DIAGNOSI / STADIAZIONE DEL TUMORE DEL POLMONE: Il ruolo del Medico Nucleare

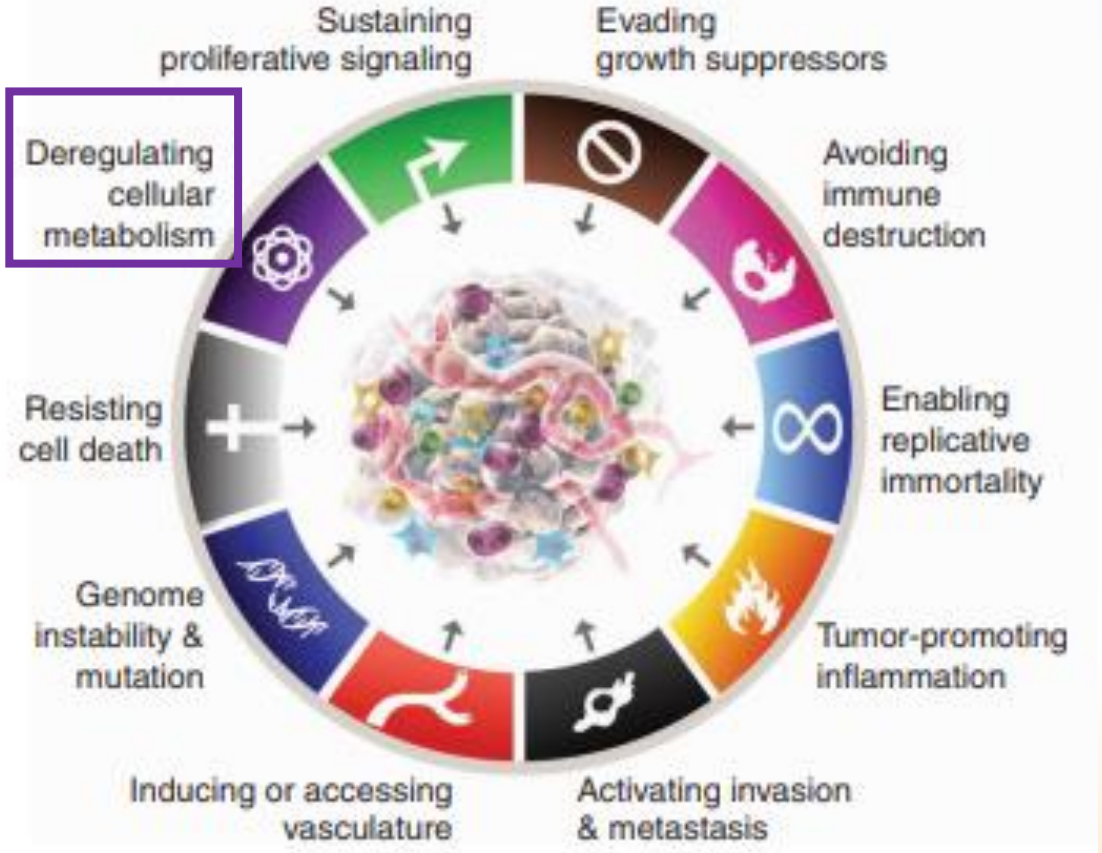
Laura Olivari
Dipartimento di Medicina Nucleare
IRCCS Sacro Cuore Don Calabria (Negrar, VR)

SACRO CUORE DON CALABRIA
IRCCS
Istituto di Ricovero e Cura a Carattere Scientifico
Sacro Cuore - Don Calabria
Ospedale Classificato e Presidio Ospedaliero Accreditato - Regione Veneto

TUMORE DEL POLMONE: dallo screening al trattamento

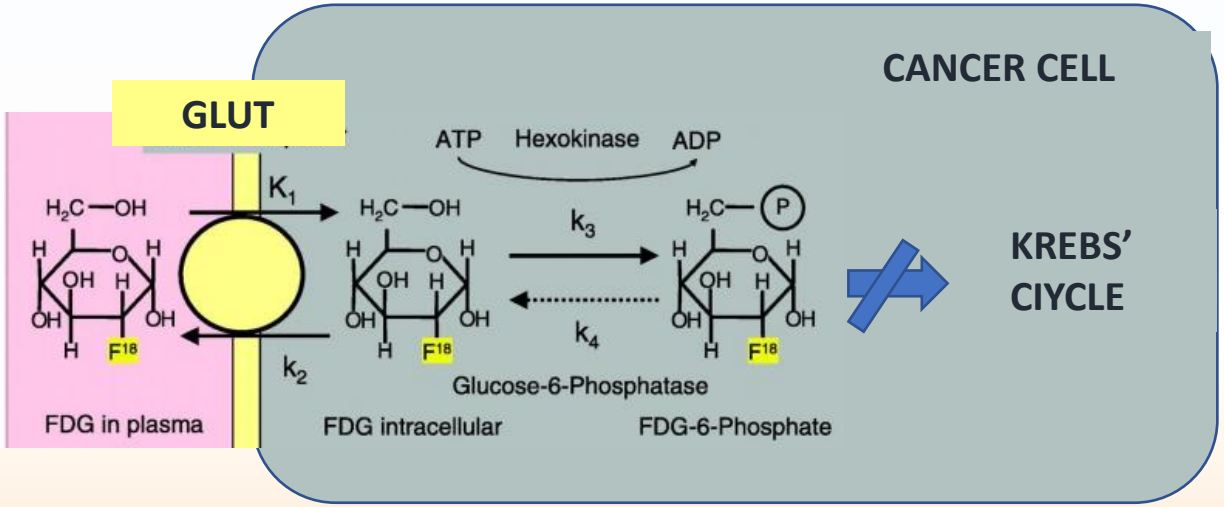
Venerdì 11 novembre 2022

18F-FDG : TRACCIANTE DI GLICOLISI



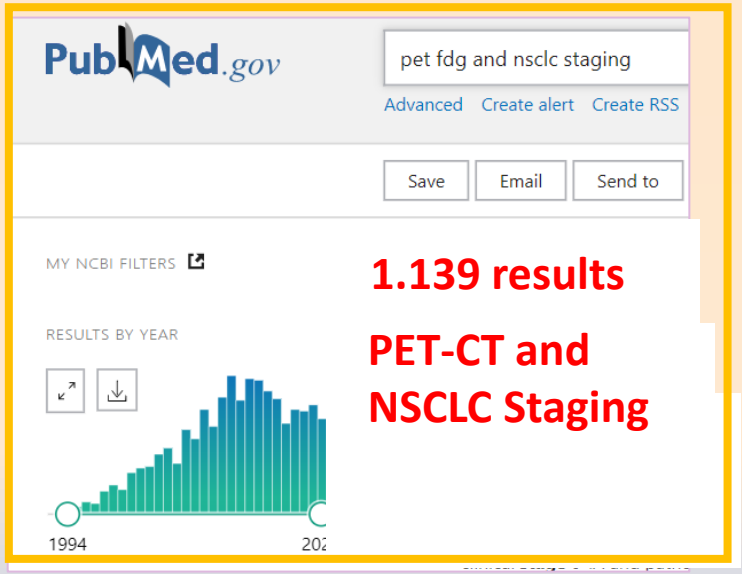
Hanahan and Weinberg, Cell 2011

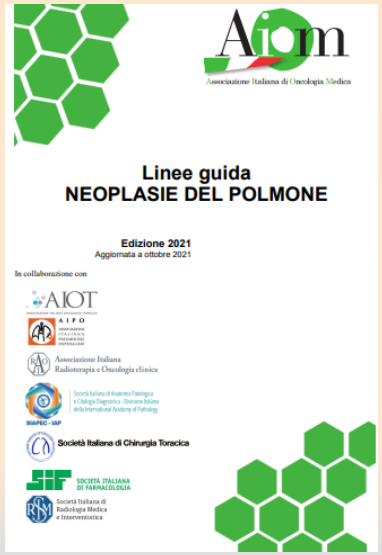
- **FDG** distribution reflects **glucose uptake and phosphorylation by cells in the body**.
- **FDG** mimics the native compounds **but** becomes **trapped in the cells**



18FDG PET/CT and NSCLC

SINCE 2000





Clinical Trial > Lancet. 2002 Apr 20;359(9315):1388-93. doi: 10.1016/s0140-6736(02)08352-6.

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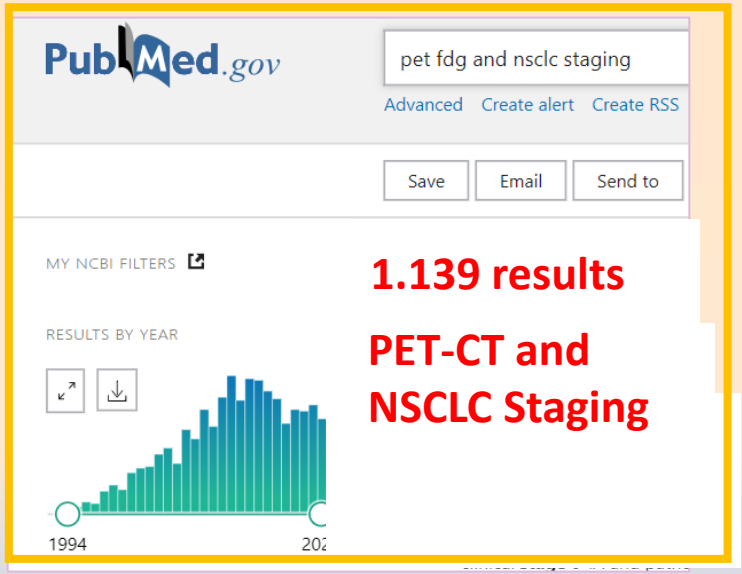

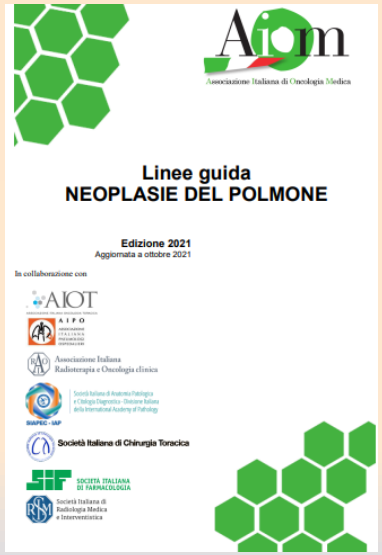

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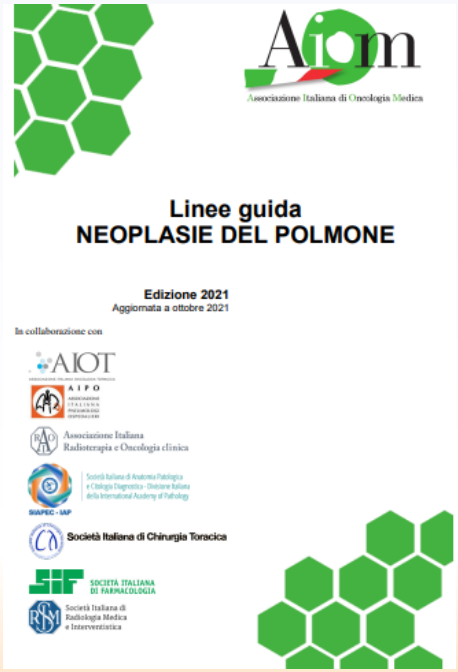
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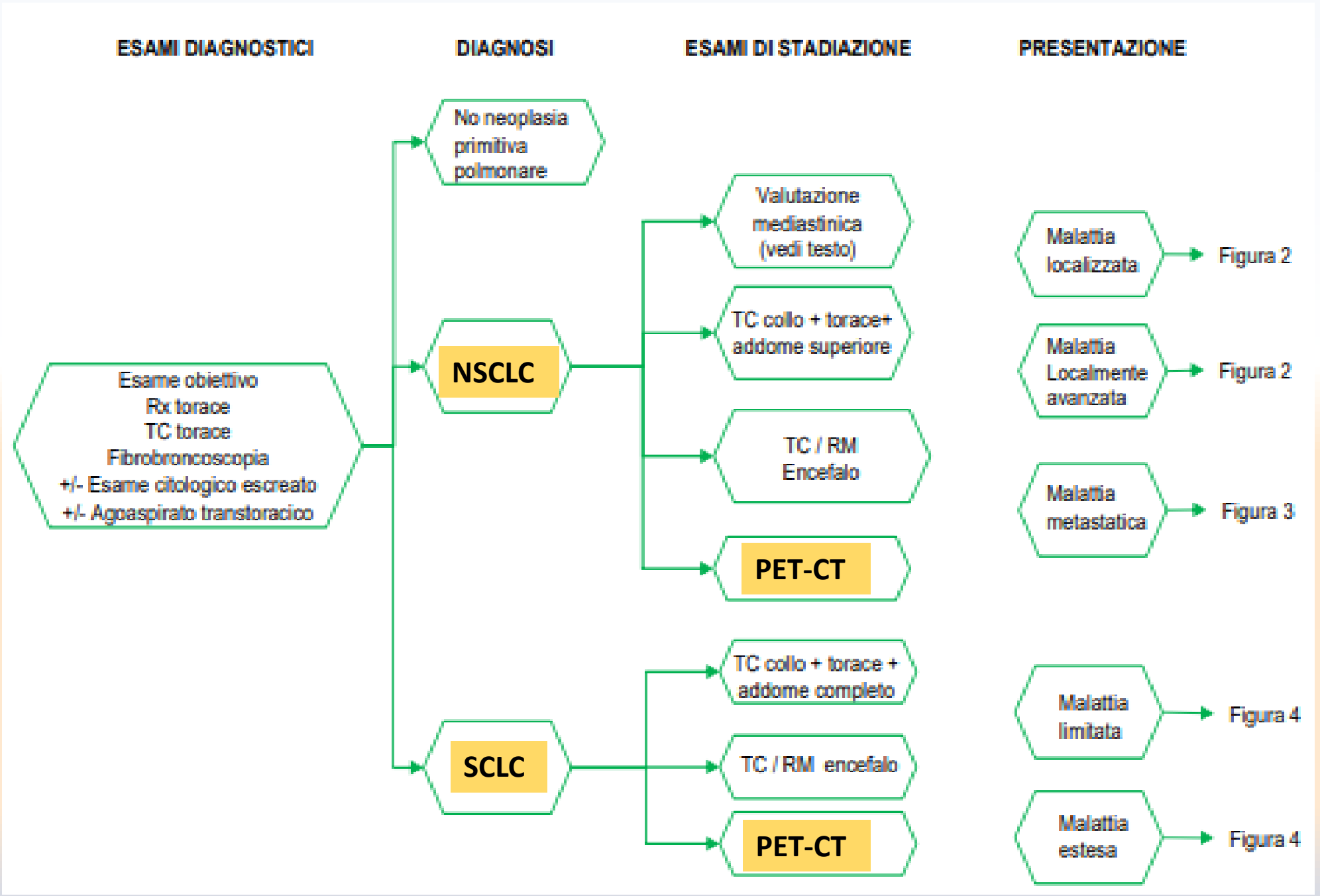
Società Italiana di Radiologia Medica e Interventistica


ESAMI DIAGNOSTICI
DIAGNOSI
ESAMI DI STADIAZIONE
PRESENTAZIONE
Esame obiettivo
Rx torace
TC torace
Fibrobroncoscopia
+/- Esame citologico escreato
+/- Agoaspirato transtoracico
No neoplasia primitiva polmonare
NSCLC
SCLC
Valutazione mediastinica (vedi testo)
TC collo + torace+ addome superiore
TC / RM Encefalo
PET-CT
TC collo + torace + addome completo
TC / RM encefalo
PET-CT
Malattia localizzata
Figura 2
Malattia Localmente avanzata
Figura 2
Malattia metastatica
Figura 3
Malattia limitata
Figura 4
Malattia estesa
Figura 4

18FDG PET/CT and NSCLC in stadiazione

PDTA REGIONE VENETO

Allegato A al Decreto n. 088 del 05 LUG. 2022 pag. 29/95

Lo studio funzionale è necessario nel paziente potenzialmente chirurgico (I e II stadio); può essere indicato anche in altri stadi a discrezione dello pneumologo e deve comprendere:
- sempre: spirometria, DLCO, EGA, valutazione del rischio cardiovascolare;
- quando richiesto: test da sforzo (stair climbing, shuttle test, test da sforzo cardiopolmonare), scintigrafia polmonare perfusoria e eventuale ventilatoria con valutazione della perfusione regionale.

PET-TC con 18FDG per stadiazione:

Nei pazienti con neoplasia periferica in stadio cIA oppure opacità tipo ground glass ≥ 1 cm o noduli a densità mista con parte solida ≤ 1 cm e senza ulteriori reperti patologici alla TC del torace, la PET-TC non è necessaria per completare la stadiazione. Negli altri casi la PET-TC è indicata per la stadiazione (eccetto cerebrale) se il paziente è candidato ad un trattamento curativo, pure con clinica negativa e TC con mdc negativa per lesioni extratoraciche.

6) VALUTAZIONE MULTIDISCIPLINARE

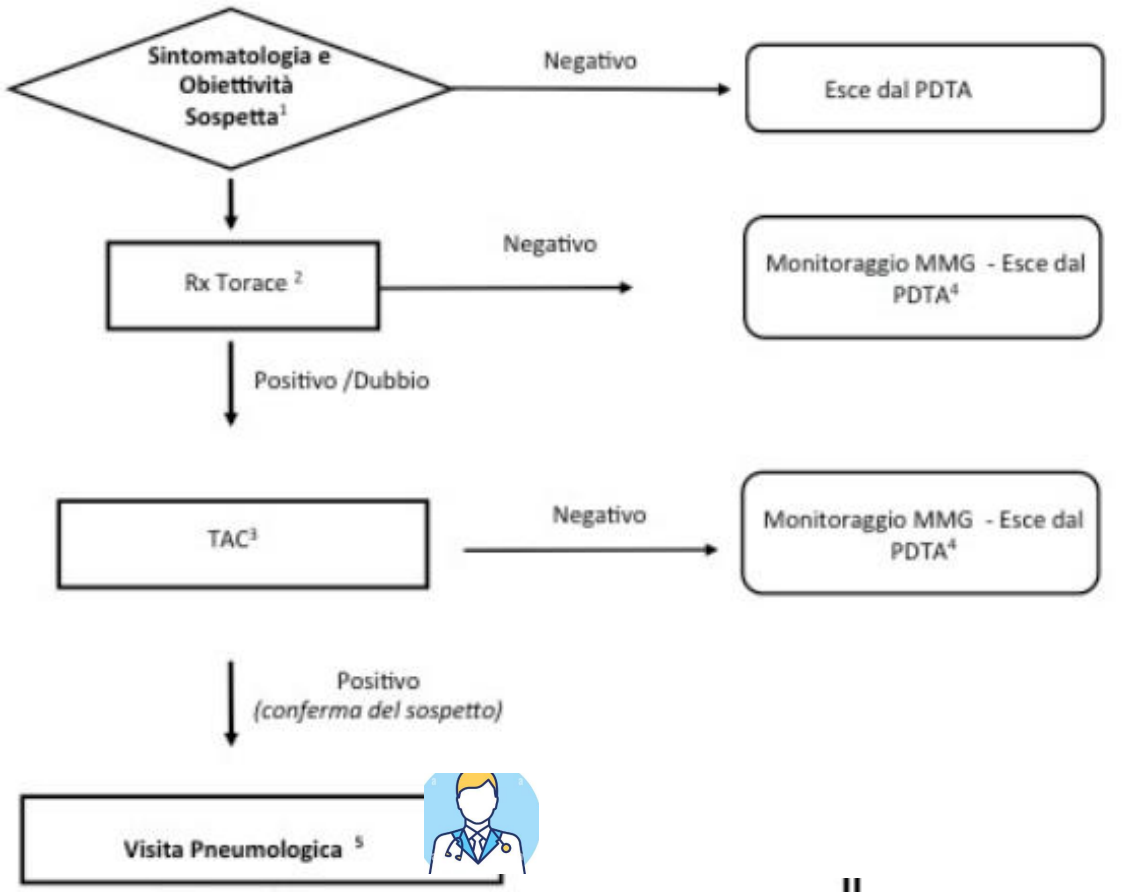
Il core team del gruppo multidisciplinare deve essere composto come minimo dalle seguenti professionalità: chirurgo toracico, oncologo medico, radioterapista oncologo, pneumologo, radiologo (in rapporto alla stadiazione) e case manager. La figura del palliativista si associa al core team nei casi che non accedono ai trattamenti e/o necessitano di cure simultanee.
A seconda della necessità o della disponibilità può essere integrato dalle seguenti figure professionali: anatomo-patologo, psicologo e medico nucleare.
Il meeting è il momento in cui avviene la discussione multidisciplinare dei casi clinici con l'intento di definire la diagnosi e lo stadio della malattia, cui segue la formulazione della strategia terapeutica con indicazioni precise sull'approccio chirurgico, radioterapico, sulle terapie oncologiche sistemiche con valutazione della relativa risposta, sugli approcci riabilitativi, cure simultanee, di supporto e di follow-up, in rapporto a linee guida condivise. In questo contesto la possibilità di arruolamento in trial clinico sarà sempre valutata in ogni setting. Il team fornisce inoltre secondi pareri su richiesta di medici, o di pazienti, e si riserva di avviare specifici casi a discussione del Molecular Tumor Board (MTB) Regionale.
Competenze gruppo: completamento diagnosi; eventuale completamento stadiazione; definizione piano terapeutico, definizione piano palliativo; selezione dei casi da avviare a discussione del MTB.

