

25th scientific day of the Geneva pulmonary league, 17.11.2011

Lung cancer screening with low-dose CT: an Update



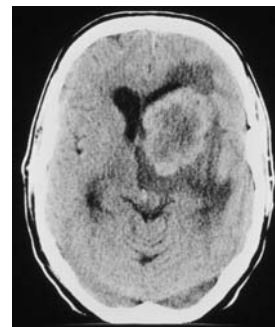
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Interventional Radiology**

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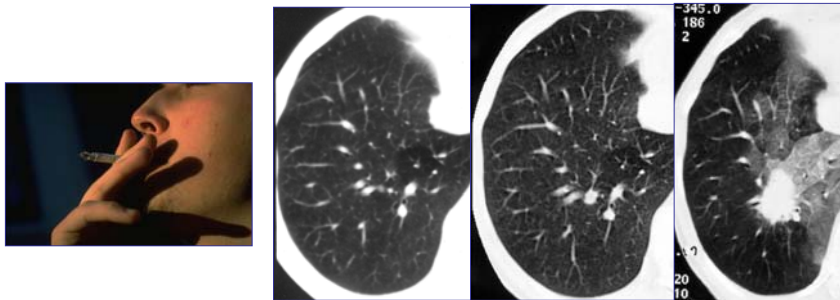
Background

- > 1.3 million deaths / year from lung cancer worldwide
- < 15% overall survival
- 5-year-survival better in early stages



Background

- Risk groups well defined
 - active, former cigarette smokers (> 85%)
 - workers with asbestos, radon, exposure
- No early symptoms → diagnostic tests for early dx



Stop smoking / never start smoking

- easiest , cheapest and best way to prevent death from lung cancer (and many other diseases)
- politically not pursued (13.4 billion €/year tax)
- only 17% of world population reached by anti-smoking programmes



Prognosis in NSCLC

Stage	TNM-classification			5-year survival (pathologic stage)
I A	T1	N0	M0	67%
I B	T2	N0	M0	57%
II A	T1	N1	M0	55% 25%
II B	T2	N1	M0	39%
	T3	N0	M0	38%
III A	T3	N1	M0	25% 25%
	T1-3	N2	M0	23%
III B	T4	N0-2	M0	7%
	T1-4	N3	M0	3%
IV	T1-4	N0-3	M1	1% 50%

Screening studies with CXR / Sputum

Studies in > 36.000 smokers in the 1970's

USA National lung cancer trial: >30.000 smokers

(Johns Hopkins, Mayo Clinic, Memorial Sloan Kettering)

Frost 1983 ARRS 130: 549

Fontana 1984 ARRS 130: 561

Melamed 1984 Chest 86: 44

Study in Czechoslovakia: > 6.000 smokers

Kubik & Polak 1986, Cancer 57: 2428

Screening studies with CXR / Sputum

- Higher detection rate of lung cancer in screening groups
- No reduction of mortality in screening group
- No recommendations to screen for lung cancer with CXR or sputum cytology

Eddy 1989, Ann Int Med 111: 232

Screening studies with CXR / Sputum


Mayo lung project

109 cancers detected

92 cancers at CXR (50 peripheral)

Size at diagnosis

< 1 cm	2	23 (27%)
1-1.9 cm	21	
2-2.9 cm	28	63 (73%)
> 2.9 cm	35	



PLCO trial

(Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial)


- since 1992 randomised controlled trial by NCI
- 155.000 participants (male and female)
- 55–74 years

assesses different screening tests for potential reduction of cancer specific mortality

Lung cancer:

- Screening arm: 4 x (smoker) / 3 x (non-smoker)
CXR p.a. 1 x year
- control arm: „usual medical care“

Prorok et al. (2000) Control Clin Trials. 21; 273S-309S



PLCO trial

(Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial)

Incidence lung cancer (per 10.000 person years)	CXR	„usual care“
	20.1	19.2
Stage 1 and 2	574	479
Stage 3 and 4	873	895
Mortality	1213	1230

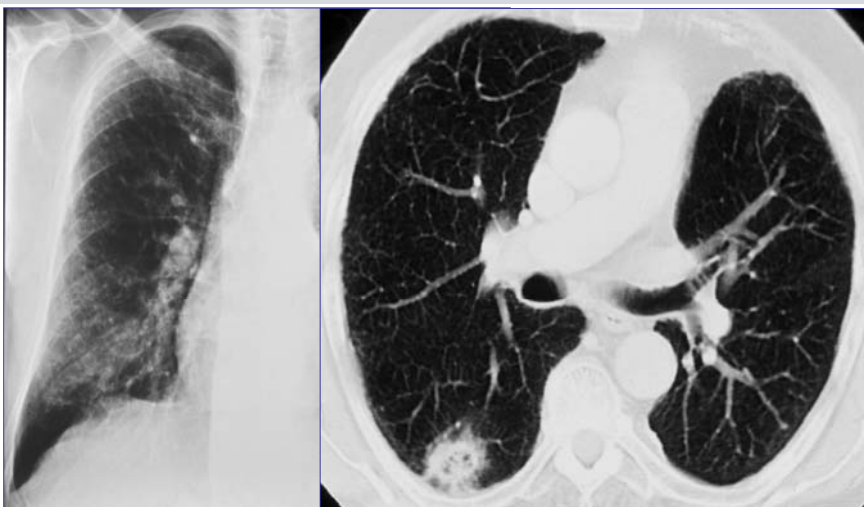
Oken et al. 2011 JAMA 306: 1865-1873

Lung cancer

Are there better tests today for early detection of lung cancer ?

