Lung cancer risk from radon and radon progeny.

Epidemiological studies

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What about radon?

- Radon is a **radioactive gas of natural origin**
- It comes from the disintegration of uranium from the soil
- It is present **everywhere** at the surface of the earth
- It is colorless and odorless
- It concentrates in **confined places**
- It is a emitter of **α particles**
- **Chronic exposure**, over the life span, for the whole population
Mechanisms of action

Inhalation of radon
- Internal exposure to radon and its short-lived progeny

Distribution of radionuclides in the whole body, mainly in the lungs → irradiation of bronchial epithelium due to radon progenies

Dosimetric models show that:
- > 90% of the received dose is delivered to the lung
- Dose delivered to the other organs ≈ 100 fold lower
- But a part of this dose can be delivered to the red bone marrow (organ at risk for leukemia)

In 1988, the International Agency for Research on Cancer (CIRC-OMS) classified radon as a known pulmonary carcinogen in humans
- Experimental studies in vivo and in vitro: inhalation of radon for three species of animals (rats, hamsters and dogs)
- Results from epidemiological studies among miners (uranium, tin, fluorspar)
Historic of knowledge

- 1567: Unusual mortality from respiratory diseases among young miners (*Mala Metallorum*, Paracelse)
- 1879: Diseases identified as cancer of bronchus
- 1898: Discovery of radium (Curie)
- 1924: First mention as occupational disease
- 1940: Inhalation of radon presented as possible (Planck)
- 1946: Beginning of intensive extraction of uranium in France
- 1956: First measures of radioprotection in France
- 1960: Launch of the first epidemiological studies among miners
- 1988: Radon classified as a known pulmonary carcinogen in humans
- 1990: Launch of the first epidemiological studies in general population
Epidemiological studies among uranium miners
Studies among miners

Epidemiological studies among miners:
- **Uranium**
  - Canada (Ontario, Port Radium, Beaverlodge)
  - United States (Colorado, Nuevo Mexico)
  - Czech Republic, France, Germany, Australia
- **Fluorspar** - Canada (Newfoundland)
- **Tin** - China, UK, Czech Republic
- **Iron** - Sweden

Miners: relevant population
- Chronic exposure to Ionizing Radiations (IR), especially to radon
- Exposure to low / relatively high doses (according to cohort/period)
- Good quality of follow-up: mortality, administrative, dosimetric data

Contribution in public health and radioprotection
- Refine knowledges on health risks due to IR for low doses exposure (to provide information allowing to describe risks associated with radon exposure)
- Contribute to improve norms of radioprotection
- Contribute to assess the risks associated with indoor radon
- **Pooled analysis of 11 underground miner cohort studies (BEIR VI, 1999)**

