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陳文茜呼吸困難確診肺腺癌!

沉默殺手肺癌如何早期發現?



倡「健康預防」 陳建仁:精準醫療找到我的微小腫 瘤



G+分享

骨列印

A- A+

2016-03-20 02:47 聯合報 記者郵桂芬/台北報導

『A誰 分字 ⟨383 | ○ 傳送 | G+1 | 0

副總統當選人陳建仁昨出席台灣外科醫 學會年會時指出,台灣的精準醫療水準 高,低劑量電腦斷層(LDCT)替他 揪出早期肺腺癌,他也因此深刻感受 到,健保應提供精準醫療更大的發揮舞 台。

此外, 健保在「撙節」前提下, 每年應 合理調整,才能在「預防保健」挹注更 多費用,為國人健康把關。

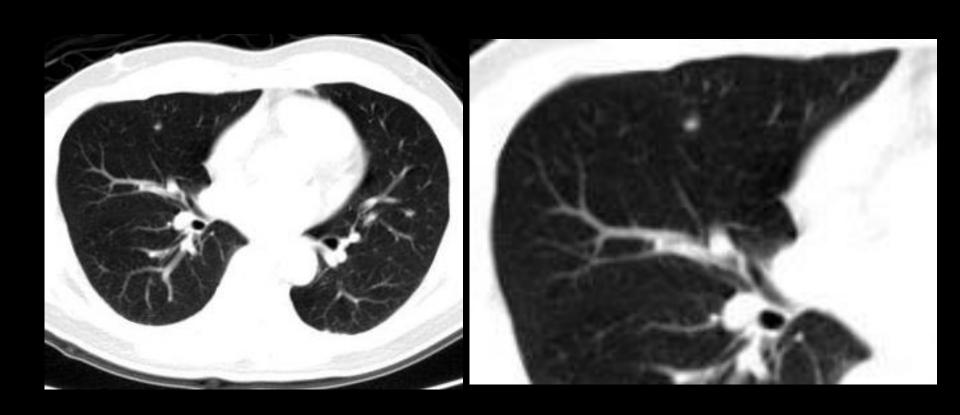
為期兩天的台灣外科醫學會年會, 昨邀 請陳建仁致詞。他一開口便稱讚台大, 利用LDCT找到他右肺零點五公分微 小結節, 「如此微小的腫瘤都能找到, 精準醫療很Amazing(驚人)」。他 說,現在微創手術非常精準,且術後傷 口小, 當初切除病灶, 隔天就上班, 連 同审的觉证期明, 「你不日土明丁



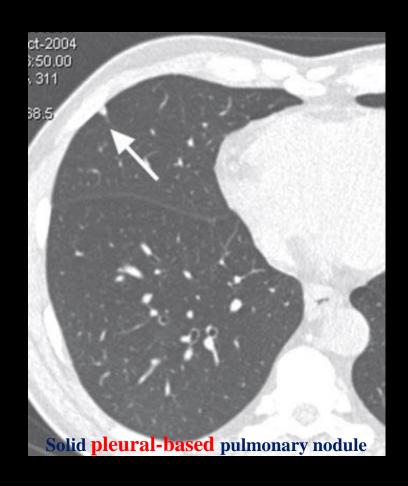
副總統黨選人陳建仁昨出席台灣外科醫學會年會,分 享接受低劑量重腦斷層撤出且期肺癌經驗,讓他更考

How to deal with incidentally detected small pulmonary nodules?

How to deal with incidentally detected pulmonary nodules less than 10 mm in size on screening LDCT?



6-month or 1-year follow-up?









The primary goal of lung cancer screening CT is to detect abnormalities that may represent lung cancer and may require further diagnostic evaluation.

低劑量電腦斷層掃描 肺癌篩檢

⊕參加醫院 ··台大醫院、臺北榮民/ 三軍總醫院、林口長

臺中榮民總醫院、中山



⇔計畫名稱 以低劑量電腦斷層掃描篩檢台灣不吸菸肺癌高危險群之研

- 3. 有三等親屬以內(含)肺癌家族史或其他肺癌高危險因子 4. 無其他排除條件(如:懷孕等...)

收案條件

- 1. 無吸菸史,或吸菸史小於10包年且已戒菸超過15年。
- 2. 符合下列肺瘍危險因子其中之一:
 - (1) 有三等親屬以內(含)肺瘍家族史
- (2) 二手菸史 (工作場所、家中)
- (3) 肺部疾病史 (肺結核、慢性阻塞性肺病病史)
- (4) 煮食頻率指數大於或等於110(註一)
- (5) 煮食時沒有使用抽油煙機
- 3. 年齡介於55歲至75歲之間(但具有肺癌家族史者,收案年齡介於50歲至75歲,若受試 者目前的年齡比肺癌指標個案發病時大,亦可收案。)。

註一:煮食指數= $2/7 \times (-週前、炒、炸天數總和) \times (煮食年)$



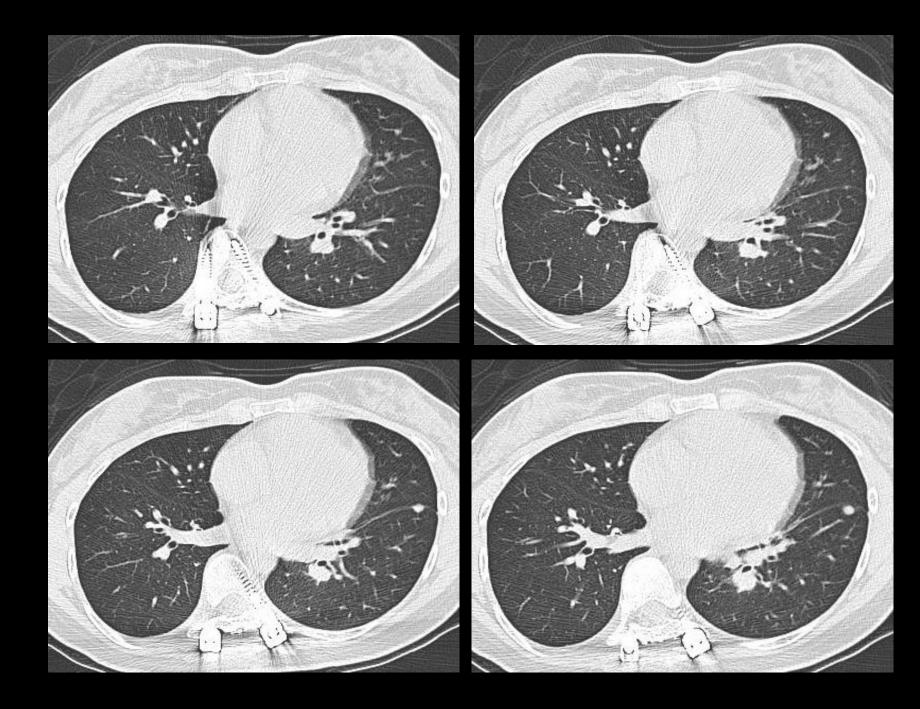
- 曾得過肺癌,或過去五年內曾罹患皮腫癌或子宮頸原位癌以外之癌症。
- 2. 無法接受胸腔穿刺或手術者。
- 3. 過去18個月內曾接受過胸部電腦斷層檢查。
- 4. 過去一個月內有不明原因之咳血。
- 5. 過去一年內有不明原因之體重減輕超過6公斤。
- 6. 懷孕中。
- 7. 過去一個月內的胸部X光檢查顯示有明顯可疑肺瘍病灶。

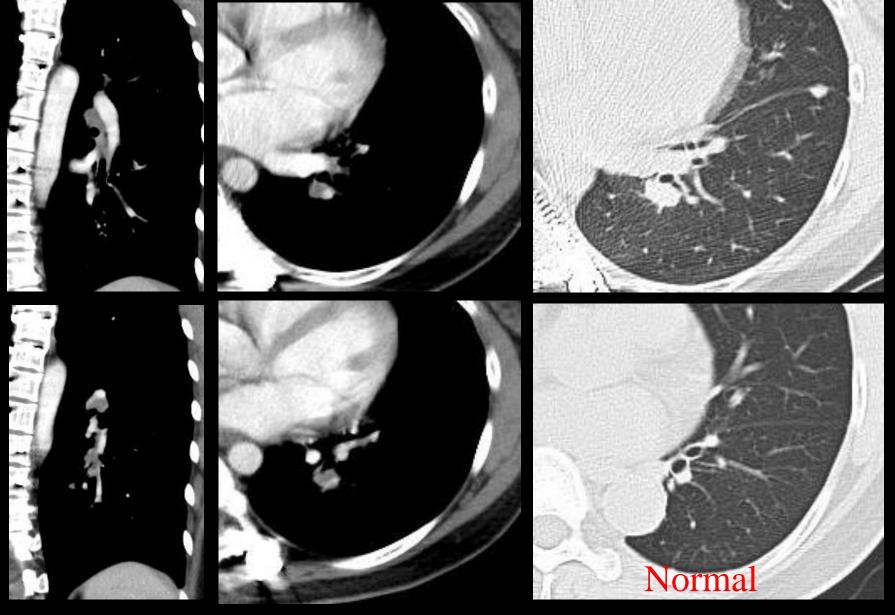


LDCT Examination

- Multidetector technique in a single breath-hold
- Without use of IV contrast medium
- In a suspended state of full inspiration
- Axial images from lung apices to CP sulci
- Viewed at axial 2 mm/2mm (≤ 2.5mm/2.5mm)(coronal image in 2.5mm/2.5mm is option)
- Characterization of small lung nodules: exam may be reconstructed at ≤ 1.0 -mm slice thickness and reconstruction intervals (sent to center)
- Postprocessing techniques: MIP or VR, MPR
- Radiation dose: $\leq 1.5 \text{ mSv (BMI} < 30)$; $\leq 2.0 \text{ mSv (BMI} > 30)$

Hospital	台大醫院	台北榮總	三總	林口長庚
	Scanner	Scanner	Scanner	Scanner
Scan type	Helical	Helical	Helical	Helical
Rotation Time (s)	0.5	0.5	0.5	0.5
Manufacturer				
CT scan manufacturer	Philips Brilliance 64 slice	Philips Brilliance 64 slice	Philips Brillance 256 slice	Toshiba 320-row
Single collimation width (mm)	0.625	0.625	0.625	0.5
Total collimation (mm)	0.625x128	0.625x128	0.625x128	0.5x320
Reconstruction (Image center)				
Convolution Kernel	Standard (B)	Standard (B)	Standard (B)	FC 02
IR	X	X	X	No
Slice thickness	1 mm	1 mm	1 mm	1 mm, 0.5 mm
Spacing between slices	1 mm	1 mm	1 mm	Equal to slice thickness
Reconstruction diameter	30-35cm (視patient size)	35-36cm (視patient size)	30-36cm (視patient size)	28-35

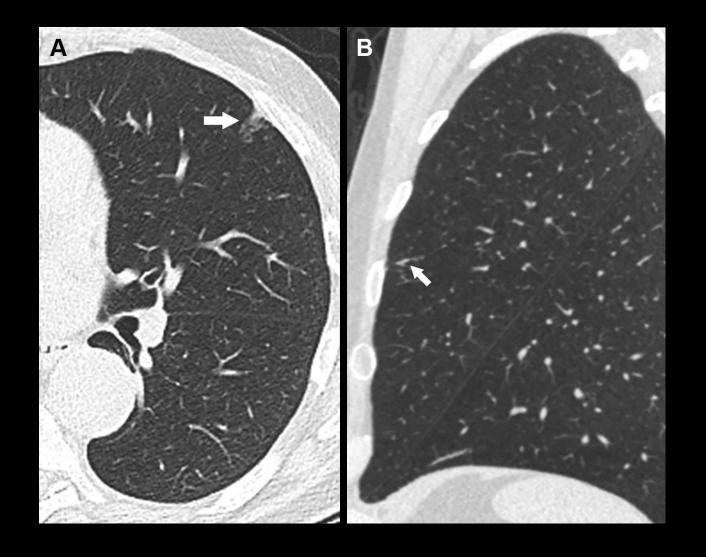




The nodule is closely associated with 4–6 mm pulmonary blood vessels. Although it is substantially larger than adjacent blood vessels, it appears less conspicuous. 儘管它比相鄰的血管大得多,但它看起來不那麼顯眼。



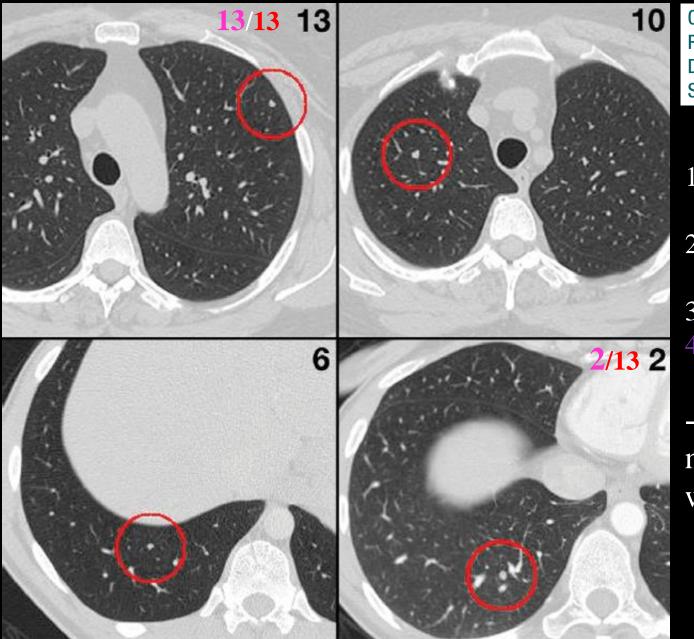
Axial LDCT image shows a LUL ground glass nodular opacity (arrow).



Usefulness of multiplanar reconstruction for the characterization of lung lesions. (A) Axial LDCT image shows a LUL ground glass nodular opacity (arrow). (B) Sagittal LDCT image reconstruction demonstrates a linear configuration of the LUL lesion, characterizing **focal scarring** rather than a true ground glass nodule (arrow).

Current State of Radiologist Performance

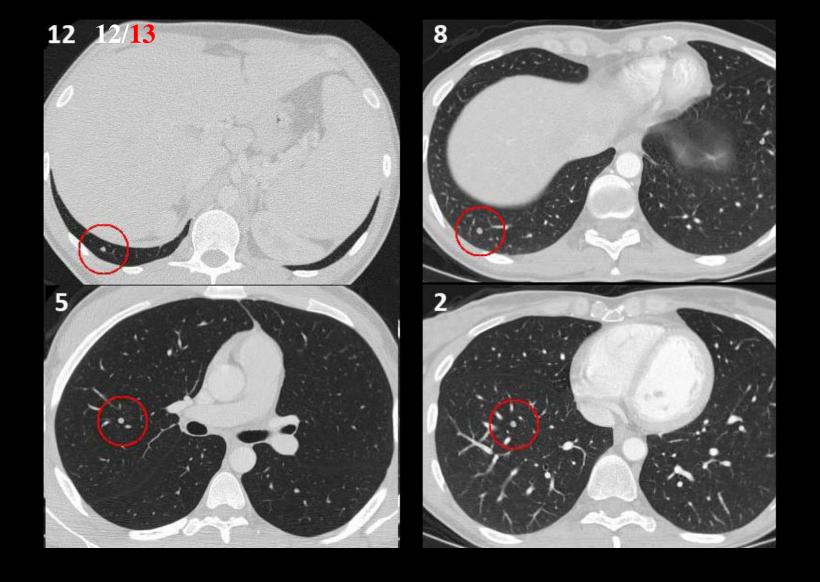
- Detection performance have been highly variable.
- Reported sensitivities range from 30–97%.
- Identification of small pulmonary nodules is very difficult.
- The *location of nodule relative to normal lung structures* appears to affect consistency of detection across readers.



Characterizing Search,
Recognition, and Decision in the
Detection of Lung Nodules on CT
Scans: Elucidation with Eye Tracking¹

- 1. Characteristics of target nodule
- 2. Quality of CT acquisition
- 3. Patient factors
- 4. Reader's experience

---- all impact nodule detection with eye tracking



Regional lung complexity and cross-sectional area of the lungs on CT cross-sections may be a key determinate in their detection.