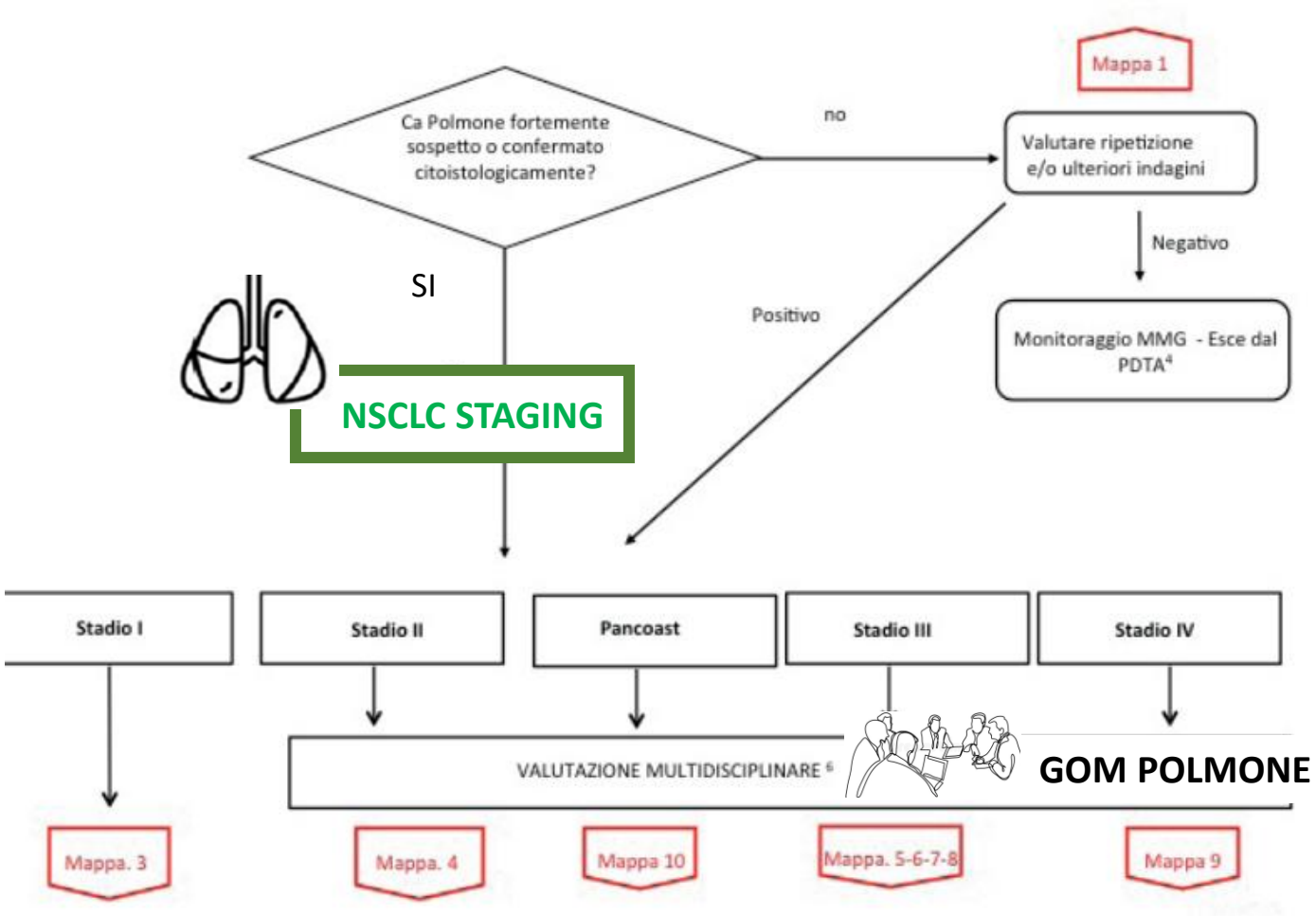
PET-CT indicata per stadiazione di paziente candidato a trattamento curativo (**anche se** TC con mdc negativa per lesioni extratoraciche)

PET-CT NON è utile valutare localizzazioni **encefaliche di NSCLC**

ECCEZIONI in cui PET-CT NON è indicata
- Neoplasia periferica cIA
- GGO >1 cm
- Noduli densità mista con parte solida < 1 cm

18FDG PET/CT and LUNG CANCER





SOLID PULMONARY NODULE > 8mm in diameter with **suspicious CT findings**

18FDG PET/CT and LUNG CANCER

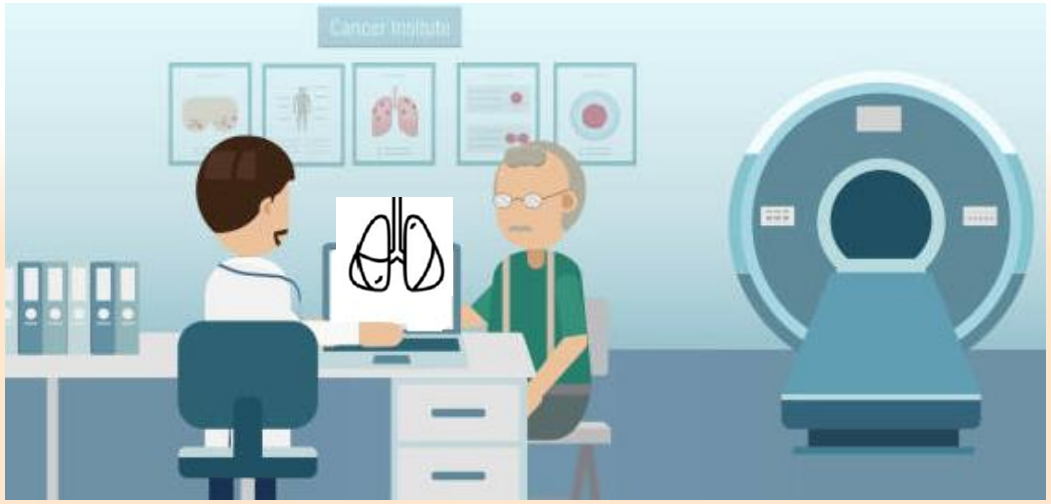
- **SOLID PULMONARY NODULE** > 8mm in diameter with **suspicious CT findings**

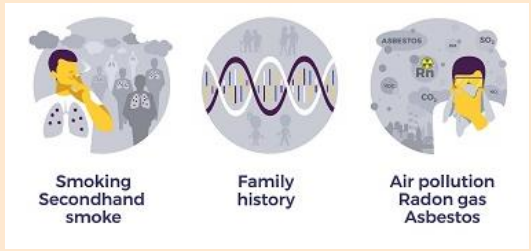
GROWTH RATE	Fast doubling time (20-400 days) more likely infectious or inflammatory cause
LOCATION	Upper lobe is more common site for malignant nodules
MARGINS	Lobulated os speculated margins are strongly associated with malignancy; notches are commonly seen in adenoCA with overt invasion
CAVIATION	Irregular thicker walls > 15 mm
CALCIFICATION	Punctate and eccentric (evidence of necrosi within nodule) calcification may occur with malignancy
SIZE	Nodules > 2 cm are more likely to be malignant
OTHER features	Vascular convergence, dilated bronchus leading into the nodule

NODULE

SOLID PULMONARY NODULE > 8mm

CLINICAL pre-test probability of malignancy





MILD pre-test probability (5-60%):

- Perform PET/CT → if positive then Biopsy

FDG PET/CT: **high VPN** → **follow up**

HIGH pre-test probability (>60%):

- Surgical Biopsy → then PET/CT for staging
- Non surgical biopsy → then PET/CT for staging
- PET/CT to guide biopsy

FDG PET/CT: **low VPN;** histologic evaluation needed

Nodule > 3 cm is more likely to be Lung Cancer

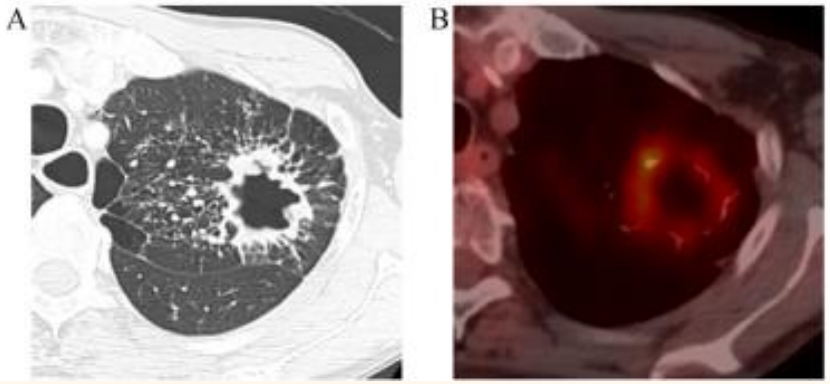
Nodules with **higher FDG-uptake compared to mediastinal blood pool**, are at greater suspicion for lung cancer, regardless of the standardized uptake value (SUV) analysis **(NCCN 2022)**

NODULE

FDG-PET/CT PITFALLS

FALSE POSITIVE

FALSI POSITIVI PET-CT

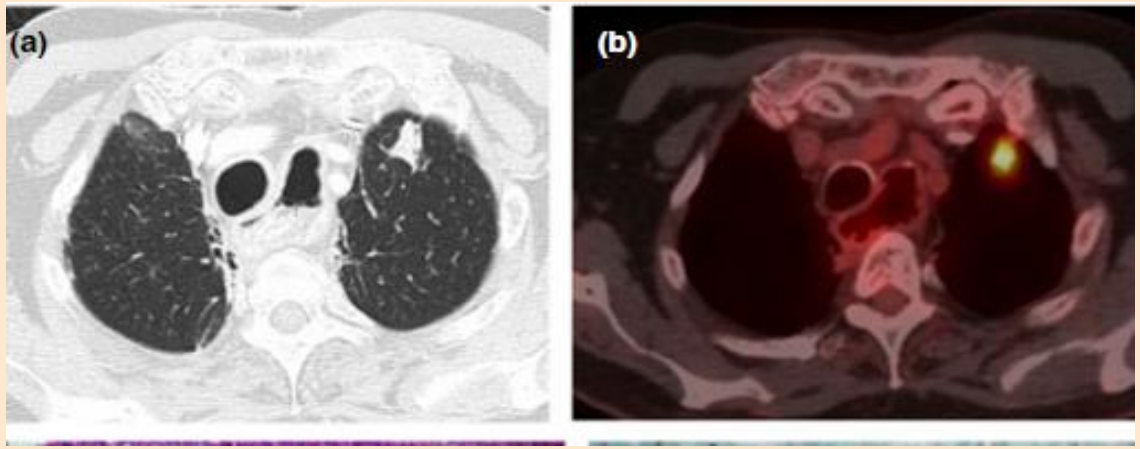


CAVITARY MASS

Positive PET-CT

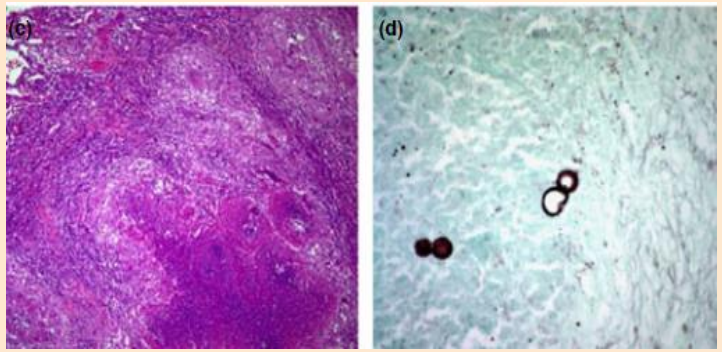
Biopsy: Mycosis

- Nontuberculous mycobacterial infection
- Fungal infection
- Granulomatosis with polyangiitis (Wegener')
- Pulmonary Langerhans cell histiocytosis



SPICULATED LESION

Positive PET/CT (SUVmax 6)



Necrotising granulomatous inflammation (blastomycosis)

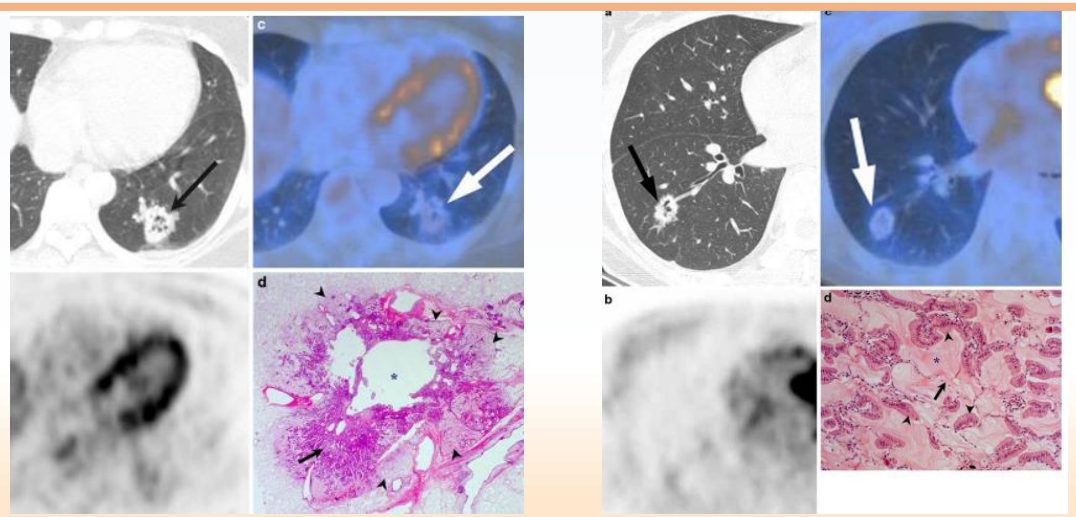
Mycoses. 2014 Apr;57(4):197-208.

NODULE

FDG-PET/CT PITFALLS

FALSE NEGATIVE

FALSI NEGATIVI PET-CT



Negative PET

Bronchioloalveolar AdenoCa
(Mucin producing NSCLC)

LOW tumour density or Ground Glass Lesion

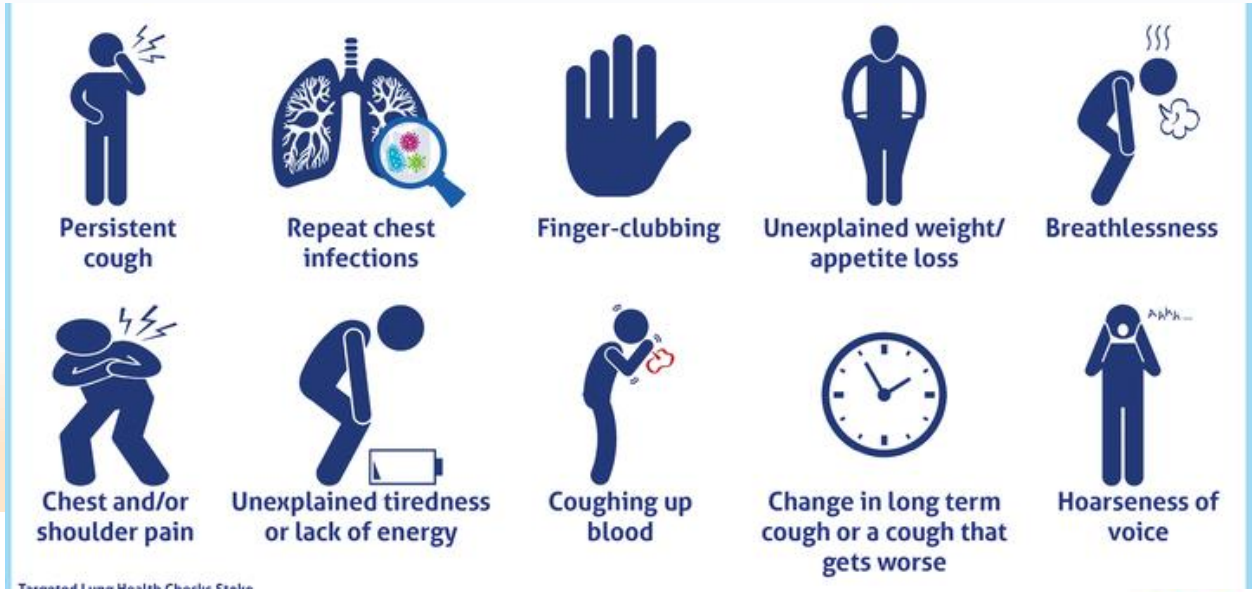
- **Mucinous** adenocarcinomas (**bronchiolo-alveolar**e 10% NSCLC)
- Adenocarcinomas with a **lepidic** growth pattern
- **Adenocarcinoma in situ**
- **Minimally invasive adenocarcinomas**
- **Carcinoid tumors**

SOLID component < 7-10 mm or SITE

- Below PET-CT sensitivity
- Small nodules **near the diaphragm or heart** where there is motion artifact

NSCLC STAGING

Fattori di rischio NSCLC e Sintomi



1) SOSPETTO CA POLMONE

Anamnesi: tosse persistente da oltre 3 settimane, o cambiamento delle caratteristiche della tosse abituale (fumatore o bronchitico cronico); emottisi; dolore toracico; dispnea di recente insorgenza; disfonia; calo ponderale; sintomi sistemici recenti suggestivi di sindromi paraneoplastiche.

Obiettività: segni toracici (ottusità, reperti a focolaio), clubbing digitale, linfoadenopatie sopraclaveari o laterocervicali.

Qualunque dei precedenti sintomi o segni che durino da più di 3 settimane. Pazienti con fattori di rischio noti possono essere presi in considerazione anche prima (es. esposizione a fumo attivo o passivo, storia di malattia polmonare cronica ostruttiva, esposizione all'asbesto, storia personale o familiare di neoplasia).

NSCLC STAGING

18FDG PET/CT and LUNG CANCER

BIOPSY (VIABLE tumour)

STAGING

Paziente è operabile (NSCLC)?
Clinical Performance*

Tumore è resecabile?
TNM STAGING

Con quale tipo di approccio?
Tumour size and location

RT planning

Malattia avanzata

Malattia metastatica

Tumore di Pancoast

ONCOGENE ADDICTED

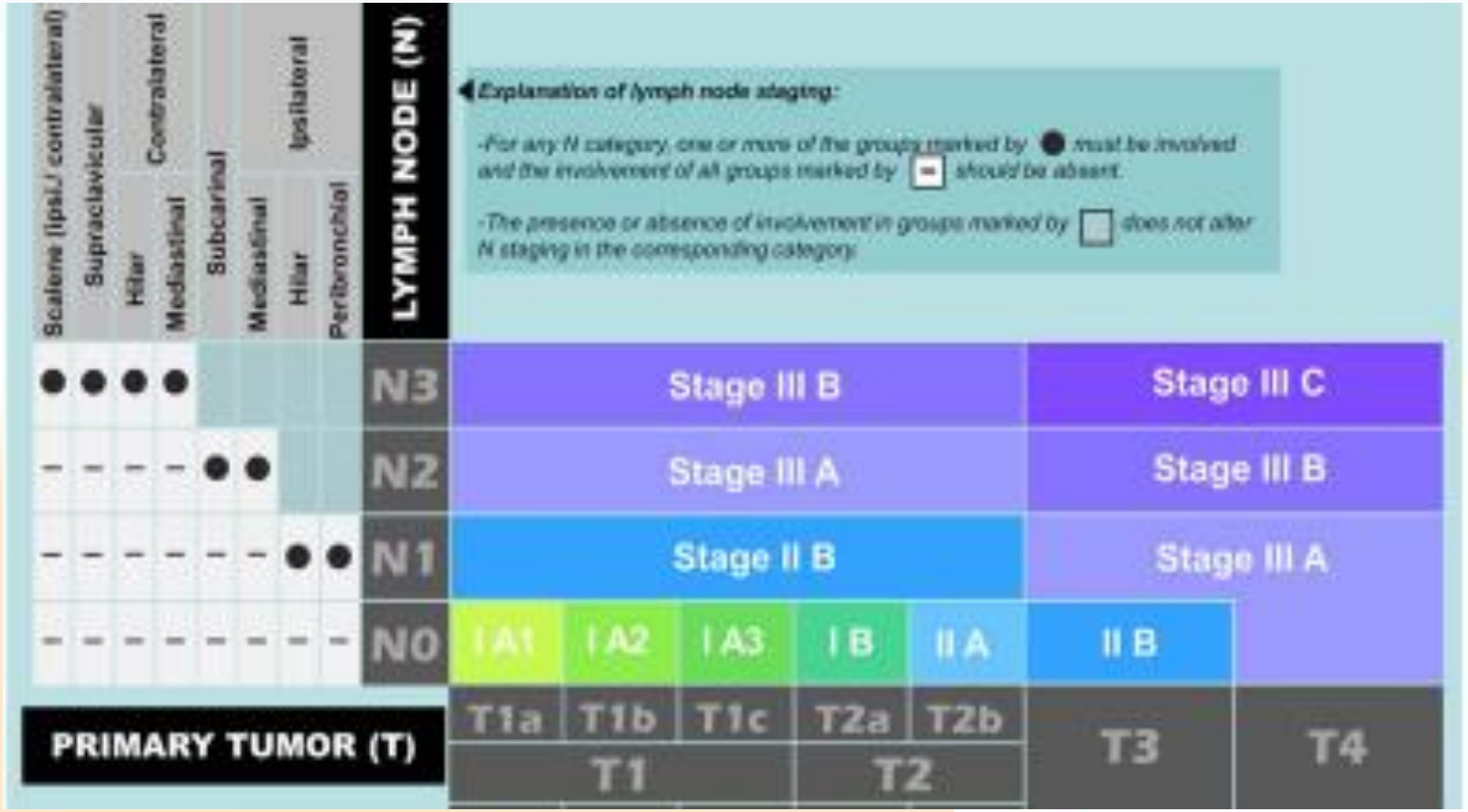
CHT

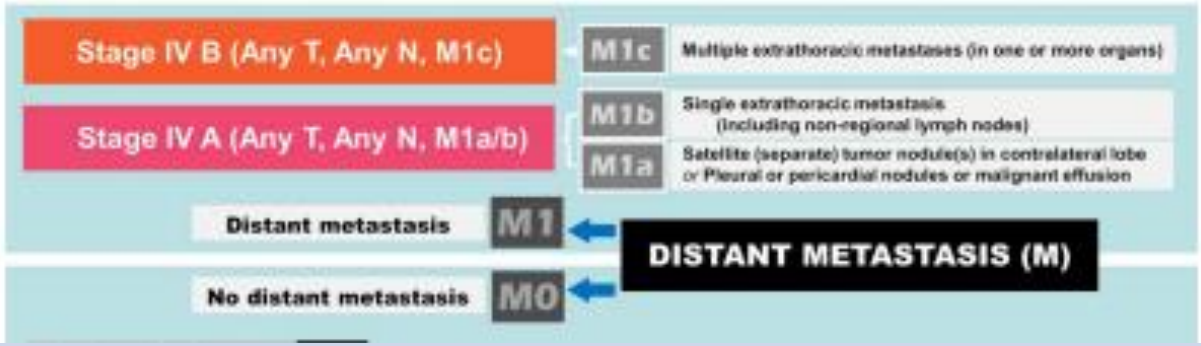
*spirometria, DLCO, EGA, rischio cardiovascolare, eventuale Scintigrafia perfusoria