<table>
<thead>
<tr>
<th>Place</th>
<th>Country</th>
<th>Type of mine</th>
<th>Follow-up period</th>
<th>N miners</th>
<th>Person-Years*</th>
<th>N lung cancer</th>
<th>Cumulative expo (WLM)</th>
<th>ERR / 100 WLM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yunnan</td>
<td>China</td>
<td>Tin</td>
<td>1976-1987</td>
<td>13,649</td>
<td>134,842</td>
<td>936</td>
<td>286.0</td>
<td>0.17</td>
</tr>
<tr>
<td>W-Bohemia</td>
<td>Czech Rep</td>
<td>Uranium</td>
<td>1952-1990</td>
<td>4,320</td>
<td>102,650</td>
<td>701</td>
<td>196.8</td>
<td>0.67</td>
</tr>
<tr>
<td>Colorado</td>
<td>US</td>
<td>Uranium</td>
<td>1950-1990</td>
<td>3,347</td>
<td>79,556</td>
<td>334</td>
<td>578.6</td>
<td>0.44</td>
</tr>
<tr>
<td>Ontario</td>
<td>Canada</td>
<td>Uranium</td>
<td>1955-1986</td>
<td>21,346</td>
<td>300,608</td>
<td>285</td>
<td>31.0</td>
<td>0.82</td>
</tr>
<tr>
<td>Newfound</td>
<td>Canada</td>
<td>Fluorspar</td>
<td>1950-1984</td>
<td>1,751</td>
<td>33,795</td>
<td>112</td>
<td>388.4</td>
<td>0.82</td>
</tr>
<tr>
<td>Malmberget</td>
<td>Sweden</td>
<td>Iron</td>
<td>1951-1991</td>
<td>1,294</td>
<td>32,452</td>
<td>79</td>
<td>80.6</td>
<td>1.04</td>
</tr>
<tr>
<td>New Mexico</td>
<td>US</td>
<td>Uranium</td>
<td>1943-1985</td>
<td>3,457</td>
<td>46,800</td>
<td>68</td>
<td>110.9</td>
<td>1.58</td>
</tr>
<tr>
<td>Beaverlodge</td>
<td>Canada</td>
<td>Uranium</td>
<td>1950-1980</td>
<td>6,895</td>
<td>67,080</td>
<td>56</td>
<td>21.2</td>
<td>2.33</td>
</tr>
<tr>
<td>Port Radium</td>
<td>Canada</td>
<td>Uranium</td>
<td>1950-1980</td>
<td>1,420</td>
<td>31,454</td>
<td>39</td>
<td>243.0</td>
<td>0.24</td>
</tr>
<tr>
<td>Radium Hill</td>
<td>Australia</td>
<td>Uranium</td>
<td>1948-1987</td>
<td>1,457</td>
<td>24,138</td>
<td>31</td>
<td>7.6</td>
<td>2.75</td>
</tr>
<tr>
<td>CEA-COGEMA</td>
<td>France</td>
<td>Uranium</td>
<td>1948-1986</td>
<td>1,769</td>
<td>39,172</td>
<td>45</td>
<td>59.4</td>
<td>0.51</td>
</tr>
</tbody>
</table>

| TOTAL     |              |              |                  | 60,606   | 888,906       | 2,674         | 164.4                | 0.59          |

* Among exposed.  WLM: Working Level Month.  ERR: Excess Relative Risk.  SE: multiplicative Standard Error

- ↑ risk of lung cancer with cumulative radon exposure
- Modifying effect of age at exposure (↓) and time since exposure (↓)
- Sub-multiplicative interaction between radon and smoking
- No evidence of other health effect associated with radon exposure
The French cohort of uranium miners: Design of the study

- Miner employed by the CEA-COGEMA company (AREVA since 2006)
- Male
- Employed for at least one year between 1946 and 1990
  (AREVA administrative database)

Possible outcomes:
- Alive
- Deceased
- Lost to follow-up
- Aged more than 85 y

Vital status from National database (RNIPP)

Population

Exposed

Non exposed

Cohort 5086 individuals

Follow-up

Exposed

Non exposed

Occupational history

(AREVA administrative database)

Annual occupational exposures

(AREVA, ALGADE)

Causes of death

from National database (CépiDC)
And Occupational medical service of AREVA (complementary)
French cohort: Assessment of IR exposures

- Setting up of radiation protection measures
- Retrospective reconstruction by experts
- Individual recording from ambient measurements
- Individual measurements
Radon exposure

<table>
<thead>
<tr>
<th></th>
<th>Mean (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual exposure &lt; 1956 (WLM)</td>
<td>21.3 (0.1 - 99.0)</td>
</tr>
<tr>
<td>Annual exposure ≥ 1956 (WLM)</td>
<td>1.7 (0.1 - 15.3)</td>
</tr>
<tr>
<td>Cumulative exposure (WLM)</td>
<td>36.6 (0.1 - 960.1)</td>
</tr>
<tr>
<td>Duration of exposure (year)</td>
<td>11.8 (1.0 - 37.0)</td>
</tr>
</tbody>
</table>

