



DUTCH
THORACIC
GROUP

DTG Congres 18 oktober 2024

Radiologische en nucleair geneeskundige ontwikkelingen in primaire longkanker stadiëring en herstadiëring na neoadjuvante (chemo-immuno)therapie



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A medical illustration of a human torso from the shoulders down to the waist, rendered in a semi-transparent, blue-tinted style. The internal organs, specifically the lungs and the branching network of bronchi and blood vessels, are clearly visible. The background is a solid dark blue.

DUTCH THORACIC GROUP

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18 oktober 2024

MULTIDISCIPLINAIR

=

TEAM

Disclosures



Format disclosure-slide voor sprekers op nascholingsbijeenkomsten

Disclosure belangen spreker	
Geen (potentiële) belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relaties¹	Bedrijfsnamen
• Sponsoring of onderzoeksgeld² • Honorarium of andere (financiële) vergoeding³ • Aandeelhouder⁴ • Andere relatie, namelijk ...⁵	• NEE • NEE • NEE • NEE

Inhoud

- Technische ontwikkelingen beeldvorming
 - Hardware (scanners) vs Software (AI)
- Ontwikkelingen kwaliteit verslaglegging/stadiering
- Restadiëring
- Uitdagingen NSCLC imaging

Technische ontwikkelingen beeldvorming

➤ Hardware

- Total body PET-CT (sensitiviteit, maar ook FP resultaten)
 - Incl. ontwikkeling tracers
- Photon-counting CT

➤ Software/Artificial intelligence

Maximum sensitivity by “long axial field-of view”

“total body PET-CT”: where MedTech and BioTech meet



~40-fold increase
for adult total-body imaging

~20-fold increase
for pediatric total-body
imaging

~4-fold increase
for single organ imaging

Ronald Boellaard



ADORE

✗ City of
✗ Amsterdam
✗



Europese Unie
Europees Fonds voor
Regionale Ontwikkeling

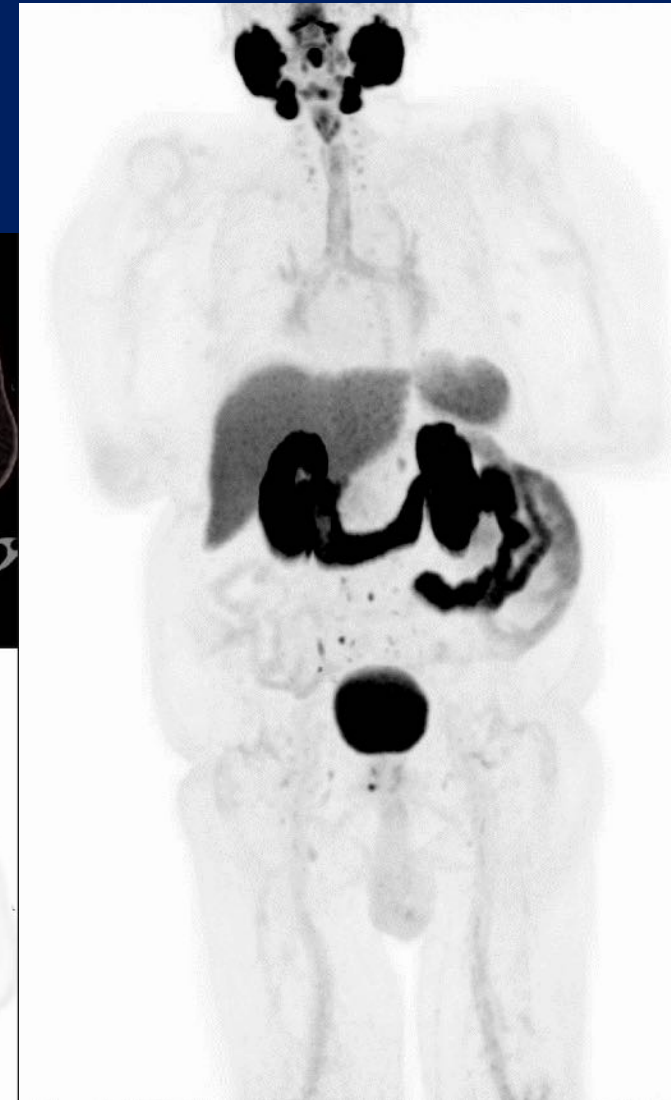
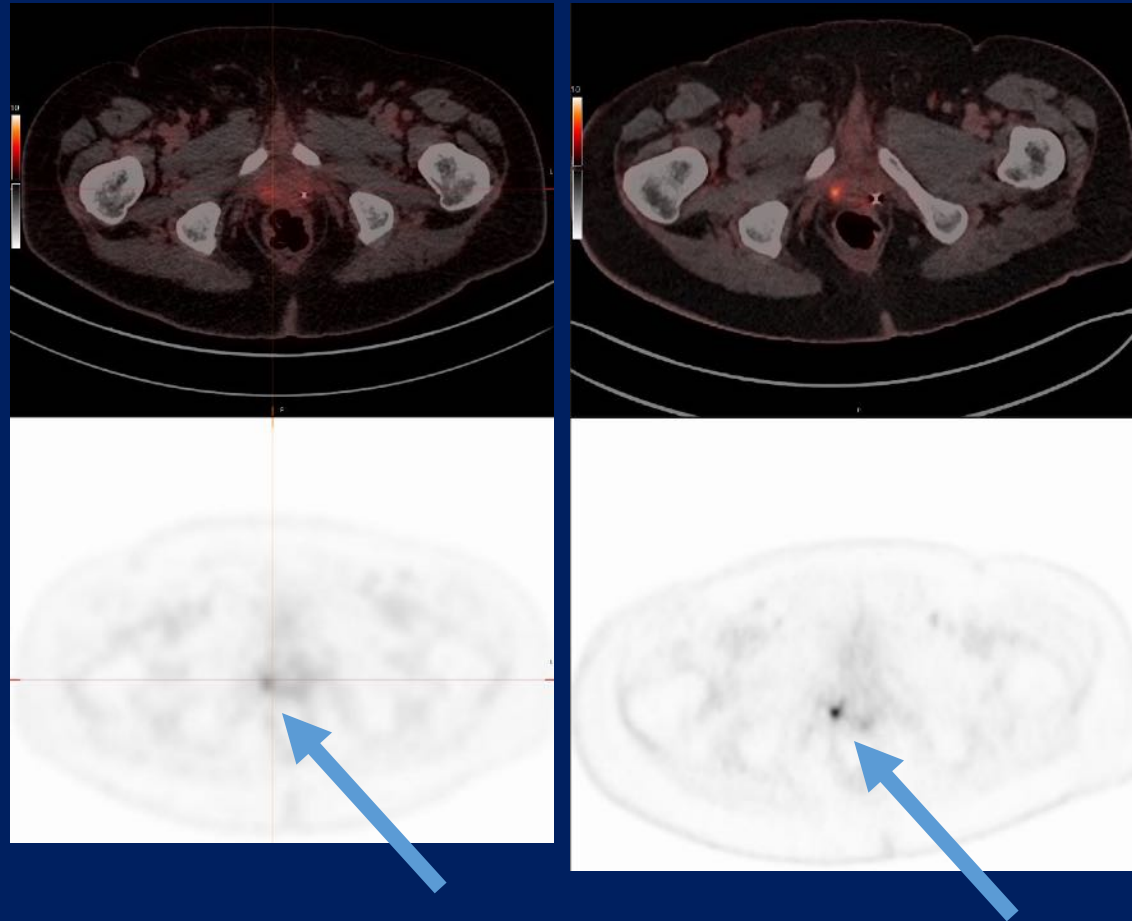
Kansen voor West

Total body PET

Zeer nauwkeurige detectie!



40 min standaard scanner



8 min total body scanner

RESEARCH ARTICLE

Open Access



[¹⁸F]FAPI adds value to [¹⁸F]FDG PET/CT for diagnosing lymph node metastases in stage I-IIIa non-small cell lung cancer: a prospective study

Youcai Li^{1†}, Yin Zhang^{2†}, Zhihua Guo³, Peng Hou¹, Jie Lv¹, Miao Ke¹, Shaoyu Liu¹, Siwen Li⁴, Weiqiang Yin³, Jianxing He³ and Xinlu Wang^{1*} 

Abstract

Background This study investigates the value of fluorine 18 (¹⁸F)-labeled fibroblast activation protein inhibitor (FAPI) for lymph node (LN) metastases in patients with stage I-IIIa non-small cell lung cancer (NSCLC).

Methods From November 2021 to October 2022, 53 patients with stage I-IIIa NSCLC who underwent radical resection were prospectively included. [¹⁸F]-fluorodeoxyglucose (FDG) and [¹⁸F]FAPI examinations were performed within one week. LN staging was validated using surgical and pathological findings. [¹⁸F]FDG and [¹⁸F]FAPI uptake was compared using the Wilcoxon signed-ranks test. Furthermore, the diagnostic value of nodal groups was investigated.

Results In 53 patients (median age, 64 years, range: 31–76 years), the specificity of [¹⁸F]FAPI for detecting LN metastasis was significantly higher than that of [¹⁸F]FDG ($P < 0.001$). High LN risk category, greater LN short-axis dimension (≥ 1.0 cm), absence of LN calcification or high-attenuation, and higher LN FDG SUV_{max} (≥ 10.1) were risk factors for LN metastasis ($P < 0.05$). The concurrence of these four risk factors accurately predicted LN metastases (Positive Predictive Value [PPV] 100%), whereas the presence of one to three risk factors was unable to accurately discriminate the nature of LNs (PPV 21.7%). Adding [¹⁸F]FAPI in this circumstance improved the diagnostic value. LNs with an [¹⁸F]FAPI SUV_{max} < 6.2 were diagnosed as benign (Negative Predictive Value 93.8%), and LNs with an [¹⁸F]FAPI SUV_{max} ≥ 6.2 without calcification or high-attenuation were diagnosed as LN metastasis (PPV 87.5%). Ultimately, the integration of [¹⁸F]FDG and [¹⁸F]FAPI PET/CT resulted in the highest accuracy for N stage (83.0%) and clinical decision revisions for 29 patients.

Conclusion In patients with stage I-IIIa NSCLC, [¹⁸F]FAPI contributed additional valuable information to reduce LN diagnostic uncertainties after [¹⁸F]FDG PET/CT. Integrating [¹⁸F]FDG and [¹⁸F]FAPI PET/CT resulted in more precise clinical decisions.