NSCLC STAGING

18FDG PET/CT and NSCLC

STAGING

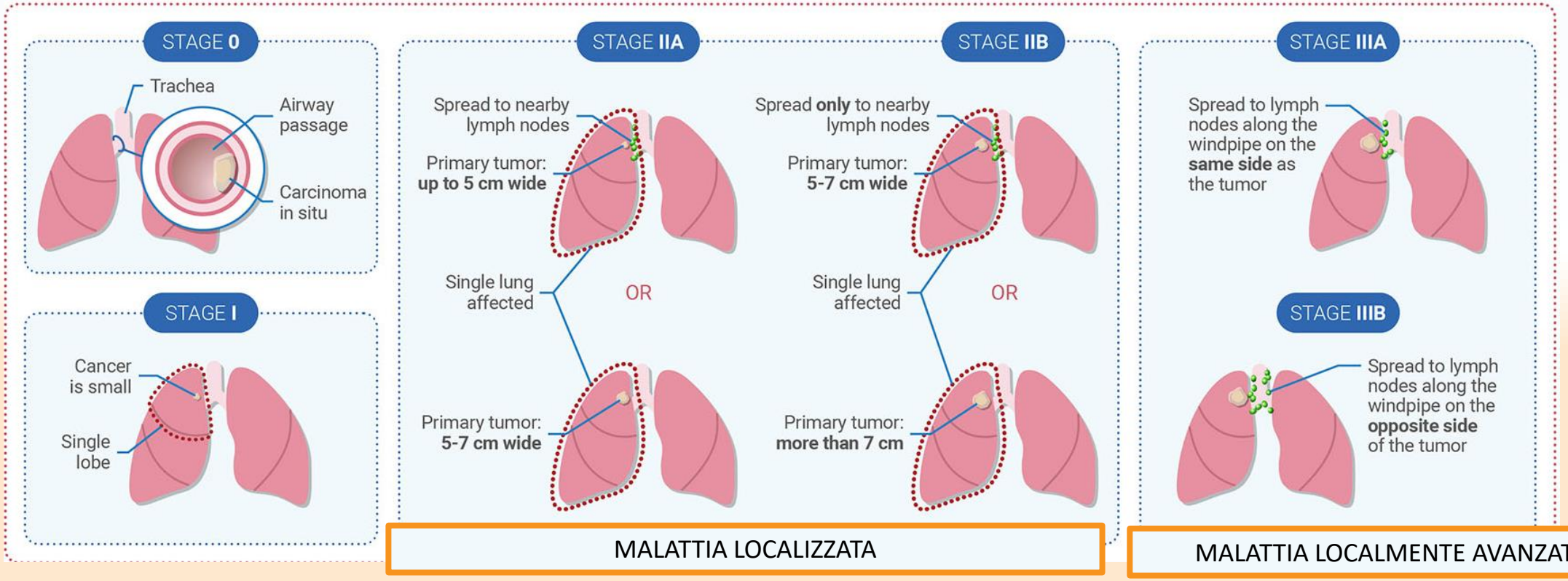




NSCLC STAGING

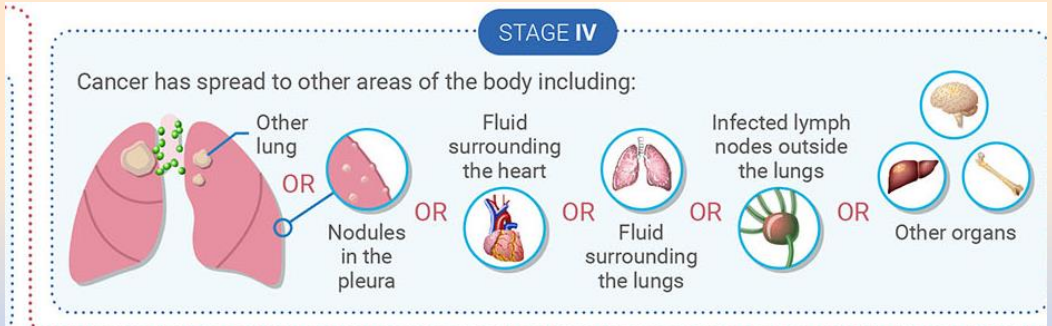
18FDG PET/CT and NSCLC

TREATMENT INDICATION



MALATTIA LOCALIZZATA

MALATTIA LOCALMENTE AVANZATA



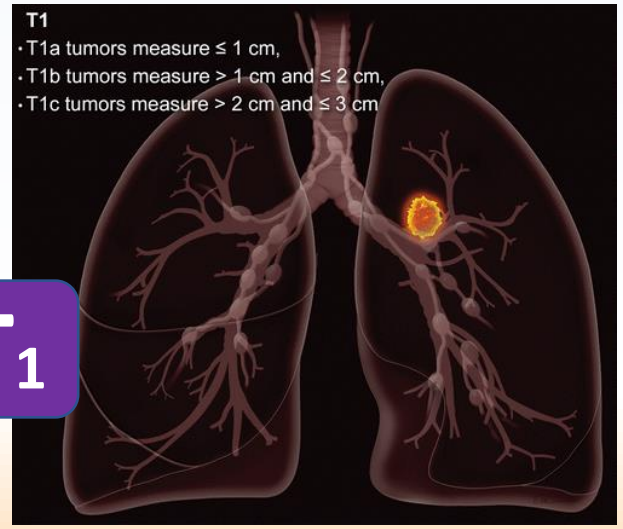
MALATTIA METASTATICA

CHEMOTHERAPY

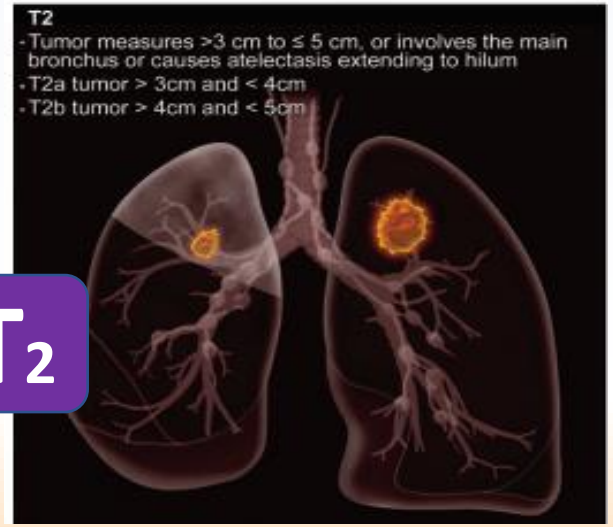
ONCOGENE ADDICTED

PET-CT STAGING : TUMOUR

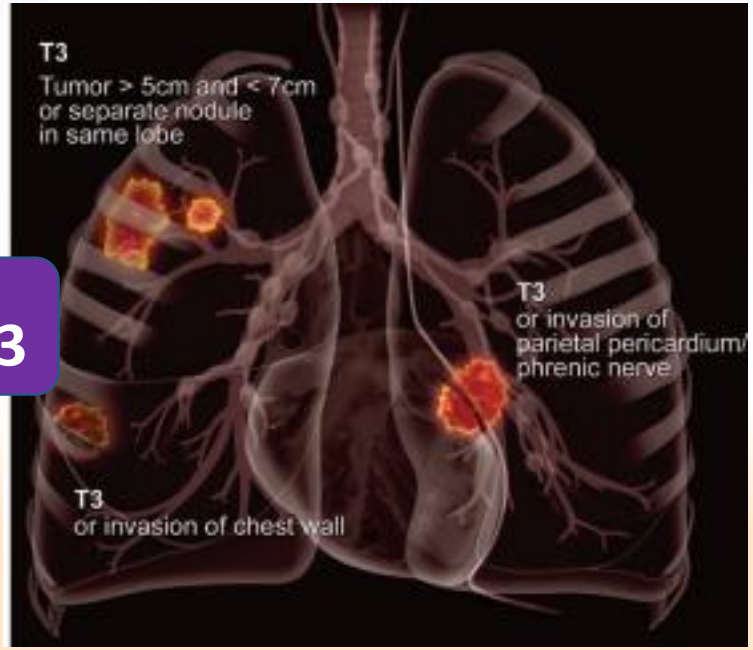
T



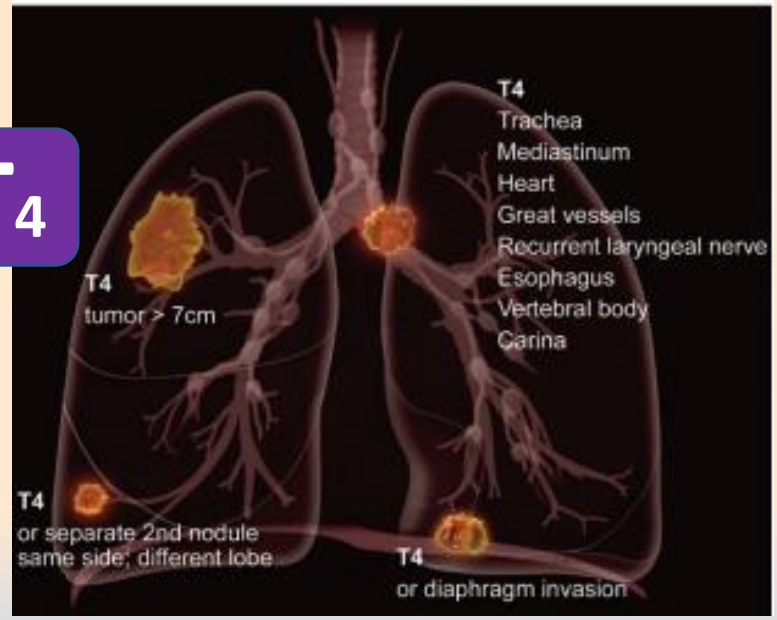
T1



T2



T3



T4

Primary Tumor Detection, Staging and Treatment Planning (T)

CT is the first-line modality for accurate T staging. Hybrid [^{18}F]-FDG-PET/CT imaging has revolutionized NSCLC staging and treatment planning. Conventional chest radiography has limited utility in T staging. Although a chest x-ray can show obvious mediastinal or chest wall invasion with advanced disease or large tumors, its sensitivity is limited; so, patients are referred to more advanced imaging to better delineate disease extent and potential resectability.[27] In all stages, surgeons need precise imaging characterization such as proximity of the tumor to vasculature, the bronchial tree, and pulmonary fissures, as the operative approach will alter accordingly.[10]

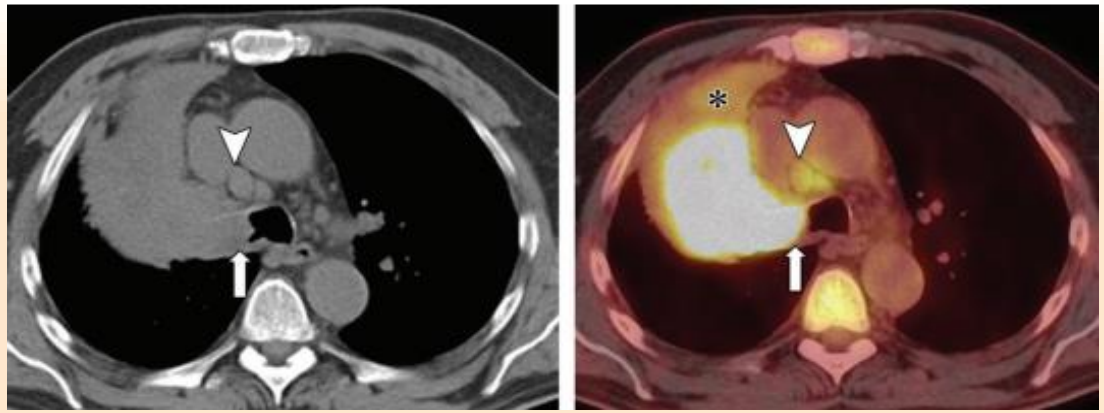
JCO Glob Oncol. 2022 May;8:e2100100.

PET-CT STAGING : TUMOUR

T

ADDED VALUE OF PET-CT

- GROSS TUMOUR VOLUME definition for RT planning **and VIABLE TUMOUR assessment**
- Identification of OTHER **FDG nodule in the LUNG → BIOPSY PLANNING** (same lobe T3 vs different lobe T4)
- Add specificity to CT findings of **LYMPHANGITIC CARCINOMATOSIS**
  Sensitivity and Specificity 86% and 100%.
- Differentiate between tumor **and post-obstructive atelectasis**



NSCLC
occluding bronchus

BUT is **suboptimal to assess chest wall invasion, brachial plexus invasion or diaphragm (T4)** owing to blooming artifact. (better ce-CT and MRI)

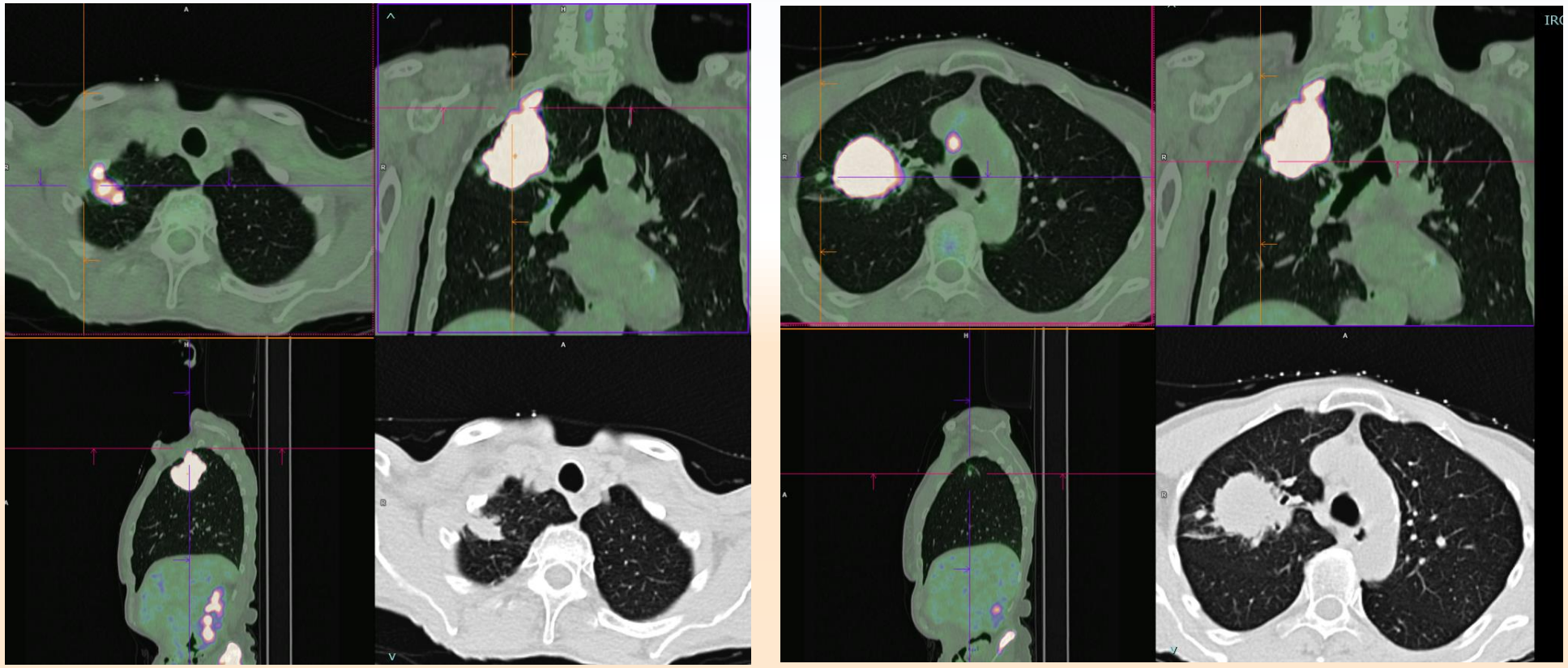
NEEDED TO KNOW: Transfissural growth, pulmonary vascular invasion, main bronchus invasion, involvement of upper and lower lobe bronchi

Radiographics. 2018 Nov-Dec;38(7):2134-2149

PET-CT STAGING : TUMOUR

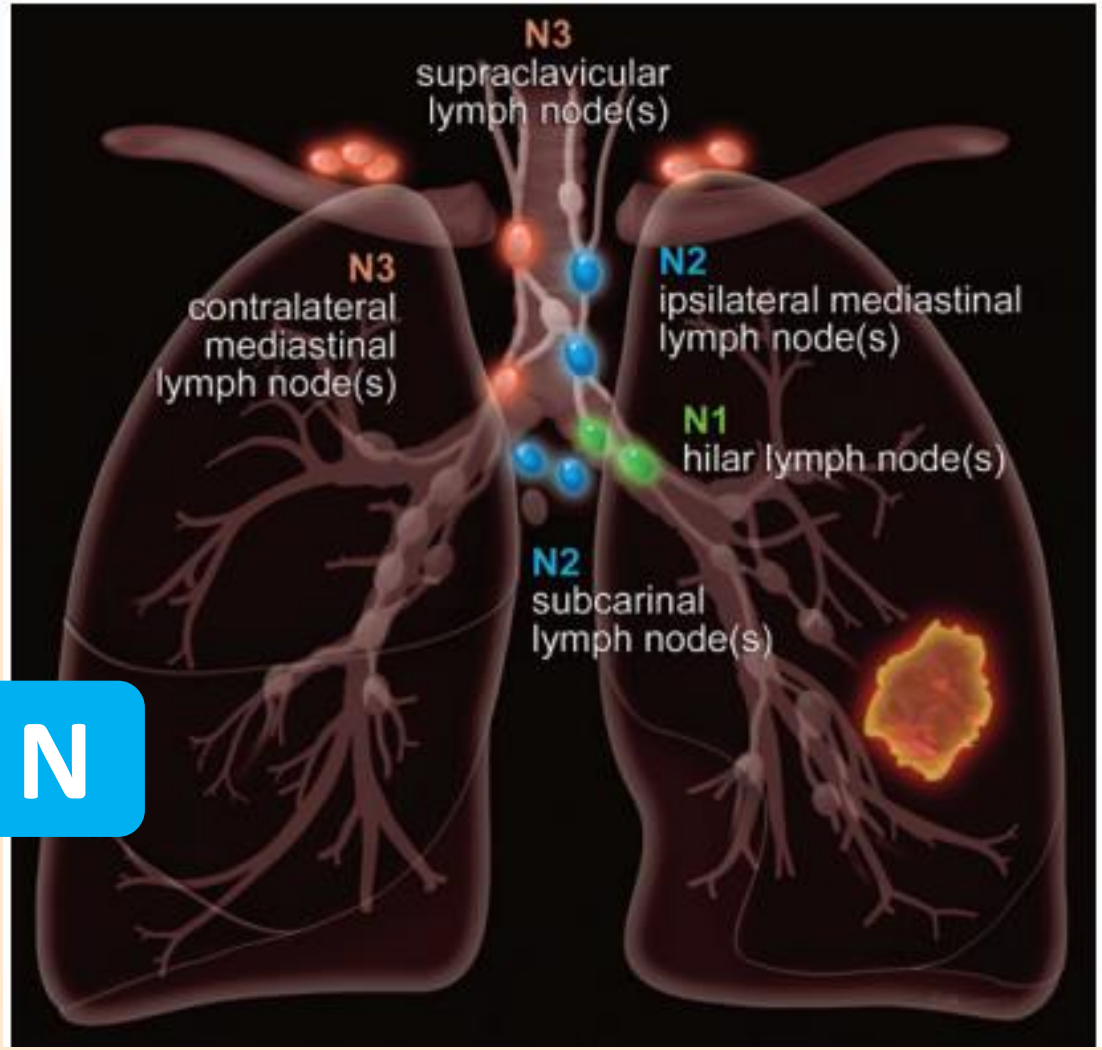
T

T STAGE



PET-CT STAGING : NODAL ASSESSMENT

N



N

Nodal Assessment (N)

[^{18}F]-FDG-PET/CT in lung cancer staging has improved the capacity to evaluate mediastinal and hilar nodal disease accurately. [^{18}F]-FDG-PET demonstrates better staging accuracy than CT, with a respective sensitivity (79%) and specificity (91%) for [^{18}F]-FDG-PET compared with 60% and 77% for CT.[31] A recent meta-analysis of [^{18}F]-FDG-PET illustrated sensitivity (72%) and specificity (91%) for mediastinal nodal disease.[27] [^{18}F]-FDG-PET/CT can direct surgical or image-guided mediastinal nodal sampling to the most suspicious nodes. As discussed above, NCCN and ESMO guidelines recommend definitive histologic sampling and staging.

.JCO Glob Oncol. 2022 May;8:e2100100.

PROGNOSTIC DETERMINANT:

- Number of involved nodes in N1 and N2
- Presence / Absence of skip metastases

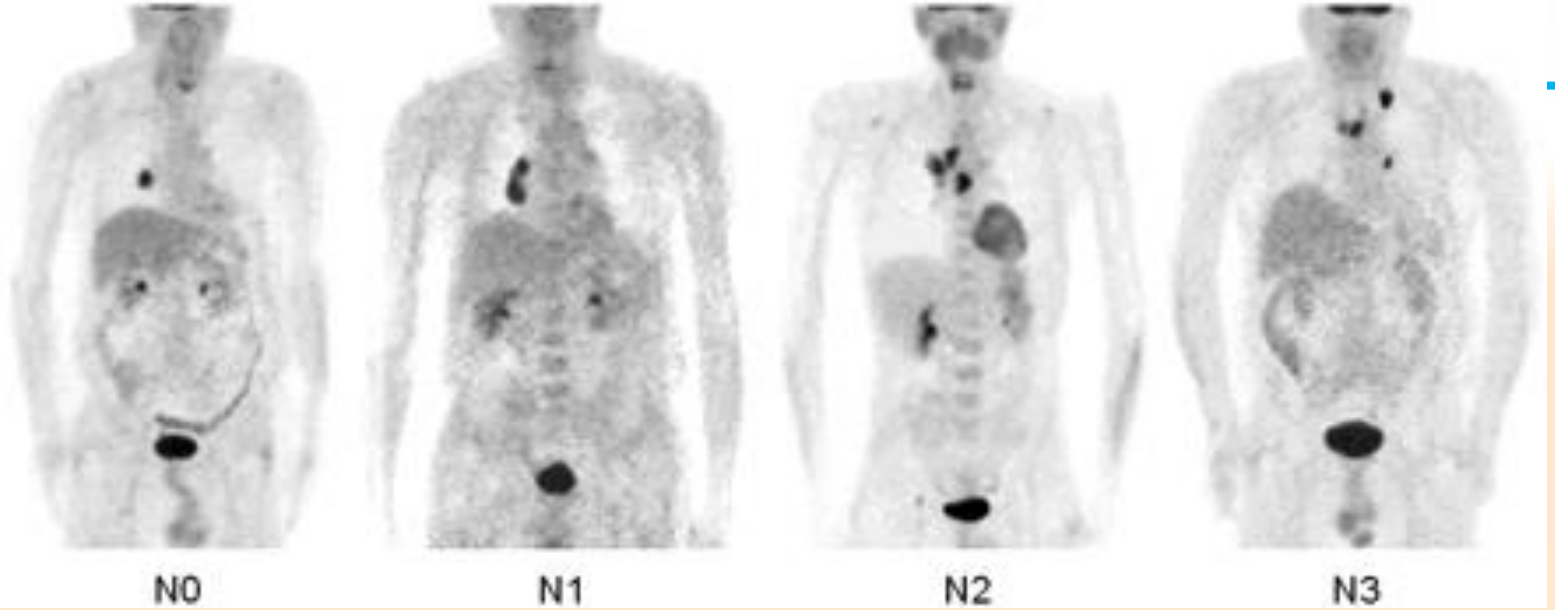
PET-CT STAGING : NODAL ASSESSMENT

N

N+

- **Sensibilità 58%–94% e specificità of 76–96% per LN**
- LN positivi che ostacolano la chirurgia → necessaria confermata endoscopica / FNAC EBUS

FP PET-CT 20%



N_0

- Meta-analysis of 10 studies: **VPN** for mediastinal metastases was 94% in T1 and 89% in T2

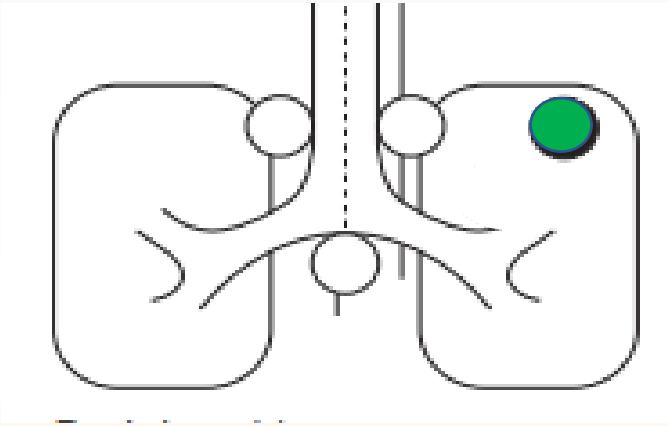
Clin. Lung Cancer 2012, 13, 81–89.

