Cancer risks associated with internal alpha emitters

ICRP-ERPW

October 11, 2017

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ICRP Committee 1, Task Group 64

Cancer risks related to alpha emitters

Current system of Radiation Protection

Detriment based on A-Bomb survivors (external exposure)

=> Instantaneous exposure (in a few seconds, whole body exposure)

In front of other exposed populations : major hypotheses are necessary

- Specific cancer risk depends on its organ dose
- If chronic exposure, additivity of annual doses, weighted by time since exposure, lag time…..
- Internal contamination: different exposures present at the same time (external + internal) (ex.: gamma and alpha emitters)
- Radiation quality for different radiation types

Importance of studies in populations with internal exposure

- Validation of presently used RP parameters
- Opportunity to compare a specific cancer risk (example : lung cancer) based on organ dose (mGy or mSv)

Experience of ICRP C1 Task Group 64

For Cancer risks related to alpha emitters :

- **Criteria: studies able to quantify the dose-risk relationship**
  - Quality of individual exposure/dose data
  - Quality and lenght of follow-up
  - Size of the population

- **TG64 : Review of publications over last 10-15 years**
  - Radon (uranium miners, indoor studies)
  - Plutonium (nuclear weapon industry workers)
  - Uranium (nuclear fuel cycle workers, drinking water)
  - Take in account synthesis done already on international level : WHO, UNSCEAR, others

Experience of ICRP C1 TaskGroup 64

- **Difficulty in exposure reconstruction**
  - Monitoring of exposures (miners) period dependent
  - Monitoring of excreted activity (bioassays, industry workers)
  - Job-exposure-matrix (workers)
  - Chronic exposure, incorporation: importance of considering the time dimension of the exposure
  - In most situations, concomitant exposure : external gamma exposure, uranium dust, chemicals, smoking...
- **Complexity of dose assessment**
  - How to take in account lack of individual information depending on periods and criteria for registration
  - Complex biokinetic models, numerous parameters and associated uncertainties

ICRP Task Group 64 – List of members

Publication 115 (radon) (2010)

Members

M. Tirmarche (Chairperson), E. Blanchardon, M. Blettner, E. Ellis, J.D. Harrison (C2), D. Laurier, J.W. Marsh, F. Paquet (C2), N. Shilnikova, J.F. Lecomte (C4), M. Sokolnikov

Corresponding members

B. Grosche, J. Lubin, C.R. Muirhead

Present composition

Members

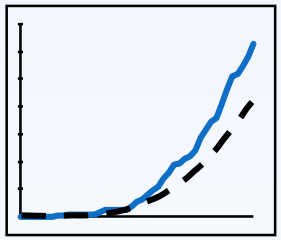
M. Tirmarche (Chair), E. Blanchardon (C2), E. Ellis, D. Laurier (MC), J.W. Marsh (C2), M. Sokolnikov (C1), I. Apostoaei, R. Wakeford (C1)

Corresponding members

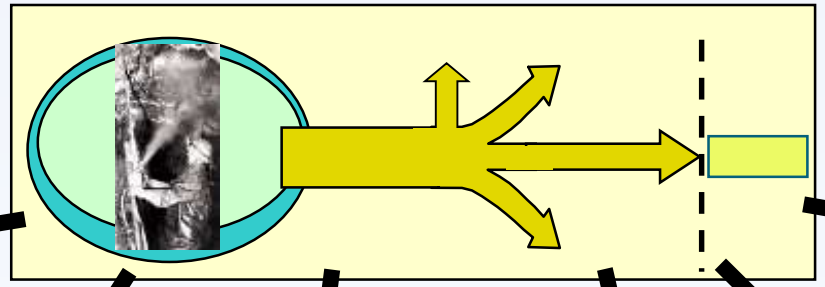
E. Gilbert, J. Harrison (C2), Sergey Zhivin ...

