Longkanker screening door het oog van de radioloog

A radiologist's perspective

Annemie Snoeckx





TOGA najaarssymposium 19 oktober 2012

I. Introduction



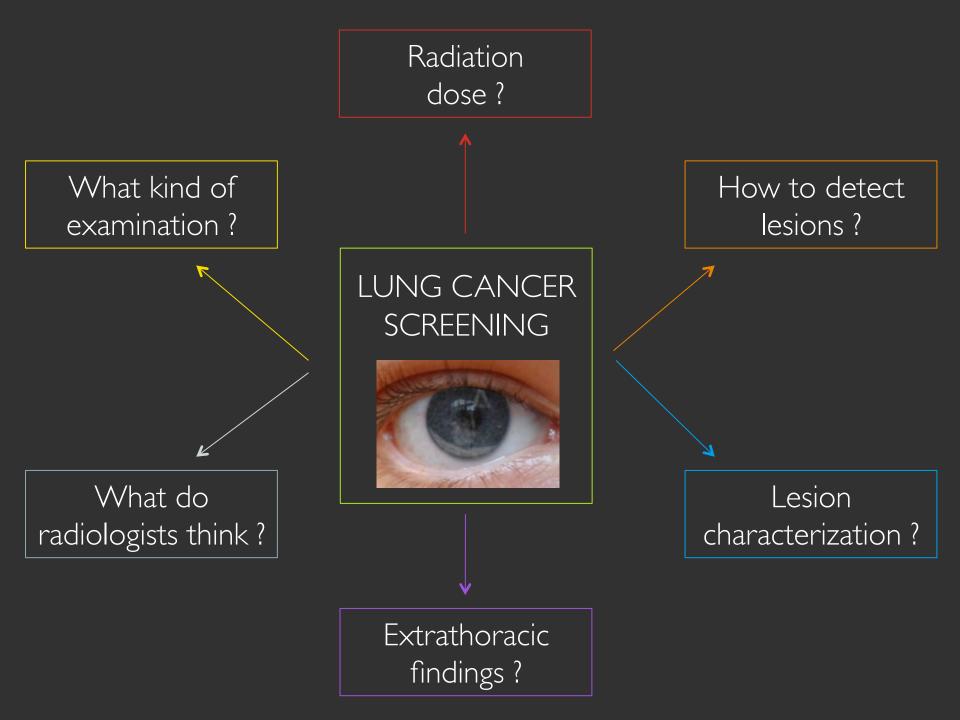
Lung cancer screening: A radiologist's perspective

I am ...

a radiologist @ UZAthoraco-abdominal imaging

l am not ...

involved in lung screening trialsan engineer/specialist in radiation protection



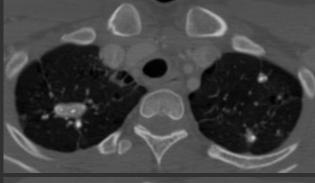
2. What kind of examination ?

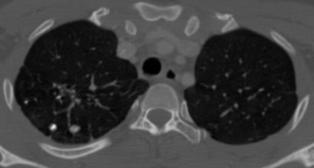




- The most commonly used technique in clinical practice
 - **7** To rule out chest disease
 - To study the effects of treatment
 - To monitor patients with chest abnormalities
- ➤ Short examination time low cost easy access
- Low sensitivity and specificity
- ◄ High interreader variability



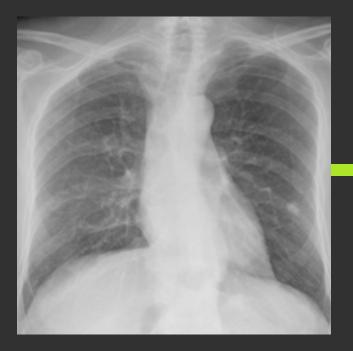


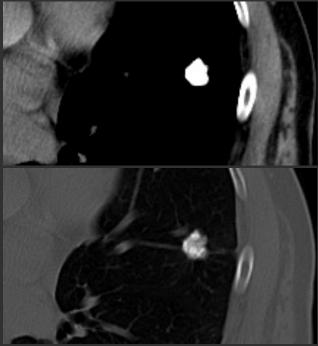


Radiography

- ↗ Often reveals nodules
- 77% of nodules smaller 7 mm visualized on a chest radiograph → calcified
- Higher probability of representing calcified granulomas
- Detection is limited by overlapping structures and low contrast of the nodule

Ketai et al. Chest 2000





Radiography

- 77% of nodules smaller 7 mm visualized on a chest radiograph → calcified
- Higher probability of representing calcified granulomas
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Ketai et al. Chest 2000

Radiograph

or

CT





Screening with chest radiography

- Purpose: to estimate the performance of digital chest radiography for detection of lung cancer
- Patients recruited from two screening sites, participating in the NELSON trial
- Conclusion:
 - High rates of lung cancer detection can be achieved at a stage when lesions are seen at CT screening
 - BUT only at the expense of a low specificity that results in an excessive number of work-up CT examinations