Radiographics. 2018 Nov-Dec;38(7):2134-2149
Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561

PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT



PERIPHERAL TUMOUR < 3 cm

NORMAL MEDIASTINUM AND HILUM on CT and
NEGATIVE MEDIASTINUM AND HILUM on FDG/PET

NO FURTHER ASSESSMENT NEEDED
(Recommendation C ESR)

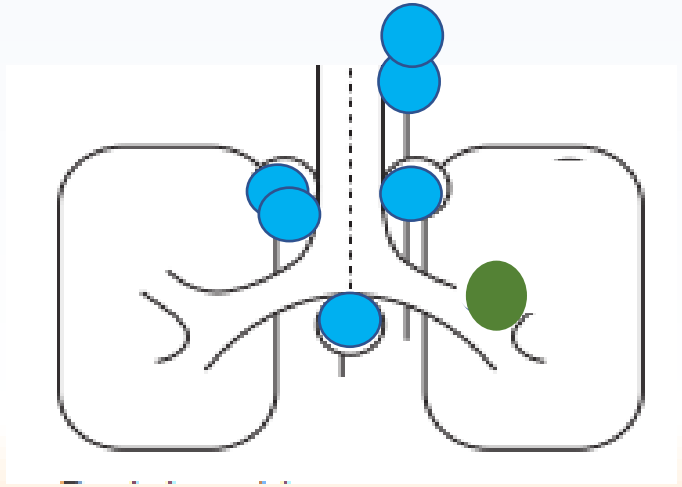
A Meta-analysis of 56 studies: pooled sensitivities and specificities of FDG-PET/CT for identifying mediastinal lymph node metastasis were 72% and 91%

. JCO Glob Oncol. 2022 May;8:e2100100

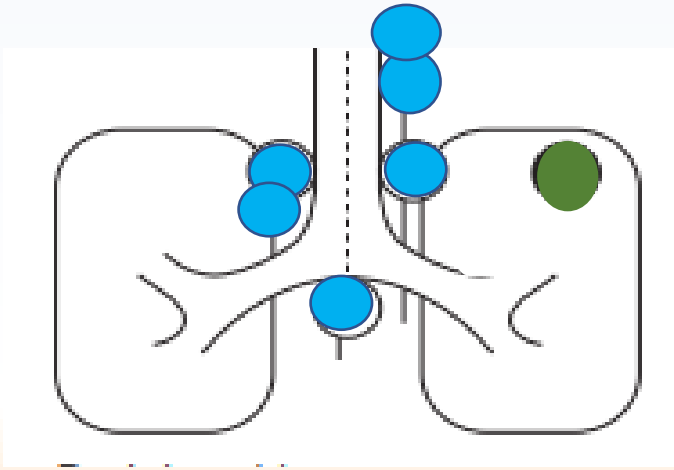
PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT



ANY SIZE CENTRAL LESION



PERIPHERAL TUMOUR

EXTENSIVE involvment MEDIASTINUM AND HILUM on CT
EXTENSIVE involvment MEDIASTINUM AND HILUM on PET-CT

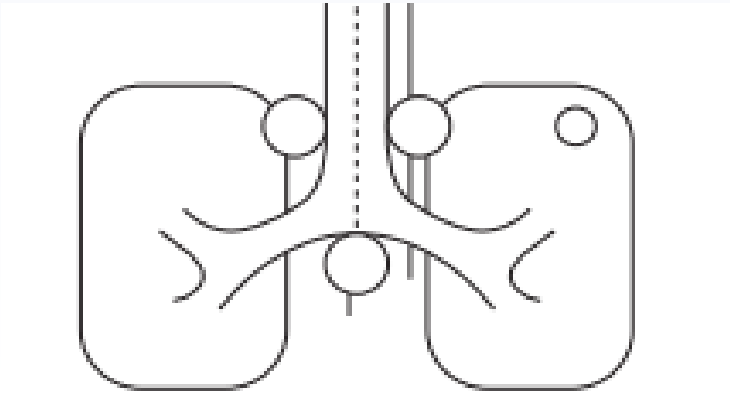
NO FURTHER ASSESSMENT NEEDED
NO invasive Lypmh node evaluation is needed
(Recommandation C ESR; ESMO LoE A GoR 1)

. JCO Glob Oncol. 2022 May;8:e2100100

PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT



NORMAL MEDIASTINUM on CT

PERIPHERAL TUMOUR < 3 cm

NO TUMOUR UPTAKE

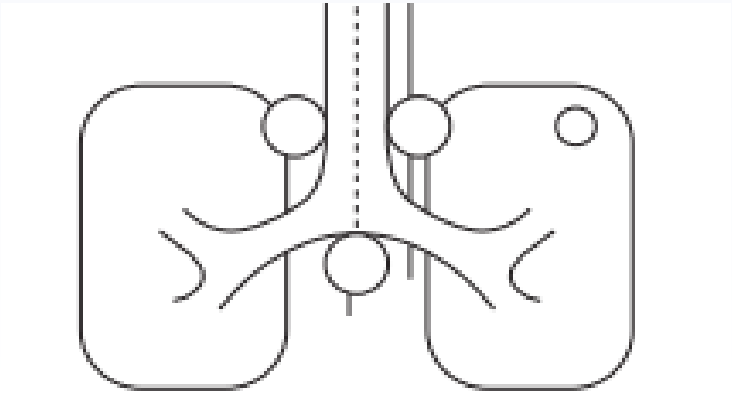
EBUS /TBNA or EUS / FNA before treatment
IF Endoscopy is negative but suspected N1/2 disease than Mediastinoscopy
Reccomendation Grade C

ERS

PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT



NORMAL MEDIASTINUM on CT

PERIPHERAL TUMOUR < 3 cm

NO TUMOUR UPTAKE

FALSE NEGATIVE

- **Mucinous** adenocarcinomas (**bronchiolo-alveolar**e 10% NSCLC)
- Adenocarcinomas with a **lepidic** growth pattern
- **Adenocarcinoma in situ**
- **Minimally invasive adenocarcinomas**
- **Carcinoid tumors**

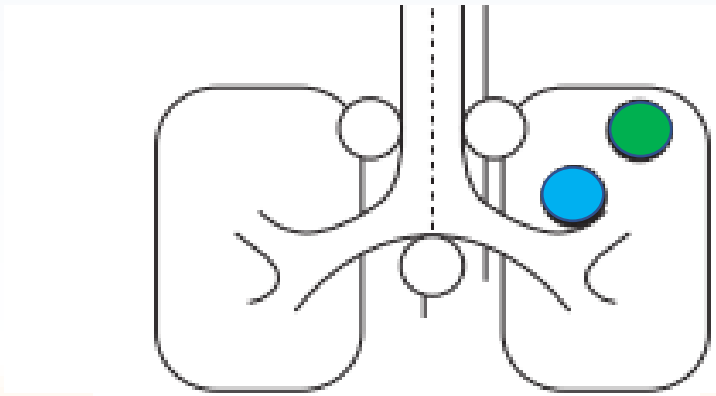
EBUS /TBNA or EUS / FNA before treatment
IF Endoscopy is negative but suspected N1/2 disease than Mediastinoscopy
Reccomendation Grade C

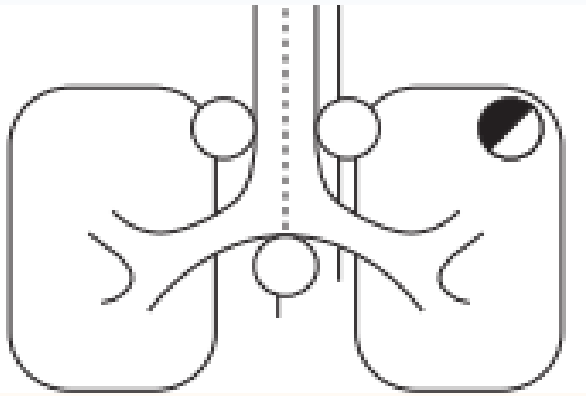
ERS

PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT





NORMAL MEDIASTINUM on CT

PERIPHERAL TUMOUR < 3 cm

PERIPHERAL TUMOUR > 3 cm

FDG AVID IPSILATERAL HILAR NODE (cN1)

WITH / WITHOUT TUMOUR UPTAKE

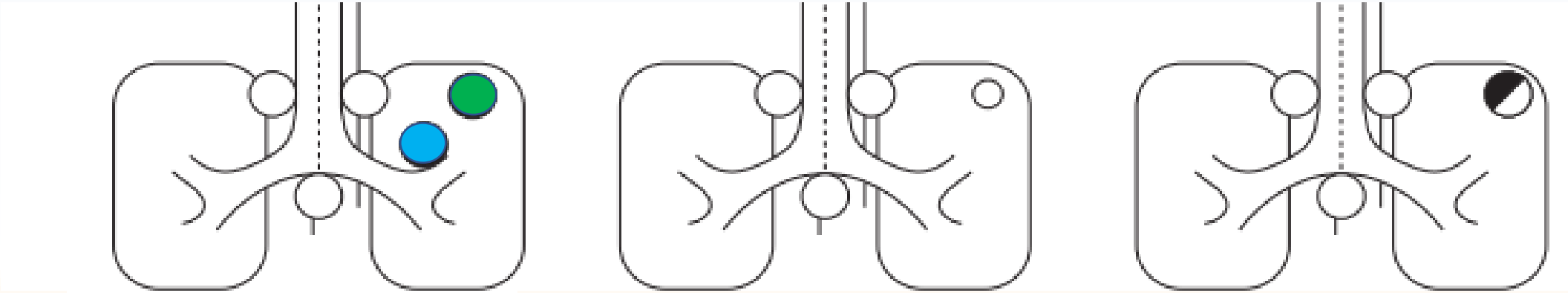
EBUS /TBNA or EUS / FNA before treatment
IF Endoscopy is negative but suspected N1/2 disease than Mediastinoscopy
Reccomendation Grade C

ERS

PET-CT STAGING : NODAL ASSESSMENT

N

NODAL ASSESSMENT



SE la PRESENZA DI LINFONODI POSITIVI CAMBIA L'approccio TERAPEUTICO

EBUS /TBNA or EUS / FNA before treatment
IF Endoscopy is negative but suspected N1/2 disease than Mediastinoscopy

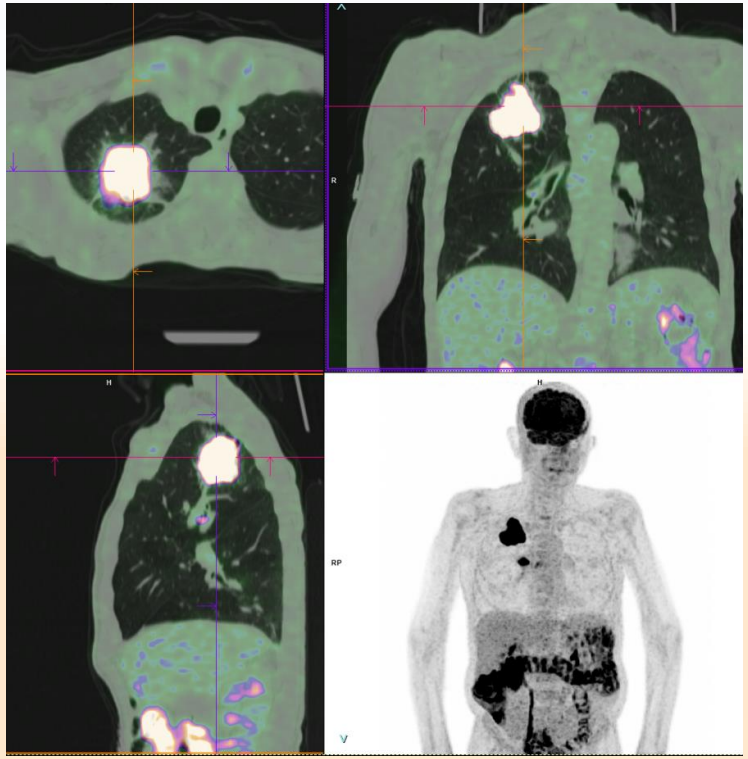
Reccomendation Grade C

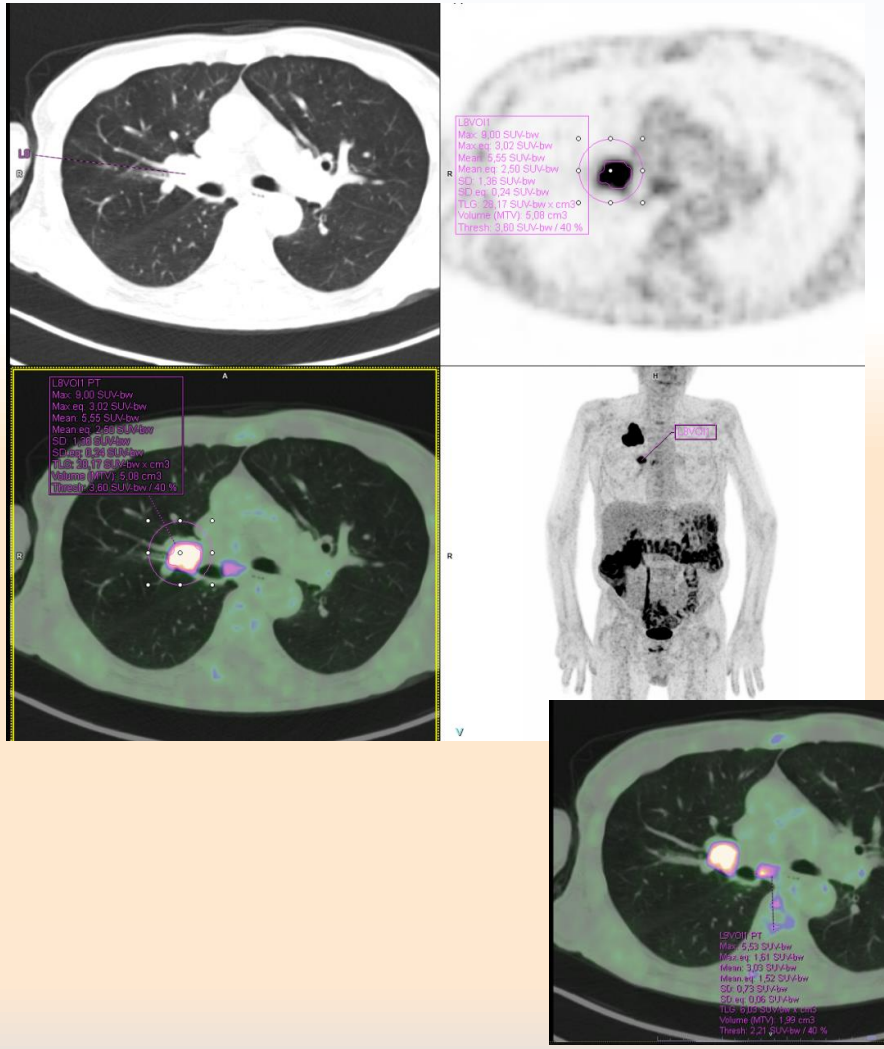
ERS

PET-CT STAGING : NODAL ASSESSMENT

N

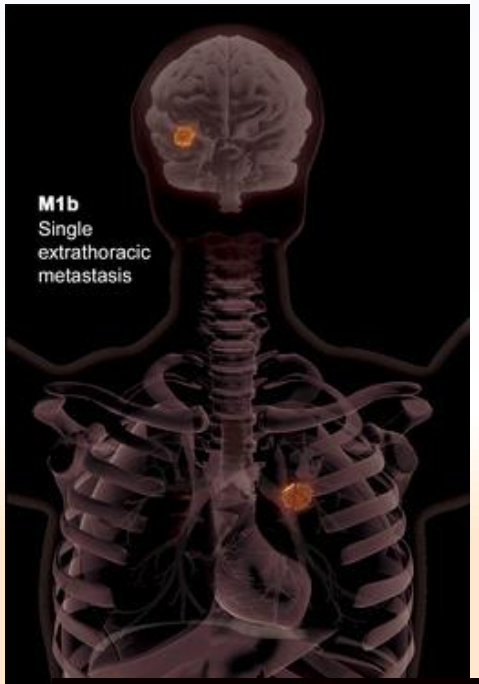
NODAL ASSESSMENT



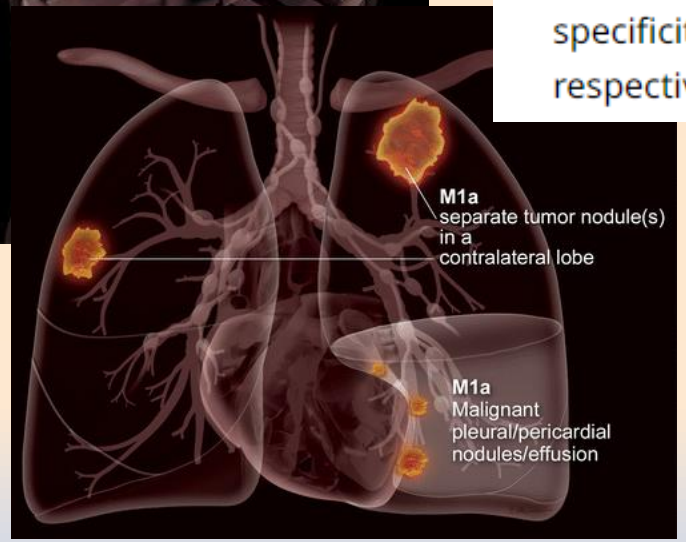


PET-CT STAGING : METASTASIS

M



M



Detection of Metastatic Disease (M)

Both intrathoracic and extrathoracic metastatic disease is characterized on the basis of imaging including nuclear medicine findings. Since more than half of the patients with lung cancer present with metastasis at initial diagnosis,[7] reporting suspected distant metastases to the care team dramatically changes clinical management. Adrenal, skeletal, intracranial, and hepatic metastatic lesions are particularly common in NSCLC. Of note, [^{18}F]-FDG-PET/CT is not recommended for the detection of brain metastases, where MRI is preferable. Skeletal metastatic disease can be evaluated by [^{18}F]-FDG-PET/CT or, when PET/CT is not available, bone scintigraphy (eg, ^{99}m-Tc diphosphonate bone scan); both are more sensitive than conventional x-rays, although [^{18}F]-FDG-PET/CT shows greater sensitivity and specificity (92% and 98%, respectively) than bone scans (86% and 87% respectively).[10] FDG-PET/CT can reduce the number of futile thoracotomies.[29]

. JCO Glob Oncol. 2022 May;8:e2100100.

PET-CT STAGING : METASTASIS ASSESSMENT

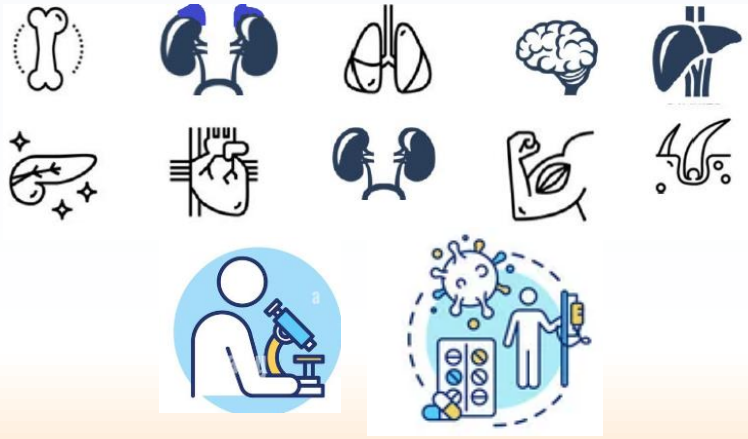
M

POSITIVE M+

M1 occur in 11%–36% of patients with NSCLC.In the results of a 2013 meta-analysis of nine studies, Detection of distant metastases with FDG PET/CT had a

- sensitivity of 93%, specificity of 96%,
- positive likelihood ratio of 28.4%,
- negative likelihood ratio of 0.08%

Diagnostics 2020, 10, 561



35) OLIGOMETASTATICO

PDTA Regione Veneto

Recentemente la Consensus EORTC Lung Cancer Group ha definito come sincronc oligometastatico da tumore del polmone non a piccole cellule un numero massimo di 5 localizzazioni e 3 organi coinvolti.
Le opzioni terapeutiche locali di prima scelta disponibili sono l'exeresi chirurgia e il trattamento radioterapico.

