Progress in understanding radon risk

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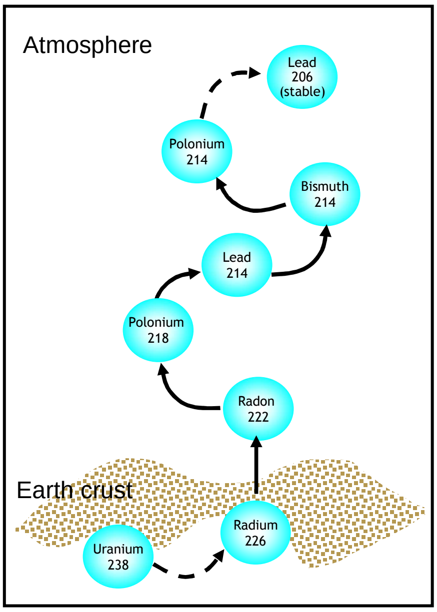
Radon and lung cancer

Radioactive gas of natural origin: formed as the decay product of uranium and radium present in soil and rocks

Present everywhere in the air in various concentrations; can accumulate in confined places (mines, caves, houses…)

Inhalation: decay products deposit in the different part of the lungs and lead to a irradiation of the epithelium cells

Recognised as a human lung carcinogen in 1988 (WHO IARC) on the basis of experimental and epidemiological results



Progress in understanding radon risk

Summary of recent results about radon risk

1. Results of miner studies at low levels of exposure
2. Estimates of lifetime risk
3. Coherence of results from miners and indoor studies
4. Organ dose calculation
5. Risks other than lung cancer

Results of miner studies at low levels of exposure

Miners cohort studies

The Alpha-Risk Project

(EC FP6, 2005-09, Contract n°516483, Coord M Tirmarche IRSN)
Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures

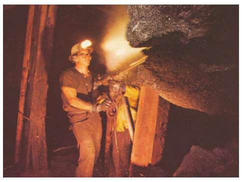
http://www.alpha-risk.org

	France	Czech Republic	Germany	Total
Population size	5,086	9,979	35,084	50,149
Follow-up period	1946 – 1999	1952-1999	1955-1998	1946 – 1999
Person-years	153,047	262,507	908,661	1,324,215
Duration of follow-up (y)	30.1	26.3	25.9	26.4
Number of death	1,467	3,947	4,519	9,933
Lung cancer	159	922	462	1 543
Radon				
Cumulative exposure (WLM)	36.6	72.8	55.9	58.0
Duration of exposure (y)	11.7	6.9	8.9	8.8

Working Level Months *(WLM): unit of radon exposure. any combination of radon progeny in 1l of air which results in the emission of 130,000 MeV of energy from alpha particles x a monthly working time of 170 hours)*

(Tirmarche et al., Alpha-Risk 2010)

Exposure-risk relationship at low levels of exposure



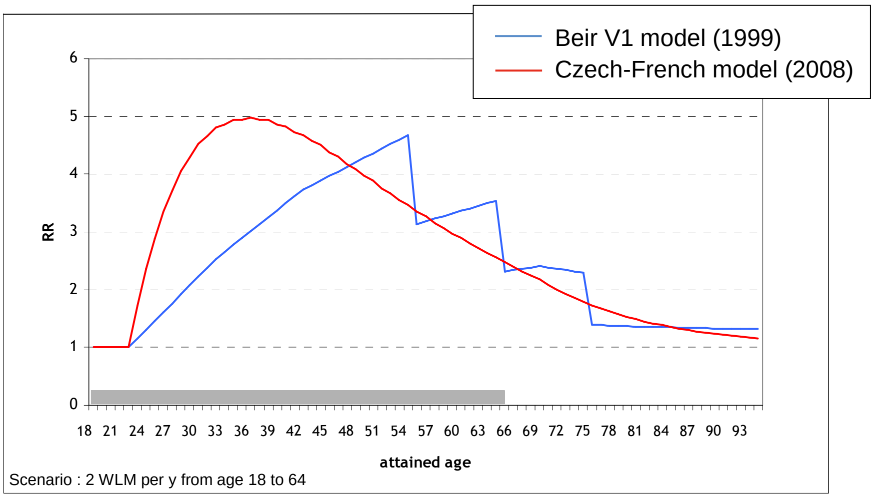
	Whole cohorts		Low exposure rate period *	
Cohort	**ERR/ 100 WLM**	**95%CI**	**ERR/ 100 WLM**	**95%CI**
Czech	1.13	0.74-1.53	2.14	1.21-3.08
French	0.60	0.17-1.03	2.11	0.78-3.44
German	0.41	0.27-0.55	3.76	2.13-5.39
Joint	-		2.60	1.83-3.36