- **molecular markers in blood, sputum, exhaled air**
- **autofluorescence fibroptic bronchoscopy**
- **low-radiation-dose CT**

Sensitivity of CXR/CT



Sensitivity of Spiral CT for pulmonary nodules

Single slice-spiral-CT sensitivity for pulm. nodules

< 6 mm	69 %
> 5 mm	95 %
> 10 mm	100 %

Diederich et al. 1999; Am J Roentgenol 172: 353

Dose reduction to 10-20% of standard dose chest-CT is feasible (Low-dose CT): 2 – 5 x CXR p.a. and lat.

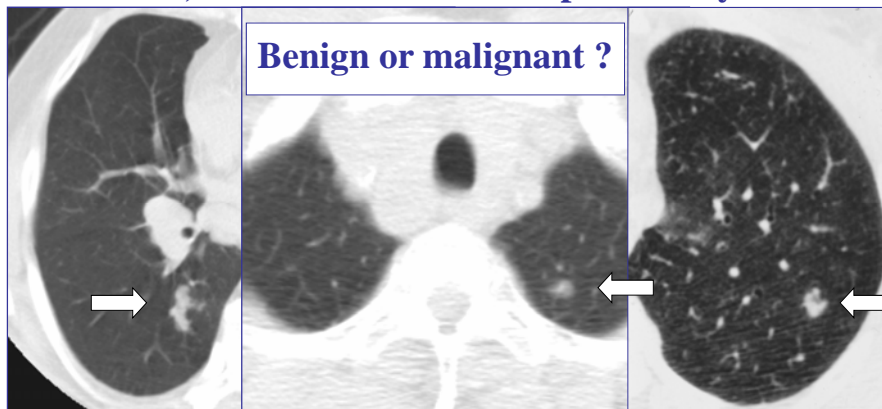
Gartenschläger et al. 1996; Eur Radiol 8: 609

Rusinek et al. 1998; Radiology 209: 243

Diederich et al. 1999; Radiology 213: 289

CT-presentation of early lung cancer ?

- 95% pulmonary nodule, (5% endobronchial lesion)
- however, > 100 other causes for pulmonary nodules



Feasibility studies

- Kaneko 1996, Radiology 201: 798
- Sone 1998; Lancet 351: 1242
- Henschke 1999, Lancet 354: 99
- Diederich 2002, Radiology 222: 773
- Swensen 2002, Am J Respir Crit Care Med 165: 508
- Nawa 2002, Chest 122: 15
- Tiitola 2002, Lung Cancer 35: 17
- Pastorino 2003, Lancet 362: 593
- and many more

Feasibility studies

- Most focussed on risk group of smokers

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Feasibility studies

- **Most focussed on risk group of smokers**
- **Most annual unenhanced low-dose CT**

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Feasibility studies

- **Most focussed on risk group of smokers**
- **Most annual unenhanced low-dose CT**
- **Work-up of detected lesions based on size**
 - small lesions → follow-up with low dose CT
 - large lesions → biopsy, CE-CT, PET
 - (small: ≤ 10 mm maximum diameter or ≤ 8 mm average diameter)

Kaneko 1996, Radiology 201: 798
Sone 1998; Lancet 351: 1242
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Feasibility studies: CT Screening in smokers

Prevalence

	Patients	NSCLC	Stage I
ALCA	1369	15 (1,1%)	14 (93%)
Shinshu	3967	19 (0,5%)	16 (84%)
ELCAP	1000	27 (2,7%)	23 (85%)
Münster	817	11 (1,3%)	7 (64%)
Mayo Clinic	1520	19 (1,2%)	12 (63%)
Hitachi	7956	37 (0,5%)	31 (82%)
Helsinki	602	5 (0,8%)	3 (64%)
Milan	1035	11 (1,1%)	6 (55%)

Feasibility studies: CT Screening in smokers

Incidence

	Patients	NSCLC	Stage I
ALCA	11911	39 (0,3%)	34 (87%)
Shinshu	10045	40 (0,4%)	35 (88%)
ELCAP	1184	6 (0,5%)	5 (84%)
Münster	668	10 (1,5%)	7 (70%)
Mayo Clinic	1478	8 (0,5%)	5 (63%)
Hitachi	7956	37 (0,5%)	31 (82%)
Helsinki	602	2 (0,3%)	
Milan	1035	11 (1,1%)	11 (100%)

Feasibility studies: CT Screening in smokers

Invasive procedures for benign lesions

	Biopsies	benign	(%)
ALCA	49	27	(55%)
Shinshu	43	9	(21%)
ELCAP	7	1	(14%)
Münster	13	3	(23%)
Mayo Clinic	40	8	(20%)
Hitachi	6	2	(33%)
Milan	28	6	(22%)
	186	56	(30%)

Results of feasibility studies

- High proportion (- 66%) of subjects with non-calcified nodules

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- **High proportion (- 66%) of subjects with non-calcified nodules**
- **High number of nodules detected**

Results of feasibility studies

- **High proportion (- 66%) of subjects with non-calcified nodules**
- **High number of nodules detected**
- **> 95 % of nodules small (≤ 8 mm / 10 mm)**