Screening with chest radiography

De Hoop et al. Radiology 2010

Quekel et al. Eur J Radiol 200 l

Potchen et al. Radiology 2000

Gavelli et al. Cancer 2000

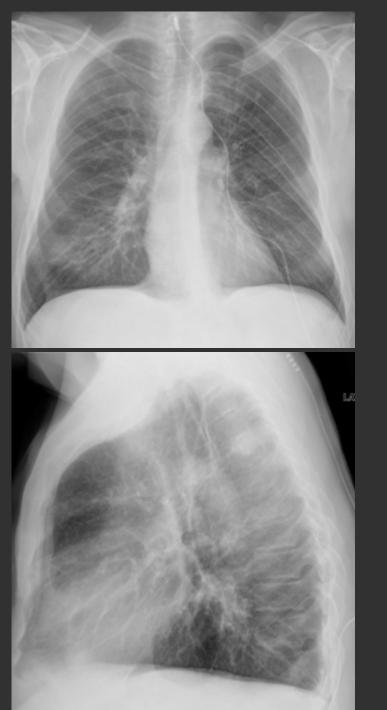
Toyoda et al. Br J Cancer 2008

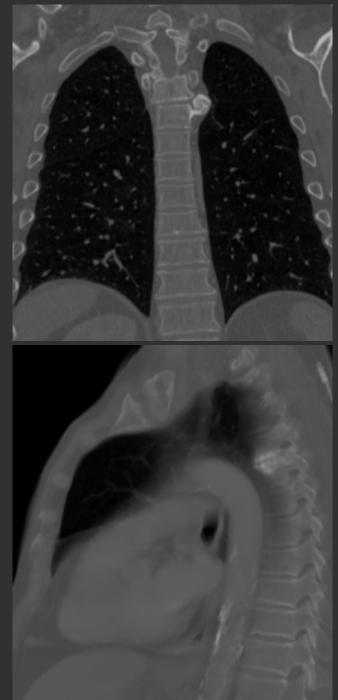
Monnier-Cholley et al. Radiology 2004

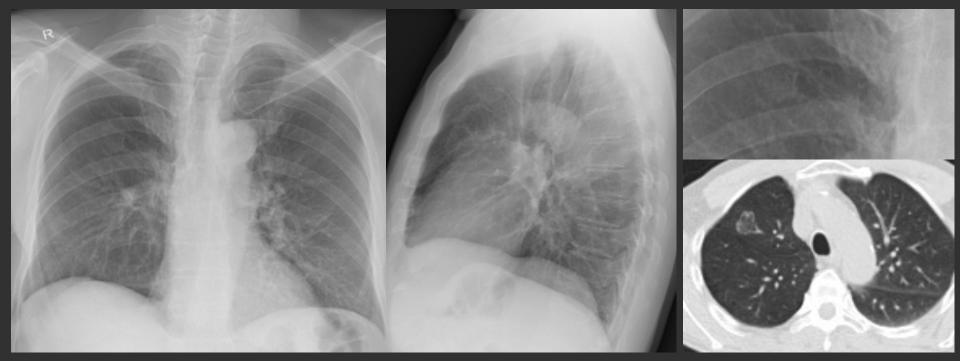
- ✓ Sensitivity of conventional digital chest radiography → range from 36% to 84%
- Depending on the study population
- Smokers → more COPD → more difficult interpretation of chest radiographs
- Low specificity that results in an excessive numer of work-up CT examinations



VEK 6-10-37





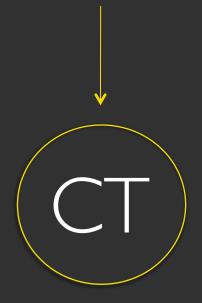


Mucinous adenocarcinoma broncho-alveolar growth p<u>attern</u>

DCR = 31 - 12 - 54



What kind of examination ?



Lung cancer screening with CT

CT affords several advantages over chest radiography

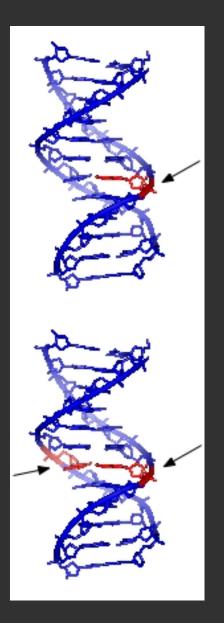


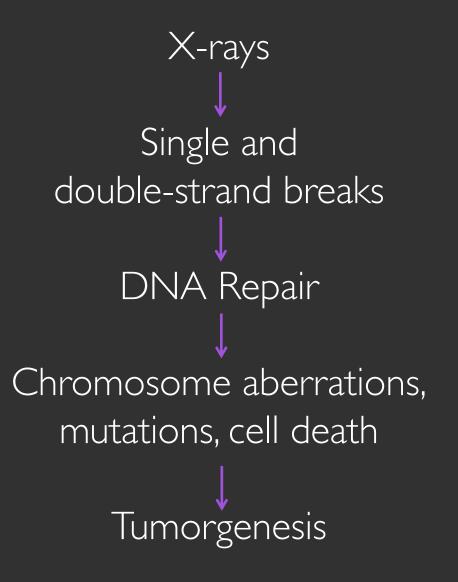
- Cross-sectional data acquisition and display → reduces the problem of overlying structures
- Contrast in the lung parenchyma is greater with CT \rightarrow visualization of more subtle abnormalities



- Screening population = healthy population \rightarrow minimize radiation exposure for screening

3. Radiation dose







De Standaard

NIEUWS INFOTHEEK E-KRANT ARCHIEF+ DIENSTEN IPAD/IPHONE

voor abonnees Infotheek



Medische beelden zijn geen familiekiekjes

woensdag 01 augustus 2012, 05u00 Bron: www.gezondheid.be gezondheid.bewww.zuinigmetstraling.be ;www.health.belgium.be/richtlijnen-medische-beeldvorming

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'Medische beeldvorming' is een verzamelnaam voor verschillende technieken om het lichaam in beeld te brengen. Medische beeldvorming heeft een enorme vooruitgang mogelijk gemaakt in de moderne geneeskunde. Röntgenfoto's, MRI of CT-scans zijn onmisbaar om diagnoses te

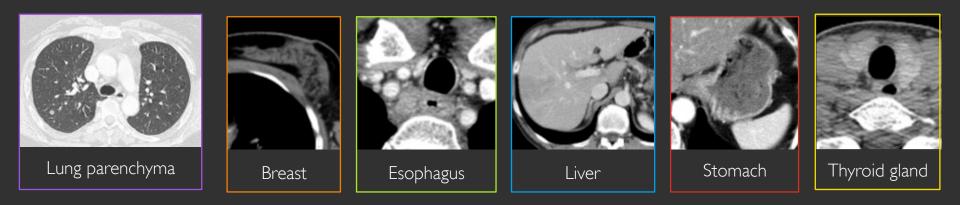


"Radiation can be used for great benefit to humanity and with minimal risk, a risk comparable to or lower than those commonly accepted as ordinary part of daily life such as driving to work"

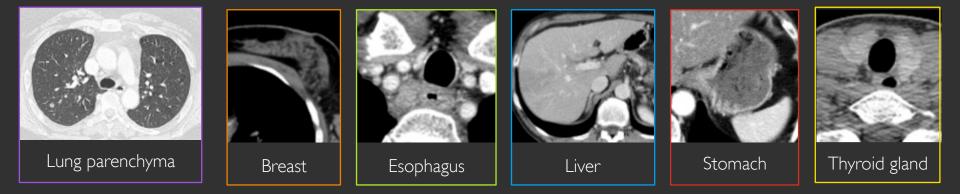
> National Institutes of Health April 2000

Is radiation dose an issue in lung cancer screening ?

