

LA DIAGNOSI PRECOCE E LO SCREENING: IL RUOLO DEL RADIOLOGO

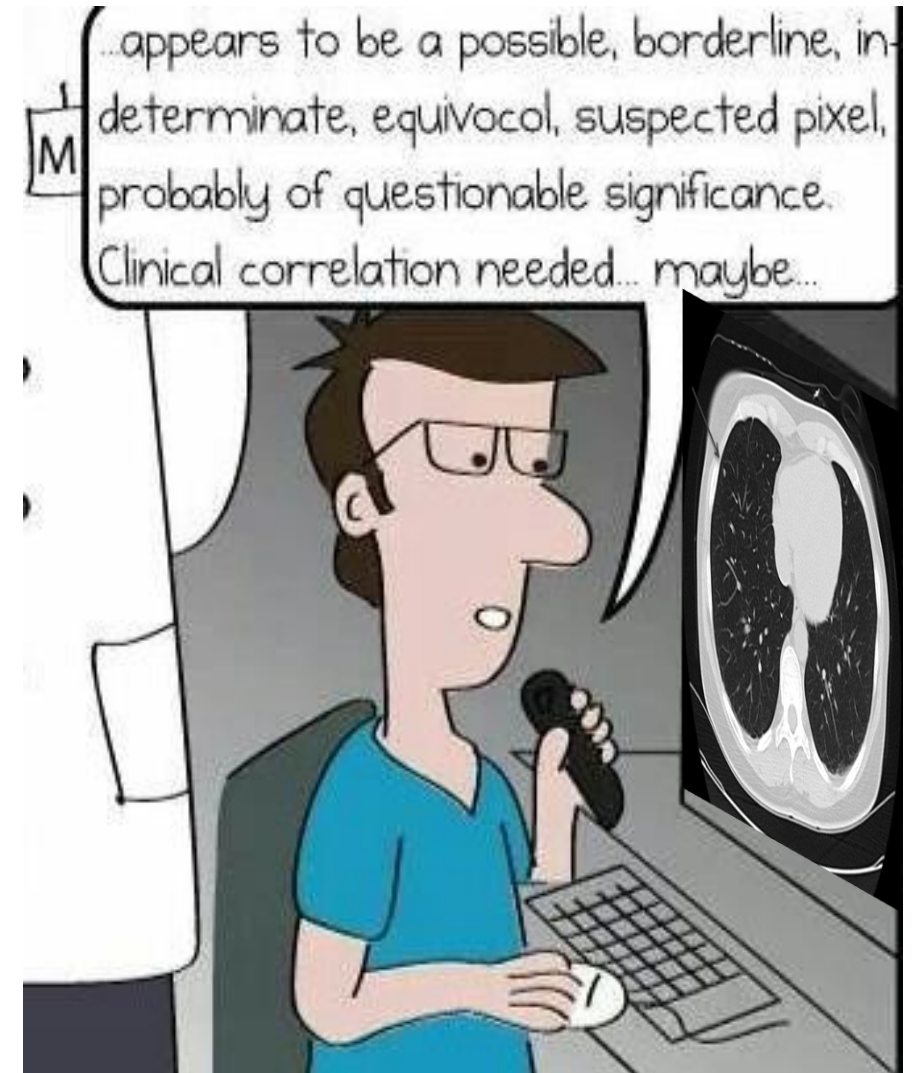
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School of Medicine,



SOMMARIO

- **INTRODUZIONE:** diagnosi precoce
- **MATERIALI E METODI:** interpretazione dell'imaging
 - parametri di valutazione
 - algoritmi
- **RISULTATI:** vantaggi e svantaggi dello screening
 - riduzione della mortalità
 - rischio di overtreatment
- **CONCLUSIONI:** responsabilità del radiologo



Recent Trends in the Identification of Incidental Pulmonary Nodules

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Abstract

Rationale: Pulmonary nodules are common incidental findings, but information about their incidence in the era of computed tomography (CT) is lacking.

Objectives: To examine recent trends in pulmonary nodule identification.

Methods: We used electronic health records and natural language processing to identify members of an integrated health system who had nodules measuring 4 to 30 mm. We calculated rates of chest CT imaging, nodule identification, and receipt of a new lung cancer diagnosis within 2 years of nodule identification, and standardized rates by age and sex to estimate the frequency of nodule identification in the U.S. population in 2010.

Measurements and Main Results: Between 2006 and 2012, more than 200,000 adult members underwent 415,581 chest CT examinations. The annual frequency of chest CT imaging increased from 1.3 to 1.9% for all adult members, whereas the frequency of nodule identification increased from 24 to 31% for all scans performed. The annual rate of chest CT increased from 15.4 to 20.7 per 1,000 person-years, and the rate of nodule identification increased from 3.9 to 6.6 per 1,000 person-years, whereas the rate of a new lung cancer diagnosis remained stable. By 2012, more than 4.8 million Americans underwent at least one

chest CT scan, and 1.57 million had a nodule identified, including 63,000 who received a new lung cancer diagnosis within 2 years.

Conclusions: Incidental pulmonary nodules are an increasingly common consequence of routine medical care, with an incidence that is much greater than recognized previously. More frequent nodule identification has not been accompanied by increases in the diagnosis of cancerous nodules.

Keywords: coin lesion; lung cancer; computed tomography

At a Glance Commentary

Scientific Knowledge of the Subject: Use of chest computed tomography is increasing over time, but large epidemiological studies of incidental pulmonary nodules and trends in their incidence have not been performed.

What This Study Adds to the Field: Between 2006 and 2012, the annual rate of pulmonary nodule identification in a large, integrated health system increased from 3.9 to 6.6 per 1,000 person-years. By extrapolation, more than 1.5 million adult Americans will have a pulmonary nodule identified each year, a number that is an order of magnitude greater than recognized



PARAMETRI VALUTAZIONE

ORIGINAL ARTICLE

Probability of Cancer in Pulmonary Nodules Detected on First Screening CT

Annette McWilliams, M.B., Martin C. Tammemagi, Ph.D., John R. Mayo, M.D., Heidi Roberts, M.D., Geoffrey Liu, M.D., Kam Soghrati, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Simon Martel, M.D., Francis Laberge, M.D., Michel Gingras, M.D., Sukhinder Atkar-Khattra, B.Sc., Christine D. Berg, M.D., [et al.](#)

Article [Figures/Media](#)

[Metrics](#)

[September 5, 2013](#)

[N Engl J Med 2013; 369:910-919](#)

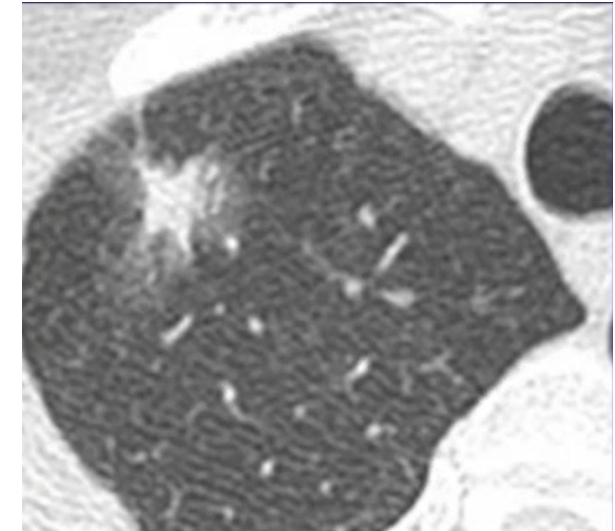
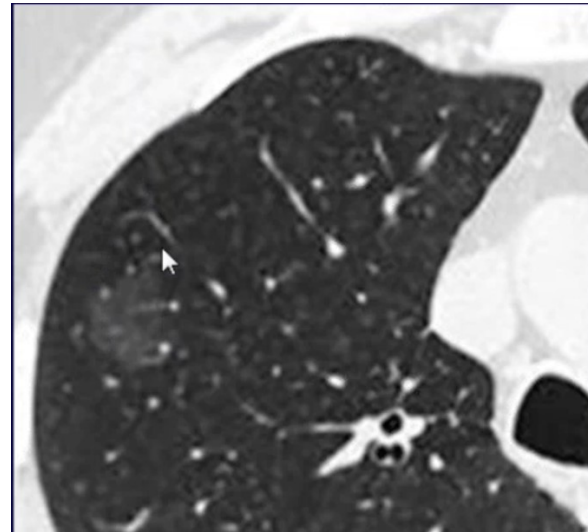
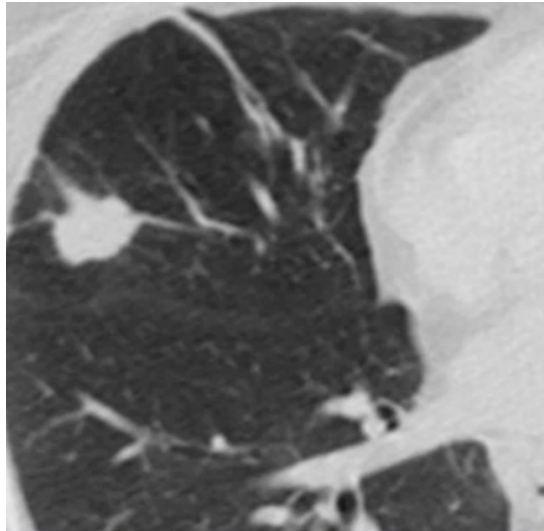
[DOI: 10.1056/NEJMoa1214726](#)