Results of feasibility studies

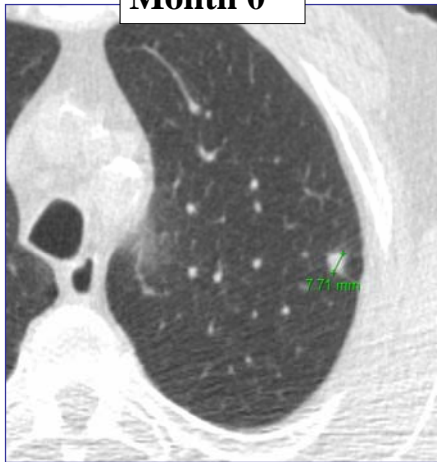
- **High proportion (- 66%) of subjects with non-calcified nodules**
- **High number of nodules detected**
- **> 95 % of nodules small (≤ 8 mm / 10 mm)**
- **Only 3 % of nodules malignant**

Results of feasibility studies

- **High proportion (- 66%) of subjects with non-calcified nodules**
- **High number of nodules detected**
- **> 95 % of nodules small (≤ 8 mm / 10 mm)**
- **Only 3 % of nodules malignant**
- **mainly non-invasive work-up with f-u CT**

Detection of growth

Month 0



Month 12



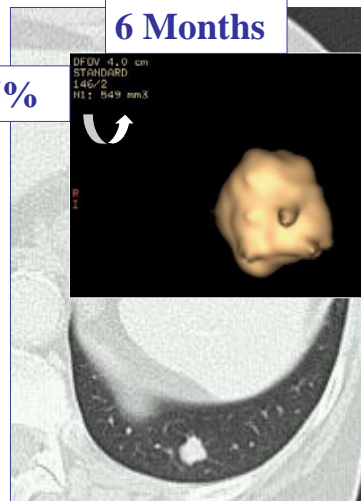
Computer-assisted Diagnosis: Growth ?

0 Month



V: +25%

6 Months



Spread of malignancy during follow-up ?

5201 baseline CT scans, 4821 annual follow-up (93%)

<= 5 mm: follow-up after 12 months

> 5-8 mm: follow-up after 3 months

> 8 mm: PET / CE-CT

2754 subjects (53%) with non-calcified nodule(s)

37 incidence cancers

17 baseline nodule → stage 1 after 12 months

7 baseline nodule → > stage 1 after 12 months (0.25%)

13 new nodule

Veronesi et al., 2008. Lung cancer 61: 340

Results of feasibility studies

- **High (0.7-3.7%) prevalence of NSCLC**

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Results of feasibility studies

- **High (0.7-3.7%) prevalence of NSCLC**
- **Lower (0.3-1.5%) incidence of NSCLC**

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Results of feasibility studies

- **High (0.7-3.7%) prevalence of NSCLC**
- **Lower (0.3-1.5%) incidence of NSCLC**
- **High (55-100%) proportion of stage I NSCLC**

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Results of feasibility studies

- **High (0.7-3.7%) prevalence of NSCLC**
- **Lower (0.3-1.5%) incidence of NSCLC**
- **High (55-100%) proportion of stage I NSCLC**
- **Acceptabel (30%) proportion of invasive procedures for benign lesions**

Kaneko 1996, Radiology 201: 798
Sone 1998; Lancet 351: 1242
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Mortality reduction ?

Results of multi center LDCT-Studie

- **>30.000 subjects**
- **if:**
 - **clinically stage 1**
 - **therapy within 1 month**
- **estimated 10 year-survival: 92%**

I-ELCAP, NEJM 2006; 355: 1763

Mortality reduction ?

comparison

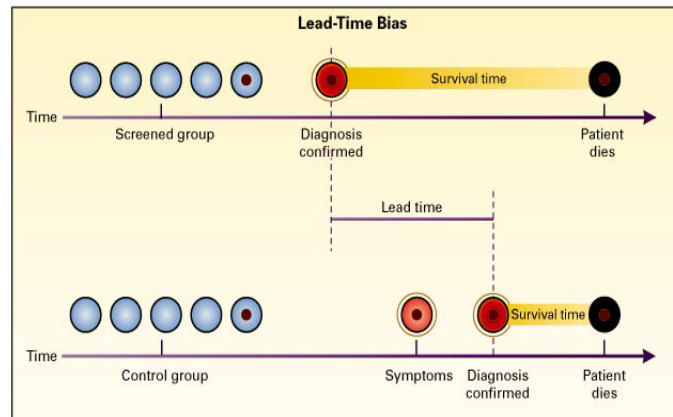
- Results of 3 CT-Screening studies
 - Prediction of results from models
- more: cancers, lung resections
 - identical: advanced stage cancer, mortality

Bach PB, JAMA 2007; 297: 953

Why may lung cancer screening not work ?

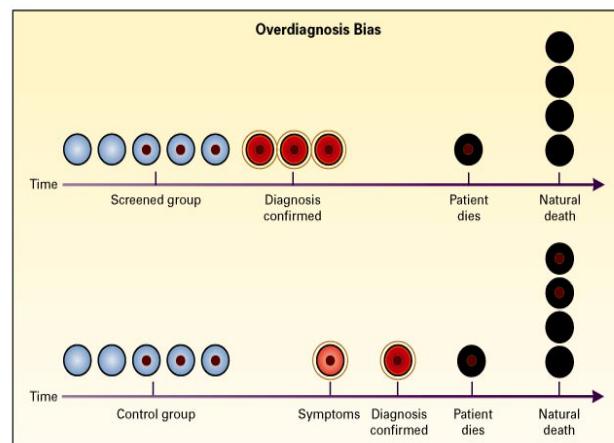
- screen detected cancer may be insignificant
 - cancer may grow slowly and may not metastasize
 - Patient may die from other cause (CAD, stroke, other cancer)
- screening may be unable to detect aggressive cancers
- detection of suspicious lesions may cause more harm than good (concerns in benign lesions, biopsy, surgery)