關鍵決定因素



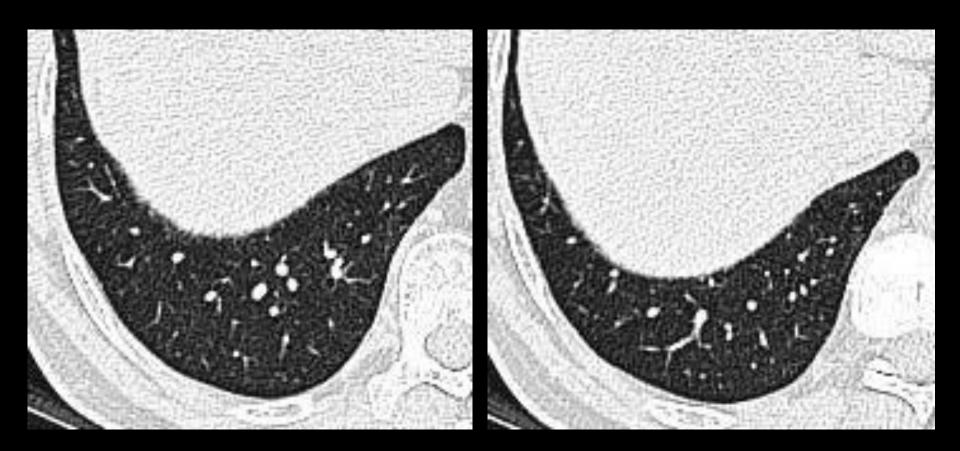


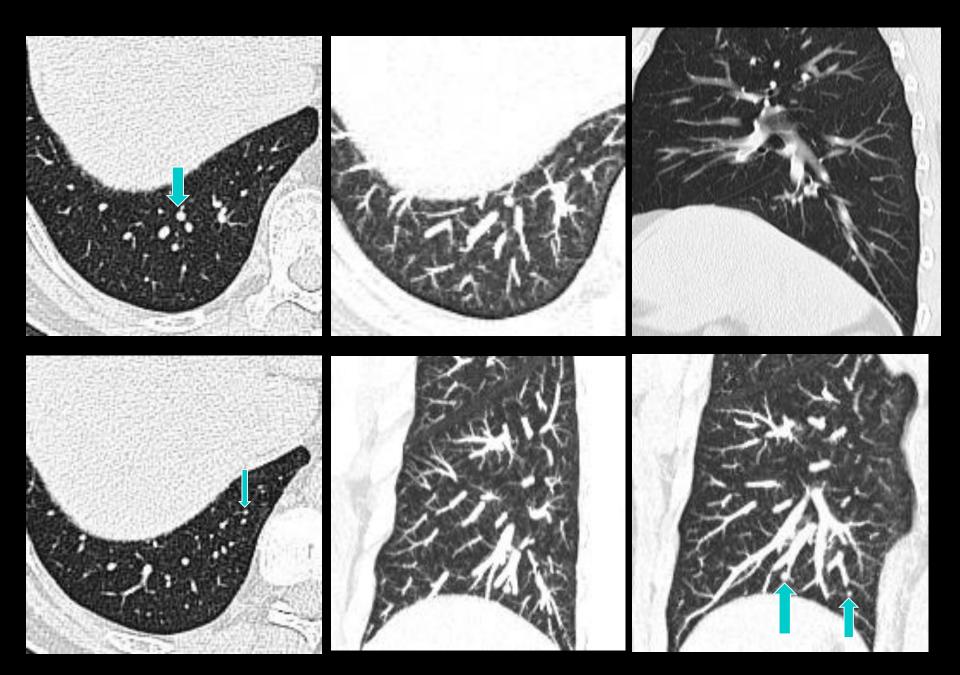


MIP images <u>enhanced detection</u> and <u>characterization of</u> <u>tiny nodules</u> because of improved depiction of pulmonary vessels and enhanced anatomic orientation.

TS-MIP images displaying the longitudinal course of the vessels and enabling their discrimination from nodules.







- * Nodule detection remains imperfect even with the addition of MIP and VR processing.
- * Further research in computerassisted diagnosis (CAD) and other methods of image processing is essential.



THE WAS GENERAL WINDS

人工智慧醫療:醫療是根本,人工智慧是手段

目前人工智慧的現況可以幫助放射科醫生到甚麼程度?

- 效率
- 敏感度



Artificial intelligence is changing radiology. How are you keeping up?

傳統CAD & 深度學習AI 在技術原理上的差異

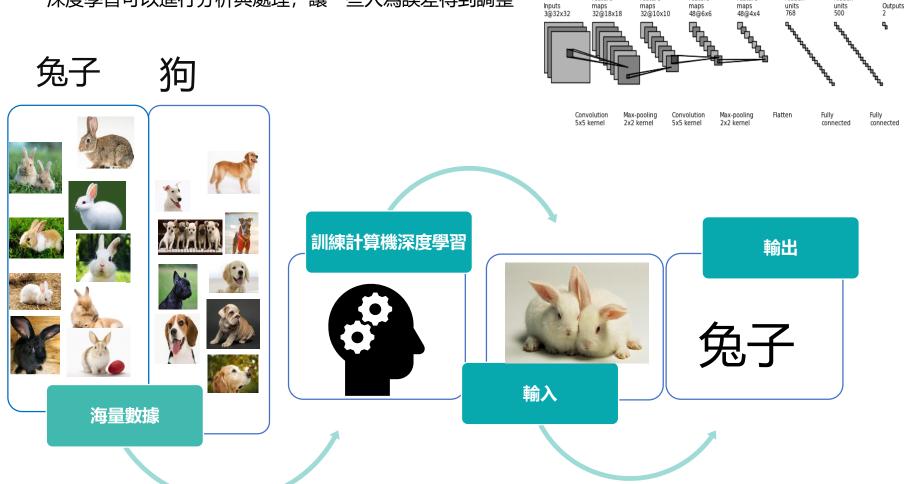
	傳統 CAD	深度學習AI	
原理	根據先驗知識制定規則, 尋找並判斷病灶	基於影像大數據和標註信息, 從原始數據中提取高維度的抽象特徵, 實現對病灶的自動 <mark>定位、分割、分類等</mark>	
精準度	低	高	
耗時	長	短	
準確度優 化	困難	不斷基於優質數據訓練可快速提升性能	
可解釋性	強	弱(目前研究趨勢)	



深度學習 AI能自動尋找特徵,非常適合智慧醫療影像



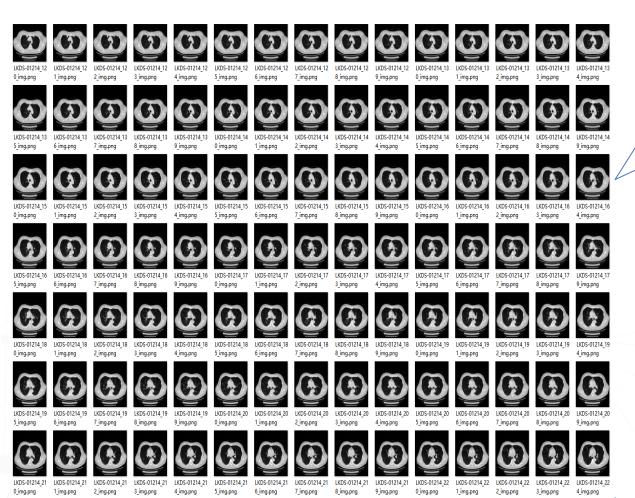
深度學習可以進行分析與處理,讓一些人為誤差得到調整





Deep Learning for Lung Nodule Detection / Classification How do a Radiologist Find Lung Nodules?





- . 300~400 slices per patient
- 2. 5~10 mins to **locate** the nodules
- 3. Nodules classification takes even longer time to handle (30 mins~2hours).



Deep Learning for Lung Nodule Detection / Classification How do a Radiologist Find Lung Nodules?

















































nodules



Nodules classification takes even longer time to handle (30 mins~2hours).



































































































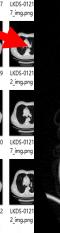






































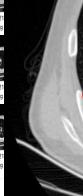








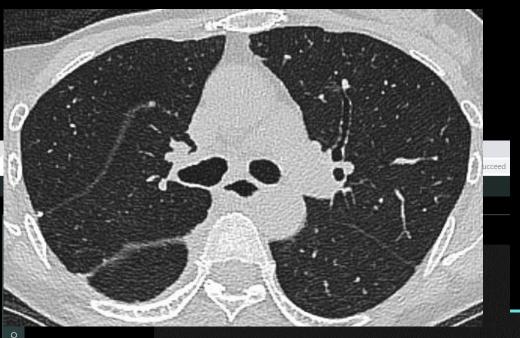






Dear all:

我覺得最近 AI 非常熱門, radiologists 一直被看衰??? 另一方面工作量大, missed detection 機會就大。 是否增加 computed aided detection (CADe) / computer aided diagnosis (CADx) 或 AI 在 CT nodule 偵測及診斷輔助應用。 可以找IT老師(如台大張瑞峰教授,亞大沈偉誌教 授,也許還有更多我不知道的老師?) 或各家應用廠商(我知道的有 clear-read, Riverrain, 點內 DNA) 來介紹目前現況或今後前景, 也許聽眾也 會有興趣~~



lung: right lung lobe: middle 結節概率: 38%

結節大小: 3.57mm/3.07mm

結節體積: 22mm³ 最長直徑: 3.46mm 癌症機率: 27%

疑似類型:

結節類型: Partially Solid

AAH

鈣化情況: 非鈣化結節

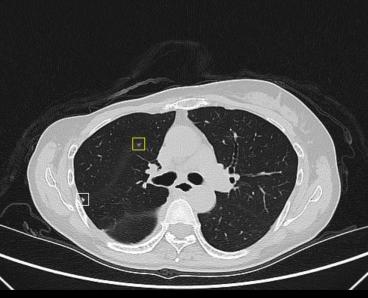
Central attenuation: -299HU

Mean density: -410.82HU

Maximal attenuation: -182HU Minimal attenuation: -587HU

當前AI版本可更有效檢出3CM以内的結節





Partially 3.57/3.07 27% AAH Solid Intrapulmonary V 4.58/3.57 17% ① Pleural ① 1.43/0.71 19% Solid **Pulmonary** V 2.58/2.08 16% ① **Pulmonary** 4.17/3.57 **Pulmonary** 7.99/6.39 16% ① Pleural 6.74/6.15 17%

影像所見

right lungupper見。, Pleural Solid (IMG 32-33),最長徑約3.85mm right lungupper見。, Intrapulmonary Calcification (IMG 33),最長徑約3.2mm right lungupper見。, Ground Glass (IMG 36-37),最長徑約6.78mm right lungupper見。, Intrapulmonary Calcification (IMG 44-45),最長徑約3.65mm right lungmiddle見。, Partially Solid (IMG 44-45),最長徑約3.57mm right lungmiddle見。, Intrapulmonary Calcification (IMG 61),最長徑約4.58mm right lungmiddle見。, Pleural Solid (IMG 61),最長徑約1.43mm

■ 一键複製

AI結果僅供參考,最終結果以臨床醫生診斷為準



lobe:

結節概率:

結節大小:

結節體積:

最長直徑

寫症機率:

疑似類型

結節類型 鈣化情況



Minimal attenuation: -587HU 當前AI版本可更有效檢出3CM以內的結節





right lung

3.57mm/3.07mm

Partially Solid

非鈣化結節

-410.82HU

-299HU

middle

22mm³ 3.46mm

27%

AAH

38%



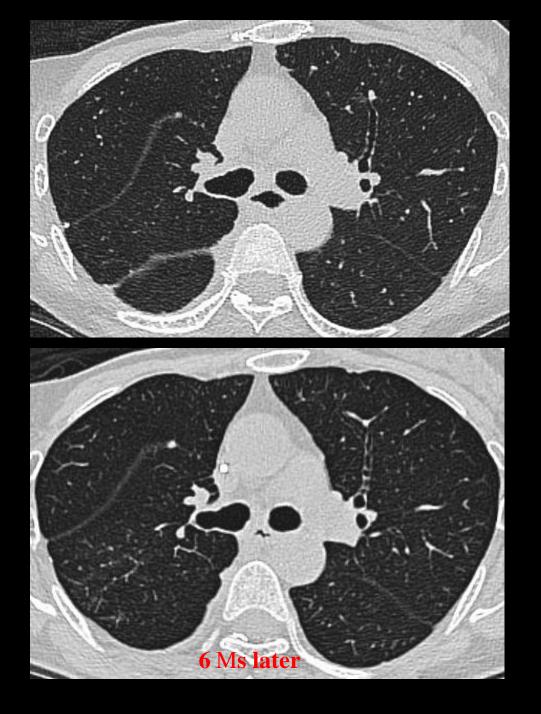


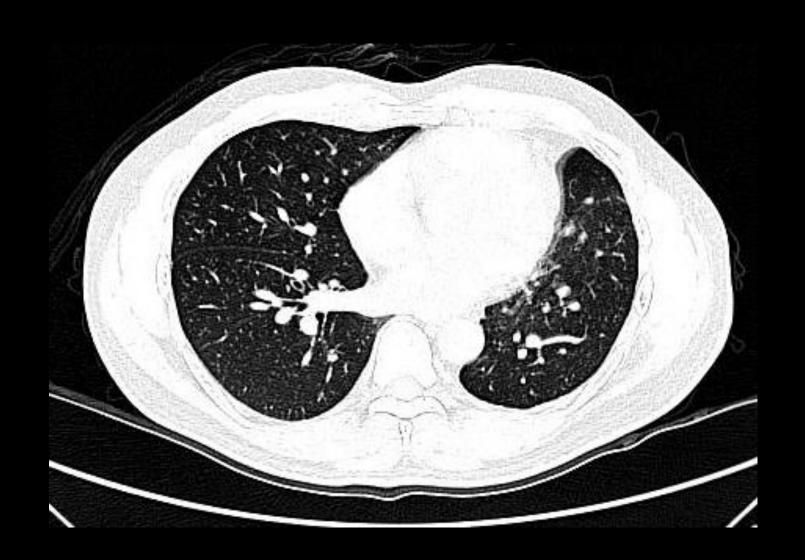




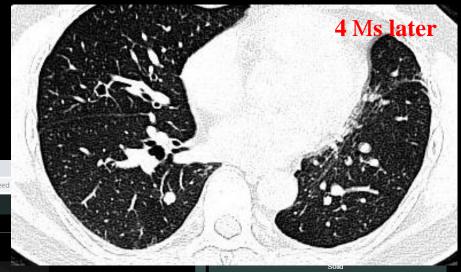












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lung: right lung lower 結節概率: 5.96mm/5.25mm 結節大小: 結節體積 89mm^s 最長直徑 5.54mm

癌症機率: 結節類型: Pulmonary Solid 非鈣化結節 鈣化情況 Central attenuation: 92.7HU Mean density:

當前AI版本可更有效檢出3CM以內的結節

Maximal attenuation: 506HU Minimal attenuation: -296HU

AI結果僅供參考,最終結果以臨床醫生診斷為準

影像所見	

right lungupper見,-Pleural Solid (IMG 6),最長徑約5.7mm left lungupper見,-Intrapulmonary Calcification (IMG 12),最長徑約3.5mm left lungupper見,-Pulmonary Solid (IMG 19), 最長徑約4.22mm left lungupper見,-Pulmonary Solid (IMG 20), 最長徑約2.48mm left lungupper見,-Ground Glass (IMG 22), 最長徑約4.22mm right lunglower見,-Pulmonary Solid (IMG 32), 最長徑約5.96mm

Intrapulmonary Calcification 11%

Ground

Glass Pulmonary Solid 12%

21%

19%

3.50/2.82

4.22/4.22

2.48/1.75

4.22/2.82

5.96/5.25

■ 一键複製















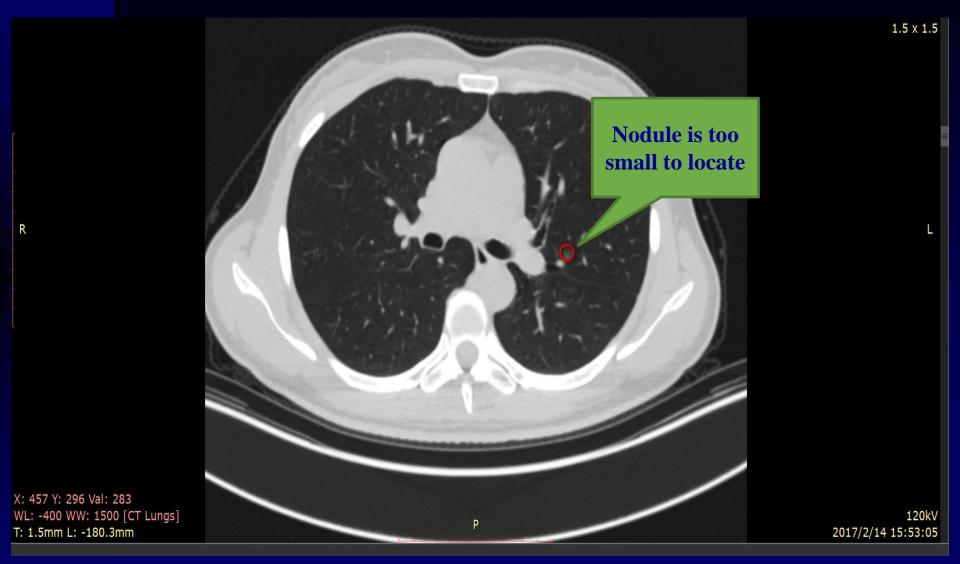




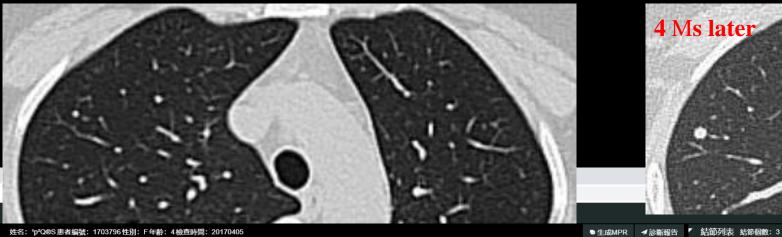




Deep Learning for Lung Nodule Detection / Classification Challenge: Nodule Localization (1)



CT肺結節偵測 (定位) 的限性: 太小、太模糊、太複雜、太靠近縱隔腔和肺門。



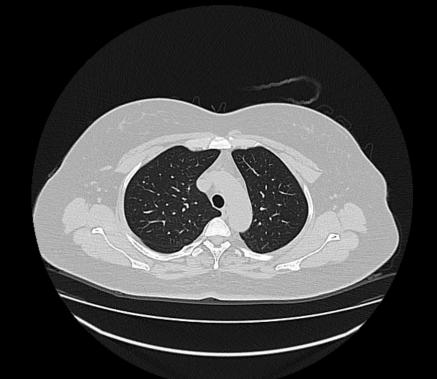
4 Ms later

當前張數: 29

總張數: 154 window width: 1500HU window level: -400HU

頂

Q



2	第幾張 ▲	大小	類型 ~	風險▲	病理預測
☑	23	2.88/2.88	Intrapulmonary Calcification	13%	0
94—AV	142		Pulmonary	3.42	_

