



Über Faktoren, die die Strahlenreaktion von Zellen beeinflussen

Andrzej Wojcik

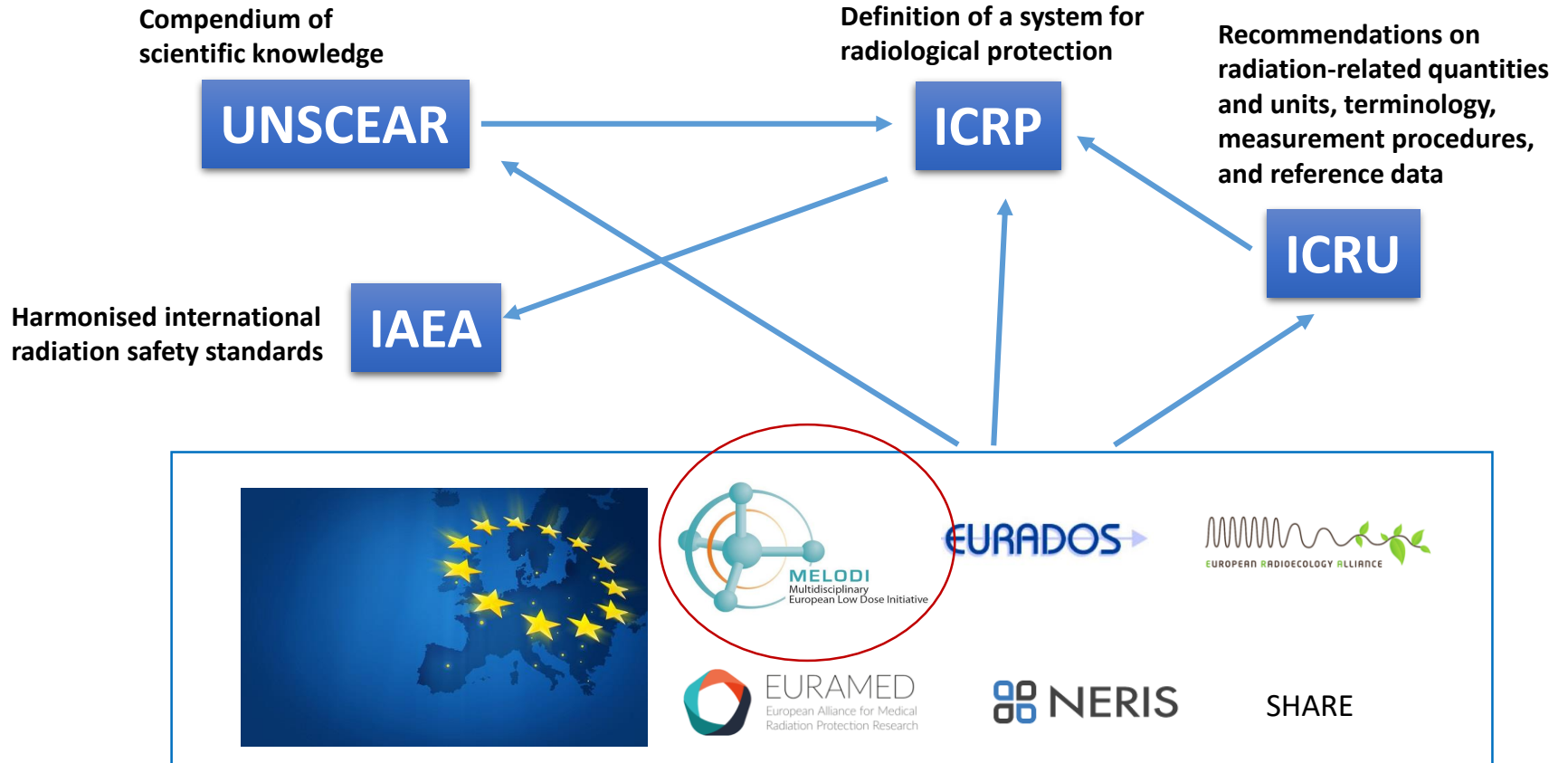
*Centre for Radiation Protection Research
Stockholm University, Sweden*

1992	H. Fritz-Niggli, Zürich
1993	H.-S. Stender, Hannover
1994	J.R. Maisin, Brüssel
1995	L.-E. Feinendegen, Jülich
1996	M. Abe, Kyoto
1997	U. Hagen, München
1998	A.W.T. Konings, Groningen
1999	K. Aurand, Berlin
2000	T.M. Fliedner, Ulm
2001	I. Szumiel, Warschau
2002	R. H. Clarke, Didcot
2003	A. Kaul, Wolfenbüttel
2004	J.J. Broerse, Leiden
2005	D. Harder, Göttingen
2007	Ch. Streffer, Essen
2010	L.E. Holm, Stockholm
2011	H. Schicha, Essen
2014	W.-U. Müller, Essen
2014	P. Gourmelon, F.-aux-Roses
2015	S. Yamashita, Fukushima
2019	R. Loose, Nürnberg





Relevant organisations in radiological protection: ICRP, UNSCEAR, IAEA, plus the European radiation research platforms