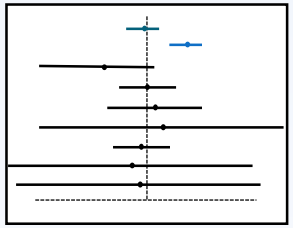
Radon

Cohorts of uranium miners

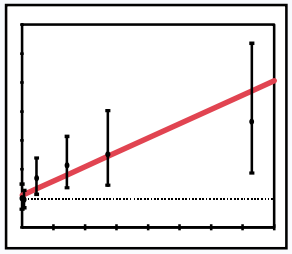


Excess lung cancer mortality





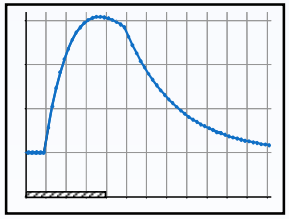
Uncertainties on potential associations with diseases other than lung cancer (stomach, kidney, leukemia, CVD)



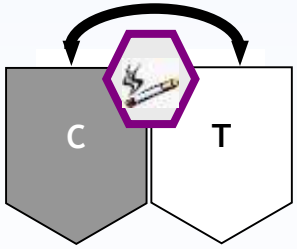
Exposure-risk relationship for lung cancer

Persisting among low exposed miners

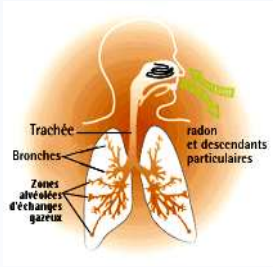
Persisting after consideration of exposure measurement errors



Decrease of risk with time since exposure



Persisting relationship after adjustment on smoking



Major contribution of radon decay products to lung dose

Dose-risk relationship

Studies in the general population

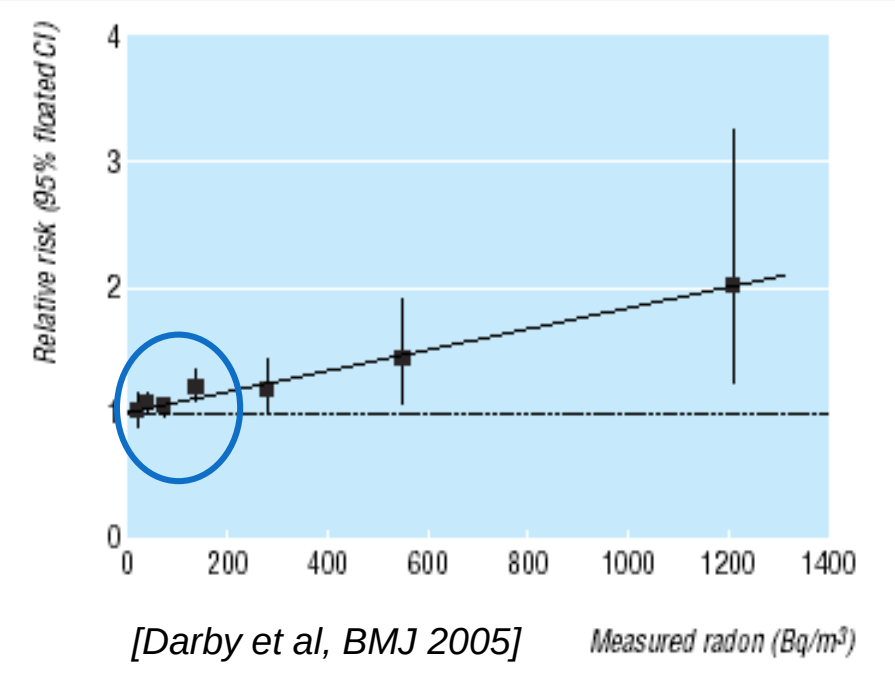
Pooled analyses in Europe, North-America and China

- Increase in lung cancer risk with indoor radon concentration

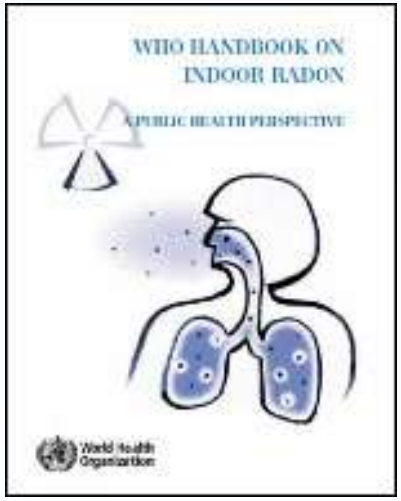
  RR=1.08 per100 Bq/m^3 [1.03 – 1.16]