Ontwikkelingen: PET tracers

- F-18 Fapi PET? Minder FP?
- Voorlopig niet in richtlijn

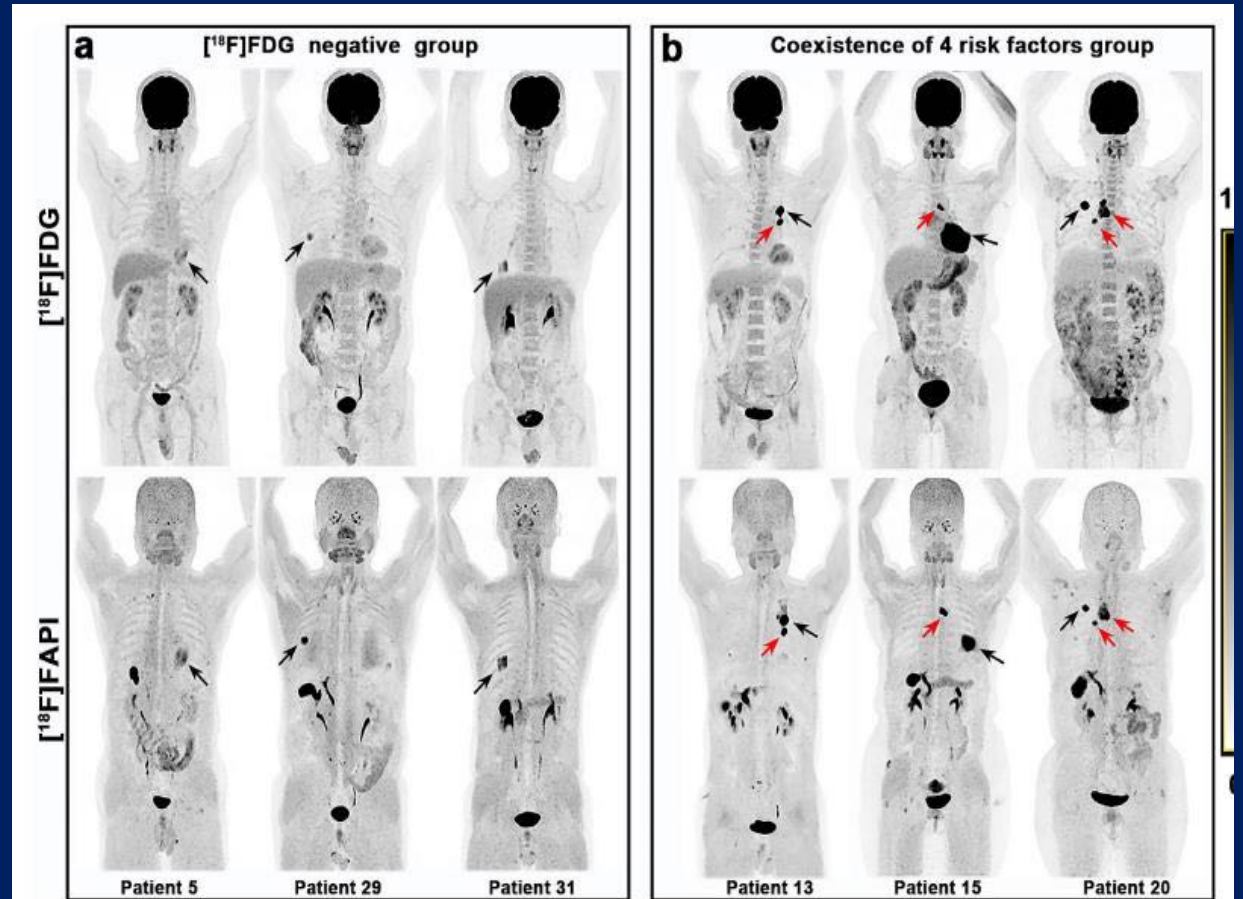


Fig. 3 (a) $[^{18}\text{F}]\text{FDG}$ and $[^{18}\text{F}]\text{FAPI}$ PET/CT of 3 representative patients in the $[^{18}\text{F}]\text{FDG}$ negative group. Lymph nodes with negative $[^{18}\text{F}]\text{FDG}$ PET/CT findings were also negative on $[^{18}\text{F}]\text{FAPI}$ PET/CT. (Note: The right hilar lymph nodes in the second and third patients display slight FDG uptake, precluding their classification as $[^{18}\text{F}]\text{FDG}$ negative group, while the other lymph nodes fall into the $[^{18}\text{F}]\text{FDG}$ negative group). (b) $[^{18}\text{F}]\text{FDG}$ and $[^{18}\text{F}]\text{FAPI}$ PET/CT of 3 representative patients in the coexistence of 4 risk factors group. Lymph nodes indicated by the red arrows were high-risk regional lymph nodes with a diameter greater than 1.0 cm and no CHA. These lymph nodes exhibited high uptake on both $[^{18}\text{F}]\text{FDG}$ ($\text{SUV}_{\text{max}}=10.9\text{--}21.3$) and $[^{18}\text{F}]\text{FAPI}$ ($\text{SUV}_{\text{max}}=12.5\text{--}22.9$) imaging. Subsequent surgical pathology confirmed these lymph nodes as metastatic (Black arrows indicated primary lesion)

Photon-counting CT

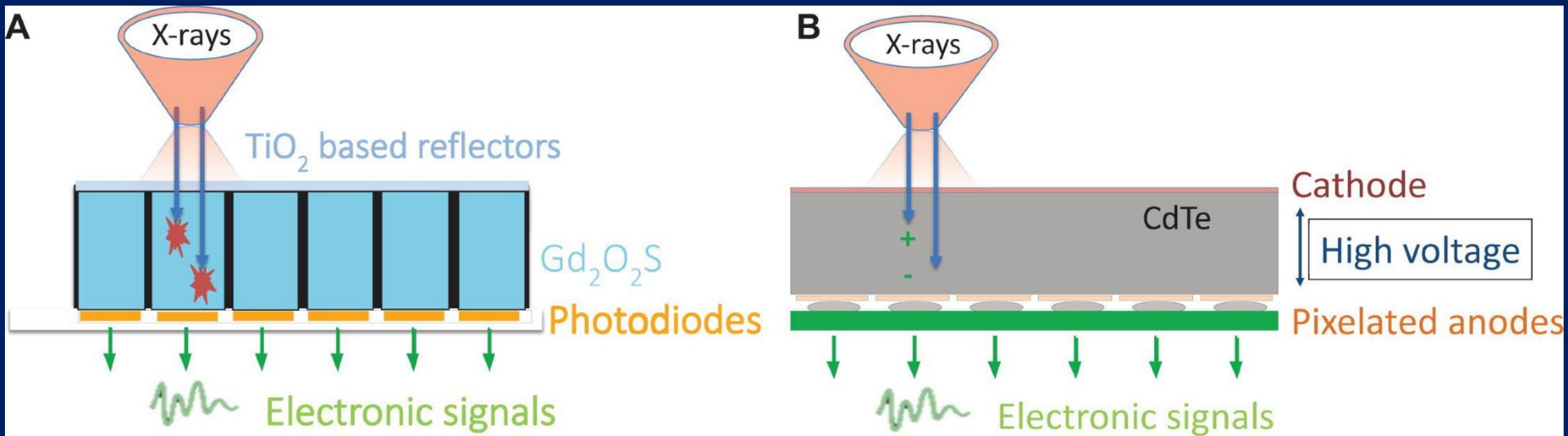


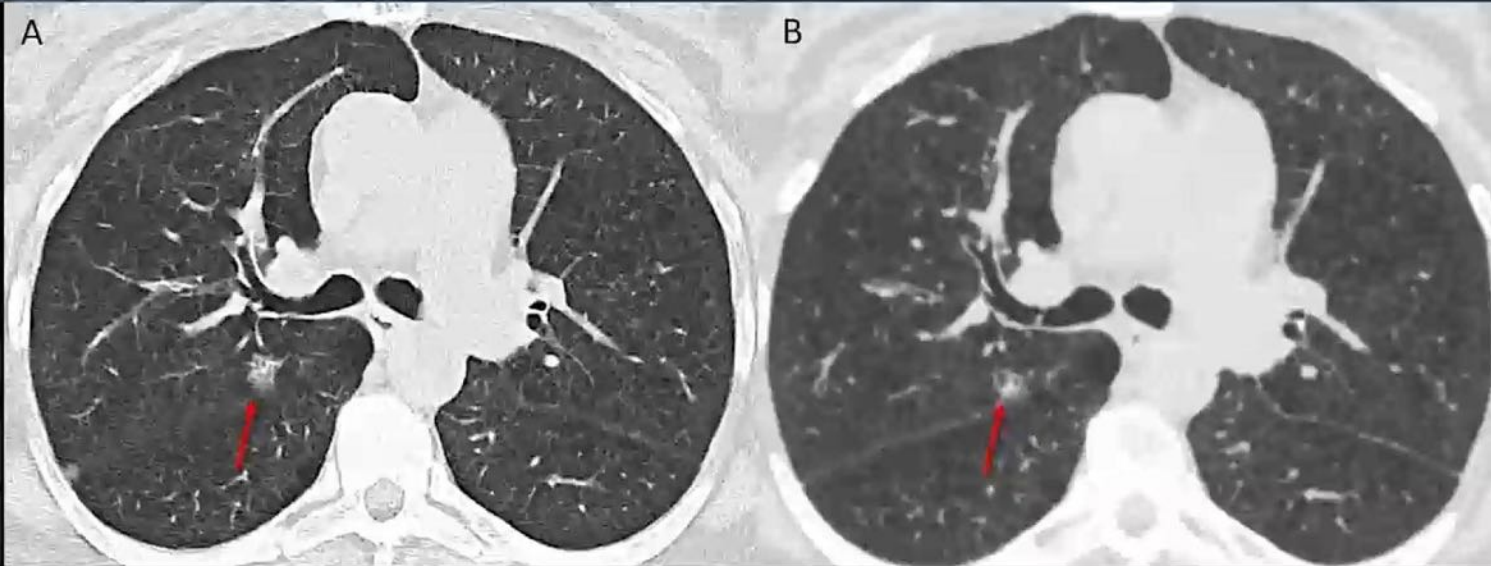
Figure 1. **(A)** Illustration shows a conventional energy-integrating CT detector. Pixels are separated by reflective septa, which reduce cross talk but increase geometric radiation dose inefficiency. The signal produced is proportional to the sum of all photon energies. **(B)** Illustration shows a cadmium telluride photon-counting detector. Note that septa are not used in the design. The signal is proportional to the energy of each individual photon, and individual photons are directly recorded as electric signals without the intermediate conversion to visible light. The energy of each photon is recorded and can be used in multienergy applications.

Photon Counting CT

Seeing More with Less: Clinical Benefits of Photon-counting Detector CT

Clinical Applications

Spatial Resolution



56-year-old female patient with BMI of 27 kg/m² with suspected adenocarcinoma of the lung:

A) PCCT at 0.4 mm resolution, Bl64f kernel

B) EID at 0.6 mm resolution, SHARP kernel (GE Revolution Apex)

PCCT vs conventionele CT

- ✓ Hogere resolutie
0.2mm vs 0.6mm
- ✓ Betere signaal- (en contrast-) ruisverhouding
- ✓ Lagere stralingsdosis
- ✓ Kortere scanduur
- ✓ Minder iv contrast
- ✓ Cardiale imaging, HRCT thorax, ...