Chest CT

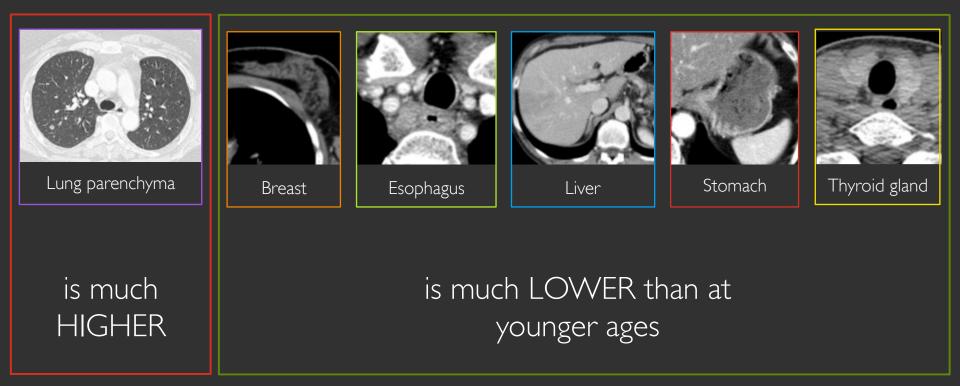


Chest CT Radiation-associated cancer risk at age 55



is much HIGHER is much LOWER than at younger ages

Chest CT Radiation-associated cancer risk at age 55



Is radiation dose an issue in lung cancer screening ?

Yes it is

Radiation-associated lung cancer risk

Radiology

Radiology is a monthly journal devoted to clinical radiology and allied sciences, owned and published by the Radiological Society of North America, Inc.

HOME CURRENT ARCHIVE COLLECTIONS 中国 (ABSTRACTS) RADIOLOGY SELECT RADIOGRAPHICS RSNA.org



David J. Brenner, PhD, DSc

Index terms: Cancer screening, 60.1211, 60.32 Computed tomography (CT), radiation exposure Lung, effects of irradiation on, 60.47 Special Reports

Published online 10.1148/radiol.2312030880 Radiology 2004; 231:440-445

Abbreviation: CI - credibility interval

¹ From the Center for Radiological Besearch, Columbia University, 630 W 168th St, New York, NY 10032, Beceived June 4, 2003; revision requested August 14; revision received September 16; accepted October 22. Supported by U.S. Department of Energy Low-Dose Radiation Research Program grants DE-I-C-0-10186326 and DL-I-G-02-981862686, and by National institutes of Health grant R8-11623. Address correspondence to the author (e-mail: dg)3@culumbia.edu). ⁶ 85NA, 2004

Radiation Risks Potentially Associated with Low-Dose CT Screening of Adult Smokers for Lung Cancer¹

PURPOSE: To estimate the radiation-related lung cancer risks associated with annual low-dose computed tomographic (CT) lung screening in adult smokers and former smokers, and to establish a baseline risk that the potential benefits of such screening should exceed.

MATERIALS AND METHODS: The estimated lung radiation dose from low-dose CT lung examinations corresponds to a dose range for which there is direct evidence of increased cancer risk in atomic bomb survivors. Estimated dose, sex, and smoking status-dependent excess relative risks of lung cancer were derived from cancer incidence data for atomic bomb survivors and used to calculate the excess lung cancer risks associated with a single CT lung examination at a given age in a U.S. population. From these, the overall radiation risks associated with annual CT lung screening were estimated.

RESULTS: A 50-year-old female smoker who undergoes annual CT lung screening until age 75 would incur an estimated radiation-related lung cancer risk of 0.85%, in addition to her otherwise expected lung cancer risk of approximately 17%. The radiation-associated cancer risk to other organs would be far lower. If 50% of all current and former smokers in the U.S. population aged 50–75 years received annual CT screening, the estimated number of lung cancers associated with radiation from screening would be approximately 36,000, a 1.8% (95% credibility interval: 0.5%, 5.5%) increase over the otherwise expected number.

CONCLUSION: Given the estimated upper limit of a 5.5% increase in lung cancer risk attributable to annual CT-related radiation exposure, a mortality benefit of considerably more than 5% may be necessary to outweigh the potential radiation risks.

* RSNA, 2004

Radiation-associated lung cancer risk

- Risk is highest in those aged 55 years at exposure
- 2. Evidence that radiation damage and smoking damage interact synergistically

 - ◄ Interaction is near multiplicative
 - Estimated risks are higher for current smokers than for former smokers
 - Higher for heavy ever-smokers compared with light ever-smokers

David Brenner, Radiology 2004

Radiation-associated lung cancer risk

- Radiation risks = difficult calculations \rightarrow data based on Japanese atomic bomb survivors
- Yearly screening, from age 50 (to 75) in a female smoker
 - \rightarrow 5% increase in risk
- → Yearly screening, from age 50, in a male smoker
 - \rightarrow 1,5% increase in risk

A mortality benefit of considerably more than 5% may be necessary to outweigh the potential radiation risks

David Brenner, Radiology 2004 Is radiation dose an issue in lung cancer screening ?

