Update on CT Lung Cancer Screening in Japan

Ryutaro Kakinuma, MD

National Cancer Center
Research Center for Cancer Prevention and Screening
Tokyo, Japan
Disclosure slide

• Nothing to Declare
Trends in Incidence of Lung Cancer According to Age 1975 - 2008

(c) Center for Cancer Control and Information Services, National Cancer Center
Trends in Lung Cancer Mortality According to Age 1958 - 2011

(c) Center for Cancer Control and Information Services, National Cancer Center
Trends in Lung Cancer Incidence by Histological Type in Osaka, Japan

Toyoda et al. Jpn J Clin Oncol 2008
Trends in the Number of Lung Cancer Incidence Per Year According to All Histological Type in Osaka, Japan 1975 - 2003

Cases

- Men
- Women

Toyoda et al. Jpn J Clin Oncol 2008
Trends in the Number of Lung Cancer Incidence Per Year According to Histological Type in Men 1975 - 2003

Adenocarcinoma
Squamous cell carcinoma
Small cell carcinoma
Others

Toyoda et al. Jpn J Clin Oncol 2008
Trends in the number of lung cancer incidence per year according to histological type in Women

1975 - 2003

- Adenocarcinoma
- Squamous cell carcinoma
- Small cell carcinoma
- Others

Toyoda et al. Jpn J Clin Oncol 2008
Experience in Reading of Chest CT

Single-Slice CT (Jpn) 1978

EMI CT scanner (UK) 1973
CT Lung Cancer Screening in Japan

1993 Anti-Lung Cancer Association, Tokyo
1994 Society of CT Screening
1998 Hitachi Project, Nawa, Chest 2002
2004 Research Center for Cancer Prevention and Screening, Tokyo
2009 Accreditation Council
2011 JECS Study (Randomized controlled trial)
CT Lung Cancer Screening in Japan

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2004 Research Center for Cancer Prevention and Screening, Tokyo
2009 Accreditation Council
2011 JECS Study (Randomized controlled trial)
Japanese Society of CT Screening

http://www.jscts.org/

Established in 1994

- Scientific Meeting
- Seminar
  - Technologist section
  - Emphysema section
  - Nodule Management section

- Journal
  (in Japanese)
Guidelines for Pulmonary Nodule Management

The size is the average of length and width of a nodule

- c.: component

Definition of Increase: GGO component > 15 mm, or solid component > 5 mm in maximal diameter

GGN: ground-glass nodule

GGO: ground-glass opacity

**An option exists to proceed to a workup if the size of the solid component is ≤5 mm, based on each hospital's decision tree.**

Figure 1. Guidelines for Pulmonary Nodules Management, Version 3 © The Japanese Society of CT Screening
Accreditation Council for Lung Cancer CT Screening

http://www.ct-kensin-nintei.jp/

Established in 2009

- **Accuracy Control**

- **Board-certified Doctors**

- **Board-certified Technologists**

- **In the near future, facilities will also be certified**
CT Lung Cancer Screening in Japan

- 1994 Society of CT Screening
- 1993 Anti-Lung Cancer Association, Tokyo
- 1998 Hitachi Project, Nawa, Chest 2002
- 2004 Research Center for Cancer Prevention and Screening, Tokyo
- 2009 Accreditation Council
- 2011 JECS Study (Randomized controlled trial)


1993 Anti-Lung Cancer Association, Tokyo

2011 JECS Study (Randomized controlled trial)
A decrease in lung cancer mortality was seen following the introduction of low-dose chest CT screening in Hitachi, Japan

Objective

To analyze the trend in lung cancer mortality in Hitachi city, which has a high participation rate in CT screening.
Numbers of Participants According to Gender and Number of Smokers (Between 1998 and 2009)

- Number of participants: 31,739
  - Men, 18,273
  - Women, 13,466

- Hitachi Health Care Center (1998-)
- Hitachi Medical Center (2001-)