French cohort: Assessment of IR exposures

Distribution of the number of exposed miners and of Radon exposure per year

1956: forced ventilation
Radon exposure and lung cancer risk:

Main results among uranium miner studies

- Excess of mortality from lung cancer
- Radon exposure - lung cancer risk relationship
  - Persistence among miners with low exposure
  - Persistence after taking into account for measurement errors
- Multi IR Exposure
  - Persistence of the risk associated with radon exposure after taking into account for other IR exposure
- Organ doses
  - Main contribution of radon to the lung dose
- Smoking habits
  - Persistence of taking into account smoking habits
- Modifying factors
  - Decrease of the risk with the time since exposure
Mortality Analyses

Standardized Mortality Ratio (SMR)

To assess mortality risks in the cohort in comparison to a reference (general population)

\[
SMR = \frac{\text{number of observed deaths for the cohort}}{\text{number of expected deaths for the cohort}}
\]

Example of the French cohort

- Whole cohort
  N=5,086; follow-up 1946-2007
  N cases=211

Significant increase of mortality from lung cancer

\[
SMR = 1.34 \quad [95\% \text{ CI}: 1.16-1.53]
\]
Relationship between Radon exposure - Lung cancer Risk

Risk assessment: Excess Relative Risk (ERR) - Linear model

- $RR(t,w)$: Relative Risk of death from lung cancer for a cumulative exposure to radon $w$ at a $t$ moment compared to the baseline risk.

$$RR(t,w) = 1 + \beta w(t)$$

- $\beta$: Excess of Relative Risk (ERR)
- $w(t)$: Cumulative exposure at $t$ time
- Poisson Regression
- 5-years lag

Example of the French cohort

- Whole cohort
  N=5,086; follow-up 1946-2007
  N cases=211
- ERR for lung cancer death:
  $$ERR/100 \text{ WLM} = 0.71 \ [95\% CI: 0.31-1.30\%]$$
- Interpretation
  71% in the RR lung cancer death

[Estelle RAGE, EURADOS Winter School - Lodz, Poland - 14 February 2019]
Radon exposure - Lung cancer Risk relationship

Low level of radon exposure

- Example of the French cohort
  - + 1955 cohort
    N=3,377; N cases = 94; follow-up 1956-2007;
  - ERR/100 WLM = 2.42 [0.09-5.14]
    [Rage et al, Int Arch Occup Environ Health 2015]

- Example of the German Wismut cohort
  - Whole cohort  N=58,987; N cases = 3,016
    follow-up 1946-2003;
    [Walsh et al, Radiat Res 2010]
  - + 1960 sub-cohort  N=26,766; N cases = 334
    follow-up 1960-2008;
    [Kreuzer et al, Br J Cancer 2015]

Excess Relative Risk for lung cancer remained significant at low exposures
Multiple exposure to ionizing radiation (1)

IR exposure in uranium mines:
- Radon, external gamma ray, long-lived radionuclides (LLR)
- Some of uranium miner cohorts have assessed radon and other IR exposures

Relationship between Radon exposure - Lung cancer risk

- French +1955 sub-cohort (N = 3377 miners / N = 94 cases of lung cancer)

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>Type of exposure</th>
<th>ERR (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>Radon (WLM)</td>
<td>2.42</td>
<td>(0.90 - 5.14)</td>
</tr>
<tr>
<td></td>
<td>Gamma (mGy)</td>
<td>0.74</td>
<td>(0.23 - 1.73)</td>
</tr>
<tr>
<td></td>
<td>LLR (Bq.m⁻³ h)</td>
<td>0.032</td>
<td>(0.009 - 0.073)</td>
</tr>
</tbody>
</table>

→ Significant ERR associated with radon, but also to LLR and gamma separately
→ But models including all exposures together could not be fitted

- Limitation due to:
  - high collinearity between exposures (correlation coefficients r > 0.70)
  - size of the cohort and a lack of statistical power

[Rage et al, Int Arch Occup Environ Health 2015]
Multiple exposure to ionizing radiation (2)