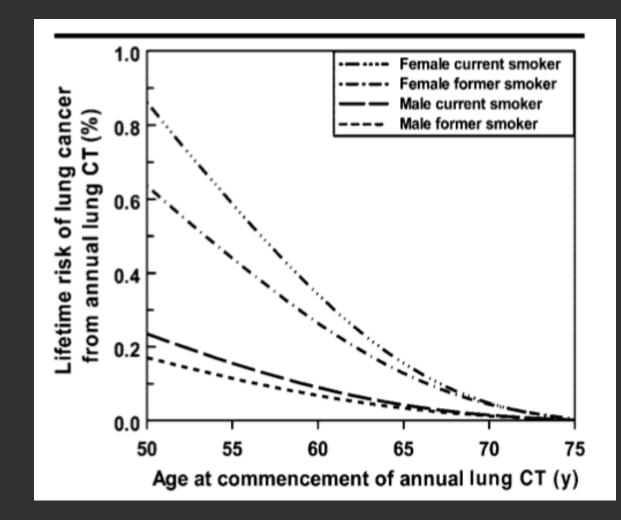
Yes It Is !

Can we reduce this risk ?

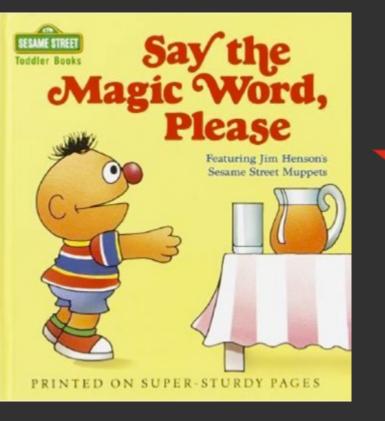
Yes We Can !



"It is clear that radiation-related risks decrease rapidly with increasing age at commencement of screening"







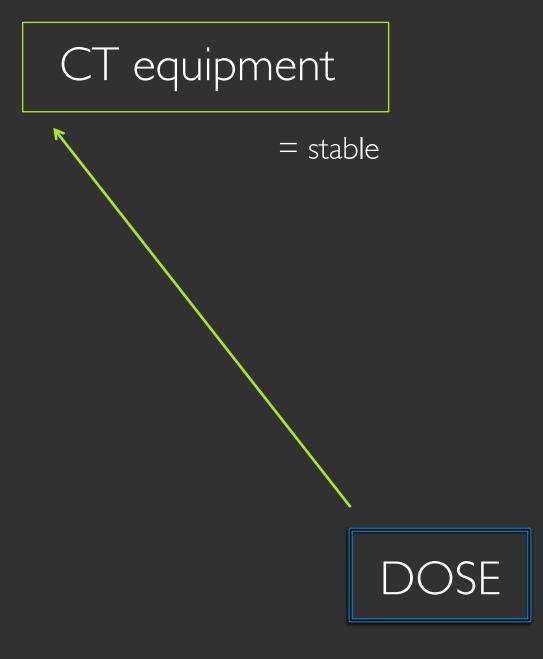
LOW DOSE

Definition of "low-dose CT"

"Lower than standard dose"

Definition of "standard dose"

No definition No standardization



Scan protocol

= highly variable

Vendor specific

Equipment specific

Protocol naming

Patient adjusted

. . .

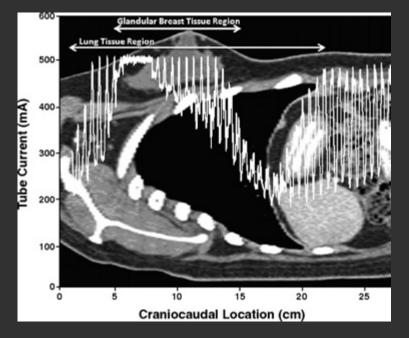
What are we doing ? What can we do ?

Tube current modulation

Adaptive dose technology that automatically adjusts tube output (mA) to compensate for changes in patient thickness



McCollough C, Bruesewitz MR et al. Radiographics 2006



Angel E et al. AJR 2009;193:1340-1345

What are we doing ? What can we do ?

Iterative reconstruction

- **7** CT images are reconstructed from raw data
- **Reconstruction technique to lower image noise**
- 7 Lower dose \rightarrow same image quality
- **↗** Protocol adjustment
- Education of technicians, nurses, ...
- Pressure on vendors
- Awareness: "Image Wisely", "Dose watch", ...

How low can we go ?

\rightarrow all protocols

- Image quality standardization is difficult
- Radiologists want "nice looking images"
- Diagnostic performance *
 - \rightarrow no difference up to 50% dose reduction
 - \rightarrow at 30% \rightarrow level of expertise becomes important



Estimated radiation dose NLST and ITALUNG trial

Larke F, Kruger R et al. AJR 2011

NLST

- Study to determine the distribution of effective dose associated with single low-dose CT chest of average-size participants
- Average dose |,4 − |,6 mSv
 - $\leftarrow \rightarrow$ average dose standard

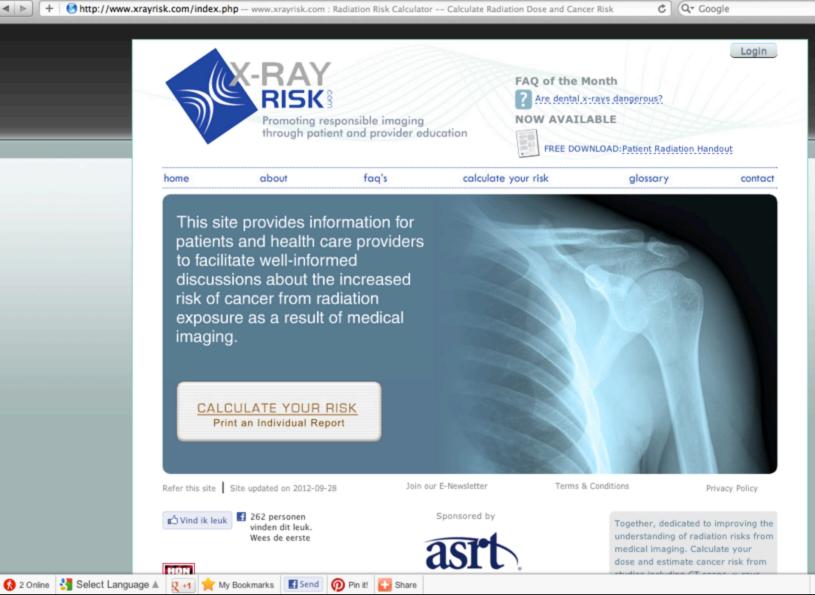
chest CT 7,0 mSv

Mascalchi M, Mazzoni LN et al. Br J Radiol 2012

◄ Four LDCT's + related further investigations (FDG PET and CT-guided biopsy)