Calcification

影像所見

right lungupper見,-Intrapulmonary Calcification (IMG 22-23), 最長徑約2.88mm left lungupper見,-Pulmonary Solid (IMG 41-42), 最長徑約3.75mm right lunglower見,-Intrapulmonary Calcification (IMG 64-65), 最長徑約2.88mm

AI結果僅供參考,最終結果以臨床醫生診斷為準

■ 一键複製













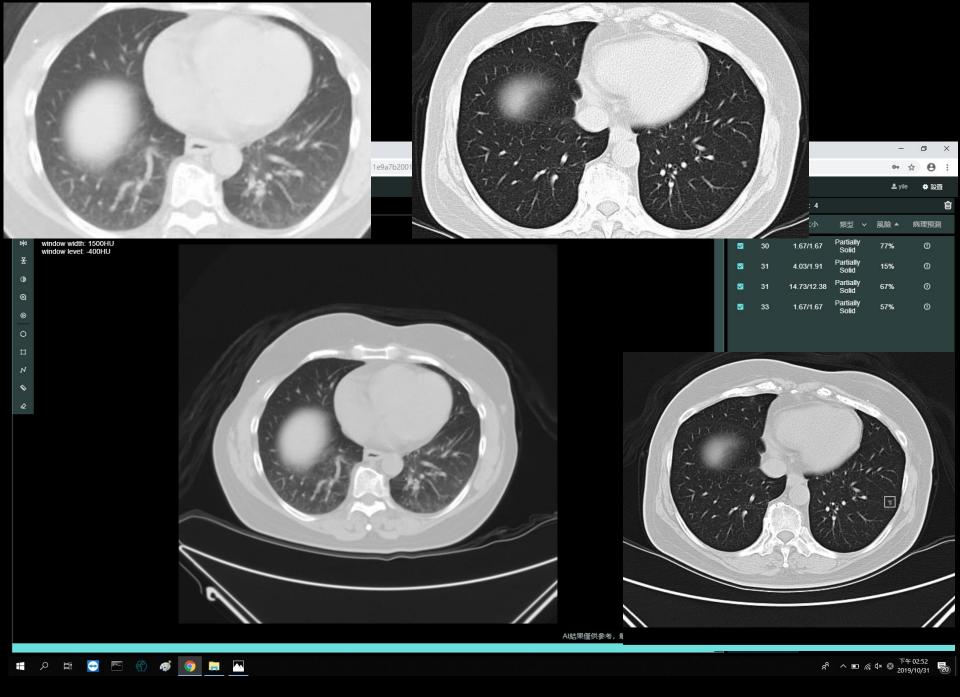


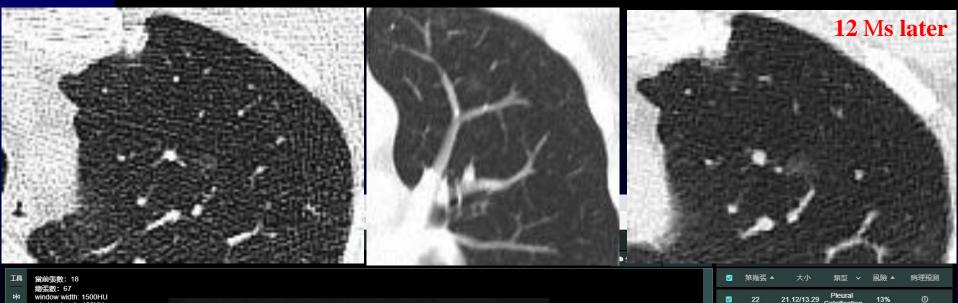












當前張數: 18 總張數: 67 window width: 1500HU window level: -400HU •

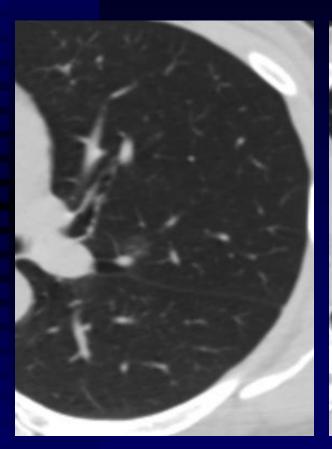
21.12/13.29 Pleural Calcification 影像所見 left lungupper見,-Pleural Calcification (IMG 21-24),最長徑約21.12mm

AI結果僅供參考,最終結果以臨床醫生診斷為準

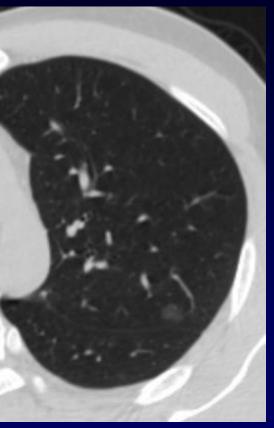
■ 一键複製

Deep Learning for Lung Nodule Detection / Classification Challenge: Nodule Classification (2)

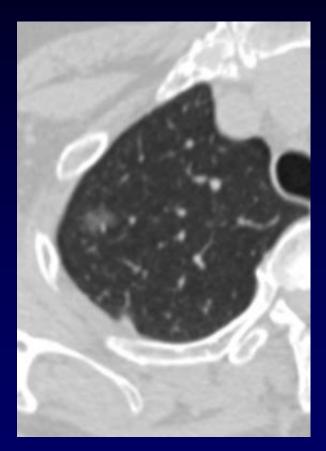
Three different classed ground-glass nodules (GGN)



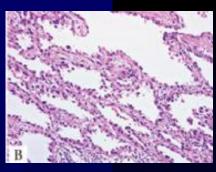
Atypical adenomatous hyperplasia (AAH)



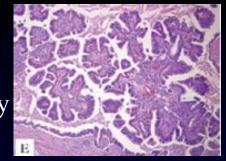
Adenocarcinoma in situ (AIS)



Minimally invasive adenocarcinoma (MIA)







- Major Alteration (3): Predominant Pattern Replaces Former Mixed Subtype in <u>Invasive Adenocarcinoma</u>: comprehensive histologic subtyping improves <u>molecular</u>, <u>therapeutic</u>, and <u>prognostic</u> correlations.
- A, Lepidic predominant pattern with mostly lepidic growth (right) and a smaller area of invasive acinar adenocarcinoma (left). B, Lepidic pattern consists of a proliferation type II pneumocytes. C, Acinar adenocarcinoma. E, Papillary adenocarcinoma. F, Micropapillary adenocarcinoma. G, Solid adenocarcinoma.

AI不會取代醫生,但用AI的醫生會取代不用AI的醫生



在不犧牲診斷的品質下提供更全面、正確、快速的結果

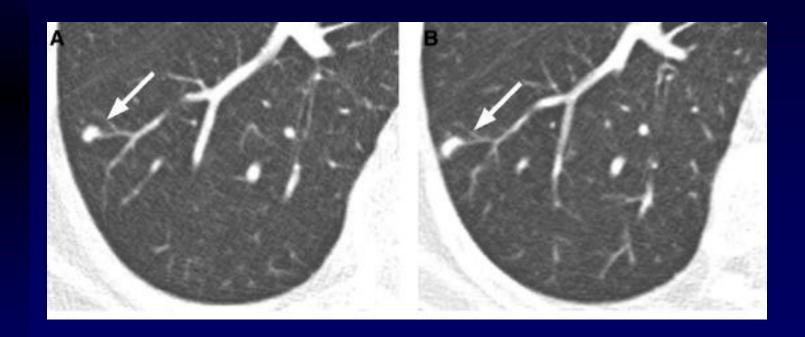


Artificial intelligence (AI) is the future of radiology --- and the future is happening now!

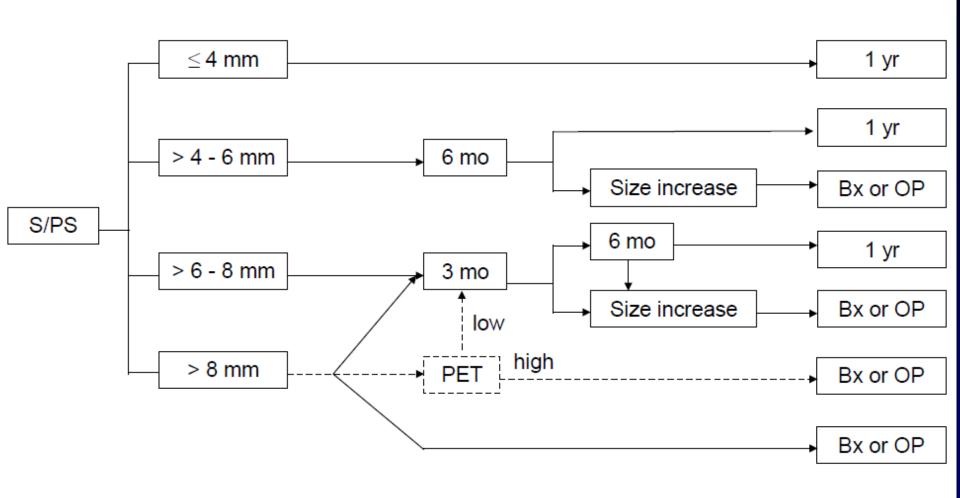
REPORTING

- anatomic location (lung lobe, segment)
- size, attenuation (soft tissue, type of calcification, fat), opacity (solid, part-solid, GGO), and margins (eg, smooth, lobulated, spiculated)
- series/image number: to facilitate comparison
- When comparing changes in nodule size, opacity, and contour, efforts should be made to compare the oldest scans available in addition to the most recent prior scan to assess for changes over time.

(1) Solid nodules

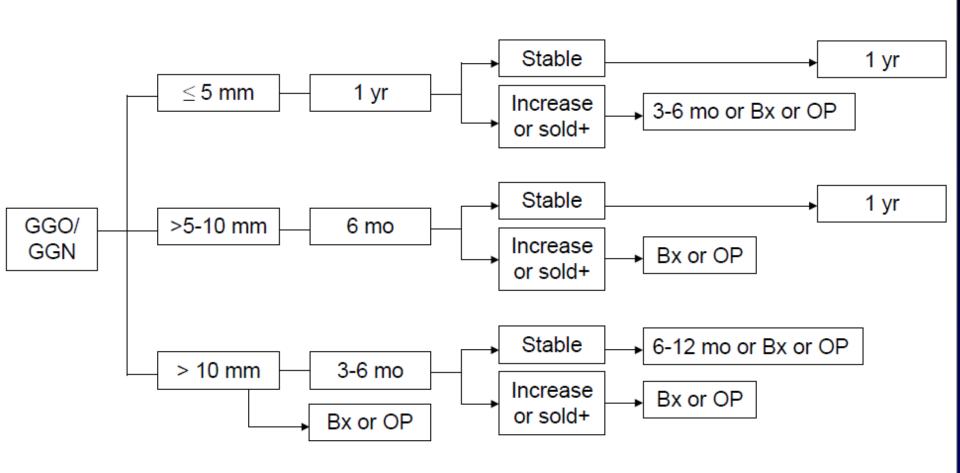


以低劑量電腦斷層掃描篩檢台灣不吸菸肺癌高危險群之研究



AATS 2013, ACCP 2013, Fleischner Society 2013, NCCN 2014 v1

以低劑量電腦斷層掃描篩檢台灣不吸菸肺癌高危險群之研究



AATS 2013, ACCP 2013, Fleischner Society 2013, NCCN 2014 v1



A solid spiculated 15×10 -mm nodule in the LLL (arrow).

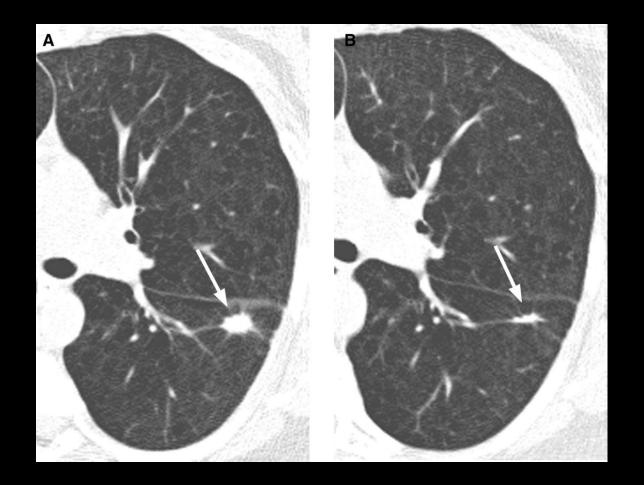


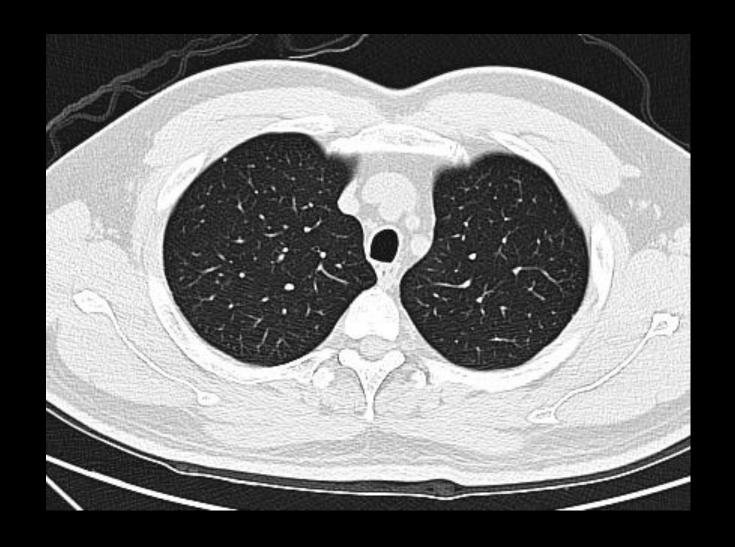
Figure. Transient spiculated nodule in a patient with a recent history of pneumonia. (A) Baseline computed tomography (CT) in a patient who was asymptomatic, demonstrating a **solid spiculated** 15 × 10-mm nodule in the LLL (arrow). The patient was found to have had consolidation in the LLL on a chest radiograph obtained for cough and fever 3 months before the baseline CT, and, therefore, the nodule was classified as Lung Reporting and Data System (LU-RADS) 3L (indeterminate; requires serial CT). (B) **Follow-up** <u>6 weeks later</u>, *demonstrating marked size decrease* (arrow). Classification is now LU-RADS 2.

Approximately 10% of solid, intermediate-sized, intraparenchymal nodules resolved during F/U.

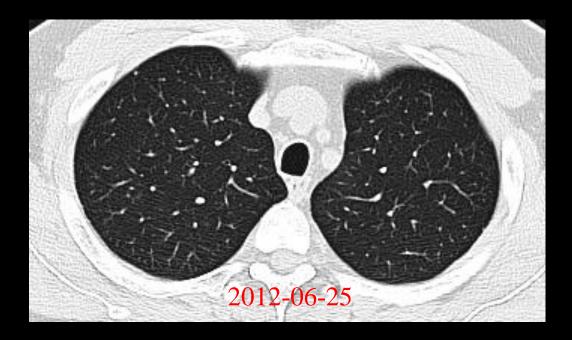
Small pulmonary nodule (< 5 mm)

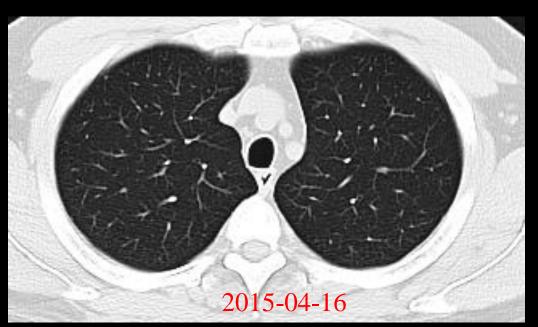


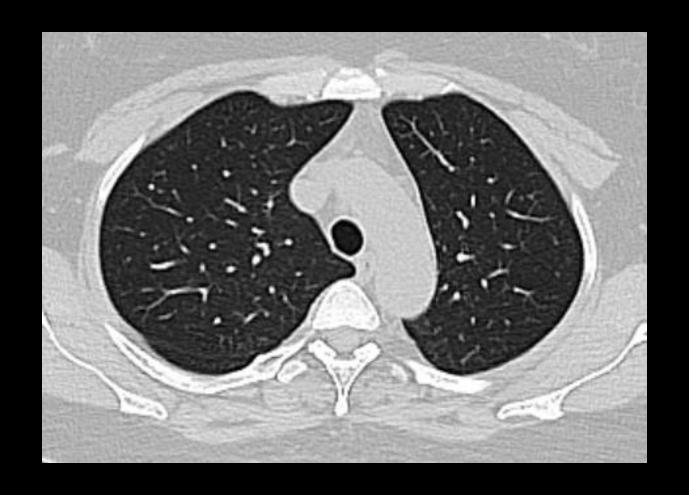
- An approximately 2-mm lung nodule (arrow): There is essentially **no role for reporting** this nodule within the context of *lung cancer screening*.
- Because nodules of this size are overwhelmingly benign there is no relevance to their identification unless *disseminated* or *presenting as a new finding in a patient with documented malignancy*.