Relationship between Radon exposure - Lung cancer risk

- German +1960 sub-cohort (N = 26,766 miners / N = 334 cases of lung cancer)

<table>
<thead>
<tr>
<th></th>
<th>ERR /WLM)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude model</td>
<td>0.013</td>
<td>(0.007 - 0.021)</td>
</tr>
<tr>
<td>Separate adjustment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>for</td>
<td></td>
<td></td>
</tr>
<tr>
<td>external gamma rays</td>
<td>0.011</td>
<td>(0.004 - 0.019)</td>
</tr>
<tr>
<td>LLR</td>
<td>0.014</td>
<td>(0.007 - 0.022)</td>
</tr>
</tbody>
</table>

- Sufficient statistical power to adjust for other IR exposures
- Significant ERR associated with radon remains after considering other IR exposures

[Kreuzer et al, Br J Cancer 2015]
Dosimetric approach (1)

- European collaborative Alpha-Risk Project (2005-2009)
  - Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures:
    - Epidemiological studies: French, Czech, German cohorts of U miners
    - Calculation of doses to target organs

- Alpha Miner Software
  - Dosimetric Model (Human Respiratory Tract Model - ICRP Publication 66)
  - Parameters of the aerosol
  - Definition of different categories of job, mechanisation, type of mines, ...
    → Different scenarios of exposure and different levels of physical activity
      

- Calculation of lung doses
  - Absorbed doses (in gray) for each miner and for each year
### Distribution of the cumulative absorbed lung doses

<table>
<thead>
<tr>
<th></th>
<th>French cohort</th>
<th>Czech cohort</th>
<th>German cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>N miners</td>
<td>3,271</td>
<td>9,979</td>
<td>29,086</td>
</tr>
<tr>
<td>Mean (min-max) (in mGy)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non Alpha</td>
<td>55.97 (0.01-472.36)</td>
<td>54.29 (0.66-338.42)</td>
<td>39.52 (0.00-709.90)</td>
</tr>
<tr>
<td>Alpha</td>
<td>77.92 (0-700.00)</td>
<td>373.54 (0.36-4550.44)</td>
<td>272.73 (0.01-7282.36)</td>
</tr>
</tbody>
</table>

→ In terms of dose contribution:

<table>
<thead>
<tr>
<th>Contribution of:</th>
<th>French cohort</th>
<th>Czech cohort</th>
<th>German cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha dose to the total lung dose</td>
<td>58 %</td>
<td>87%</td>
<td>87%</td>
</tr>
</tbody>
</table>
 Dosimetric approach (3)

Relationship between Lung Doses - Lung cancer Risk

---

<table>
<thead>
<tr>
<th>Alpha Risk Joint cohort (n = 1444 cases)</th>
<th>Separate regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERR / Sv</td>
</tr>
<tr>
<td>Total dose</td>
<td>0.07</td>
</tr>
<tr>
<td>Non alpha</td>
<td>15.70</td>
</tr>
<tr>
<td>Rn gas + progeny</td>
<td>0.07</td>
</tr>
<tr>
<td>LLR alpha</td>
<td>9.38</td>
</tr>
</tbody>
</table>

- Significant association with **Total and Non-Alpha lung doses** in separate models
- Significant association with **Alpha component**, but large uncertainties on estimates for LLR
- In multivariate analyses, **ERR remained significant for Rn gas + progeny and LLR alpha**, whereas significant association with non alpha lung dose did not remain.

