Longkanker screening door het oog van de radioloog

A radiologist’s perspective

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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

- Often reveals nodules
- 77% of nodules smaller 7 mm visualized on a chest radiograph → calcified
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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

*De Hoop et al. Radiology 2010*
Screening with chest radiography

- 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 number of work-up CT examinations

De Hoop et al. Radiology 2010
Quekel et al. Eur J Radiol 2001
Potchen et al. Radiology 2000
Gavelli et al. Cancer 2000
Toyoda et al. Br J Cancer 2008
Monnier-Cholley et al. Radiology 2004
Mucinous adenocarcinoma
broncho-alveolar growth pattern
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 |
| Tumorigenesis |
Medische beelden zijn geen familiekiekjes. Wees er zuinig mee.

www.zuinigmetstraling.be

De Standaard

Medische beelden zijn geen familiekiekjes

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

AANRADEN 1

Medische beeldvorming is een verzamelaan 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
Which button do I push?

Usually we just punch 'em both.

Detect cancer cause cancer

Mammogram 5000 control panel

Concept: Mike Adams  Art: Dan Berger

www.NaturalNews.com
“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

- Lung parenchyma
- Breast
- Esophagus
- Liver
- Stomach
- Thyroid gland
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

Lung parenchyma is much HIGHER
Breast is much LOWER than at younger ages
Is radiation dose an issue in lung cancer screening?

Yes it is
Radiation-associated lung cancer risk
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!
“It is clear that radiation-related risks decrease rapidly with increasing age at commencement of screening”
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*
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

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
X-RAY RISK
Promoting responsible imaging through patient and provider education

This site provides information for patients and health care providers to facilitate well-informed discussions about the increased risk of cancer from radiation exposure as a result of medical imaging.

CALCULATE YOUR RISK
Print an Individual Report

Refer this site | Site updated on 2012-09-28

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Together, dedicated to improving the understanding of radiation risks from medical imaging. Calculate your dose and estimate cancer risk from radiation exposure.
Calculate your risk

Plain Films (x-rays)

CT Scans
- Brain CT (Standard)
- Brain and Neck CTA/CTP
- Neck CT
- Chest CT (Low Dose Screening)
- Chest CT (PE Study)
- Chest CT (Standard)
- Cardiac CT (Coronary CTA)
- Cardiac CT (Calcium Scoring)
- Abdomen CT
- Abdomen CT (Dedicated Liver)
- Abdomen and Pelvis CT
- Chest, Abdomen and Pelvis CT
- Pelvis CT
- Virtual Colonoscopy CT
- Dental CT

Fluoroscopy
- Nuclear Medicine
- Interventional Procedures
- MRI and Ultrasound

Please see Glossary for description of different studies.

Choose a study from the panels

Click on the panel titles to slide open additional studies.
Risk Calculator

Plain Films (x-rays)
- Chest x-ray (2 views)
- Abdomen x-rays
- Pelvis x-rays
- Hip x-rays (unilateral)
- Neck x-rays
- Upper Back x-rays
- Lower Back x-rays
- Extremity x-rays (Arm, Leg, etc)
- Mammogram (unilateral)
- Dental x-ray (panoramic)
- Dental x-ray (4 intraoral bitewings)
- Skull x-rays
- DEXA Scan (Bone Density)

Dose is based on multiple views

CT Scans
Fluoroscopy
Nuclear Medicine
Interventional Procedures
MRI and Ultrasound

Please see Glossary for description of different studies.

Chest CT (Standard)

Gender: Female
Age at Time of Study: 34 (years)
Number of Exams: 1
Average Dose: 7.000 (mSv)
DLP (Optional for CT): Optional (mGy · cm)

Calculate

Total Effective Dose: 7 (mSv)
Additional Cancer Risk: 0.082 (%)
Baseline Cancer Risk: 37.5 (%)
Baseline + Additional Risk: 37.582 (%)

Add This Exam to your Report

To learn more about how these calculations are made, see the About page.
Your X-ray Risk Report

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender</th>
<th>Age</th>
<th># of exams</th>
<th>Dose (mSv)</th>
<th>Additional Cancer Risk(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest CT (Standard)</td>
<td>Male</td>
<td>34</td>
<td>1</td>
<td>7</td>
<td>0.055%</td>
</tr>
<tr>
<td><strong>Totals:</strong></td>
<td></td>
<td></td>
<td><strong>1</strong></td>
<td><strong>7</strong></td>
<td><strong>0.055%</strong></td>
</tr>
</tbody>
</table>

Said another way, the chance of not getting cancer as a result of the above studies is 99.945%.

Comparison Doses

<table>
<thead>
<tr>
<th>Natural Background</th>
<th>3.1 mSv/year(^{10})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average US Exposure</td>
<td>6.2 mSv/year(^{10})</td>
</tr>
<tr>
<td>Chest x-ray (2 views)</td>
<td>0.10 mSv</td>
</tr>
</tbody>
</table>

| Domestic Pilots        | 2.2 mSv/year\(^{11}\)  |
| 7 Hour Airline Flight  | 0.02 mSv\(^{12}\)       |
| Chest CT               | 7.0 mSv                 |

Estimated Lifetime Risk of Death from Various Sources\(^{13}\)

<table>
<thead>
<tr>
<th></th>
<th>1% or 1 in 100 chances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Vehicle Accident</td>
<td></td>
</tr>
<tr>
<td>Drowning</td>
<td>0.1% or 1 in 1000 chances</td>
</tr>
<tr>
<td>Bicycle Accident</td>
<td>0.01% or 1 in 10,000 chances</td>
</tr>
<tr>
<td>Lightning</td>
<td>0.001% or 1 in 100,000 chances</td>
</tr>
</tbody>
</table>

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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262 personen vinden dit leuk.
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

- 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!
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?
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

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


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

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

Probably benign

Solid - sharp
Polygonal

Ground glass

Adeno

SCLC

Probably malignant

Solid
Spiculated
Benign

Probably benign

Probably malignant

Malignant

Solid - sharp

Polygonal

Ground glass

Solid

Spiculated

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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- Irregular or spiculated margins are highly suggestive
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Characterization

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

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

Aspergillus  
Wegener’s  
NSCLC  
Candida
Characterization

3. Density and internal characteristics

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Girvin F, Ko JP
AJR 2008

Grewal RG, Austin JH.
JCAT 1994
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 JP
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 than 5 mm can be malignant
- “Guidelines for management of small pulmonary nodules detected on CT scans: A statement from the Fleischner Society”

*Ginsberg et al. Radiology 1999
Grewal RG, Austin JH. JCAT 1994
Girvin F, Ko JP AJR 2008
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
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 \(\Rightarrow\) variation in measurement
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 $\rightarrow$ 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
ISOTOPE MAN TO THE RESCUE
73-y-old man
Dyspnea
No previous history
73-y-old man
Dyspnea
No previous history

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

Saghiri Z et al. Am J Respir Crit Care 2012
7. What do radiologists think about lung cancer screening?

- 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