models stratified on the birth year and the country, using a modified external background rate estimation method
* exposures since 1953, 1956 and 1967, respectively in the Czech, French and German cohort

(Tirmarche et al., Alpha-Risk 2010)

Higher risk coefficients at low levels of exposure
Good coherence between estimates from the 3 cohorts

Modifying factors of the exposure-risk relationship



(Tomasek et al., Rad Res 2008)

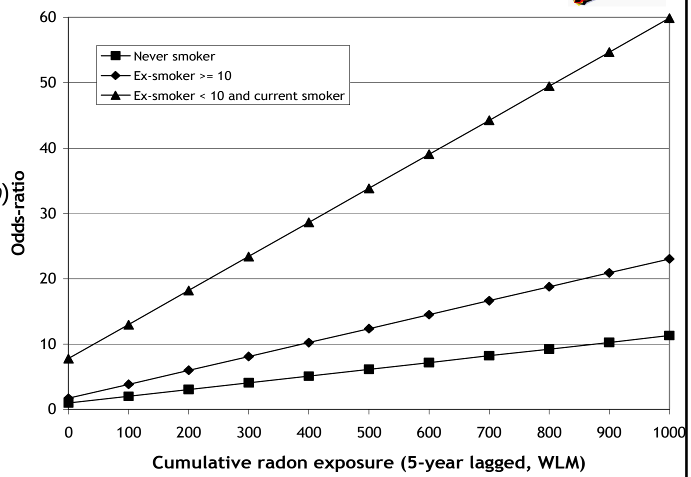
Decrease of risk with time since exposure and age at exposure/ attained age

Risk associated to radon and smoking

Joint nested case-control study

French (*Leuraud, Health Phys 2007*)
German (*Schnelzer, Health Phys 2010*)
Czech (*Tomasek, Rad Prot Dosim in press*)

1236 cases - 2678 controls



- **Relationship with radon persists after controlling for smoking**
- **Risk increases with radon exposure in each smoking category**
- **Sub-multiplicative interaction**

Estimates of lifetime risk

Radon lifetime risk

ICRP report 65 (1993)
Lifetime Excess Absolute Risk : $2.8\ 10^{-4}$ per WLM

New results at low levels of exposure
BEIR VI (1999) $5.4\ 10^{-4}$ per WLM
Czech-French joint analysis (2008) $4.8\ 10^{-4}$ per WLM

ICRP TG64 (2010)
Lifetime Excess Absolute Risk **$5\ 10^{-4}$ per WLM**

(ICRP 2010, http://new.icrp.org/)

Direction de la radioprotection de l'homme IRSN

Exposure-dose Conversion convention

For workers

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

(Marsh et al. Health Phys 2010)

Also new results from dosimetry

→ **ICRP will propose new conversion coefficients based on dosimetry in near future**

Coherence of results from miners and indoor studies

Pooled residential studies

Joint analysis	Number of studies included	Cases	Controls	Relative risk per 100 Bq m-3	95% CI
Chinese *(Lubin et al.,Int J Cancer 2004)*	2	1050	1995	1.13	(1.01-1.36)
European *(Darby et al.,BMJ 2005)*	13	7148	14208	1.08	(1.03-1.16)
North American *(Krewski et al.,Epidemiol 2006)*	7	3662	4966	1.10	(0,99-1.26)

Very good coherence of results from indoor studies
RR increase ≈ 10% per 100 Bq.m^{-3} (cumulated over 30 y)

Comparison of miner and residential results

ICRP

Comparison of Lifetime Excess Absolute Risks (10^{-4} per WLM)

	Beir VIc 1999	CzFr 2008	Darby 2005
18-59	1.64	1.30	0.73
18-69	3.53	2.72	2.71
18-89	5.58	4.68	7.58