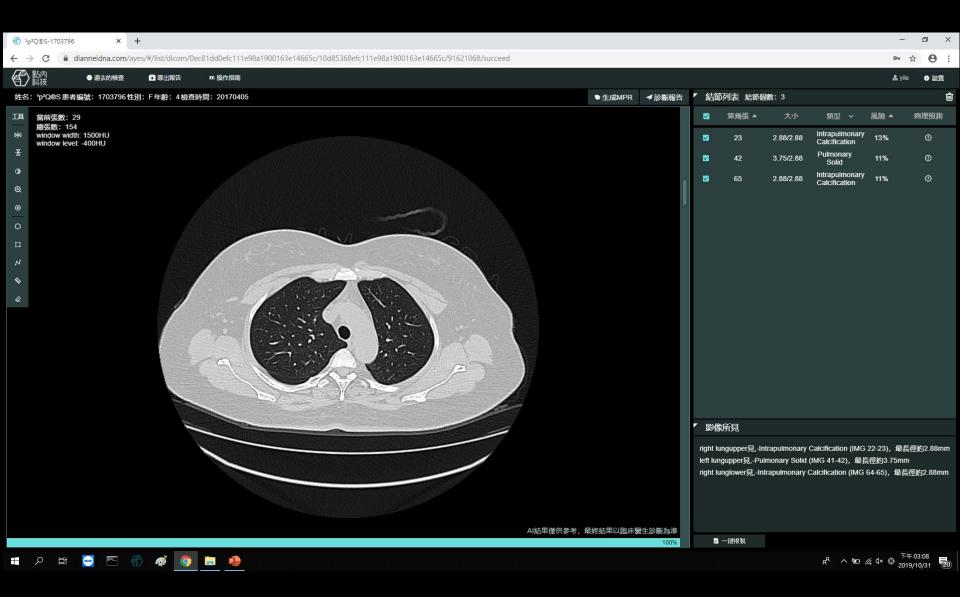
A 43-year-old male with history of colon cancer

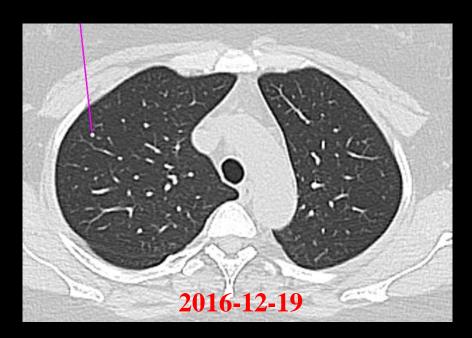






A 53-year-old female with history of RCC





lung: right lung lobe: upper 結節概率: 100%

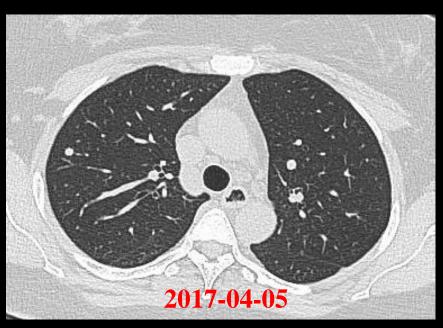
結節大小: 6.15mm/6.15mm

結節體積: 131mm³ 最長直徑: 6.31mm 寫症機率: 17%

結節類型: Pulmonary Solid 鈣化情況: 非鈣化結節 Central attenuation: 198HU Mean density: 62.52HU Maximal attenuation: 469HU

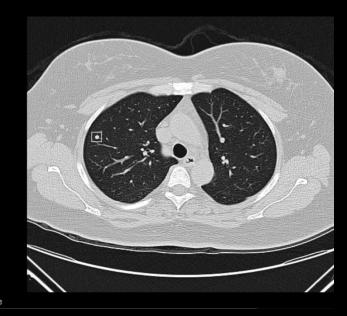
Maximal attenuation: 469HU Minimal attenuation: -290HU

當前AI版本可更有效檢出3CM以内的結節



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tung: right tung upper shote. ship make: 100% ship make: 100% ship make: 11mm* 最長直徑: 6.31mm 最長直徑: 6.31mm 扇症機率: 17% ship make: 17% ship make: 1981HU for 2.52HU Maximal altenuation: 499HU Minimal altenuation: 499HU Minimal altenuation: 499HU Minimal altenuation: 499HU Ship make: 489HU Minimal altenuation: 499HU Minimal altenuation: 499HU Minimal altenuation: 490HU Minima



Follow-Up of Small (4 mm or Less) Incidentally Detected Nodules by Computed Tomography in Oncology Patients

- In oncologic patients, 28% of small pulmonary nodules detected at initial CT will increase in size, suggesting metastasis.
- This increase in size tends to occur early, and follow-up CT in 3 months and 6 months would be appropriate in further evaluation.
- Small nodules that are stable in size for more than 365 days are unlikely to be pulmonary metastasis.

Small Incidental Pulmonary Nodules (≤ 4 mm) How Useful is Short-Term Interval CT Follow-Up?

The chance of growth in ≤ 4 mm NCNs in a 3- to 6-month period in patients with no previous history of malignancy or immune disorder is small; therefore, short-term follow-up imaging (<12 month) for nodules ≤ 4 mm is not necessary.</p>

ORIGINAL ARTICLE

Small Incidental Pulmonary Nodules
How Useful is Short-Term Interval CT Follow-Up?

Smooth or attached indeterminate solid NCNs

6-month or 1-year follow-up?

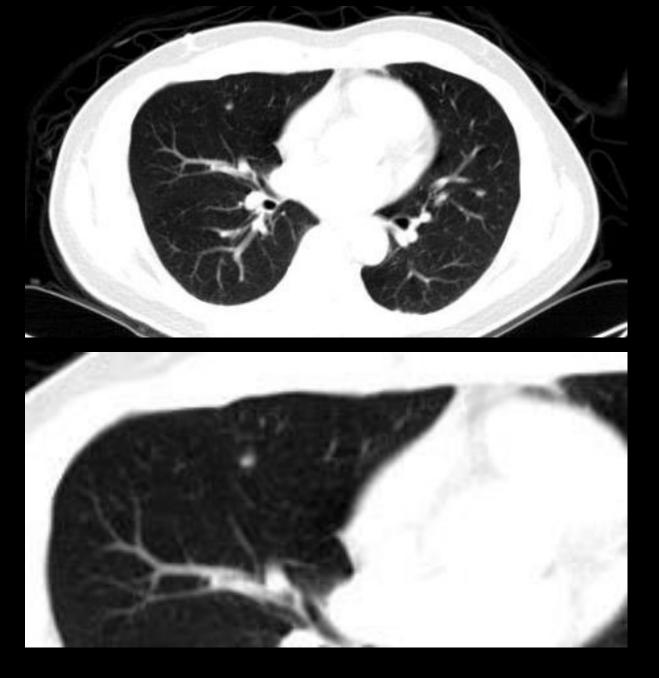




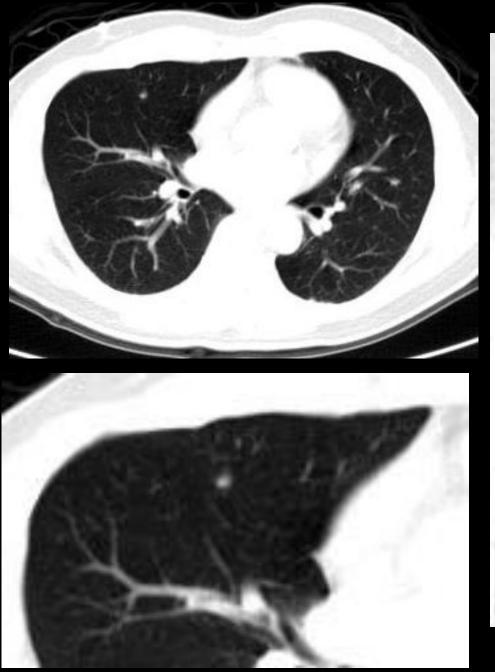


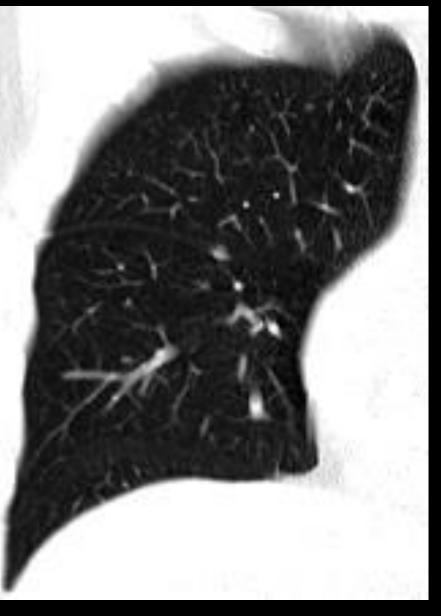


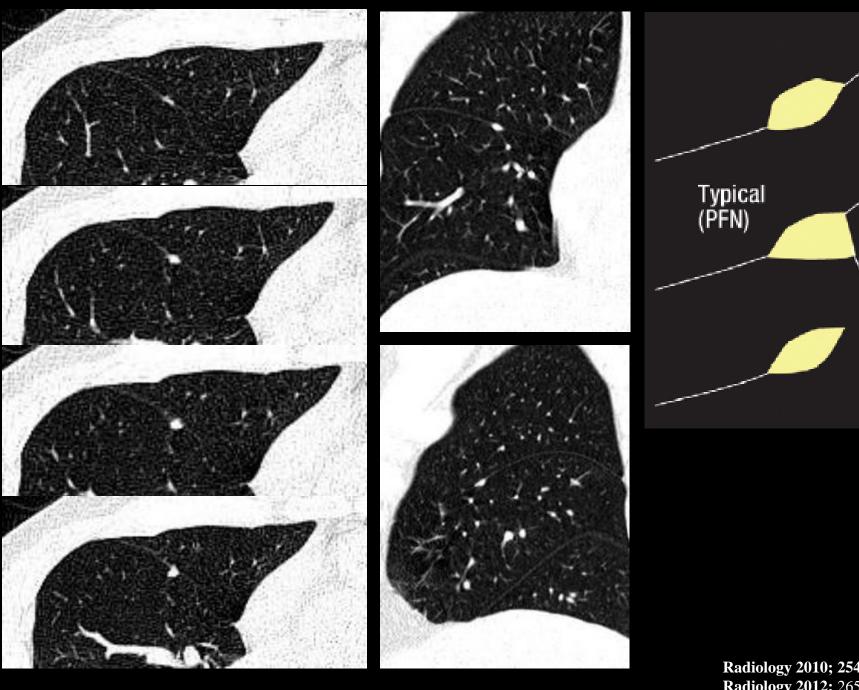
In smooth or attached indeterminate solid NCNs, no malignancies were found at 1-year follow-up (NELSON study).



Low-dose CT screening







Radiology 2010; 254:949–956 Radiology 2012; 265:611–616

Perifissural nodules (PFN)

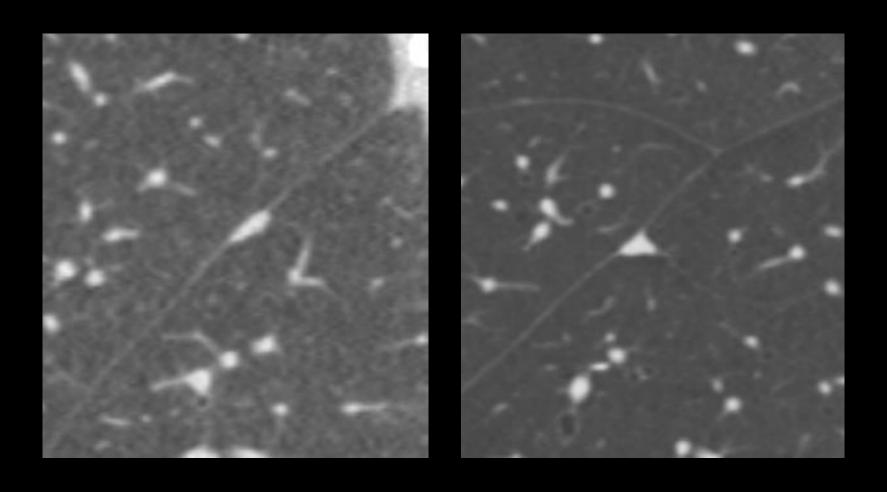
Typical PFN

We defined a typical PFN as a fissure-attached, homogeneous, solid nodule that had smooth margins and an oval, lentiform, or triangular shape.

Perifissural Nodules Seen at CT Screening for Lung Cancer¹

Typical (PFN)

Typical PFN

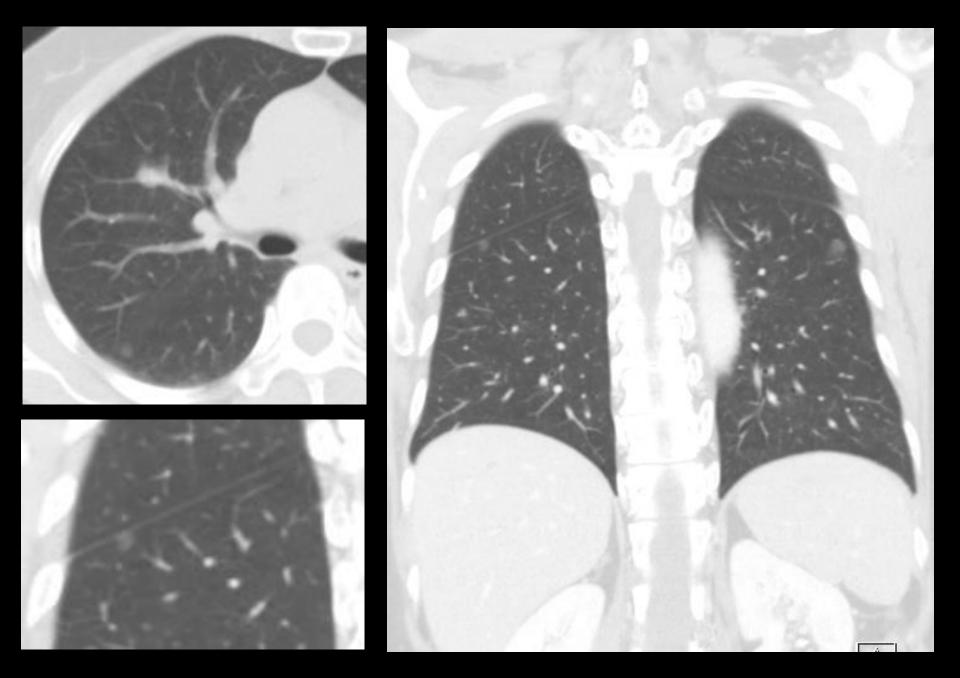


Non-PFN

All other nodules were defined as non-PFN.
This included nodules that showed features typical of malignancy, like spiculation.
Spherical nodules were also classified as non-PFN because a spherical shape suggests that the nodule is not influenced by the fissure, but is instead growing through the fissure.

Pulmonary Perifissural Nodules on CT Scans: Rapid Growth Is Not a Predictor of Malignancy

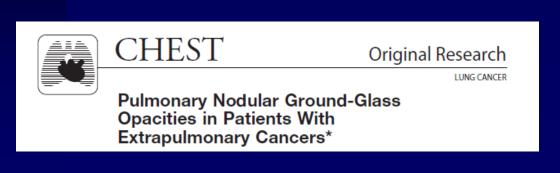
Pulmonary Perifissural Nodules on CT Scans: Rapid Growth Is Not a Predictor of Malignancy¹



Pulmonary Nodular Ground-Glass Opacities (NGGOs) in Patients With Extrapulmonary Cancers

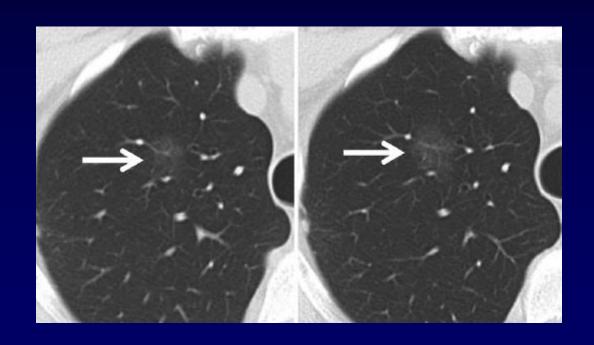
What is Their Clinical Significance and How Can We Determine Whether They Are Malignant or Benign Lesions?

- Pulmonary NGGOs in patients with extrapulmonary cancers tend to have high malignancy rates and are very often primary lung cancers.
- All malignant NGGOs were primary lung cancers.



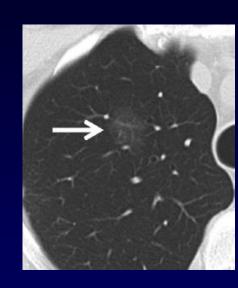


(2) Ground-glass opacity (GGO) or GGN



Ground-glass nodules (GGNs)

- A GGN is an area of increased pulmonary attenuation with preservation of the bronchial and vascular margins.
- GGN can be partly solid or nonsolid.
- A large range of benign diseases (eg, inflammatory disease or fibrosis) can manifest as GGN, most GGNs that persist longer are AAH, AIS, or MIA.





CT scan obtained with 5-mm-thick sections

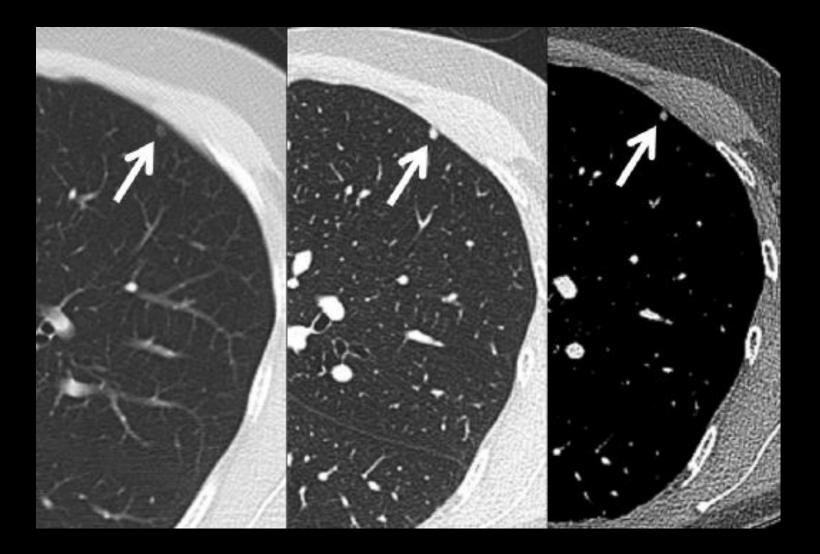
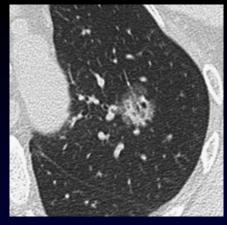


Image reconstruction at 1 mm or less *minimizes* <u>volume-averaging effects</u> and, therefore, *should be available to optimize characterization of small lung nodules*, particularly in the assessment of <u>nodule size</u> and <u>morphology</u> pertaining to solid and subsolid components.