**Strategic Research Agenda of the
Multidisciplinary European Low Dose Initiative
(MELODI) – 2019**



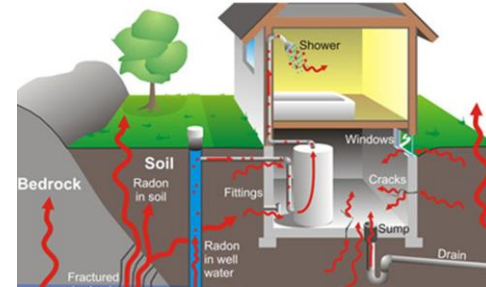
Selected topics from the Strategic Research Agenda

- Effects of spatial and temporal variation in dose delivery
- Dose and dose-rate dependence of cancer risk
- Individual variation in cancer risk

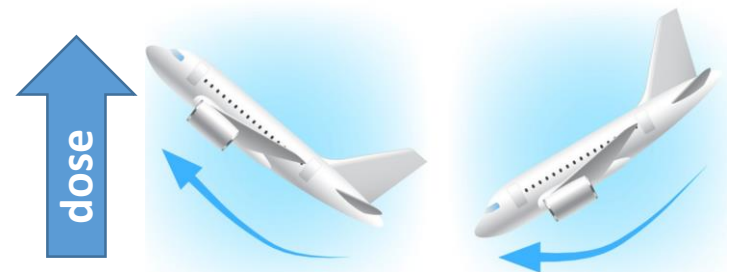


Major lines of radiobiology research at SU

Cellular effects of exposure to mixed beams of high and low LET radiation



Cellular effects of changing dose rate



Cellular effects of very high dose rate



Our main sponsor



Individual variation in cancer risk



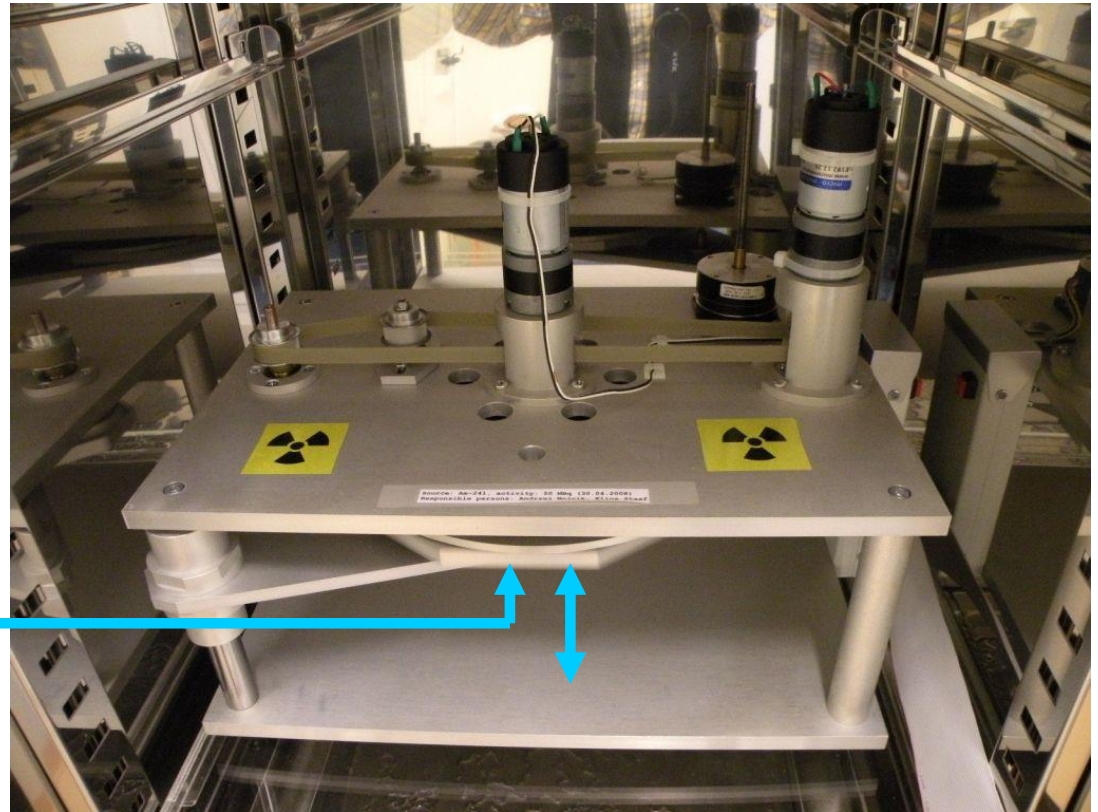


The mixed beam exposure facility at the Stockholm University

The ^{241}Am alpha irradiator – dose rate: 0.21 Gy/min

Alpha irradiator
in an incubator

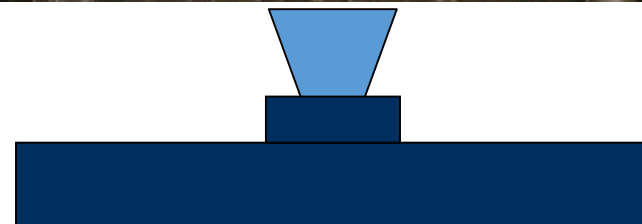
An exposure dish
covered by 1.5 μm Mylar



