Radon and risk of cancer

Updated results of the German uranium miners cohort study, 1946-2003

KREUZER M, WALSH L, SCHNELZER M, TSCHENSE A, DUFYE F, GROSCHE B

Federal Office for Radiation Protection, Department Radiation Protection and Health, Munich/Germany, mkreuzer@bfs.de
Previous knowledge

• 1988, Radon classified a known human pulmonary carcinogen (IARC)
  → causal for lung cancer
  → no clear evidence for other cancers

• Major recipient of the radon dose is the lung, doses to other organs about 1,000 times lower

• Evidence mainly based on results of a pooled miner study (heterogeneity !!) or small single studies (low statistical power)
German cohort study

- 59,000 male former employees of the uranium mining company WISMUT

Objectives:
- Risk of death from extrapulmonary cancers by radon
- Lung cancer and radon: exposure-response-relationship, influence of effect modifiers
Wismut uranium mining company

- Location: East Germany
- Operation period: 1946-1990
- Third largest uranium producer
- ≈ 400,000 employees
- Early years: high exposure to dust and radiation
## Cohort description, 1946-2003

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of miners</td>
<td>58,987</td>
</tr>
<tr>
<td>Person-Years</td>
<td>1,997,041</td>
</tr>
<tr>
<td>Mean duration of follow-up</td>
<td>34 years</td>
</tr>
<tr>
<td>Loss to Follow-Up</td>
<td>4.7 %</td>
</tr>
<tr>
<td>Deceased cohort members</td>
<td>20,920</td>
</tr>
<tr>
<td>Cause of death available</td>
<td>19,588 (93.6 %)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>3,016</td>
</tr>
<tr>
<td>Cancers other than lung</td>
<td>3,355</td>
</tr>
</tbody>
</table>
Assessment of radon exposure

- Detailed job-exposure-matrix (JEM)
- Radon values in Working Level Months (WLM) for each
  - calendar year (1946 - 1989)
  - type of job (≈ 900)
  - place of work (surface/underground/milling/open pit mining)
  - mining facility (≈ 40)
- 1955-1989: Estimates based on area measurements
  1946-1954: no radon measurements available (expert rating)
Mean annual exposure to radon in WLM among exposed cohort members

Ever exposed: 50,773 (86%)
Information on other risk factors

Job-exposure-matrix for

- External gamma radiation \([\text{mSv}]\)
- Longlived radionuclides \([\text{kBq/h/m}^3]\)
- Arsenic \([\mu g/m^3 \times \text{ys}]\)
- Fine/silica dust \([\text{mg/m}^3 \times \text{ys}]\)

Smoking (from a nested ca-co study on lung cancer)
Statistical Methods

• External comparisons (1960-2003)
  - Ratio of observed to expected deaths (SMR= O/E) based on national mortality rates adjusted for age, calendar year
  - corrected for missing causes of death

• Internal poisson regression (1946-2003)
  - Categorical analysis
  - Linear regression model → Excess Relative Risk (ERR) per unit of exposure
  - 0-year lag (leukemia), 5-year lag for all other cancer sites
External comparisons (1960-2003)

*Ratio of observed (O) to expected (E) deaths and 95% CI for specific cancer sites*

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Deaths</th>
<th>O*/E</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O</td>
<td>O*</td>
<td>E</td>
</tr>
<tr>
<td>Lung</td>
<td>2,999</td>
<td>3,180</td>
<td>1,567.5</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>3,340</td>
<td>3,543</td>
<td>3,488.2</td>
</tr>
</tbody>
</table>

*O* is number of observed deaths (O) corrected for missing causes of deaths

*Kreuzer et al., Br J Cancer 2008*
Ratio of observed to expected deaths (O/E) and 95% CI for specific cancer sites

Kreuzer et al., Br J Cancer 2008
Internal Poisson Regression
Relative risk by cum. radon exposure

Extrapulmonary cancers (n = 3,355) Lung cancer (n = 3,016)

ERR/WLM = 0.014%

ERR/WLM = 0.19%
Excess Relative Risk per 100 WLM and 95% CI for cancer sites with 35+ deaths
## Lung cancer

### Modifying factors

- **Wismut**
  - 3,016 cases
  - 2 Mio person-years

- **11 miner studies**
  - 2,705 cases
  - 0.9 Mio person-years
  - *(BEIR VI, 1999)*

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Wismut</th>
<th>BEIR VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERR/WLM %</td>
<td>0.6 (0.2-0.9)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time-since exposure (ys)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5 - 14</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>15 - 24</td>
<td>0.7</td>
<td>(0.4-1.1)</td>
</tr>
<tr>
<td>25 - 34</td>
<td>0.5</td>
<td>(0.3-0.7)</td>
</tr>
<tr>
<td>35+</td>
<td>0.4</td>
<td>(0.2-0.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Attained age (ys)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;55</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>55 - 64</td>
<td>0.5</td>
<td>(0.3-0.7)</td>
</tr>
<tr>
<td>65 - 74</td>
<td>0.3</td>
<td>(0.2-0.5)</td>
</tr>
<tr>
<td>75+</td>
<td>0.3</td>
<td>(0.2-0.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure rate (WL)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td>4.6</td>
<td>(2.5-8.7)</td>
</tr>
<tr>
<td>0.5 - 1.0</td>
<td>2.8</td>
<td>(1.6-5.1)</td>
</tr>
<tr>
<td>1.0 - 3.0</td>
<td>2.2</td>
<td>(1.6-3.2)</td>
</tr>
<tr>
<td>3.0 - 5.0</td>
<td>2.0</td>
<td>(1.4-2.8)</td>
</tr>
<tr>
<td>5.0 - 15.0</td>
<td>1.7</td>
<td>(1.2-2.4)</td>
</tr>
<tr>
<td>15+</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>
Summary: Lung cancer

• Approximately linear increase in risk with cumulative radon exposure

• ERR/WLM decreases with increasing time since exposure, increasing attained age and increasing exposure rate

• No major confounding by
  - gamma radiation, long-lived radionuclides, arsenic, dust
  - smoking (results by nested case-control studies)

• Results largely compatible with that of the pooled 11 miners studies, but risk estimates slightly lower
Summary: Extrapulmonary cancers

• Evidence for a positive relationship between radon and risk of extrapulmonary cancers combined

• Significant excess only present above 1,000 WLM

• Positive ERR/WLM for 15 out of 18 cancer sites
  - non-significant, or insignificant after adjustment for confounder (stomach)

• Highest risk for cancers of the pharynx, tongue/mouth, liver

⇒ Compatible with dosimetric calculations for organ doses
Strengths and limitations

• Strengths
  - Large number of cancer deaths, wide exposure range
  - Internal comparison group
  - Information on potential confounders (gamma-radiation, LRN, arsenic, fine and silica dust) available

• Potential limitations
  - Accuracy of cause of death
  - Uncertainty of exposure to radon in the early years
  - Missing information on other potential confounders
Conclusion

• Previous radon-related lung cancer risk estimates and temporal effect modifiers largely confirmed

• Some evidence for an increased risk of extra-pulmonary cancers due to radon, but chance and confounding by unconsidered factors cannot be excluded (organ doses)

• Risk for extrapulmonary cancers is – if not a chance finding – appreciably lower than for lung cancer
Outlook

Opening of the dataset of the WISMut cohort for interested scientists ⇒ information on how to send proposals will follow in June 2009

see: http://www.bfs.de/de/bfs/forschung/Wismut

Setup of a biobank from German uranium miners ⇒ see poster GOMOLKA et al.