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

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

- 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
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

“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 parts 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
Is radiation dose an issue in lung cancer screening? Yes it is

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

Radiation-associated cancer risk at age 55

- Radiation-associated cancer risk at age 55 is much LOWER than at younger ages is much LOWER than at younger ages

- 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
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."

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Definition of "low-dose CT"

"Lower than standard dose"

Definition of "standard dose"

No definition
No standardization

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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.

References:
- Tamm EP, Rong XJ et al. Radiographics 2011
- McCollough C, Bruesewitz MR et al. Radiographics 2006
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 \(\rightarrow\) 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% \(\rightarrow\) level of expertise becomes important

Estimated radiation dose
NLST and ITALUNG trial

- 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
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.”

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
- 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
**Reader variability:** What’s the cause and what can we do to become better?

**Nodule detection**

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**
  - MP reconstructions
  - MP 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

**Imaging in trials**

- **NLST-trial**
  - Interpretations were made by using soft-copy 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

Probably benign

Probable benign

Ground glass

Benign

Probably benign

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

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

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Characterization

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

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Characterization

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"

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 → 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 → 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

Extrathoracic findings

- Detection of incidental findings outside the lung
- NLST 75% \( \rightarrow \) clinically significant abnormality
- Danish Lung Cancer Screening trial
  - In 6.8% of patients
  - 7.7% of these findings were malignant
- Health benefits \( \leftrightarrow \) additional diagnostic examinations / procedures with no health benefit
- Difficult interpretation on low-dose CT
7. What do radiologists think about lung cancer screening?

National survey of radiologists


- 298 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