Technische ontwikkelingen beeldvorming

Hardware

- Total body PET-CT (sensitiviteit, maar ook FP resultaten)
- Photon-counting CT

Verbeteringen op gebied van:

- Beeldkwaliteit
- Scansnelheid
- Gevoeligheid
- Stralingsbelasting

Software/Artificial intelligence

Technische ontwikkelingen beeldvorming

Hardware

- Total body PET-CT (sensitiviteit, maar ook FP resultaten)
- Photon-counting CT
- Beeldkwaliteit, scansnelheid, gevoeligheid en stralingsbelasting

Software/Artificial intelligence

- Verlagen dosis FDG
- Verkorten scanduur
- Patroonherkenning?
- Screening IdCT

Ontwikkelingen: Kwaliteit verslaglegging/stadiering

➤ Context kennis

- TNM 9^e editie IASLC (standaardisatie verslaglegging) en single-multilevel N2 ziekte
- Correlatie beeldvorming-pathologie
- MDO ondersteuning

➤ Artificial intelligence/software ondersteuning

- Detectie kleine noduli/screening
- Patroonherkenning
- Respons evaluatie

Ontwikkelingen: Kwaliteit verslaglegging/stadiering

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- Respons evaluatie

T: Primary tumor	
Tx	Primary tumor cannot be assessed ^d
T0	No evidence of primary tumor
Tis	Carcinoma in situ ^b
T1	Tumor surrounded by lung or visceral pleura or in a lobar or more peripheral bronchus ^c
T1mi	Minimally invasive adenocarcinoma ^d
T1a	Tumor ≤1 cm in greatest dimension
T1b	Tumor >1 cm but ≤2 cm in greatest dimension
T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2	Tumor with any of the following features:
T2a	Tumor >3 cm but ≤4 cm in greatest dimension invades visceral pleura invades an adjacent lobe involves main bronchus (up to but not including the carina) or is associated with atelectasis or obstructive pneumonitis, extending to the hilar region, involving either part of or the entire lung
T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3	Tumor with any of the following features: tumor >5 cm but ≤7 cm in greatest dimension invades parietal pleura or chest wall invades pericardium, phrenic nerve, or azygos vein ^e invades thoracic nerve roots (i.e., T1, T2) or stellate ganglion separate tumor nodule(s) in the same lobe as the primary
T4	Tumor with any of the following features: tumor >7 cm in greatest dimension invades mediastinum, thymus, trachea, carina, recurrent laryngeal nerve, vagus nerve, esophagus, or diaphragm invades heart, great vessels (aorta, superior or inferior vena cava, intrapericardial pulmonary arteries or veins), supra-aortic arteries, or brachiocephalic veins invades subclavian vessels, vertebral body, lamina, spinal canal, cervical nerve roots, or brachial plexus (i.e., trunks, divisions, cords, or terminal nerves) separate tumor nodule(s) in a different ipsilateral lobe than that of the primary
N: Regional lymph node involvement	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial or ipsilateral hilar or intrapulmonary lymph nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal or subcarinal lymph node(s)
N2i	Metastasis in ipsilateral mediastinal or subcarinal lymph node(s)
N2a	Metastasis(es) in a single ipsilateral mediastinal or in the subcarinal nodal station
N2b	Metastases in multiple ipsilateral mediastinal nodal stations with or without involvement of the subcarinal nodal station
N3	Metastases in contralateral mediastinal or contralateral hilar lymph nodes, or in ipsilateral or contralateral mediastinal or subcarinal lymph nodes
M: Distant	
M0	No distant metastasis
M1	Metastasis
M1a	Tumor with pleural or pericardial nodules or malignant pleural or pericardial effusions, separate tumor nodule(s) in a contralateral lobe
M1b	Single extrathoracic metastasis in a single organ system ^g
M1c	Multiple extrathoracic metastases in a single or multiple organ system(s)
M1c1	Multiple extrathoracic metastases in a single organ system ^h
M1c2	Multiple extrathoracic metastasis in multiple organ systems

Note: Changes to the eighth edition are in bold.

ORIGINAL ARTICLE



The International Association for the Study of Lung Cancer Staging Project for Lung Cancer: Proposals for the Revision of the N Descriptors in the Forthcoming Ninth Edition of the TNM Classification for Lung Cancer



James Huang, MD,^{a,*} Raymond U. Osarogiagbon, M.B.B.S., FACP,^b Dorothy J. Giroux, MS,^c Katherine K. Nishimura, PhD, MPH,^c Andrea Bille, MD, PhD,^{d,e} Giuseppe Cardillo, FRCS, FETCS,^{f,g} Frank Detterbeck, MD,^h Kemp Kernstine, MD, PhD,ⁱ Hong Kwan Kim, MD, PhD,^j Yolande Lievens, MD, PhD,^k Eric Lim, MB, ChB, MD, MSc, FRCS(C-Th),^{l,m} Edith Marom, MD,ⁿ Helmut Prosch, MD,^o Paul Martin Putora, MD, PhD, MA, MHI,^{p,q} Ramon Rami-Porta, MD,^{r,s} David Rice, MB, BCh,^t Gaetano Rocco, MD, FACS, FRCSEd, FEBTS,^a Valerie W. Rusch, MD,^a Isabelle Opitz, MD,^u Francisco Suarez Vasquez, MD,^v Paul Van Schil, MD, PhD,^w Chi-Fu Jeffrey Yang, MD,^x Hisao Asamura, MD,^y Members of the Staging and Prognostic Factors Committee, Members of the Advisory Boards, and Participating Institutions of the Lung Cancer Domain

Systematische beoordeling CT-thorax

- **Pulmonale nodule/ massa**

- Grootte, ligging, ingroei, gespiculeerd/glad begrensd, aankleuring, holtevorming, necrose, aangrenzende noduli, enz
- T stadium

- **Vergrote lymfeklieren**

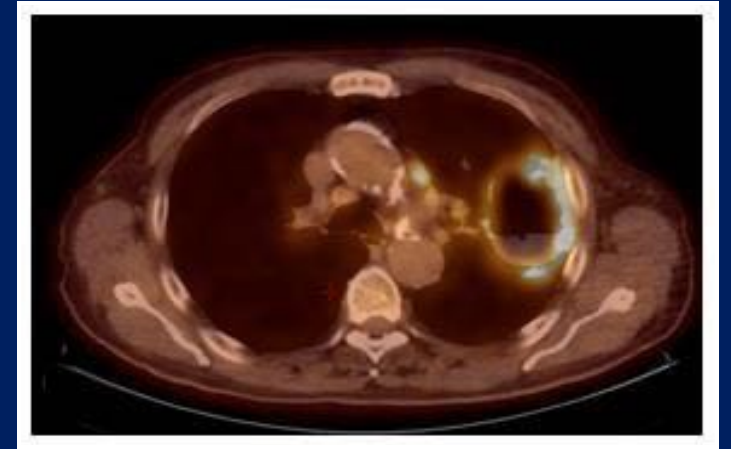
- Lokatie (en verspreidingspatronen kennen), aankleuring, necrose
- N stadium

- **Metastasen op afstand**

- Verspreidingsroutes (bijnieren, lever, lymfeklieren op afstand)
- M stadium

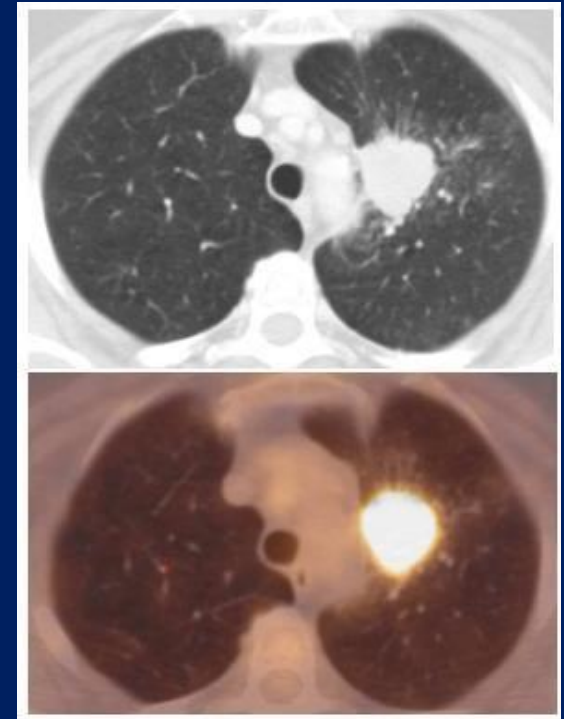
Patroon plaveiselcelcarcinoom

- Meer centraal (bronchus)
- Centrale necrose (altijd) met cavitatie
- Nicotine
- Hemoptoë
- Post-obstructie atelectase
- Inflammatie en infectie
- Reactieve klieren (aankleurend, doorgroei in N1)
- Altijd intense FDG opname (zelfs kleine tumoren)
- BSE, koorts, leucocytose, waisting



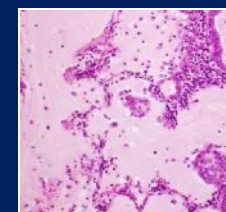
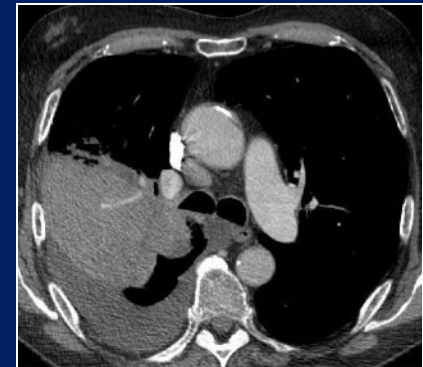
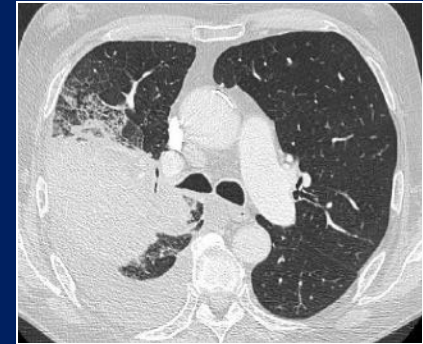
Patroon adenocarcinoom

- Meer perifeer
- Minder obstructie
- Minder infectie/inflammatie
- Minder necrose (betere perfusie, pneumonia like op ceCT)
- Minder reactieve klieren (meer lymfkliermetastasen)
- Variabele FDG uptake (fotopenie in colloid carcinoom, intens in papillair AC)