ITALUNG

Mean effective dose to a single subject ranged between 6,2 and 6,8 mSv



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+ Shttp://www.xrayri	sk.com/calcula	ator/calculator.php ww	vw.xrayrisk.com :		Reader C Q+ G	oogle		
	D	RISK Promoting re through pati	sponsible imaging ent and provider e	ducation	x-rays dangerous?	Login		
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+ Ohttp://www.xrayrisk.com/calculator/calcul	lculator-normal-studies.php — w	www.xrayrisk.com :	Reader C Q+ Goo	ogle	0
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Plain Films (x-ra					
Chest x-ray (2 vi Abdomen x-rays Pelvis x-rays Hip x-rays (unila Neck x-rays Upper Back x-ray Lower Back x-ray Extremity x-rays Mammogram (un Dental x-ray (pai Dental x-ray (4 i Skull x-rays DEXA Scan (Bore	iteral) ys ; (Arm, Leg, etc) hilateral) noramic) ntraoral bitewings)	Study: Gender: Age at Time of Study: Number of Exams: Average Dose: DLP (Optional for CT):	Chest CT (Standard) Male Female 34 (years) 1 7.000 (mSv) Optiona (mGy · cm) Calculate		
CT Scans Fluoroscopy		Total Effective Dose: Additional Cancer Risk: Baseline Cancer Risk: Baseline + Additional Risk:	7 (mSv) 0.082 (%) 37.5 (%) 37.582 (%)		
Nuclear Medicin Interventional F MRI and Ultraso Please see Glossa different studies.	Procedures	Add This To learn more about how these o	Exam to your Report	About page.	
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Your X-ray Risk Report # of Dose Additional Cancer Gender Age Study exams (mSv) Risk(%) Chest CT (Standard) 7 Male 34 0.055% 1 × Totals: 1 7 0.055% Said another way, the chance of NOT getting cancer as a result of the above studies is 99.945%. Preview Report Save Report **Comparison Doses** 3.1 mSv/year¹⁰ 2.2 mSv/year¹¹ Natural Background **Domestic Pilots** 0.02 mSv¹² 6.2 mSv/year¹⁰ Average US Exposure **7 Hour Airline Flight** Chest x-ray (2 views) 0.10 mSv Chest CT 7.0 mSv

Estimated Lifetime Risk of Death from Various Sources¹³

Motor Vehicle Accident	1% or 1 in 100 chances
Drowning	0.1% or 1 in 1000 chances
Bicycle Accident	0.01% or 1 in 10,000 chances
Lightning	0.001% or 1 in 100,000 chances

Keep in mind, the overall lifetime risk of developing an invasive cancer is 37.5% (1 in 3) for women and 44.9% (1 in 2) for men regardless of imaging history. These statistics are averages and do not predict what is going to happen to you. They do not take into consideration individual risk factors including lifestyle (smoking, diet, exercise, etc), family history (genetics) or radiation exposure. The majority of cancers occur later in life and the average lifetime risk of dying from cancer is 25% (1 in 4).

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4. Lesion detection

Pulmonary nodules

Common incidental finding on CT

"What is so hard about finding a pulmonary nodule ? "

"It is not finding the nodule, but how you deal with the result."



Is low-dose as good as standard dose for detection of nodules ?

Detection: low-dose versus conventional CT

Rusinek H et al. Radiology 1998

Karabulut N et al. Eur Radiol 2002

Leader JK, Warfel TE et al. AJR 2005

Gierada DS, Pilgram TK et al. Radiology 2008

- ➤ High contrast between air and pulmonary parenchyma
 → lung is well-suited for investigation with lowdose
- Sensitivities between low-dose and conventional images was not statistically significant
 - **刀** For detection
 - More likely to miss small nodules
 - **◄** For characterization
 - オ Reader variability

 \rightarrow More studies needed !

Reader variability @ diagnosis

- Purpose of the study: to assess relative intraand interobserver agreement in detecting pulmonary nodules when interpreting low-dose chest CT screening examinations
- Inconsistent measurements of nodule size
- Agreement is relatively low

Leader JK, Warfel TE et al. AJR 2005

Gierada DS, Pilgram TK et al. Radiology 2008 Reader variability: What's the cause and what can we do to become better ?

Nodule detection

Peloschek P, Sailer J et al. Radiology 2007 Detection is mainly limited by visual perception problems and errors



- I. Increasing number of transverse images
- 2. Anatomic noise (from normal structures in the lung parenchyma: vascular structures, airways, interstitium)
- 3. Human errors: interpretation mistakes, lack of concentration, disturbances, ...

What can we do ?



Cine review

Distinguishing nodules from vessels

- 3D data volume reconstruction
 - MIP reconstructions
 - MIP enhances nodule detection by more than twofold compared with the use of conventional transverse images

Coakley F, Cohen M Peloschek P, Sailer J et al. et al. Br J Radiol 1998 Radiology 2007

Is computer-aided detection (CAD) of any use ?

