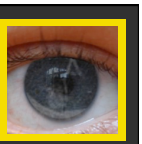
Longkanker screening door het oog van de radioloog

A radiologist's perspective

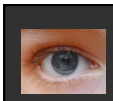


Annemie Snoeckx

UZA
Antwerp University Hospital

TOGA najaarssymposium
19 oktober 2012

I. Introduction



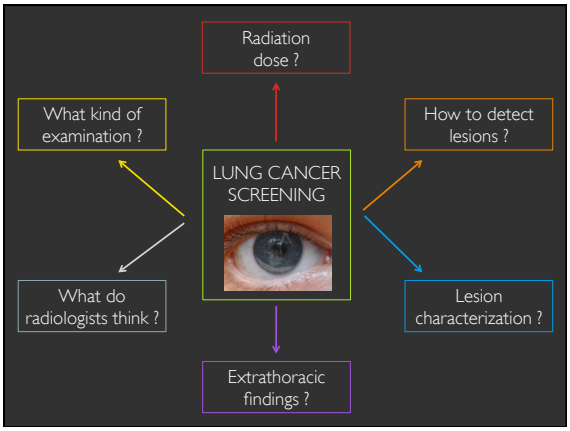
Lung cancer screening: A radiologist's perspective

I am ...

- a radiologist @ UZA
- thoraco-abdominal imaging

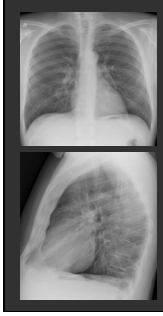
I am not ...

- involved in lung screening trials
- an engineer/specialist in radiation protection

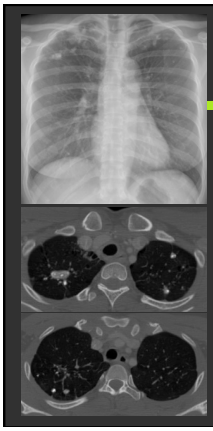


2. What kind of examination ?

Radiography



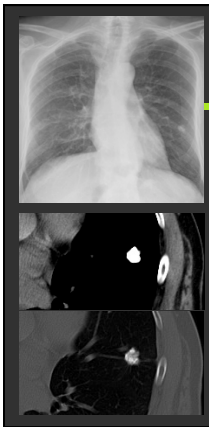
- The most commonly used technique in clinical practice
  - To rule out chest disease
  - To study the effects of treatment
  - To monitor patients with chest abnormalities
- Short examination time – low cost – easy access
- Low sensitivity and specificity
- High interreader variability



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

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- Detection is limited by overlapping structures and low contrast of the nodule