- Significant relationship from 200 Bq/m^3

  Significant relationship for non smokers



[Darby et al, BMJ 2005]

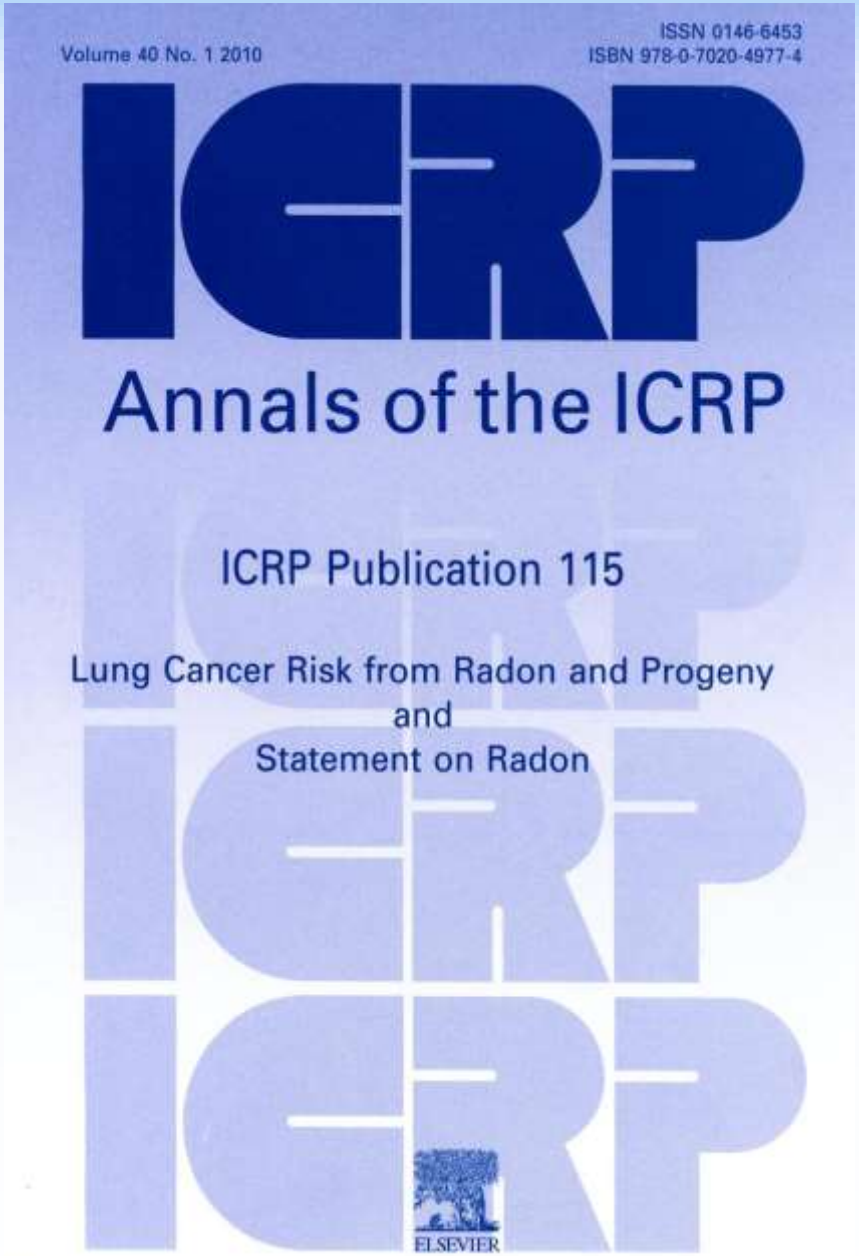


Demonstrated lung cancer risk associated with indoor radon exposure [WHO 2009]

New evaluation of radon risk

ICRP Publication 115 (2010)

- Update of scientific literature review since ICRP Publication 65 (1993)
- Good agreement of risk estimates from low-exposed miners and from indoor studies
- Calculation **of lung cancer lifetime detriment** due to radon and radon decay products
- No evidence of associated risk outside lung cancer



Conversion from radon exposure to dose

For a worker

	Lifetime Lung cancer risk (WLM^{-1})	*Detriment* (Sv^{-1})	Effective dose ($mSv.WLM^{-1}$)
1993	$2.8\ 10^{-4}$ *(ICRP 65)*	$5.6\ 10^{-2}$ *(ICRP 60)*	**5**
2010	$5\ 10^{-4}$ *(ICRP 115)*	$4.2\ 10^{-2}$ (*ICRP 103*)	**x 2**