Il trattamento locale chirurgico (incluso o meno il primitivo polmonare) potrebbe essere preferito nei pazienti definiti operabili in caso di localizzazioni secondarie che causano sintomi da effetto massa, localizzazioni secondarie ossee a rischio di frattura patologica, in caso di necessaria diagnosi istologica e/o molecolare (es. localizzazione secondaria encefalica), oppure in presentazione di malattia oligometastatica dove approccio radioterapico è contro-indicato.

Il trattamento radioterapico (incluso o meno il primitivo polmonare) dovrebbe essere privilegiato nei pazienti in cui la resezione chirurgica è contro-indicata o rifiutata da parte del paziente, oppure in pazienti con multiple lesioni in un singolo organo. In tale scenario, l'approccio chirurgico potrebbe aumentare il rischio di perdita funzionale d'organo e il trattamento radioterapico risulterebbe maggiormente perseguibile. Nei pazienti eleggibili a trattamenti radioterapici è consigliato perseguire dosi ablative (radioterapia stereotassica).
Ogni decisione terapeutica deve essere condivisa a livello multidisciplinare, includendo l'Oncologo Medico per l'approccio integrato sistemico di malattia e in tale discussione sono inclusi anche i pazienti oligoprogressivi e oligoricorrenti.

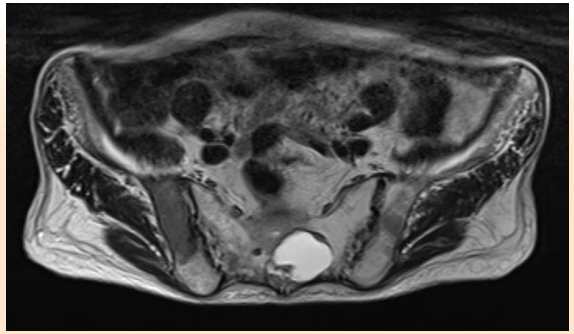
PET-CT STAGING : METASTASIS ASSESSMENT

M

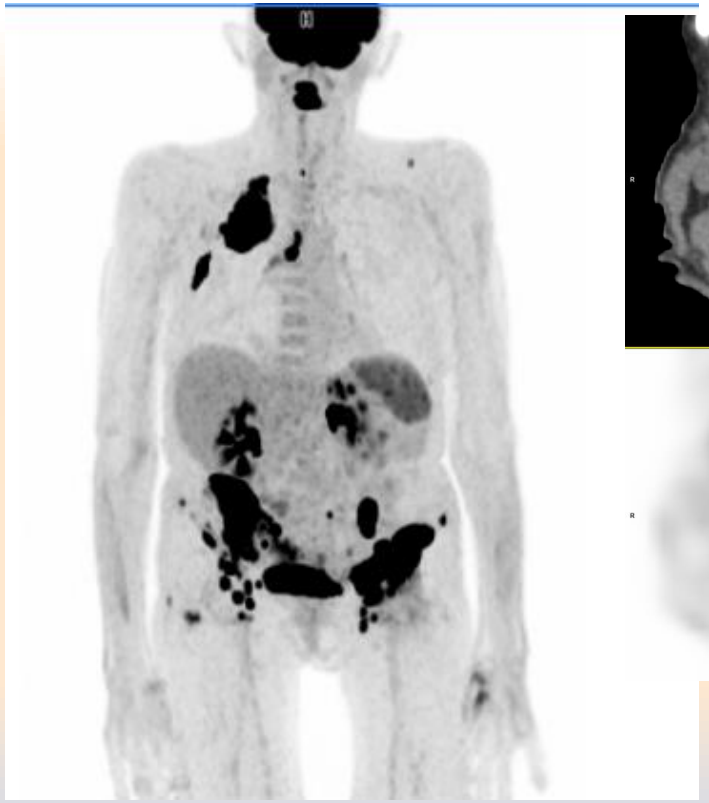
POSITIVE M+

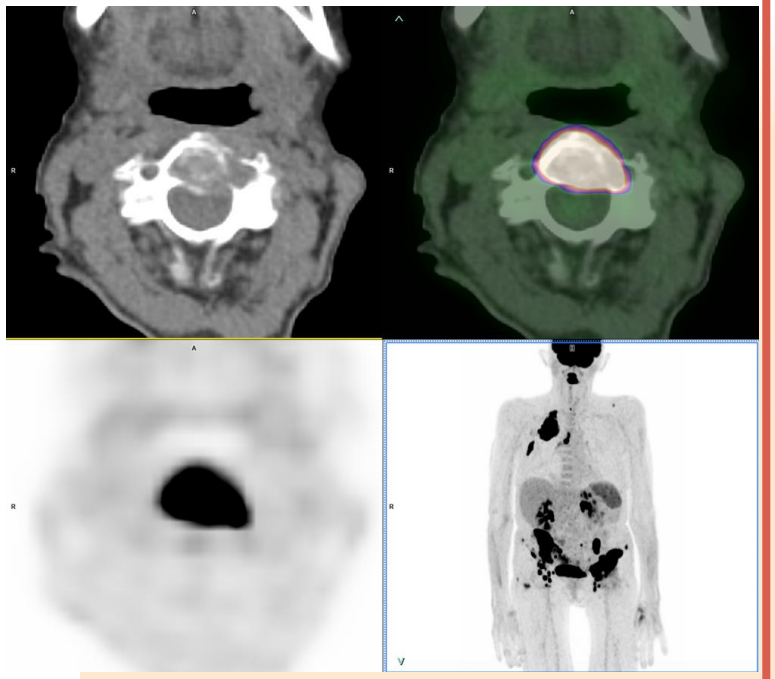
BONE METASTASIS The results of a meta-analysis of patients with lung cancer, investigators found that FDG PET/CT and FDG PET were more accurate methods for the diagnosis of bone metastases than MRI or bone scintigraphy, **and FDG PET/CT has a higher diagnostic value than any other method**

Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561



Weight loss and bone mts of unknown origin





PET-CT STAGING : METASTASIS ASSESSMENT

M

POSITIVE M+

BRAIN METASTASIS. The results of a metaanalysis of prospective studies showed pooled **sensitivities of 21% and 77%** for PET and MRI, respectively, and specificities of 100% and 99%. **NCCN guidelines recommend MRI** n patients with stage II to stage IV

Radiographics. 2018 Nov-Dec;38(7):2134-2149
Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561

- Nei pazienti con adenocarcinoma con diametro > 3 cm, nei tumori di Pancoast o con adenopatie mediastiniche anche in assenza di sintomatologia neurologica è necessaria la stadiazione con MR con mdc;
- Nei pazienti con sintomi neurologici o controindicazione all'uso del gadolinio o della RMN va eseguita la TC con mdc.

→ Nei pazienti con neoplasia polmonare N0,1 resecabile e una singola metastasi cerebrale (sincrona o metacrona), in assenza di altre localizzazioni, è indicata la resezione chirurgica o il trattamento radiochirurgico della metastasi cerebrale in associazione al trattamento chirurgico della neoplasia primitiva polmonare. La radiochirurgia è una opzione terapeutica in caso di localizzazioni multiple preferibilmente fino 5 lesioni encefaliche, in pazienti con ottimo perfomance status e controllo di malattia extracranica*

*Chang et al Lancet Oncol 2009, 10:1037-44 ; Yamamoto et al, Lancet Oncol 2014, 15:387-95; Alongi et al Lancet Oncol 2014, 15(7):e246-7; Kocher et al, JCO 2011; 29:134-41
PDTA Regione Veneto

PET-CT STAGING : METASTASIS ASSESSMENT

M

POSITIVE M+

ADRENAL METASTASTASIS Incidental adrenal nodules are found in 20% of patients with NSCLC; most nodules are benign adrenal adenomas
The combination of a **mean CT attenuation greater than 10 HU and SUVmax > 3,. had a sensitivity and specificity of 97% and 86%** for identifying metastatic disease

Radiographics. 2018 Nov-Dec;38(7):2134-2149
Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561

M1 Surrenalica

→ Nei pazienti con neoplasia polmonare N0,1 resecabile e una singola metastasi surrenalica (sincrona o metacrona), in assenza di altre localizzazioni, è indicata la resezione chirurgica della metastasi surrenalica in associazione al tumore primitivo. In caso di inoperabilità o in pazienti che rifiutano procedure invasive la radioterapia stereotassica è una opzione, se tecnicamente effettuabile.**

Nodulo polmonare controlaterale

→ Nei pazienti con NSCLC e una localizzazione polmonare controlaterale, in assenza di metastasi mediastiniche (linfonodali) o a distanza, è indicata l'asportazione di entrambe le lesioni, purchè il paziente abbia una adeguata riserva polmonare. In caso di inoperabilità o in pazienti che rifiutano procedure invasive la radioterapia stereotassica è una opzione, se tecnicamente effettuabile**

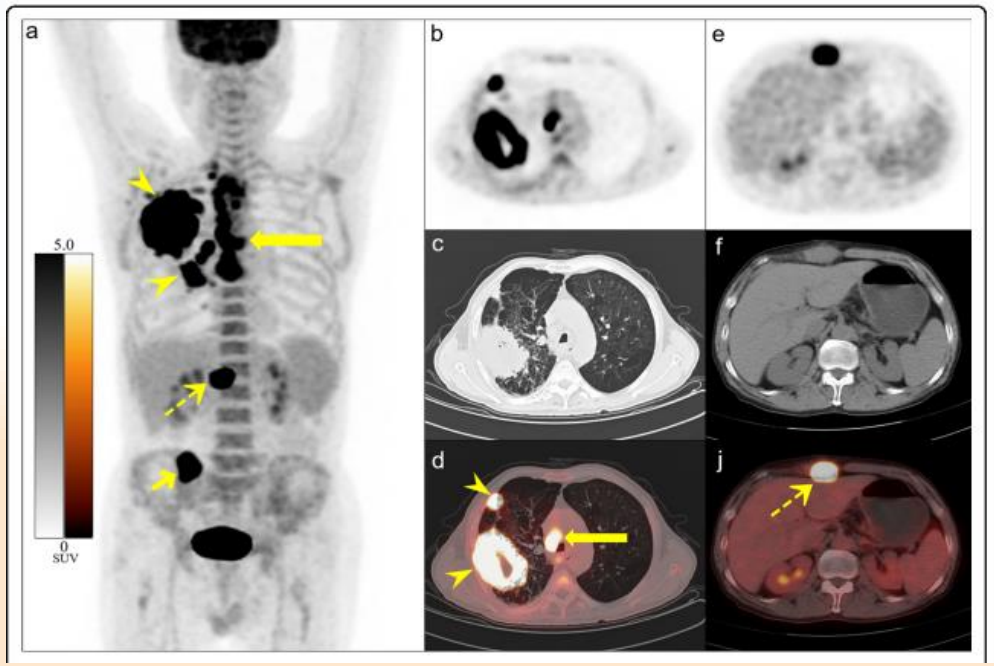
Histopathologic confirmation is necessary in surgical candidates with a single atypical lesion

**Corbin et al, JCO 2013, 31(11):1384-90; Alongi et al. Oncologist. 2012;17(8):1100-7; Gomez et al.LancetOncol.2016Dec;17(12):1672- 1682
PDTA Regione Veneto

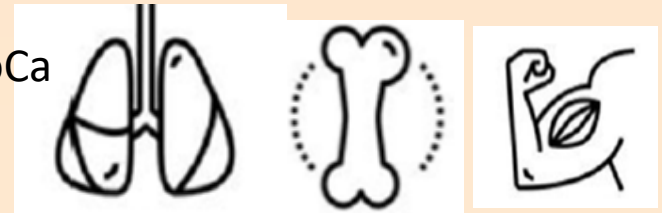
PET-CT STAGING : METASTASIS ASSESSMENT

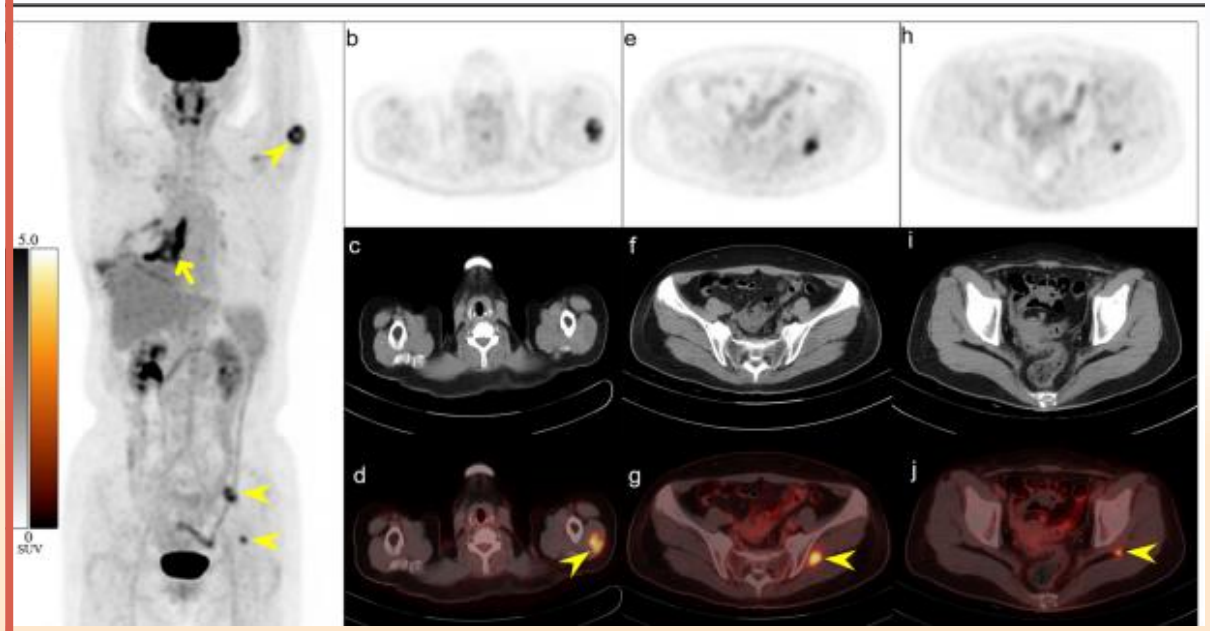
M

POSITIVE M+



AdenoCa





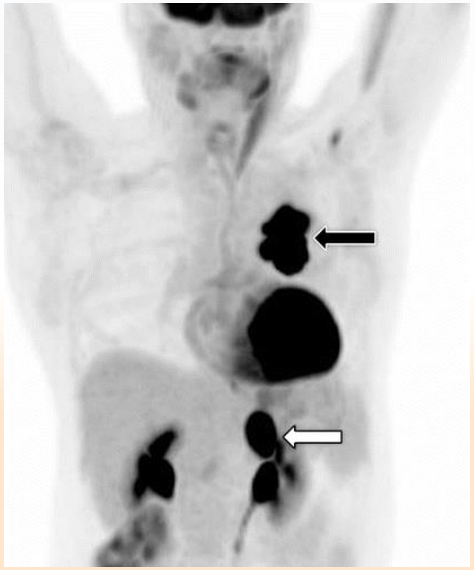
SCC

Radiographics. 2018 Nov-Dec;38(7):2134-2149
Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561

PET-CT STAGING : METASTASIS ASSESSMENT

M

POSITIVE M+



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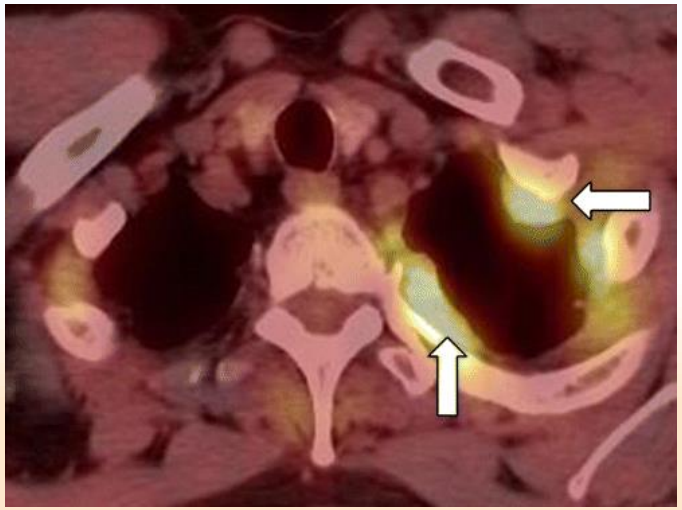

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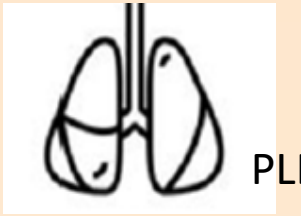


PLEURA

Radiographics. 2018 Nov-Dec;38(7):2134-2149
Diagnostics 2020, 10, 561; doi:10.3390/diagnostics10080561

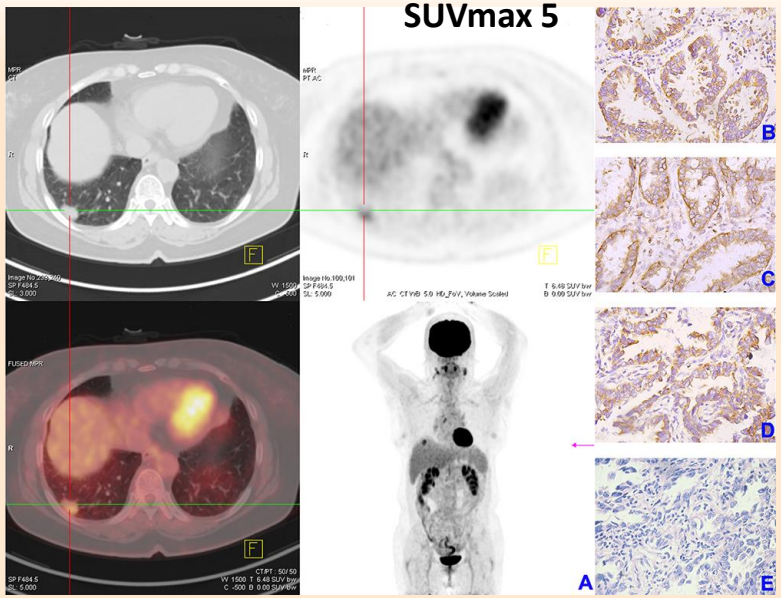
PROGNOSTIC ROLE of PET/CT in NSCLC

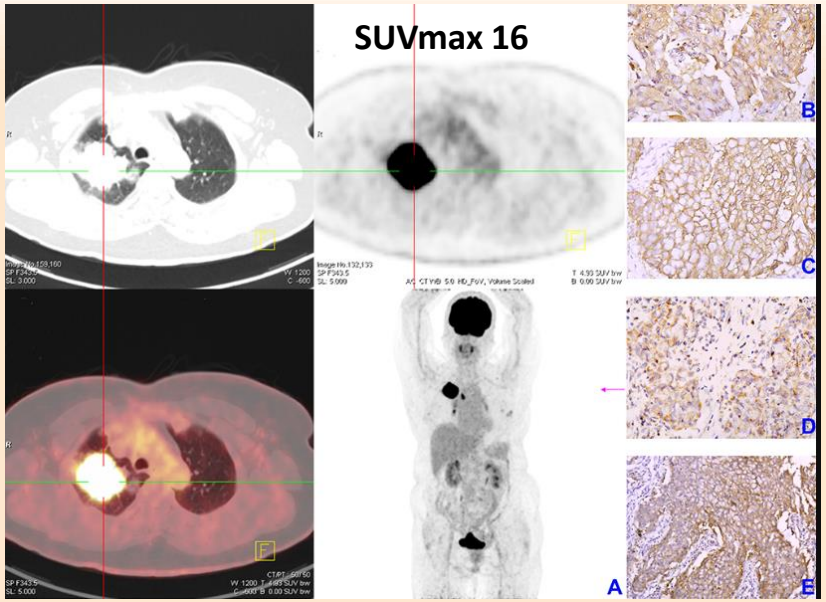
SUVmax (and other parameters)

- **Enhanced TUMOUR glycolytic** gene expression is related to **poor clinical outcomes** (OS, PFS)

(**increased of lactic acid, one of the products of glycolysis,** can increase the function of T regulatory cells and inhibit tumor immunity)

- Increased Hesokinase II expression and Ki67
- Increased PD-L1 expression (SUVmax cuf off 9.5**)





IHC: image B Hesokinase II, Image C: GLUT1; Image D: PD1; image E: PD-L1

**Cancer Manag Res. 2020 Jul 27;12:6385-6395.

WHAT'S NEW ON PET/CT in NSCLC

TRACERS BEYOND 18F-FDG

OTHER TRACERS: elenco dei farmaci è lungo..

Table 3. Immuno-PET tracers applied in preclinical studies.

