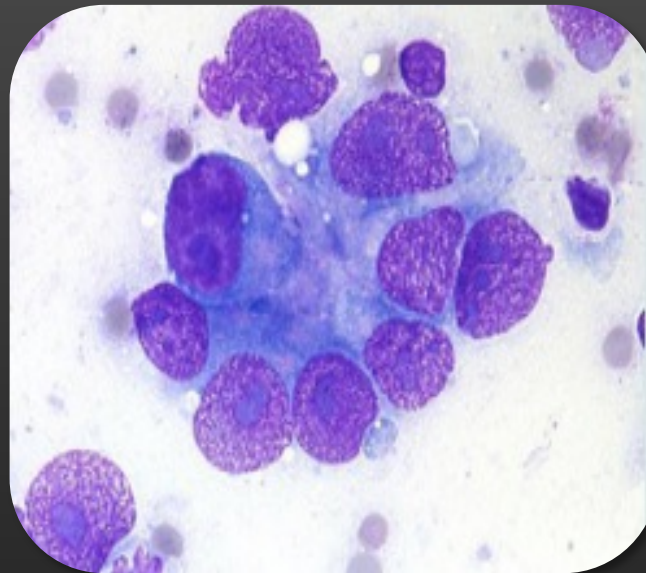
Torakoskopisk pleurabiopsi bäst för diagnos av metastaserande pleurautgjutning

Adekvat vävnadsprovtagning för histologisk och molekylär karakterisering av lungcancer är av största vikt

Patfall 2



Specialbronkoskopi med MP, GL



TTF-1+, CK7+, Napsin A+

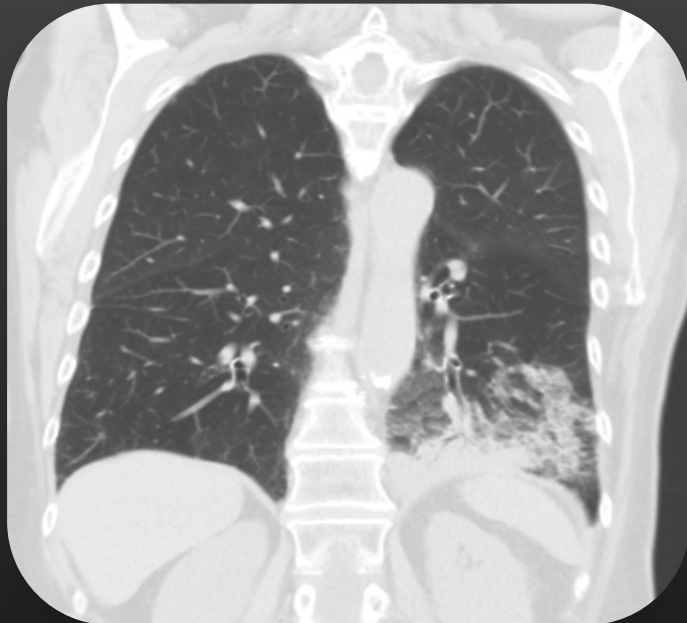
LUAD

Patfall 3

76 år, exrökare. KOL, PMR, kortison. Följs på lungmottagningen pga 'oklar förändring i vä underlob'

Sista 3 månader ökad produktiv hosta.

Vidare handläggning?



Januari 2021



Juli 2021

Januari 2021

Juli 2021

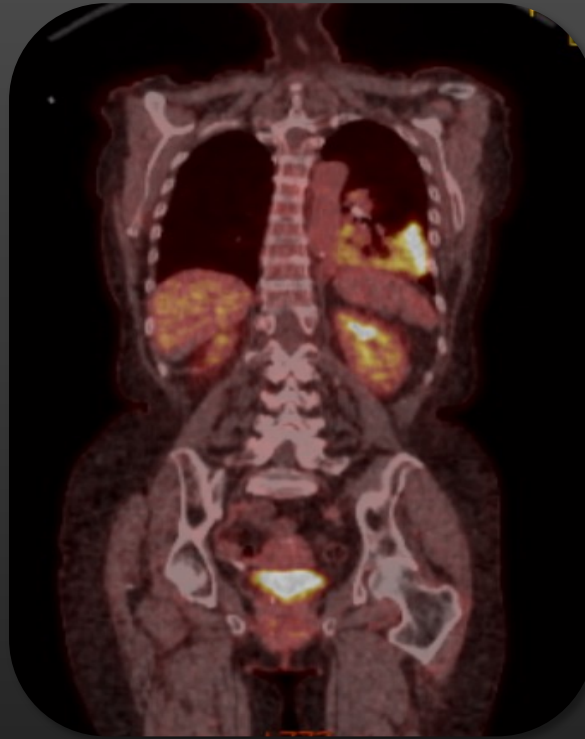
Patfall 3

PET CT juli 2021

Vilken typ av invasiv undersökning?

Bronkoskopi med kryobiopsering

PAD: Mucinöst adenocarcinom



Bronkoskopi med kryoprob

Joule –Thompson effekt

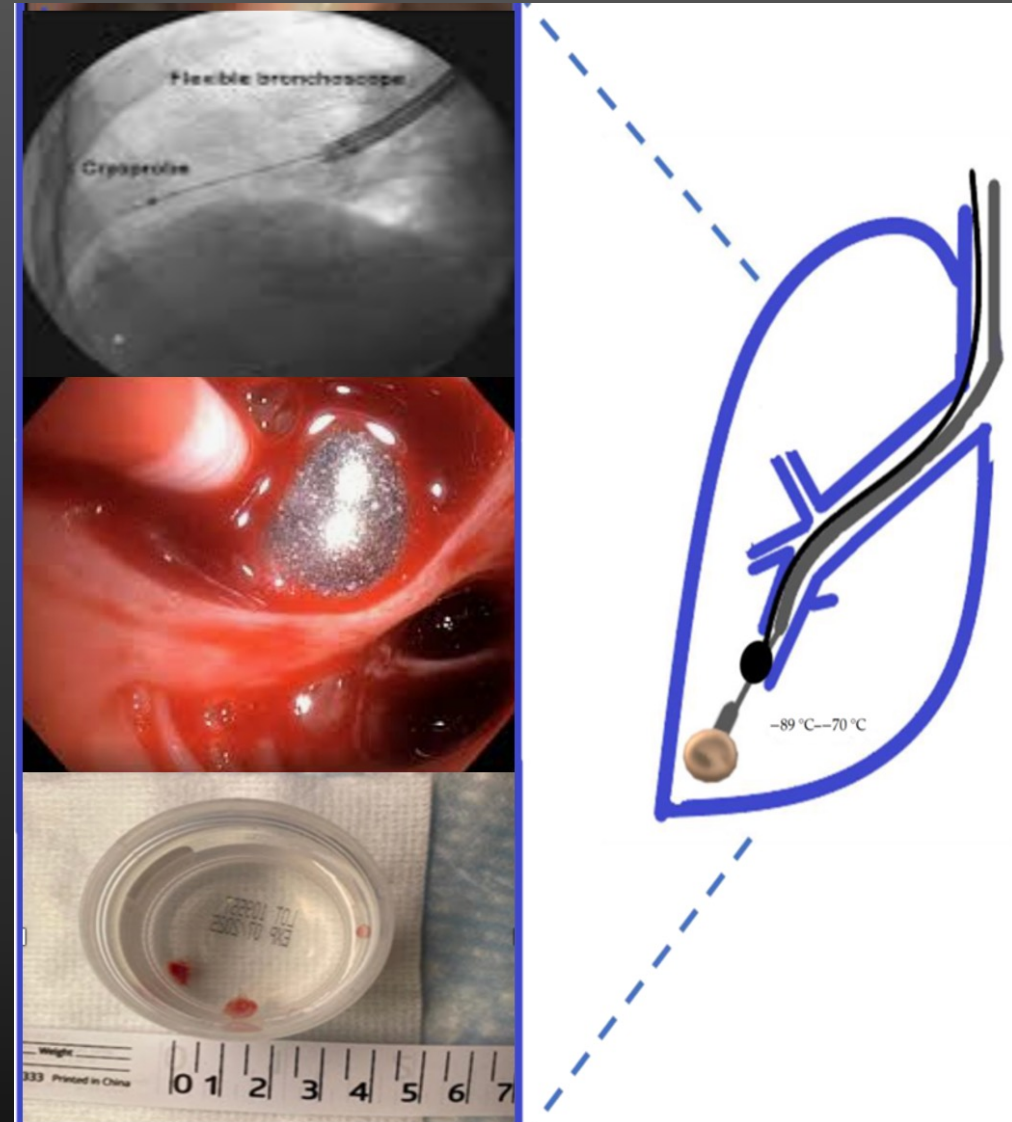
høgt fløde av komprimerad gas (CO_2 , N_2O) i proben
expanderar snabbt och sänker temp till $-89\text{ }^\circ\text{C}$

Kryogen – CO_2

Kryoprob: 1.1mm, 1.7mm, 2.4mm

Syfte:

- transbronkiella kryobiopsier (lungtransplanterade)
- interstitiell lungsjukdom - diagnostik
- biopsiering av misstänkt tumör (i sbd med EMN, MP och GL)
- EBUS-TBMCB
- rekanalisering av centrala luftvägar med rigid bronkoskop



Patfall 4

61 år, rökare 25 pktår. Frisk sedan tidigare. Mor dog i lymfom 65 år gammal.
Snabbt tilltagande andfåddhet, rtg i hemlandet



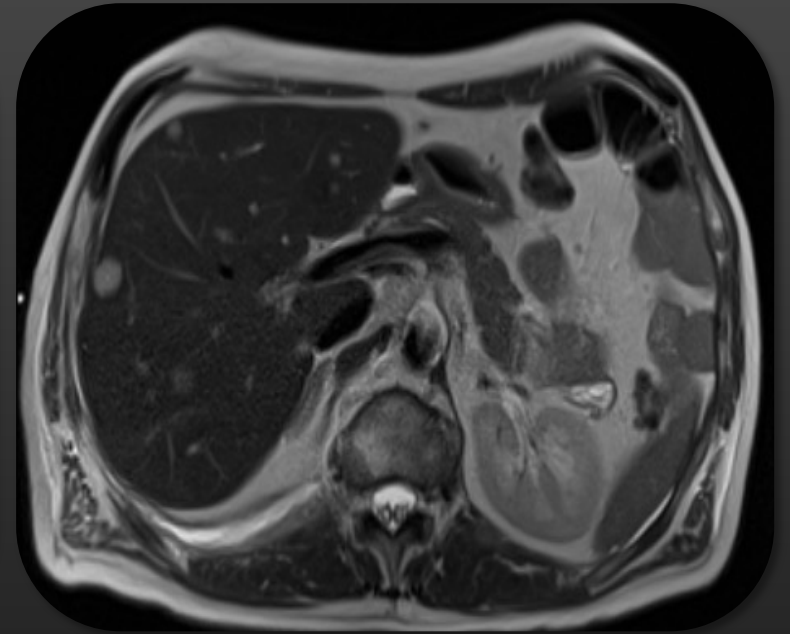
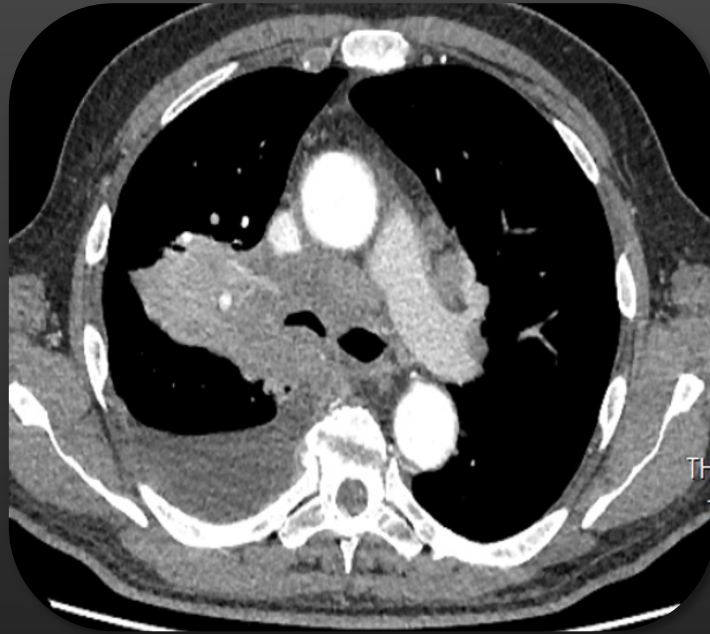
Flyger till Sverige och söker akuten - CT thorax

Vad göra? Tappning eller dränage?

Pleuradränage – inlagd på Lung avd 3 – Malmö

Pleuravätska – sparsamt med maligna celler , otillräckligt för dg

Patfall 4



CT thorax efter dränage. MR lever - metastaser
Pleurodes?
Vävnadsprovtagning?

Bronchoscopy med EBUS-TBNA

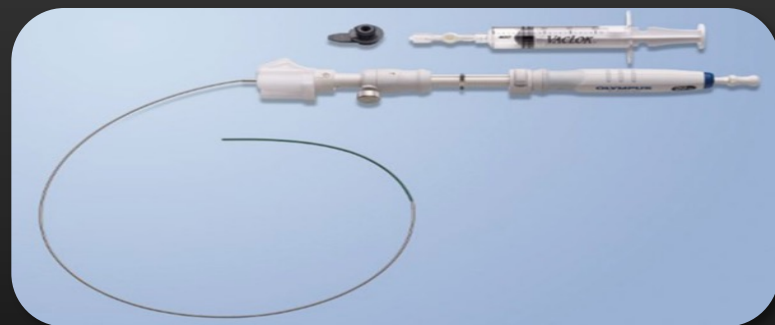
EndoBronchial UltraSound guided - TransBronchial Needle Aspiration



Att se runt hörn och gå igenom väggar

You can use a stick!

But there's more hope with an EBUS bronchoscope!



Convex transducer
5–12 MHz
(vanligtvis 7 MHz)
Arbetskanal 2.0 mm

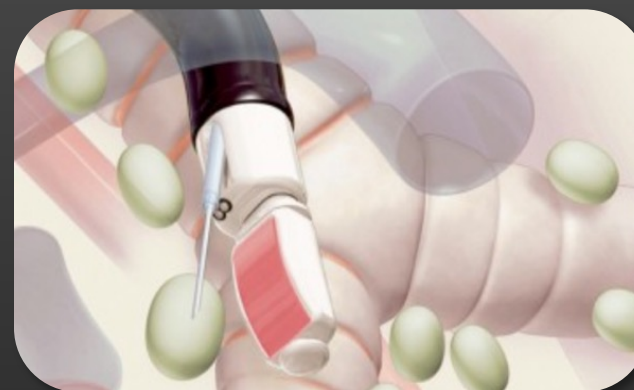
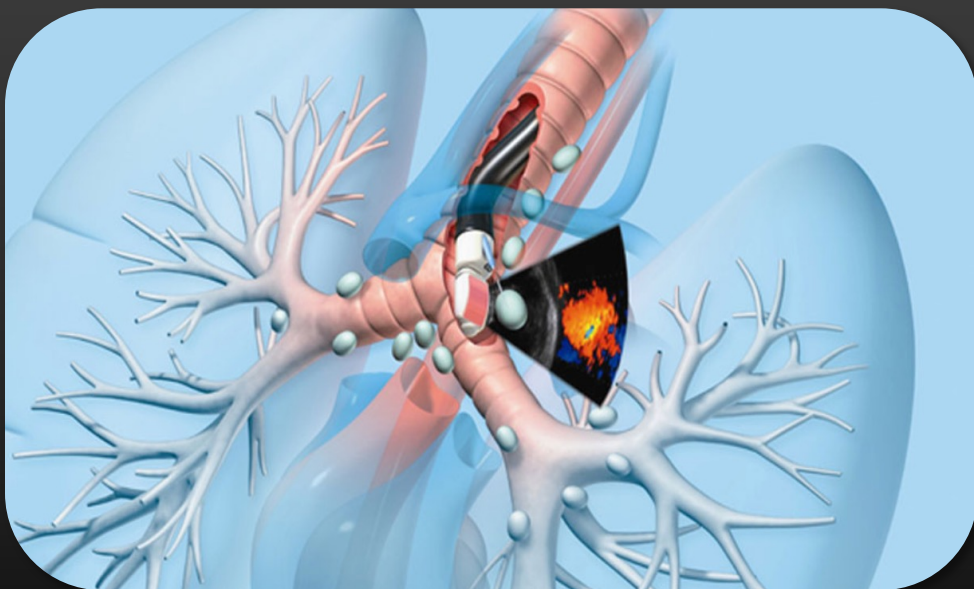
TBNA nålar 19G, 21G, 22G, 25G

Indikationer för EBUS-TBNA

Diagnos av centrala intratorakala expansiviteter

Oklar mediastinal lymfadenopati: benignt? malignt?