Ground-glass nodules (GGNs)

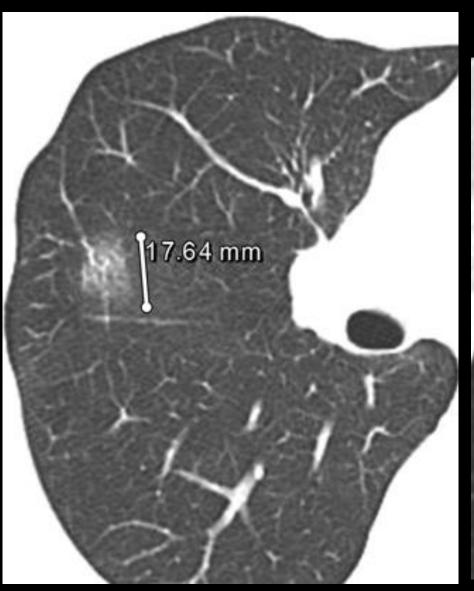
- GGNs are regularly encountered during CT screening for lung cancer.
- These GGNs pose a challenging task for the clinician because they grow slowly but, at the same time, have *a malignancy rate as high as 63%*.

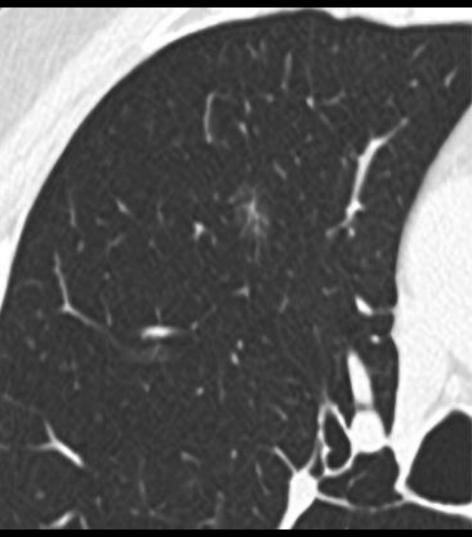




- Predictive CT findings of malignancy: a size of
 - > 10 mm, a lobulated margin and bubble-like appearance on initial CT were indicative of the future growth of pure GGNs, which implies probable malignancy.
- Resolving pulmonary nodules share CT features with malignant nodules.

There are no predictive CT features to aid in differentiating lesions likely to *progress* versus those that *remain stable*.





Case 1 Case 2

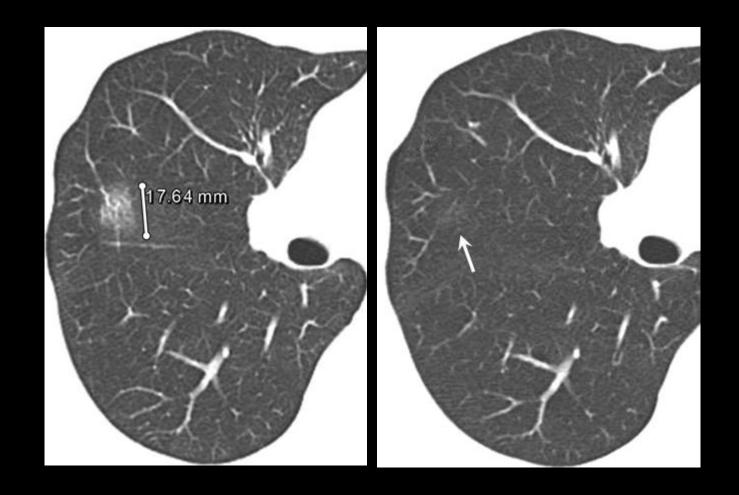


Fig. Focal inflammation mimicking adenocarcinoma. (a) Magnified 1-mm CT section through the right upper lobe shows nodules with GGO initially diagnosed as probable BAC. (b) Follow-up CT scan obtained 3 months later shows near complete resolution of the lesion (arrow), now presumed to represent focal nonspecific inflammation.

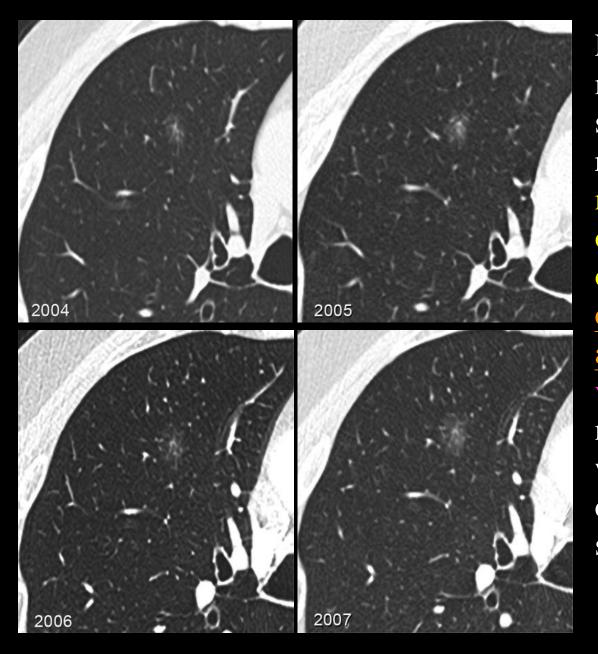
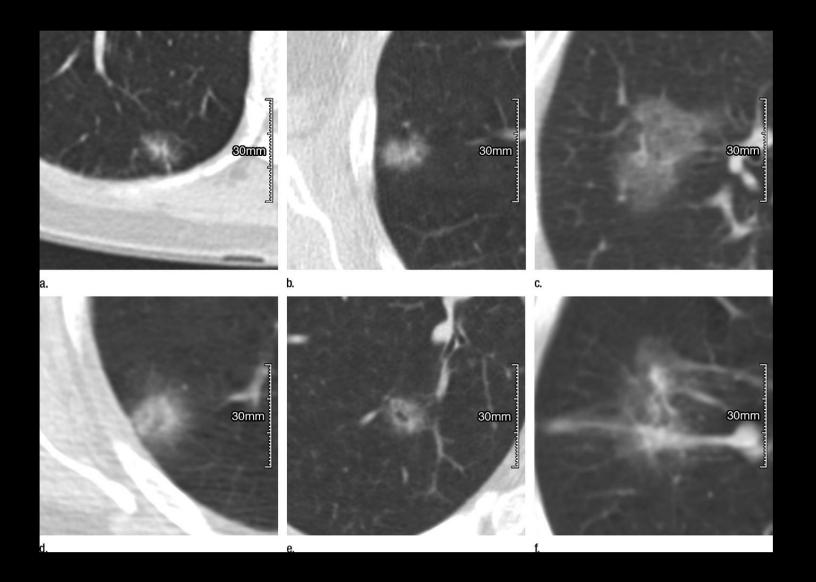


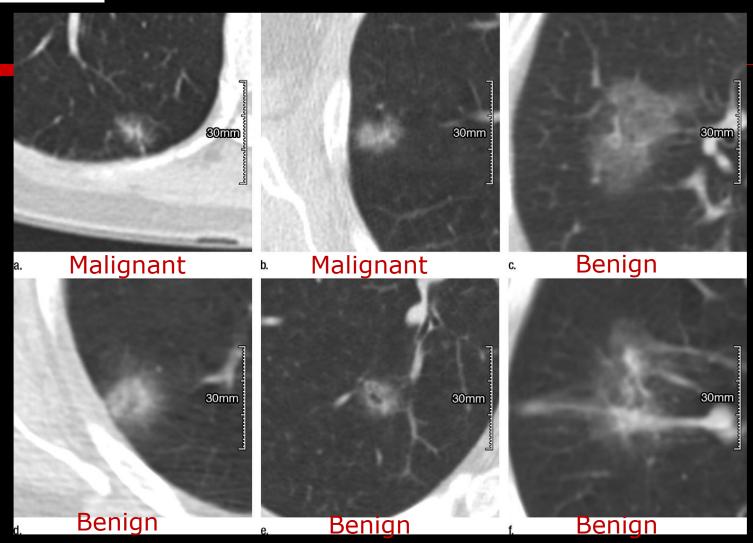
Figure. ADC. Sequential magnified 1-mm CT sections through the right upper lobe show minimal increase in size of a nodule with GGO over a 3-year period. The central area of higher attenuation represents a vessel bifurcation and not a solid component, which was better characterized on sequential images.



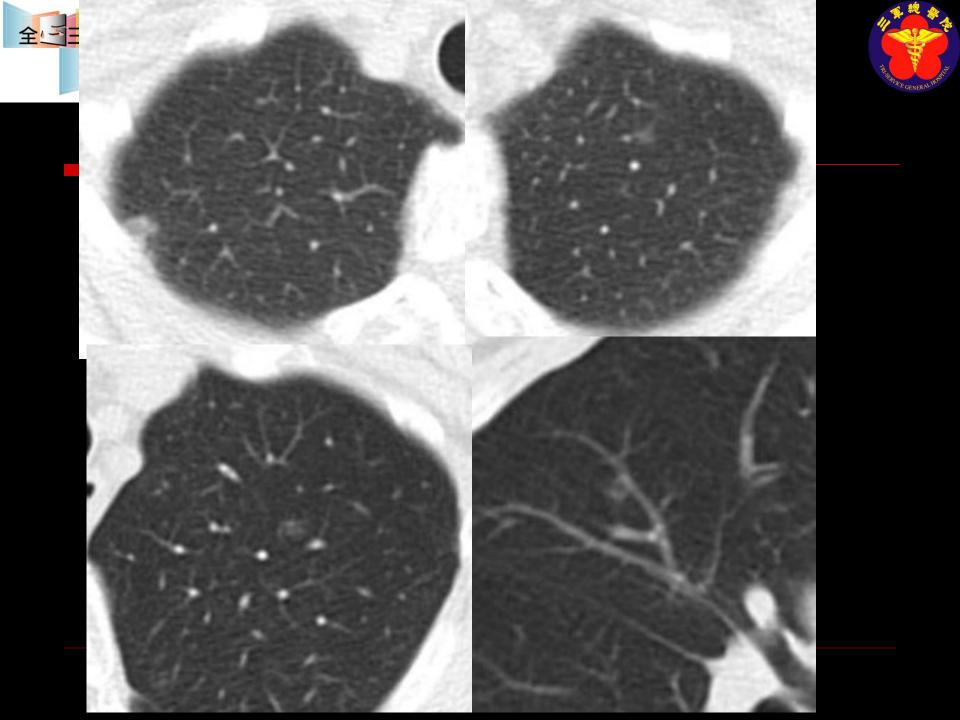
Radiology: Volume 284: Number 1—July 2017

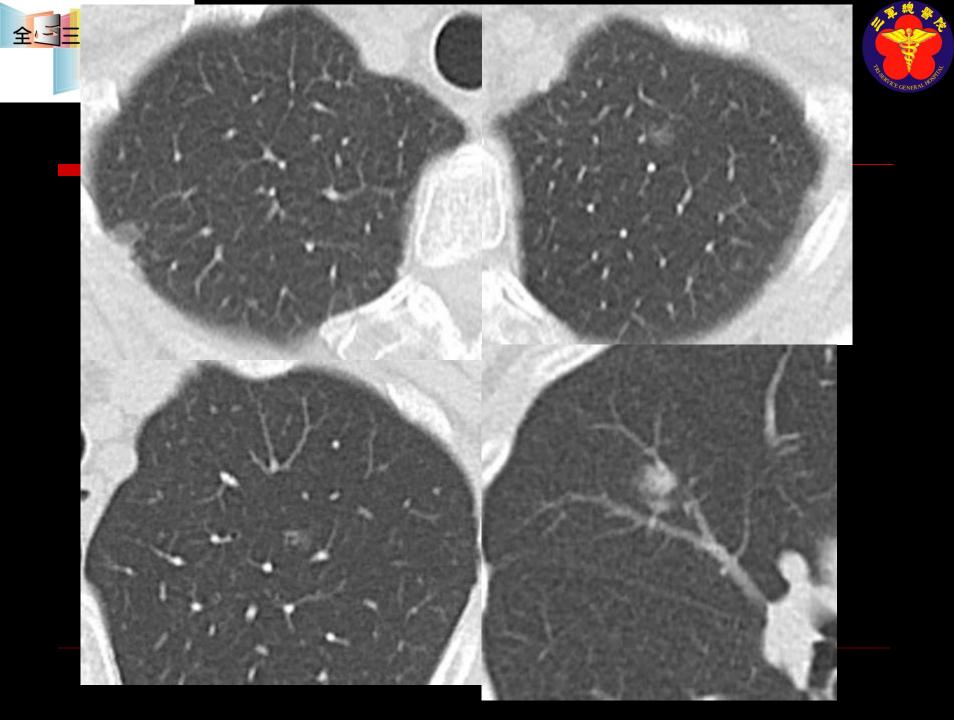






Radiology: Volume 284: Number 1—July 2017





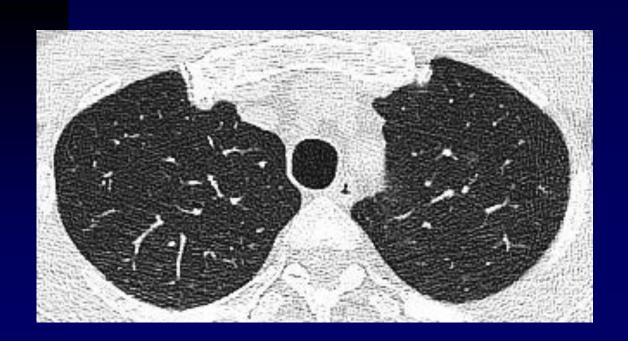


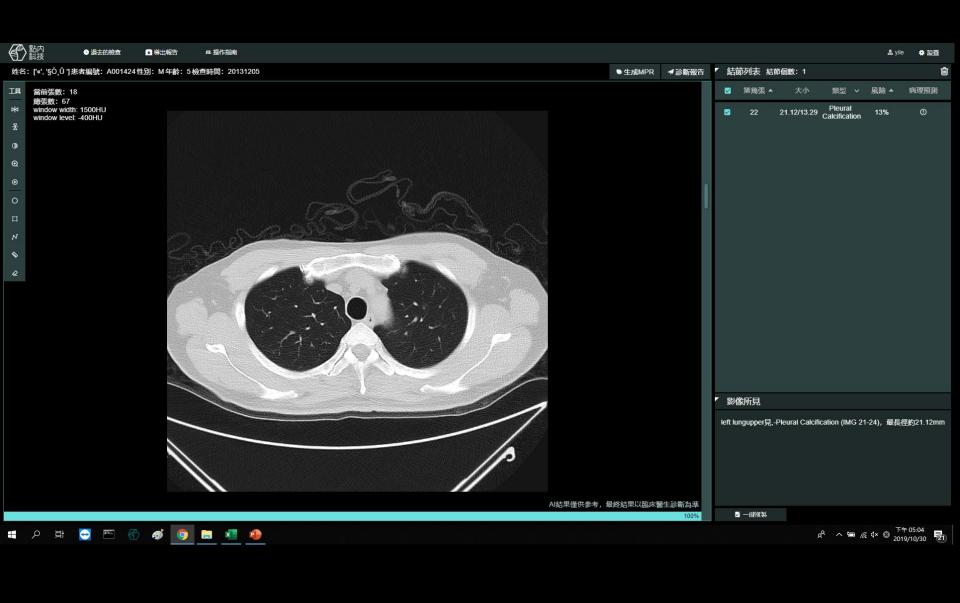
Solitary subsolid GGN

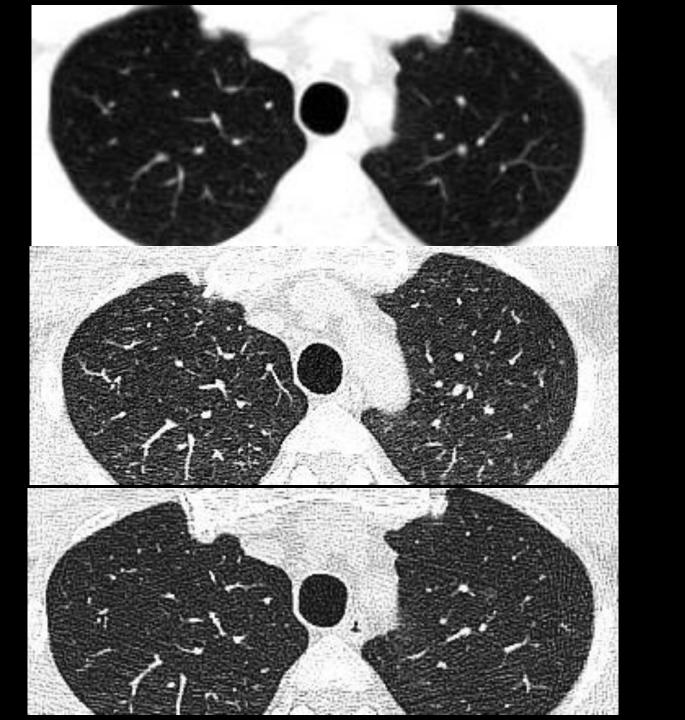
- Solid: 7%; Part-solid: 63%; GGN: 18%.
- Large pure GGNs are more likely to be invasive.
- Solid component > 5 mm: malignancy should be considered.
- Development of a solid component within lesions is also strong evidence of an invasive adenoCA.