[1 References](#) [697 Citing Articles](#) [Letters](#)

- ATTENUAZIONE = TIPO DI NODULO
- DIMENSIONI
- SEDE
- MORFOLOGIA
- MARGINI
- RETRAZIONE PLEURICA
- SPAZI CISTICI
- ACCRESIMENTO



SOLIDO – NON SOLIDO – PARZIALMENTE SOLIDO



	ELCAP	PanCan dataset	BCCA dataset
PARZIALMENTE SOLIDO	63 %	6.6 %	22.2%
NON SOLIDO	18 %	1.9%	1.3%
SOLIDO	7%	1.1%	0.6%



NODULI SOLIDI

- Linfonodi intrapolmonari
- Tumori benigni
- Lesioni infiammatorie
- Tumore polmone



**Formazioni
benigne**

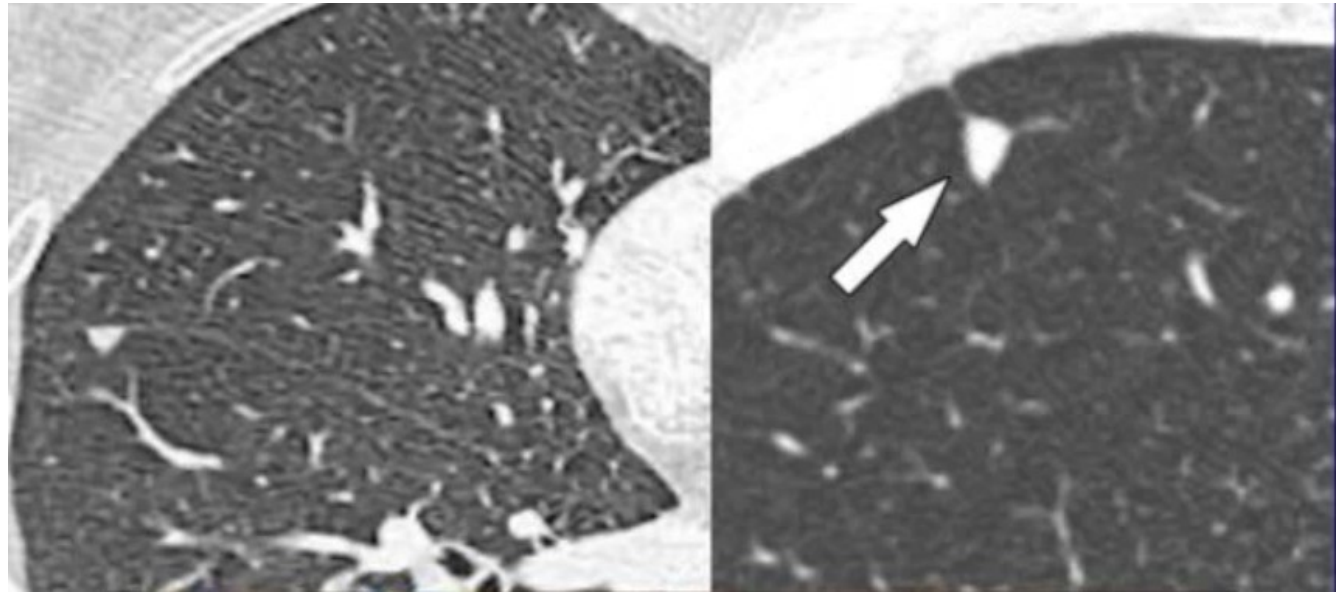


NODULI SOLIDI

- **Linfonodi intrapolmonari**

(24-44% dei noduli non calcifici in contesto di screening)

- Forma → lenticolare, triangolare, poliedrica
- Margini → lisci, d fino 12 mm
- Localizzazione → ai lobi inferiori a distanza di 10-15 mm dalla pleura viscerale o adeso alla scissura
- Fini strutture radiopache di raccordo con la pleura
- Variabilità dimensionale nel tempo



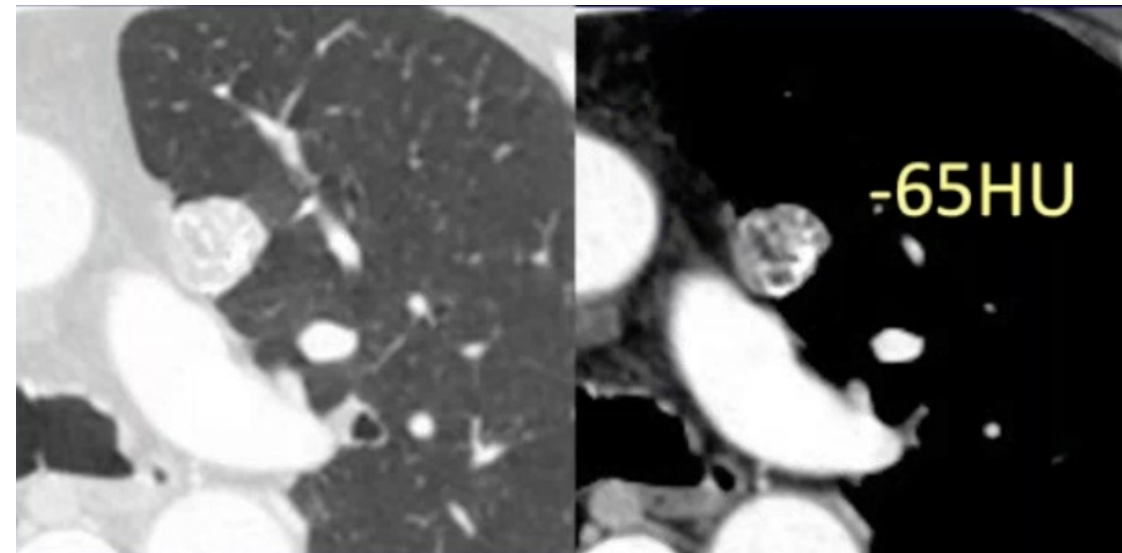
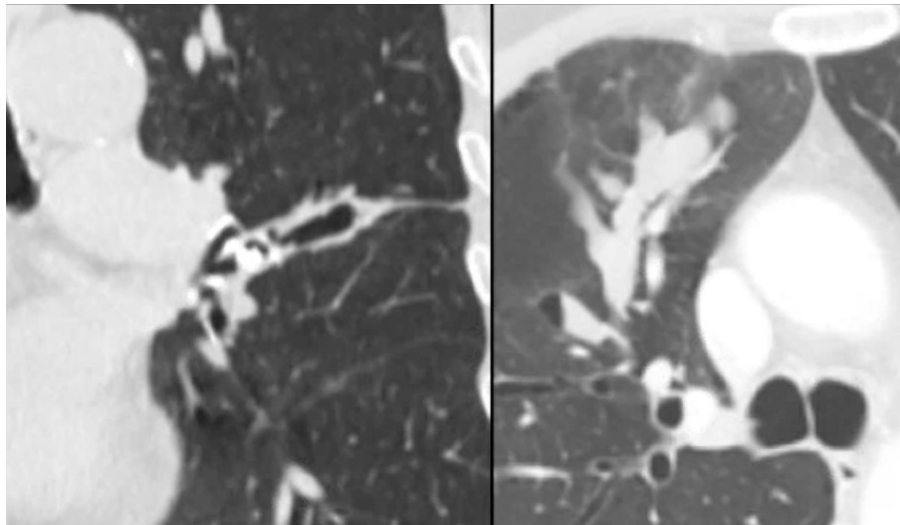
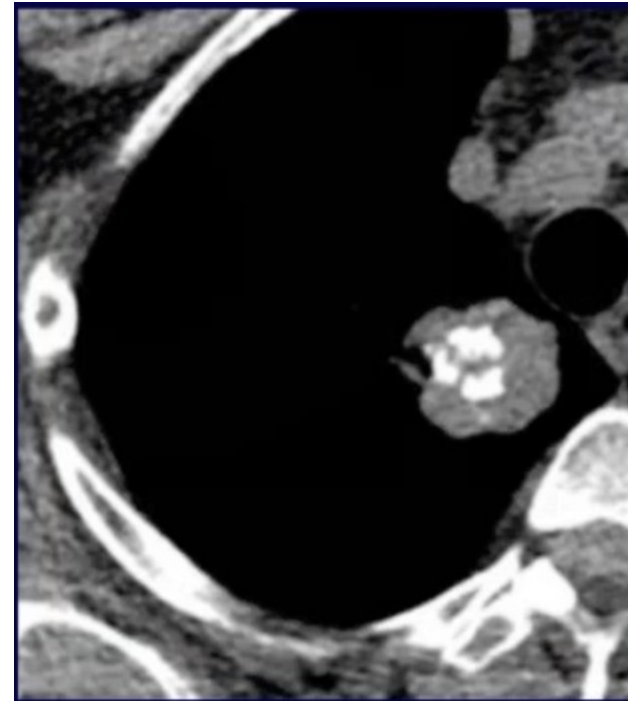
Bueno J. – RadioGraphics 2018;38:1337