Minimalt invasiv nodal staging vid lungcancer



Typer av EBUS-TBNA

1. **Staging EBUS** – nodal staging av lungcancer
2. **Diagnostisk EBUS** – hilära och medoiastinala lymfkörtlar samt expansiviteter nära centrala luftvägar

Diagnostisk EBUS-TBNA

Diagnostisk EBUS-TBMCB (kryo EBUS)

Dooms C et al Revised **ESTS** guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J Cardiothorac Surg. 2014

Silvestri et al. Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines (**ACCP**) Chest. 2013

Ettinger et al. **NCCN** Clinical Practice Guidelines in Oncology (NCCN Guidelines). Non-small cell lung cancer. Version 3. 2017

Maribel Botana-Rial et al. A systematic review: Is the diagnostic yield of mediastinal lymph node cryobiopsy (cryoEBUS) better for diagnosing mediastinal node involvement compared to endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)? Resp Med 2023

EBUS-TBNA - proceduren

Icke-invasiv och patientsäker metod

Poliklinisk procedur, lokalbedövning i svalget + Alfentanyl iv \pm Rmimazolam iv

Först inspektionsbronkoskopi

Sedan EBUS bronkoskop transoralt

Via larynxmask / rakbronkoskop vid generell anestesi

Vid dg EBUS punkteras förstorade och hypermetabola LN eller expansivitet

Vid staging EBUS provtagningsordning N3 \rightarrow N2 \rightarrow N1

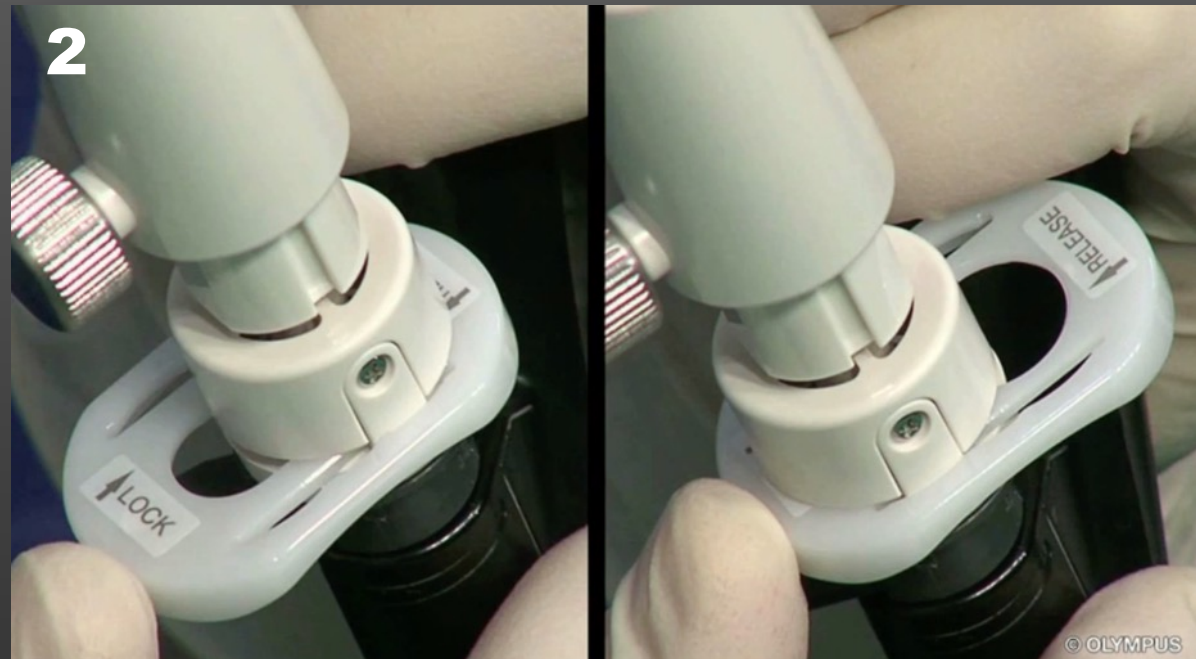
Rapid On Site Examination, preliminär cytologi

Kontraindikationer: som vid konventionell bronkoskopi

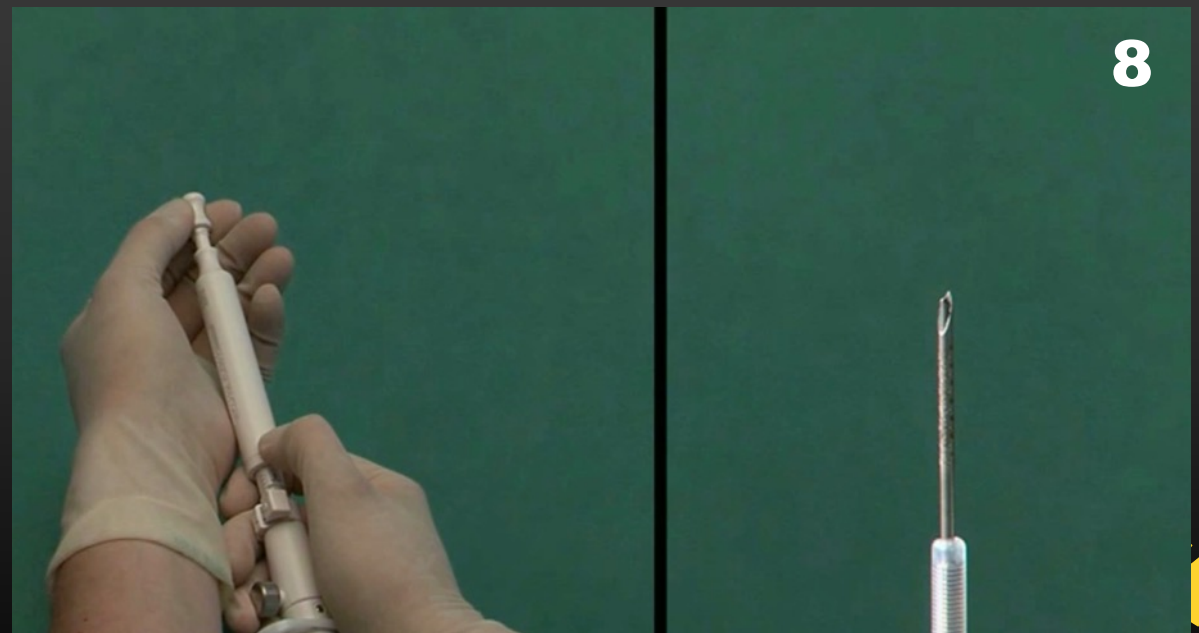
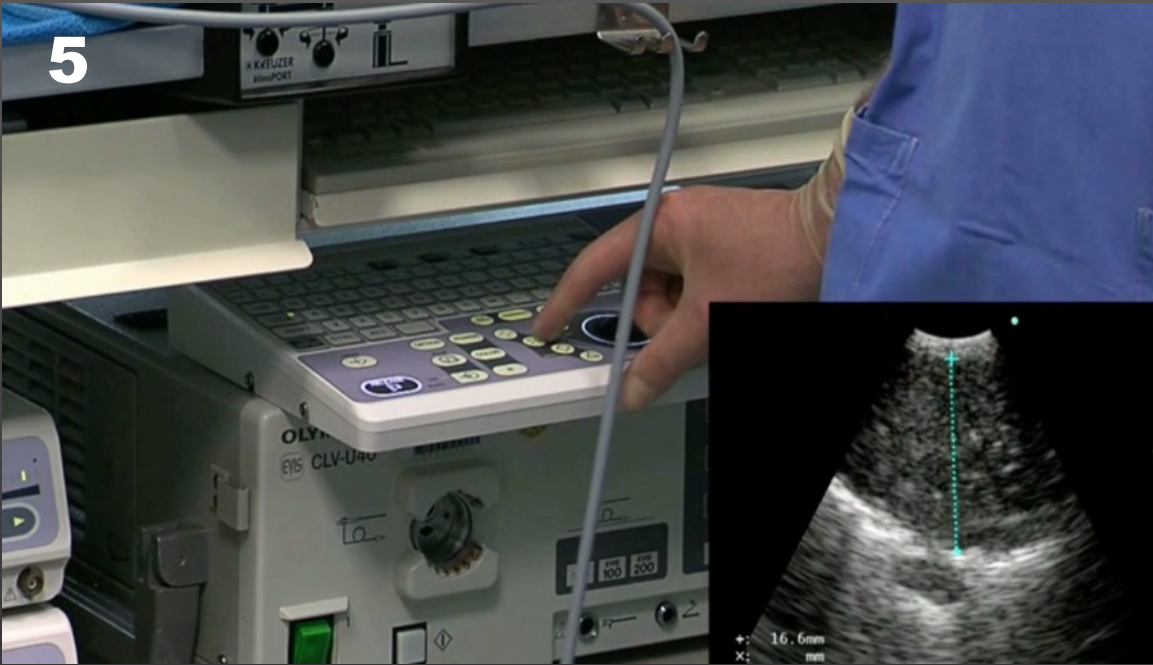
Komplikationer: blödning, pneumothorax, mediastinit



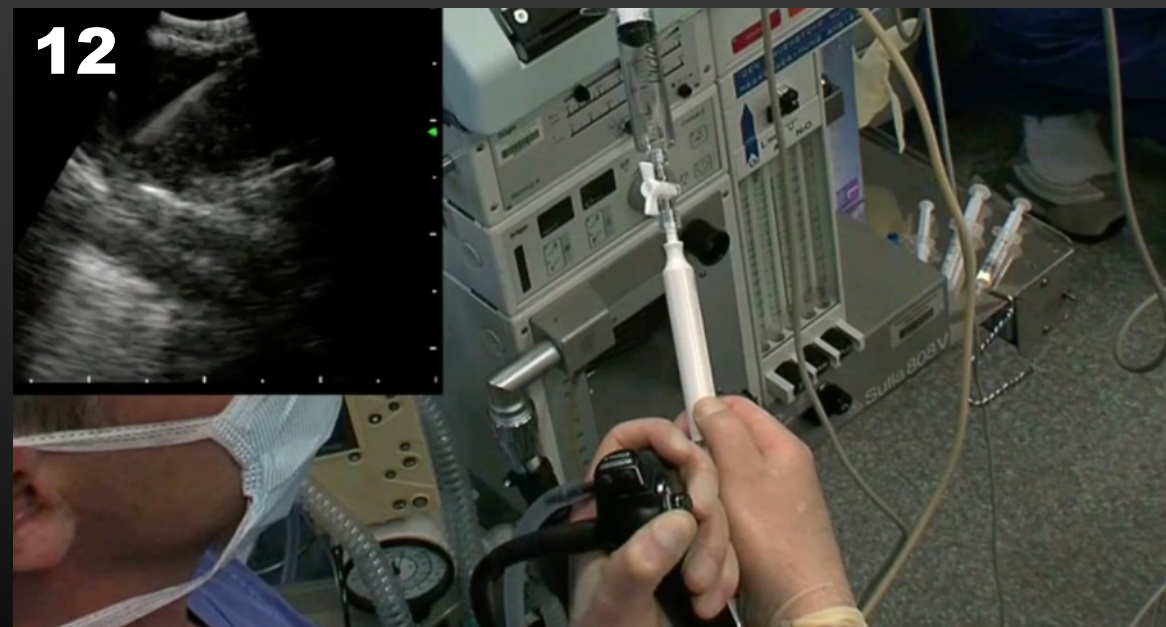
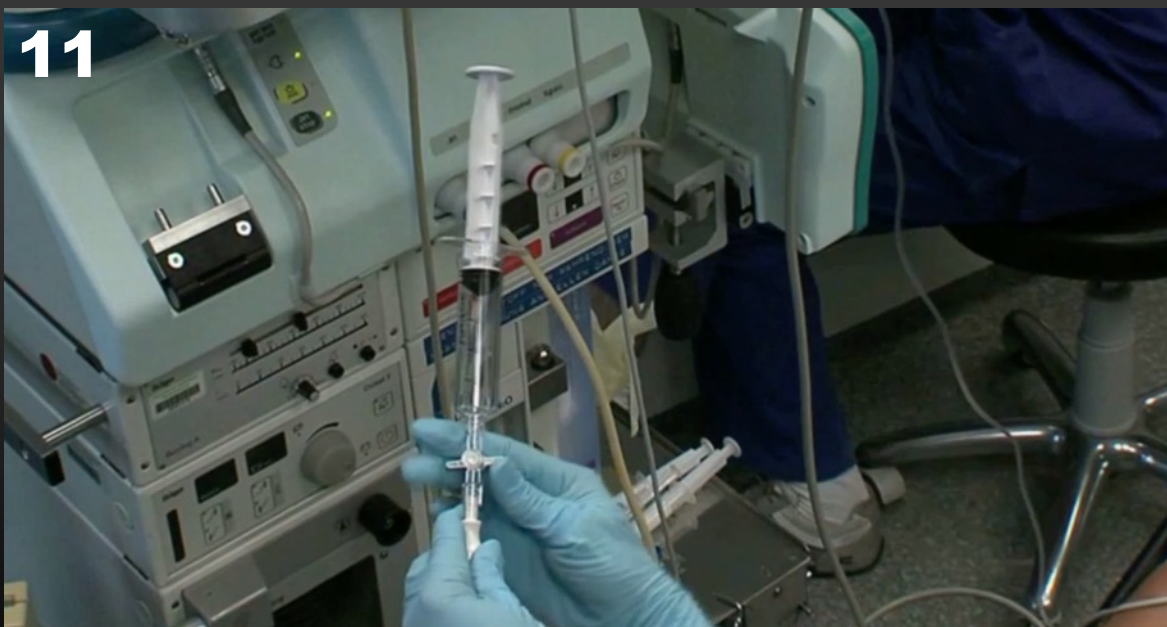
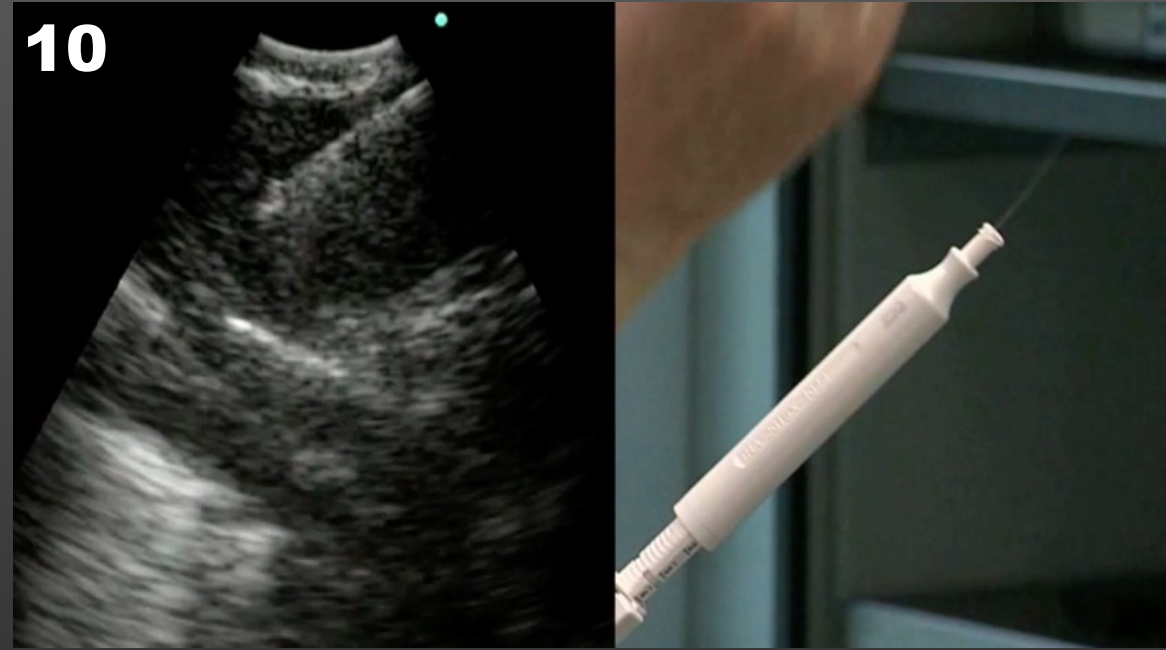
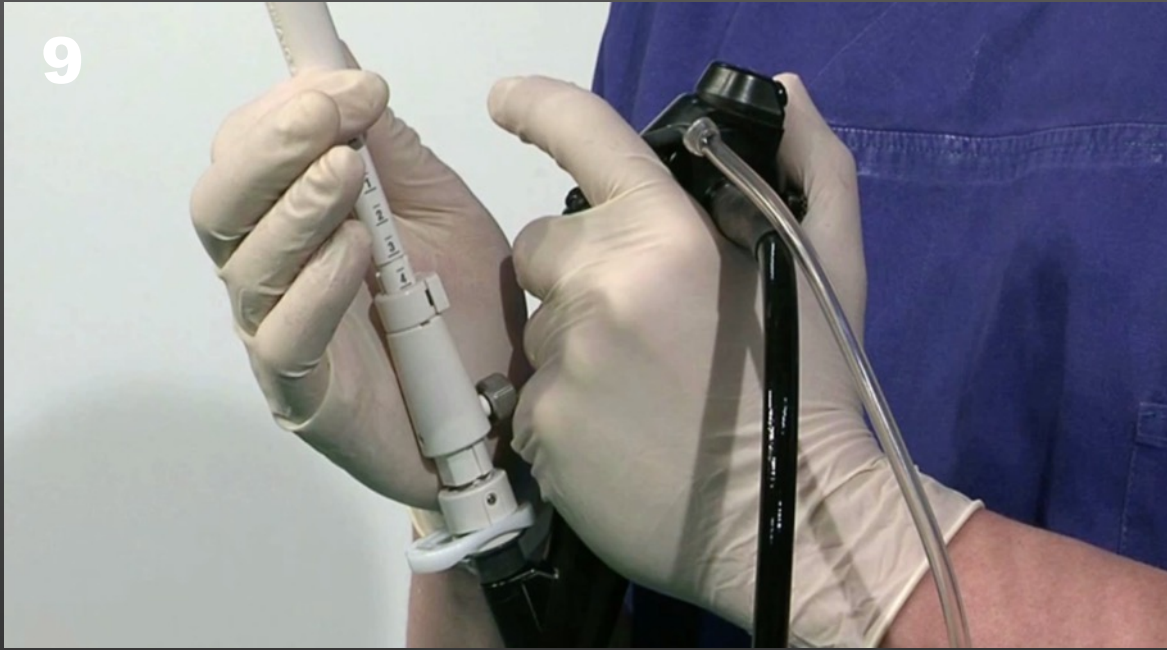
EBUS-TBNA – step by step