Although the surgical indications for GGO lesions are not well established, generally, when the size of a pGGO lesion grows or when a newly developed solid component is observed, the operation may be performed.

For subsolid nodules, the limitations in assessing growth are compounded because these lesions are *typically small* and *poorly defined* with growth that may be indolent and difficult to perceive.



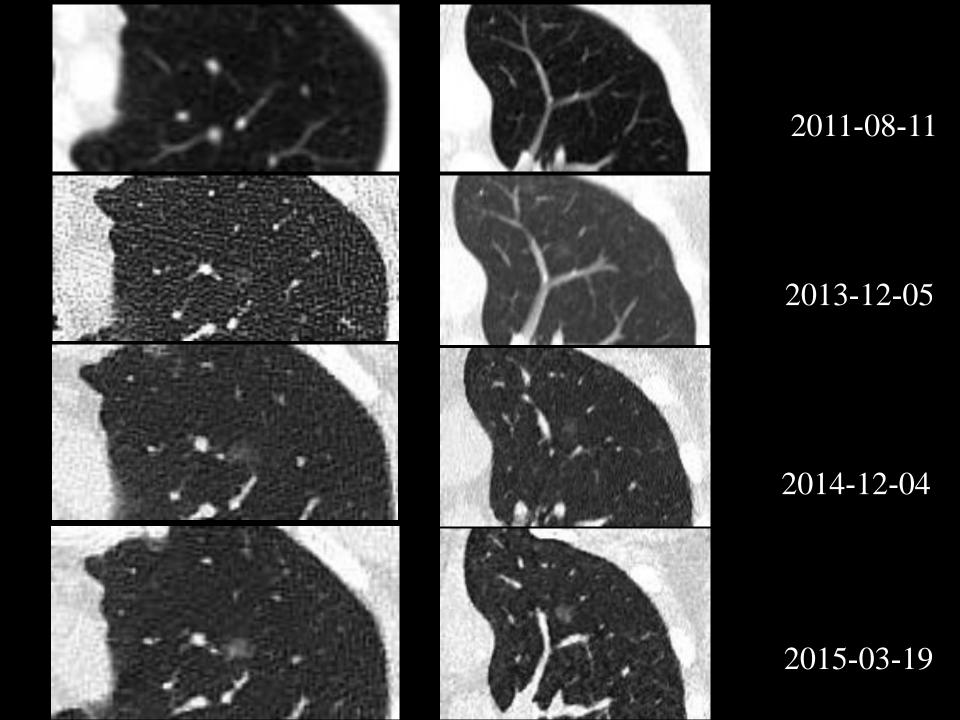




2011-08-11

2012-12-06

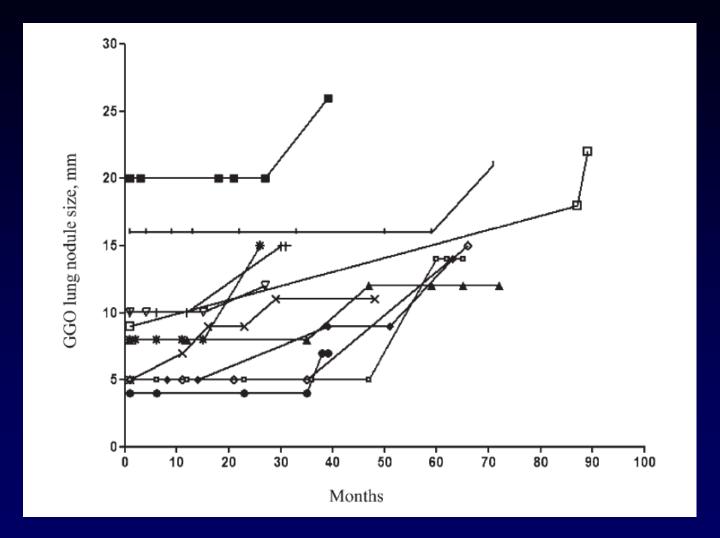
2013-12-05



Natural history of pGGNs

- 10-25% of pure GGNs increases in size or grow solid component, while others remain unchanged for years.
- GGN: 122 GGNs (Chest 2013- screening-detected GGNs, median F/U period: 59 months): median size of 5.5 mm (range, 3–20 mm; 5 of the 12 pure GGNs ≤ 5 mm): 9.8% (12/122 GGNs) growth, VDT: 769 days (2.1 years: 330-3031 days) for growing pGGNs, 2/12: developing solid component.
- lung nodules did not grow during long-term follow-up in subjects with no history of malignancy and most growing nodules had an indolent clinical course. A strategy of long-term follow-up and selective surgery for growing nodules should be considered for pure GGO lung nodules.

Growth Patterns of Pure GGNs



91% of the pure GGN were dormant for > 12 months and subsequently grew, but one (9.1%) exhibited a linear growth pattern without dormancy.

Solitary Pure Ground-Glass Nodules 5 mm or Smaller:

Frequency of Growth¹

Purpose:

To clarify the percentage of solitary pure ground-glass nodules (SPGGNs) 5 mm or smaller that grow and develop into invasive adenocarcinomas.

Results:

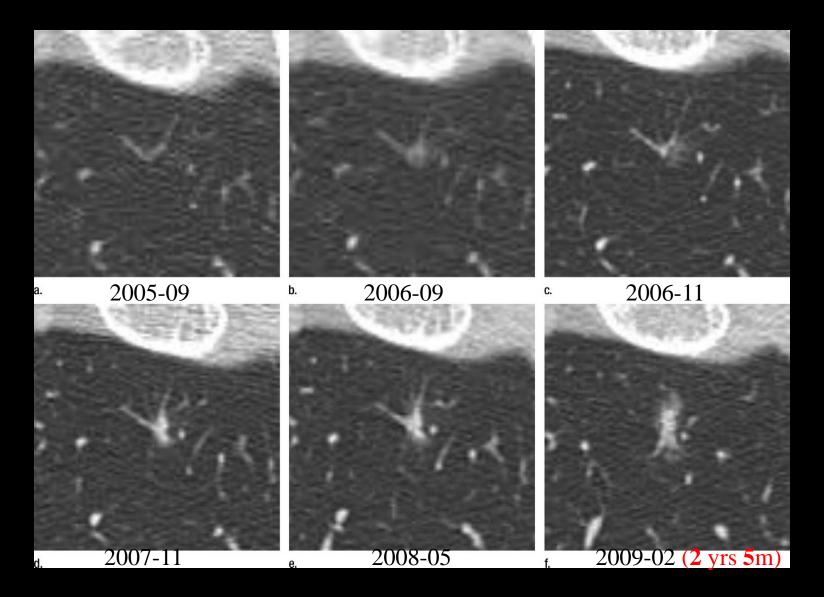
At baseline screening, 438 SPGGNs 5 mm or smaller were identified, and during the study period one SPGGN 5 mm or smaller developed de novo. Of the 439 SPGGNs, 394 were stable and 45 (10.3% [95% confidence interval: 7.5%, 13.7%]), including newly developed SPGGN, grew. Of the 45 SPGGNs that grew, 0.9% (four of 439 [95% confidence interval: 0.3%, 2.3%]) developed into adenocarcinomas (two minimally invasive [including the newly developed SPGGN] and two invasive). The mean period between baseline CT screening and the appearance of solid components in the four adenocarcinomas was 3.6 years.

Conclusion:

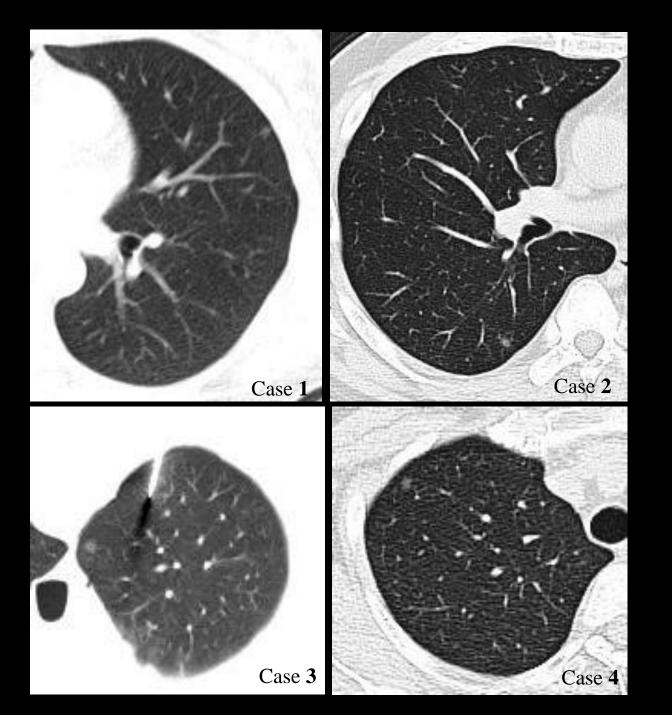
Of SPGGNs 5 mm or smaller, approximately 10% will grow and 1% will develop into invasive adenocarcinomas or minimally invasive adenocarcinomas. SPGGNs 5 mm or smaller should be rescanned 3.5 years later to look for development of a solid component.

°RSNA, 2015

- 1. 在CT篩檢中檢測 到的大約10%
 - (439個GGNs中的45個)5毫米或更小的SPGGN將增長 大。
- 這些≤5mm的
 SPGGN中大約
 1% (439個中的4個)
 將發展成<u>侵襲性</u>
 腺癌或MIA。
- 3. 這些≤5mm的
 SPGGN在病理證實的腺癌中,基線CT篩查與固體
 成分出現之間的
 平均時間為3.6年。

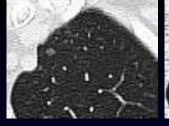


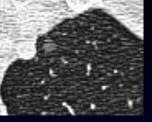
MIA, tumor size: 0.8 cm; invasive focus: 2 mm; TNM stage IA1: pT1miN0M0; segment 3 of the left upper lobe; VDT, 265 days.



林秀燕16051 殷維偉70112 黃亦平24903 鍾碧雲18171

Growth of pure GGN





- of patients with GGO nodules who underwent surgery, 27.3% had *invasive* adenocarcinoma and 9.1% had microscopic mediastinal nodal metastasis.
- A portion of pure GGO lung nodules could develop into invasive adenocarcinoma.

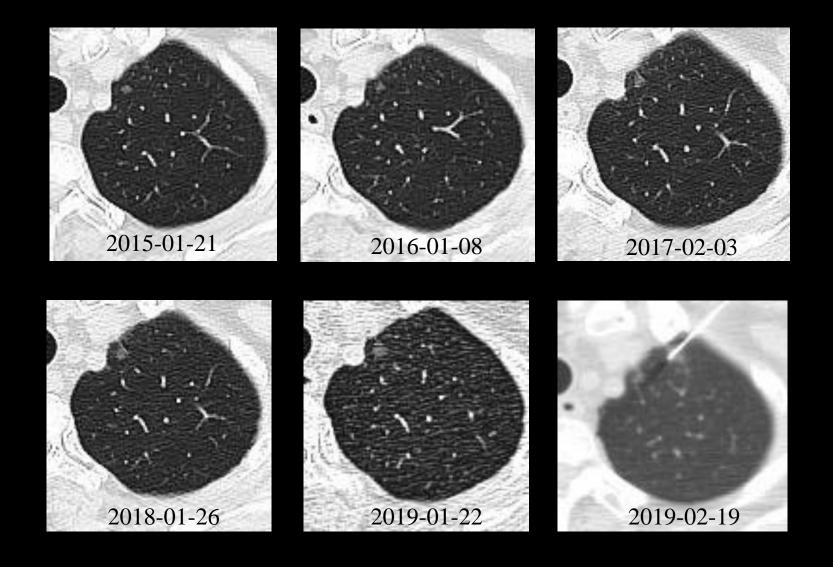
Background: Although focal ground-glass opacity (GGO) lung nodules are generally reported to grow slowly, their natural course is unclear. The purpose of this study was to elucidate the natural course of screening-detected pure GGO lung nodules in patients with no history of malignancy. Methods: We retrospectively reviewed the database of subjects who had undergone screenings involving low-dose CT scans. We included patients with pure GGO lung nodules who were followed for > 2 years after the initial screening.

Results: Between June 1997 and September 2006, 122 pure GGO nodules were found in 89 patients. The median nodule size was 5.5 mm (range, 3-20 mm) in the largest diameter on initial low-dose CT scan. The median follow-up period per patient was 59 months. On a per-person basis, the frequency of growth was 13.5% (12 of 89 patients). On a per-nodule basis, the frequency of growth was 9.8% (12 of 122 nodules). Nodule growth was significantly associated with initial size and new development of an internal solid portion. The median volume doubling time was 769 days for growing pure GGO nodules. A total of 11 growing nodules were surgically validated, and all lesions were confirmed as primary lung cancer.

Conclusions: About 90% of the screening-detected pure GGO lung nodules did not grow during long-term follow-up in subjects with no history of malignancy and most growing nodules had an indolent clinical course. A strategy of long-term follow-up and selective surgery for growing nodules should be considered for pure GGO lung nodules.

CHEST 2013; 143(1):172–178

Abbreviations: GGO = ground-glass opacity; HU = Hounsfield unit; LDCT = low-dose CT; TDR = tumor shadow disappearance rate



Well-differentiated adenocarcinoma, tumor size: 7 mm; TNM stage IA1; the left upper lobe.

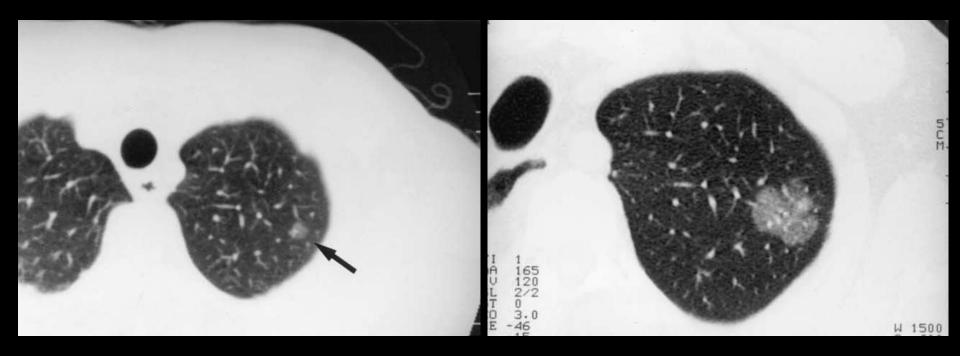


Fig. CT from 57-year-old with long-term follow-up of pure ground-glass opacity (**PGGO**) for more than 10 years. Patient had undergone operation for ADC originating in right upper lobe 10 years previously. (A) Small PGGO in left upper lobe (arrow) was pointed out as a function of the retrospective review of conventional *CT taken at that operation*. (B) On follow-up *124 months later*, high-resolution CT shows *enlargement of PGGO from 8 mm (A) to 25 mm in diameter*. Most of the resected specimen reveals **bronchioloalveolar carcinoma** (hematoxylin and eosin, × 2.5). **Focus of invasive adenocarcinoma** can also be recognized. (Hematoxylin and eosin, × 66.)

Natural History of Pure Ground-Glass Nodule (pGGN)

Table	1.	Patient	U	demographics (
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a Involving recurrence from prior cancer.

AAH = atypical adenomatous hyperplasia;

VATS = video-assisted thoracic surgery;

Patient No.	Age at Discovery (y)	Sex	No. of Lesions	Means of Detection	Location (lobe)	Preoperative Follow-up (mo)	Initial/Final Size (mm)	Surgery	Histology	Outcome
1	57	M	1	Postoperative follow-up	Left upper	124	8/25	WWR	AC with MS	Disease-free ^a
2	66	M	1	Postoperative follow-up	Right lower	96	18/20	Segmentectomy	BAC	Disease-free
3	70	M	1	Postoperative follow-up	Right upper	32	4/10	WWR	BAC	Disease-free
4	76	M	2	Postoperative follow-up	Left upper	28	15/25 & ?/10	Segmentectomy	BACs	Dead without recurrence
5	66	M	1	CT screening	Middle	26	7/7	VATS WWR	BAC	Disease-free
6	60	F	1	Incidentally	Right upper	29	6/6	VATS WWR	AAH	Disease-free
7	47	M	1	CT screening	Right upper	39	6/10	Segmentectomy	PLD	Disease-free
8	35	M	1	CT screening	Middle	24	11/14	WWR	PLD	Disease-free
9	64	F	1	Postoperative follow-up	Left lower	52	10/25	WWR	PLD	Disease-free
10	62	F	1	CT screening	Right upper	37	8/8	VATS WWR	Fibrosis	Disease-free
11	65	F	Many	CT screening	All lobes	37	$\leq 10 / \leq 10^{\rm b}$	ND	BAC or AAH ^c	Alive with lesions
12	74	F	1	Postoperative follow-up	Left upper	48	18/20	ND	Unknown	Alive with lesion
13	53	F	1	CT screening	Left lower	36	6/6	ND	Unknown	Alive with lesion
14	52	F	1	CT screening	Right upper	34	5/5	ND	Unknown	Alive with lesion
15	75	M	1	CT screening	Right upper	30	10/13	ND	Unknown	Alive with lesion
16	67	M	1	CT screening	Left upper	30	8/14	ND	Unknown	Alive with lesion
17	65	F	1	Postoperative follow-up	Left lower	26	5/5	ND	Unknown	Alive with lesion
18	53	F	1	CT screening	Left upper	26	8/8	ND	Unknown	Alive with lesion
19	65	M	1	CT screening	Right lower	30	8/8	ND	Unknown	Alive with lesion

AC with MS = adenocarcinoma with mixed subtypes;

WWR = wide wedge resection.

b Some of lesions have shown only a slight increase in size or density, but remained within 10 mm in diameter;

CT = computed tomography;

PLD = pulmonary lymphoproliferative

^c Probably.

