Task Group 91: Radiation Risk Inference at Low-dose and Low-dose Rate Exposure for Radiological Protection Purposes

ICRP Workshop « 30 Years of Scientific Achievements for International Radiological Protection: Summary of the Southern Urals Health Studies Program »

May 25, Vienna

ICRP: UK Registered Charity 1166304

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INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

Task Group TG91: "Radiation Risk Inference at Low-dose and Low-dose Rate Exposure for Radiological Protection Purposes: Use of Dose and Dose Rate Effectiveness Factors"

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Current Situation

- ICRP uses risk estimates from high dose rate study (atomic bomb survivors)
- Suggests a dose and dose rate effectiveness factor (DDREF) of 2 to apply those risk estimates to the occupational setting

>> TG91 to review the current scientific evidence with focus on LDEF (low dose effectiveness factor) and DREF (dose rate effectiveness factor), not on DDREF!

- **Low dose: < 100 mGy**
- **Low dose rate: < 0.1 mGy / min averaged over 1 hour**

A Bit of History

NCRP 1980

- Introduced the “dose-rate effectiveness factor (DREF)”
- For a variety of endpoints **in animal models values between 2 and 10 were observed**

UNSCEAR 1988

- *“… such a factor certainly **varies very widely with individual** (human) **tumour type** and with dose rate range. However, an appropriate range to be applied … should lie between 2 and 10”*

ICRP 1991

- Introduced the “Dose and Doserate Effectiveness Factor (DDREF)” **with a value of 2**
- Acknowledged that the chosen **value of 2 might be somewhat arbitrary**, and it was felt that **it may be conservative**.

UNSCEAR 2006 (approach confirmed recently in 2017)

- Fitted the LSS data using a dose-response curve that included a quadratic component
- In this way, an LDEF was implicitly taken into account
- *Values of DDREF of about 2 consistent with this approach*

Work done by TG91

Historical Review

- Rühm, W., Woloschak, G. E., Shore, et al. (2015) Dose and dose-rate effects of ionizing radiation: a discussion in the light of radiological protection. Radiat Environ Biophys 54: 379-401

Review of typical dose rates and doses in radiobiological and epidemiolgoical studies

- Rühm., W., Azizova, T., Bouffler, S., Cullings, H., Grosche, B., Little, M.P., Shore, R., Walsh, L., Woloschak, G. (2018) Typical Doses and Dose Rates in Studies Pertinent to Radiation Risk Inference at Low Doses and Low Dose Rates. J. Radiat Res 59 (S2): ii1-ii10

- D. Lowe, L. Roy, M.A. Tabocchini, W. Rühm, R. Wakeford, G.E. Woloschak, D. Laurier. *Radiation dose rate effects: what is new and what is needed?* Radiat. Environ. Biophys. 61:507-543, 2022.

Review of molecular and cellular studies

- S. Bouffler in Rühm, W., Woloschak, G. E., Shore, et al. (2015) Dose and dose-rate effects of ionizing radiation: a discussion in the light of radiological protection. Radiat Environ Biophys 54: 379-401

Analyses of animal studies

- Haley, B., Paunesku, T., Grdina, D.J., Woloschak, G.E. (2015) Animal Mortality Risk Increase Following Low-LET Radiation Exposure is not Linear-Quadratic with Dose. PLOS One, 10(12): e0140989

- Haley B, Zander A, Popović J, Paunesku T, Woloschak GE. Findings from international archived data: Fractionation reduces mortality risk of ionizing radiation for total doses below 4 Gray in rodents. Mutat Res Genet Toxicol Environ Mutagen. 2022 Oct;882:503537. doi: 10.1016/j.mrgentox.2022.503537. Epub 2022 Jul 29. PMID: 36155139.