Ketai et al. Chest 2000

SCREENING

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

De Hoop et al. Radiology 2010

Screening with chest radiography

De Hoop et al. Radiology 2010

Quekel et al. Eur J Radiol 2001

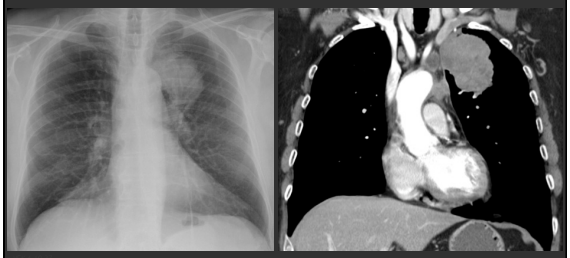
Patchen et al. Radiology 2000

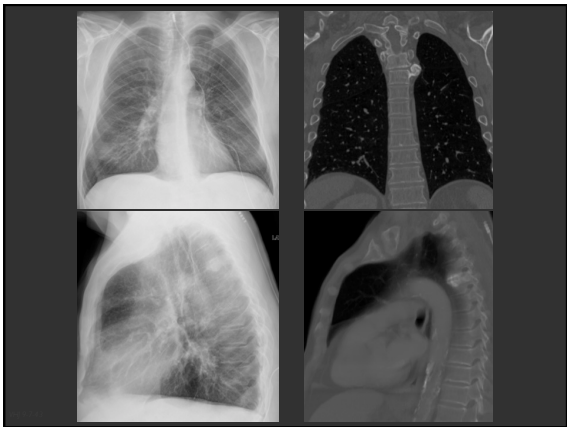
Gavelli et al. Cancer 2000

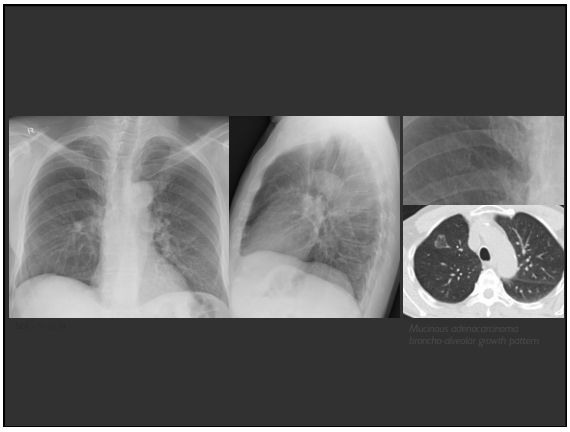
Toyoda et al. Br J Cancer 2008

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







What kind of examination ?

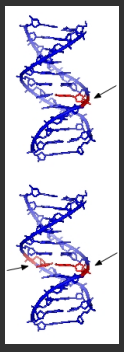
CT

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 → visualization of more subtle abnormalities

- Higher cost
- Screening population = healthy population → minimize radiation exposure for screening

3. Radiation dose



X-rays

↓

Single and
double-strand breaks

↓

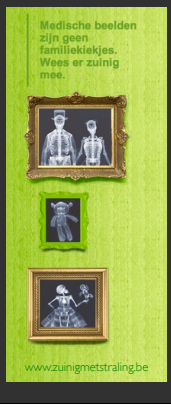
DNA Repair

↓

Chromosome aberrations,
mutations, cell death

↓

Tumorgenesis

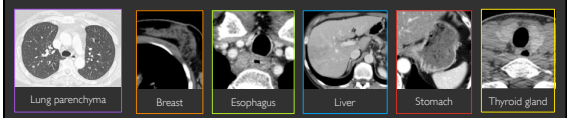


"Radiation can be used for great benefit to humanity and with minimal risk, a risk comparable to or lower than those commonly accepted as ordinary part of daily life such as driving to work"

National Institutes of Health
April 2000

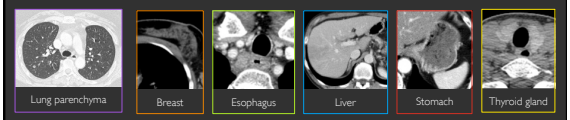
Is radiation dose an issue in lung cancer screening ?

Chest CT



Chest CT

Radiation-associated cancer risk at age 55

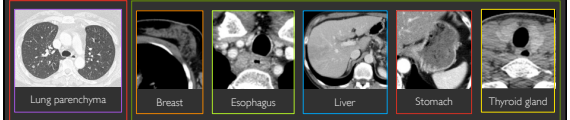


is much HIGHER

is much LOWER than at younger ages

Chest CT

Radiation-associated cancer risk at age 55



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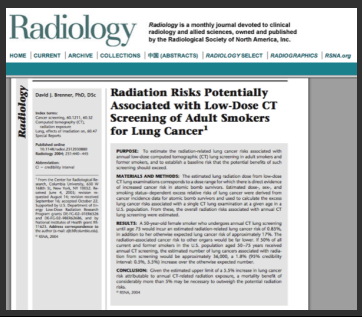
Is radiation dose an issue in lung cancer screening ?

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.

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David J. Brenner, PhD, DSc

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

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 age-dependent risk models developed from the atomic bomb survivor lung 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 current or former smoker who undergoes annual CT lung screening from age 55 would incur an estimated radiation-related lung cancer risk of 0.81%, in addition to her otherwise expected lung cancer risk of approximately 7.7%. 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 lung screening, the number of lung cancer deaths associated with radiation from screening would be approximately 14,500, ± 1.8% (95% credibility interval: 0.3%, 3.3%) increase over the otherwise expected number.

CONCLUSION: Given the estimated upper limit of a 5.3% 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.

Radiation-associated lung cancer risk

1. Risk is highest in those aged 55 years at exposure
2. Evidence that radiation damage and smoking damage interact synergistically
   - Hard to quantify
   - 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 → data based on Japanese atomic bomb survivors
- Yearly screening, from age 50 (to 75) in a female smoker
  - → 5% increase in risk
- Yearly screening, from age 50, in a male smoker
  - → 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 ?