(Laurier et al. IRPA 2010)

Scenario: 0.43 WLM (100 Bq/m3) per y from age 40 to 64; Ref rates ICRP male+female/asian+euroamerican

Good agreement of estimated cumulated risk
High sensitivity to lifetime duration

Organ dose calculation

Organ dose calculation

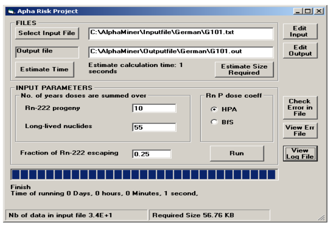
European project Alpha Risk

WP1: Cohorts of uranium miners

- French, Czech and German cohorts (>50,000 miners)
- Individual exposure to radon, gamma and long lived radionuclides
- Reconstruction of exploitation methods and mine atmosphere

WP5: Organ doses

- Adapted parameters / job types / aerosol characteristics
- Use of ICRP biocinetic and dosimetric models
- Setting up of the *Alpha Miner* software



Calculation of doses to different organs for each miner / each year

(Marsh et al. Rad Prot Dosim 2008)

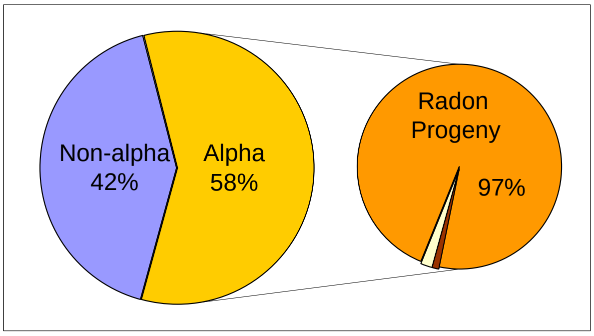
Lung dose calculation

French cohort post 1955 (n=3377)

Cumulative exposures	mean	[min – max]
Radon (WLM),	17.8	[0.01 – 128.4]
Gamma (mSv)	54.7	[0.2 - 470.0]
Long lived radionuclides (kBq.m^{-3}.h)	1.6	[0.01 - 10.2]

Cumulative absorbed dose (mGy)

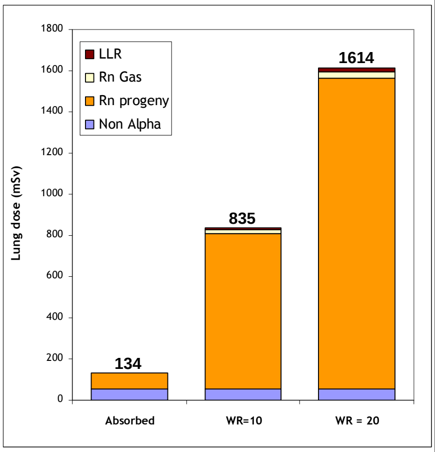
Total	**134**	[0.1-1113.3]
Non Alpha	56	[0,1 – 472]
Alpha	78	[0 – 700]
Long-lived Rn	1	[0 – 5.90]
Radon gas	1	[0 – 12.4]
Radon Progeny	76	[0 – 683]



Dose-risk relationship for lung cancer

French cohort post 1955 (n=3377)

Sensitivity analyses: weighted lung dose



w	Alpha contribution (%)	ERR per Sv	95% CI	p value
1	58	**2.97**	(0.82 – 7.57)	0.001
10	93	**0.43**	(0.13 – 1.06)	0.001
20	97	**0.22**	(0.06 – 0.54)	0.001

(Rage et al. 2010)

Dose-risk relationship for lung cancer

Studies	ERR per Sv lung cancer	90% CI
Mortality analyses		
15-country study, *Cardis et al, 2007*	1.86 (all)	0.49-3.63
Life Span Study, *Preston et al 2003*	0.89* (all) 0.48 (men)	 0.23-0.78
Incidence analyses		
Life Span Study, *Preston et al 2007*	0.81 (all) 0.28 (men)	0.56-1.10 0.12-0.49
UK NRRW, *Muirhead et al 2009*	0.11 (all)	-0.35-0.67

* at 60 years old

Estimated ERR/Sv can be compared with ERR observed in the literature for external exposure