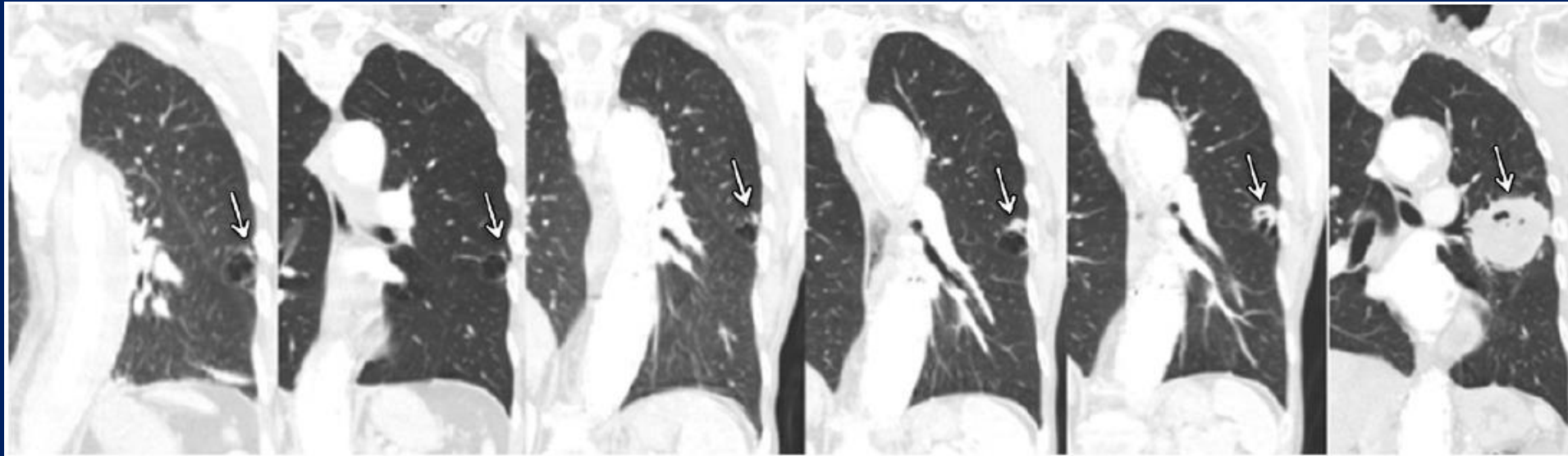
Pneumonia like adenocarcinoom

- Deels matglas
- Luchtbronchogrammen
- Vaten
- Vaak mucineus
- Uitbreiding via luchtwegen (aerogeen)
- Multifocaal
- FDG stapeling varieert
- Voorheen ~~BAC~~



Cyste gerelateerd primair longca

- Zeldzaam kenmerk van NSCLC, incidentie onderschat
- Frequent bij (ex)rokers (field carcinogenese!)
- Meestal (ca 80%) adenocarcinoom
- Voorafgaand of gelijktijdig met longcarcinoom in ca 50%
- Geen voorkeurslokalisatie, perifere distributie



baseline

2 months

15 months

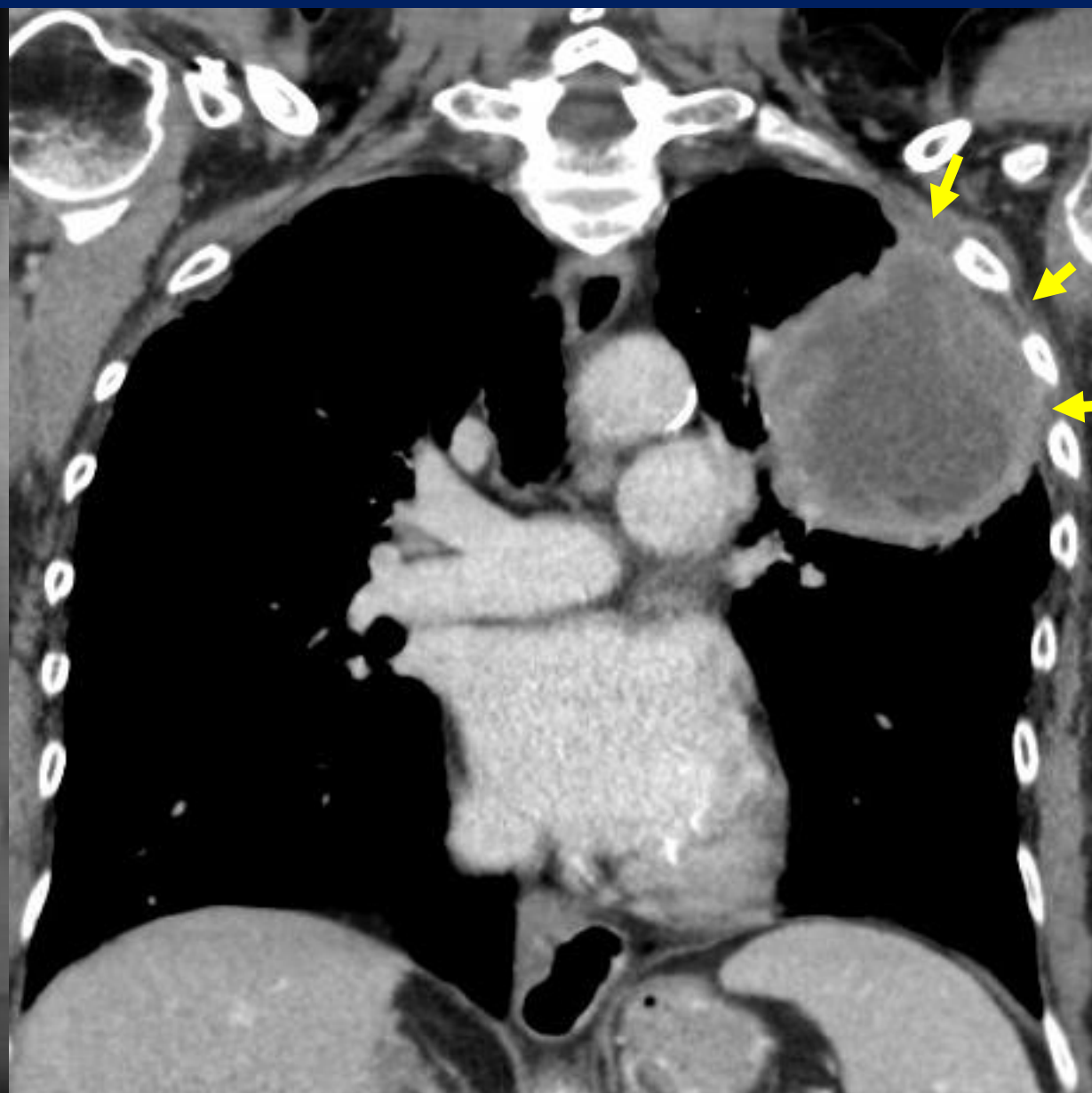
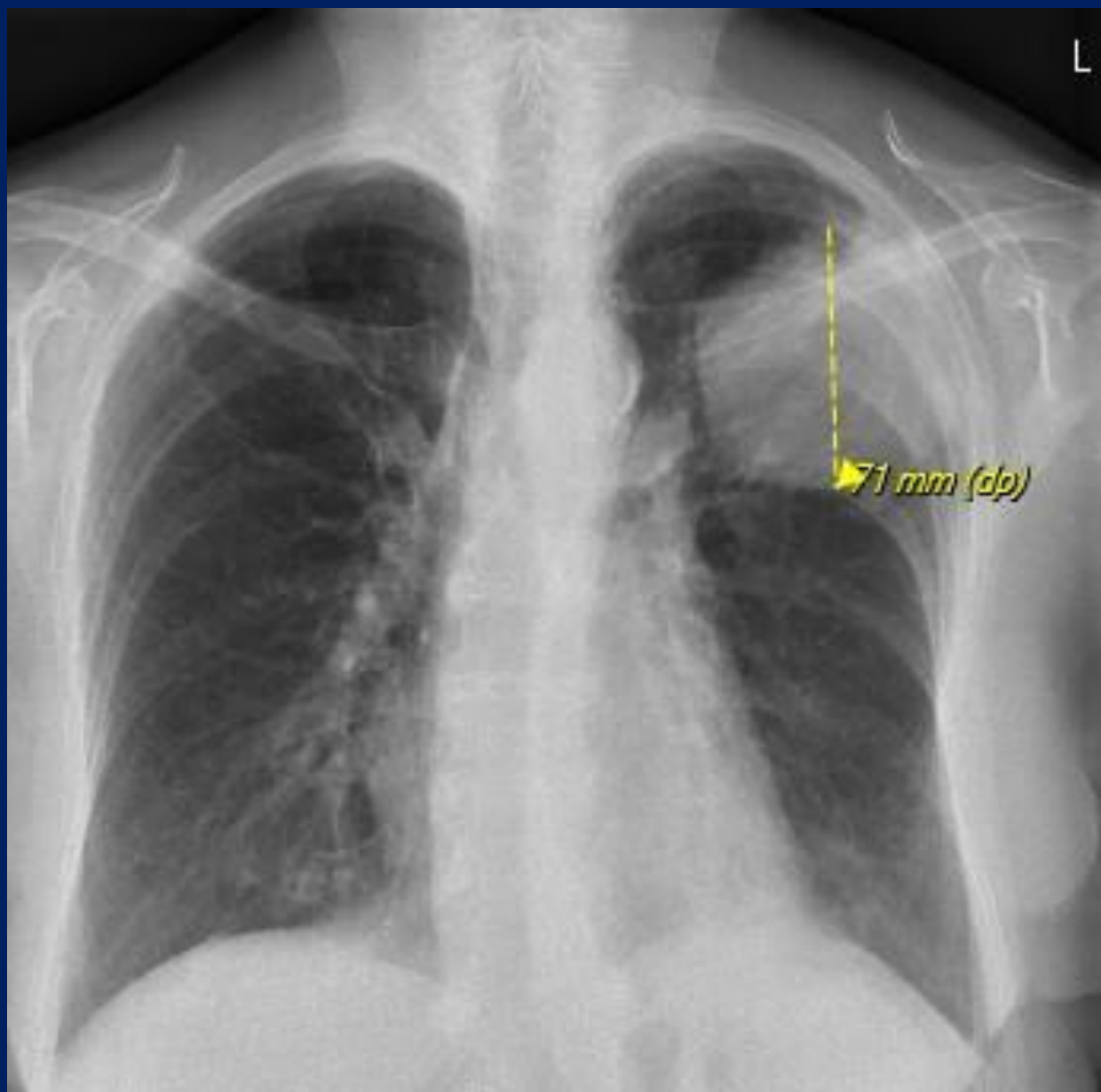
33 months