Modifying factors of the exposure-risk relationship

Decrease of lung cancer risk
- with Time since exposure
- with Age at exposure (attained age)

Scenario: 2 WLM per y from age 18 to 64

[Beir V1 model (1999)]
[Czech-French model (2008)]

[Tomasek et al., Radiat Res 2008]
Impact of Smoking habits

Joint European cohort

Nested case-control study
- France
- Germany
- Czech Republic

1,236 cases (lung cancer)
2,678 controls

- Significant Relationship between Radon exposure - Lung cancer risk remained after taking into account smoking habits
- The risk increased in each category of smoking
- Sub-multiplicative interaction

[Leuraud et al. Radiat Res 2011]
Epidemiological studies in the general population
### Indoor radon and lung cancer: case-control studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of publication</th>
<th>Country</th>
<th>Case/controls</th>
<th>RR per 100 Bq.m⁻³</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schoenberg</td>
<td>1990</td>
<td>USA (New Jersey)</td>
<td>480/442</td>
<td>1,49</td>
<td>0,89 - 1,89</td>
</tr>
<tr>
<td>Blot</td>
<td>1990</td>
<td>China</td>
<td>308/356</td>
<td>0,95</td>
<td>* - 1,08</td>
</tr>
<tr>
<td>Pershagen</td>
<td>1992</td>
<td>Sweden</td>
<td>201/378</td>
<td>1,16</td>
<td>0,89 - 1,92</td>
</tr>
<tr>
<td>Pershagen</td>
<td>1994</td>
<td>Sweden</td>
<td>1 281/2 576</td>
<td>1,10</td>
<td>1,01 - 1,22</td>
</tr>
<tr>
<td>Letourneau</td>
<td>1994</td>
<td>Canada</td>
<td>738/378</td>
<td>0,98</td>
<td>0,87 - 1,27</td>
</tr>
<tr>
<td>Alavanja</td>
<td>1994</td>
<td>USA (Missouri)</td>
<td>538/1 183</td>
<td>1,08</td>
<td>0,95 - 1,24</td>
</tr>
<tr>
<td>Auvinen</td>
<td>1996</td>
<td>Finland</td>
<td>517/517</td>
<td>1,11</td>
<td>0,94 - 1,31</td>
</tr>
<tr>
<td>Ruosteenoja</td>
<td>1996</td>
<td>Finland</td>
<td>164/331</td>
<td>1,80</td>
<td>0,90 - 3,50</td>
</tr>
<tr>
<td>Darby</td>
<td>1998</td>
<td>UK</td>
<td>982/3 185</td>
<td>1,08</td>
<td>097 - 1,20</td>
</tr>
<tr>
<td>Alavanja</td>
<td>1999</td>
<td>USA (Missouri)</td>
<td>247/299</td>
<td>0,85</td>
<td>0,73 - 1,00</td>
</tr>
<tr>
<td>Field</td>
<td>2000</td>
<td>USA (Iowa)</td>
<td>413/614</td>
<td>1,24</td>
<td>0,95 - 1,92</td>
</tr>
<tr>
<td>Kreienbrock</td>
<td>2001</td>
<td>Germany</td>
<td>1 449/2 297</td>
<td>0,97</td>
<td>0,82 - 1,14</td>
</tr>
<tr>
<td>Pisa</td>
<td>2001</td>
<td>Italy</td>
<td>138/291</td>
<td>1,40</td>
<td>0,30 - 6,66</td>
</tr>
<tr>
<td>Lagarde</td>
<td>2001</td>
<td>Sweden</td>
<td>436/1 649</td>
<td>1,10</td>
<td>0,96 - 1,38</td>
</tr>
<tr>
<td>Wang</td>
<td>2002</td>
<td>China</td>
<td>763/1 659</td>
<td>1,19</td>
<td>1,05 - 1,47</td>
</tr>
<tr>
<td>Lagarde</td>
<td>2002</td>
<td>Sweden</td>
<td>110/231</td>
<td>1,33</td>
<td>0,88 - 3,00</td>
</tr>
<tr>
<td>Kreuzer</td>
<td>2003</td>
<td>Germany</td>
<td>1 192/1 640</td>
<td>1,75</td>
<td>0,96 - 5,30</td>
</tr>
<tr>
<td>Baysson</td>
<td>2004</td>
<td>France</td>
<td>486/984</td>
<td>1,04</td>
<td>0,99 - 1,11</td>
</tr>
<tr>
<td>Bochicchio</td>
<td>2005</td>
<td>Italy</td>
<td>384/404</td>
<td>1,14</td>
<td>0,89 - 1,46</td>
</tr>
<tr>
<td>Wichmann</td>
<td>2005</td>
<td>Germany</td>
<td>2 963/4 232</td>
<td>1,10</td>
<td>0,98 - 1,30</td>
</tr>
<tr>
<td>Sandler</td>
<td>2006</td>
<td>USA (Connecticut, Utah)</td>
<td>1 474/1 811</td>
<td>1,002</td>
<td>0,79 - 1,21</td>
</tr>
<tr>
<td>Wilcox</td>
<td>2008</td>
<td>USA (New Jersey)</td>
<td>561/740</td>
<td>1,05</td>
<td>0,86 - 1,56</td>
</tr>
<tr>
<td>Turner</td>
<td>2011</td>
<td>USA</td>
<td>3 493/811 961</td>
<td>1,15</td>
<td>1,01 - 1,31</td>
</tr>
<tr>
<td>Brauner</td>
<td>2012</td>
<td>Danemark</td>
<td>589/52 692</td>
<td>1,04</td>
<td>0,69 - 1,56</td>
</tr>
</tbody>
</table>
**European case-control study (1/3)**