X-ray tube below
the incubator

0.052 Gy/min

0.068 Gy/min

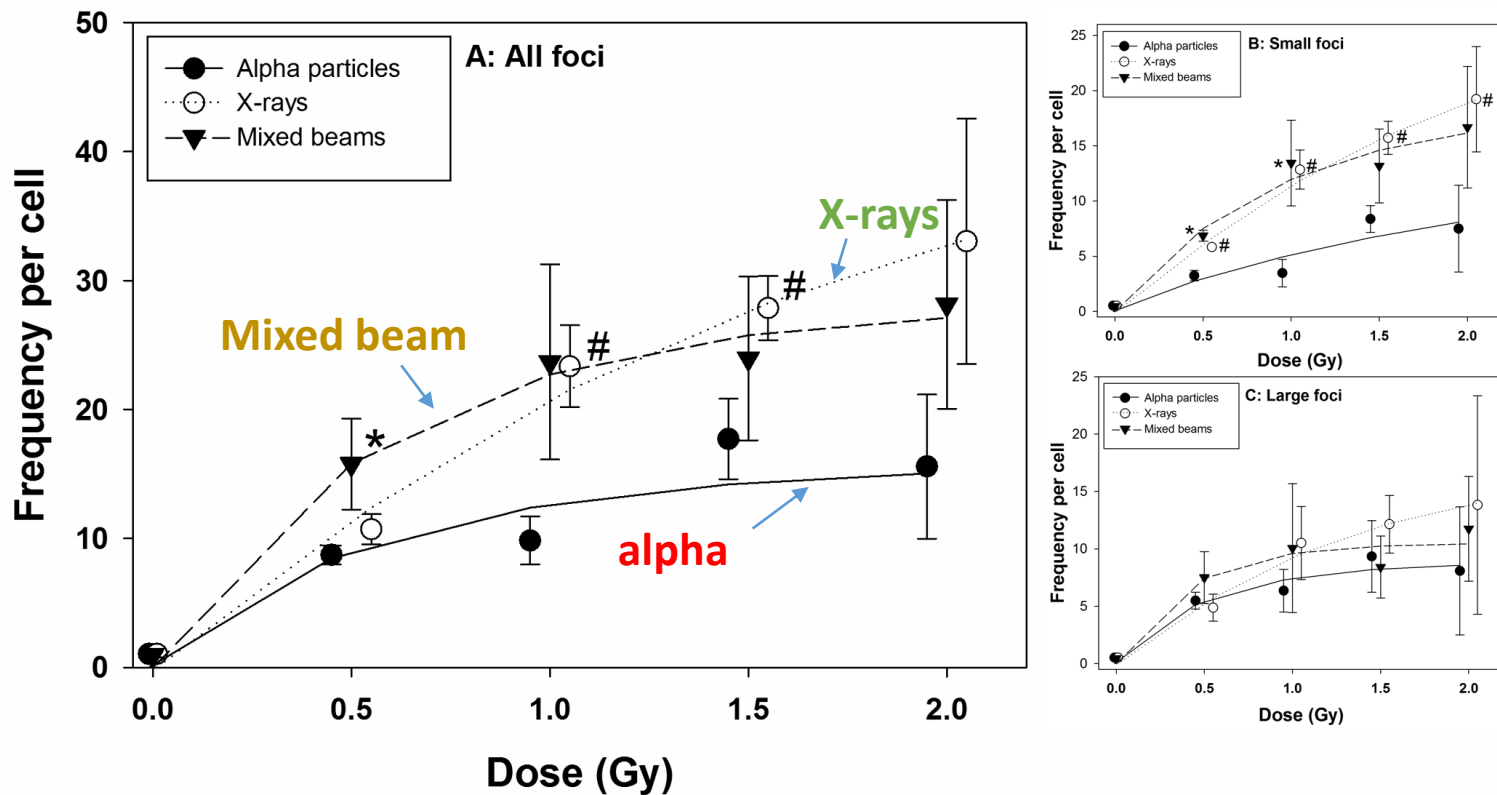


X-ray tube 190 kV
(peak at 80 keV)



53BP1 foci in U2OS cells – dose response

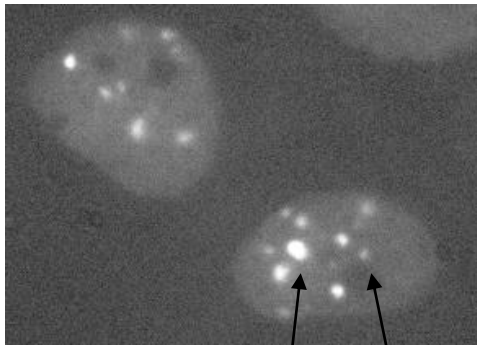
*Mixed beam-induced foci are more frequent than those induced by alphas
The effect is strongest for small foci*