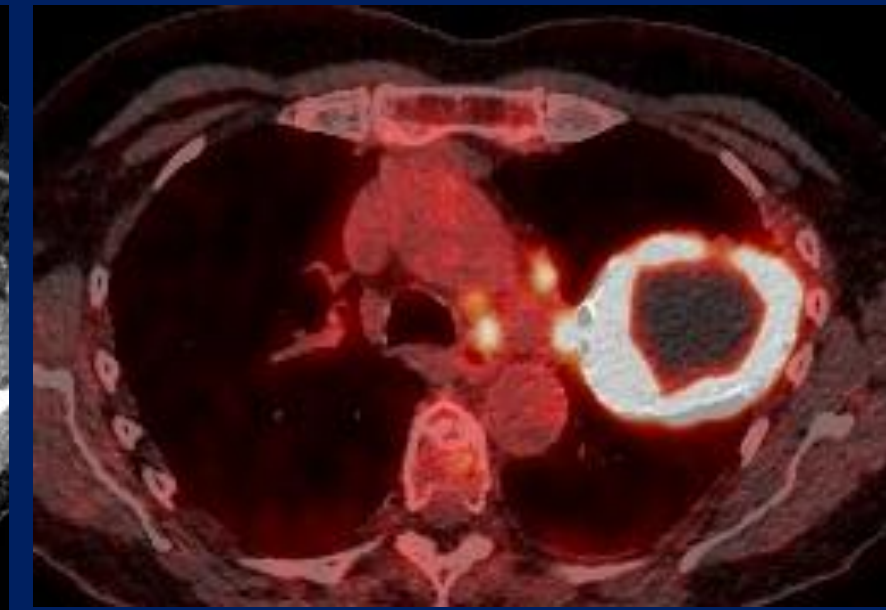
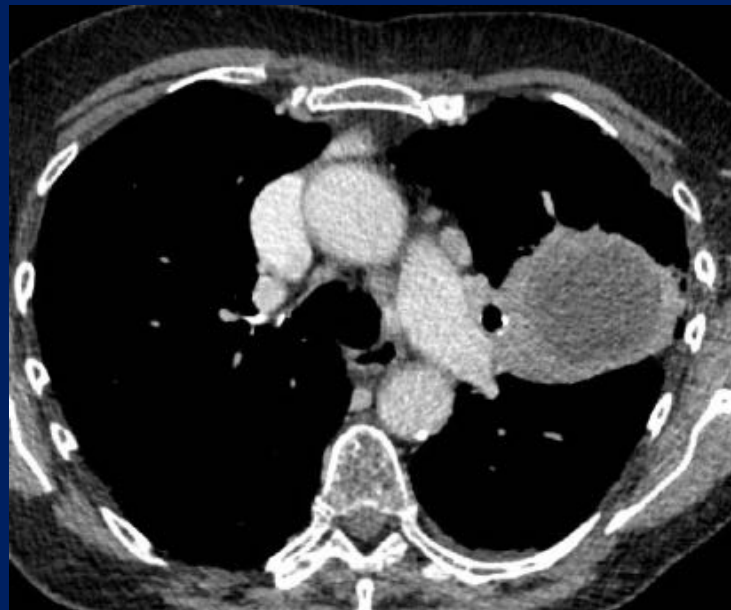
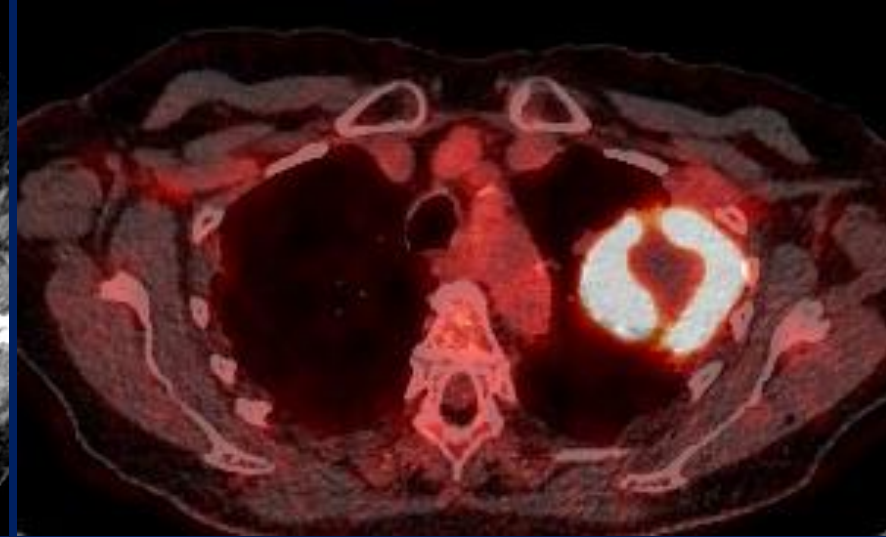
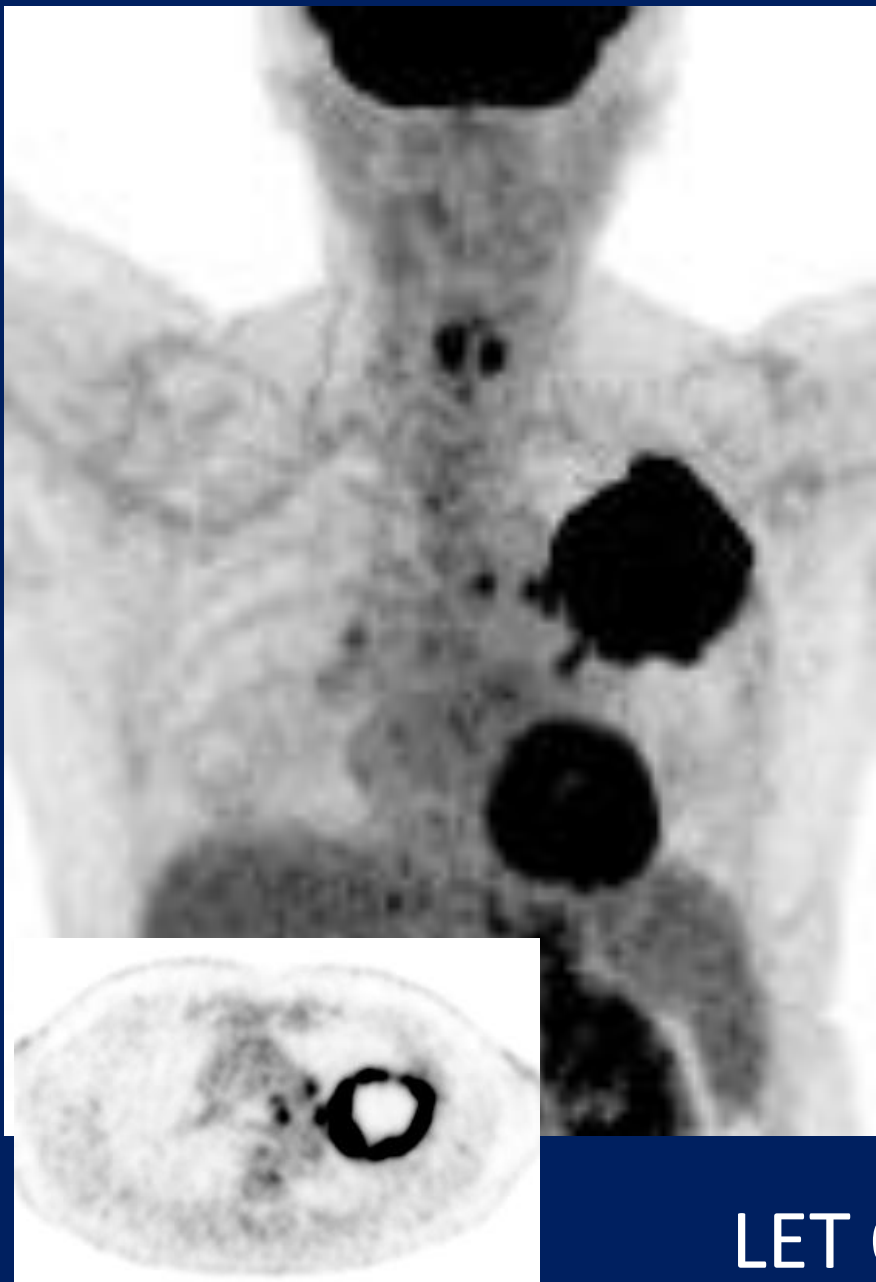
45 months