ND = not done;

^{1.} pGGN (4–18 mm) after long-term F/U of more than 2 years: 1) no change: 8/19 (42%); 2) increased slightly (up to 5 mm): 6/19 (32%); 3) increased by more than 5 mm: 5/19 (26%).

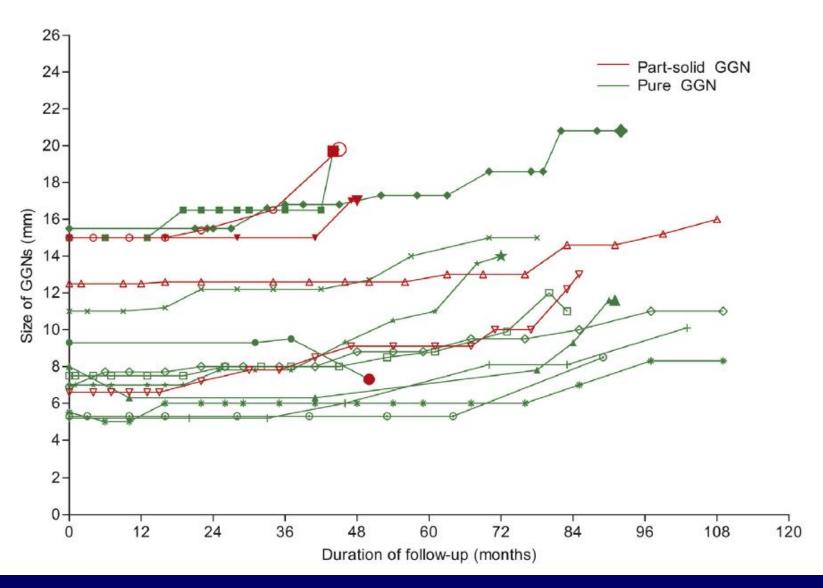
^{2.} These data suggest that **some pGGNs will never progress to clinical disease** and would be included in the category of *overdiagnosis bias*.

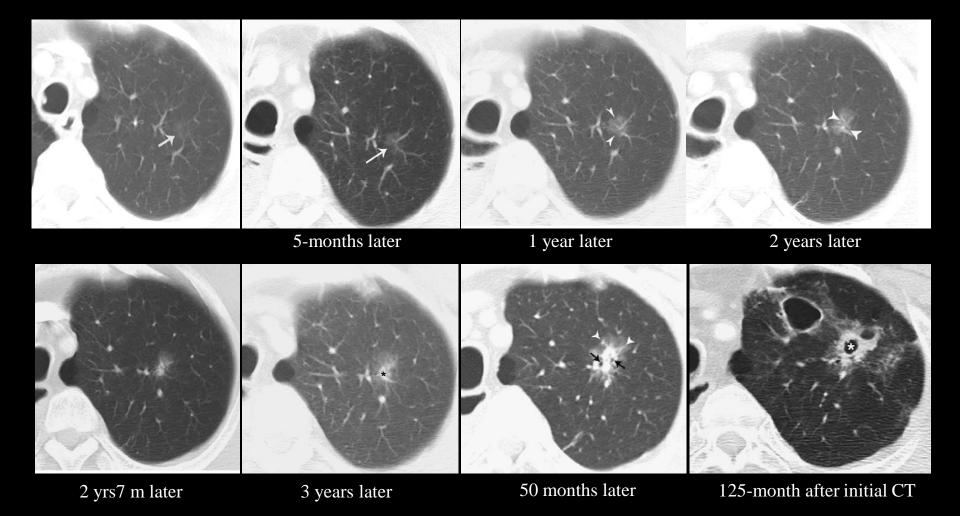
Natural history of GGNs: Long-term follow-up of small pulmonary GGNs stable for 3 Years

- *Introduction*: How long persistent and stable GGNs should be followed is uncertain, although a minimum of 3 years is suggested.
- Results: 2003-2015, 453 GGNs (438 pGGNs and 15 part-solid GGNs; size: 2-31 mm, median size: 5 mm) were found in 218 pts. Of the 218 pts, 14 had 15 GGNs showing subsequent growth after the initial 3 yrs during the median follow-up period of 6.4 years.

For the <u>person-based</u> analysis, the frequency of subsequent growth of GGNs that had been stable during the initial 3 yrs was 6.7% (14/218). For the <u>nodule-based</u> analysis, the frequency was 3.3% (15/453).

Growth patterns of 15 GGNs: 6.7% (14/218)





Serial HRCT over the 126 months of a 51-year-old man with a history of right upper lobectomy for lung cancer (squamous cell carcinoma) (pT2N2M0).

Stepwise evolution from a focal pure pulmonary ground-glass opacity nodule into an invasive lung adenocarcinoma: An observation for more than 10 years.

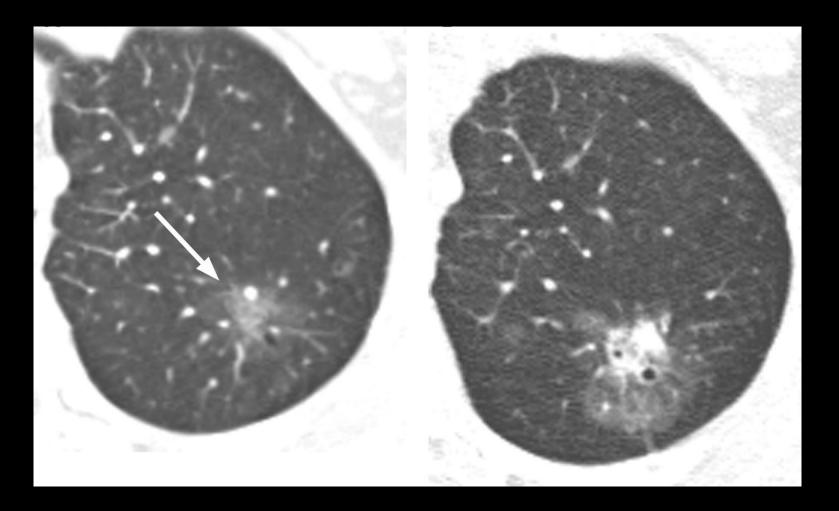
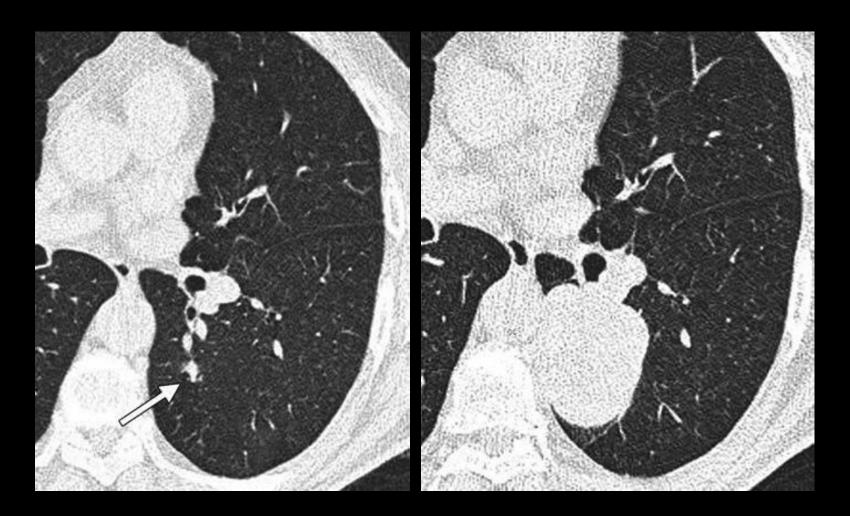


Fig.—Subsolid nodule, demonstrating worrisome change. (A) An annual CT, demonstrating a persistent 14-mm pure GGO (arrow). This is a Lung Reporting and Data System (LU-RADS) 4B nodule (likely low-grade adenocarcinoma). The patient was not referred to surgery and did not return for recommended follow-up. (B) CT 3 years later, showing the nodule has enlarged to 34 mm and contains a 12 mm solid portion. The nodule is now classified as LU-RADS 4C (likely malignant).



57-year-old man with visible but unidentified 6.3-mm nodule (arrow) in left lower lobe *similar in size and shape to surrounding blood vessels*.



a, 57-year-old man with visible but unidentified 6.3-mm nodule (arrow) in LLL similar in size and shape to surrounding blood vessels. b, CT image obtained 12 months after a. *shows substantial increase in diameter to 56 mm* (T3). Diagnosis was small cell carcinoma with N1 lymph node metastasis (stage IIIA).

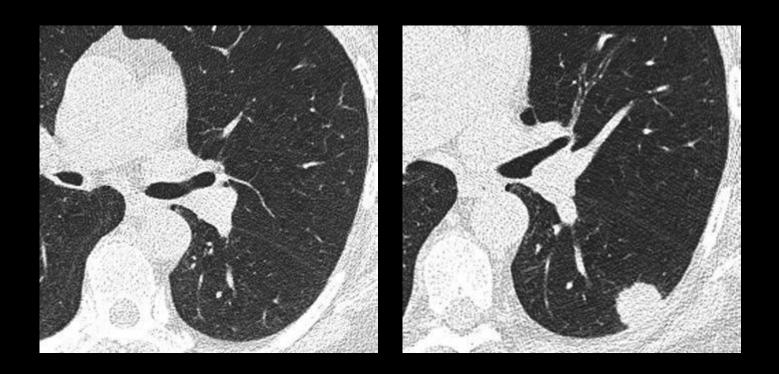
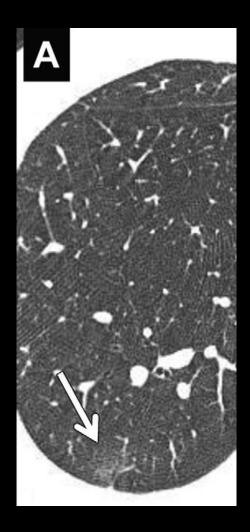


Fig. — 61-year-old woman with cancer not visible at previous CT screening (category 1). A, CT image shows no nodule in left lower lobe.

B, CT image 11 months after A shows new nodule measuring 22.0×19.0 mm. Diagnosis was large cell carcinoma (stage I).



Value of initial short-term follow-up of malignant GGNs. Consecutive 1-mm-thick sections through RLL section obtained at same anatomic level over a 6-month period (A, baseline.

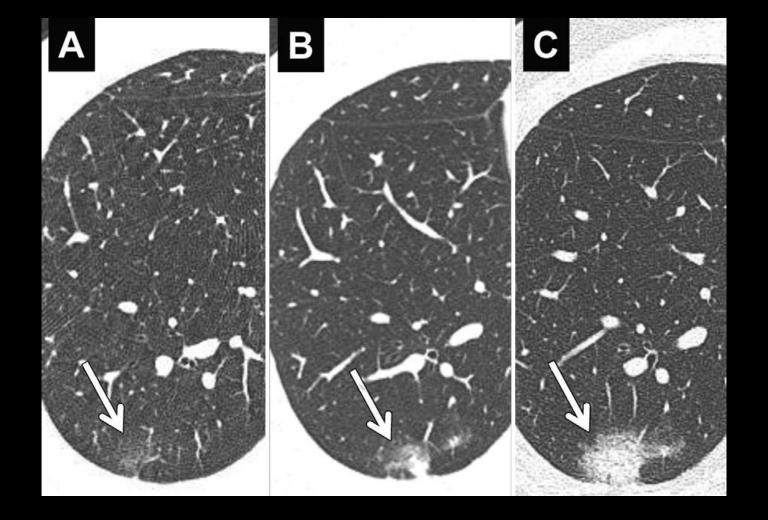
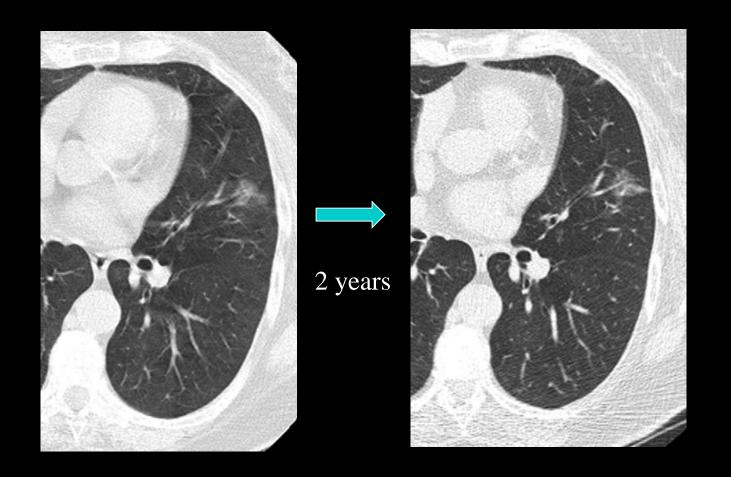


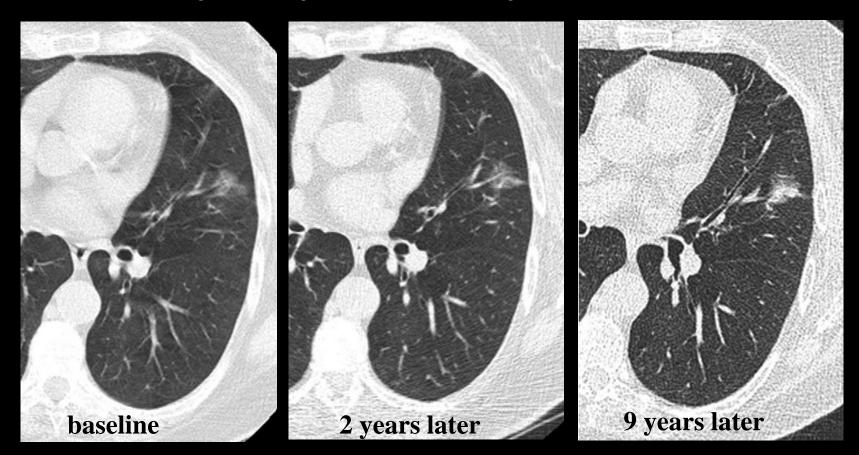
Fig: **Value of initial short-term follow-up** of malignant GGNs. Consecutive 1-mm-thick sections through RLL section obtained at same anatomic level over a 6-month period (A, baseline; **B, 3 months**; **C, 6 months**) show *rapid transformation of initial pure GGN* (arrow in A) *to a predominantly part-solid lesion* (arrow in B and C), which subsequently proved to be **mucinous adencarcinoma**.

It is sometimes difficult to determine proper follow-up examinations, particularly in case of GGO nodule growing slowly on serial CT scans.



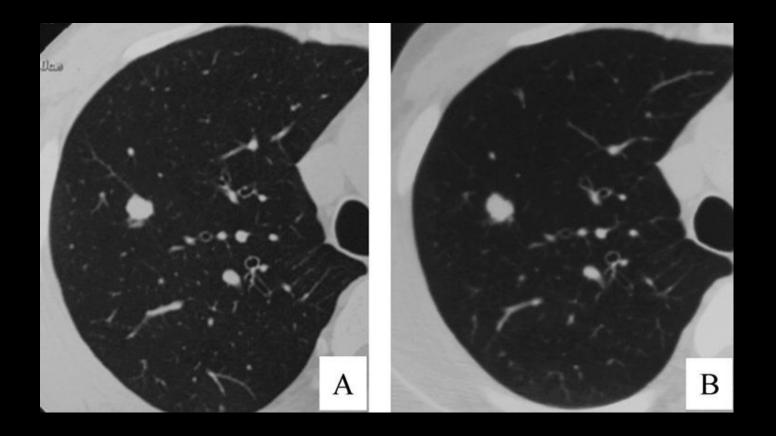
CT images in a 68 y/o smoker show (a) a nonsolid nodule ($17 \times 13 \text{ mm}$) in the LUL at baseline screening, (b) the nodule remained nonsolid at follow-up 2 years later.

The follow-up duration should be extended to 5 or 10 years, considering the long volume doubling time.



CT images in a 68 y/o smoker show (a) a nonsolid nodule (17×13 mm) in the LUL at baseline screening, (b) the nodule remained nonsolid at follow-up 2 years later, and (c) a solid component emerged at follow-up 9 years later. At that time, it was resected, and the final diagnosis was 2.1-cm invasive adenocarcinoma.

If such change should be considered as a benign lesion?



(A) A solid nodule was detected by conventional CT screening in the RUL and considered as granuloma and followed up (10 mm \times 9 mm). (B) The nodule unchanged in size by the follow up CT (*after 2 years and 6 months*).