EBUS-TBNA – step by step



EBUS-TBNA – step by step



EBUS / EUS-B-FNA träning

- Structured, evidenced-based training programmes
- ERS course EBUS TBNA
- Part 1 – Theory
- Part 2 – Clinical and simulations training
- Part 3 - Supervised training
- The Essential EBUS Bronchoscopist
<https://www.bronchoscopy.org/downloads/The%20Essential%20EBUS%20Bronchoscopist%20eBook.pdf>
- EBUS assessment tool (EBUSAT) <https://www.bronchoscopy.org/downloads/BEP%20EBUS%20assessment%20tools.pdf>

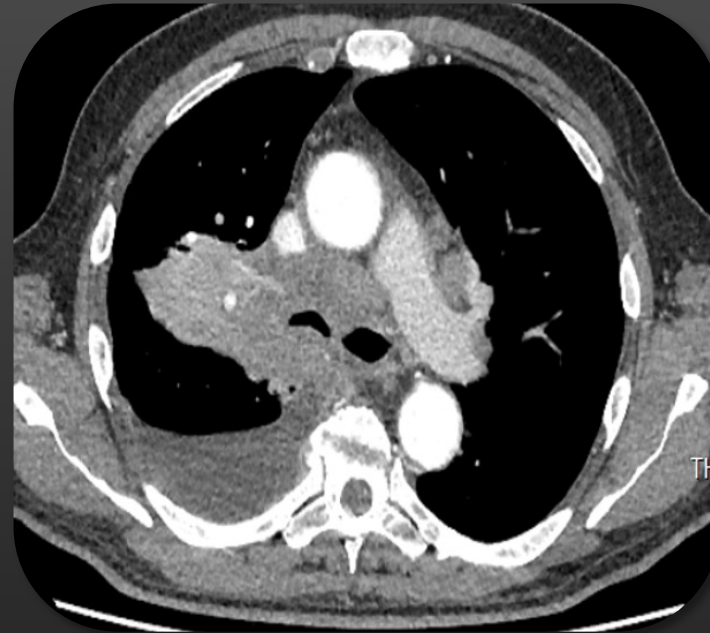
Diagnostisk EBUS

Hög träffsäkerhet - diagnos i 89%-98%

Molekulär profilering av lungcancer

Komplikationer:

- Mediastinit 0,2%, blödning 0,2%, pneumothorax 0,5%
- Fatal blödning 1 case report
- Övriga: pneumoni, perikardit, sepsis, hypoksi
- Needle breakage 4 case report, samtliga pat hostat upp nålen



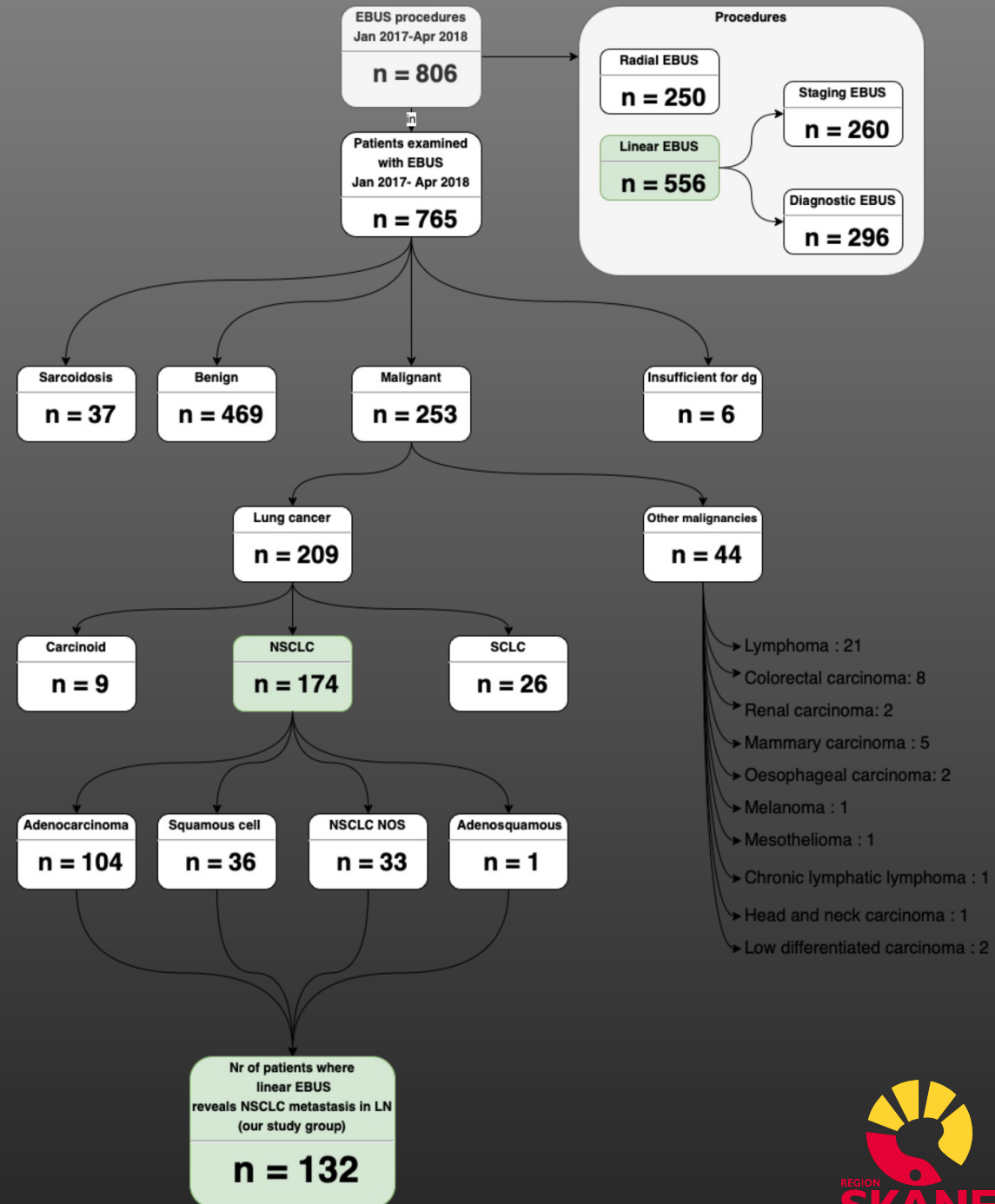
Vaidya et al. Endobronchial ultrasound-guided transbronchial needle aspiration: Risks and repairs. *Respirology* 2017 "The cumulative number of clinical complications reported in these large studies were 26 of 1235 (1.02%) procedures"

Feasibility of EBUS-TBNA for histopathological and molecular diagnostics of NSCLC—A retrospective single-center experience

Marija Karadzovska-Kotevska, Hans Brunnström, Jaroslaw Kosieradzki, Lars Ek, Christel Estberg, Johan Staaf, Stefan Barath, Maria Planck

Published: February 2, 2022 • <https://doi.org/10.1371/journal.pone.0263342>

Retrospective review of 765 patients' records of all patients examined with EBUS bronchoscopy between January 2017 and April 2018



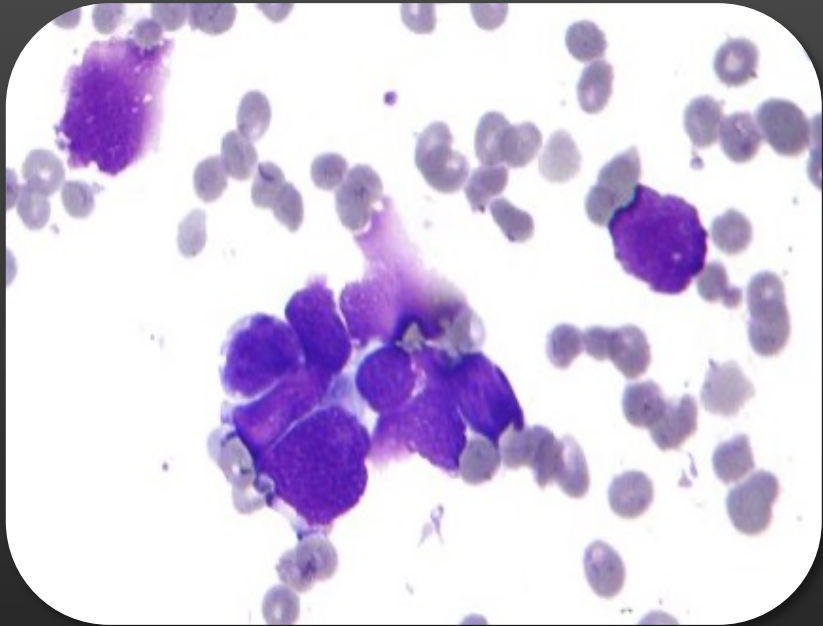
Resultat

(Feasibility of EBUS-TBNA for histopathological and molecular diagnostics of NSCLC)

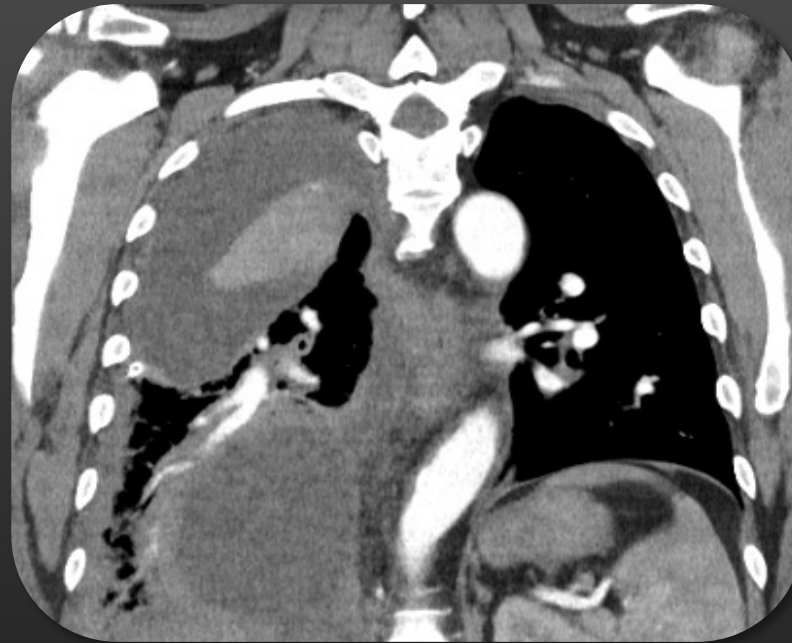
The EBUS-TBNA specimen proved to be sufficient:

- for subtyping of NSCLC in **83%**
- for analysis of treatment-predictive biomarkers in **77%**
- for analysis of multiple oncogenes by NGS in **53%**

Patfall 4 – dg? **SCLC**



EBUS-TBNA på avd 3
EBUS-TBNA cytology:
Synaptophysin +
Chromogranin +
CD56 +



Söker 2 veckor senare med dyspné
Fackbildningar efter talkpleurodes

TNM – stadieindelning av lungcancer

TNM 1st Edition - 1968, 2155 - lungcancer pat

TNM 5th Edition - 1997, 5319 - lungcancer pat

1997 – etableras IASLC

TNM 8th Edition - 2018 i Sverige, 77200 lungcancer pat (Europa, Asien, Nord Amerika)

TNM 9th Edition börjar tillämpas i januari 2025

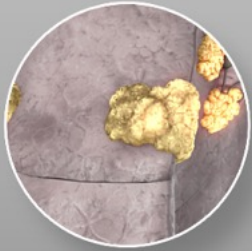


Dr. Pierre Denoix
cancerkirurg
Paris

Vad är TNM?

Obligatoriska parametrar

Andra parametrar: PL, R, STAS, LIV



Tumor size



Lymph Nodes



Metastases

| Prefix | Name | Definition |
|--------|------------|---|
| c | Clinical | Prior to initiation of any treatment, using any and all information available (eg, physical examination, imaging, biopsy results) |
| p | Pathologic | Following resection, based on pathologic assessment and all clinical information |
| y | Restaging | After part or all of the treatment has been given, and can be used in a nonsurgical setting (ycTNM) or after resection (ypTNM) |
| r | Recurrence | Stage at time of a recurrence |
| a | Autopsy | Stage as determined by autopsy (cancer not suspected prior to death) |

cTNM, pTNM, yTNM, rTNM, aTNM

TNM – varför?

Grundläggande för behandlingsval



Stage I
Tumor only in the lung



Stage II
Tumor in the lung and LN



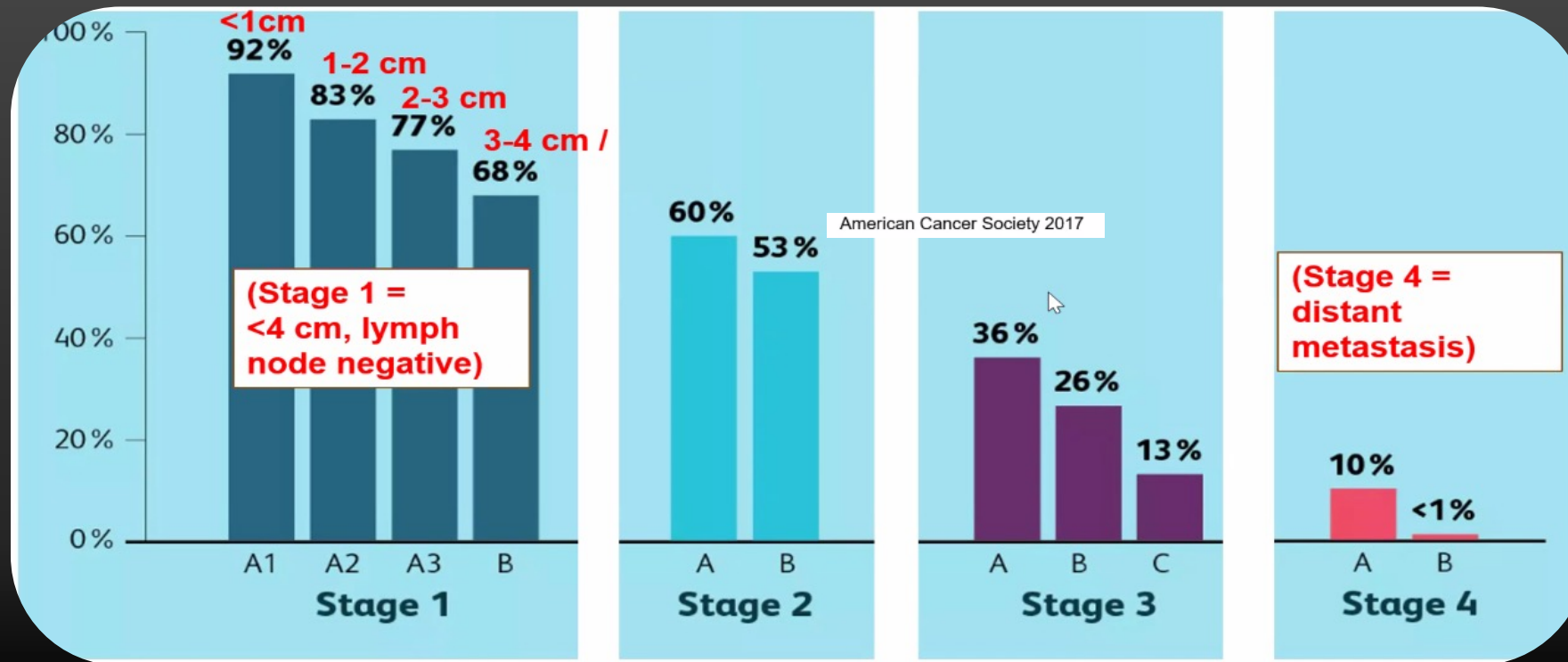
Stage III
Tumor in the lung and
surrounding tissue



Stage IV
Tumor in other organs
or the other lung

TNM – varför?