- 40% of the population of Hitachi city (47% of men, 33% of women) screened using CT at least once as of 2009

Provided by Dr. Takeshi Nawa
Numbers of Participants According to Gender and Number of Smokers (Between 1998 and 2009)

• Number of participants: 31,739 (smokers, 14,661 [46%])
  Men, 18,273 (smokers, 13,456 [74%])
  Women, 13,466 (smokers, 1,115 [8%])

• Hitachi Health Care Center (1998-)
• Hitachi Medical Center (2001-)

• 40% of the population of Hitachi city (47% of men, 33% of women) screened using CT at least once as of 2009

Provided by Dr. Takeshi Nawa
Time Trend of Standardized Mortality Ratio and Standardized Incidence Rate

Standardized Incidence Rate per 100,000

1.2

1.0

0.8

0.6

0.4

0.2

0.0

1995~1999
2000~2004
2005~2009

Provided by Dr. Takeshi Nawa

Standardized Mortality Ratio

<table>
<thead>
<tr>
<th>Period</th>
<th>Value</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995~1999</td>
<td>0.95</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>2000~2004</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>2005~2009</td>
<td>0.76</td>
<td></td>
</tr>
</tbody>
</table>

Hitachi Health Care Center
Hitachi Medical Center
Time Trend of Standardized Mortality Ratio and Standardized Incidence Rate

Standardized Incidence Rate per 100,000

Provided by Dr. Takeshi Nawa

1995~1999: 0.95
2000~2004: 0.97
2005~2009: 0.76

P <0.001

2010~2013
CT Lung Cancer Screening in Japan

1993 Anti-Lung Cancer Association, Tokyo


2004 Research Center for Cancer Prevention and Screening, Tokyo

2009 Accreditation Council

2011 JECS Study (Randomized controlled trial)
Lung Cancer Screening in Nagano Prefecture

Provided by Dr. Yuichiro Maruyama
Komoro General Hospital, Nagano, Japan
Population-based Lung Cancer Screening in Nagano Prefecture
Dedicated Optical Fiber Network for CT Lung Cancer Screening by Japan Agriculture Nagano Medical Network

Provided by Dr. Yuichiro Maruyama
Mobile CT Unit in Nagano

4-Multislice CT (Hitachi Ltd.), 10mA, 0.8s/rotation, 8mAs, Reconstruction Interval 5mm

Provided by Dr. Yuichiro Maruyama
Implementation Status of Lung Cancer Screening in Nagano Prefecture’s 77 Municipalities

Provided by Dr. Yuichiro Maruyama
Implementation Status of Lung Cancer Screening in Nagano Prefecture’s 77 Municipalities

Provided by Dr. Yuichiro Maruyama
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RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer
(Pack-years <30)

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

50-64 years old
35,000 participants

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

Assuming 60% mortality reduction

50-64 years old
35,000 participants

Total cost €6,000,000/15y

Assuming 60% mortality reduction

5-10 years Screening

5-5 Year Follow-up and Comparison of mortality

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

- Assuming 60% mortality reduction
- 50-64 years old 35,000 participants
- Total cost €6,000,000 / 15y

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RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

- Assuming 60% mortality reduction
- 50-64 years old 35,000 participants
- Total cost €6,000,000 / 15y

CT Group: 2 CT + 8 Chest X-ray Screening

Randomization Stratified according to age, gender and smoking status

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

Assuming 60% mortality reduction

50-64 years old
35,000 participants

Total cost
€ 6,000,000 / 15y

CT Group

Randomization
Stratified according to age, gender and smoking status

CXR Group

Provided by Dr. Motoyasu Sagawa

 Assuming 60% mortality reduction

50-64 years old
35,000 participants

Randomization
Stratified according to age, gender and smoking status

CT Group

2 CT + 8 Chest X-ray Screening

CXR Group

1 CXR + 9 CXR Screening

Total cost
€ 6,000,000 / 15y

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)