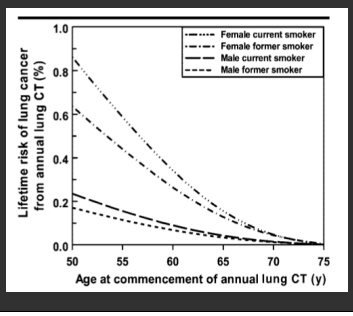
Yes It Is !

Can we reduce this risk ?

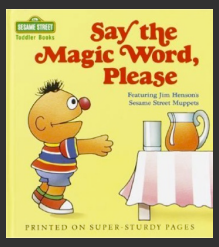
Yes We Can !

Age

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



Dose



LOW DOSE

Definition of "low-dose CT"

"Lower than standard dose"

Definition of "standard dose"

! No definition
No standardization

CT equipment

= stable

Scan protocol

= highly variable

Vendor specific

Equipment specific

Protocol naming

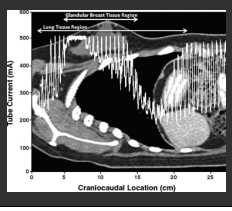
Patient adjusted

…

DOSE

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



Tamm EP, Rong XJ et al. Radiographics 2011

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
  - CT images are reconstructed from raw data
  - Reconstruction technique to lower image noise
  - Lower dose → same image quality
- Protocol adjustment
- Education of technicians, nurses, …
- Pressure on vendors
- Patient dose registration: required in future
- Awareness: "Image Wisely", "Dose watch", …

How low can we go ?

- ALARA - "As low as reasonably achievable"
  → all protocols
- Image quality standardization is difficult
- Radiologists want "nice looking images"
- Diagnostic performance *
  → no difference up to 50% dose reduction
  → at 30% → level of expertise becomes important

* D. Zhang UCLA, 2010

Estimated radiation dose NLST and ITALUNG trial

Larke F, Kruger R et al. AJR 2011

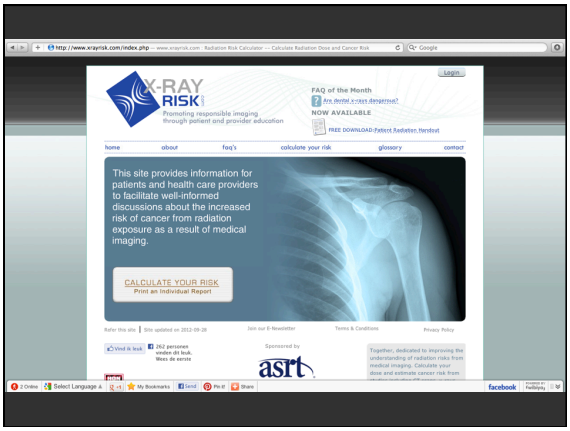
NLST

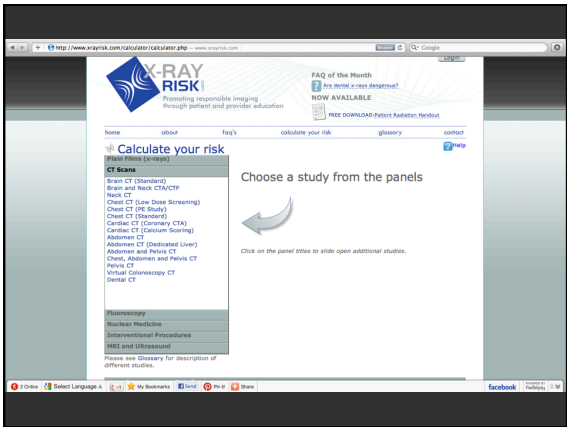
- Study to determine the distribution of effective dose associated with single low-dose CT chest of average-size participants
- Average dose 1,4 – 1,6 mSv
  ←→ average dose standard
  chest CT 7,0 mSv

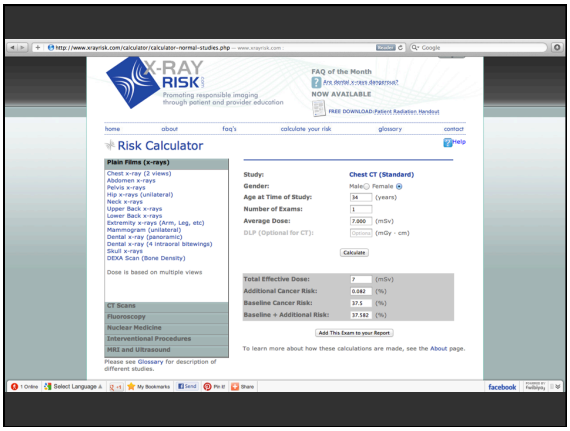
Mascalchi M, Mazzoni LN et al. Br J Radiol 2012