- Tran., V., Little, M.P. (2017) Dose and dose rate extrapolation factors for malignant and non-malignant health endpoints after exposure to gamma and neutron radiation. Radiat Environ Biophys 56, 299-328

Work done by TG91

Analyses of epidemiological studies - DREF

Computed "matching" cancer risks in sub-cohorts of the atomic bomb survivors with matching distributions according to sex, age at exposure, grouping of cancer types and follow-up time

- Shore, R., Walsh, L., Azizova, T., Rühm, W. (2017) Risk of Solid Cancer in Low-dose and Low Dose-Rate Radiation Epidemiological Studies and the Dose Rate Effectiveness Factor. Int J Radiat Biol 93, 1064-1078

Analyses of epidemiological studies - LDEF

Followed recent UNSCEAR approach

- Little MP, Pawel D, Misumi M; Hamada N; Cullings HM; Wakeford R; Ozasa K (2020) Lifetime Mortality Risk from Cancer and Circulatory Disease Predicted from the Japanese Atomic Bomb Survivor Life Span Study Data Taking Account of Dose Measurement Error. Radiat Res 194(3): 259–276

Review of biologically-based mechanistic models to describe epidemiological data

- Rühm, W., Eidemüller, M., Kaiser, J.C. (2017) Application of Biologically-Based Models of Radiation-Induced Carcinogenesis to Epidemiological Data. Int J Radiat Biol 93, 1093-1117

Review of current epidemiological evidence

- W. Rühm, D. Laurier, R. Wakeford. Cancer risk following low doses of ionising radiation – Current epidemiological evidence and implications for radiological protection. Mutat. Res. - Gen. Tox. Environ. Mutag. 873:503436, 2022.

2024 Meta Analysis – Comparison with LSS cohort

Recent (2024) meta-analysis of epidemiological data: Risk estimates from **29 human cohorts** exposed to low dose rates including those from **Mayak workers** and **Techa River population**

Study Identifiers [a]	Mean reported external dose (mGy)	No. of cancers	LDR Study Risk: ERR Gy^{-1} (90% or 95% CI) [a]	Corresponding LSS Risk: ERR Gy^{-1} (90% or 95% CI…	LDR/LSS: Risk ratio of this study to th… 90% or 95% …
Occupational Radiation Exposures and Mortality					
Mayak workers, Russia (Sokolnikov, Preston et al. 2015, Sokolnikov, Preston et al. 2017) *	354[b1] 235[b1]	1,825 [c4] 593 [c4]	0.16 (0.07, 0.2… [illegible]	[illegible]	…, 0.68) …0.45 (0.34, 0.66)[a]
….					
Environmental Radiation Exposures and Mortalit…					
Techa River, Russia (Schonfeld, Krestinina et al. 2013) *	[illegible]	[illegible]	…1 (0.04, 1.27)[d]	0.53 (0.42, 0.64)	1.15 (-0.01, 2.42)
…					
Radiation S… …ong with Mortality Data)					
Russi… (Hunte…	510[b1]	1,447[c4]	0.07 (0.01, 0.15)	0.45 (0.36, 0.54)	0.16 (0, 0.33)
Russia, … residents (Davis et al. 20…)	52[b5]	1,933[c1]	0.77 (0.13, 1.5)[d]	0.71 (0.60, 0.82)	1.08 (0.12, 2.10)
…					

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2024 Meta-Analysis: Leave-One-Out Approach

Mortality Studies Only:			
	All Mayak (N=24) [b]	Non-Pu Mayak [c] (N=24)	Mayak Excl[illegible] (N=23)
DREF	1.99 (1.36, 3.71)	1.37 (0.91, 2.73)	[illegible]3)
Incidence Studies Only			
	(N=9)	[illegible]	(N=8)
DREF	1.73 (1.04, 5.06) [d]	[illegible]	1.40 (0.92, 2.95) [e]
Combined Mortality and Nonredund[illegible]			
	[illegible]	(N=29)	(N=28)
[illegible]	[illegible]4)	1.48 (1.06, 2.46)	1.26 (0.89, 2.16)
Studies [illegible] under 100 mGy (excludes Mayak and Chornobyl cleanup worker studies)			
	Combined Mortality and Nonredundant Incidence Studies (N=27)		Mortality Studies Only (N=22)
DREF	1.30 (0.90, 2.28)		0.86 (0.56, 1.84)

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Mayak worker cohort dominates overall outcome (see Shore et al. 2017)!

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