Agent	Targeting
^{64}Cu -DOTA-antimouse-PD-1	PD-1 expression on TILs and primary lymphoid organs in a transgenic mouse model bearing melanoma
^{89}Zr-Keytruda®	Antihuman PD-1 antibody, imaging PD-1 expression on hPBMCs adoptively transferred to mice (hNSG) bearing A375 human skin melanoma tumors
^{64}Cu-Keytruda®	
^{89}Zr-Df-pembrolizumab	Biodistribution and pharmacokinetics in a humanized mouse model implanted with hPBMCs
^{64}Cu-DOTA-HAC-PD-1	PD-L1 expression in engrafted mice with PD-L1–negative and hPD-L1–positive tumors
^{64}Cu-NOTA-PD-1	Determination of PD-1 and PD-L1 expression in malignant tumors and the biodistribution of antimurine checkpoint-blocking antibodies

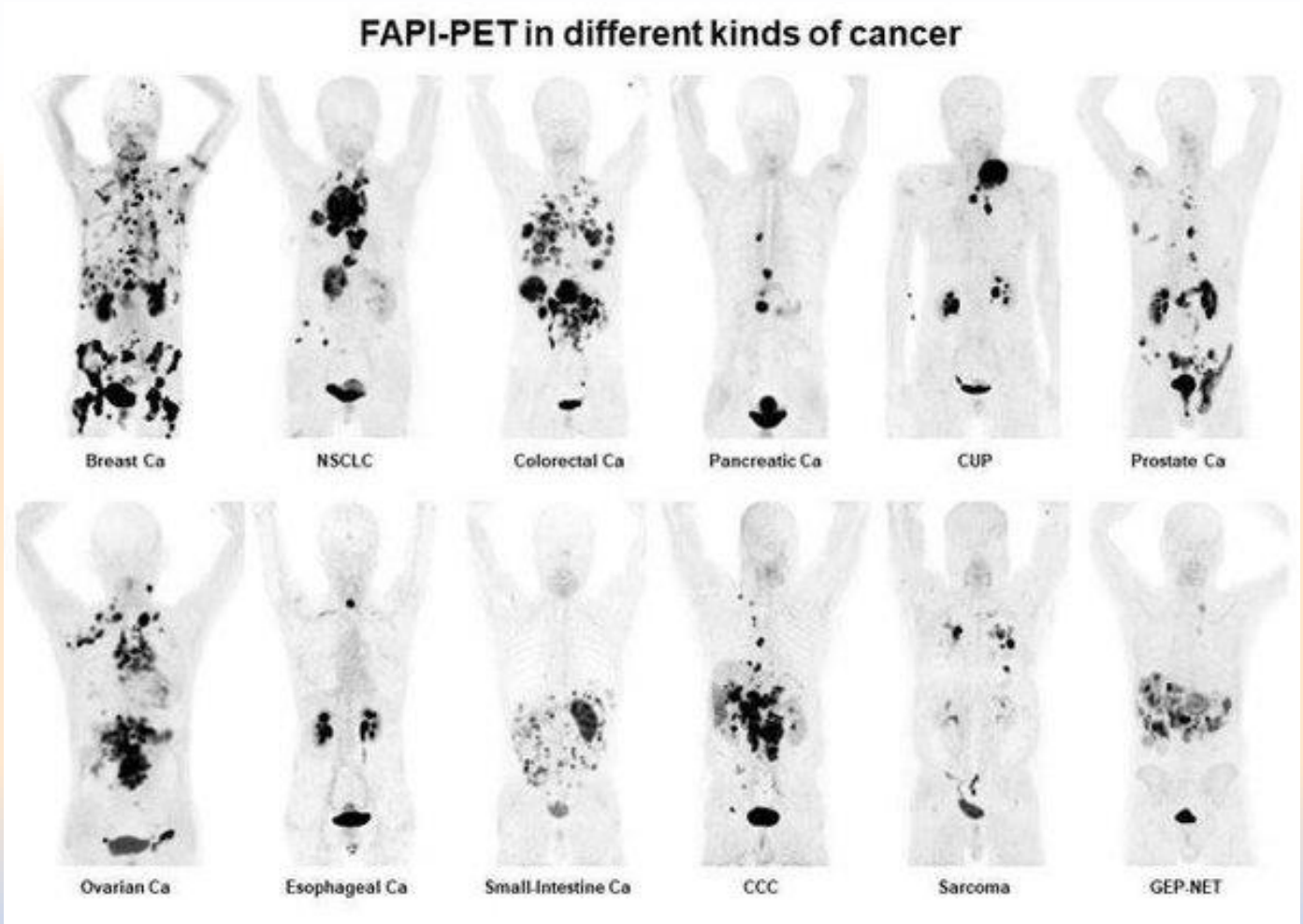
HAC: High-affinity consensus; hPBMC: Human peripheral blood mononuclear cell; PD: Programmed death; TIL: Tumor-infiltrating lymphocyte.

ma.. sono principalmente utilizzati in studi pre-clinici

WHAT'S NEW ON PET/CT in NSCLC

TRACERS BEYOND 18F-FDG

68Ga/18F-FAPI



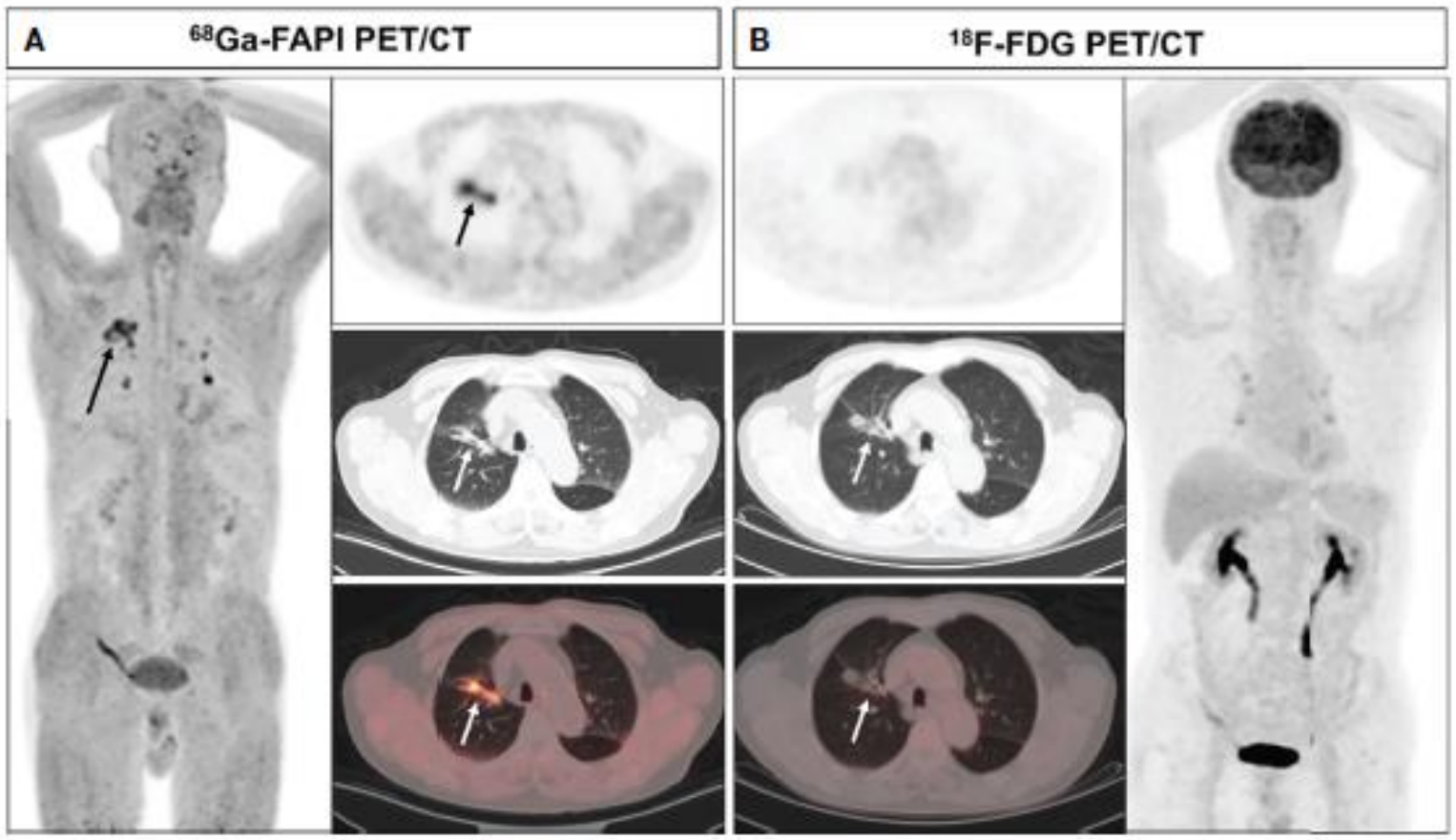
Cancer associated fibroblasts (CAF) express elevated levels of the type II transmembrane serine protease fibroblast-activated protein (FAP) which plays key-roles in migratory, invasive, and angiogenic activity in oncogenic contexts

Front. Oncol. 12:924223.
doi: 10.3389/fonc.2022.924223

WHAT'S NEW ON PET/CT in NSCLC

TRACERS BEYOND 18F-FDG

68Ga/18F-FAPI



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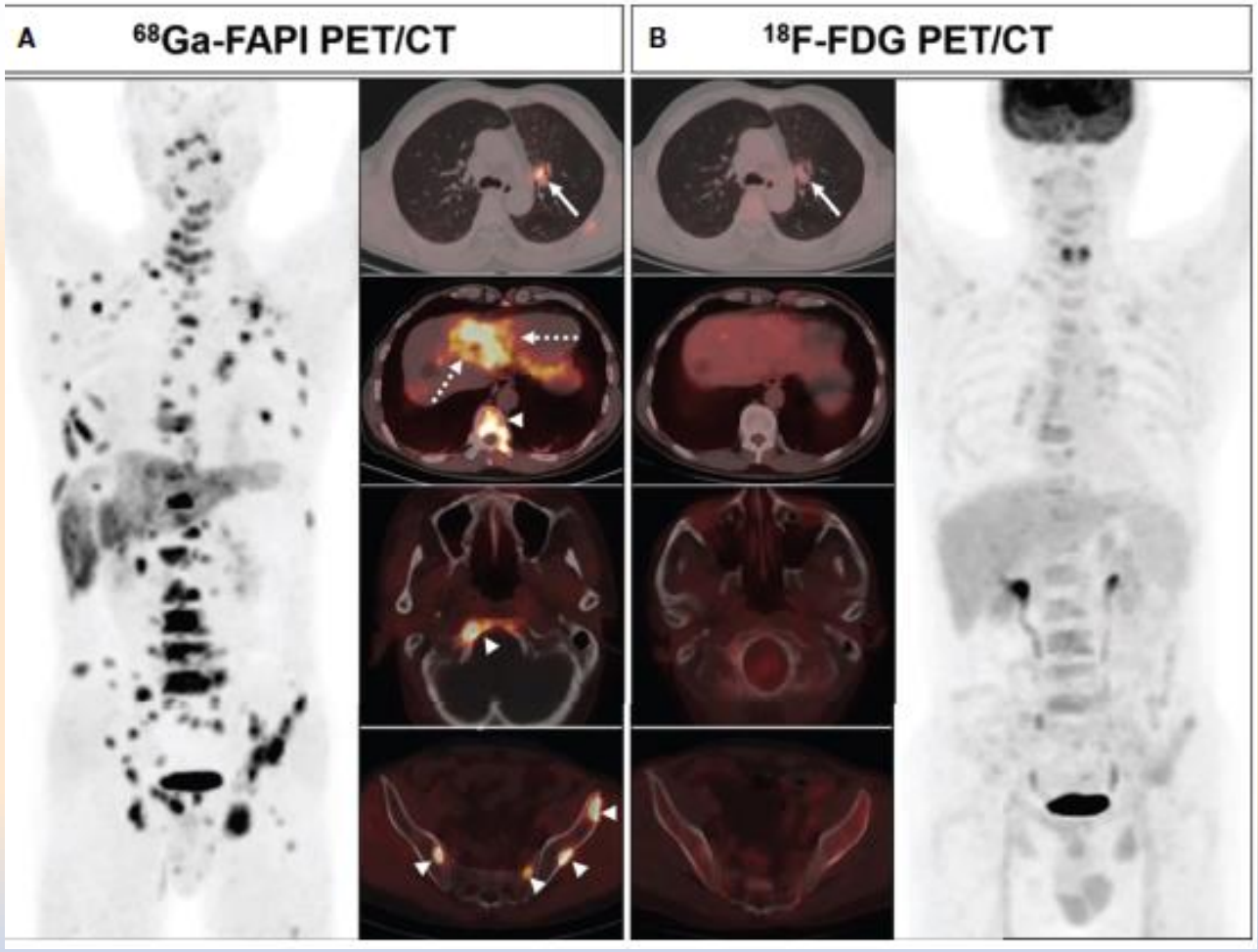
WHAT'S NEW ON PET/CT in NSCLC

TRACERS BEYOND 18F-FDG

68Ga/18F-FAPI



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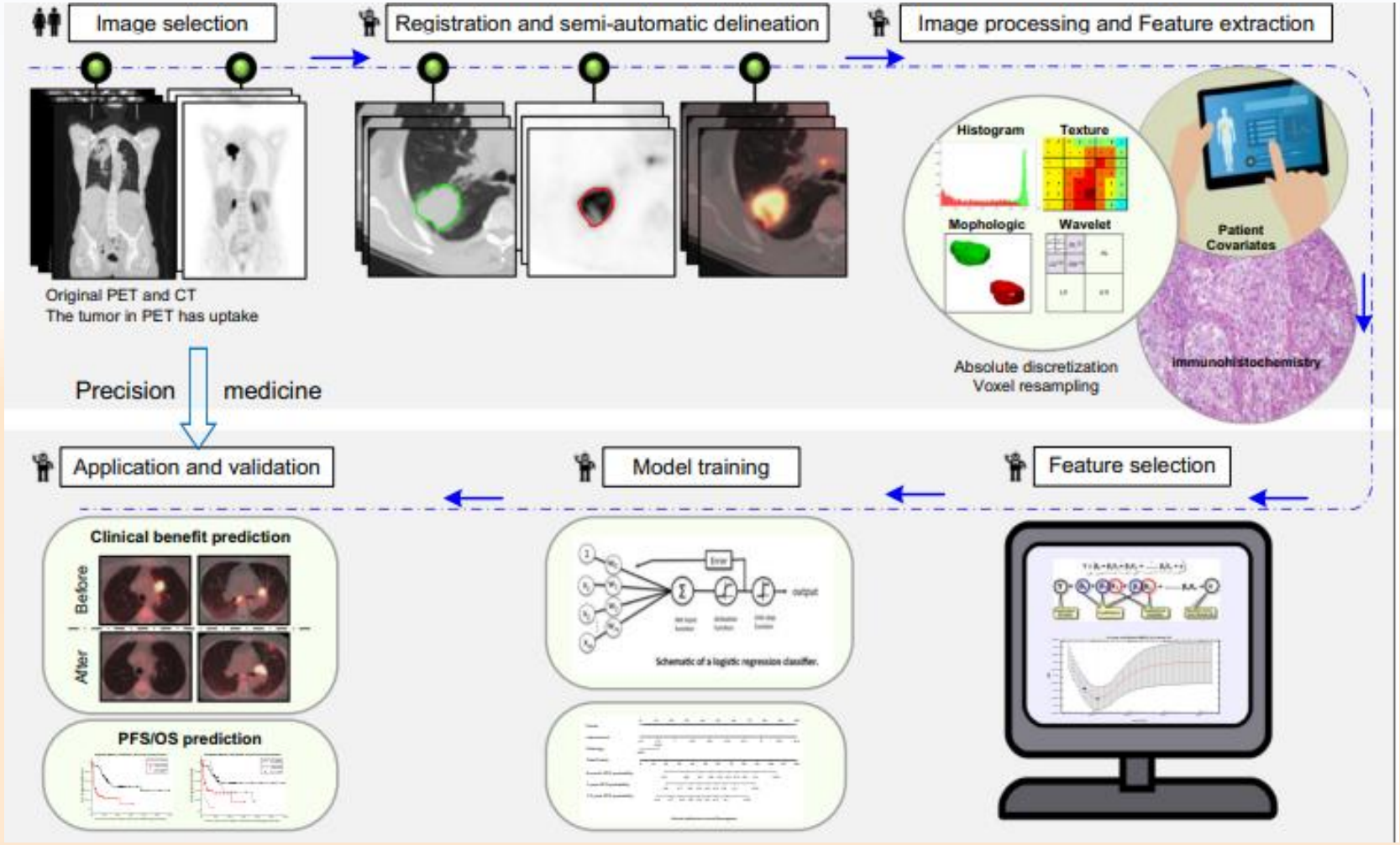
WHAT'S NEW ON PET/CT in NSCLC

RADIOMICS and AI



Radiomics is **quantitative extraction** of imaging features from medical scans.
It may **detect prognostic features and patterns unnoticed to the human eye**

WHAT'S NEW ON PET/CT in NSCLC

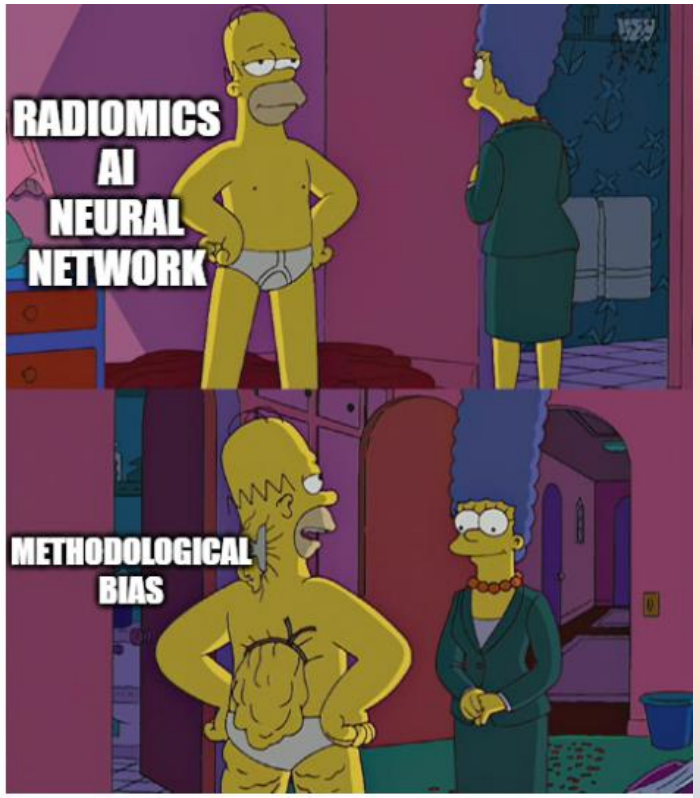
RADIOMICS and AI

Review > Diagnostics (Basel). 2020 May 30;10(6):359. doi: 10.3390/diagnostics10060359.

Imaging-Based Prediction of Molecular Therapy Targets in NSCLC by Radiogenomics and AI Approaches: A Systematic Review

The objective of this systematic review was to analyze the current state of the art of imaging-derived biomarkers predictive of genetic alterations and immunotherapy targets in lung cancer. We included original research studies reporting the development and validation of imaging feature-based models. The overall quality, the standard of reporting and the advancements towards clinical practice were assessed. Eighteen out of the 24 selected articles were classified as "high-quality" studies according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). The 18 "high-quality papers" adhered to Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) with a mean of 62.9%. The majority of "high-quality" studies (16/18) were classified as phase II. The most commonly used imaging predictors were radiomic features, followed by visual qualitative computed tomography (CT) features, convolutional neural network-based approaches and positron emission tomography (PET) parameters, all used alone or combined with clinicopathologic features. The majority (14/18) were focused on the prediction of epidermal growth factor receptor (EGFR) mutation. Thirty-five imaging-based models were built to predict the EGFR status. The model's performances ranged from weak (n = 5) to acceptable (n = 11), to excellent (n = 18) and outstanding (n = 1) in the validation set. Positive outcomes were also reported for the prediction of ALK rearrangement, ALK/ROS1/RET fusions and programmed cell death ligand 1 (PD-L1) expression. Despite the promising results in terms of predictive performance, image-based models, suffering from methodological bias, require further validation before replacing traditional molecular pathology testing.

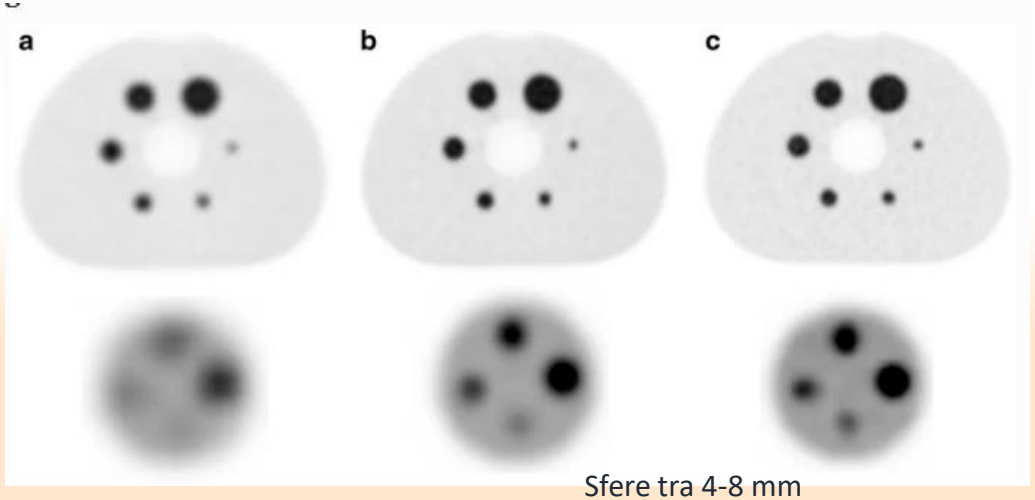
PROMISING results
BUT
Further validation NEEDED
before replacing traditional pathological test



WHAT'S NEW ON PET/CT in NSCLC

TECHNOLOGIC PET-CT implementation

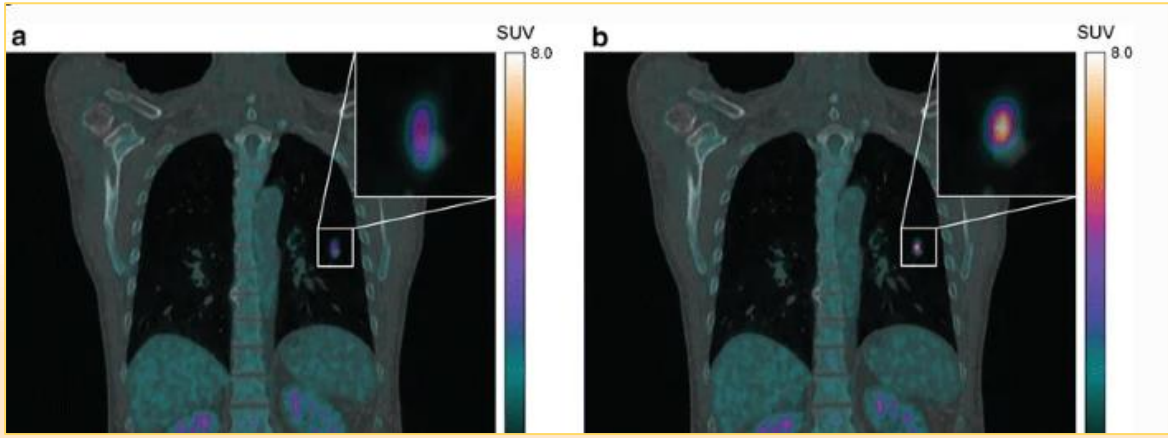
Better imaging quality



Sfere tra 4-8 mm

- Miglior efficienza del cristallo (aumento Annichilazioni reali)
- TOF riduzione coincidenze Casuail Random
- Algoritmi iterativi Riduzione Coincidenze Scatter
- Maggior visualizzazione di eventi di annichilazione per unità di tempo

Respiratory gating



- Riduzione dell'effetto "volume dilution"
- Incremento del SUVmax fino al 70%
- Riduzione del volume fino al 80%

WHAT'S NEW ON PET/CT in NSCLC

TECHNOLOGIC PET-CT implementation

Patient dose ↓ = **Acquisition time**

KEEPING HIGH QUALITY

Patient dose = **Acquisition time** ↓

KEEPING HIGH QUALITY

WHAT'S NEW ON PET/CT in NSCLC

TECHNOLOGIC PET-CT implementation

Patient dose

RAPPORTI ISTISAN 20|22

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Livelli diagnostici di riferimento per la pratica nazionale di radiologia diagnostica e interventistica e di medicina nucleare diagnostica