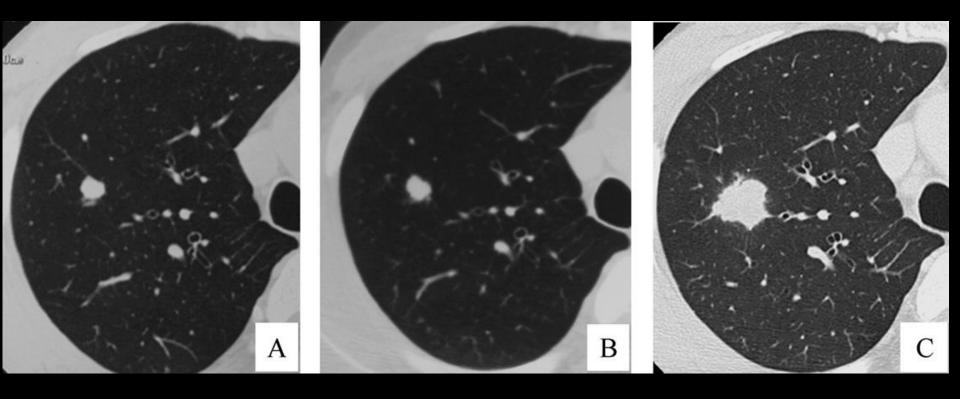
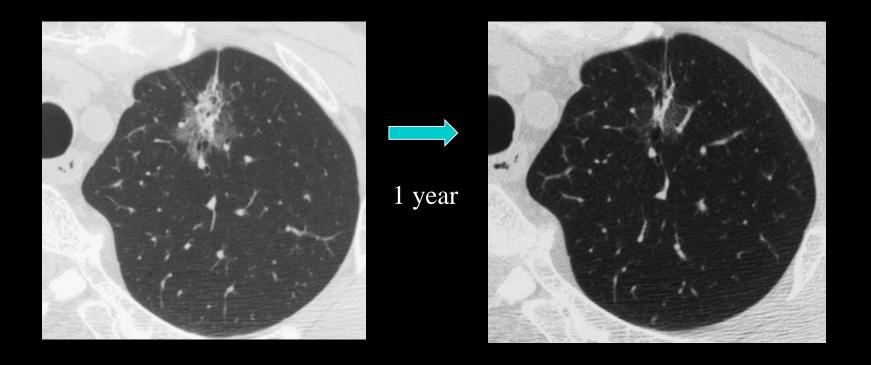
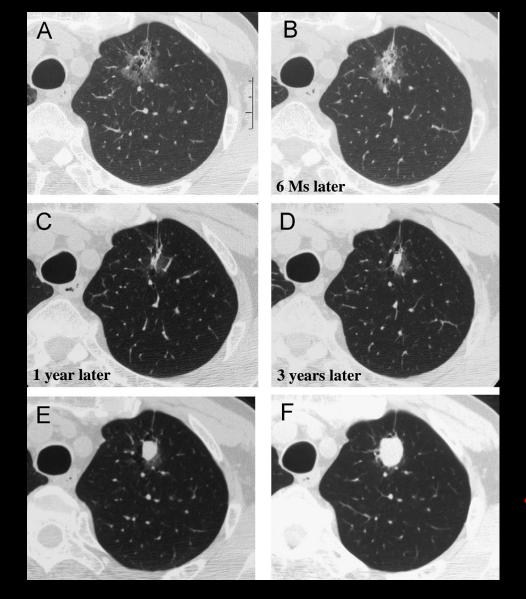


Fig. A case of the VDT changed during follow up period. In this case, the follow up durations was **3 years and 4 months**. (A) A solid nodule was detected by conventional CT screening and followed up (10 mm × 9 mm). (B) The nodule unchanged in size by the follow up CT (*after 2 years and 6 months*), but grew rapidly during next 8 months. (C) The pathological findings was mucoepidermoid carcinoma.

If such change should be considered as a benign lesion?



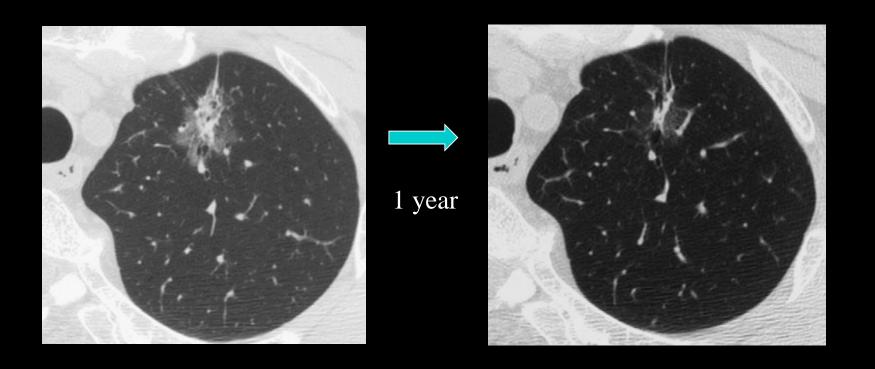
Nodule diameter (with 36-mm diameter at initial CT image) has decreased to 16mm and solid component has become linear at 1 year after initial CT.



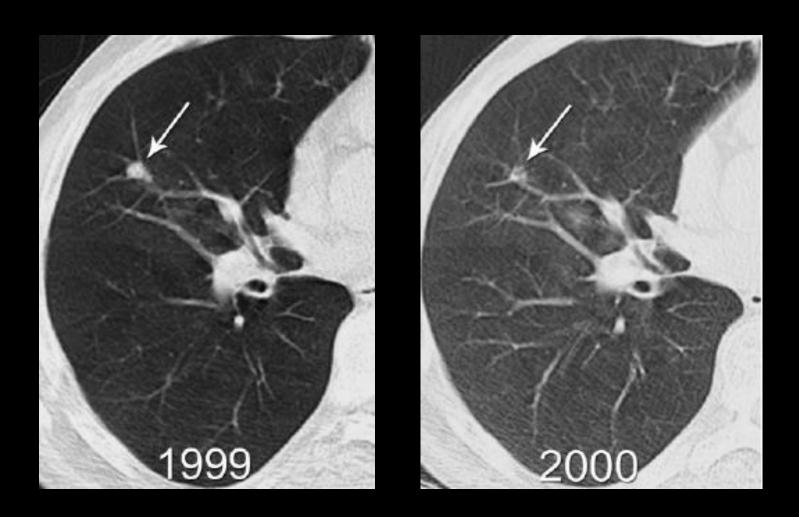
4 years and 6 months

Adenocarcinoma: (A) Nodule with 36-mm diameter shows ground-glass opacity (GGO) with high attenuation in LUL. (B) Solid component in GGO 6 months later. (C) Nodule diameter has decreased to 16mm and solid component has become linear at 1 year after initial CT. (D) Linear solid component is slightly enlarged at 3 years after initial CT. (E) Solid round nodule of 10-mm diameter and focal GGO at 4 years after initial CT. (F) At 6 months thereafter, solid nodule has increased to 20mm in diameter, and GGO has disappeared.

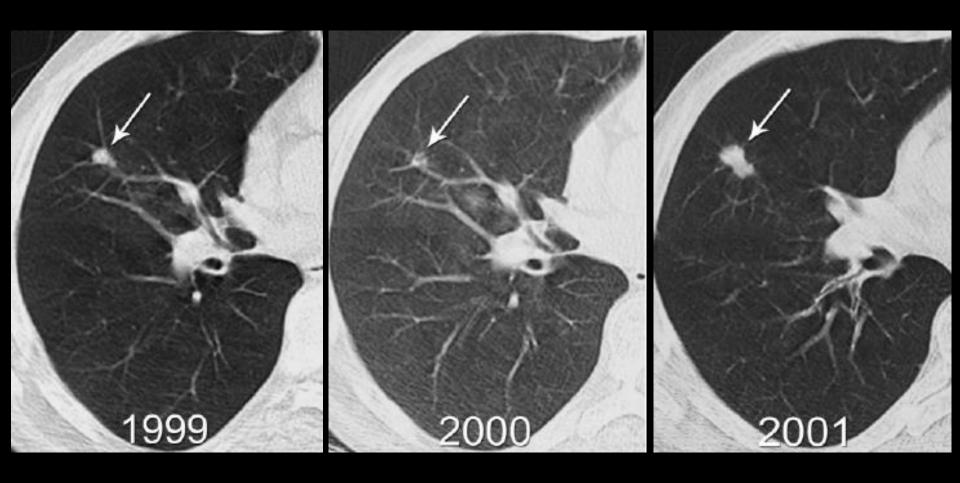
Malignant lesions may occasionally show a temporary decrease in size, due to contraction of a fibrotic or atelectatic component.



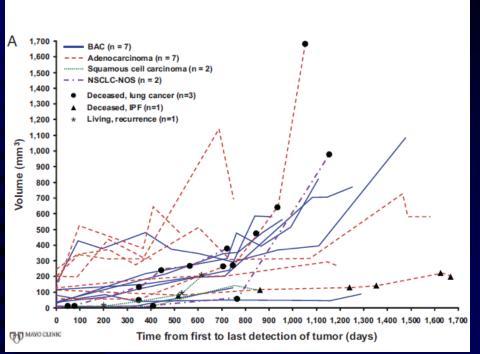
If such change should be considered as a benign lesion?

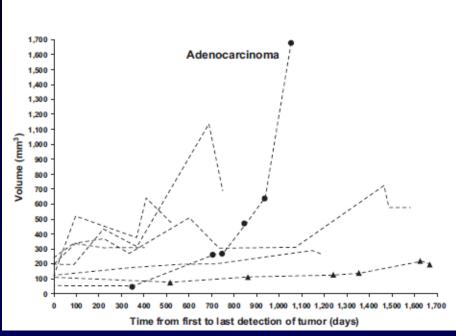


Two sequential transverse CT scans (5-mm section width) obtained 1 year apart show a nodule (arrow) in the RML that became smaller after initial screening CT.



Three sequential transverse CT scans (5-mm section width) obtained 1 year apart show a grade 3 **adenocarcinoma** (arrow) in the RML that **became smaller after initial screening CT** but enlarged on the subsequent scan.





11 growth curves suggested a decrease in volume at some point.

A small number of tumors become smaller, decreased in attenuation, or become more smoothly marginated -- such changes should not negate follow-up of an indeterminate tumor.

少數腫瘤變小、attenuation變淡、或邊緣變得更加平滑 ---- 這種變化不應該否定不確定腫瘤的追蹤

Conclusion

There remains a growing need to reexamine the radiologic approach to small nodules, particularly when CT is performed for indications other than screening. 仍有越來越多的需要重新審視

Conclusion

 Guideline awareness among clinicians is widespread, but conformance shows large heterogeneity.

 Overmanagement is common, which may lead to avoidable financial and physical burden.



T Descriptor Subsolid Nodules

cī* ı	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‡‡	06-3.0 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‡‡	cTla	cTlb	cTlc

總結了第8版小型 (≤3 cm: Tis/T1mi/T1a) 肺腺癌之T描述分類的提議: solid component size 被新採用(8th edition TNM)作為分類T分類的重要參數:

- If pure GGO > 3 cm, classified as cT1a.
- If GGO predominant part-solid nodule has solid component ≤ 0.5 cm but total size > 3 cm, classified as cT1a.
- Tis [AIS] cT: These lesions typically show pure GG nodules (GGNs) measuring 3 cm or less.

Long-Term Follow-up of Small Pulmonary Ground-Glass Nodules Stable for 3 Years: Implications of the Proper Follow-up Period and Risk Factors for Subsequent Growth



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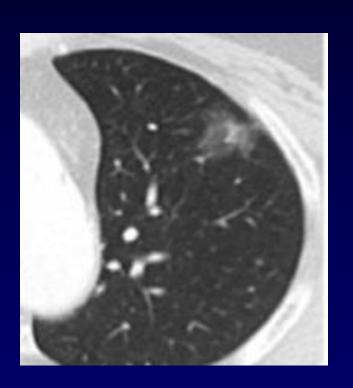
Results: Between May 2003 and June 2015, 453 GGNs (438 pure GGNs and 15 part-solid GGNs) were found in 218 patients. Of the 218 patients, 14 had 15 GGNs showing subsequent growth after the initial 3 years during the median follow-up period of 6.4 years. For the person-based analysis, the frequency of subsequent growth of GGNs that had been stable during the initial 3 years was 6.7% (14 of 218). For the nodule-based analysis, the frequency was 3.3% (15 of 453). In a multivariate analysis, age 65 years or older (OR = 5.51, p = 0.012), history of lung cancer (OR = 6.44, p = 0.006), initial size 8 mm or larger (OR = 5.74, p = 0.008), presence of a solid component (OR = 16.58, p = 0.009), and air bronchogram (OR = 5.83, p = 0.015) were independent risk factors for subsequent GGN growth.

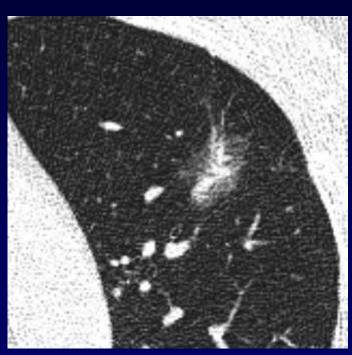
1. 穩定3年的small GGNs的長期追蹤:

對於基於人的分析,在最初的3年中穩定的GGN的後續長大的頻率為6.7%(218個中的14個)對於基於結節的分析,頻率為3.3%(453中的15)。

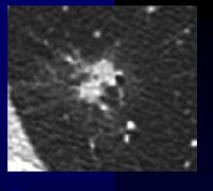
2. 在增長的15個GGN中,有7個透過手術切除: 所有切除的GGN被診斷為IA期肺腺癌,包括兩個結節是MIA和五個是invasive ADC。

(3) Part-solid nodules

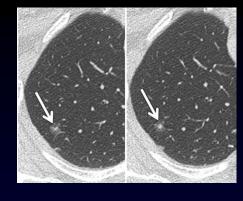




The **solid component** of PSNs is known to represent the invasive foci of adenocarcinomas although other histologic changes, such as alveolar collapse, inflammation, fibrosis, and, occasionally, *mucus*, may also appear as a solid region of PSNs on CT.



Part-solid nodules



- Such a nodule is more likely to be malignant than a solid one.
- Persistent part-solid GGNs with a solid portion size greater than 5 mm usually are considered to be invasive adenocarcinomas and are recommended for biopsy or surgical resection according to the Fleischner society statement.
- In contrast to growth in solid nodules, which is based solely on size, in subsolid nodules, *growth* may manifest as an increase in size, an increase in attenuation, development of a solid component, or an increase in size of a solid component.

Importance of solid component in PSNs

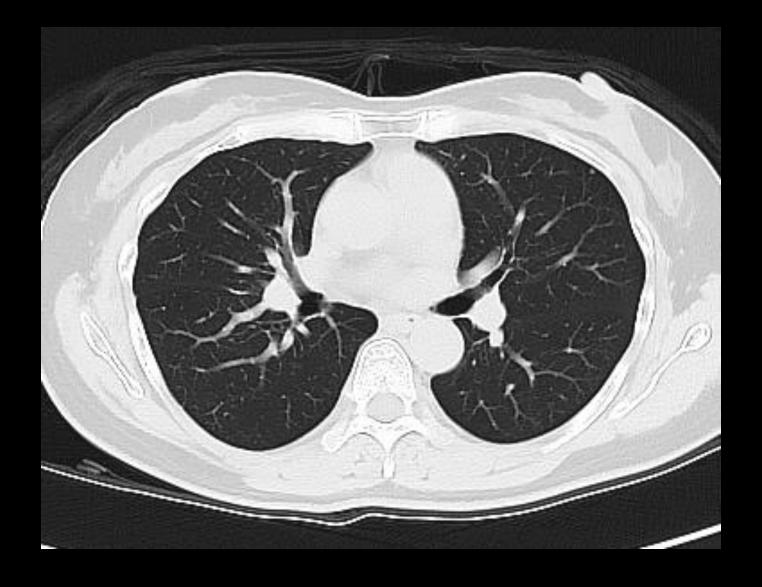
- represent invasive foci of ADCs.
- is related to prognosis: size of solid region is found to be predictive of **nodal involvement**, **high-grade malignancy** (positive lymphatic, vascular, or pleural invasion) and **disease-free survival** in clinical stage IA lung ADCs.
- a T factor measured by the solid component might be a more accurate prognostic parameter.

Persistent part-solid nodules with solid part of 5 mm or smaller: Can the 'follow-up and surgical resection after interval growth' policy have a negative effect on patient prognosis?

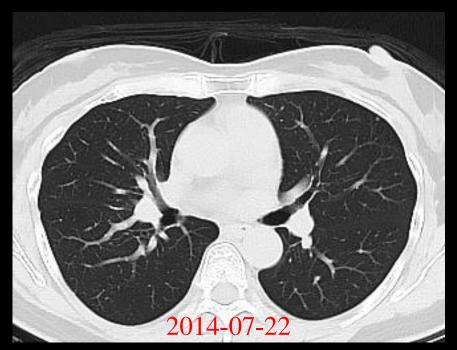
Persistent part-solid nodules with solid part of 5 mm or smaller: Can the 'follow-up and surgical resection after interval growth' policy have a negative effect on patient prognosis?

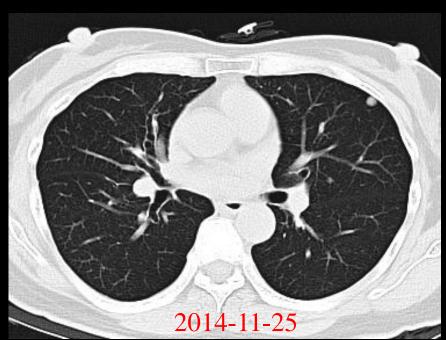
Conclusion: did not negatively influence the prognosis of patients.

追蹤至interval長大再手術,對於prognosis不會產生負面的影響。



A 54-year-old female with history of colon cancer





Multiple Ground-glass/Lepidic Lesions.—Lung cancers manifesting as multiple pulmonary lesions with ground-glass or lepidic features are associated with various demographics, excellent patient outcomes, and infrequent recurrences.



Multifocal adenocarcinoma should be classified by the T category of the lesion with the highest-level T descriptor and by the number of lesions (#)—or simply "(m)" for multiple—indicated in parentheses (Fig).



Fig. Multiple ground-glass/lepidic lesions (**multifocal adenocarcinoma**). MDCT image shows approximately 16 ground-glass nodules bilaterally, the largest of which is in the RUL and measures approximately 2.2 cm in focal diameter. In the setting of multiple ground-glass lesions or lepidic tumors, the IASLC recommends *use of the dominant lesion for T staging purposes*. In this case, 2.2 cm corresponds to a T1c lesion, and the overall descriptor can be listed as either T1c(16) or T1c(m).