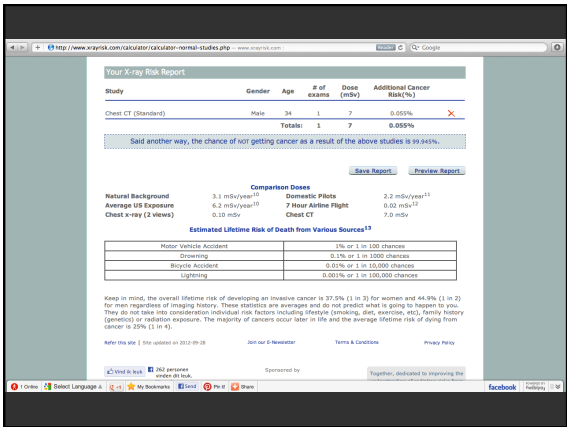
ITALUNG

- Four LDCT's + related further investigations (FDG PET and CT-guided biopsy)
- Mean effective dose to a single subject ranged between 6,2 and 6,8 mSv









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."

J. Jelinek

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 low-dose
- Sensitivities between low-dose and conventional images was not statistically significant
  - For detection
    - More likely to miss small nodules
  - For characterization
  - Reader variability

→ More studies needed !

Reader variability @ diagnosis

- Purpose of the study: to assess relative intra- and 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 ?

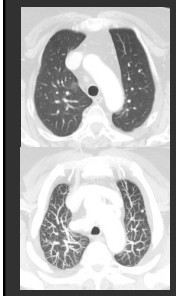
Nodule detection

Peloschek P, Sailer J et al. Radiology 2007

Detection is mainly limited by visual perception problems and errors

1. 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 et al. Br J Radiol 1998

Peloschek P, Sailer J et al. 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
- 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