### Three joint studies

<table>
<thead>
<tr>
<th></th>
<th>Studies n</th>
<th>Cases n</th>
<th>Controls n</th>
<th>RR / 100 Bq.m⁻³ (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>Darby 2005</td>
<td>13</td>
<td>7 148</td>
<td>14 208</td>
</tr>
<tr>
<td>North American</td>
<td>Krewski 2006</td>
<td>7</td>
<td>3 662</td>
<td>4 966</td>
</tr>
<tr>
<td>Chinese</td>
<td>Lubin 2004</td>
<td>2</td>
<td>1 050</td>
<td>1 995</td>
</tr>
</tbody>
</table>

- Increase in the RR about 10% per 100 Bq.m⁻³

**Joint European study in general population**

- 13 studies in 9 countries: Belgium, Czech Republic, Finland, France, Germany, Great-Britain, Italia, Spain, Sweden

- **Standardized protocol:**
  - Identical inclusion criterias
  - Common questionnaire
  - Reconstruction of indoor exposure for 30 years
  - Inter-comparison of the methods of measure
  - Joint analysis of individual data

- Population: 7,148 cases / 14,208 controls
European case-control study (2/3)

- Indoor mean radon concentration
  - Cases = 104 Bq.m⁻³
  - Controls = 97 Bq.m⁻³

- Risk of lung cancer with radon concentration
  - \( RR = 1.08 \text{ per } 100 \text{ Bq.m}^{-3} \) [1.03 - 1.16]
  - \( RR = 1.16 \text{ per } 100 \text{ Bq.m}^{-3} \) [1.05 - 1.31]
  - After consideration of uncertainties related to estimations of radon concentration

- Significant relationship for exposures < 200 Bq.m⁻³

[Darby et al. BMJ 2005]
European case-control study (3/3)

- Joint effect of radon and smoking

Significant relationship with radon among smokers and non-smokers

[Darby et al. Scand J Work Environ Health 2006]
### Population attributable fraction of lung cancer mortality from residential radon