Bedömning av prognos



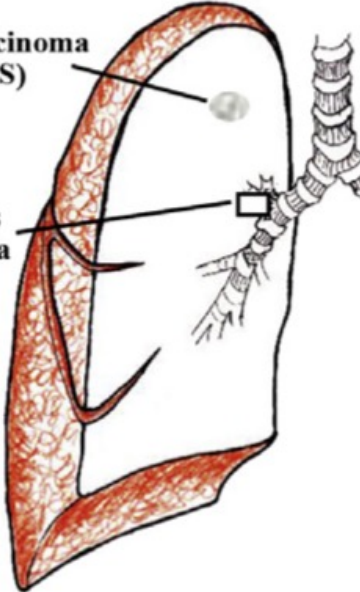
Stadieindelning lungcancer TNM 8

Stage 0

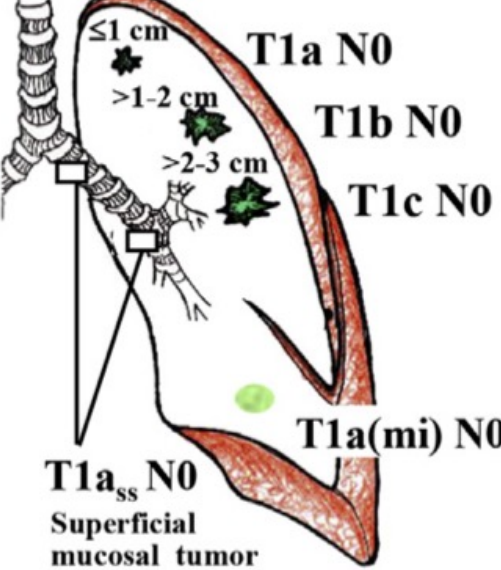
Adenocarcinoma in situ (AIS)

Tis N0

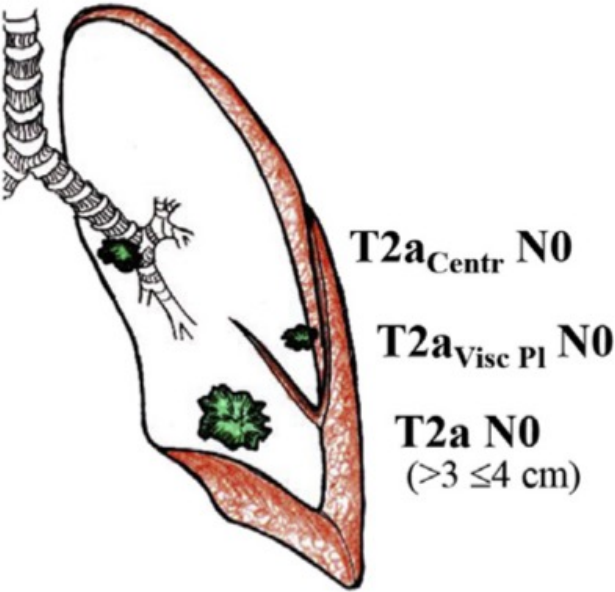
Squamous Carcinoma in situ



Stage IA



Stage IB



Stadieindelning lungcancer TNM 8

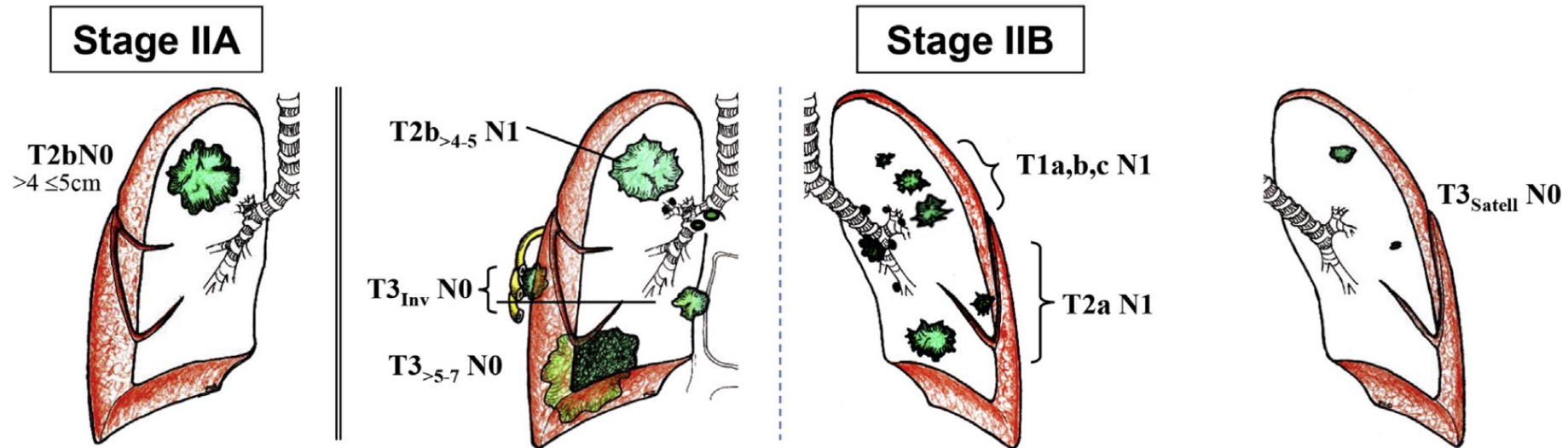
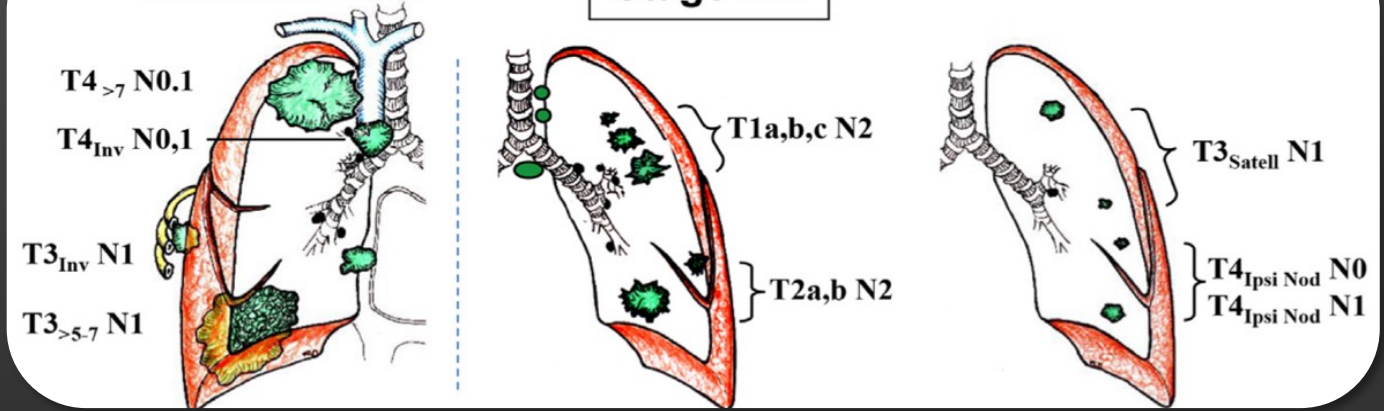


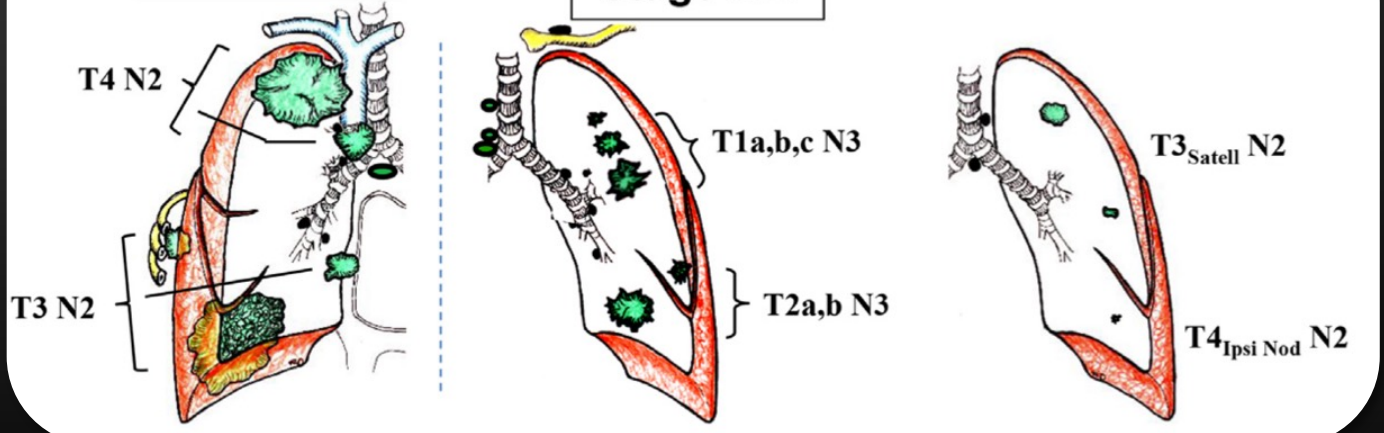
Figure 2 – Graphic illustration of stages 0, I, and II.

Stadieindelning lungcancer TNM 8

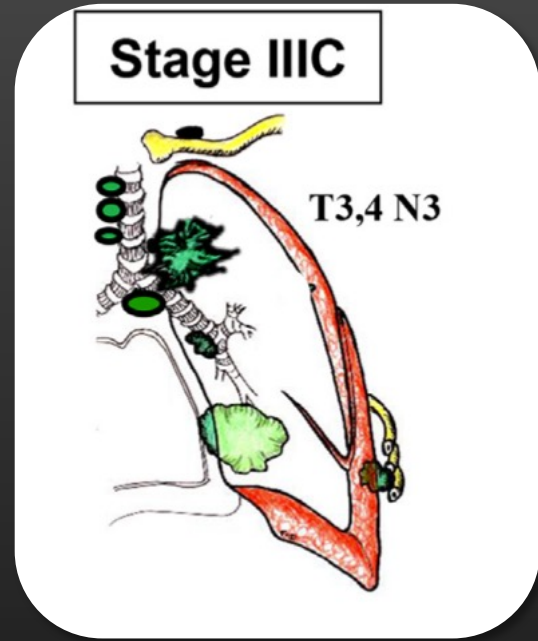
Stage IIIA



Stage IIIB



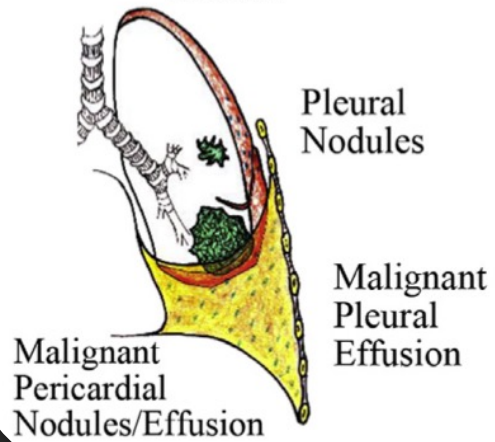
Stage IIIC



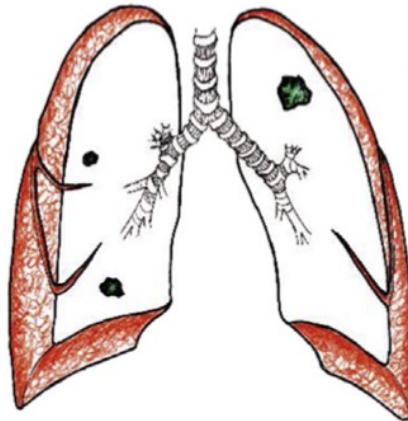
Stadieindelning lungcancer TNM 8

Stage IVA

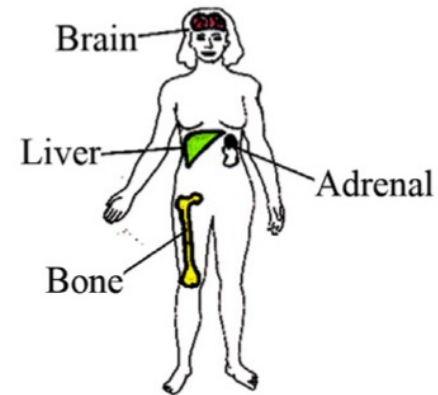
M1a Pl Dissem



M1a Contra Nod

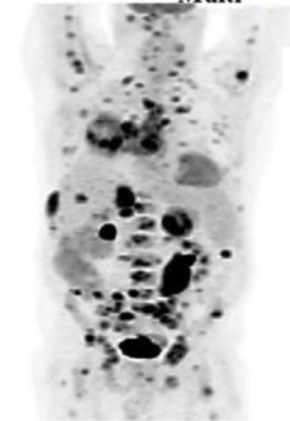


M1b Single



Stage IVB

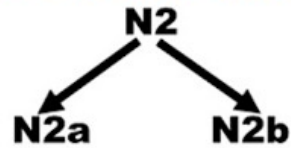
M1c Multi



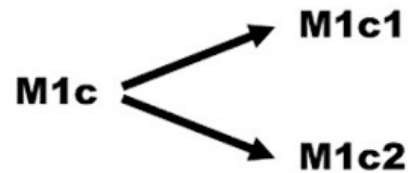
Förändringar i kommande TNM 9

Changes in the 9th Edition

N2 involvement is split into:
 N2a (single station)
 N2b (multiple stations)



M1c involvement is split into:
 M1c1 (single organ system)
 M1c2 (multiple organ systems)



| T/M category | Subcategory, Descriptor | N0 | N1 | N2 | | N3 |
|--------------|-------------------------|------------|------------|-------------|-------------|------|
| | | | | N2a | N2b | |
| T1 | T1a T1b T1c | IA | IIA | IIB | IIIA | IIIB |
| T2 | T2a | IB | IIIB | IIIA | IIIB | IIIB |
| | T2b | IIA | | | | |
| T3 | Size Invasion Nodule | IIB | IIIA | IIIA | IIIB | IIIC |
| T4 | Size Invasion Nodule | IIIA | IIIA | IIIB | IIIB | IIIC |
| M1 | M1a, M1b | IVA | | | | |
| | M1c1, M1c2 | IVB | | | | |