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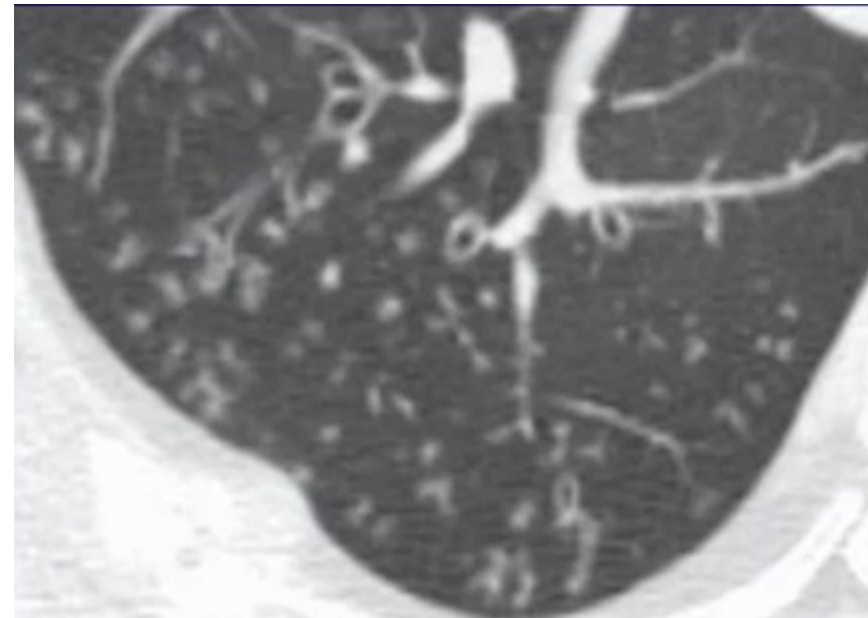
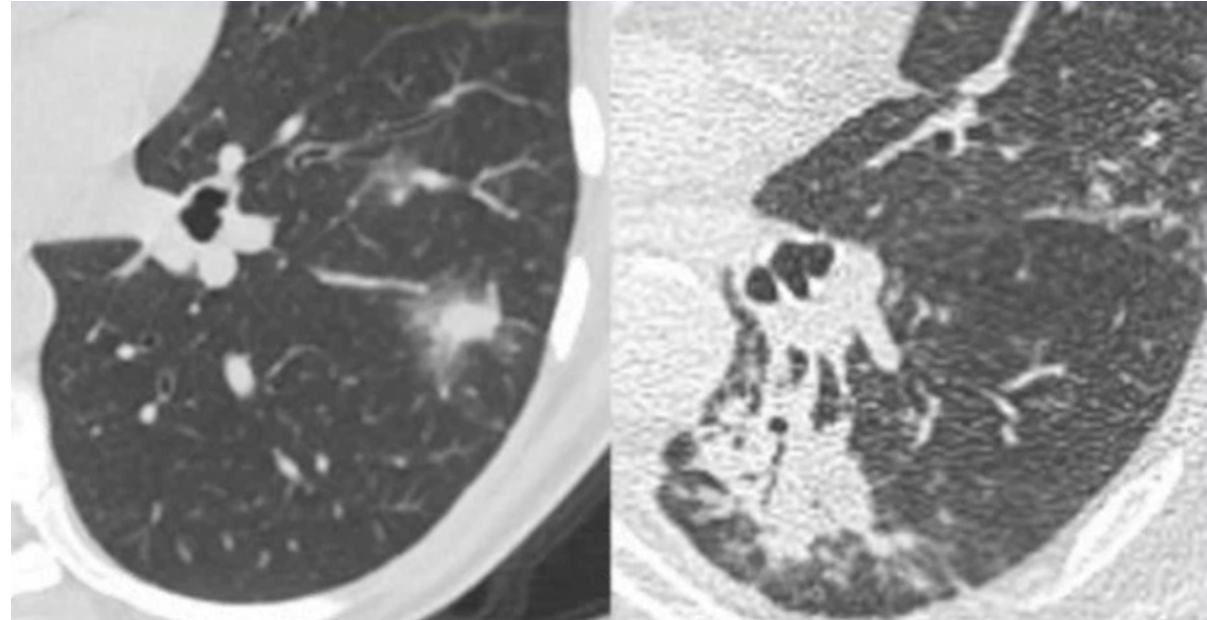
NODULI SOLIDI

- ***Tumori benigni***
 - Amartomi
 - Calcificazioni a «pop corn» →
DD con amorse e puntiformi
 - Componenti adipose →
escludere storia liposarcoma o RCC
 - Granulomi
 - Ristagni mucosi endobronchiali



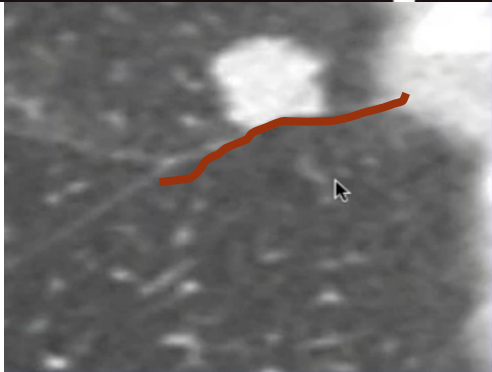
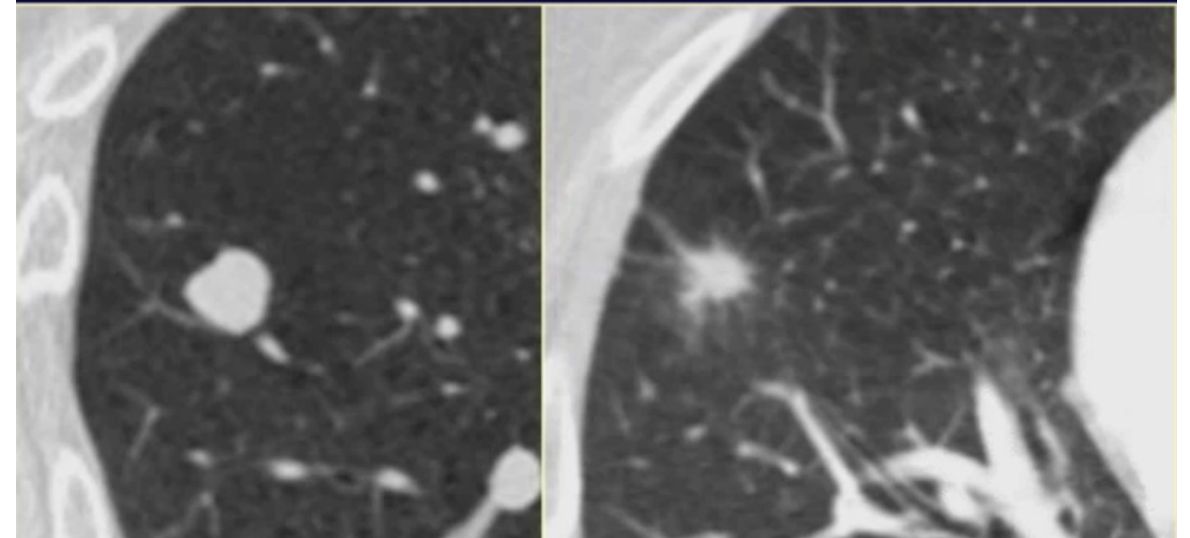
NODULI SOLIDI

- ***Lesioni infiammatorie***
 - « alterazione ad albero in gemma» o micronodiuli centrolobulari
 - Ampie consolidazioni parenchimali, anche con margini irregolari, sono primariamente da riferire a infiammazioni piuttosto che a neoplasie se si ha un precedente (recente) negativo; soprattutto se presente broncogramma aereo