Aggiornamento del Rapporto ISTISAN 17/33

- 18F-FDG: **2 - 5.4** MBq/kg (AIMN)
- 18F-FDG : 14 MBq (min/bed)/kg (EANM)

SACRO CUORE DON CALABRIA I R C C S

Negrar FDG: 0,06 mCI/kg (2.2 MBq/Kg)

WHAT'S NEW ON PET/CT in NSCLC

TECHNOLOGIC PET-CT implementation

Patient dose ↔ **Acquisition time**

- 18F-FDG: 2 - 5.4 MBq/kg (AIMN)
- 18F-FDG : 14 MBq (min/bed)/kg (EANM)

Negrar FDG: 0,06 mCI/kg (2.2 MBq/Kg)

- NON Digital imaging : 14 minutes
- New Digital PET-CT: **8 minutes**

PET/CT TAKE HOME MESSAGE

TNM STAGING

- IDENTIFY VIABLE TUMOUR
- TREATMENT PLANNING

- DIRECT SAMPLING ON SUSPECT LN
- INCREASE PREDICTIVE VALUE OF TESTS OF MORPHOLOGIC IMAGING

- Identification of METASTATIC DISEASE

FUTURE

- NEW TRACERS
- RADIOMICS

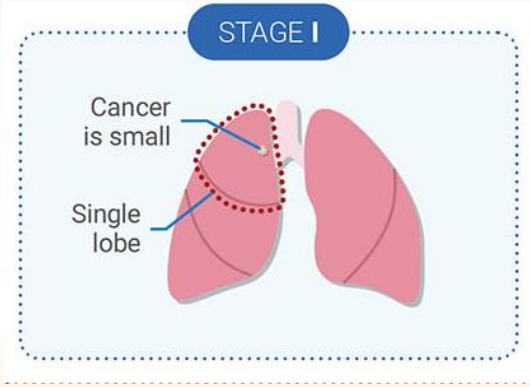
Near FUTURE

- TECHNOLOGICAL IMPROVEMENTs

laura.olivari@sacrocuore.it

18FDG PET/CT and NSCLC

TREATMENT INDICATION



MALATTIA LOCALIZZATA (STADIO 1)

pT1a-c N0
pT2a N0

RADICAL SURGERY (Stage I) Esame istologico e molecolare

Raccomandazioni intervento chirurgico

→ **Esecuzione di esame istologico estemporaneo nei casi senza diagnosi preoperatoria se fattibile;**

→ **Resezioni anatomiche:**

- Lobectomie (preferibili)
- Segmentectomie (se paziente unfit per lobectomia)
- Wedge resection con margini adeguati (se paziente unfit per resezione segmentaria)

→ **Linfadenectomia sistematica**

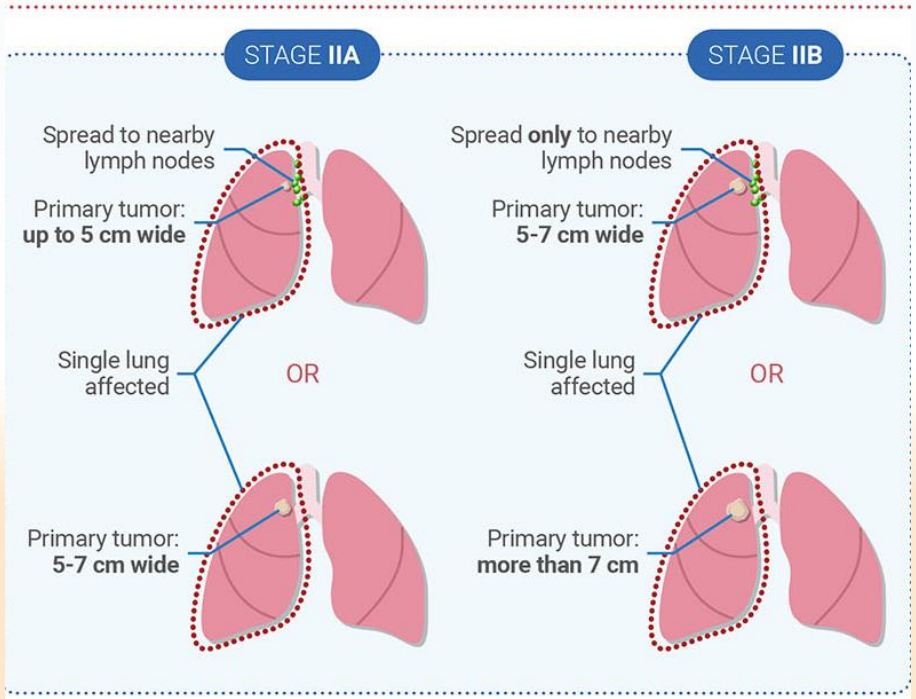
→ **Approccio VATS** se possibile

RT stereotassica (non operabile)

Stadio IA-B (T1 – T2a N0) i pazienti ritenuti non operabili o che rifiutano l'intervento chirurgico sono candidabili ad un trattamento radicale esclusivo con tecniche di precisione a dosi ablative(SBRT/SABR), cioè equivalenti ad una dose biologicamente efficace uguale o superiore a 100-105Gy. In questo setting, i dati di controllo locale si attestano a valori superiori all'80-85%. In caso di lesioni centrali (≤ 1 cm dal mediastino) si valuterà la fattibilità del trattamento o una prescrizione adattata al rischio.

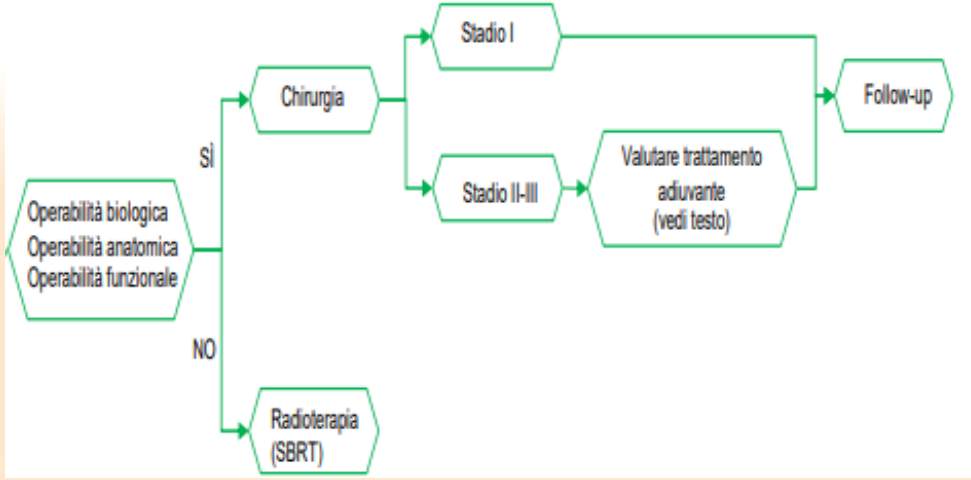
18FDG PET/CT and NSCLC

TREATMENT INDICATION



MALATTIA LOCALIZZATA

RADICAL SURGERY → **CHT / RT adiuvate**



RT a scopo curativo

CHT + RT a scopo curativo

18FDG PET/CT and NSCLC

TREATMENT INDICATION

MALATTIA LOCALIZZATA (stadio 2A e 2B)

RADICAL SURGERY → **CHT / RT adiuvate**

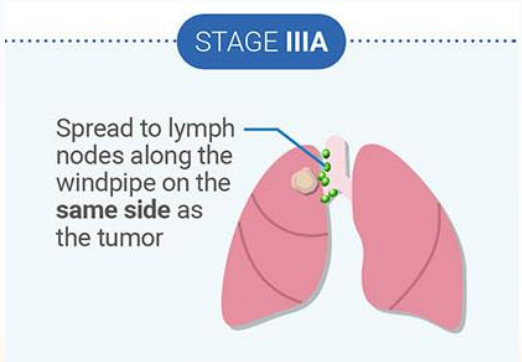
RT a scopo curativo

CHT + RT a scopo curativo

Stadio IIA (T1-T2a N1 – T2b N0), Stadio IIB (T2b N1 – T3 N0 per dimensione o nodulo satellite) e nei pazienti non operabili o che rifiutano intervento chirurgico sono candidabili a trattamento radioterapico esclusivo se cN0. In caso di cN1 il trattamento standard è rappresentato da chemo-radioterapia concomitante. Il trattamento chemioterapico e radioterapico sequenziale o radioterapico esclusivo deve essere considerato nei pazienti fragili non in grado di tollerare concomitanza.

18FDG PET/CT and NSCLC

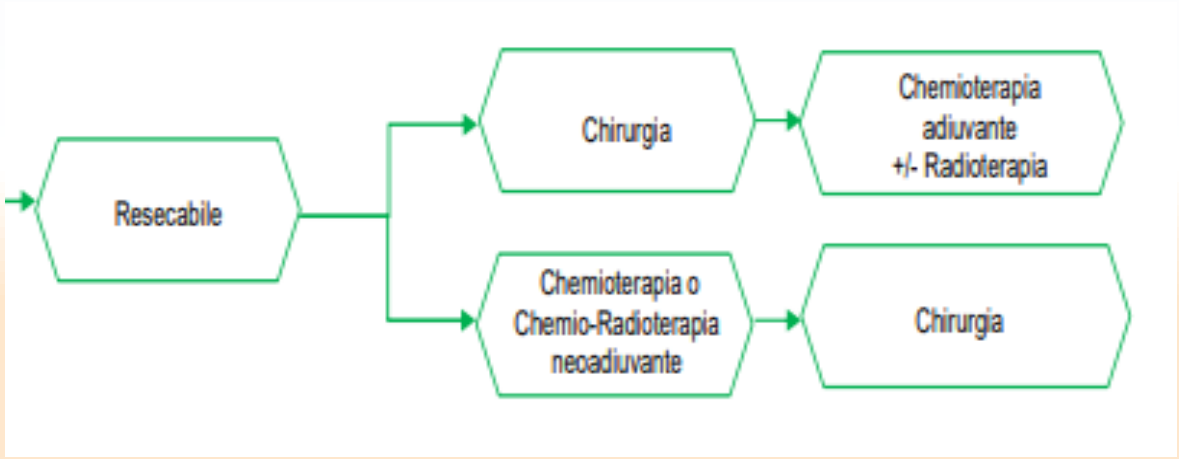
TREATMENT INDICATION



MALATTIA LOCALMENTE AVANZATA

- pT3pN1
- pT4pN0
- pTxpN2
- Pluristazione selezionato
- - Monostazione

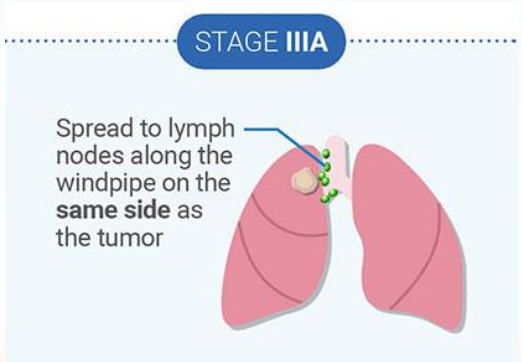
Resecabile



NON resecabile (N2bulky)