- Materials and methods: mainly 'standard' examinations – some low-dose
- General conclusion: "use of CAD system improved detection of pulmonary nodules"
- CAD algorithms can assist radiologists, but cannot replace them
- **7** CAD as second reader ?
- Concerns
 - False-positives (COPD in screening population)
 - Not widely available
 - Time consuming

Rubin G, Lyo J et al. Radiology 2005

Awai K, Murao K et al. Radiology 2004

Beigelman C, Raffy P et al. AJR 2007

Girvin F, Ko J AJR 2008

Imaging in trials

NLST-trial

Rubin G, Lyo J et al. Radiology 2005

Awai K, Murao K et al. Radiology 2004

Beigelman C, Raffy P et al. AJR 2007

Girvin F, Ko J AJR 2008

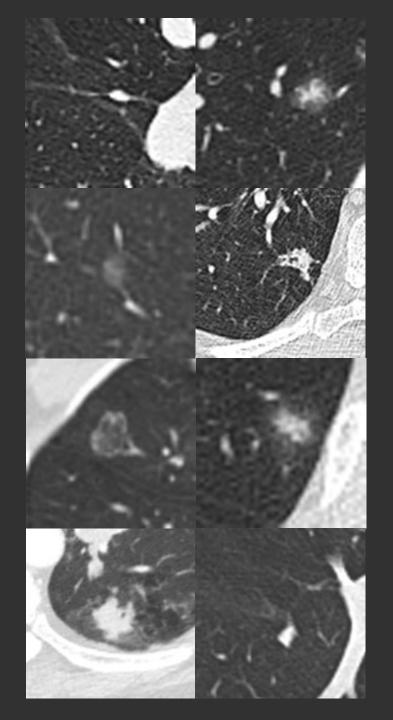
- Interpretations were made by using softcopy display at lung and soft-tissue windows
- ➤ Without computer-assisted diagnosis

5. Lesion characterization

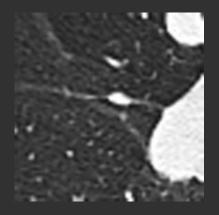


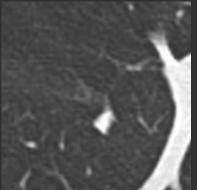
"'All nodules are not equal"

The difficult part is to find the malignant one...



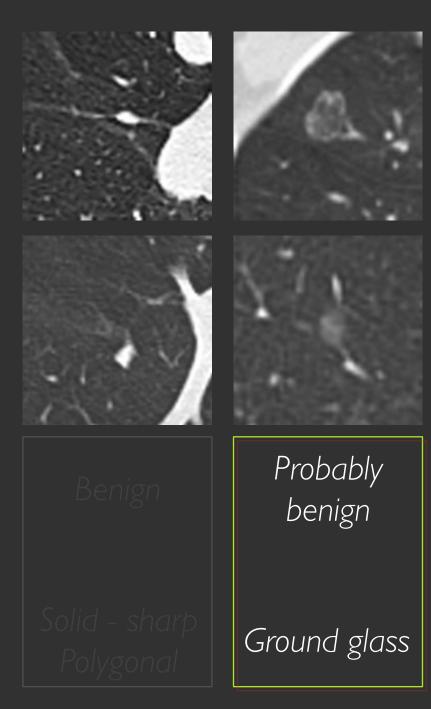
Benign Probably benign Probably malignant Malignant

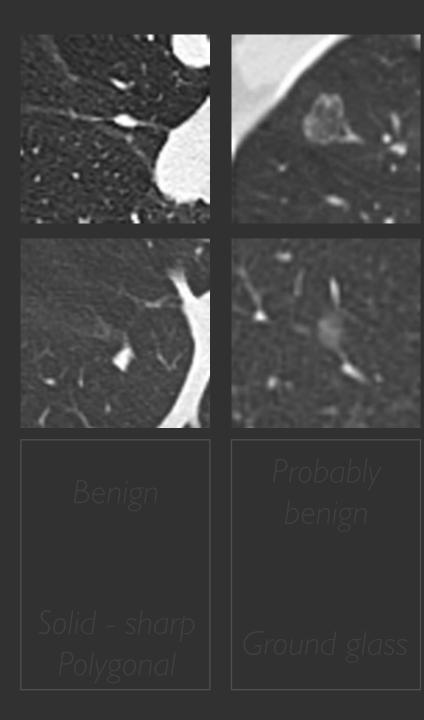




Benign

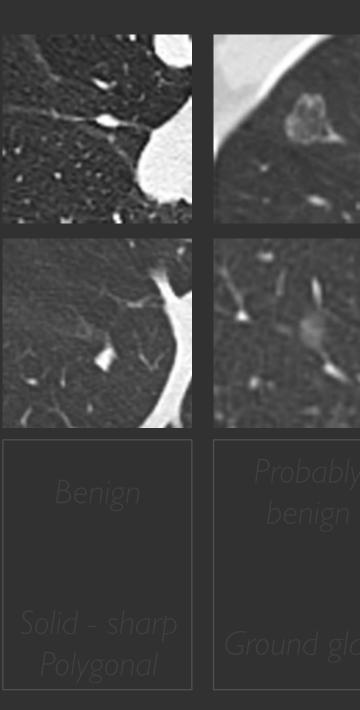
Solid - sharp Polygonal

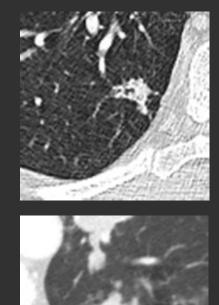






Spiculated

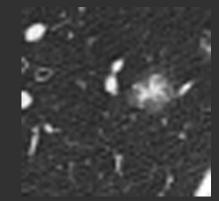






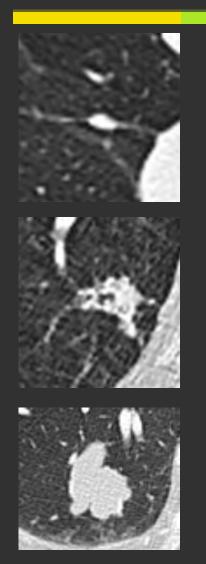






Malignant

Part solid

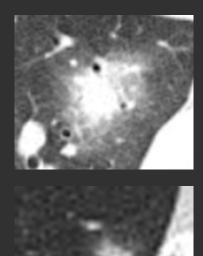


I. Margin

- Irregular or spiculated margins are highly suggestive
- Lobulation smooth borders pleural tail: both malignant and benign nodules

2. Halo sign

- Pathology: perinodular hemorrhage tumor infiltration – inflammation
- More common in infection, but does not exclude malignancy