Nodal staging - Metoder

Non-invasiva

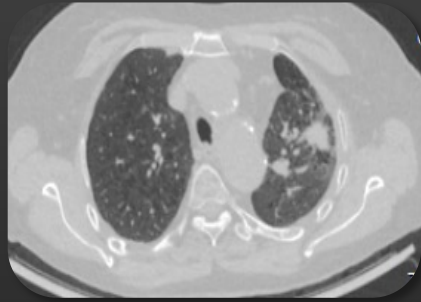


Minimalt invasiva



Invasiva - kirurgiska

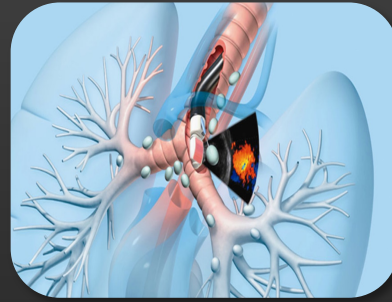
Anatomisk



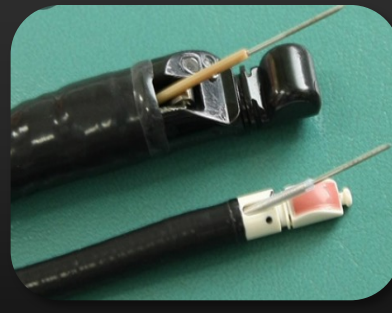
Metabol



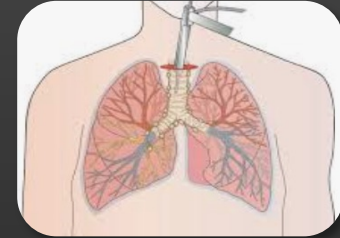
EBUS-TBNA



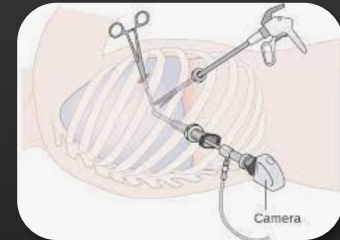
EUS-B-FNA



Mediastinoskopi



VATS



TEMLA



Non-invasiva metoder för nodal staging

Radiologiskt suspekt mediastinum: LN med kort axis > 1cm och FDG-upptag

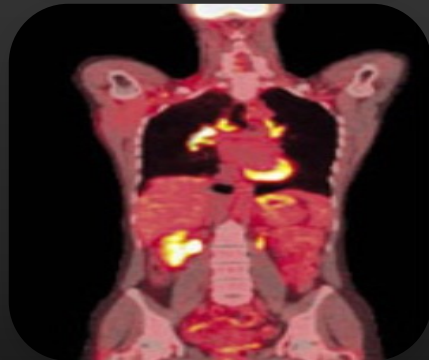


Sensitivitet 55%

PPV 56% - Falskt positiva LN - Central tumörväxt, TB, sarcoidos

NPV 88% Falskt negativa LN - Adenocarcinom, tumorstorlek > 3cm

Ingen vävnadsdiagnostik



Sensitivitet 48 - 77%
beroende av SUV_{max} och LN
storlek (LN<10mm sensitivitet 32%)

Prenzel KL, Mönig SP, Sinning JM, et al. Lymph node size and metastatic infiltration in non-small cell lung cancer. Chest 2003

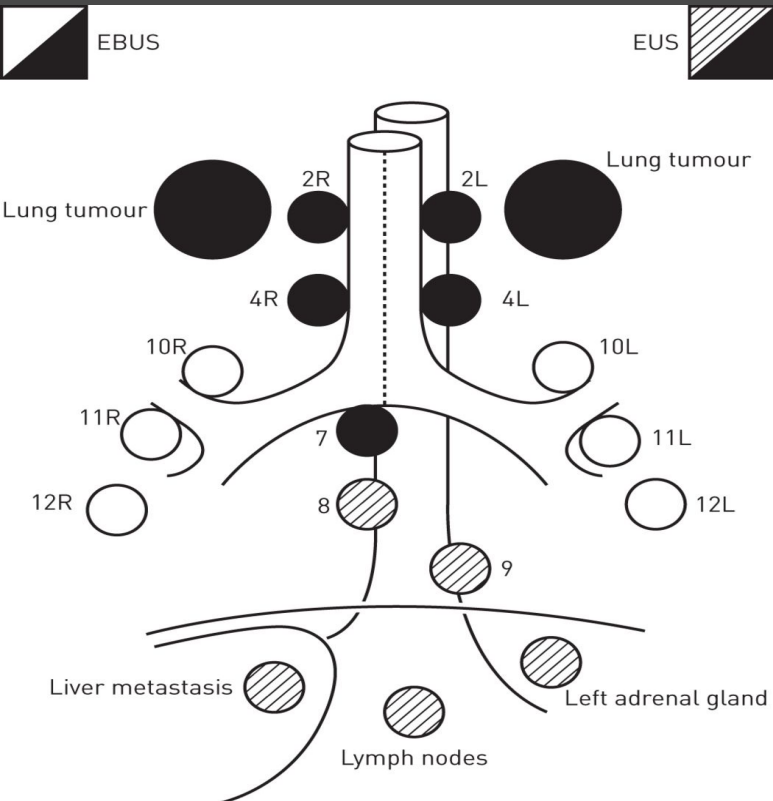
Prenzel KL, Mönig SP, Sinning JM, et al. Lymph node size and metastatic infiltration in non-small cell lung cancer. Chest 2003

Kaseda, K et al Identification of false-negative and false-positive diagnoses of lymph node metastases in non-small cell lung cancer patients staged by integrated ^{18}F -fluorodeoxyglucose-positron emission tomography/computed tomography: A retrospective cohort study. Thorac Cancer, 2016

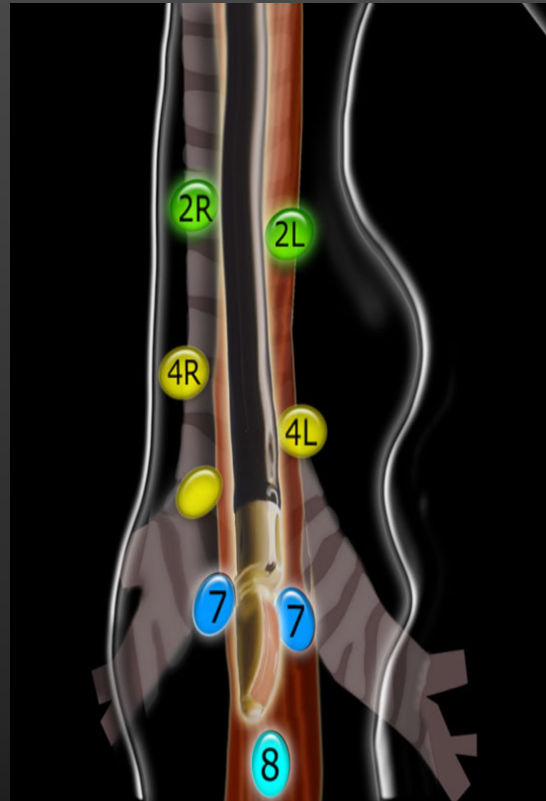
Schmidt-Hansen M et al. PET-CT for assessing mediastinal lymph node involvement in patients with suspected resectable non-small cell lung cancer. Cochrane Database Syst Rev. 2014

Schmidt-Hansen M et al. PET-CT for assessing mediastinal lymph node involvement in patients with suspected resectable non-small cell lung cancer. Cochrane Database Syst Rev. 2014