[Marsh et al. Health Phys 2010]

Increased lifetime risk (Pub 115)

New dose coefficient to be provided soon (OIR 3)

Conclusion on radon

- TG64 and the Publication115 was a support for the conversion convention between radon exposure and effective dose (ICRP Publication OIR 3, in press)
- Support to radon protection recommendations (ICRP Publication 126, 2015)

- Need for continuation of research on open questions: interaction between radon and smoking, lung cancer risk associated with childhood exposure, potential association with diseases other than lung cancer

→ **Elaborated dosimetric system** **[see presentation of Marsh et al.]**

→ **New international study of uranium miners** (USA, Canada, Germany, Czech Republic, France): the **PUMA project**

Plutonium

Plutonium studies

Main studies of workers

- Russia (Mayak)
- UK (Sellafield)
- USA (Handford, Rocky Flats, Oak Ridge NL, Los Alamos…)

Elaborated dosimetric models play a major role in final analysis of plutonium risk

International collaborations through research programs exist :

- on European level : Alpha-Risk, SOUL and SOLO programs…
- on international level : JCCRER

Cancer risk among Mayak workers

- Large cohort (>22,000 workers hired in the period 1948–1982)
- Several elaborated dosimetric systems to describe this chronic internal contamination
- *Publ. by Sokolnikov et al, 2008* : 5572 workers with a positive plutonium dose :
  - Mean plutonium dose to lung : 0.19 Gy liver : 0.3 Gy bone : 0,98 Gy
  - End of follow up : Dec. 2003

ERR/Gy plutonium dose

	Males (n=3874)	Females (n=1698)
Lung:	**7.1 (4.9 – 10)**	**15 (7.6 – 29)**
Liver:	**2.6 (0.7 – 6.9)**	**29 (9.8 – 95)**
Bone:	**0.8 (<0 – 5.2)**	**3.4 (0.4 – 20)**

[Sokolnikov M,. et al *IJC 2008]*

- No association for other cancer types after adjustment on monitoring status [Sokolnikov M, et al. PLoS1 2015]
- No significant association for leukemia [Kuznetsova IS, et al. PLoS1 2016] ERR/Gy = 2.13 (90% CI: <0-9.45)

Lung cancer risk among Mayak workers

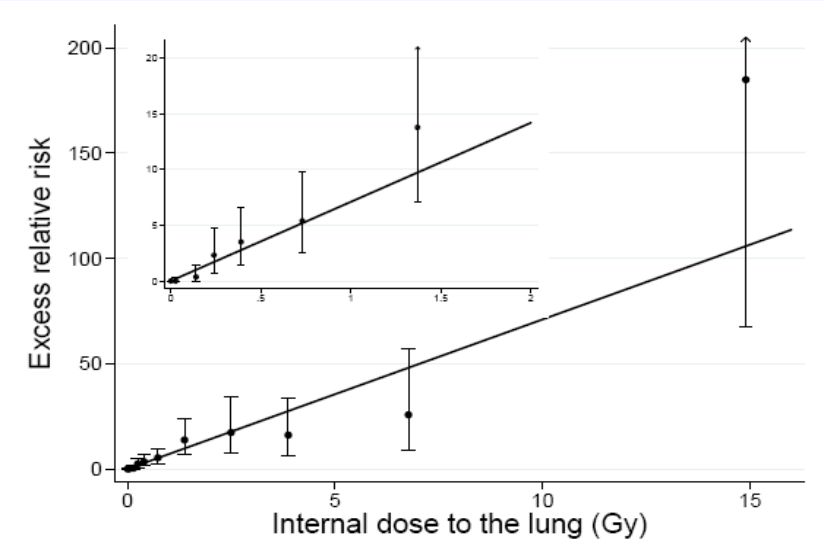
[Gilbert ES,. et al *Radiat Res 2013]*

> 14,000 workers, follow-up to 2008, 486 lung cancer deaths

Dose estimates (MWDS-2008)