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

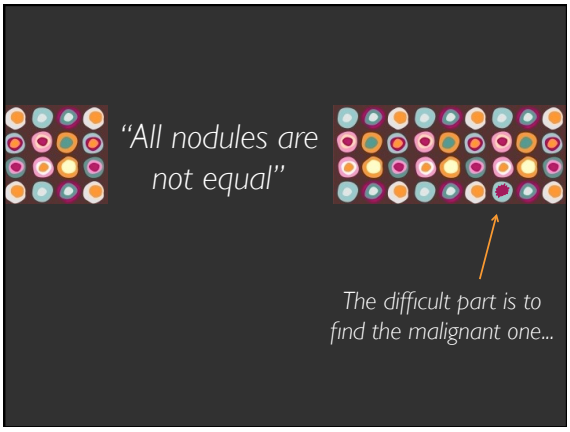
Rubin G, Lyo J et al. Radiology 2005

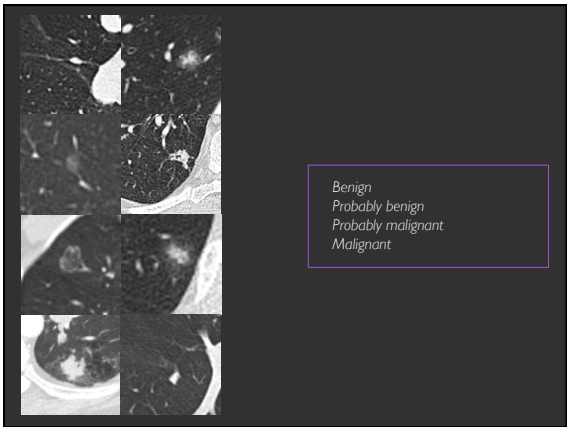
Awai K, Murao K et al. Radiology 2004

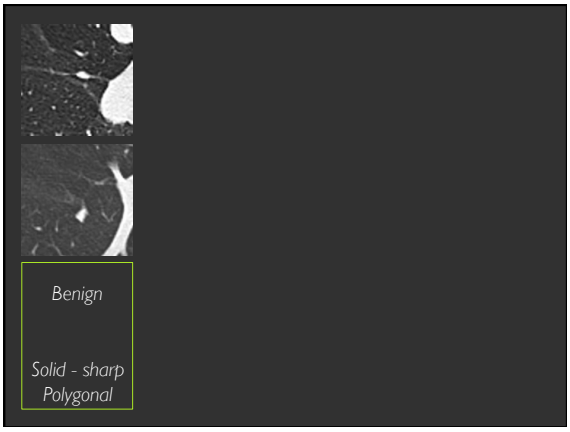
Beigelman C, Raffy P et al. AJR 2007

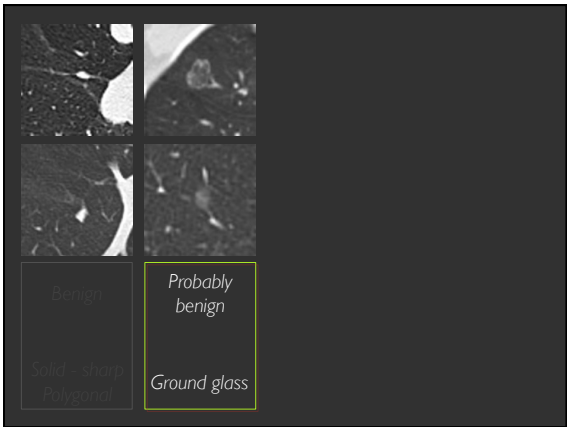
Girvin F, Ko J AJR 2008

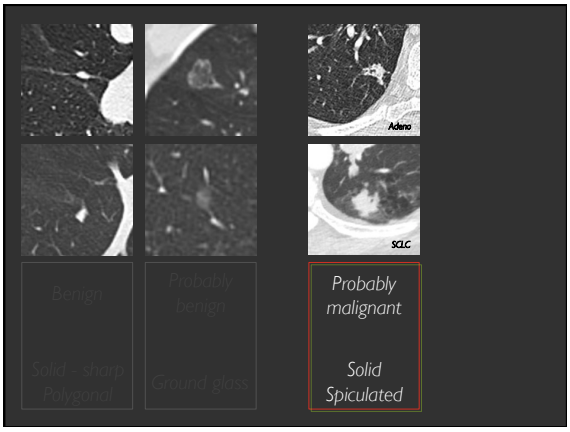
5. Lesion characterization

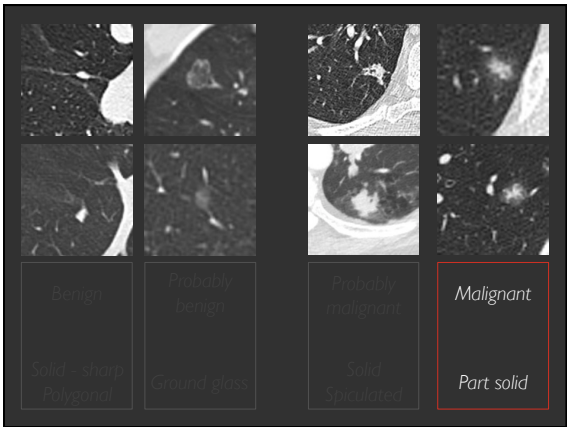

"All nodules are not equal"
The difficult part is to find the malignant one...


Benign
Probably benign
Probably malignant
Malignant

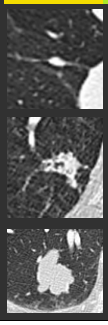

Benign
Solid - sharp
Polygonal


Benign
Solid - sharp
Polygonal
Probably benign
Ground glass


Adeno
SCLC
Benign
Solid - sharp
Polygonal
Probably benign
Ground glass
Probably malignant
Solid
Spiculated


Benign
Solid - sharp
Polygonal
Probably benign
Ground glass
Probably malignant
Solid
Spiculated
Malignant
Part solid

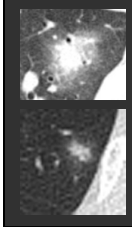
Characterization



1. 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

Characterization



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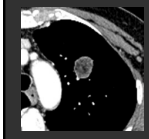
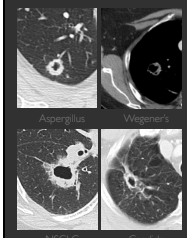


3. Density and internal characteristics
   - Macroscopic fat: benign lesions
   - Cavitation: necrotic tumors – infectious and inflammatory lesions
   - Calcification
     - Can be seen in 10% of patients with lung cancer
     - Benign patterns: laminated – central – diffuse – popcorn calcifications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

Characterization



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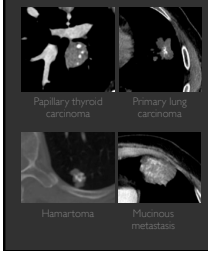