Screening: Lead-time Bias



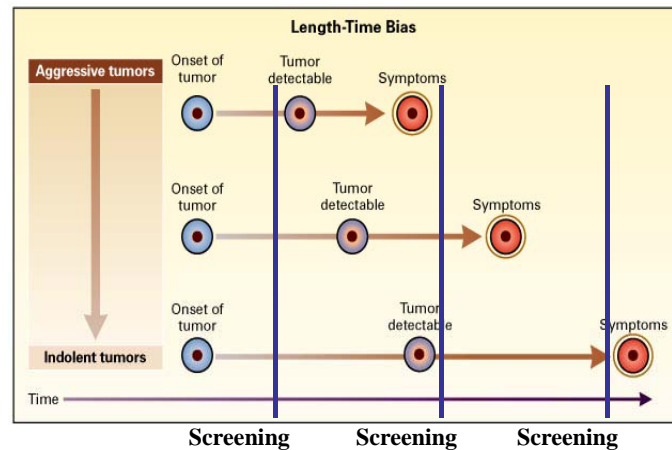
Patz et al. NEJM 2000; 343: 1627

Screening: Overdiagnosis Bias



Patz et al. NEJM 2000; 343: 1627

Screening: Length Bias



Patz et al. NEJM 2000; 343: 1627

Efficacy of cancer screening

not useful:

- size of tumor at diagnosis
- resectability of tumor
- stage distribution
- median survival
- percentage of 5-year survival

Screening: proof of efficacy

prospective, randomised controlled trials (RCT):

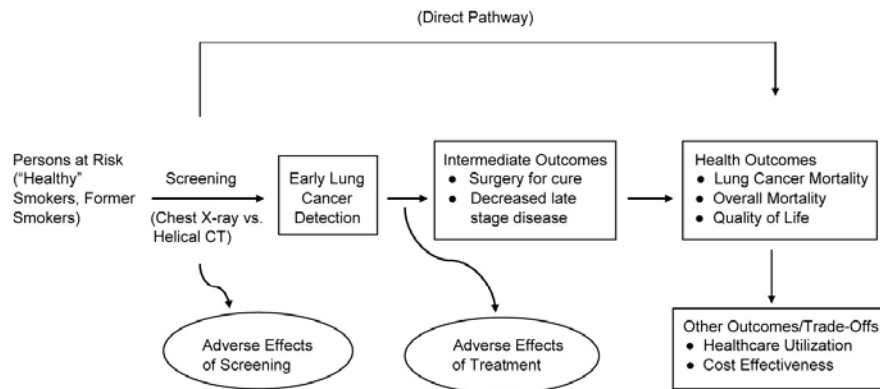
- screening arm with diagnostic test
- control arm without diagnostic test

→ comparison of cancer mortality

Randomised controlled trials (RCT)

- USA: NLST (National Lung Screening Trial):
> 53.000 subjects recruited from 2002 - 2004
- Netherlands/Belgium (NELSON):
20.000 subjects: not yet recruited
- several smaller studies: most likely no significant
results → pooling of data (Pisa-Statement)

Process and outcomes in the NLST



Radiology 2011;258:243-253

NLST (National Lung Screening Trial)

- **active or ex-smokers (<= 15 years)**
- **55-74 years at inclusion**
- **>= 30 pack years**
- **3 x annual screening**
 - low-dose CT
 - CXR p.a. and lateral
- **5 year follow-up**

participating institutions

Study Group and Screening Center	Location	Accrual No.
NLST-ACRIN		
Beth Israel Deaconess Medical Center*†	Boston	629
Brigham and Women's Hospital†	Boston	540
Brown University, Rhode Island Hospital*†	Providence	827
The Cancer Institute of New Jersey*†	New Brunswick	88
Dartmouth-Hitchcock Medical Center*†	Lebanon	575
Emory University	Atlanta	1231
Jewish Hospital Rudd Heart and Lung Institute*†	Louisville	1971
Johns Hopkins University*†	Baltimore	1670
Mayo Clinic, Jacksonville*†	Jacksonville	288
Mayo Clinic, Rochester*†	Rochester	1183
Medical University of South Carolina	Charleston	578
Moffitt Cancer Center*†	Tampa	787
Northwestern University	Chicago	426
Ochsner Medical Center	New Orleans	504
St. Elizabeth Health Center*†	Youngstown	1046
University of California, Los Angeles*†	Los Angeles	1587
University of California, San Diego*†	San Diego	155
University of Iowa	Iowa City	1154
University of Michigan Medical Center*†	Ann Arbor	857
University of Pennsylvania	Philadelphia	386
University of Texas M.D. Anderson Cancer Center*†	Houston	782
Vanderbilt University	Nashville	465
Wake Forest University*†	Winston-Salem	1113
NLST/ACRIN total		18 842
NLST-LSS		
Georgetown University Medical Center	Washington	1827
Henry Ford Health System	Detroit	3395
Marshfield Clinic Research Foundation	Marshfield	2520
Pacific Health Research & Education Institute‡	Honolulu	2359
University of Alabama at Birmingham	Birmingham	5052
University of Colorado Denver	Aurora	3743
University of Minnesota School of Public Health	Minneapolis	6618
University of Pittsburgh Medical Center	Pittsburgh	2177
University of Utah Health Sciences Center	Salt Lake City	3159
Washington University School of Medicine	St Louis	3764
NLST/LSS total		34 614
NLST total		53 456