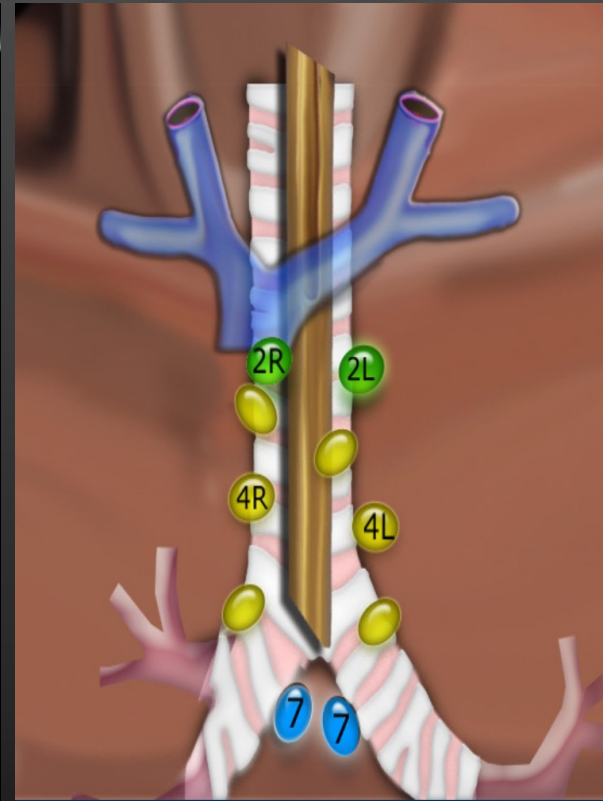
Invasiva metoder för nodal staging



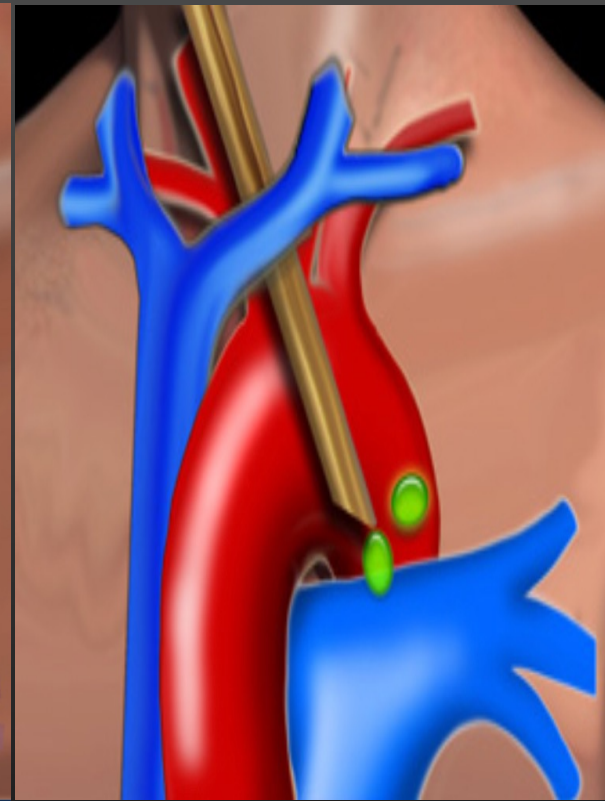
EBUS+EUS



EUS-B-FNA



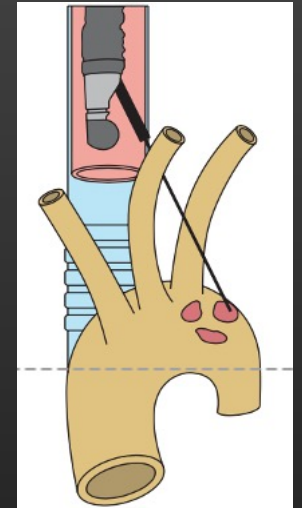
VAM



ECM

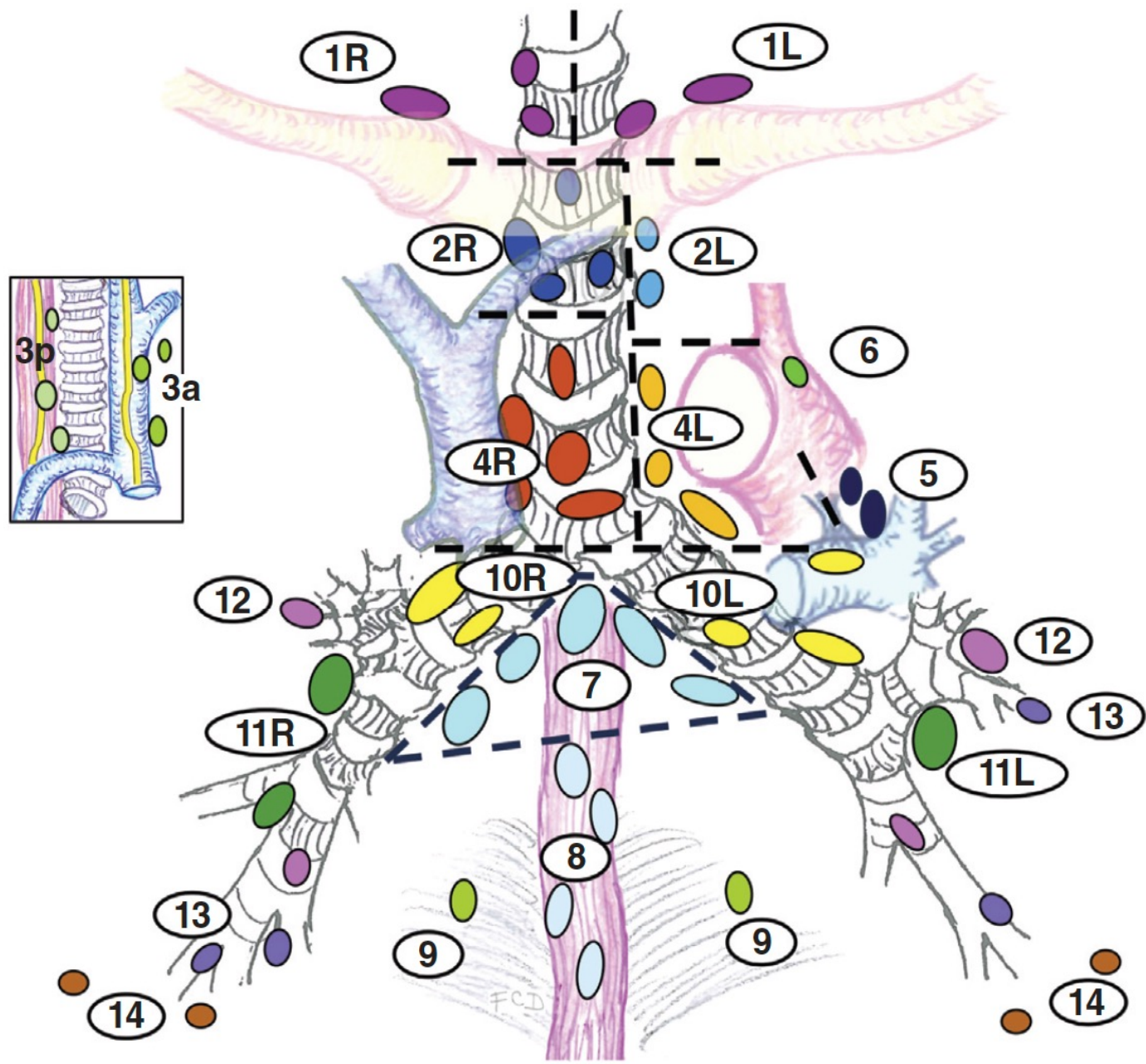
Guidelines for invasive nodal staging

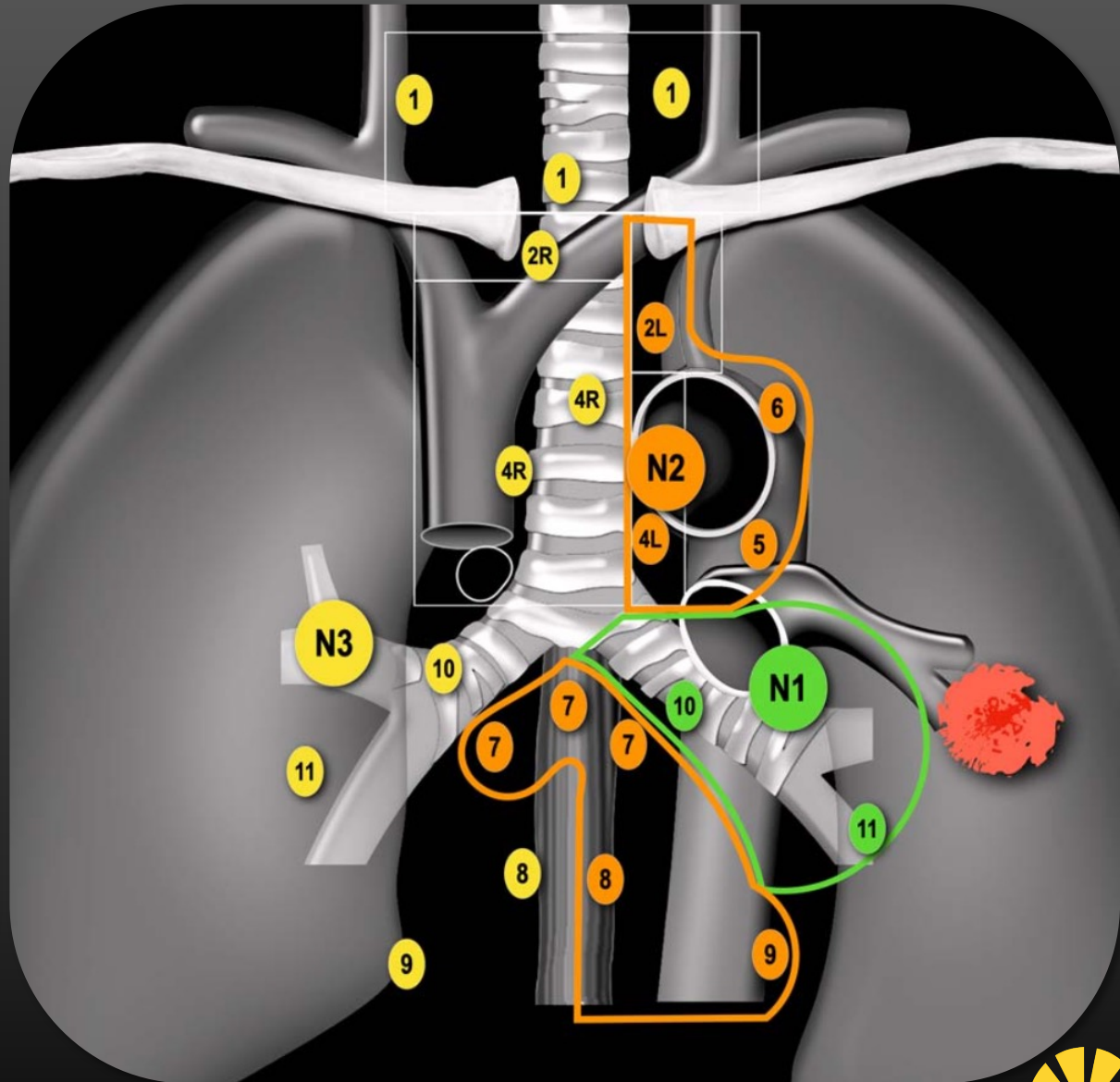
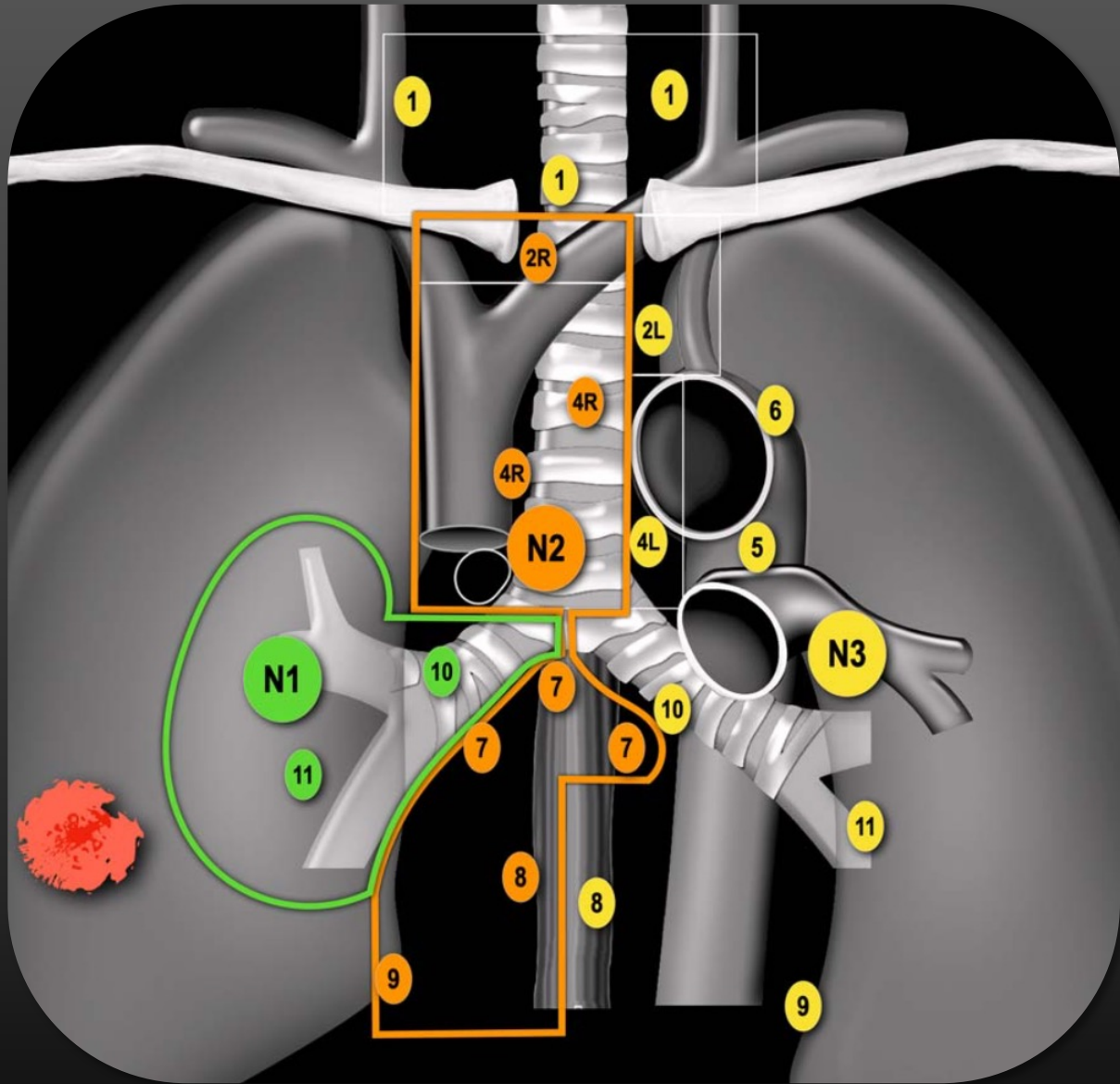
| Nodal basin | EBUS | EUS | CM | AM | VATS |
|-------------------------------|------|----------------|----|----|------|
| 1: Highest mediastinal | ✓ | | | | |
| 2: Upper paratracheal | ✓ | ✓ | ✓ | | ✓ |
| 3: Pre-vascular retrotracheal | ✓ | ✓ | | | ✓ |
| 4: Lower paratracheal | ✓ | ✓ | ✓ | | ✓ |
| 5: Subaortic (AP window) | | ✓ | | ✓ | ✓ |
| 6: Para-aortic | | ✓ [#] | | ✓ | ✓ |
| 7: Subcarinal | ✓ | ✓ | ✓ | | ✓ |
| 8: Paraoesophageal | | ✓ | | | ✓ |
| 9: Pulmonary ligament | | ✓ | | | ✓ |
| 10: Hilar | ✓ | | ✓ | | ✓ |
| 11: Interlobar | ✓ | | | | ✓ |



Lymph node stations accessible by different techniques

IASLC Lymph Node Map





Guidelines for invasiv nodal staging

Rekommendation för mediastinal stadiindelning inför kurativ behandling

PET-DT inkl. diagnostisk DT av torax är grundläggande undersökning

Mediastinal provtagning (EBUS-TBNA, ev. i komb med EUS-B-FNA, i andra hand mediastinoskopi) om:

- PET-positiva lymfkörtlar i N1-,N2- eller N3-position
- Centrallt växande tumörer även om PET-negativa mediastinala lymfkörtlar
- Tumör > 3 cm oavsett lokalisation

Vid stark misstanke (PET positiv eller "bulky nodes") och EBUS/EUS-B-FNA benign **Mediastinoskopi** preop

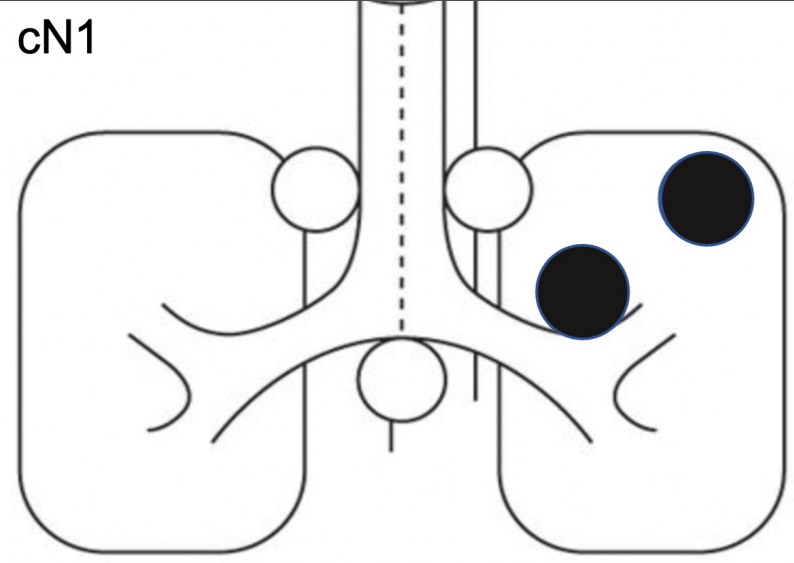
Table 1. Summary of staging guidelines

| | ACCP [1] | ESTS [3] | ESGE/ERS-ESTS [4] |
|--|---|--|---|
| Indications of invasive staging | Central tumor ($\leq 1/3$) cN1 stage ^a cN2/3 stage | Central tumor ($\leq 2/3$) Tumor >3 cm cN1 and cN2/3 stage ^b | Central tumor ($\leq 1/3$) Tumor ≥ 3 cm cN1 and cN2/3 stage ^b FDG-non-avid tumor |
| First procedure | EBUS/EUS | cN0/N1: EBUS/EUS or mediastinoscopy cN2/N3: EBUS/EUS | EBUS/EUS(-B) |
| Systematic endosonographic procedure | No clear recommendation as to how staging should be performed | Complete assessment of mediastinal and hilar nodal stations Sampling the largest node >5 mm on ultrasonography within each of these stations and PET-avid nodes within each of these nodal stations | Complete assessment of mediastinal and hilar nodal stations Sampling of at least three different mediastinal nodal stations (4R, 4L, 7) in cN2/N3 stage ^b and all abnormal lymph nodes ^b |
| Surgical staging if first procedure negative | When the clinical suspicion of mediastinal node involvement remains high ^c | cN2/3 stage ^{b, d} | Central tumor ($\leq 1/3$) Tumor ≥ 3 cm FDG-avid tumor cN1 and cN2/N3 stage ^b (CT or PET) |

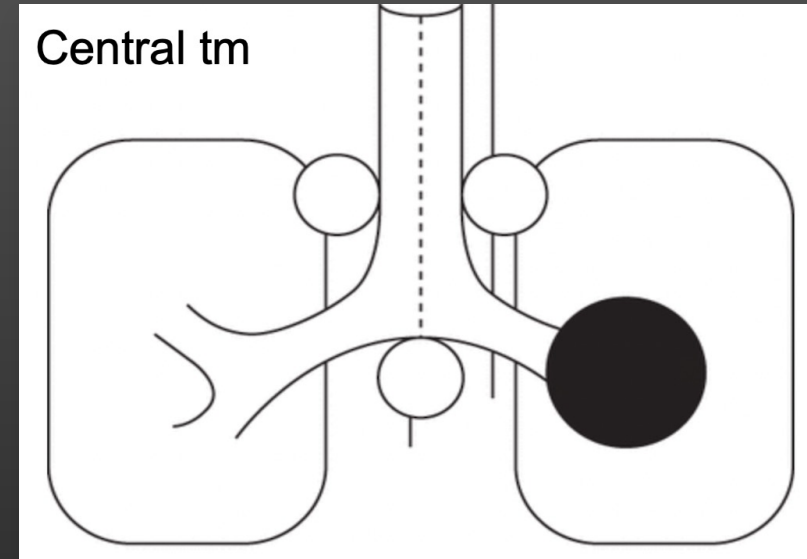
ACCP, American College of Chest Physicians; ESTS, European Society for Thoracic Surgery; ESGE, European Society of Gastrointestinal Endoscopy; ERS, European Respiratory Society; $\leq 1/3$, inner third of the lung; $\leq 2/3$, inner two thirds of the lung; FDG, fluorodesoxyglucose; CT, computed tomography; PET, positron emission tomography. ^a Node with a short axis >10 mm. ^b Node with a short axis >10 mm or node that is FDG-PET-avid. ^c With mediastinoscopy, video-assisted thoracic surgery, etc. ^d With video-assisted mediastinoscopy.

Indikationer för invasiv staging

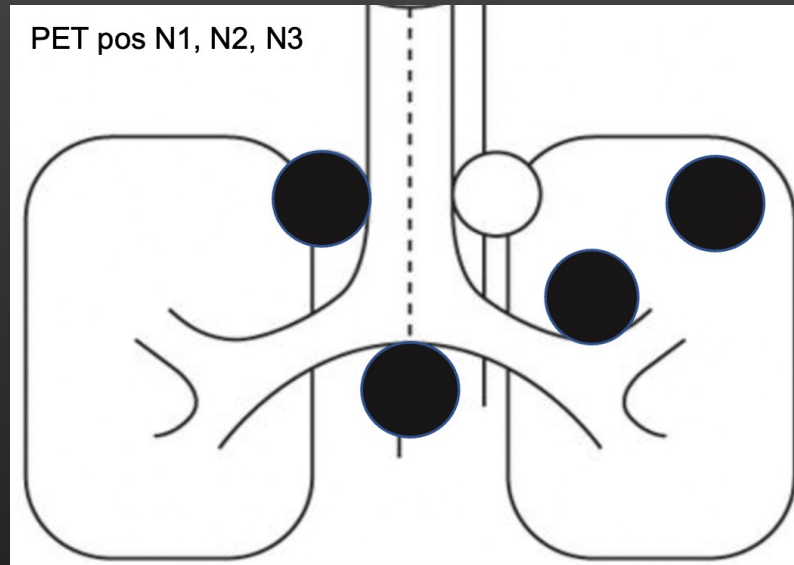
cN1



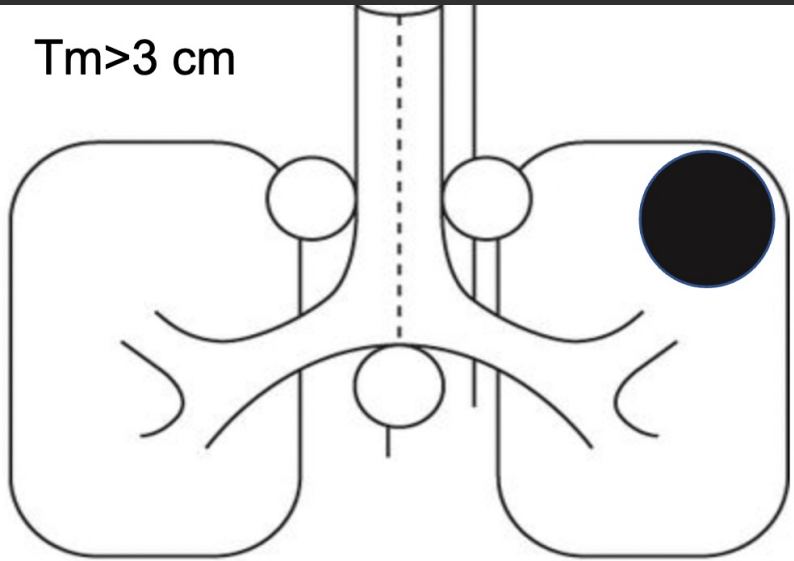
Central tm



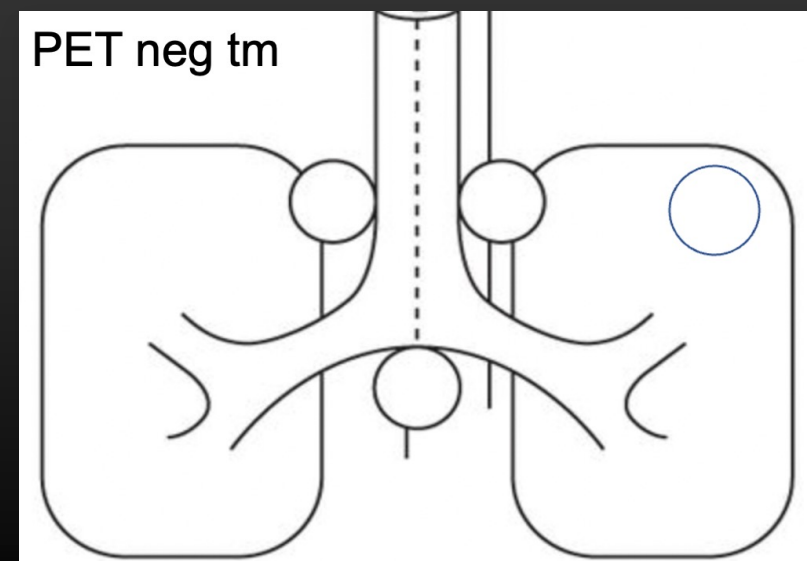
PET pos N1, N2, N3



Tm > 3 cm



PET neg tm



Staging EBUS

Systematisk endosonografisk undersökning och provtagning av hilära och mediastinala LN