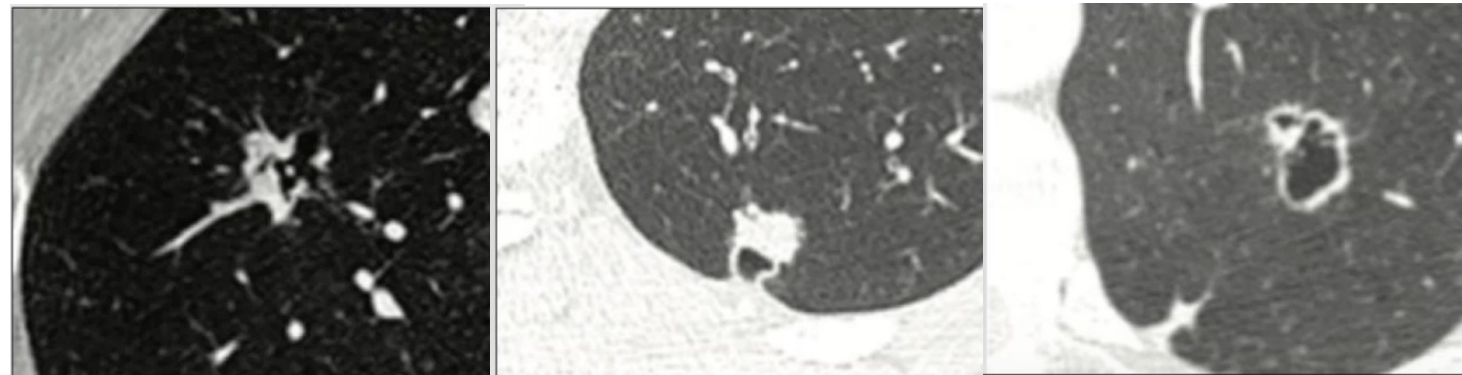
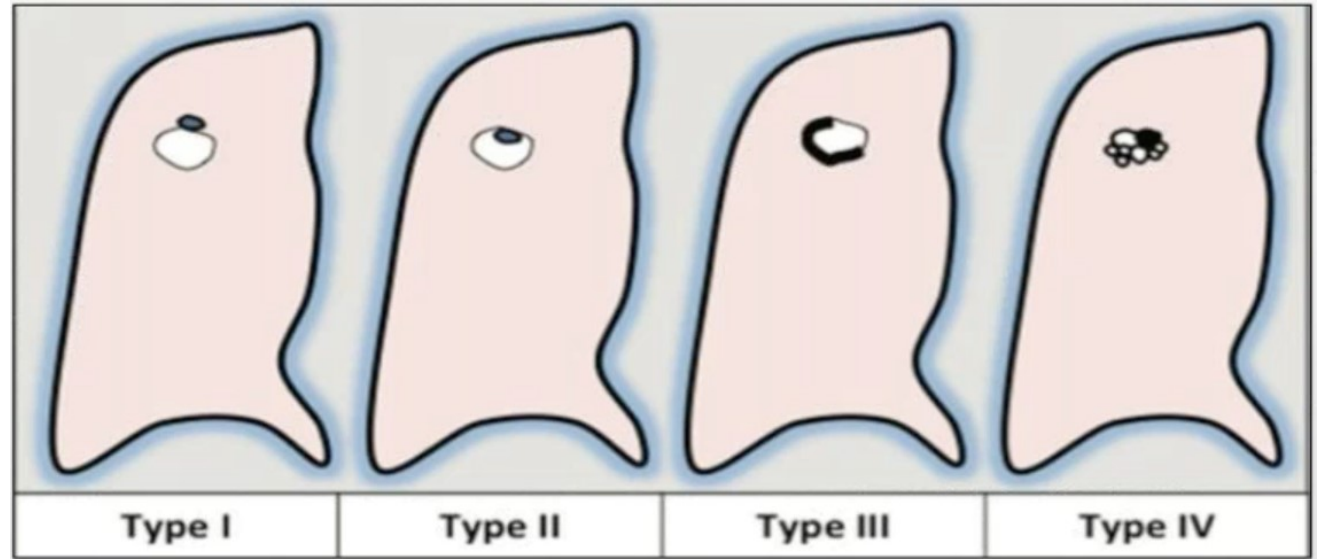
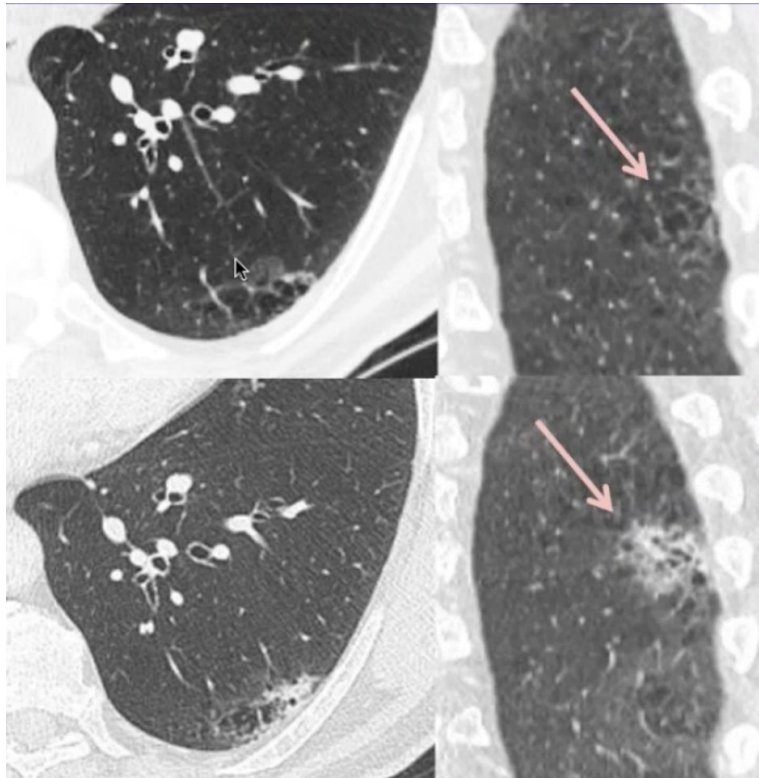
NODULI SOLIDI

- ***Tumore polmone***
 - Localizzazione → lobi superiori
 - Forma → irregolare
 - Margini → spiculati (PPV 90%)
 - NB. Se lisci escludere carcinoidi o metastasi
 - Retrazione pleurica

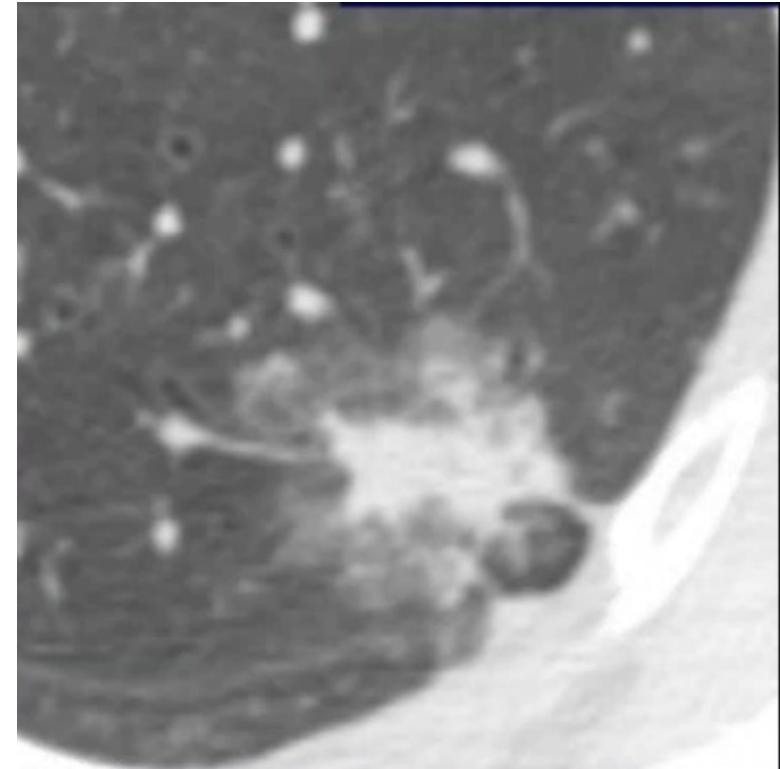
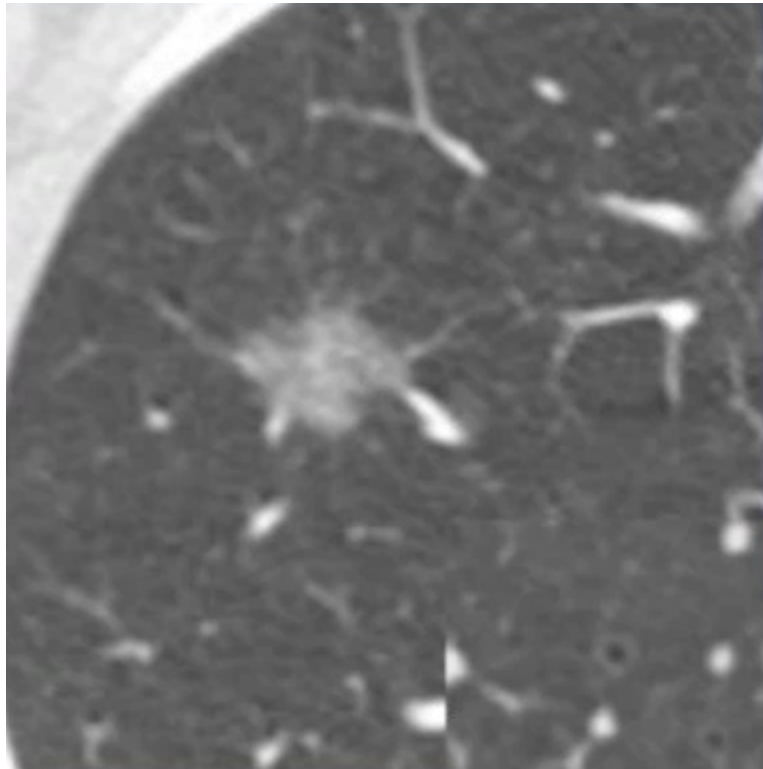