53BP1-GFP foci in U2OS cells

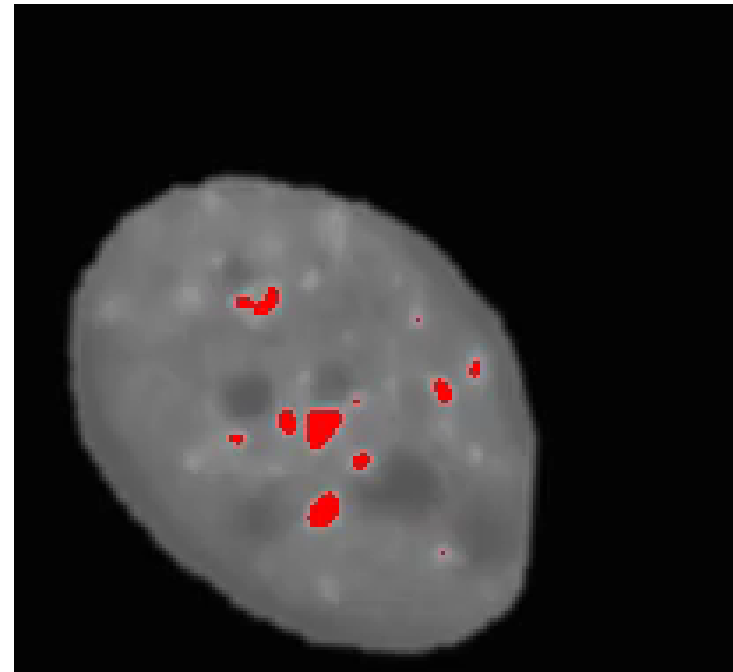
Foci in fixed cells



Small focus
(Simple damage)

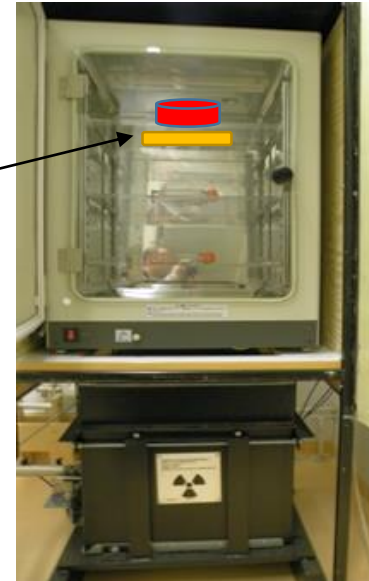
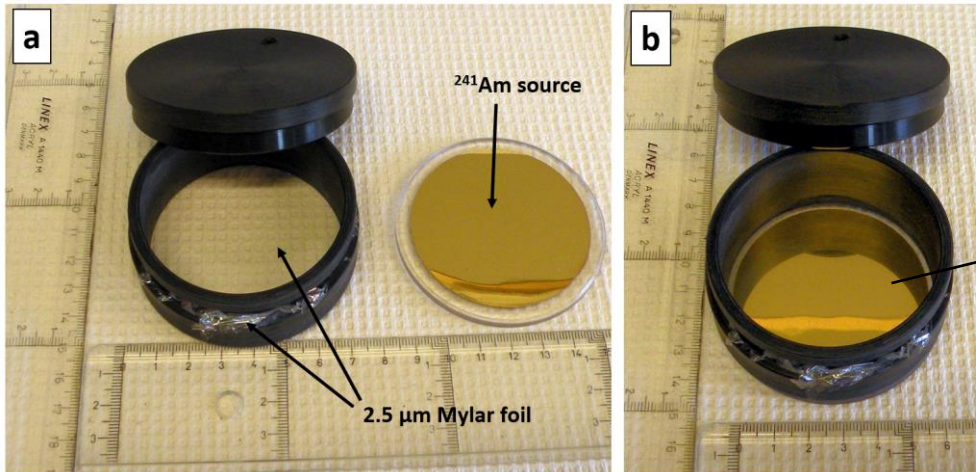
Large focus
(Complex damage)

Live image of foci identified by Image J
Time: 0-80 min post irradiation, image every 60s





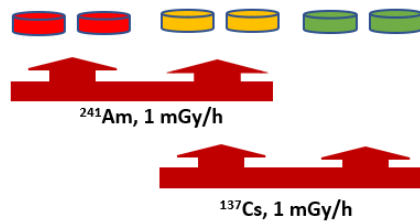
Effect of mixed beams at low doses and low dose rates



Two cell lines differing in sensitivity: VH10 and AHH-1

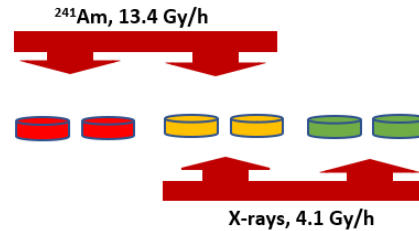
Chronic exposure

Doses: 0.05, 0.1, 0.15, 0.2 Gy



Acute exposure

Doses: 0.05, 0.1, 0.15, 0.2, 1.0 Gy

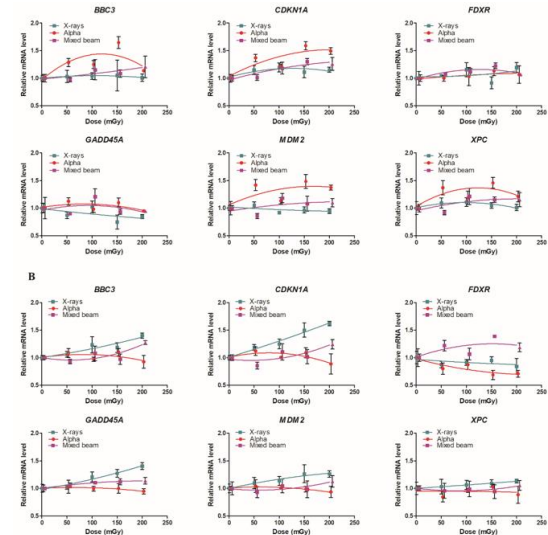


Analysed endpoints:

Gene expression: BBC3, CDKN1A, FDXR, GADD45A, MDM2, XPC

Cell proliferation

Chromosomal aberrations



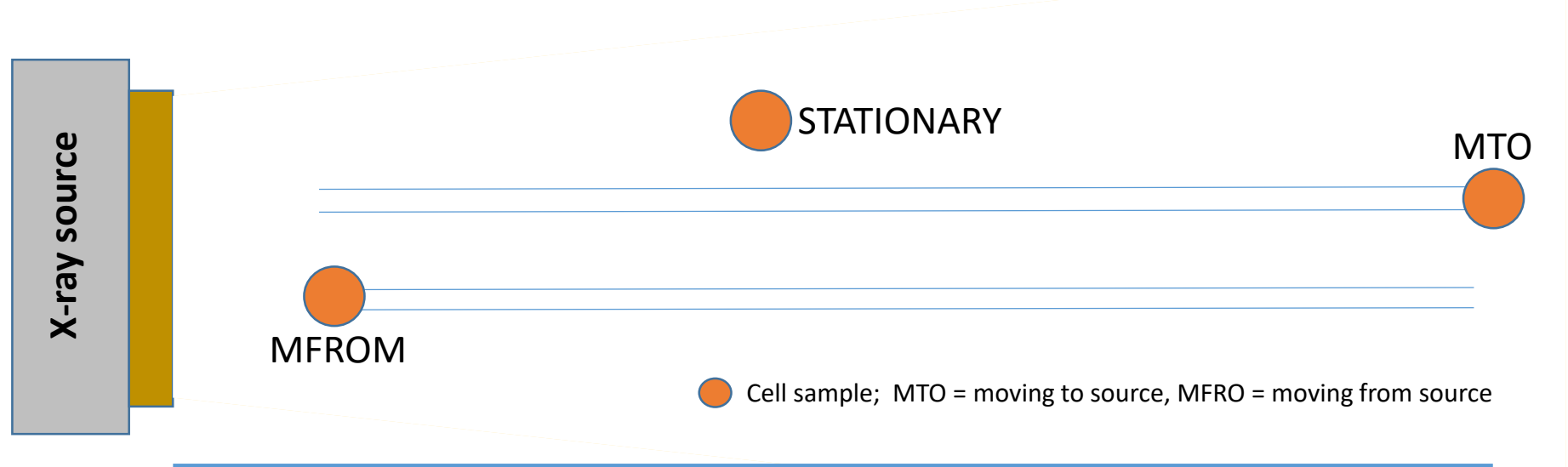
VH10

AHH-1



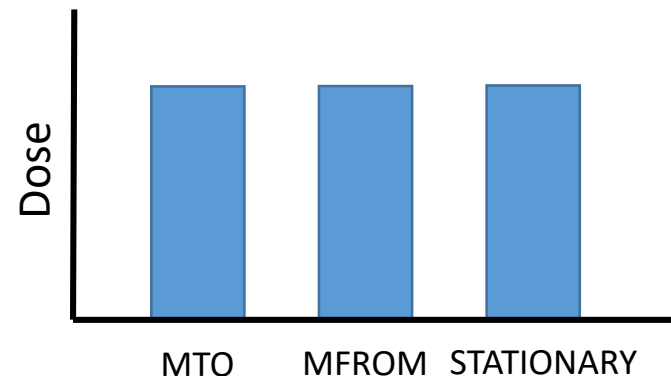
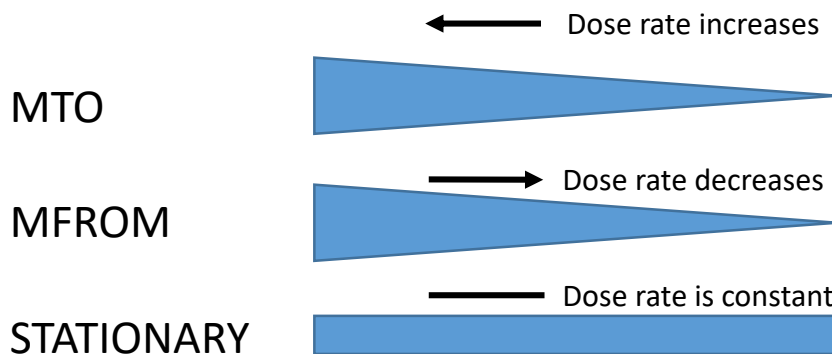
Cellular effects of changing dose rate

Motion experiments



Dose rate

Dose



The total dose is the same in all samples.