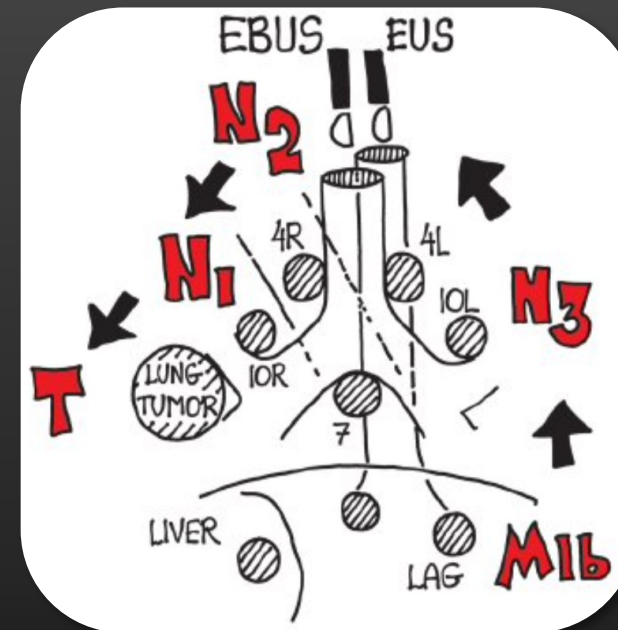
Poliklinisk procedur

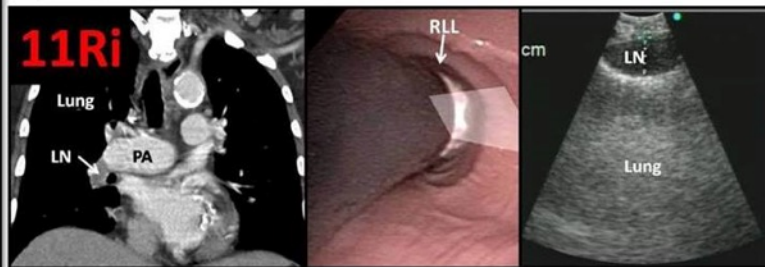
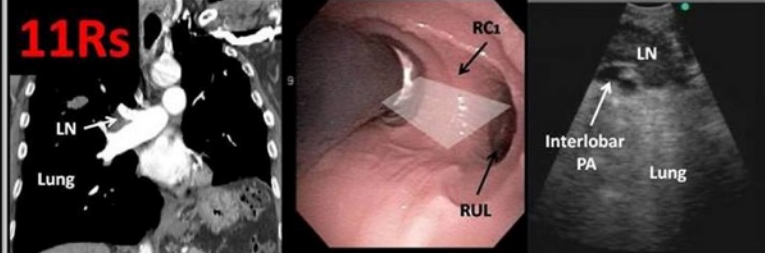
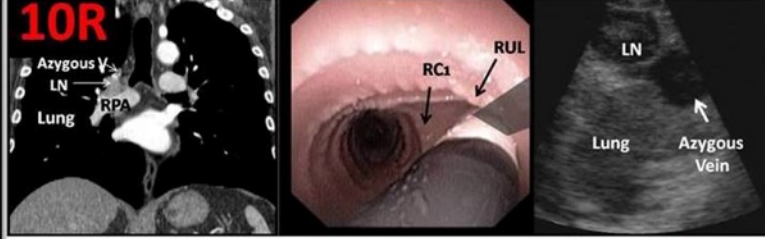
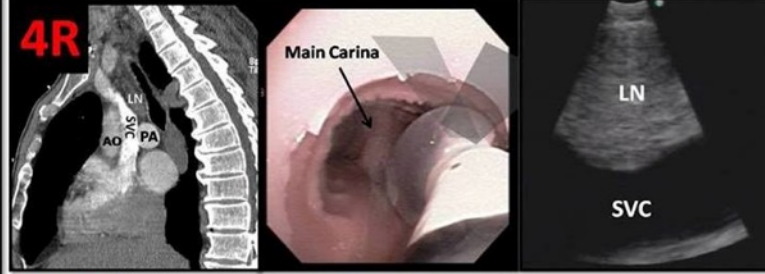
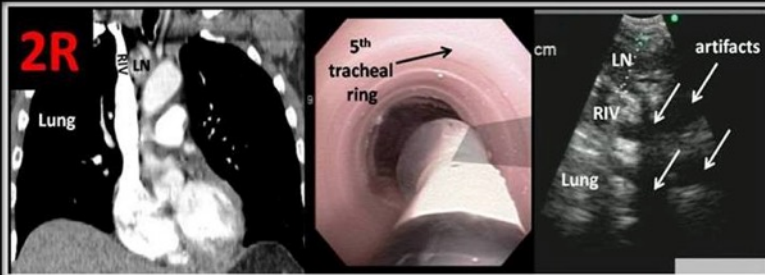
Lokalbedövning i svalget + Alfentanyl iv ± Remimazolam (Midazolam) iv

Först inspektionsbronkoskopi, sedan EBUS bronkoskop transoralt

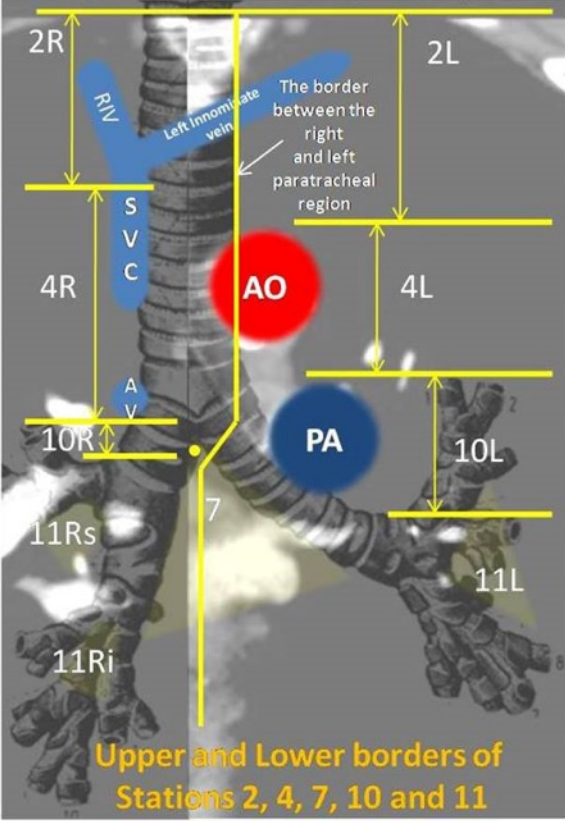
N3→ N2→N1, åtminstone 4R, 7 och 4L

Komb med EUS-B-FNA





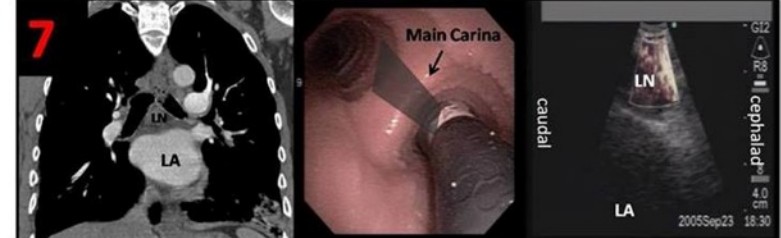
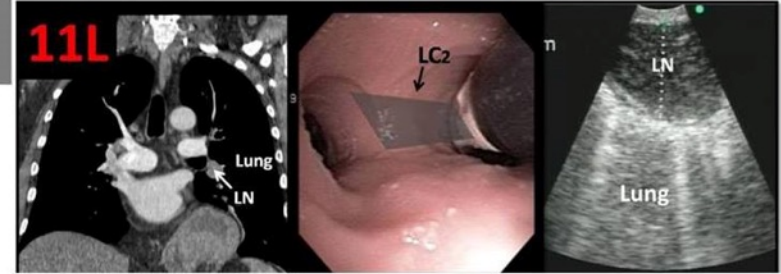
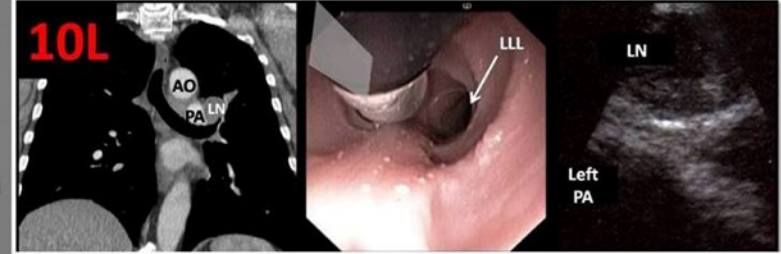
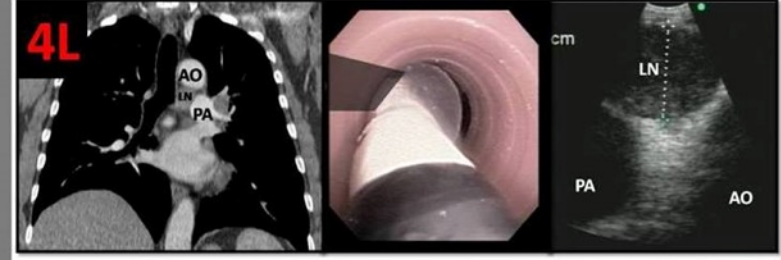
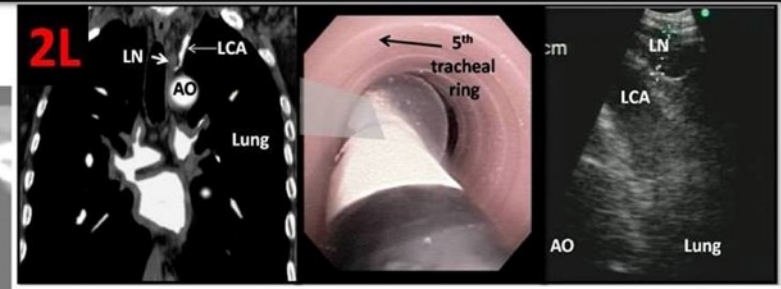
CT-WLB-EBUS correlations for regional lymph nodes by IASLC system



Upper and Lower borders of Stations 2, 4, 7, 10 and 11

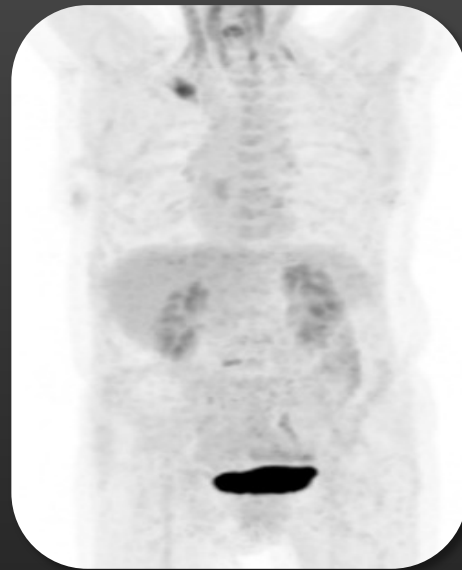
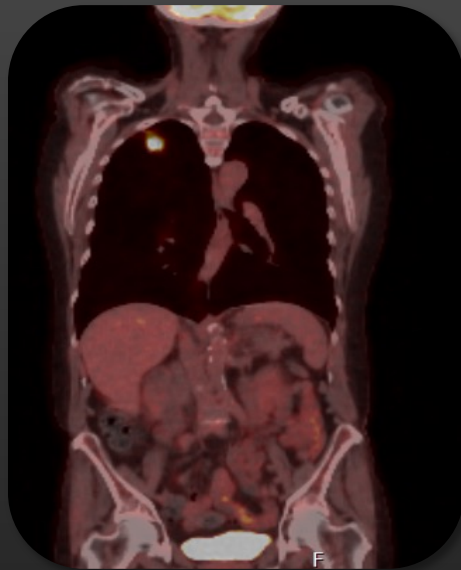
- AV: azygous vein
- AO: aorta
- LN: lymph node
- PA: pulmonary artery
- SVC: superior vena cava
- RC1: primary right carina
- RIV: right innominate vein
- RUL: right upper lobe
- RLL: right lower lobe
- LCA: left carotid artery
- LC2: secondary left carina
- LUL: left upper lobe

© Bronchoscopy International 2010
Septimiu Murgu, MD & Henri Colt, MD



Endosonografi för cN0/N1

UPSTAGING



Risk för ockult spridning i LN 15-25%

EBUS-TBNA – förhindrar onödiga operationer – ockult spridning till N2, N3

Överlägsen metod för bedömning av cN1 inför SBRT

(Endosonography for Mediastinal Nodal Staging of Clinical N1 Non-small Cell Lung Cancer - A Prospective Multicenter Study - Christophe Doooms et al, *Chest* 2015)

Endosonografi för cN2/N3

DOWNSTAGING

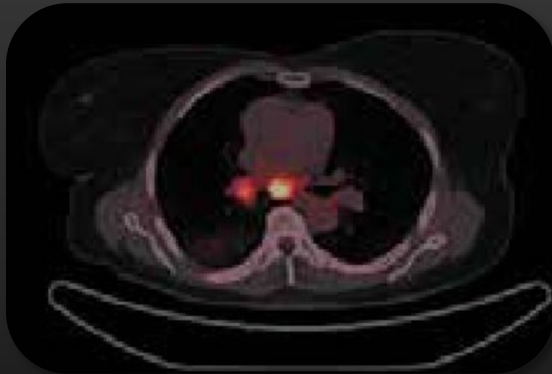


Hög risk för mediastinal spridning

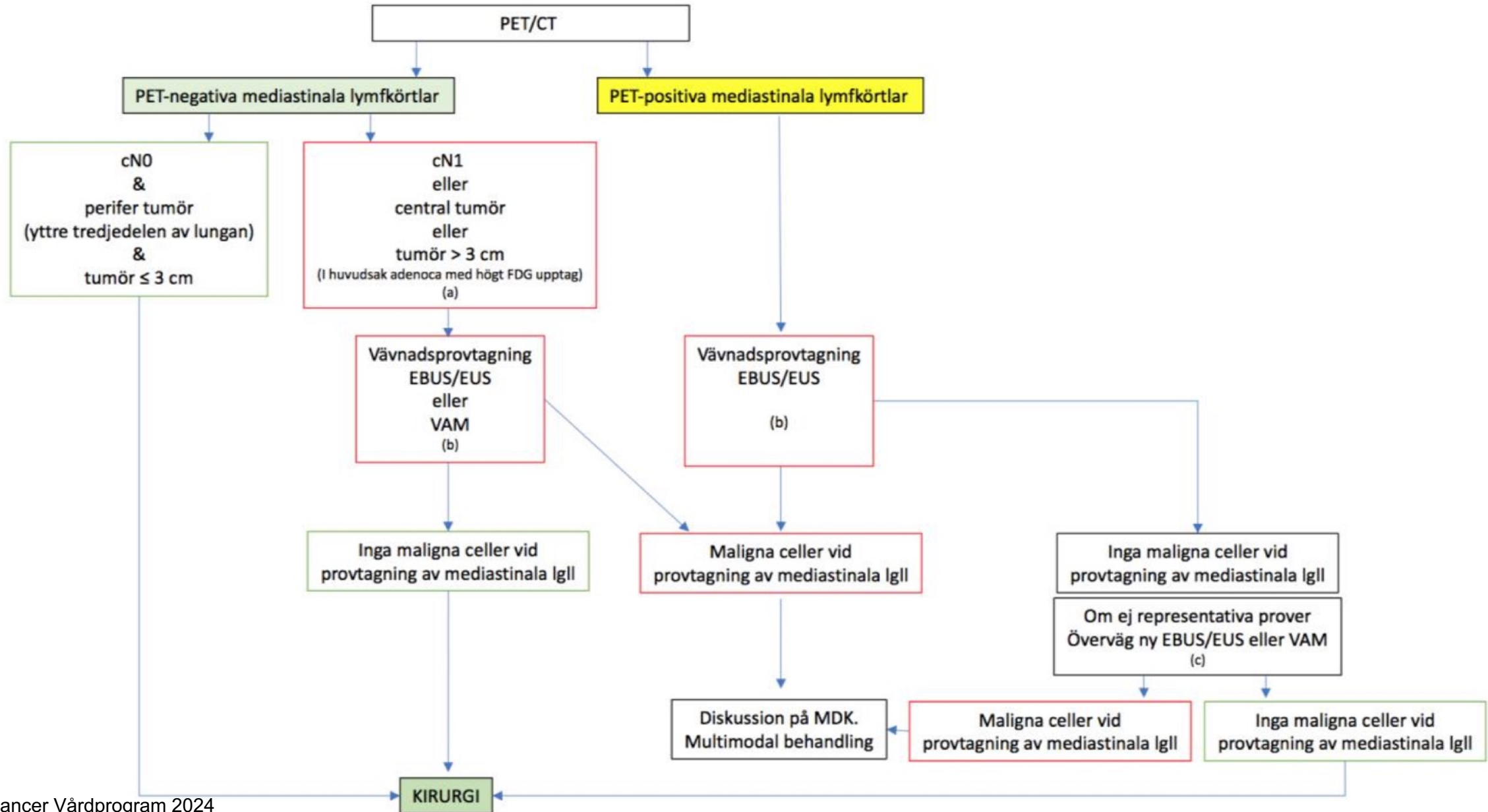
Endosonografi (EBUS-TBNA ev komb med EUS-B-FNA (EUS) – sens 88%

Mediastinoskopi – sensitivitet 79%

Mediastinoskopi som komplement (vid negativ EBUS) – 97%

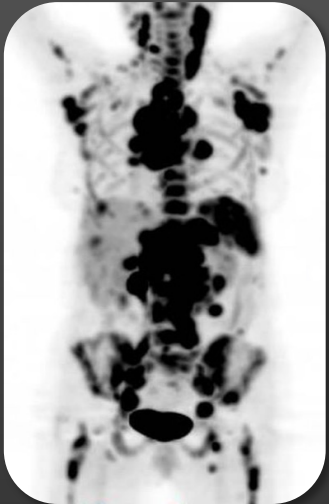


Figur 9.2 Mediastinal staging hos patienter med NSCLC inför kurativt syftande behandling. Algoritm modifierad från ESMO-guidelines.