NODULI SOLIDI

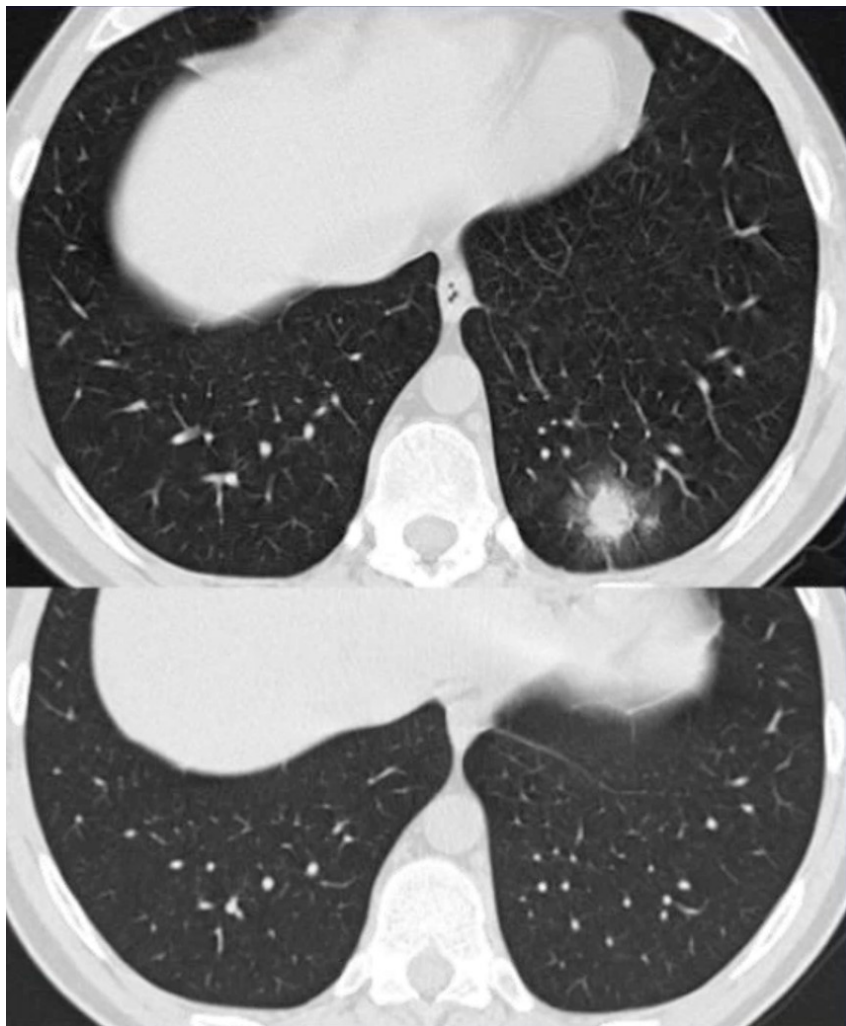
- ***Tumore polmone***
 - *Lesione pericistica*



NODULI SUB-SOLIDI O PARZIALMENTE SOLIDI DUE FACCE DELLA STESSA MEDAGLIA?



NODULI SUB-SOLIDI O PARZIALMENTE SOLIDI LO SCOPRIREMO COL TEMPO

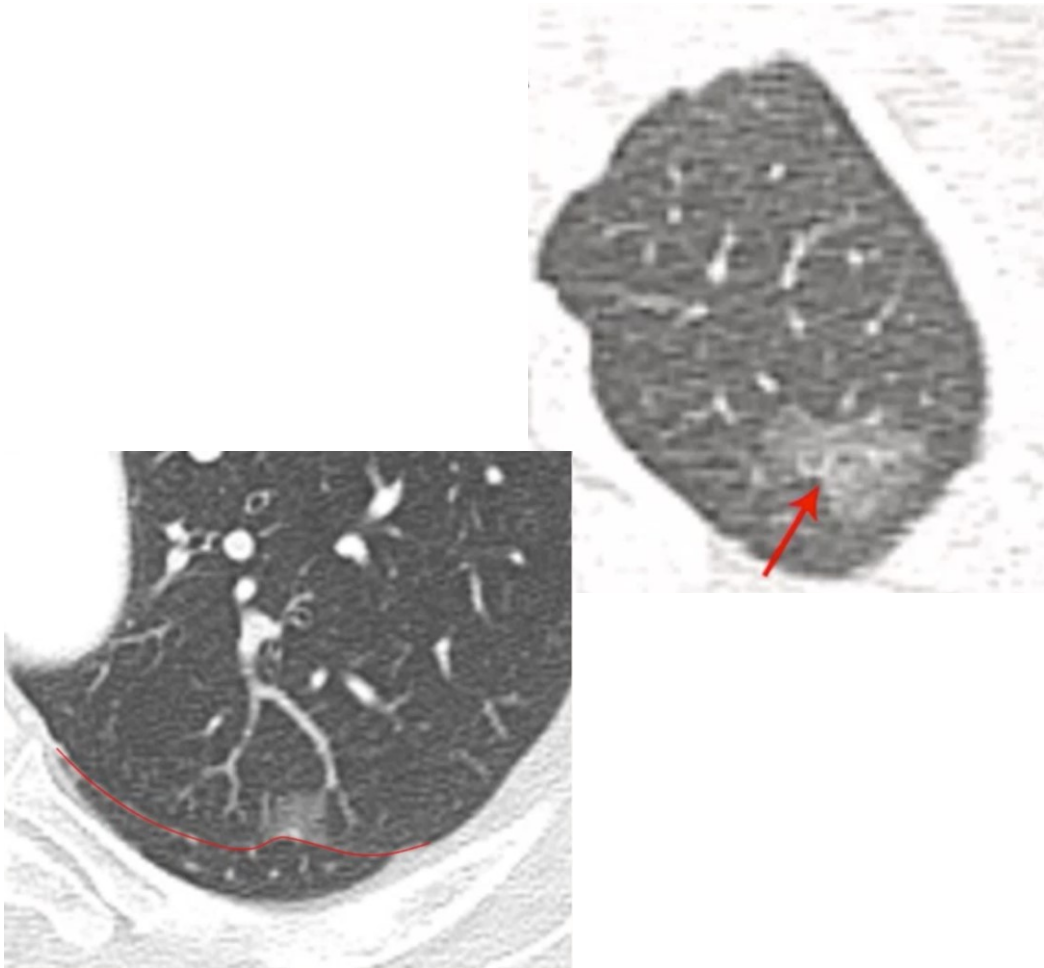


- Transitorie o persistenti?
 - Nel 67% dei casi si risolvono (NELSON)
 - Spesso presentazione di alterazioni infettivo - infiammatorie o vasculitiche
- Caratteristiche suggestive di risoluzione spontanea:
 - M, giovane,
 - Fumatore
 - Eosinofilia
 - Margini poco definiti
 - Componente solida ampia
 - Assenza in TC precedente recente



NODULI SUB-SOLIDI O PARZIALMENTE SOLIDI


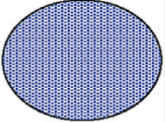

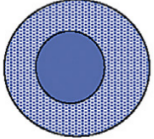
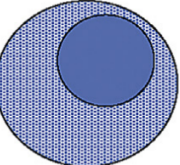
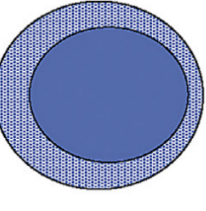
SOSPETTA IPERPLASIA ADENOMATOSA ATIPICA VS ADENOCARCINOMA IN SITU