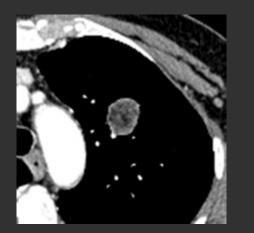
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- Pathology: perinodular hemorrhage tumor infiltration inflammation
- More common in infection, but does not exclude malignancy

3. Density and internal characteristics



Macroscopic fat: benign lesions

- Cavitation: necrotic tumors infectious and inflammatory lesions
- Calcification
 - Can be seen in 10% of patients with lung cancer
 - Benign patterns: laminated central diffuse – popcorn calcifications
 - Malignant patterns: stippled or eccentric

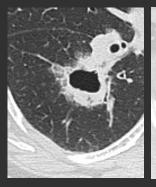
Girvin F, Ko JP AJR 2008 Grewal RG, Austin JH, JCAT 1994

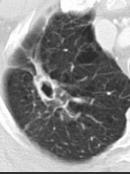
3. Density and internal characteristics



Aspergillus

Wegenei





Macroscopic fat: benign lesions

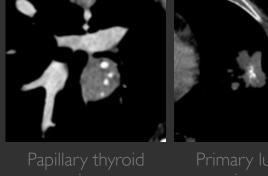
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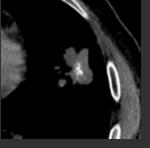
Girvin F, Ko JP AJR 2008 Grewal RG, Austin JH. JCAT 1994

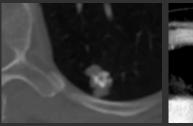
NSCLC

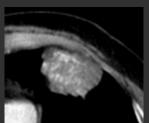
Candic

3. Density and internal characteristics



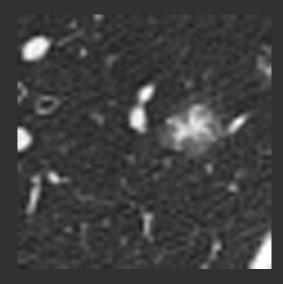






- Calcification
 - Can be seen in 10% of patients with lung cancer
 - Benign patterns: laminated central diffuse – popcorn calcifications
 - Malignant patterns: stippled or eccentric

3. Density and internal characteristics



- Subsolid nodules
 - Solid nodules with component of ground glass
 - Higher incidence of malignancy compared to ground glass nodules
 - Bronchoalveolar growth pattern

Girvin F, Ko J AJR 2008 Grewal RG, Austin JH. JCAT 1994

4. Nodule size and measurement

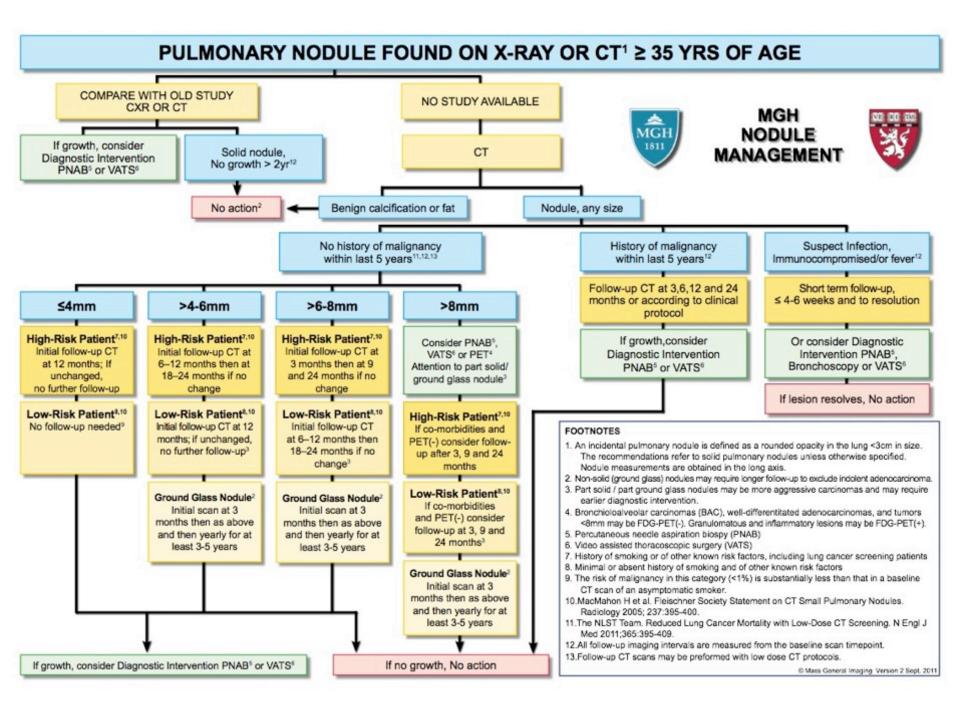
- Risk of malignancy is strongly correlated with size
- Up to 42% of nodules smaller tham 5 mm can be malignant
- "Guidelines for management of small pulmonary nodules detected on CT scans: A statement from the Fleischner Society"

	-
No follow-up needed ⁶	Follow-up CT at 12 mo; if unchanged, no further follow-up!
Follow-up CT at 12 mo; if unchanged, no further follow-up ¹	Initial follow-up CT at 6–12 mo ther at 18–24 mo if no changel
Initial follow-up CT at 6–12 mo then at 18–24 mo if no change	Initial follow-up CT at 3-6 mo then at 9-12 and 24 mo if no change
Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy	Same as for low-risk patient
etected indeterminate nodule in persons ngth and width. beent history of smoking and of other ke	
oking or of other known risk factors.	
ilignancy in this category (<1%) is substa atic smoker.	intially less than that in a baseline CT sca
	Follow-up CT at 12 mo; if unchanged, no further follow-up ¹ Initial follow-up CT at 6–12 mo then at 18–24 mo if no change Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy ttected indeterminate nodule in persons ngth and width. osent history of smoking and of other kn oking or of other known risk factors.