Hodgkins

EBUS-TBNA – Lymfom?



före behandling



efter behandling

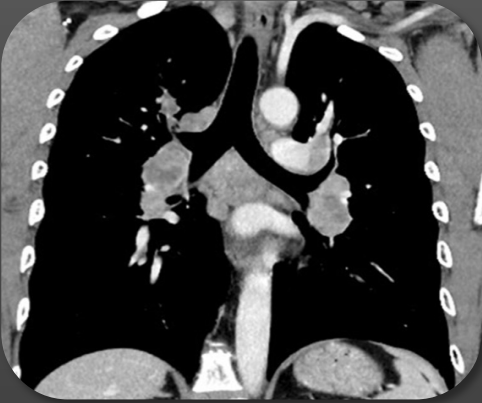
- Stor heterogenitet av dg utfall av EBUS-TBNA för diagnostik av lymfom

(Gandotra S et al. Endobronchial ultrasound transbronchial needle aspiration for the diagnosis of lymphoma. J Bronchol Interv Pulmonol. **2018**. 806 pat, dg utfall 85%

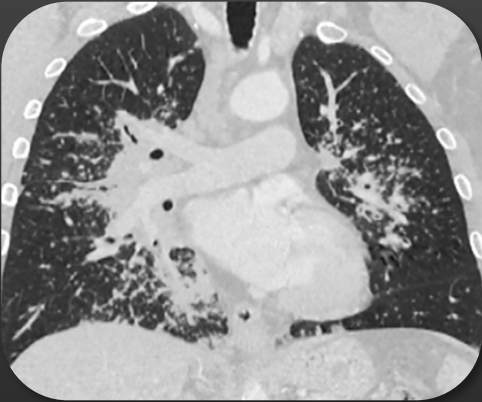
Iqbal S et al. Endobronchial ultrasound and lymphoproliferative disorders: a retro-spective study. Ann Thorac Surg **2012**. dg utfall 29%)

- Bättre sensitivitet för låg diff Non-Hodgkin lymfom jmf med Hodgkin
- Flödescytometri (transfix), nålens storlek (19G bättre?)
- EBUS TBNA vs EBUS TMCB

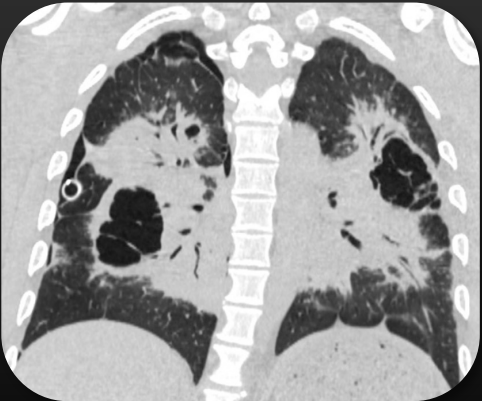
EBUS-TBNA – Sarcoidos?



Stadium I



Stadium II



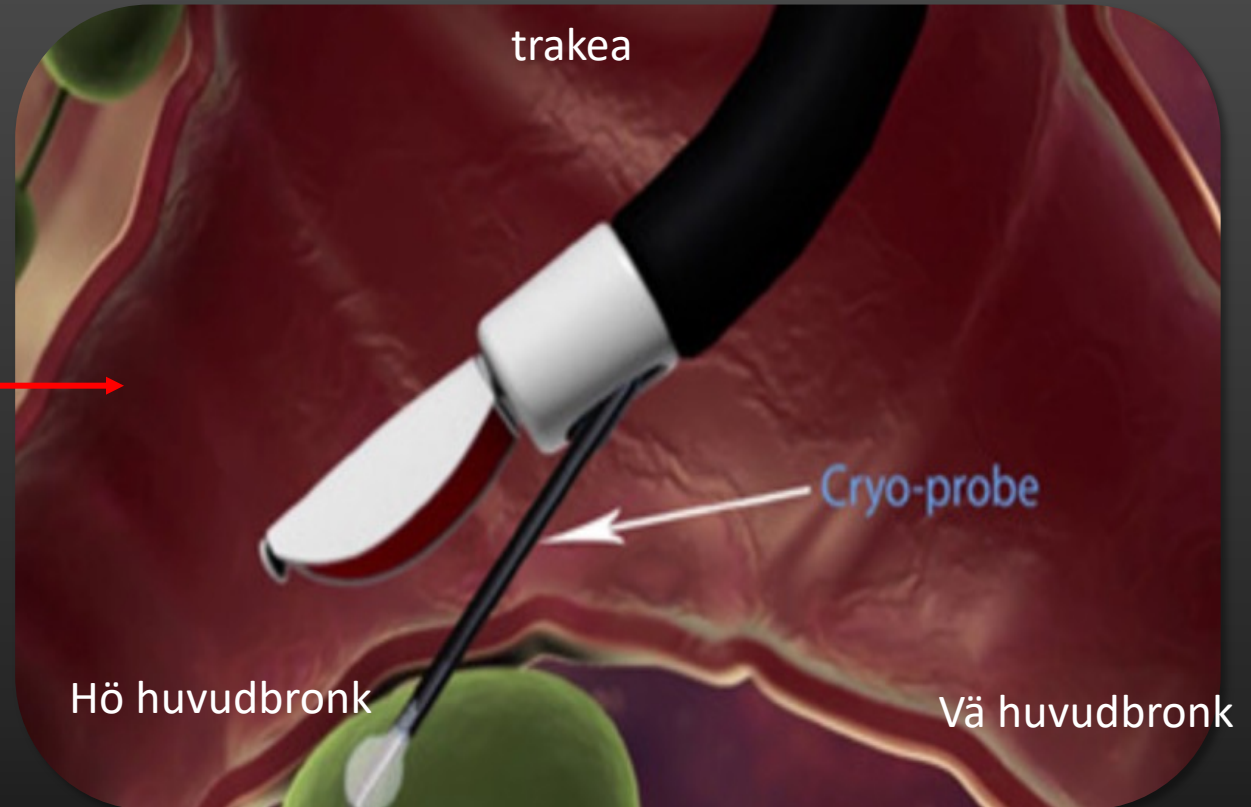
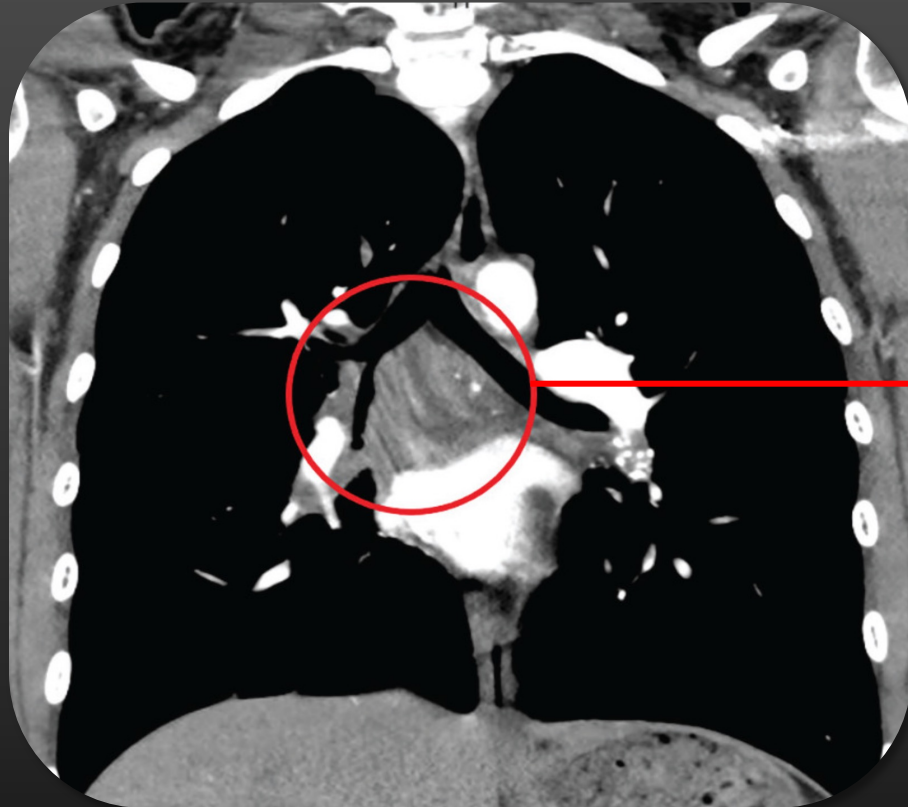
Stadium III

Respirology. 2015 Meta-analysis:

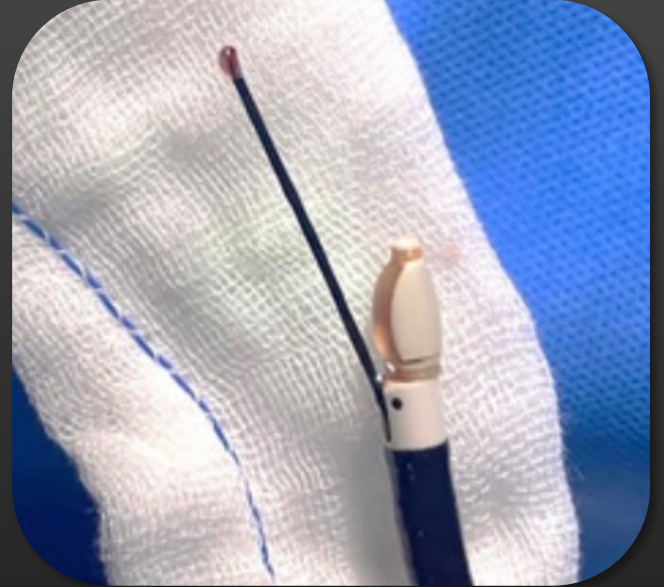
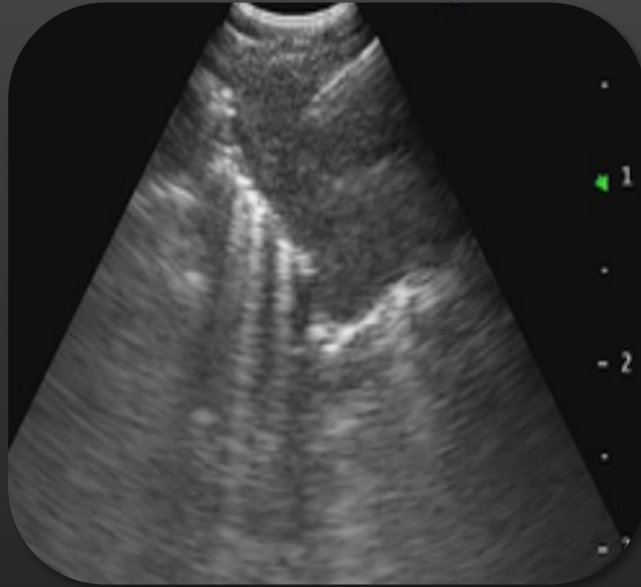
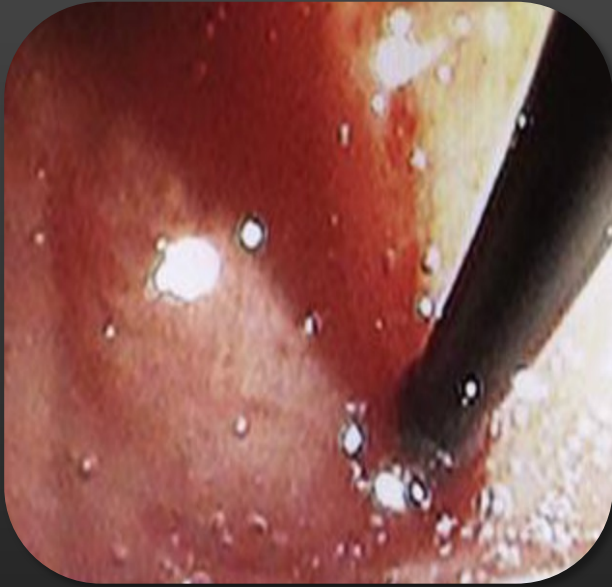
Trisolini R et al Endobronchial ultrasound-guided transbronchial needle aspiration for diagnosis of sarcoidosis in clinically unselected study populations.

- 14 studier, 11 länder, 2097 patienter
- Sensitivitet 79%
- Högre dg utfall i stadium I, jmf med st II (högre densitet av granulom i lymfkörtlar vid st I sjukdom?)
- Påverkan på dg utfallet: nr of LN punktioner, minst 4 per LN station, ROSE

KRYO EBUS (TBMCB)



KRYO EBUS (TBMCB)

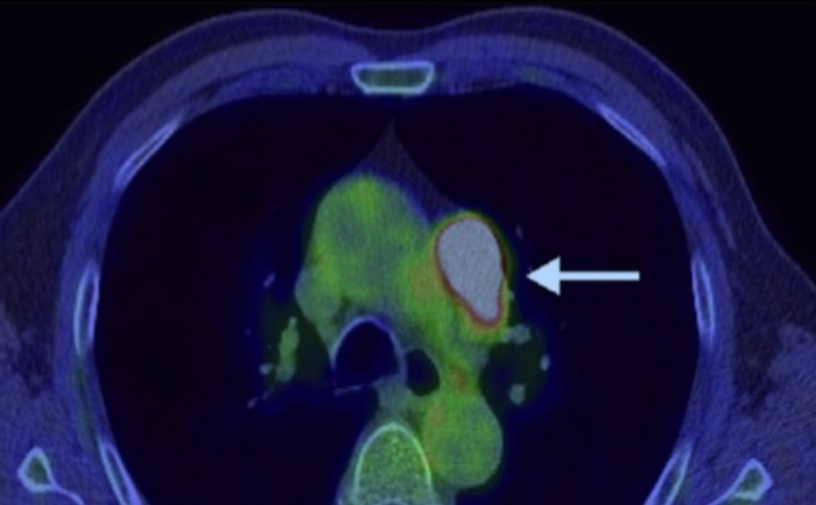
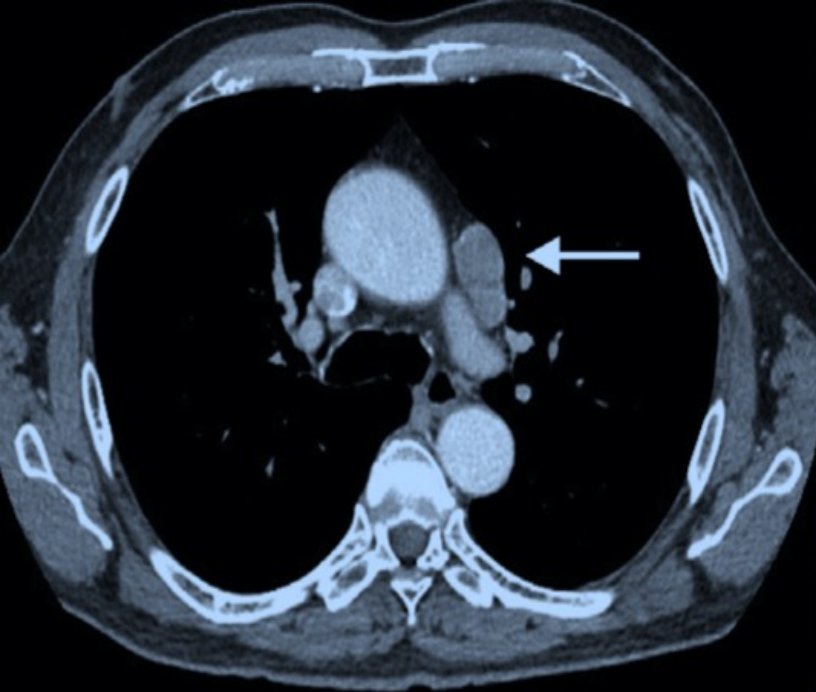


KRYO EBUS (TBMCB)

Maribel Botana-Rial et al. Resp Med 2023

A systematic review: Is the diagnostic yield of mediastinal lymph node cryo biopsy (cryo EBUS) better for diagnosing mediastinal node involvement compared to endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)?

- 7 studier, 555 pat
- Overall sensitivitet: **cryo 92%** jmf med **80% TBNA**
- Lymfom: **cryo 87% vs 12% TBNA**
- Sarkoidos: **cryo 87% vs 60% TBNA**
- PD-L1: **cryo 97% vs 79 %TBNA**



Transvascular EBUS-TBNA - new challenges?

Tack!