69 months

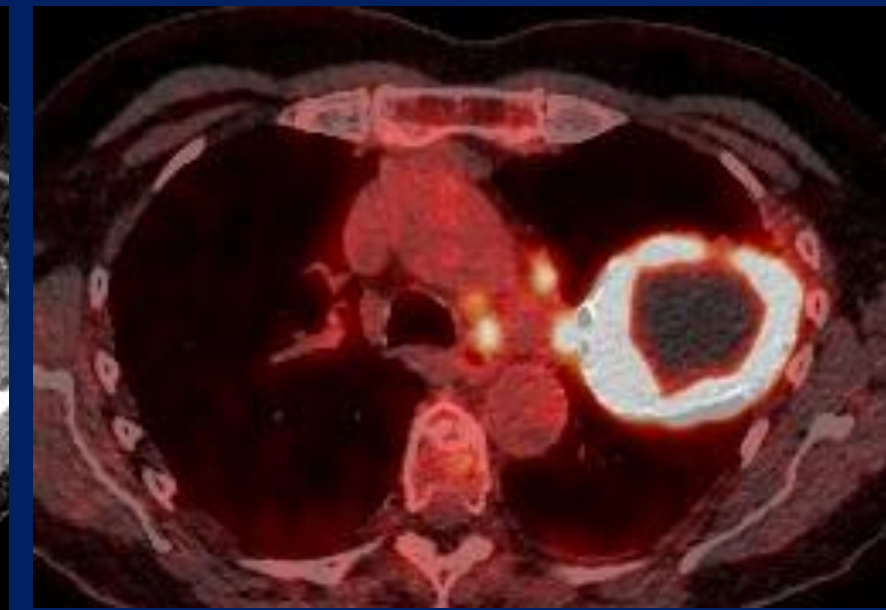
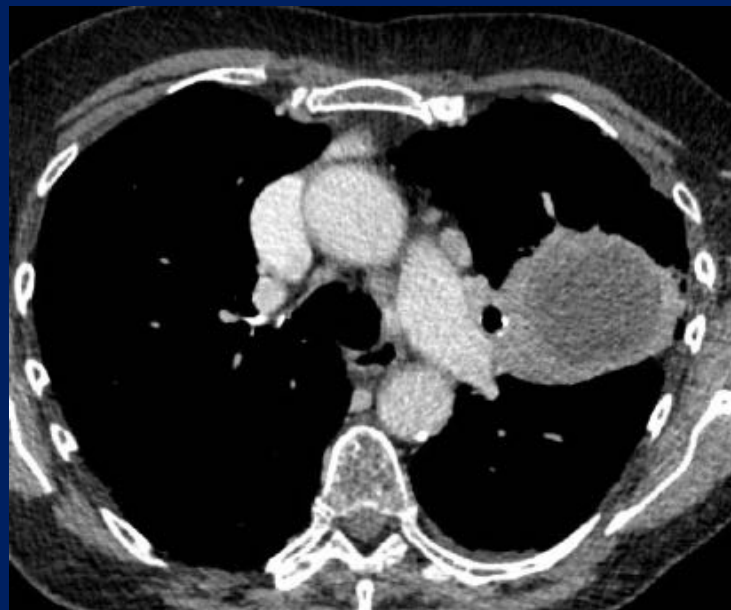
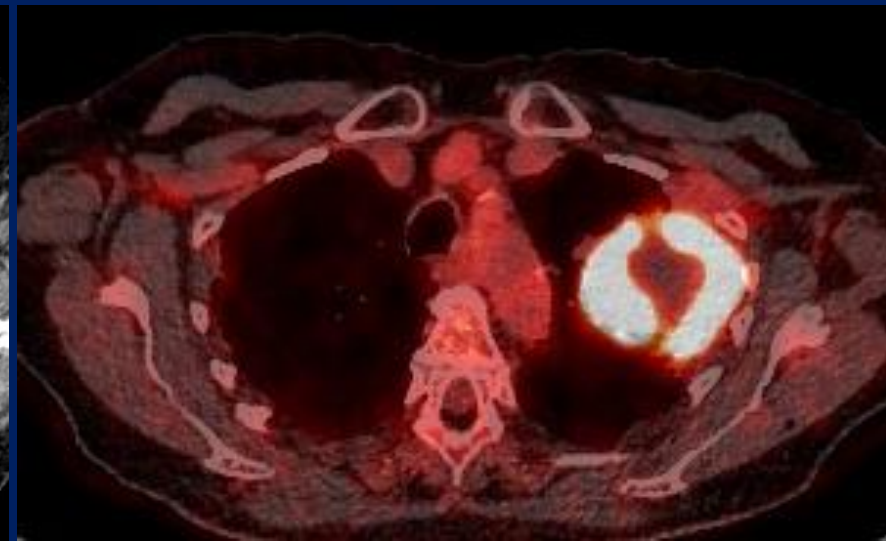
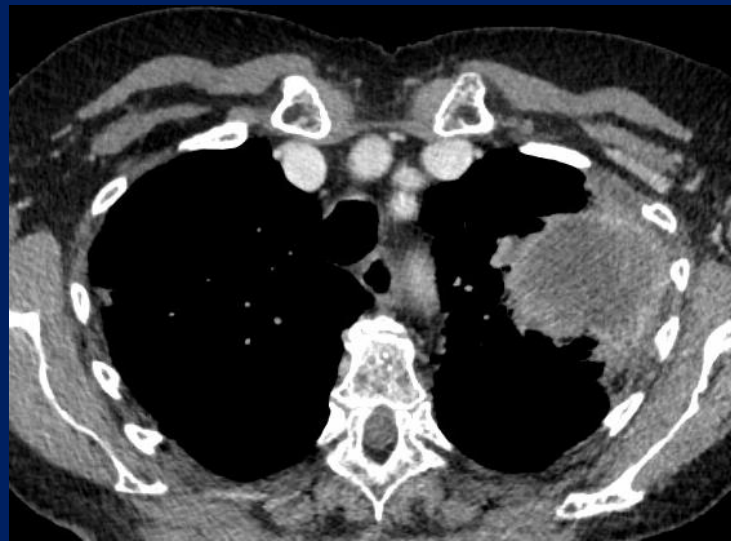
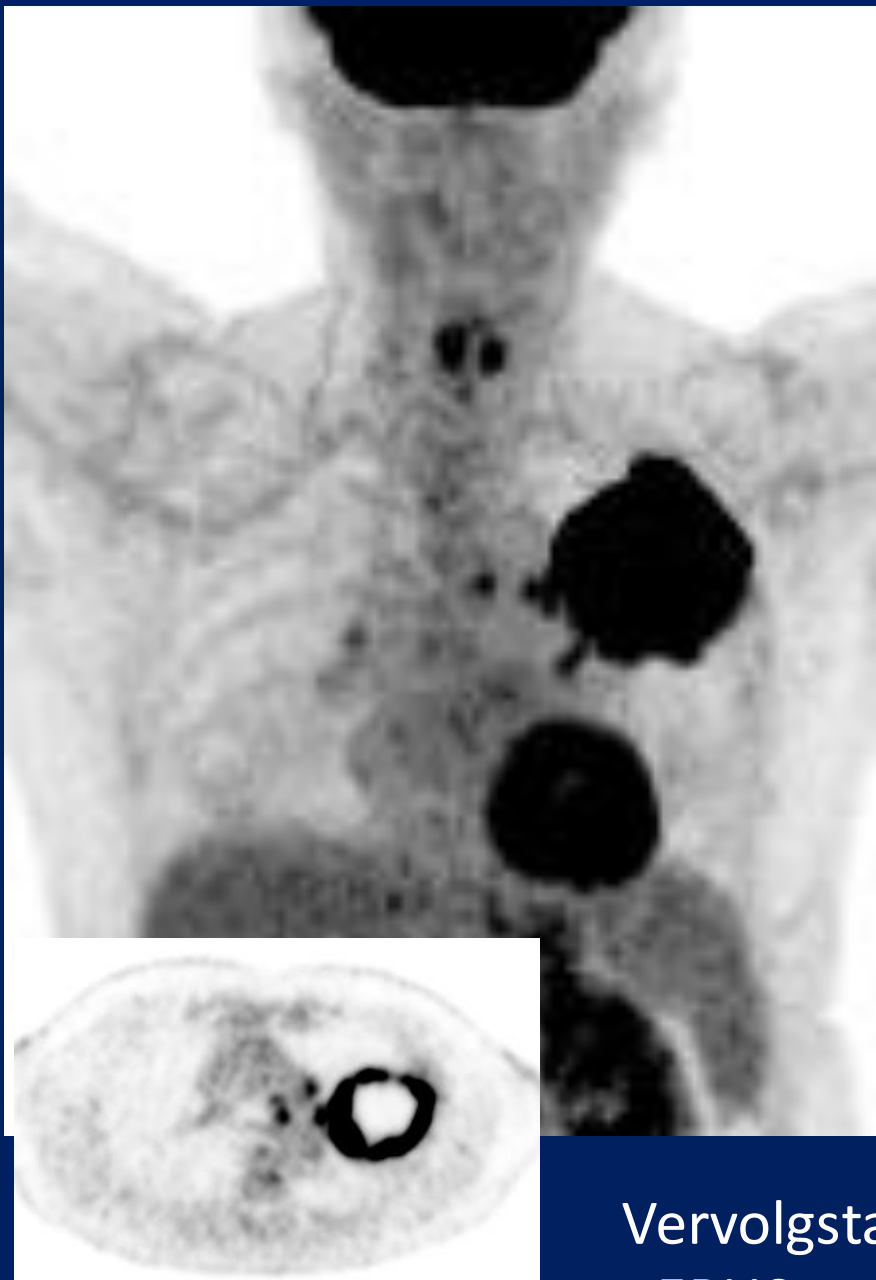
Casus: Belang MDO

- Patiënt met langdurig pijn li schouder
- Ex roker
- CRP (84), anemie, leucocytose (13), trombocytose
- Geen focus voor anemie (MDL)





LET OP DETAILS: CHIRURG, RADIOTHERAPEUT,
INTERVENTIERADIOLOOG



Vervolgstap n.a.v. PET-CT:
- EBUS station 7 en 4L
- CT geleid biopt massa LBK

Uitkomst PA:

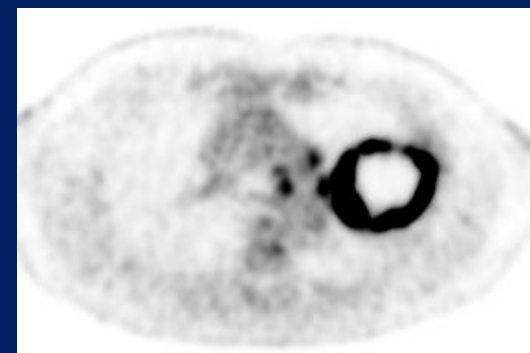
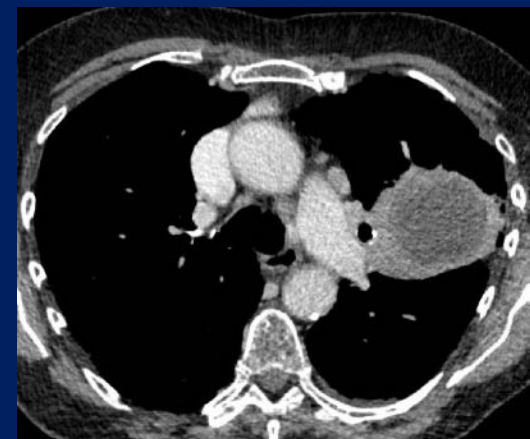
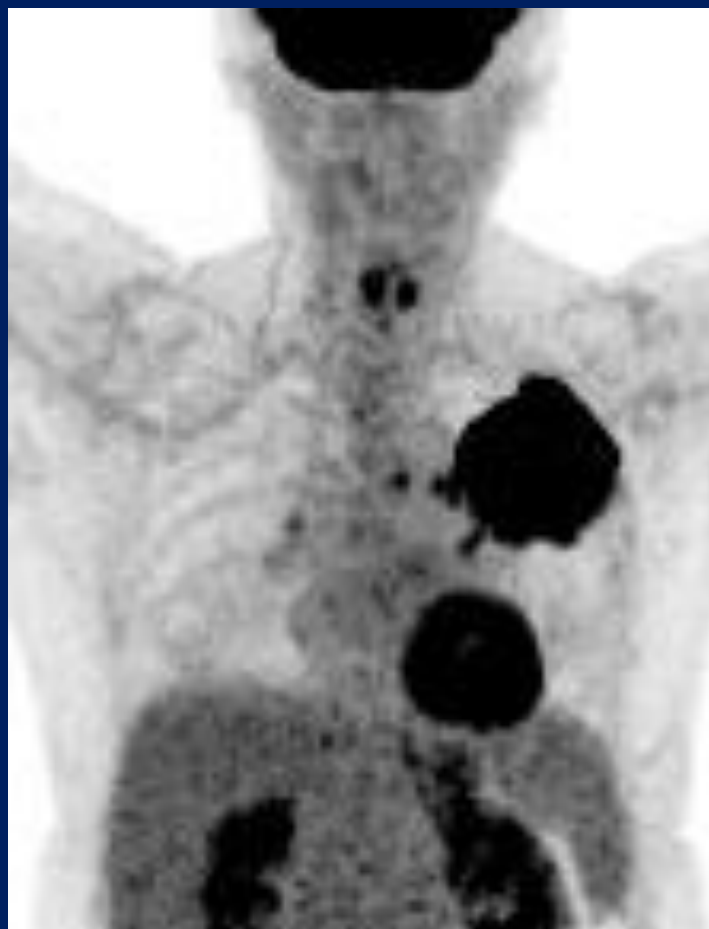
- EBUS station 7 en 4L: reactief
- CT geleid biopt massa LBK:
Enkele atypische cellen
(onvoldoende voor PD-L1 en NGS)

MDO moment of truth voor patiënt:

- Kennis van alle uitkomsten (CT, PET-CT en PA)
- Nogmaals kijken naar CT en PET-CT
- Observer variatie en lokale expertise spelen rol
- Kleine verschillen opties: OK, CRT, inductie?