*Ginsberg et al. Radiology 1999

Grewal RG, Austin JH. JCAT 1994

Girvin F, Ko JF AJR 2008



4. Nodule size and measurement

- Studies: interobserver agreement was moderate to substantial
- Similar for positive and negative interpretations
- Disagreement \rightarrow variation in measurement
 - Interobserver variability: baseline examinations and follow-up examinations

Erasmus et al. J Clin Oncol 2003

Bogot NR et al. Acad Radiol 200!

Gierada DS et al. Radiology 2008

Singh S, Pinsky P et al Radiology 2011

Interpretation of low-dose CT

Gierada DS et al. Radiology January 2008

- Radiologists involved in NLST
- Interpretation of low-dose CT as baseline NLST scan
 - Longest transverse dimension of non-calcified nodules larger than 4 mm
 - And recommendation for follow-up of positive cases
- Conclusion
 - Interobserver agreement was moderate to substantial
 - Similar for positive and negative interpretations
 - **7** Disagreement \rightarrow variation in measurement

Erasmus et al. J Clin Oncol 2003

Bogot NR et al. Acad Radiol 2005 How good are radiologists in detecting and characterizing pulmonary nodules ?

...There is room for improvement...

Nodule growth = 3D process Future: use of 3D measurement methods → computer aided detection → volumetric determination of lesion size

Volumetric measurement



- 3D techniques are susceptible to precision error
- ◄ Important factors:
 - ↗ Nodule size
 - **7** Small lesions \rightarrow higher error
 - **オ** Shape
 - ➔ Spiculated lesions = difficult
 - オ Attenuation
 - **オ** Segmentation problems

Volumetric measurement



- Lung nodule volumes in patients scanned three times in the same session
- Interscan volumetric variation of 20%

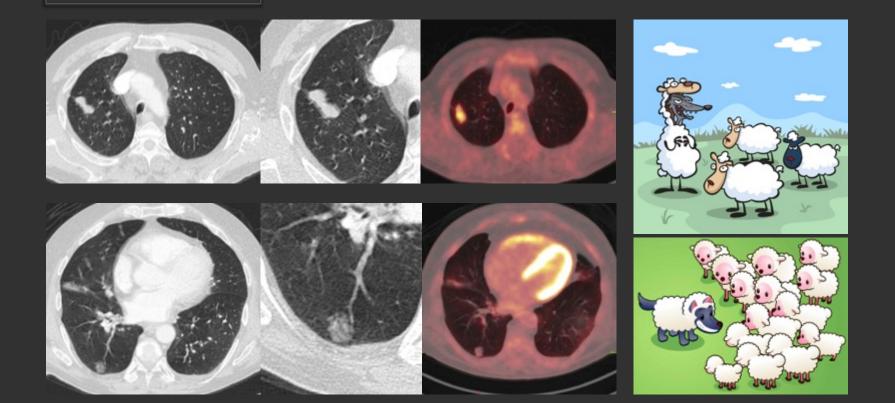
■ Boll et al.AJR 2004

- Cardiac gating
- Small nodules near the heart: 34% volume change during cardiac cycle
- De Hoop et al. Radiology 2010
 - Mass measurements can enable detection of growth of ground glass nodules
 - And are subject to less variability than are volume or diameter measurements

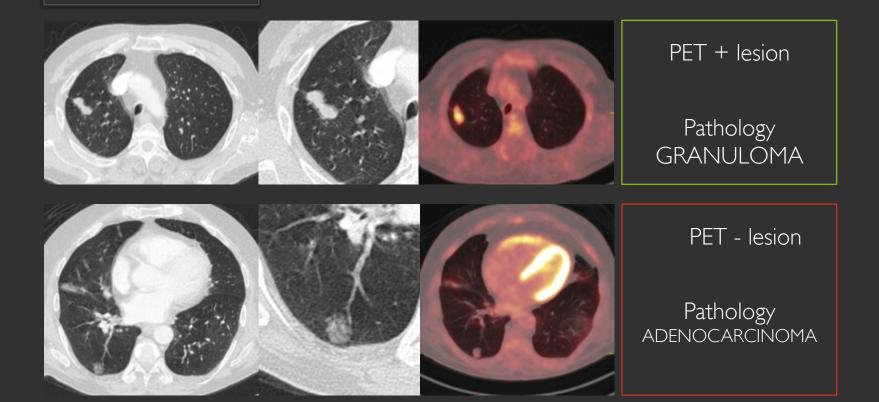


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73-y-old man Dyspnea No previous history

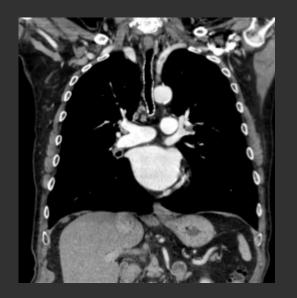


73-y-old man Dyspnea No previous history



6. Extrathoracic findings

Extrathoracic findings



- Detection of incidental findings outside the lung
- ∧ NLST 7,5% → clinically significant abnormality
- Danish Lung Cancer Screening trial
 - In 6,8 % of patients
 - 7,7% of these findings were malignant
- ➤ Health benefits ← → additional diagnostic examinations / procedures with no health benefit
- Difficult interpretation on low-dose CT

Saghir Z et al. Am J Respir Crit Care 2012

7. What do radiologists think about lung cancer screening ?

National survey of radiologistq

"The use of CT for Screening: A National Survey of Radiologists' Activities and Attitudes" – Radiology 2008

- **7** 398 US Radiologists 1/3 reading screening examinations
- Responding to physician and patient requests are more important motivations for reading CT screening studies than the belief that patients benefit from screening
- Most radiologists are in favor of lung cancer screening, while few support wholebody CT imaging
- Radiologists are significantly more likely to believe CT screening studies are appropriate if they read them than if they do not

Some final thoughts...

A lot of work is done

. . .

A lot of work still needs to be done

The interpretation of pulmonary findings is a complex task

with room for improvement in both lesion detection and characterization.

. . .

Radiation dose and dose reduction – as low as reasonably achievable – is important

and should concern every radiologist.

Management of the pulmonary nodule requires a multidisciplinary approach.



P. Tatchell

Thank you for your attention