- Persistenza con stabilità dimensionale o solo minimo aumento dimensionale
- Retrazione pleurica
- Spiculature o distorsioni
- Lobo superiore
- Fattori di rischio
- Comparsa componente solida → minimo 3 mm di diametro
- Spesso non captano alla PET



NODULI SUB-SOLIDI O PARZIALMENTE SOLIDI

cT*	CT image on HRCT						
	Solid part	0 cm	0 cm	≤0.5 cm†	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
	Total tumor size including GG	≤0.5 cm	0.6-3.0 cm‡‡	≤3.0 cm‡‡	0.6-3.0 cm‡‡	1.1-3.0 cm‡‡	2.1-3.0 cm‡‡
	Pathologic Differential Diagnosis	AAH‡, AIS, MIA	AIS, MIA, LPA	MIA, LPA, AIS	LPA, Invasive AD, MIA	LPA, Invasive AD	Invasive AD
Clinical Stage*			cTis‡‡	cT1mi‡‡	cT1a	cT1b	cT1c
pT	Invasive part	0 cm	0 cm	≤0.5 cm‡‡	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
	Total tumor size including lepidic growth part	Usually ≤0.5 cm‡	≤3.0 cm‡‡	≤3.0 cm‡‡	0.6-3.0 cm‡‡	1.1-3.0 cm‡‡	2.1-3.0 cm‡‡
	Pathology	AAH	AIS	MIA	Lepidic predominant AD or Invasive AD with lepidic component	Invasive AD with a lepidic component or lepidic predominant AD	Invasive AD with lepidic component
	Pathologic Stage		pTis‡‡	pT1mi‡‡	pT1a	pT1b	pT1c

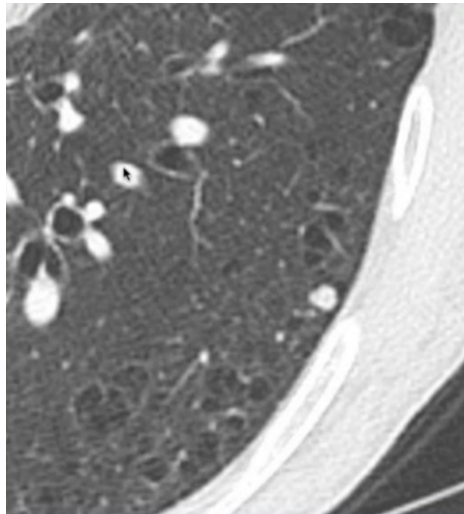
Iperplasia adenomatosa atipica

Adenocarcinoma invasivo



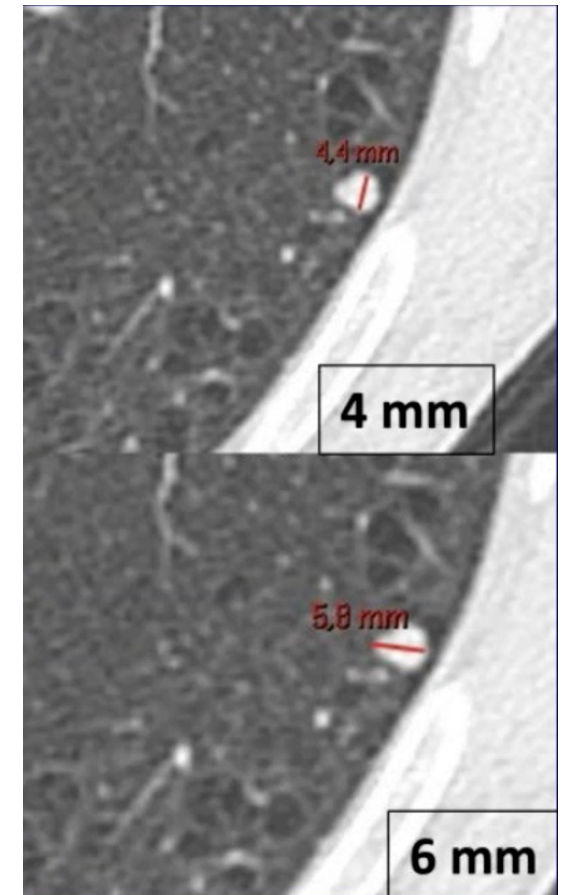
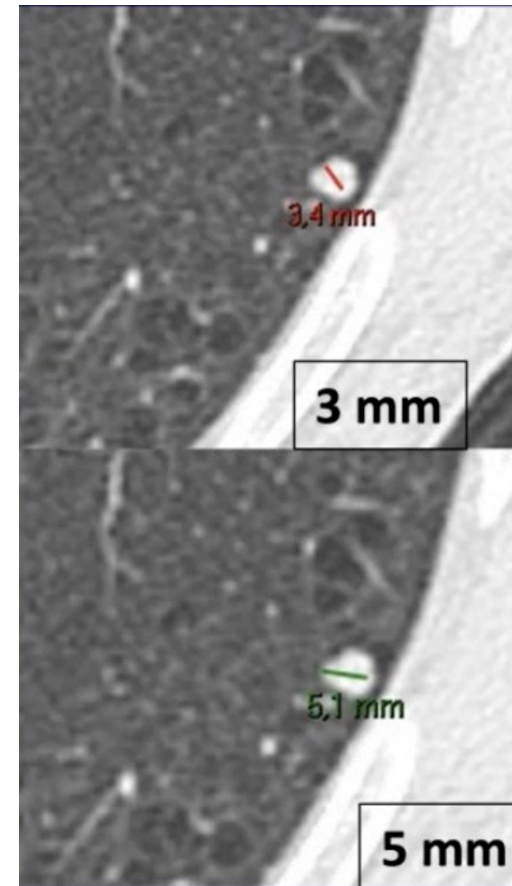
DIMENSIONI

6 mm < D < 8 mm → 1,3
% RISCHIO MALIGNITÀ
D > 10 mm → 15 %
RISCHIO MALIGNITÀ

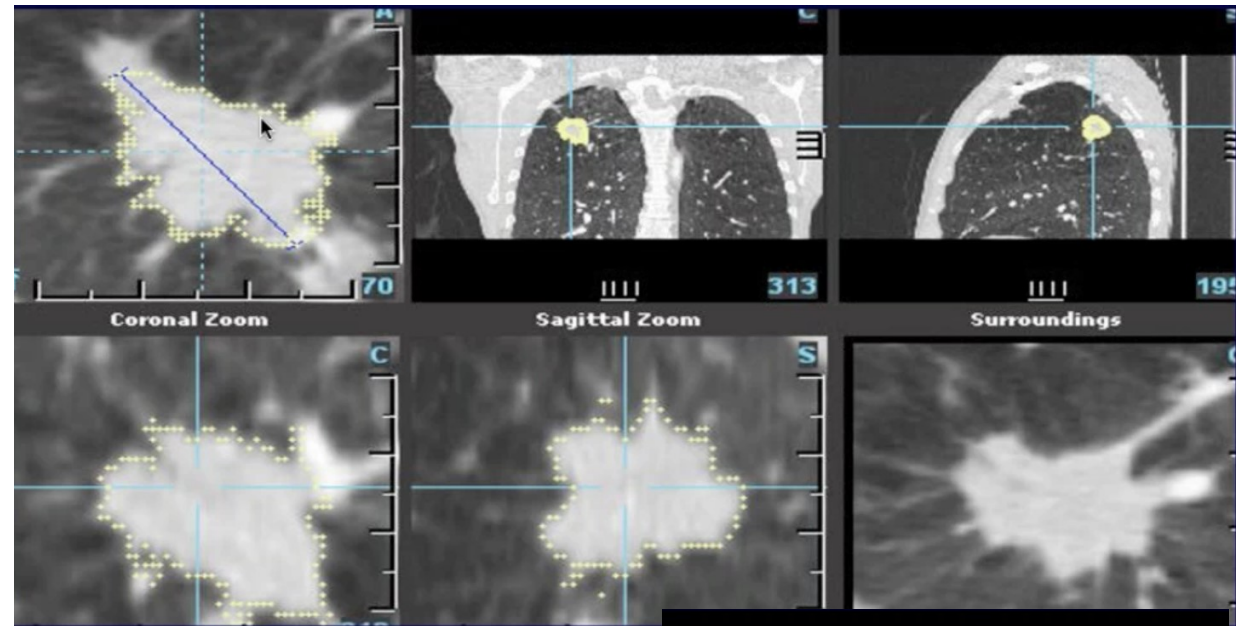
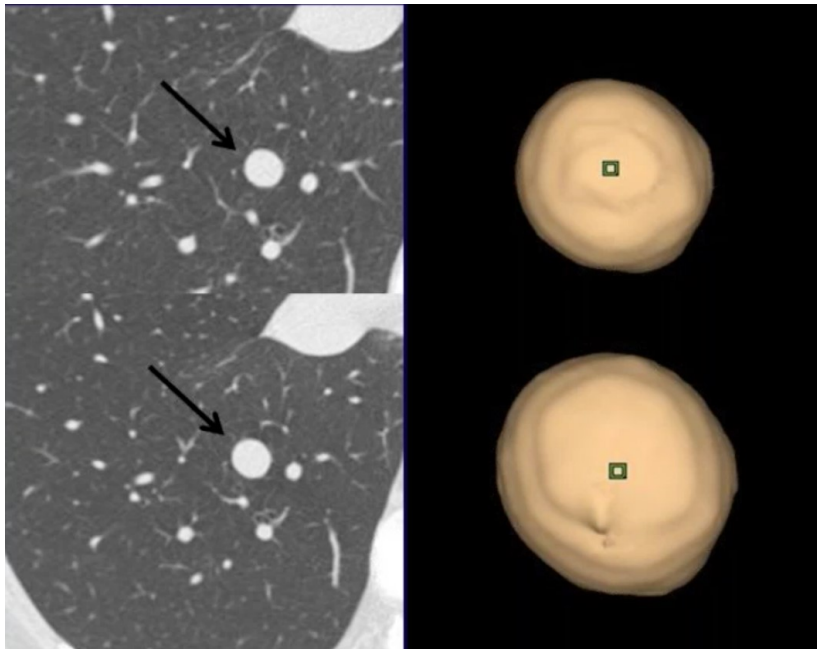