Examination parameters

Parameter	Datum
CT	
Scout view	Single posteroanterior projection; participant supine; tube below patient
Helical acquisition	
Positioning	Supine; arms elevated above the head
Inspiration	Suspended maximal
Voltage (kVp)	120–140
Tube current–time product (mAs)	40–80 (dependent on participant body habitus)
Detector collimation (mm)	≤2.5
Nominal reconstructed section width (mm)	1.0–3.2
Reconstruction interval (mm)	1.0–2.5
Reconstruction algorithm	Soft tissue or thin section
Scanning time (sec)	<25
Chest radiography	
Projection	Posteroanterior only
Voltage (kV)	100–150
Maximum exposure time (msec)	40*
Source-to-receptor distance (in.)†	≥72
Antiscatter device	≥ 10:1 ratio grid

Interpretation of Findings at CT or Chest Radiographic Screening

Arm and Result	Observation
CT	
Negative or minor abnormality: not suspicious for lung cancer	No findings or minor findings not suspicious for lung cancer, such as morphologically benign nodules or noncalcified nodules < 4 mm
Clinically important abnormality: not suspicious for lung cancer	Important findings not suspicious for lung cancer but requiring some form of clinical follow-up
Positive: suspicious for lung cancer	Findings suspicious for lung cancer, such as noncalcified nodule ≥ 4 mm, lung consolidation or obstructive atelectasis, nodule enlargement, and nodules with suspicious changes in attenuation
Chest radiography	
Negative or minor abnormality, not suspicious for lung cancer	No findings or minor findings not suspicious for lung cancer, such as nodules containing benign patterns of calcification
Clinically important abnormality, not suspicious for lung cancer	Important findings not suspicious for lung cancer, but requiring some form of clinical follow-up
Positive, suspicious for lung cancer	Findings suspicious for lung cancer, such as noncalcified nodule or pulmonary opacity

If abnormal findings

- mail to subject and „health care provider“
- if suspicious for lung cancer further procedures (different in different institutions)
- diagnostic procedures depend on „health care provider“

NLST-ACRIN Substudies

- use of resources and outcome
→ cost-effectiveness analysis
(quality-adjusted life-years)
- smoking habits → effect of screening
 - overall
 - pos. screening-result
 - neg. screening-result
- Biospecimen collection (blood, urine, sputum,
histology of resected lung cancer)

Results

- 53.456 subjects 2002 - 2004 recruited
- maximum follow-up 8 years
- annual interim analysis since 2006

Results

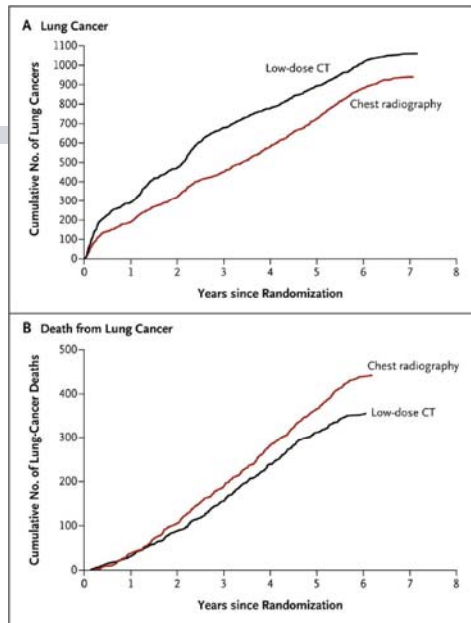
- 53.456 subjects 2002 - 2004 recruited
- maximum follow-up 8 years
- annual interim analysis since 2006
- 10/2010 data & safety monitoring board
 - press conference:
 - 354 lung cancer deaths: screening arm
 - 442 lung cancer deaths: control arm

NLST (National Lung Screening Trial)

	LDCT	CXR
Positive findings	24.2%	6.9%
Death from lung cancer	354	442
Lung cancer mortality (per 100.000 pack years)	246	308
lung cancer mortality reduction through LDCT: 20%		
overall mortality reduction: 7%		

NEJM 2011; 365: 395-409

NEJM 2011; 365: 395-409



A. cumulative numbers of lung cancer cases from randomisation until 31.12.2009

B. cumulative numbers of lung cancer deaths from randomisation until 31.12.2009

Results of 3 rounds of screening

NEJM 2011; 365: 395-409

Table 2. Results of Three Rounds of Screening.*

Screening Round	Low-Dose CT				Chest Radiography			
	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer no. (% of screened)	No or Minor Abnormality	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer no. (% of screened)	No or Minor Abnormality
T0	26,309	719 (27.3)	2695 (10.2)	16,423 (62.4)	26,035	2387 (9.2)	795 (3.0)	22,863 (87.8)
T1	24,715	690 (27.9)	1519 (6.1)	16,295 (65.9)	24,089	1482 (6.2)	429 (1.8)	22,178 (92.1)
T2	24,102	405 (16.8)	1408 (5.8)	18,640 (77.3)	23,346	1174 (5.0)	361 (1.5)	21,811 (93.4)

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. Results of screening tests that were technically inadequate (7 in the low-dose CT group and 26 in the radiography group, across the three screening rounds) are not included in this table. A screening test with low-dose CT was considered to be positive if it revealed a nodule at least 4 mm in any diameter or other abnormalities that were suspicious for lung cancer. A screening test with chest radiography was considered to be positive if it revealed a nodule or mass of any size or other abnormalities suspicious for lung cancer.