Significant dose-risk relationship

- ERR/Gy* males = 7.4 (95% CI: 5.0–11)
- Compatible with a linear no threshold model
- Declined with attained age
- ERR/Gy higher among females
- Interaction between plutonium dose and smoking likely sub-multiplicative



* ERR/Gy at age 60, after adjustment for external radiation dose and smoking

105 lung cancer deaths (22%) attributed to plutonium exposure and 29 (6%) to external exposure

Present preliminary conclusion on plutonium risk

Despite limits of Mayak cohort

- Urine samples available only for 30% of the cohort, started in 1971
- Uncertainties on when exposure started and on the chemical form of Pu
- Changes over time in biokinetic models and parameter values used to estimate deposition and clearance in organs of the body
- Migration out of Oziorsk ~ 41 %

It seems possible today to estimate Pu associated detriment for lung cancer

But TG64 considers that we need confirmation from other studies

- several papers close to publication from the parallel analysis of Sellafield and Mayak workers
- uncertainties consideration

Input of recent publication of Grellier et al (sept 2017) :

- A European case-control (n= 553-1333) study included deaths from lung cancer among nuclear workers from the UK, France and Belgium exposed to either uranium or plutonium, and made it possible to compare these results with those observed in cohort studies.

➔ the excess odds ratio (EOR) per Gy was 50 (90% CI: 17, 106), but reduced to 37 (90% CI: 0.18, 121) when workers from the UK Atomic Weapons Establishment (AWE) were excluded from the analysis.

➔ Median positive lung dose from plutonium was low (median 1.27 mGy) when compared with the median cumulative lung dose from external gamma radiation (33 mGy)

Publication of the risk coefficient linked to the analysis of the joint cohorts of plutonium workers of Sellafield and Mayak study is under press:

➔ will be of major importance before concluding on the plutonium risk coefficient