- Misurazioni manuali del d sono soggette ad elevata variabilità interosservatore
- La variabilità aumenta con la complessità del nodulo
- La variazione è di circa 1,73 mm tra gli osservatori

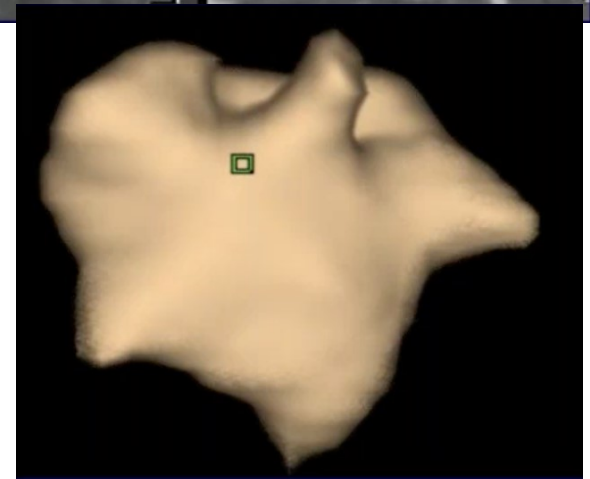
Una crescita di 2 mm è stata indicata dalle linee guida BTS; Lung-RADS > 1,5 mm



DIMENSIONI E ACCRESCIMENTO

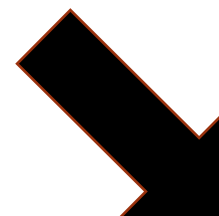


- Volume e tempo di raddoppiamento (VDT) ha un elevato accordo interosservatore ed elevata sensibilità nell'identificare crescita in tempi brevi
- **Aumenti volumetrici <25% non sono significativi**
- **VDT < 400 giorni è indice di malignità**



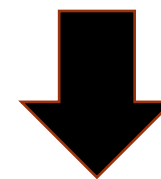
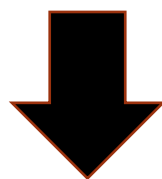


ALGORITMI



RISCONTRO INCIDENTALE
Popolazione eterogenea

SCREENING
Popolazione ad alto rischio



**Guidelines for Management of
Incidental Pulmonary Nodules
Detected on CT Images:** From the
Fleischner Society 2017¹

Radiology

European Radiology (2020) 30:3277–3294
<https://doi.org/10.1007/s00330-020-06727-7>

CHEST

ESR/ERS statement paper on lung cancer screening





Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

Nodule Type	Size			Comments
	<6 mm (<100 mm ³)	6–8 mm (100–250 mm ³)	>8 mm (>250 mm ³)	
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	

B: Subsolid Nodules*

Nodule Type	Size		Comments
	<6 mm (<100 mm ³)	≥6 mm (>100 mm ³)	
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A–4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).



Nodule Type

Single

Low risk[†]

High risk[†]

ALTO O BASSO RISCHIO ?

[†] Consider all relevant risk factors (see Risk Factors).

Risk Estimation and Risk Models

These guidelines for nodule management are based on estimations of the individual risk of malignancy. Although nodule size and morphology remain the dominant factors that we use to predict risk, it is important to consider additional clinical risk factors, including smoking, exposure to other carcinogens, emphysema, fibrosis, upper lobe location, family history of lung cancer, age, and sex. Because these factors are numerous and have differing effects on the likelihood of cancer, several sophisticated risk prediction models have been developed (Appendix E1 [online]). However, for the purposes

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10.1148/radiol.2017161659

Appendix E1

Methods

The present report updates and supersedes previously published guidelines for evaluation of incidental lung nodules (1,2). For this purpose, PubMed and Google Scholar were primarily used to search the term *solid lung nodule(s)* to update initially published guidelines from 2005, with additional search terms including, but not limited to *subsidiary nodule(s)*, *ground-glass nodule(s)*, *GGO(s)*, *nonsolid nodule(s)*, *NSN(s)*, and *part-solid nodule(s)*, with emphasis on citations appearing from 2013 through the first 3 months of 2016. Additional references were also reviewed by searching citations from the aforementioned articles and from the authors' personal reference files. Citations include randomized controlled trials, randomized observations, uncontrolled studies, retrospective studies, and cross-sectional studies examining relationships between nodules and outcomes (82). A multidisciplinary writing committee was organized and comprised thoracic radiologists, pulmonologists, a pathologist, and a surgeon. The final text was submitted to the entire membership of the Fleischner Society for comments and approval. Guidelines were subsequently graded for the quality of evidence by using criteria previously published by the American College of Chest Physicians (9).

Risk Assessment

Several clinical predictors of lung cancer risk have been developed that yield a probability for developing cancer within a defined period of time (1–10 years). Among these, the only algorithm that has been prospectively validated is the Tammemagi risk prediction tool, which was developed as a lung cancer incidence model for smokers with data from the Prostate, Lung, Colorectal, and Ovarian Trial and evaluated in the National Lung Screening Trial (NLST). It showed slightly improved sensitivity compared with the NLST eligibility criteria, and importantly, it showed that the lowest risk quintile in the NLST accounted for only 1% of the prevented lung cancer deaths (16).

Of greater interest to radiologists are models that incorporate nodule features together with clinical risk factors to arrive at a prediction of malignancy in a detected nodule. One such model that has received considerable attention is the Brock model (also referred to as the PanCan or Vancouver model), which was based on an analysis of more than 7000 nodules encountered in the PanCan screening trial (7). The full model includes age, sex, family history of lung cancer and emphysema, as well as nodule type (solid, part solid, ground glass), nodule location (upper vs lower or middle lobe), number of nodules, and spiculation. The model was validated by using images obtained in more than 1000 people in the British Columbia Cancer Agency chemoprevention trial and achieved excellent predictive accuracy in distinguishing malignant from benign nodules, with an area under the receiver operating characteristic curve of 0.94. It was also applied to data from the Danish lung cancer study and attained a receiver operating characteristic curve of 0.83. However, the reliability of this model as a decision support tool and its potential clinical role have not been established.



Calculator: Solitary pulmonary nodule malignancy risk in adults (Brock University cancer prediction equation)

Input

Age

Sex Female (0.6011)
 Male (0)

Family history of lung cancer (0.2961)

Emphysema (0.2953)

Nodule size

Nodule type Nonsolid or ground-glass (-0.1276)
 Partially solid (0.377)
 Solid (0)

Nodule in upper lung (0.6581)

Nodule count

Spiculation (0.7729)

Results

Log odds

Cancer probability

Low risk, which corresponds to an estimated risk of cancer of less than 5%, is associated with young age, less smoking, smaller nodule size, regular margins, and location in an area other than the upper lobe. To estimate high risk, we recommend combining the ACCP intermediate-risk (5%–65% risk) and high-risk (>65% risk) categories. High-risk factors include older age, heavy smoking, larger nodule size, irregular or spiculated margins, and upper lobe location. Subjects with intermediate risk share both high- and low-risk characteristics (83).