Provided by Dr. Motoyasu Sagawa
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer (Pack-years <30)
RCT to Evaluate the Efficacy of Low-dose CT Screening for Lung Cancer
(Pack-years <30)

CT Group

2 CT + 8 Chest X-ray Screening

Annual check of contamination

CXR Group

1 CXR + 9 CXR Screening

5-Year Follow-up and Comparison of mortality
The Japanese Randomized Trial for Evaluating the Efficacy of Low-dose Thoracic CT Screening for Lung Cancer
JECS Study in 20 Municipalities

Municipality

Kagoshima: 5
Ishikawa: 5
Niigata: 2
Miyagi: 3
Fukui: 2
Okayama: 2
Kagawa: 1
Kagoshima: 5

Provided by Dr. Motoyasu Sagawa
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Research Center for Cancer Prevention and Screening
## Screening CT and Follow-Up CT Protocol In RCCPS

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Nodule or No Malignancy</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
</tr>
<tr>
<td>Solid Nodule ≥5mm &amp; &lt;10mm</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
</tr>
<tr>
<td>GGO Nodule ≥5mm &amp; &lt;15mm</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
</tr>
<tr>
<td>Any Nodule &lt;5mm</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
<td>⬝</td>
</tr>
</tbody>
</table>

- ⬝: Screening CT (€245 – Fee Paid by Individual)
- ⬝: Screening CT (€112 – Fee Paid by Individual)
- ⬝: (€112 – 30% by Individual & 70% by National Health Insurance)
- Optional Screening CT by Individual

**Note:**

- Smokers: including ex-smokers
- Never Smoker Adenocarcinoma Cases Based on Gender and Histopathology
### Protocols of CT Scan

<table>
<thead>
<tr>
<th>Date</th>
<th>Equipment</th>
<th>Protocol Description</th>
<th>Exposure Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004 Apr</td>
<td>16-row multidetector CT</td>
<td>Screening CT 15 mAs</td>
<td></td>
</tr>
<tr>
<td>2010 Jun</td>
<td>64-row MDCT</td>
<td>Exposure Control (compatible with 15 mAs)</td>
<td>5-10 mAs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-resolution CT 150 mAs (range of 4 cm)</td>
<td>5 mAs</td>
</tr>
<tr>
<td>2011 Nov</td>
<td></td>
<td>HRCT ≤100 mAs</td>
<td></td>
</tr>
</tbody>
</table>

**Adaptive Iterative Dose Reduction 3D**
Never-smokers 
Pack-years <30 
Pack-years ≥30

Participants According to Gender, Ager and Smoking Status Between 2004 and March 2012 (N=12122)

Male
n=7,299

Female
n=4,823

Between 2004 and March 2012 (N=12122)
### Lung Cancers According to Gender, Diameter, Histology and Smoking Status

<table>
<thead>
<tr>
<th>Cases /Lesions §</th>
<th>Never-Smoker</th>
<th>Pack-years &lt;30</th>
<th>Pack-years ≥30</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>16/16</td>
<td>22/22</td>
<td>32/36</td>
<td>70/74</td>
</tr>
<tr>
<td>Female</td>
<td>50/59</td>
<td>10/12</td>
<td>2/2</td>
<td>62/73</td>
</tr>
<tr>
<td>Maximal Diameter (cm)*</td>
<td>1.5 ± 0.7</td>
<td>1.4 ± 0.7</td>
<td>1.5 ± 0.6</td>
<td>1.5 ± 0.7</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
<td>132/147</td>
</tr>
<tr>
<td>Adeno</td>
<td>73 (97%)</td>
<td>31 (91%)</td>
<td>28 (74%)</td>
<td>132</td>
</tr>
<tr>
<td>Sq</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Small</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Adsq</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>NSCLC</td>
<td>*Mean 0 ± SD</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
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</table>

Lesions §: nodules + other lesions
Lung Cancers According to Gender, Diameter, Histology and Smoking Status