Cellular effects of changing dose rate

Filter experiment

● = Cell sample

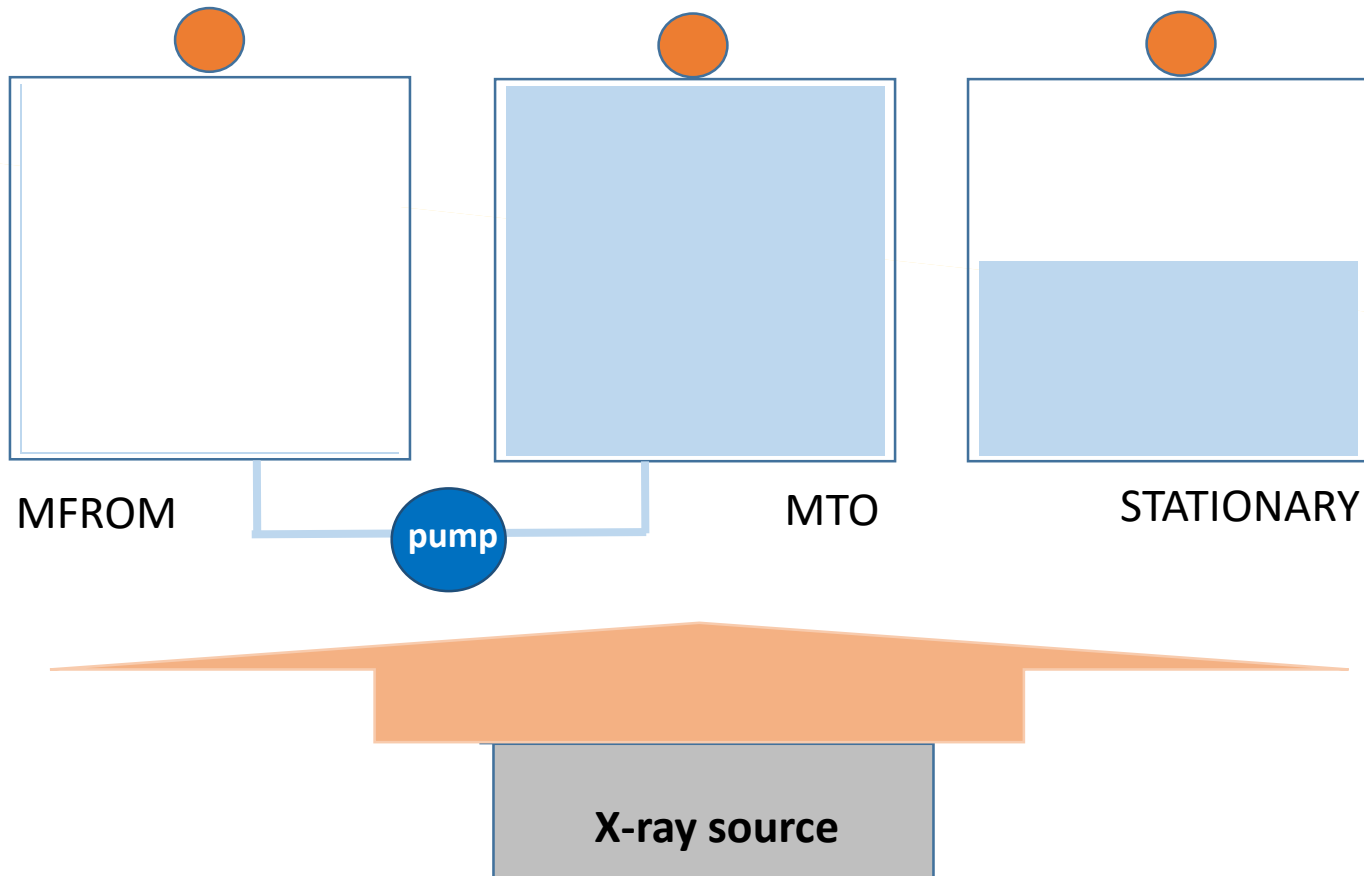
MTO = dose rate increases

MFRO = dose rate decreases

■ = BaCl₂

The total dose is again the same the same in all samples.

What about the biological effect?