Diagnostic follow-up of positive screening results in the 3 screening rounds

NEJM 2011; 365: 395-409

Table 3. Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.*

Variable	Low-Dose CT				Chest Radiography			
	T0	T1	T2	Total	T0	T1	T2	Total
	number (percent)							
Total positive tests	2101 (100.0)	6004 (100.0)	6054 (100.0)	18,146 (100.0)	2337 (100.0)	1482 (100.0)	1174 (100.0)	5043 (100.0)
Lung cancer confirmed	270 (12.8)	341 (5.7)	211 (3.5)	649 (3.6)	136 (5.8)	65 (4.4)	78 (6.6)	279 (5.5)
Lung cancer not confirmed†	5941 (96.2)	6733 (97.6)	3843 (96.8)	17,497 (96.4)	2251 (94.3)	1417 (95.6)	1096 (93.4)	4764 (94.5)
Positive screening results with complete diagnostic follow-up information	7049 (100.0)	6740 (100.0)	3913 (100.0)	17,702 (100.0)	2348 (100.0)	1456 (100.0)	1149 (100.0)	4953 (100.0)
Any diagnostic follow-up	6309 (90.4)	3966 (57.4)	2522 (94.5)	12,757 (70.3)	2176 (92.7)	1078 (74.0)	957 (83.3)	4211 (85.0)
Clinical procedure	5089 (75.2)	3190 (47.3)	2181 (85.0)	10,436 (57.9)	1414 (60.2)	723 (49.7)	658 (57.3)	2795 (56.4)
Imaging examination	5717 (81.1)	2520 (37.4)	2039 (77.3)	10,246 (57.0)	2010 (85.6)	658 (46.4)	606 (52.9)	3284 (66.4)
Chest radiography	1284 (18.2)	613 (9.1)	659 (16.6)	2,547 (14.4)	867 (36.9)	381 (26.2)	365 (31.8)	1613 (32.6)
Chest CT	5153 (73.1)	2046 (30.4)	1608 (41.1)	8,807 (49.8)	1346 (58.8)	245 (16.4)	242 (20.9)	3033 (61.0)
FDG PET or FDG PET-CT	728 (10.3)	350 (5.2)	393 (10.0)	1,471 (8.3)	179 (7.6)	105 (7.2)	113 (9.8)	397 (8.0)
Percutaneous cytologic examination or biopsy	155 (2.2)	74 (1.1)	95 (2.4)	322 (1.8)	83 (3.5)	37 (2.5)	52 (4.5)	172 (3.5)
Transbronchial	129 (1.7)	60 (0.9)	71 (1.8)	254 (1.4)	67 (2.9)	31 (2.1)	43 (3.7)	141 (2.8)
Endobronchial	39 (0.6)	17 (0.3)	24 (0.6)	80 (0.4)	20 (0.9)	6 (0.4)	11 (1.1)	37 (0.8)
Bronchoscopy	306 (4.3)	178 (2.6)	187 (4.8)	671 (3.8)	107 (4.6)	56 (3.8)	62 (5.4)	225 (4.5)
With neither biopsy nor cytologic testing	126 (1.8)	95 (1.4)	99 (2.3)	320 (1.8)	45 (1.9)	19 (1.3)	32 (2.8)	96 (1.9)
With biopsy or cytologic testing	194 (2.8)	95 (1.4)	102 (2.6)	391 (2.2)	74 (3.2)	40 (2.7)	30 (2.6)	150 (3.0)
Surgical procedure	297 (4.2)	197 (2.9)	219 (5.5)	713 (3.9)	121 (5.2)	51 (3.4)	67 (5.8)	239 (4.8)
Mediastinoscopy or mediastinotomy	60 (0.9)	32 (0.5)	25 (0.6)	117 (0.7)	22 (0.9)	12 (0.8)	21 (1.8)	55 (1.1)
Thoracoscopy	82 (1.2)	56 (0.8)	96 (2.3)	234 (1.3)	22 (0.9)	11 (0.8)	20 (1.7)	53 (1.1)
Thoracotomy	197 (2.8)	148 (2.2)	164 (4.2)	509 (2.8)	96 (4.1)	44 (3.0)	44 (3.8)	184 (3.7)
Other procedures	168 (2.4)	96 (1.4)	63 (1.6)	327 (1.8)	33 (1.4)	34 (2.3)	34 (3.0)	122 (2.5)

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. FDG PET denotes ¹⁸F fluorodeoxyglucose positron emission tomography.
† Positive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose CT group and 39 at T0, 26 at T1, and 23 at T2 in the radiography group).