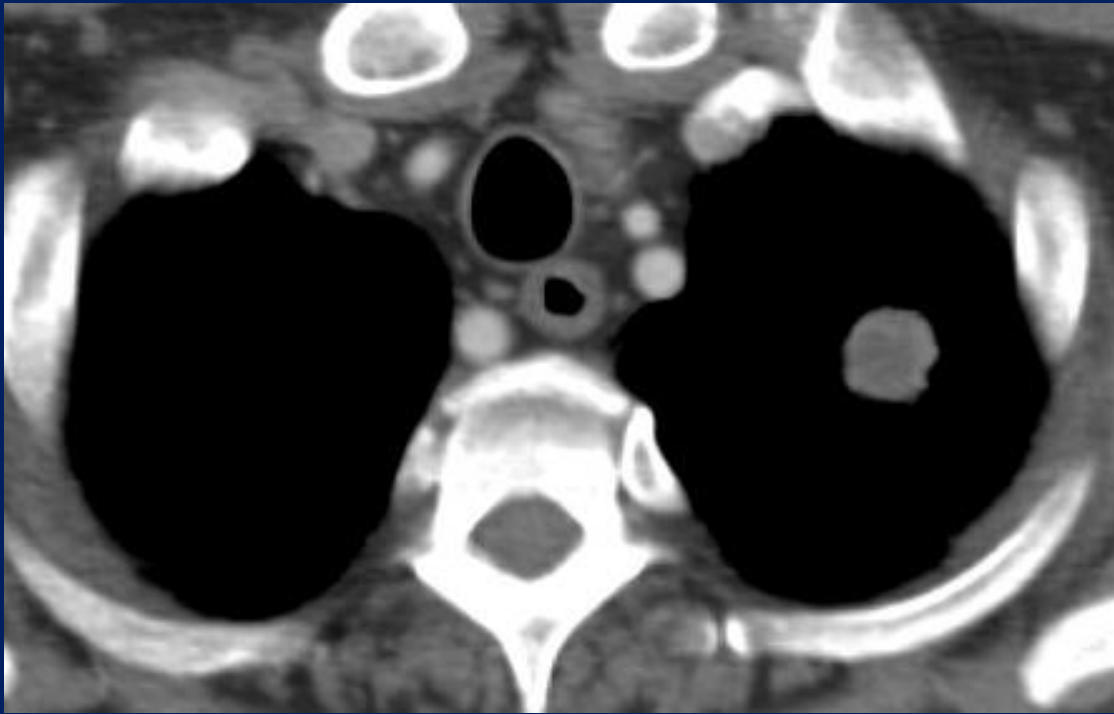
OK incl. partiele ribresecties:

- Adeno-squameus 7.8 cm -> T4N0
- Sclerosering pleura, ingroei in 1 rib (R0) -> PI-3
- Pleuraal fibrosering



Casus: kennis verspreidingspatroon en context

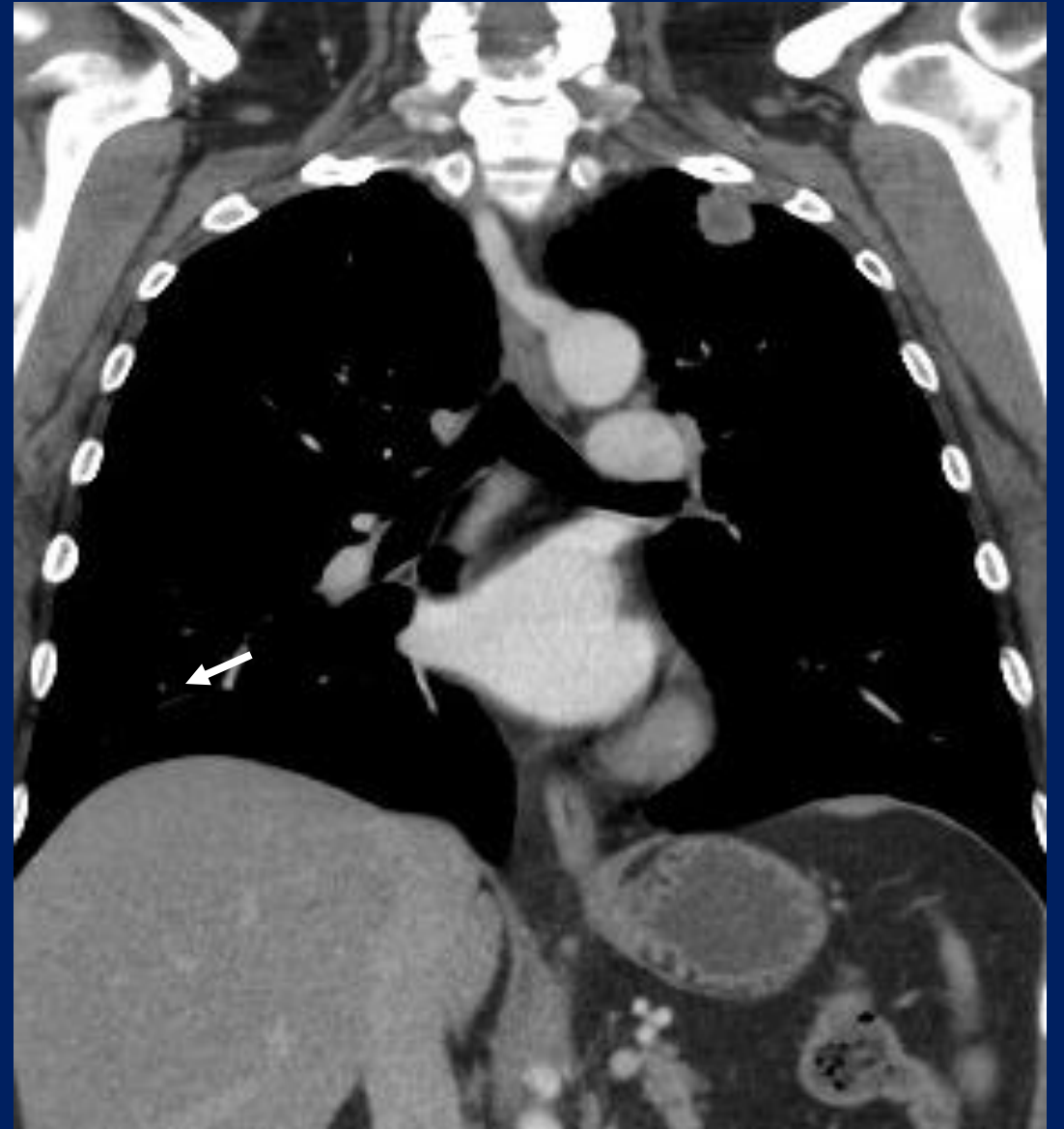
- Ex-roker met toevalsbevinding LBK (2,3 cm)
- CT-thorax en PET-CT

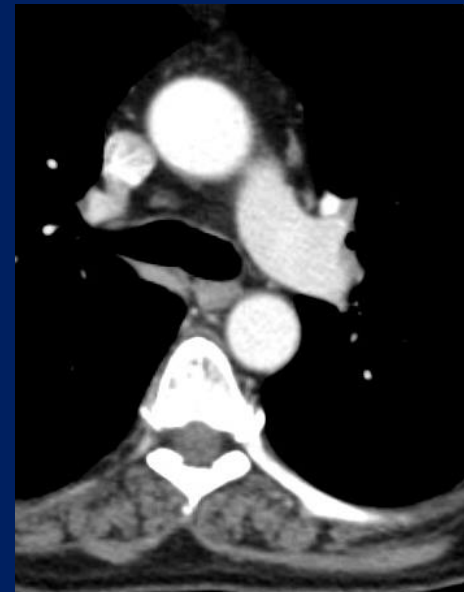
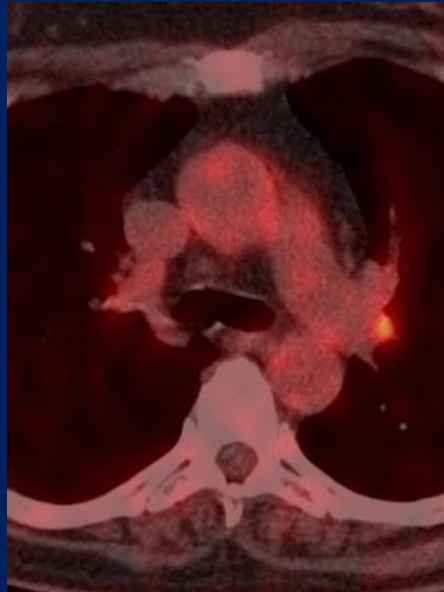
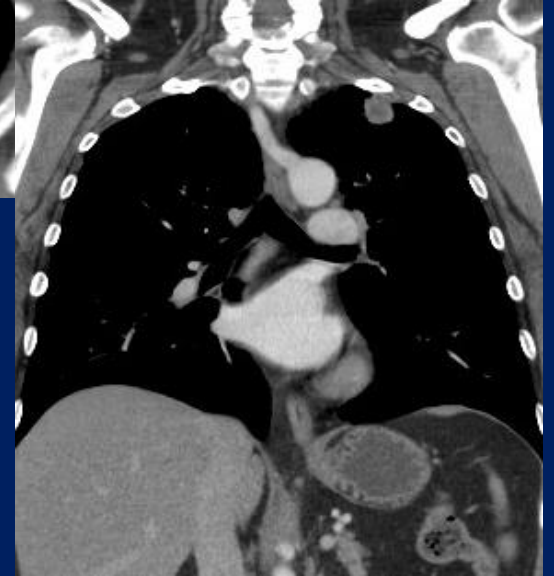
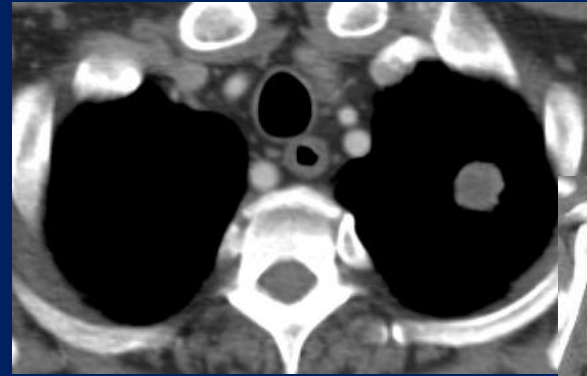
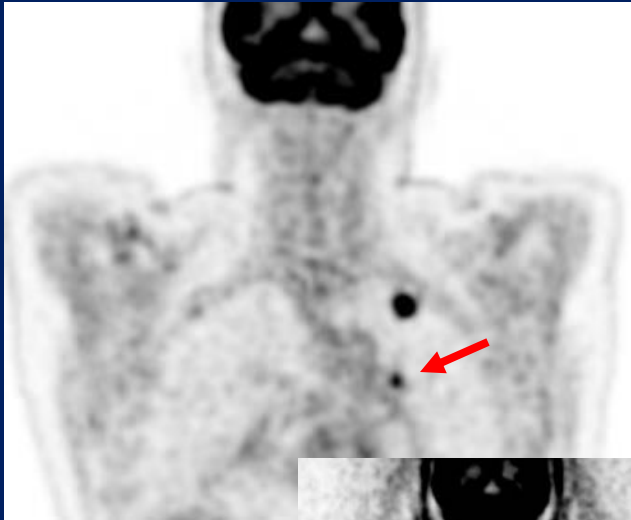