The PLCOm2012 is the lung cancer risk prediction model that has been most validated by different research teams in multiple countries around the world –including the US, Germany, Australia, the UK, Canada and Brazil



PLCOm2012 LCRC

Medicina
Progettata per iPhone

OTTIENI



SCREENING

Table 3 State-of-the-art definitions of positive screens at baseline

	Positive			Indeterminate			Negative		
	Solid	Part-solid [#]	Non-solid	Solid	Part-solid [#]	Non-solid	Solid	Part-solid [#]	Non-solid
Lung-RADS	≥8 mm	≥6 mm	–	6–<8 mm	<6 mm	≥30 mm	<6 mm ⁺		<30 mm
BTS	≥300 mm ³ and Brock ≥10%	–	–	≥300 mm ³ and Brock <10% 80–<300 mm ³	≥5 mm	<80 mm ³	<5 mm		
EUPS [*]	≥300 mm ³	–	–	100–<300 mm ³	≥5 mm	<100 mm ³	<5 mm		
NCCN	8 mm	≥6 mm		6–7 mm	≥6 mm	≥20 mm		≤5 mm	≤19 mm
I-ELCAP	≥15 mm	6–14.9 mm [¶]		<6 mm or 6–14.9 mm ⁺	<6 mm or 6–14.9 mm ⁺	Any size	No non-calcified nodules		

Lung-RADS, Lung CT Screening Reporting And Data System; *BTS*, British Thoracic Society; *EUPS*, European Union Position Statement on Lung Cancer Screening; *NCCN*, National Comprehensive Cancer Network; *I-ELCAP*, International Early Lung Cancer Action Program. [#]: may refer to size of the solid component; [¶]: long and short axis should be measured to one decimal point and mean nodule diameter should be reported (also to one decimal point); ⁺: total diameter



Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening

* *Lancet Oncol* 2014; 15: 1332–41



RISULTATI DELLO SCREENING

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

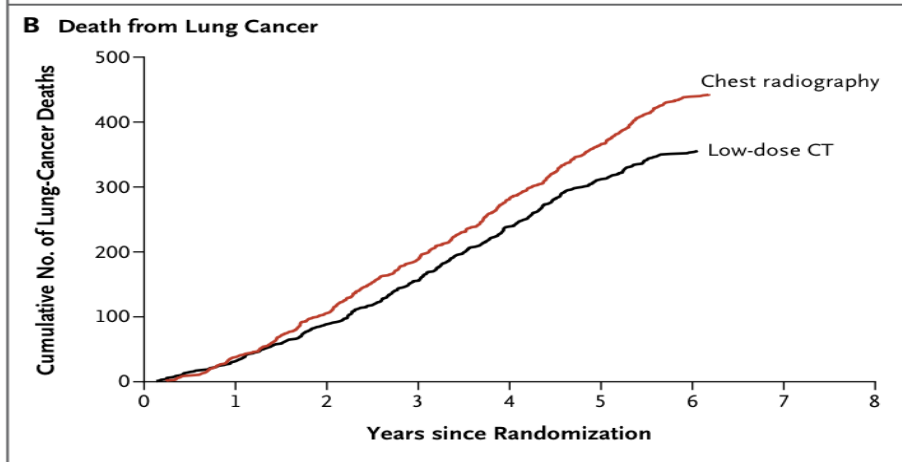
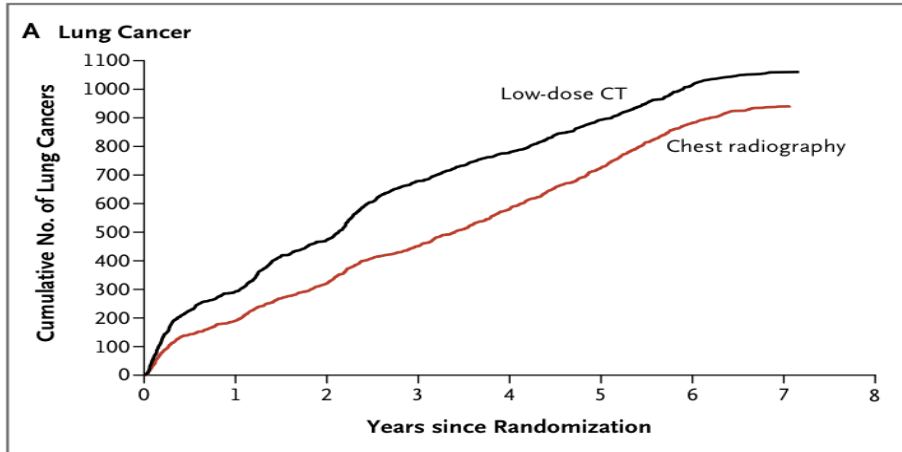


Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.

The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

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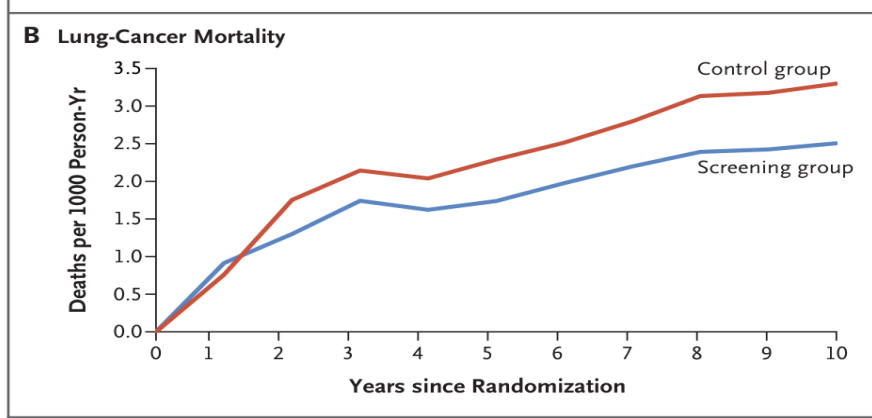
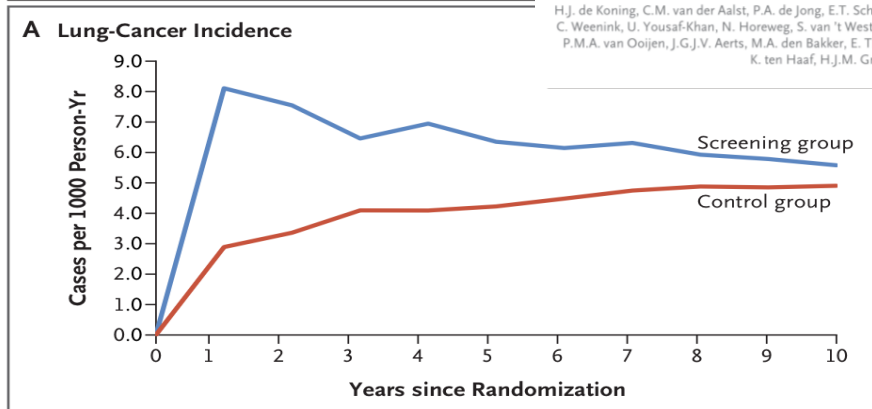


Figure 1. Lung-Cancer Incidence and Lung-Cancer Mortality among Male Participants.

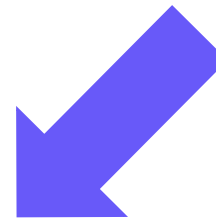
Panel A shows the cumulative lung-cancer incidence (per 1000 person-years) according to follow-up year since randomization. Panel B shows the cumulative lung-cancer mortality (per 1000 person-years) according to follow-up year since randomization. Cause of death (with known date of lung-cancer diagnosis) was defined by the cause-of-death committee, if available, or by vital-statistics registries.





RISCONTRO INCIDENTALE
Popolazione eterogenea

SCREENING
Popolazione ad alto rischio



REPERTO POSITIVO:

- Riferimento a pneumologo clinico
 - TC/PET
 - Approfondimento istologico
 - Valutazione multidisciplinare





REPERTO POSITIVO

TC/PET

- Caratterizzazione metabolica del nodulo
- Stadiazione loco-regionale

- Falsi negativi e falsi positivi

MEDICO NUCLEARE

BIOPSIA

- Caratterizzazione immunoistochimica e molecolare (targeted therapy)
- Sampling nodale

- Costi e rischi

RADIOLOGO

MDT

- Miglior valutazione del rapporto costo/beneficio
- Indirizzo terapeutico condiviso

- Insostenibilità per grandi numeri dello screening



CONCLUSIONI

- **Tipo nodulo, dimensioni ed accrescimento** sono le maggiori caratteristiche per determinare il rischio di malignità di un nodulo di tipo indeterminato alla TC
- Le caratteristiche morfologiche possono aiutare a suggerire la benignità/malignità del nodulo e cambiare eventualmente il management
- La **stratificazione del rischio** del Pz è fondamentale per capire l'algoritmo corretto da applicare
- La **valutazione multidisciplinare** e i **percorsi diagnostici organizzati**, è fondamentale per una diagnosi precoce del tumore al polmone ed evitare possibili «overdiagnosi» ed «overtreatment».





ASST Papa Giovanni XXIII

GRAZIE PER L'ATTENZIONE

« Sembra che la natura sia in grado di darci solo malattie piuttosto brevi.

La medicina ha inventato l'arte di prolungarle.»

Marcel Proust