Stage and histologic type of lung cancer in the two screening groups

NEJM 2011; 365: 395-409

Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.*

Stage and Histologic Type	Low-Dose CT				Chest Radiography			
	Positive Screening Test (N=649)	Negative Screening Test (N=441)	No Screening Test (N=3571)	Total (N=4061)	Positive Screening Test (N=278)	Negative Screening Test (N=1371)	No Screening Test (N=5211)	Total (N=6411)
	number/total number (percent)							
Stage								
IA	129/635 (11.4)	5/44 (1.1)	82/361 (22.7)	416/1040 (40.0)	40/275 (14.5)	16/115 (13.9)	40/516 (7.7)	146/808 (18.1)
IB	71/635 (11.2)	2/44 (0.5)	31/361 (8.6)	104/1040 (10.0)	41/275 (14.9)	6/115 (5.2)	46/516 (8.9)	93/808 (11.5)
IIA	25/635 (4.1)	2/44 (0.5)	7/361 (1.9)	35/1040 (3.4)	14/275 (5.1)	2/115 (1.7)	16/516 (3.1)	32/808 (4.0)
IIB	20/635 (3.1)	3/44 (0.7)	15/361 (4.2)	38/1040 (3.7)	11/275 (4.0)	4/115 (3.5)	25/516 (4.8)	42/808 (5.2)
IIIA	59/635 (9.3)	3/44 (0.7)	37/361 (10.2)	99/1040 (9.5)	35/275 (12.7)	21/115 (18.3)	53/516 (10.2)	109/808 (13.5)
IIIC	49/635 (7.7)	15/44 (3.4)	58/361 (16.1)	122/1040 (11.7)	27/275 (9.8)	24/115 (20.8)	71/516 (13.7)	122/808 (15.1)
IV	81/635 (12.8)	14/44 (3.2)	111/361 (30.7)	206/1040 (19.7)	57/275 (20.7)	60/115 (52.2)	218/516 (42.2)	335/808 (41.4)
Histologic type								
Bronchioloalveolar carcinoma	95/645 (14.7)	1/44 (2.3)	14/358 (3.9)	110/1048 (10.5)	13/276 (4.7)	1/115 (0.7)	21/520 (4.0)	35/811 (4.3)
Adenocarcinoma	258/645 (39.9)	8/44 (18.2)	111/358 (31.0)	380/1048 (36.3)	112/276 (40.6)	37/115 (32.2)	179/520 (34.4)	328/811 (40.4)
Squamous-cell carcinoma	136/645 (21.1)	13/44 (29.5)	94/358 (26.3)	243/1048 (23.2)	70/276 (25.4)	24/115 (20.8)	112/520 (21.5)	206/811 (25.4)
Large-cell carcinoma	28/645 (4.3)	3/44 (6.8)	10/358 (2.8)	41/1048 (3.9)	12/276 (4.3)	10/115 (8.7)	21/520 (4.0)	43/811 (5.3)
Non-small-cell carcinoma or other†	75/645 (11.6)	8/44 (18.2)	52/358 (14.5)	135/1048 (12.8)	40/276 (14.5)	30/115 (26.1)	88/520 (16.9)	158/811 (19.5)
Small-cell carcinoma	49/645 (7.6)	15/44 (34.1)	71/358 (19.8)	135/1048 (12.8)	28/276 (10.1)	32/115 (27.8)	66/520 (12.7)	126/811 (15.5)
Carcinoid	5/645 (0.8)	0	1/358 (0.3)	6/1048 (0.6)	1/276 (0.4)	1/115 (0.7)	0	2/811 (0.2)

* The denominators represent only cancers with a known stage or histologic type. The stage was not known in the case of 14 cancers after a positive screening test and 6 after no screening in the low-dose CT group and in the case of 4 cancers after a positive screening test, 2 after a negative screening test, and 6 after no screening in the radiography group. The histologic type was not known for 3 cancers after a positive screening test and 9 after no screening in the low-dose CT group and for 3 cancers after a positive screening test, 2 after a negative screening test, and 5 after no screening in the radiography group.
† Negative screening tests included tests that revealed either minor or clinically significant abnormalities that were not suspicious for lung cancer.
‡ The 892 lung cancers in this category in the two groups combined included 28 adenocarcinomas, 6 sarcomatoid carcinomas, 55 unclassified carcinomas, 1 anaplastic-type carcinoma, 1 carcinosarcoma, and 198 coded only as "non-small-cell carcinoma."

histologic type of lung cancer in the two screening groups according to tumor stages

NEJM 2011; 365: 395-409

Table 6. Histologic Type of Lung Cancers in the Two Screening Groups, According to Tumor Stage.*

Histologic Type	Total No. of Cancers	Stage of Cancer						
		IA	IB	IIA	IIB	IIIA	IIIB	IV
		number/total number (percent)						
Low-dose CT group								
Bronchioloalveolar carcinoma	110	83/110 (75.5)	6/110 (5.5)	3/110 (2.7)	1/110 (0.9)	1/110 (0.9)	8/110 (7.3)	8/110 (7.3)
Adenocarcinoma	380	173/376 (46.0)	48/376 (12.8)	17/376 (4.5)	10/376 (2.7)	31/376 (8.2)	33/376 (8.8)	64/376 (17.0)
Squamous-cell carcinoma	243	90/239 (37.7)	35/239 (14.6)	9/239 (3.8)	16/239 (6.7)	26/239 (10.9)	32/239 (13.4)	31/239 (13.0)
Large-cell carcinoma	41	17/41 (41.5)	4/41 (9.8)	0/41	3/41 (7.3)	7/41 (17.1)	5/41 (12.2)	5/41 (12.2)
Non-small-cell carcinoma, other†	131	38/127 (29.9)	10/127 (7.9)	1/127 (0.8)	5/127 (3.9)	16/127 (12.6)	17/127 (13.4)	40/127 (31.5)
Small-cell carcinoma	137	8/133 (6.0)	1/133 (0.8)	5/133 (3.8)	3/133 (2.3)	17/133 (12.8)	27/133 (20.3)	72/133 (54.1)
Carcinoid	6	2/2 (100.0)	0/2	0/2	0/2	0/2	0/2	0/2
Unknown	12	0/12 (0.0)	0/12	0/12	0/12	1/12 (8.3)	0/12	0/12 (0.0)
Total	1060	416/1040 (40.0)	104/1040 (10.0)	35/1040 (3.4)	38/1040 (3.7)	99/1040 (9.5)	122/1040 (11.7)	226/1040 (21.7)
Radiography group								
Bronchioloalveolar carcinoma	35	17/35 (48.6)	1/35 (2.9)	1/35 (2.9)	2/35 (5.7)	3/35 (8.6)	5/35 (14.3)	6/35 (17.1)
Adenocarcinoma	328	83/326 (25.5)	42/326 (12.9)	17/326 (5.2)	12/326 (3.7)	29/326 (8.9)	29/326 (8.9)	114/326 (35.0)
Squamous-cell carcinoma	206	51/205 (24.9)	29/205 (14.1)	6/205 (2.9)	17/205 (8.3)	24/205 (11.7)	28/205 (13.7)	50/205 (24.4)
Large-cell carcinoma	43	9/42 (21.4)	5/42 (11.9)	1/42 (2.4)	1/42 (2.4)	10/42 (23.8)	7/42 (16.7)	9/42 (21.4)
Non-small-cell carcinoma or other†	158	20/155 (12.9)	9/155 (5.8)	3/155 (1.9)	5/155 (3.2)	24/155 (15.5)	24/155 (15.5)	70/155 (45.2)
Small-cell carcinoma	159	11/157 (7.0)	6/157 (3.8)	4/157 (2.5)	5/157 (3.2)	18/157 (11.5)	28/157 (17.8)	83/157 (54.1)
Carcinoid	2	2/2 (100.0)	0/2	0/2	0/2	0/2	0/2	0/2
Unknown	10	3/7 (42.9)	1/7 (14.3)	0/7	0/7	1/7 (14.3)	1/7 (14.3)	4/7 (57.1)
Total	941	196/929 (21.1)	93/929 (10.0)	32/929 (3.4)	42/929 (4.5)	109/929 (11.7)	122/929 (13.1)	335/929 (36.1)