Belangrijkste items CT-thorax

- Nodus 23 mm
- Perifeer LBK, tegen pleura
- Geen Inn met korte as > 1 cm

C/ iT1cN0Mx



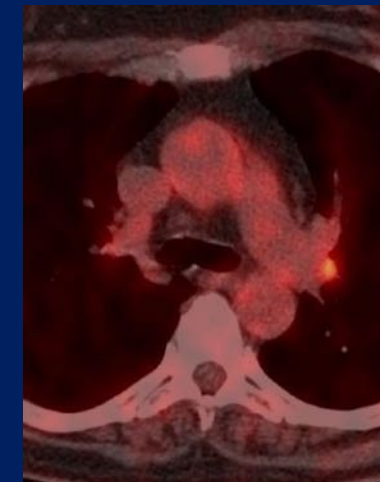
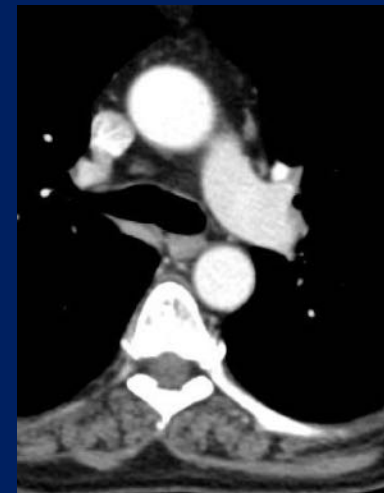
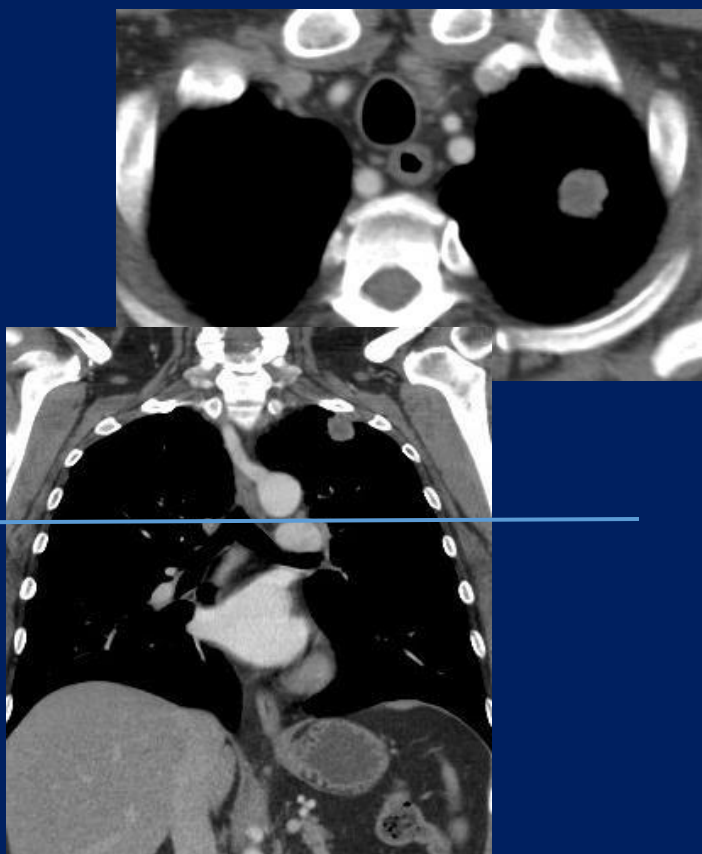


Vragen:

1. Is deze lymfeklier PET-positief?
2. Grens N1 vs N2 lokalisatie linker zijde?

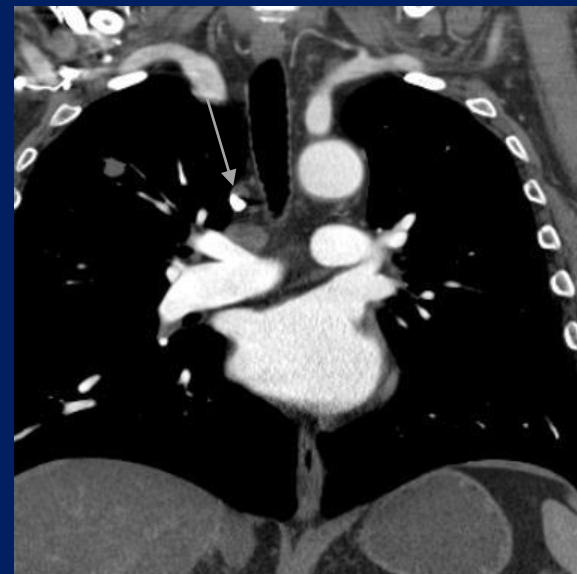
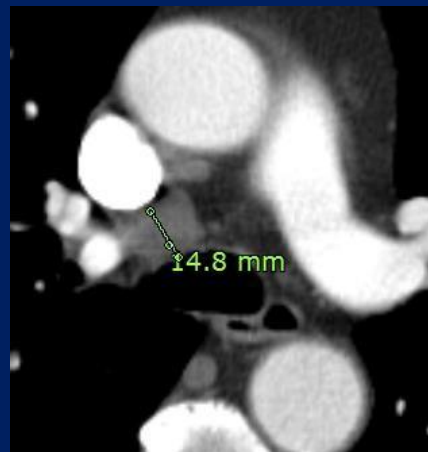


Toelichting lymfeklierdrainage (LBK)



Station 10L = N1!
Bovengrens 10L = bovenbegrenzing
pulmonaal arterie

Toelichting lymfeklierdrainage (RBK)



Station 10R = N1!

Ondergrens 4R = Caudale begrenzing v. azygos

Toelichting PET-CT en lymfeklieren

Cochrane Database Syst Rev. 2014 Nov 13;11:CD009519. doi: 10.1002/14651858.CD009519.pub2.

PET-CT for assessing mediastinal lymph node involvement in patients with suspected resectable non-small cell lung cancer.

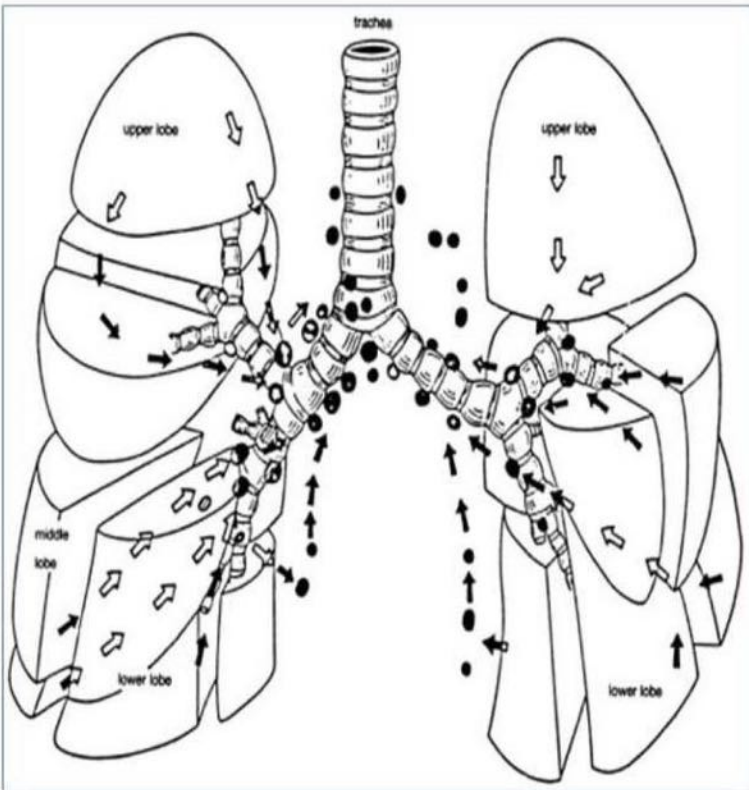
Schmidt-Hansen M¹, Baldwin DR, Hasler E, Zamora J, Abaira V, Roqué I Figuls M.

The differences in PET-CT accuracy estimates between scanner makers, NSCLCsubtypes, FDGdose, and country of study origin, along with the general variability of results, suggest that

all large centers should actively monitor their accuracy

- Sensitivity 80%
- Specificity 80%

Toelichting patroon lymfeklierdrainage



Lymph is transported from the periphery toward more proximal lymphatics and nodes. Lymphatic usually drain sequentially into the intralobular, interlobular, lobar, hilar and mediastinal nodes.

N2 ziekte:

- LBK: station 5
- LOK,ROK+MK: station 7
- RBK: station 4R

Restadiëring

- Alle diagnostiek na initiële behandeling
- Respons evaluatie
 - Visueel
 - SUV? MTV?
 - AI/software ondersteuning CT en PET/CT?
- Follow up stadium 3 (landelijke multicenter studie PET/CT)
- Oligoprogressie en oligometastasering
 - Belangrijk of enige downstaging verkregen kan worden
 - PET toont plek met nog beperkte activiteit -> vervolg = MDO beslissing
- Praktijkvoorbeeld



CONCLUSIES

- Beeldvorming (CT, FDG PET-CT) essentiële rol bij stadiëring en re-stadiëring NSCLC
- FDG PET-CT toepassingen nemen toe:
 respons evaluatie/oligo metastasering/oligo progressie
- Observervariatie belangrijke rol, ook binnen het MDO
- MDO cruciaal moment voor besluitvorming en reflexie (contextkennis)
- Behoefte aan (na)scholing in een multi-disciplinaire context?
- Correlatie beeldvorming met pathologie en kliniek verhoogt de kwaliteit van beoordeling
- Artificial intelligence gaat hierbij mogelijk (in de toekomst) helpen

Uitdagingen NSCLC imaging (rol DTG?)

- Scholing en nascholing beoordeling
 - Total body PET, CT, etc.
- Correlatie beeldvorming (anatomisch/metabool-moleculair) met PA
- Implementatie AI
- Standaardisatie verslaglegging
- MDO ondersteuning (juridische consequenties besluitvorming)
- Stimuleren contextkennis met multidisciplinaire ondersteuning
- Kennis delen m.b.t. richtlijn niet-kleincellig bronchuscarcinoom

Vragen?



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