**[Gaskin et al. Environ Health Physics 2018]**

<table>
<thead>
<tr>
<th>Countries</th>
<th>Radon exposure (Bq.m&lt;sup&gt;-3&lt;/sup&gt;)</th>
<th>Attributable fraction for lung cancer from residential radon (%)</th>
<th>BEIR VI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Hunter&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Kreuzer&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Krewski&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Darby&lt;sup&gt;e&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Cuba</td>
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<td>1,6</td>
<td>1,2</td>
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<td>3,7</td>
<td>3,5</td>
<td>2,1</td>
<td>1,6</td>
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<td>5,8</td>
<td>5,4</td>
<td>4,1</td>
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<td>6,4</td>
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<td>13,1</td>
<td>12,4</td>
<td>9,5</td>
<td>7,2</td>
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<td>16,3</td>
<td>15,5</td>
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<td>11,2</td>
<td>8,6</td>
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<td>17,8</td>
<td>16,9</td>
<td>13,0</td>
<td>10,0</td>
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<td>19,2</td>
<td>22,4</td>
<td>21,2</td>
<td>16,3</td>
<td>13,0</td>
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<td>24,9</td>
<td>19,3</td>
<td>15,4</td>
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<tr>
<td>Czech Republic</td>
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<td>28,9</td>
<td>27,5</td>
<td>21,4</td>
<td>17,3</td>
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<tr>
<td>Poland</td>
<td>133</td>
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<td>28,4</td>
<td>36,1</td>
<td>34,8</td>
<td>27,3</td>
<td>22,6</td>
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<tr>
<td><strong>66 countries (median)</strong></td>
<td><strong>38</strong></td>
<td></td>
<td><strong>16,5</strong></td>
<td><strong>14,4</strong></td>
<td><strong>13,6</strong></td>
<td><strong>10,4</strong></td>
<td><strong>8,4</strong></td>
</tr>
</tbody>
</table>

Radon exposure: national geometric mean (in 2012)

- **a** EAC Model « exposure age concentration », joint analysis 11 miner cohorts, BEIR VI (NRC 1999)
- **b** Three European joint analysis on miners (Hunter et al. 2013)
- **c** German cohort of uranium miners (Kreuzer et al. 2015)
- **d** North-American joint analysis in the general population (Krewski et al. 2003)
- **e** European joint study in the general population (Darby et al. 2006)

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Consistence in findings according to the models (based on miners studies)
Summary of knowledges on lung cancer risk and radon exposure

- Good **consistence among results** from studies among miners and in the general population
- Persistence of lung cancer risk **at low level of radon**
- Increased risk observed among smokers as well as **non smokers**
- **Smoking-radon interaction** between additive and multiplicative effect
- **Lung cancer**: to date, the only highlighted risk associated with radon (*studies on leukemia, skin cancer, brain cancer, stomach cancer, ...*)
- Lack of knowledge on the effect of radon exposure during childhood
### Perspectives

#### International joint cohort

- **Pooled Uranium Miners Analysis (PUMA)**

<table>
<thead>
<tr>
<th>Country, Place</th>
<th>Ur Miners</th>
<th>Period of Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada, Ontario</td>
<td>28,546</td>
<td>1954-2007</td>
</tr>
<tr>
<td>Canada, Beaverlodge</td>
<td>9,498</td>
<td>1950-1999</td>
</tr>
<tr>
<td>Canada, Port Radium</td>
<td>3,047</td>
<td>1950-1999</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>9,978</td>
<td>1952-2010</td>
</tr>
<tr>
<td>France</td>
<td>5,086</td>
<td>1946-2007</td>
</tr>
<tr>
<td>Germany</td>
<td>58,976</td>
<td>1946-2013</td>
</tr>
<tr>
<td>USA, Colorado Plateau</td>
<td>4,137</td>
<td>1960-2005</td>
</tr>
<tr>
<td>USA, New Mexico</td>
<td>3,469</td>
<td>1943-2012</td>
</tr>
<tr>
<td><strong>Total: Pooled study</strong></td>
<td><strong>126,733</strong></td>
<td></td>
</tr>
</tbody>
</table>

#### Objectives
- Set up a large international cohort of uranium miners
- Increase the statistical power
- Improve the assessment of the relationship between radon exposure and:
  - Risk of Lung cancer risk (refinement, modifying factors, low exposure, ...)
  - Risk of cancer other than lung
  - Risk of non cancer disease

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EURADOS Winter School - Lodz, Poland - 14 February 2019

IRSN
Thank you