18FDG PET/CT and NSCLC

TREATMENT INDICATION

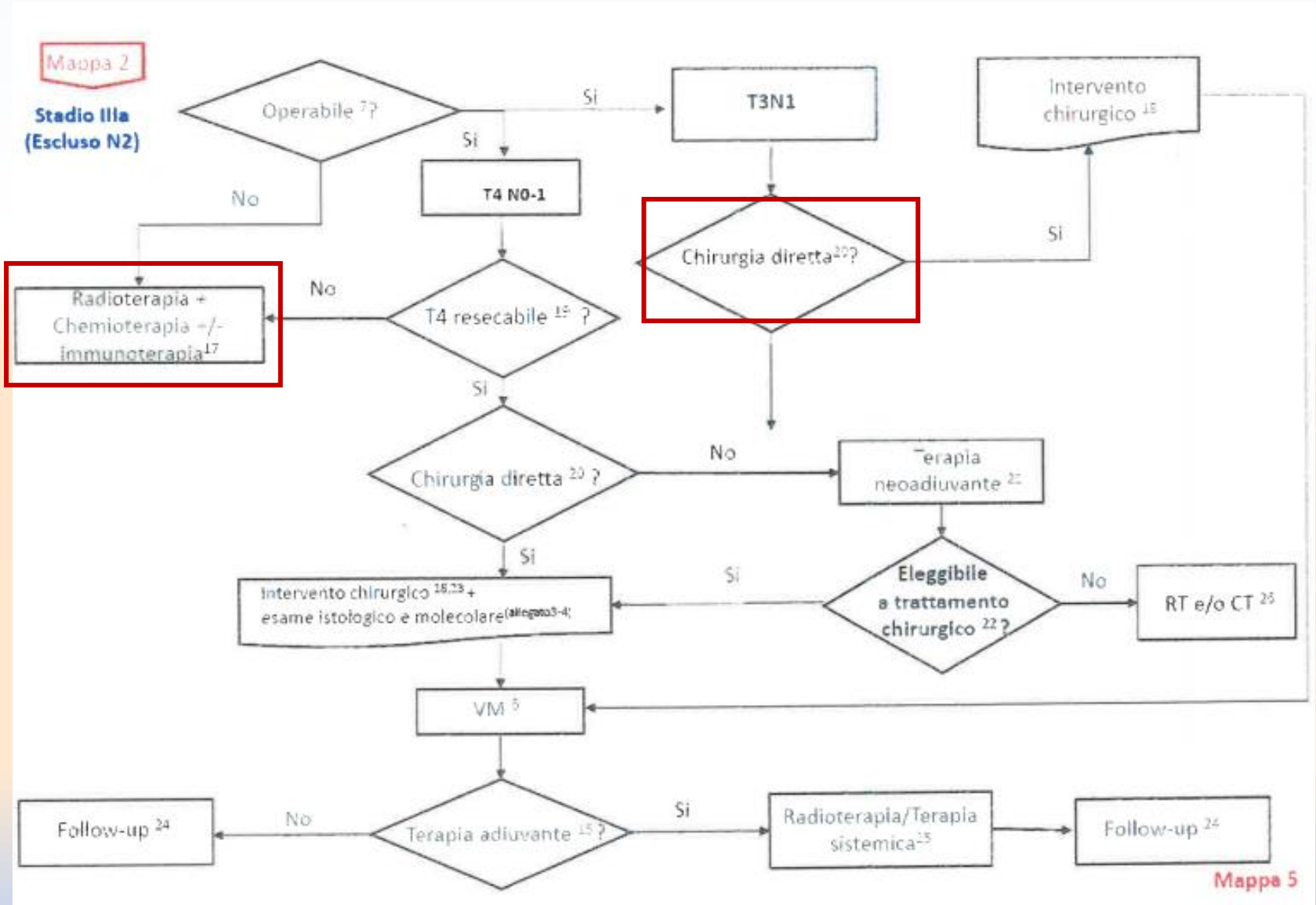


MALATTIA LOCALMENTE AVANZATA

pT3pN1

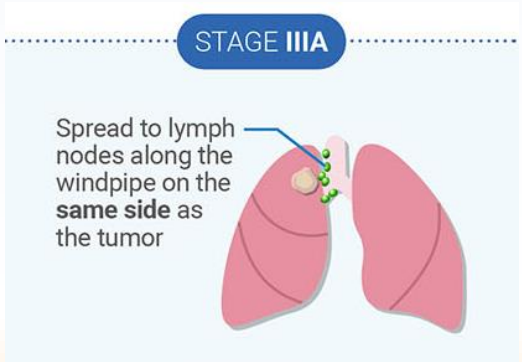
pT4pN0

Variazioni PDTA 2022 vs 2017



18FDG PET/CT and NSCLC

TREATMENT INDICATION

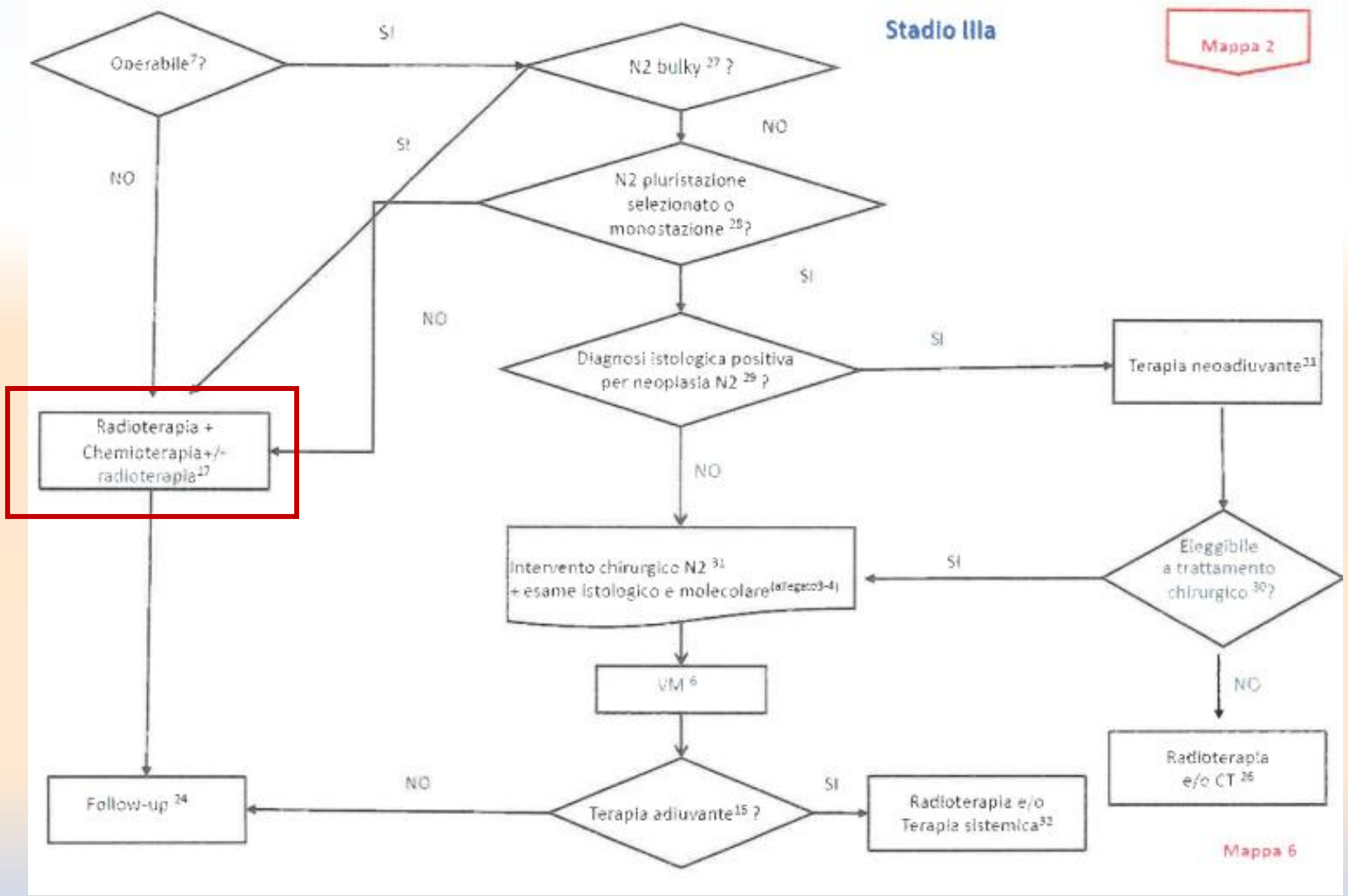


MALATTIA LOCALMENTE AVANZATA

pT3pN1

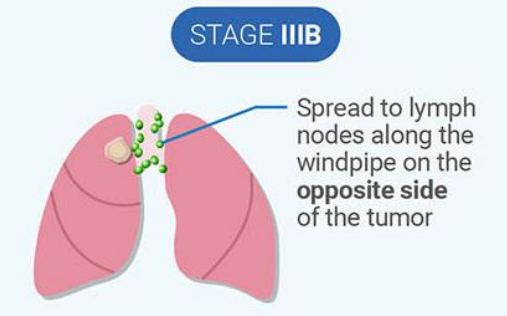
pT4pN0

Variazioni PDTA 2022 vs 2017



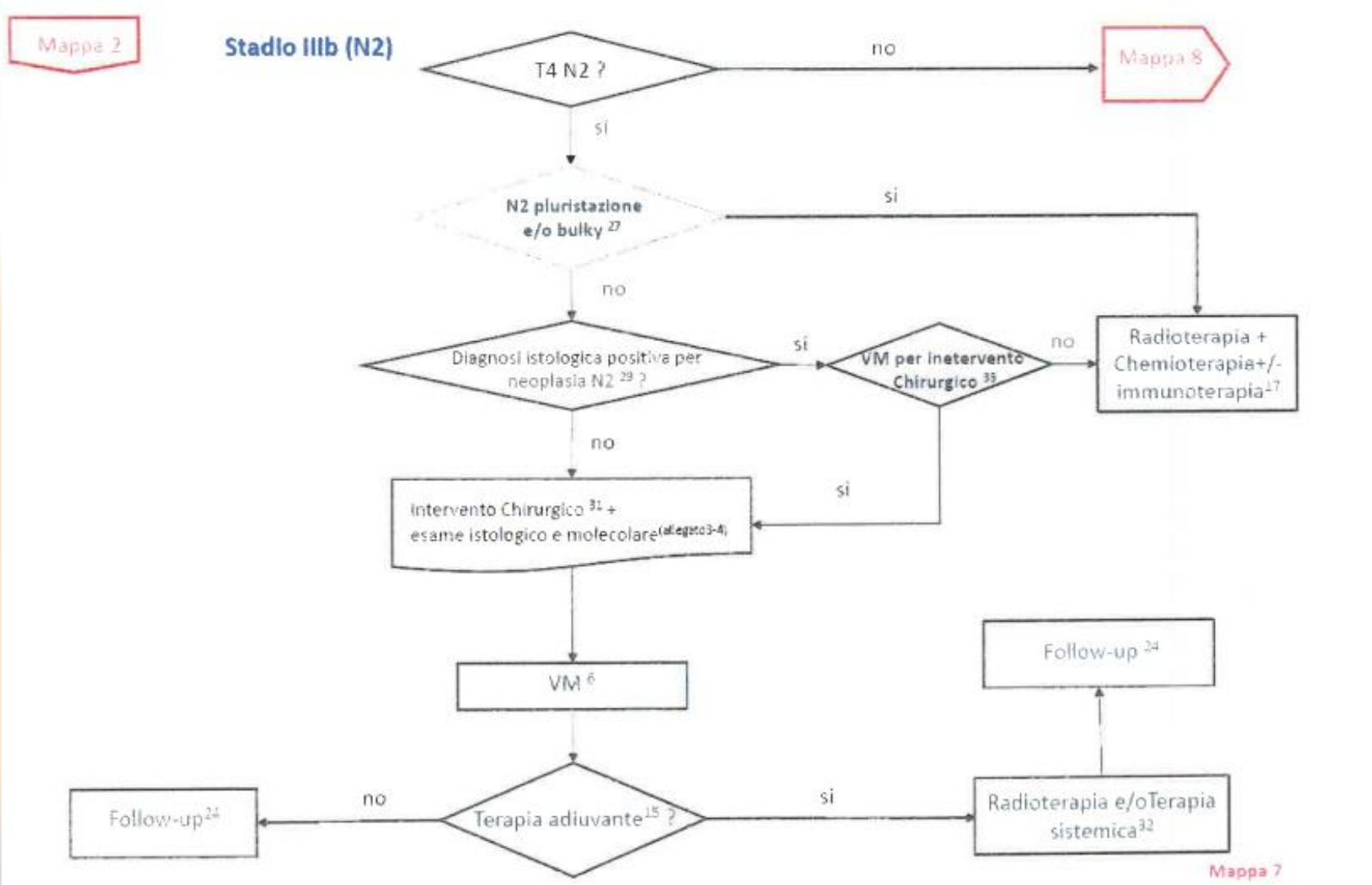
18FDG PET/CT and NSCLC

TREATMENT INDICATION



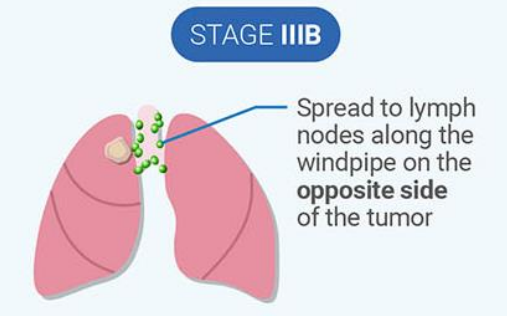
MALATTIA LOCALMENTE AVANZATA

pT4pN2



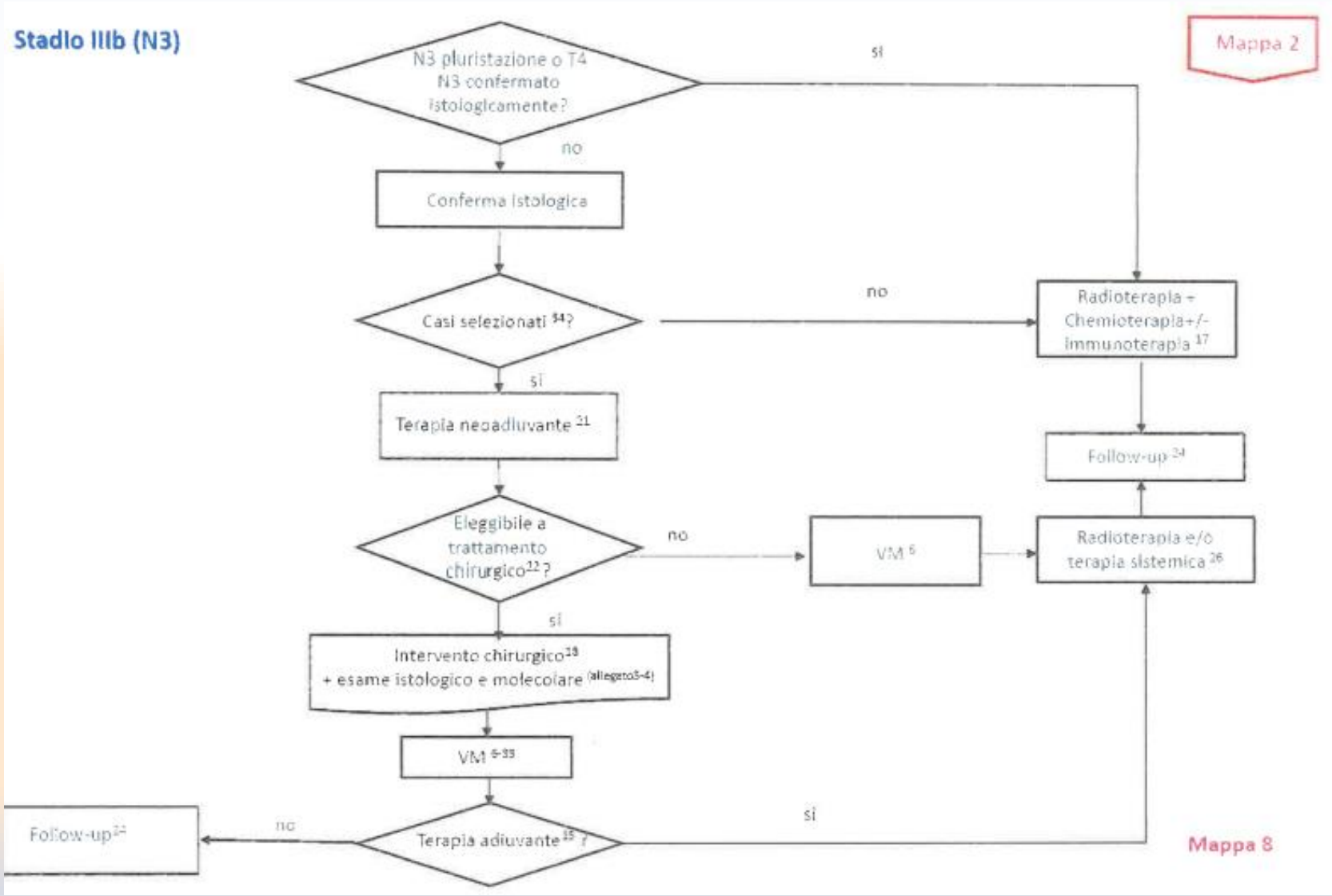
18FDG PET/CT and NSCLC

TREATMENT INDICATION



MALATTIA LOCALMENTE AVANZATA

pTxpN3

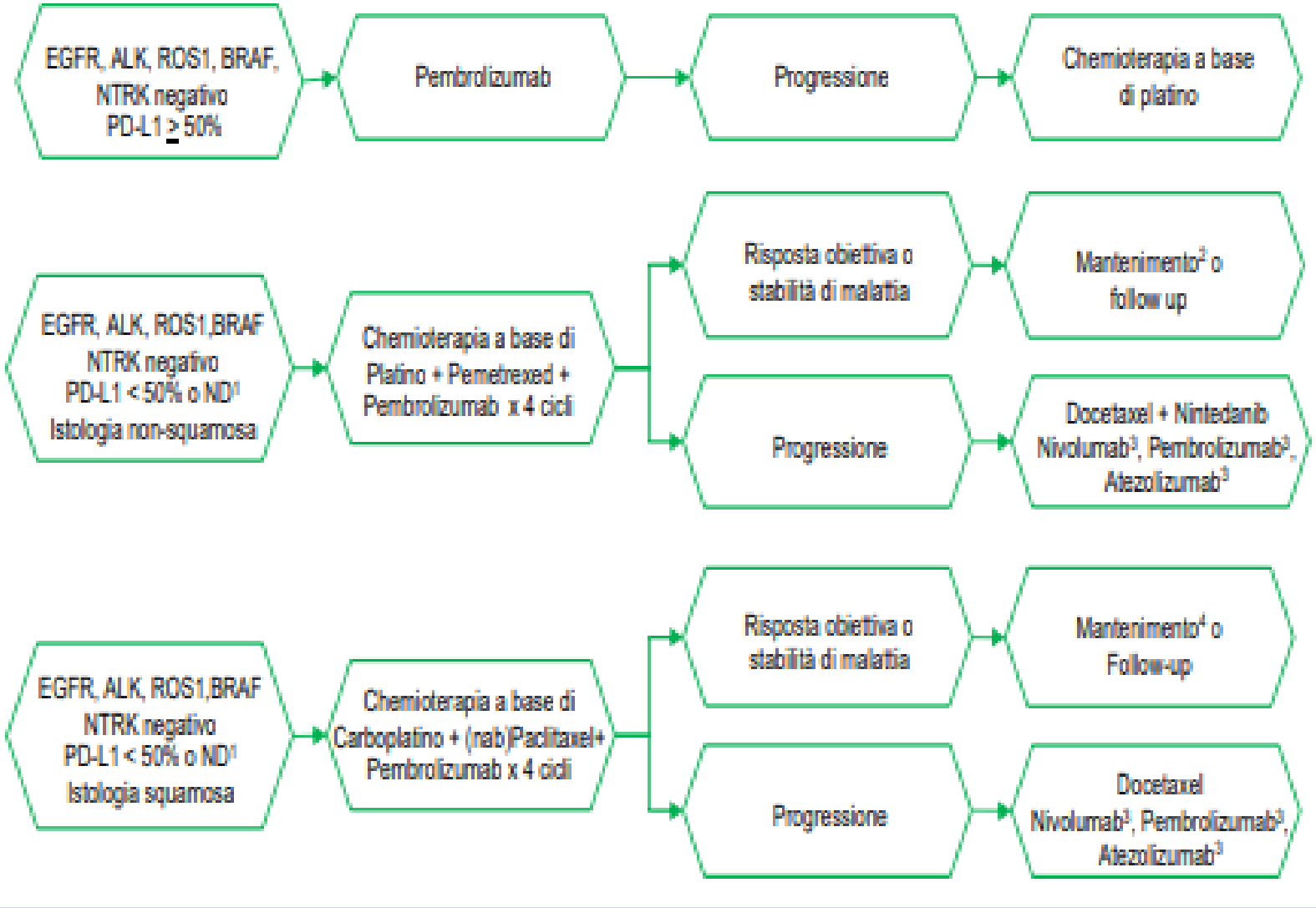


18FDG PET/CT and NSCLC

TREATMENT INDICATION

MALATTIA METASTATICA

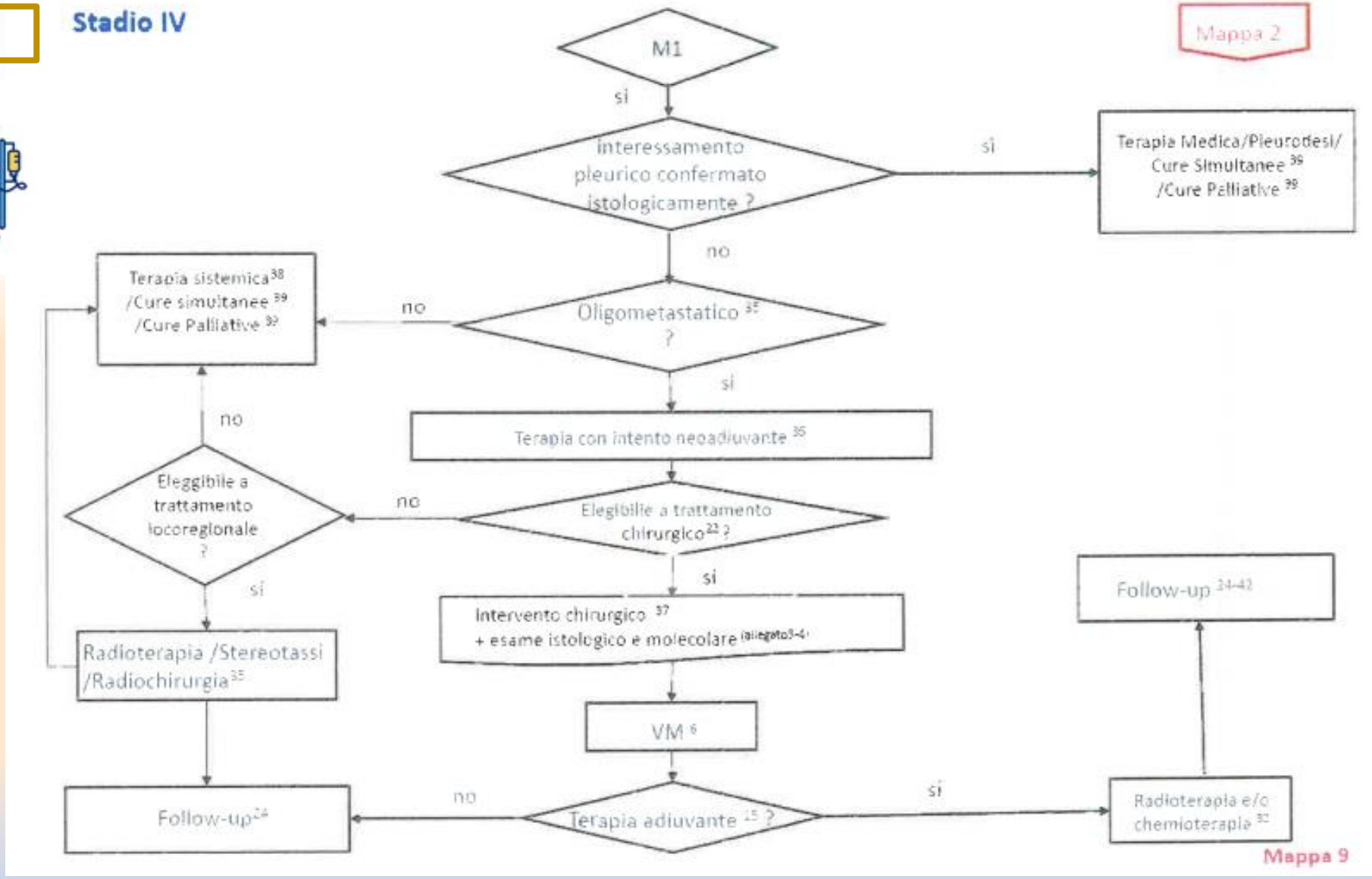
CHEMOTHERAPY



18FDG PET/CT and NSCLC

TREATMENT INDICATION

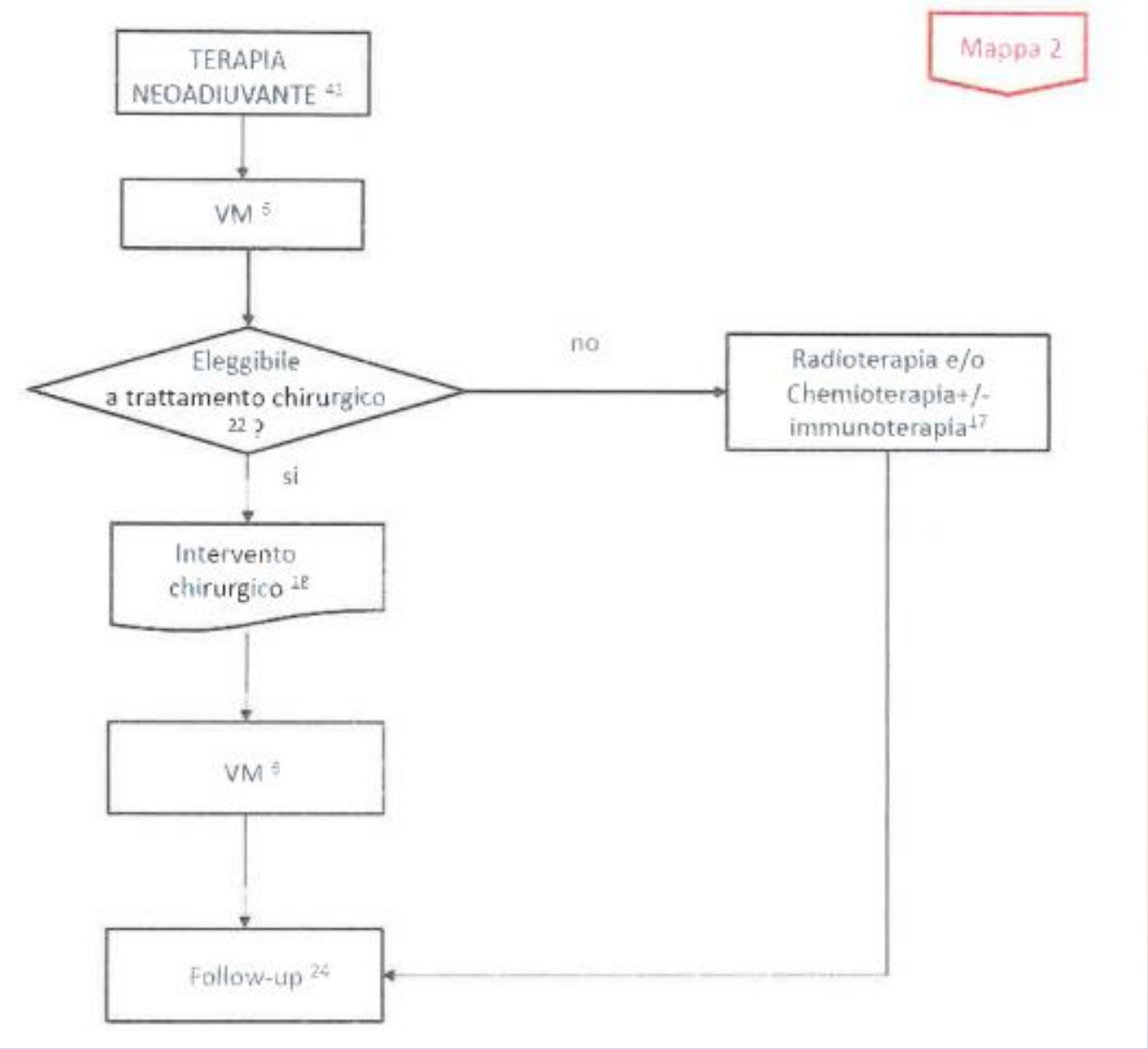
MALATTIA METASTATICA



18FDG PET/CT and NSCLC

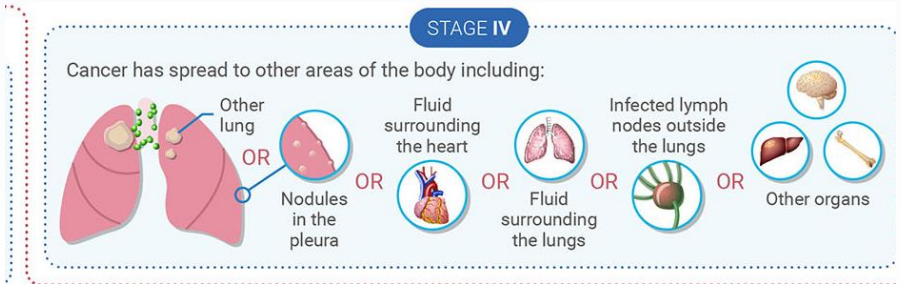
TREATMENT INDICATION

TUMORE DI PANCOST



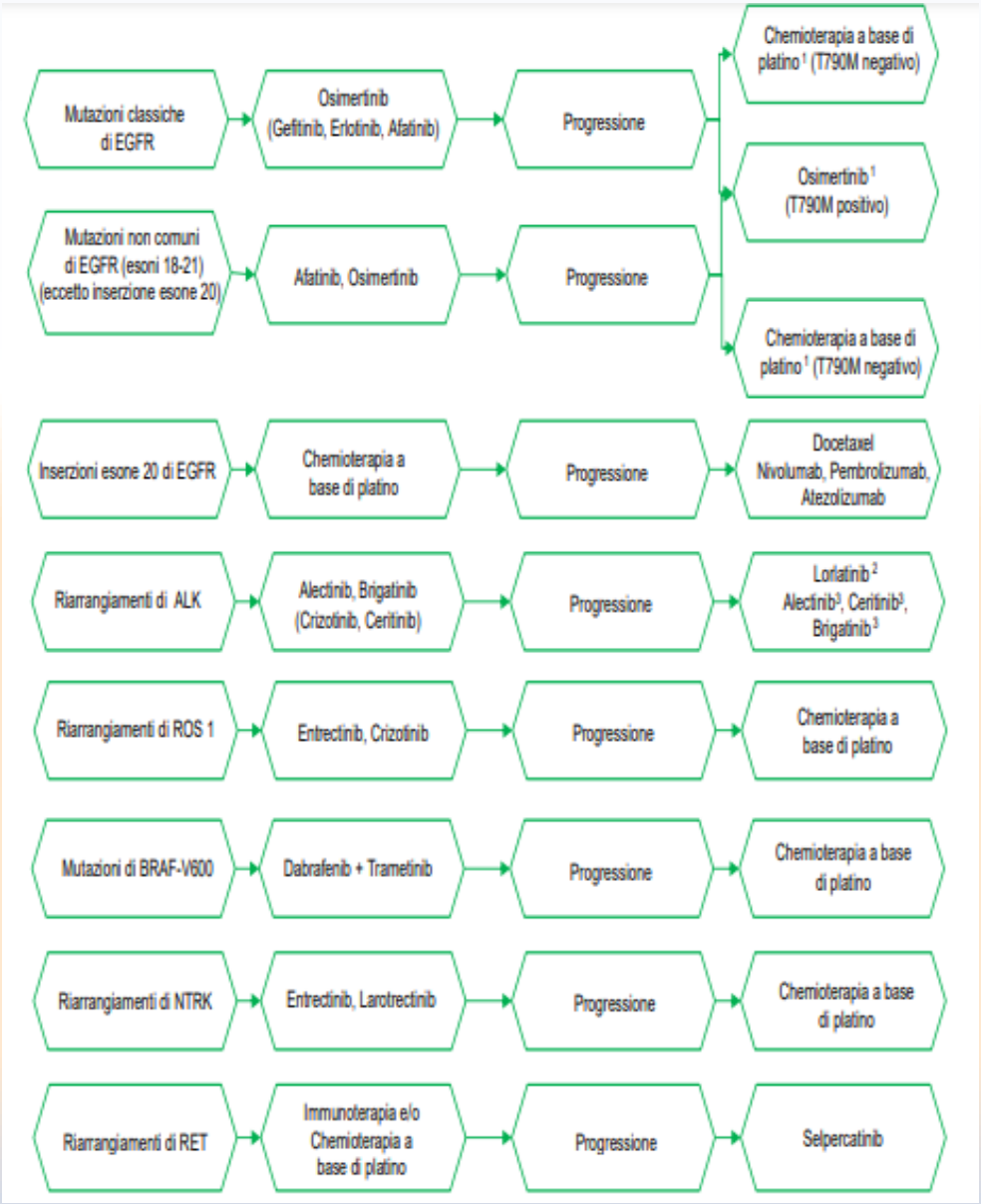
18FDG PET/CT and NSCLC

TREATMENT INDICATION



MALATTIA METASTATICA

ONCOGENE ADDICTED



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