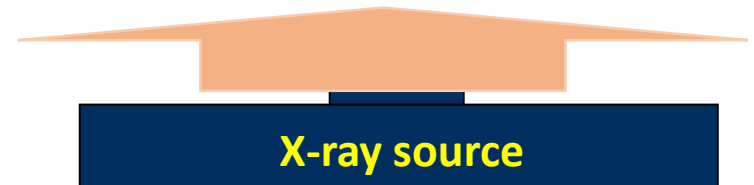
Cellular effects of changing dose rate

Images of exposure facilities

0.15 Gy/min - 0.0042 Gy/min



0.11 Gy/min - 0.0027 Gy/min



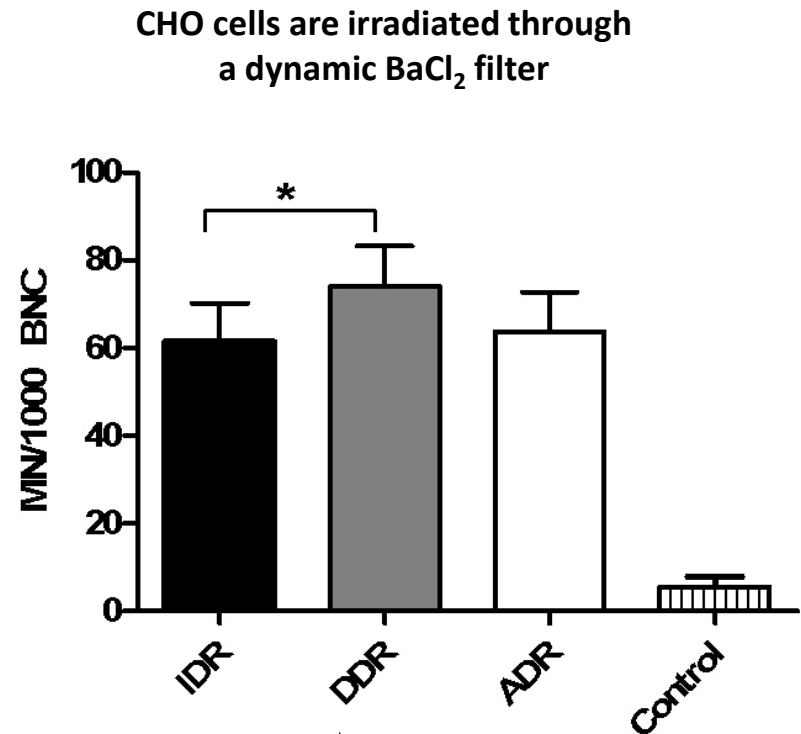
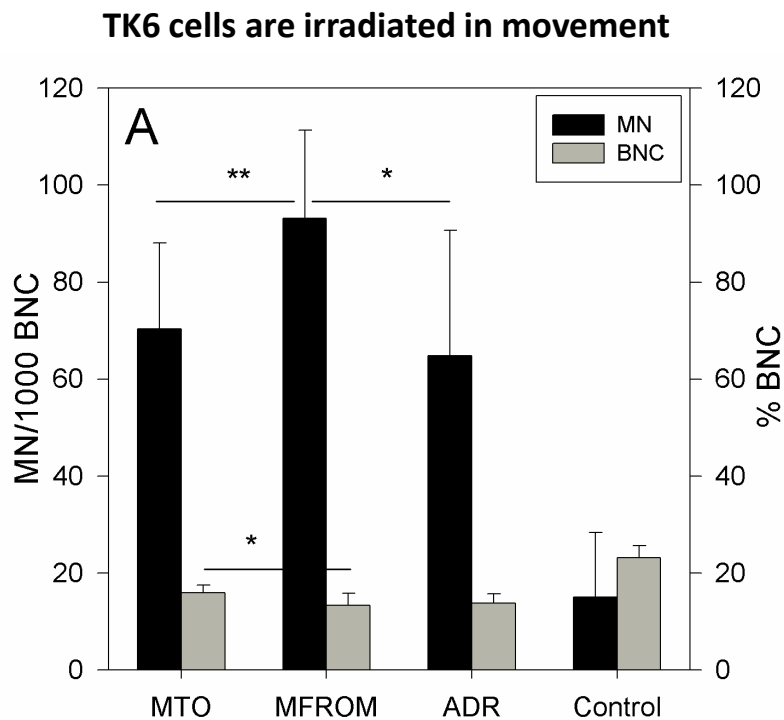


Cellular effects of changing dose rate

Some results

The highest biological effect is always seen in cells which are exposed under conditions of a decreasing dose rate