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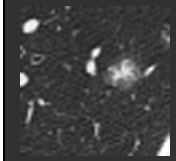
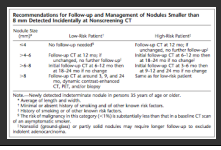


3. Density and internal characteristics
   - Subsolid nodules
     - Solid nodules with component of ground glass
     - Higher incidence of malignancy compared to ground glass nodules
     - Bronchoalveolar growth pattern

Characterization

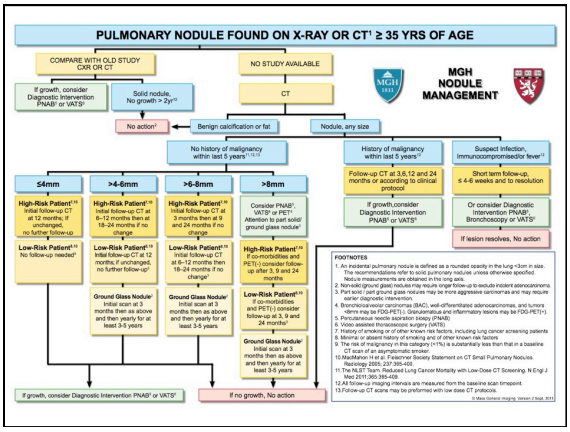
4. Nodule size and measurement

- 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"


Recommendations for Follow-up and Management of Nodules Smaller than 8 mm Detected Incidentally at Nonscreening CT

Nodule Size (mm)*	Low-Risk Patient†	High-Risk Patient†
≤4	No follow-up needed‖	Follow-up CT at 12 mo; if unchanged, no further follow-up‖
>4–6	Follow-up CT at 12 mo; if unchanged, no further follow-up‖	Initial follow-up CT at 6–12 mo then at 18–24 mo if no change
>6–8	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
>8	Follow-up CT at 3, 9, and 24 mo; dynamic contrast-enhanced CT, PET, and/or biopsy	Same as for low-risk patient

Note.—Newly detected indeterminate nodule in persons 35 years of age or older.
* Average of length and width.
† Minimal or absent history of smoking and of other known risk factors.
‡ The risk of malignancy in this category (<1%) is substantially less than that in a baseline CT scan of an asymptomatic smoker.
§ Nonsolid (ground-glass) or partly solid nodules may require longer follow-up to exclude indolent adenocarcinoma.



Characterization

4. Nodule size and measurement

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

Erasmus et al. (Curr Oncol 2007)

Bogot NR et al. Acad Radiol 2005

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
  - Disagreement → variation in measurement

Erasmus et al. (Curr Oncol 2007)

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

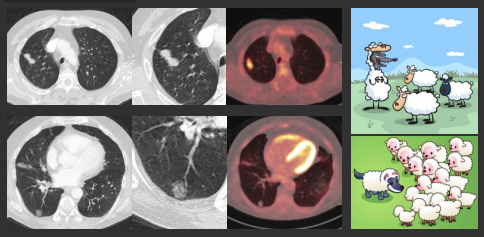
Volumetric measurement

- 3D techniques are susceptible to precision error
- Important factors:
  - Nodule size
    - Small lesions → higher error
  - Shape
    - Spiculated lesions = difficult
  - Attenuation
    - Segmentation problems

Volumetric measurement

- *Goodman et al. AJR 2006*
  - 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

73-y-old man
Dyspnea
No previous history



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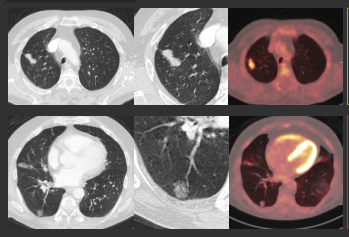


PET + lesion

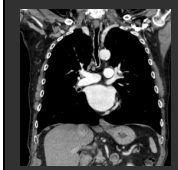
Pathology
GRANULOMA

PET - lesion

Pathology
ADENOCARCINOMA

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

- 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 whole-body CT imaging
- Radiologists are significantly more likely to believe CT screening studies are appropriate if they read them than if they do not

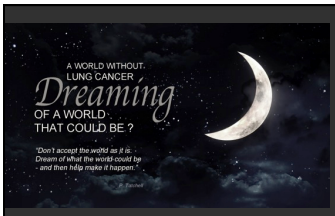
Some final thoughts...

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.



Thank you for your attention