* The denominators represent only cancers for which the stage was known.

† The 289 lung cancers in this category (in the two groups combined) included 28 adenocarcinomas, 6 sarcomatoid carcinomas, 55 unclassified carcinomas, 1 anaplastic-type carcinoma, 1 carcinosarcoma, and 198 coded only as "non-small-cell carcinoma."

NLST

Cause of death on the death certificate for CT- and control group

Table 7. Cause of Death on the Death Certificate, According to Screening Group.*

Cause of Death	Low-Dose CT Group	Radiography Group	Total
	number/total number (percent)		
Neoplasm of bronchus and lung†	427/1865 (22.9)	503/1991 (25.3)	930/3856 (24.1)
Other neoplasm	416/1865 (22.3)	442/1991 (22.2)	858/3856 (22.3)
Cardiovascular illness	486/1865 (26.1)	470/1991 (23.6)	956/3856 (24.8)
Respiratory illness	175/1865 (9.4)	226/1991 (11.4)	401/3856 (10.4)
Complications of medical or surgical care	12/1865 (0.6)	7/1991 (0.4)	19/3856 (0.5)
Other	349/1865 (18.7)	343/1991 (17.2)	692/3856 (17.9)

* A total of 3875 death certificates were received (1877 for participants in the low-dose CT group and 1998 for those in the radiography group), but the cause of death was unknown for 12 participants in the low-dose CT group and 7 in the radiography group. The denominators represent only the deaths for which the cause was known. Causes of death were categorized according to the following codes in the *International Classification of Diseases, 10th Revision (ICD-10)*: neoplasms of bronchus and lung, C33-C34; neoplasms other than bronchus and lung, C00-D48 (excluding C33 and C34); cardiovascular illness, I00-I99; respiratory illness, J00-J99; complications of medical or surgical care, S00-T17.8, T18-T90, and Y40-Y84; unknown, R96-R99 and death certificates without a coded cause of death; and other, all remaining codes.

† The number of deaths from neoplasm of the bronchus and lung in this table is not equal to the number of lung-cancer deaths in the lung-cancer mortality analysis. The lung-cancer deaths included here are those that were determined from information on the death certificate only (without review by the end-point verification team) and include deaths that occurred through December 31, 2009.

NEJM 2011; 365: 395-409

Limitations of NLST

No detailed analysis available on:

- **procedures for indeterminate findings**
- **sub group analysis of age, sex, race etc.**

Advantage of CT versus „no screening“ uncertain

Advantage of longer screening uncertain

Limitations of NLST

only (ex-)smokers 55-74 years \geq 30 pack years

→ Results transferable to other groups ?

Subjects in larger urban centers

→ Results transferable to subjects in rural areas etc. ?

Study conducted at large university hospitals

→ Results transferable to other institutions ?

Recommendations in Germany

Consensus statement of German Röntgen Society and German Society of chest medicine

Low-dose CT is acceptable in asymptomatic smokers if:

- active or ex-smoker
- 55- 74 years
- ≥ 30 pack years
- quality control

Recommendations in Germany

Quality control:

- informed consent
- examination technique
- radiation exposure
- interpretation of CT scans
- recommendations for further management

www.drg.de, Pneumologie 1-2011

Expert meeting at the German Federal office for Radiation Protection

- **representatives of German Roentgen Society, German society of chest physicians, national health insurances, private health insurances, Radiation Protection board, secretary of health, secretary of the environment etc.**
- **Project suggested**
 - **certified multidisciplinary lung cancer centers**
 - **CT funded by health insurances**
 - **smoking cessation, statistics, epidemiology etc. funded by secretaries of health and environment**

November 21st, 2011

Meeting of :

- **secretary of health**
- **secretary of environment**
- **health insurances**
- **radiation protection board**

25th scientific day of the Geneva pulmonary league, 17.11.2011

**Thank you for your
attention !**



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