Risks other than lung cancer

Radon risk outside lung cancer - Miner studies

Specific excesses: non-Hodgkin lymphoma, multiple myeloma *(Schubauer-Berigan, AJE 2009)*, kidney *(Vacquier, OEM 2008)*, stomach and liver (*Kreuzer, BJC 2008*)
No consistent pattern

German Wismut cohort: exposure risk relationship

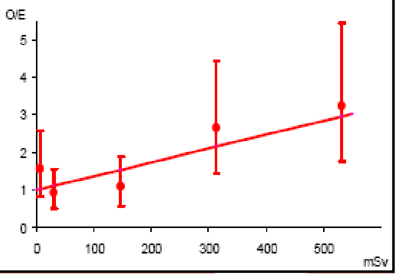
- All extra-pulmonary cancers *(Kreuzer, BJC 2008, Walsh, HP 2010)*
  ERR per 100 WLM = 0.014   95%CI=[0.006–0.023]
  linear model with modifying effect of attained age
- Stomach cancer (*Kreuzer et al., ERRS 2010*)
  absorbed dose (radon+RDP, LLR, gamma)
  ERR per Gy = 1.53   95%CI=[0.23-2.73]
  no more significant after adjustment for arsenic and fine dust exposure

Radon and leukaemia risk - Miner studies

Czech uranium miners *(Rericha, EHP 2006)*
84 leukemia cases
leukemia risk associated with cumulative radon exposure
other sources of exposure not considered

German Wismut uranium miners *(Mohner, HP 2010)*
377 leukemia cases and 980 controls
absorbed RBM dose (Rn+RDP, LLR, Gamma + medical X-rays)
contribution of radon inhalation = 31%
increased risk above 200 mGy (not significant)

Alpha-Risk European project *(Tirmarche, Alpha-Risk 2010; Tomasek, IRPA 2010)*
69 leukaemia deaths
equivalent RBM dose (Rn+RDP, LLR, Gamma)
mean RBM dose = 90 mSv
contribution of radon inhalation = 40%
ERR per Sv = 3.7   95%CI=[1.1–8.8]



Radon and leukaemia risk - general population studies

Nationwide case-control study in Denmark (*Raaschou-Nielsen, Epidemiology 2008*)
1153 leukaemia cases / 2306 controls
residential radon concentrations calculated from a model
significant association for childhood acute lymphocytic leukaemia
ERR per 1000 Bq.m^{-3}.y cumulated = 0.56 95%CI=[0.05 – 1.30]
9% of ALL cases in Denmark attributable to radon (m=59 Bq.m^{-3})

Dose and risk assessment In Great Britain
- equivalent dose due to natural exposure ≈ 1.3 mSv per year before age 15 (*Kendall, JRP 2009*)
- natural exposure may account for 15 to 20% of all cases of childhood leukaemia (*Wakeford, Leukemia 2009; Little, JRP 2009*)
- a large study (nationwide recruitment of cases over 10 or 20 years) should have sufficient power to detect the risk attributable to background radiation (*Little, Rad Res 2010*)
- poor capacity to demonstrate the proper effect of radon due to its small contribution to RBM dose (m=20 Bq.m^{-3}) (*Wakeford, Rad Prot 2010*)

Conclusions

Higher lung cancer risk coefficients estimated from recent studies of miners with low levels of radon exposure

Increased lifetime absolute risk attributable to radon compared to previous ICRP estimates

Good coherence of results from miners and indoor studies regarding lung cancer risk

Analyses based on dose calculations confirm the major contribution of radon decay products to lung dose

No consistent evidence of radon associated risks other than lung cancer (but growing concerns)

Perspectives

Conduction of pooling studies to better quantify risks at low exposure levels
- Residential exposure: World pooling project
- Miners: Euro-Can initiative

Refinement of organ dose calculations
- Analyses based on dose-risk relationships
- New exposure-dose conversion coefficients for ICRP

Correction for measurement errors
- For both miner and indoor studies
- For exposure and dose estimates

Launching of large scale studies on childhood radon exposure
- Studies of childhood leukaemia risk in the UK and France

Development of multidisciplinary research projects
- Interaction epidemiology/dosimetry/biology
- Molecular epidemiology studies