Uranium

Uranium studies

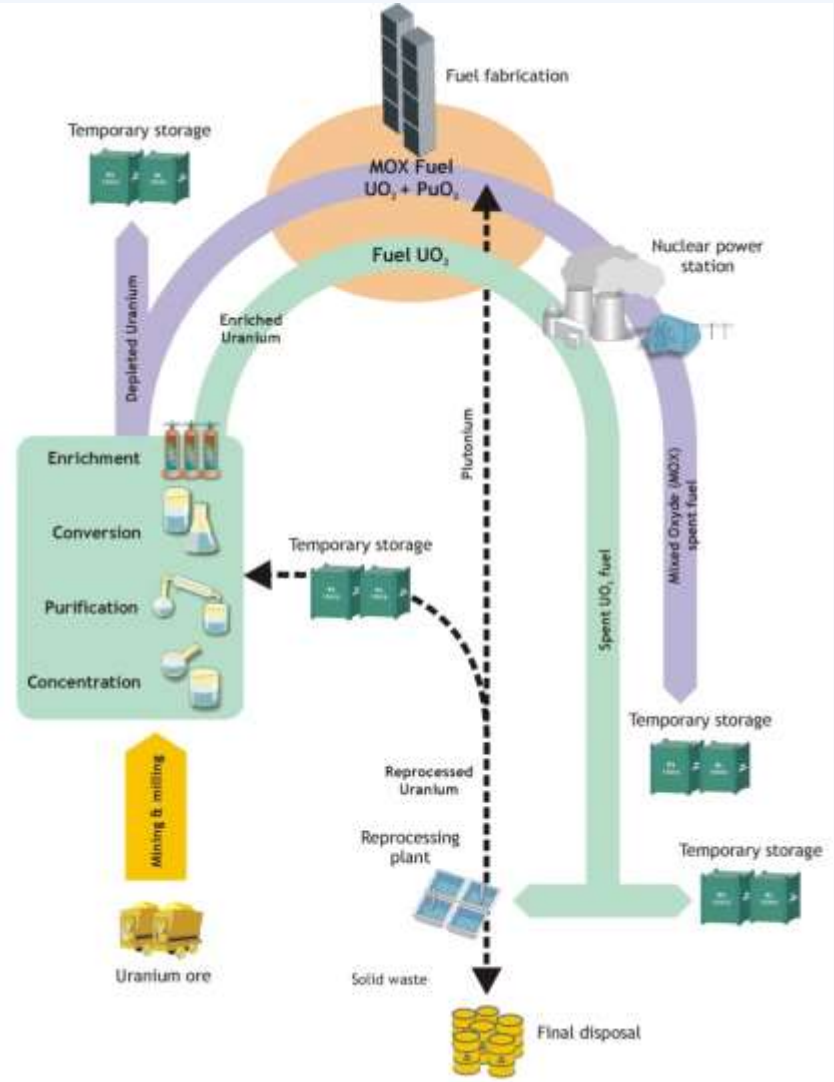
Epidemiological studies

- Nuclear workers: USA (Fernald, Rocketdyne, Oack Ridge GDP, Paducah…), UK (Spingfield, Sellafield…), France (CEA, AREVA…)
- *Uranium miners: France, Germany, Czech Republic*
- Uranium millers: USA, Canada, Germany
- Army veterans (depleted uranium)
- Drinking water (Finland)

Limits

- Sensitivity to chemical form (solubility)
- Chemical and radiological toxicity
- Very low doses
- Small size
- Poor control of confounding factors

Studies of nuclear fuel cycle workers



- Nuclear fuel cycle workers constitute the best population to assess the risk of uranium exposure (stability, long duration follow-up, individual monitoring…)
- Carcinogenicity depends on the physical and chemical nature of U compounds and isotopy [Guseva-Canu et al. CCC 2011]
- Only a few studies were able to estimate individual doses
- Very low estimated doses associated to very large uncertainties
- Excesses / positive associations observed for lung cancer, lymphatic and hematopoietic malignancies, multiple myeloma, kidney cancer

Position of TG64

- The majority of selected studies have shown no increase in lung cancer risk with exposure to uranium.
- A French study (Canu 2011) revealed significant increases after exposure to reprocessed but not natural uranium.
- Cohorts of uranium enrichment workers in France (Zhivin 2016) and in USA (Yiin 2017), exposed mostly to rapidly soluble uranium compounds, were in line with this finding.
- The studies of Grellier and of Silver indicate a positive dose response relationship, but both with a large confidence interval that cannot exclude the absence of a trend. In the study of Grellier et al. (2017), when testing for the influence of specific worker groups, the UK AWE and BNFL workforces influence the risk coefficient in an opposite directions.

Conclusion on uranium

Limits of existing studies

- Only a few allowed quantification of a dose-risk relationship
- Difficulty of dosimetric reconstruction

Current results

- Comprehensive review published by UNSCEAR end of 2016
- Grellier et al paper (sept 2017) based on individually reconstructed exposure of the past:
- From cohorts of nuclear workers, nested case control studies could be a way to go further ?

Need for improved studies

- *Consideration of new populations (nuclear fuel cycle workers in other countries)*
- *Segmentation of industrial processes : focus on those with the highest organ dose*
- *Improved reconstruction of exposure and dosimetric assessment*
- *Consideration of uncertainties*
- *Importance of international collaborative projects + integration with biology*

Global Conclusion

- **Risks linked to radon:** Assessment performed (Publication 115), supported management recommendations (Publication 126) and dose conversion convention (Publication OIR 3)
  - Communication to public and decision makers out of the field of nuclear industry is now a major task
  - In research : risks other than lung cancer ? risks linked to childhood exposure ?
- **Risk linked to plutonium:** More results expected in very near future, from joint analysis (Sellafield and Mayak), consideration of uncertainties (JCRRER project).
- **Risk linked to uranium:** Limited data presently available.
  - Unscear published a large report on uranium and possible health effects, including review of experimental data.
  - Improved studies are undertaken on a large scale : USA, Europe…..

Global Conclusion 2

For improvement in RP, based on cancer risks associated with alpha emitters

- TG64 is able to estimate the detriment linked to lung cancer:
  - By comparing risk coefficients obtained from populations exposed to external gamma exposure (A bomb survivors, nuclear workers, Inworks, Mayak chemical workers…) with those observed after inhalation of alpha emitters : Rd progeny, Pu.
  - using a specific scenario of chronic exposure, applied on the same population caractersitics (age structure, followed up to age 90) as defined in ICRP publication103

- That may contribute to the discussion of RBE [Marsh et al., IJRB 2014]

More research needed as there is a suggestion of risks for non-cancer diseases, to be followed

- Cerebrovascular and cardiac diseases ?

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