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| Maximal Diameter (cm)* | 1.5 ± 0.7 | 1.4 ± 0.7 | 1.5 ± 0.6 | 1.5 ± 0.7 |

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<tr>
<td></td>
<td>Adsq</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Carcinoid</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
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<tr>
<td></td>
<td>NSCLC</td>
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Lesions§: nodules + other lesions
# Lung Cancers According to Gender, Diameter, Histology and Smoking Status

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<td>*Mean 0 ± SD</td>
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Lesions §: nodules + other lesions
Lung Cancers According to Histology and Smoking Status

Never-smokers
n=75

Pack-years <30
n=34

Pack-years ≥30
n=38

- Ad 73(97%)
- Cd 2(3%)

- Ad 31(91%)
- Adsq 1(3%)
- Sm 2(5%)

- Ad 28(74%)
- Sq 8(21%)
- Sm 2(5%)

- Never-smokers n=75
- Pack-years <30 n=34
- Pack-years ≥30 n=38

Ad = Adenocarcinoma
Sm = Small Cell Lung Cancer
Sq = Squamous Cell
Adsq = Adenocarcinoma Sq
Cd = Carcinoid
NSCLC = Non-Small Cell Lung Cancer
Lung Cancers According to Stages and Smoking Status

Never-smokers
n=75

- IA 92%
- IB 5%
- IIIB 3%

Pack-years <30
n=34

- IA 83%
- IB 9%
- IIA 3%
- IIIB 3%

Pack-years ≥30
n=38

- IA 79%
- IB 11%
- IIA 3%
- IIIB 3%
- IIIA 5%

Legend:
- Red: IA
- Blue: IB
- Yellow: IIA
- Black: IIIB
- Gray: IIIA
- Green: IIIB
## Lung Cancer Cases According to Gender and Smoking Status

$P < 0.0001$

<table>
<thead>
<tr>
<th></th>
<th>Never-smokers</th>
<th>Smokers*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>16</td>
<td>54</td>
<td>70</td>
</tr>
<tr>
<td>Women</td>
<td>50</td>
<td>12</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
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<td>66</td>
<td>132</td>
</tr>
</tbody>
</table>

* Smokers: including ex-smokers
Lung Cancer Cases According to Gender and Smoking Status

\[ P < 0.0001 \]

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* Smokers: including ex-smokers
Adenocarcinoma Cases
According to Smoking Status and Histopathology

<table>
<thead>
<tr>
<th></th>
<th>AIS+MIA</th>
<th>Invasive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never-smokers</td>
<td>42</td>
<td>23</td>
<td>65</td>
</tr>
<tr>
<td>Smokers*</td>
<td>29</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>47</td>
<td>118</td>
</tr>
</tbody>
</table>

Smokers: including ex-smokers
AIS: adenocarcinoma in situ
MIA: minimally invasive adenocarcinoma
Invasive: invasive adenocarcinoma

$P = 0.274$
### Adenocarcinoma Cases According to Smoking Status and Histopathology

\[ P = 0.274 \]

<table>
<thead>
<tr>
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Smokers: including ex-smokers  
AIS: adenocarcinoma in situ  
MIA: minimally invasive adenocarcinoma  
Invasive: invasive adenocarcinoma
Never-smoker Adenocarcinoma Cases According to Gender and Histopathology

\[ P < 0.05 \]

<table>
<thead>
<tr>
<th></th>
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<th>Invasive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>7</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Women</td>
<td>35</td>
<td>14</td>
<td>49</td>
</tr>
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Smokers: including ex-smokers
AIS: adenocarcinoma in situ
MIA: minimally invasive adenocarcinoma
Invasive: invasive adenocarcinoma
Lung Nodule Database

Division of Epidemiology and Prevention
Nodule Epidemiology

Outpatient Clinic
Natural History of Subsolid Nodules

Solid Nodule Mapping

Solid Nodule Follow-up System

Research Center
Division of Genome Biology
SNP of Participants with Subsolid Nodules

Solid Nodule Mapping