A risk assessment of the potential impacts of radon, terrestrial gamma and cosmic rays on childhood leukemia in France

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Natural radioactivity (NR)

- **Major source** of exposure to ionizing radiation (IR) for most of the world population

- Exposure from **various sources** and via different **pathways**, notably:
  - Inhalation of radon gas and its decay products
  - External irradiation by cosmic and terrestrial gamma rays (TGR)
  - Food and water ingestion

- **Lung cancer** following radon inhalation is the only clearly established health effect of NR

- Can there be **other health effects**?
Childhood Leukemia

- One of the cancers most strongly associated with exposure to IR
- Shorter latency than most solid cancers
- Association with IR higher in children

- Several ecological studies suggested an association between NR and CL, including in France (Evrard et al. 2005, 2006)

- In the UK, the proportion of CL attributable to NR was estimated by a risk assessment approach to be circular around 15-20% (Wakeford et al 2009, Little et al 2009)

  ... although considerable uncertainties surround these figures
Objectives

To estimate, via a risk assessment approach, the proportion of childhood leukemia cases potentially related to 3 components of NR in France

- radon
- terrestrial gamma rays (TGR)
- cosmic rays

... these components being those for which doses to children can most reliably be estimated at large scales for epidemiological studies
Data

**Exposure**: average estimates (Billon et al, *RPD* 2005)

- radon concentration in buildings (63 Bq.m$^{-3}$)
- dose rates from TGR (0.49 mSv.y$^{-1}$)
- dose rates from cosmic rays (0.28 mSv.y$^{-1}$)

**Conversion to RBM doses**

**Leukaemia rates** for French children (0-14 y)
provided by the National Registry of Childhood Blood Malignancies (INSERM - RNHE), period 1990-2004
Risk prediction models

Proposed by international scientific committees:

- U.S. National Research Council, Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation (BEIR VII, NRC 2007)

Derived from the cohort of Japanese A-Bomb survivors (LSS)

Multiplicative and additive models proposed

Consider attained age (and age at exposure for some), as modifiers of the relation between IR and leukemia
Results: doses

RBM dose estimates (in mSv) for average French child

<table>
<thead>
<tr>
<th></th>
<th>Radon</th>
<th>TGR</th>
<th>Cosmic rays</th>
<th>Summed doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>In utero (9 months)</td>
<td>0.03</td>
<td>0.33</td>
<td>0.19</td>
<td>0.55</td>
</tr>
<tr>
<td>Infant (yearly)</td>
<td>0.29</td>
<td>0.61</td>
<td>0.35</td>
<td>1.24</td>
</tr>
<tr>
<td>Child (yearly)</td>
<td>0.34</td>
<td>0.55</td>
<td>0.31</td>
<td>1.21</td>
</tr>
<tr>
<td>Cumulated (in utero - 14 years)</td>
<td>5.08</td>
<td>8.64</td>
<td>4.88</td>
<td>18.73</td>
</tr>
<tr>
<td>% of cumulated dose</td>
<td>27</td>
<td>47</td>
<td>26</td>
<td>100</td>
</tr>
</tbody>
</table>

TGR is the major contributor to RBM dose
Results: attributable risk

Point estimates for the attributable % of CL cases for summed doses

<table>
<thead>
<tr>
<th>Model</th>
<th>UNSCEAR multiplicative</th>
<th>UNSCEAR additive</th>
<th>BEIR VII multiplicative</th>
<th>BEIR VII additive</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL percentage attributable to NR</td>
<td>19.8</td>
<td>4.6</td>
<td>13.8</td>
<td>14.9</td>
</tr>
</tbody>
</table>

- large contrasts depending on the model considered
Results: variation with attained age

Models behave differently according to attained age: point estimates of the % of cases attributable to summed exposures (radon, TGR, cosmic)

Consistent with findings in the UK (Wakeford et al, Leukemia 2009)
Uncertainties and extrapolation hypotheses

- Uncertainties in red bone marrow dose estimates (especially for radon)
- Difference in radiation quality between LSS exposure and NR in France
- Dose level extrapolation (some influential observations at high doses in the LSS)
- Dose rate extrapolation (acute LSS exposure vs chronic NR exposure)
- Risk at young ages: sparse data on risk at youngest ages and shortest time since exposure periods
- Transposition: from a mid-20th century Japanese population to contemporary French children
Uncertainties

So far, “point estimates” only! Uncertainties not quantified…

- Under the Bayesian paradigm:

- To characterize the full posterior distributions of leukemia risk model coefficients by fitting these anew to the LSS data*

- To propagate these distributions throughout the risk assessment process

*by applying the methodology described in Little et al, Rad Res 169, 660–676 (2008)
Uncertainties: preliminary results

UNSCER 2006 EAR model: All 3 exposures (Male)

- 95% posterior predictive CI
- posterior predictive median
- point predictive value obtained from frequentist analysis
Conclusion and perspectives

- Point estimates suggest that an important proportion of CL cases might be attributable to radon, TGR and cosmic rays.

- Preliminary results reveal important uncertainties related to leukemia risk predictions models.

  - Need for further analysis of uncertainties
  - Need to better investigate the relation between NR and CL

- An INSERM-IRSN epidemiological study of NR and CL is ongoing in France as part of the Geocap program *

  *Presentation by C Demoury, TS10c: Radon Thursday, May 17, 10:15
Thank you for your attention
Generalized ERR model

$$h_0(s, a) \cdot \left[1 + (\alpha \cdot D + \beta \cdot D^2) \cdot \exp[\kappa_1 \cdot \ln[a]]\right]^a$$

Generalized EAR model

$$h_0(s, a) + (\alpha \cdot D + \beta \cdot D^2) \cdot \exp[\kappa_1 \cdot 1_{s \text{= female}} + \kappa_2 \cdot \ln[a - e]]^a$$

$^aD =$ radiation dose (Sv); $a =$ attained age, $e =$ age at exposure, $s =$ sex,

Wakeford et al, *Leukemia* 2009
BEIR VII leukemia models (NRC, 2006)

Generalized ERR model

\[ h_0(s,a) \cdot \left[ 1 + \beta_s \cdot (D + \theta \cdot D^2) \cdot \exp \left[ \gamma_- \cdot \min(e-30,0)/10 + \delta \cdot \ln[(a-e)/25] + \phi \cdot \ln[(a-e)/25] \cdot \min(e-30,0)/10 \right] \right]^a \]

Generalized EAR model

\[ h_0(s,a) + \beta_s \cdot (D + \theta \cdot D^2) \cdot \exp \left[ \gamma_- \cdot \min(e-30,0)/10 + \phi \cdot \ln[(a-e)/25] \cdot \min(e-30,0)/10 \right]^a \]

\[ D = \text{radiation dose (Sv)}; \ a = \text{attained age}; \ e = \text{age at exposure}; \ s = \text{sex}, \]

Wakeford et al, *Leukemia* 2009