The effect has nothing to do with the adaptive response



Increasing dose rate

Decreasing dose rate

Stationary - average dose rate



Effect of very high dose rate on gene expression in peripheral blood lymphocytes

High dose rate ^{137}Cs sources available at the Stockholm University

Scanditronic
0.39 Gy/min



Gammacell Extactor
0.80 Gy/min



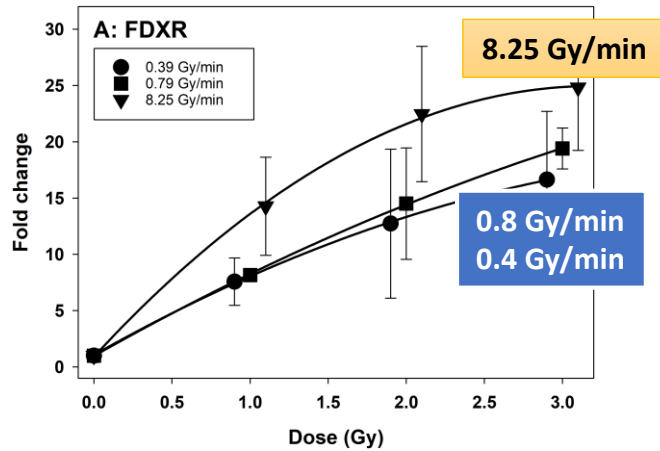
Gammacell 1000
8.25 Gy/min



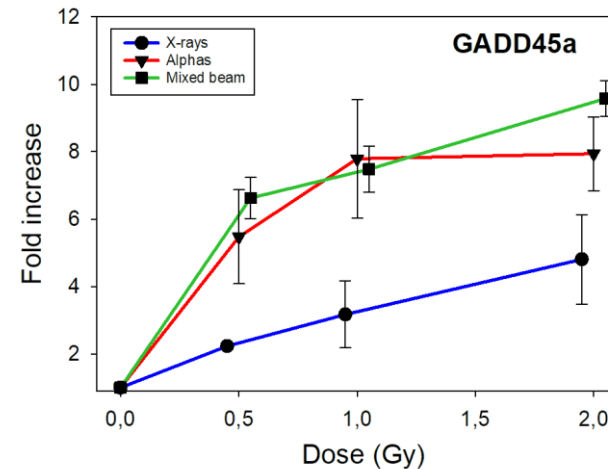
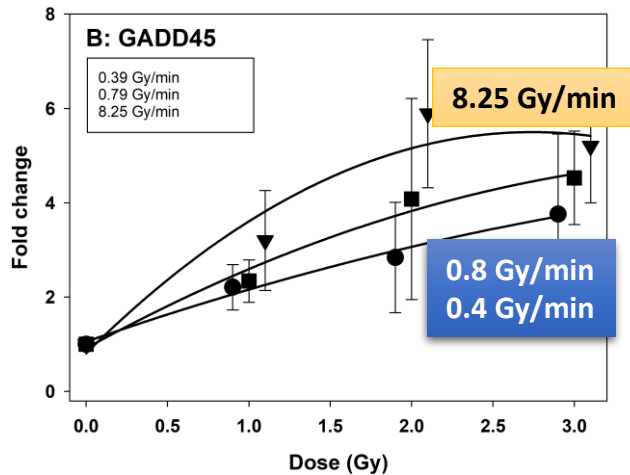
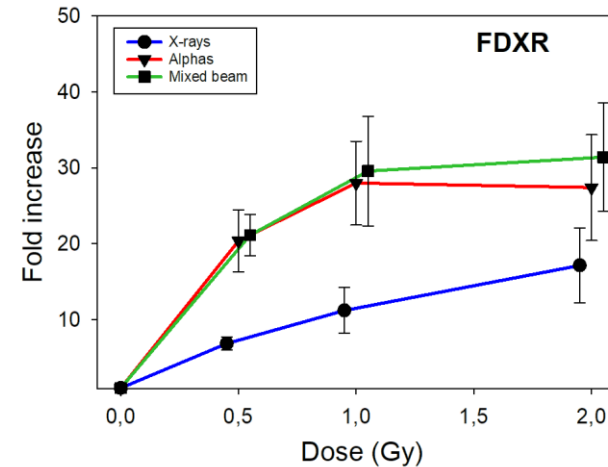


Effect of very high dose rate on gene expression in peripheral blood lymphocytes

Acute gamma radiation,
various dose rates



Acute alpha, X-ray and
mixed beam exposure



Currently running experiments at > 10 Gy/min



Individual and seasonal variability in response to radiation



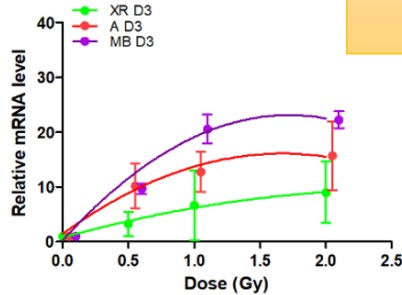


In human peripheral blood lymphocytes the effect of mixed beam radiation is individually and seasonally variable

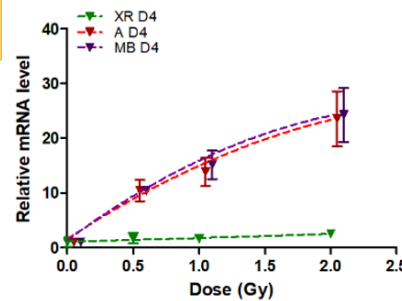
FDXR PP1

Donor 3

3 experiments
in spring

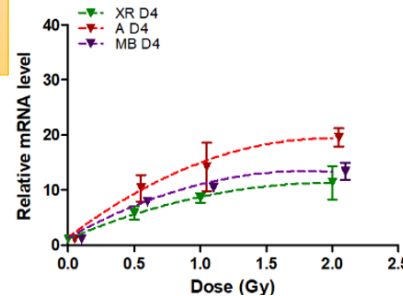
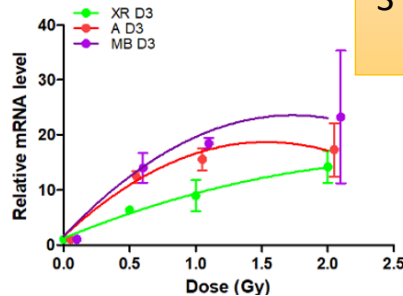


Donor 4



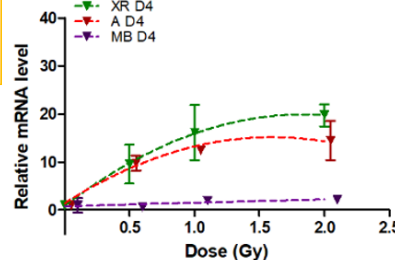
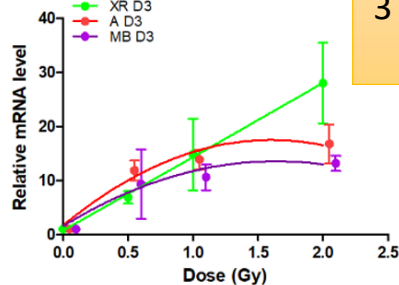
FDXR PP1

3 experiments
in summer



FDXR PP1

3 experiments
in autumn



Dose response of relative mRNA level FDXR splice variant PP1 24 hours after exposure to X-rays (green), alpha particles (red) and mixed beams in PBL from donors 3 (left) and 4 (right) obtained on three different occasions

Frequencies of chromosomal aberrations are being scored as we speak



Hans Langendorff



“Thus, Langendorff focused during his early years of radiobiology research on questions of great scientific interest, **many aspects of which remain unanswered even today**: mechanisms of cell proliferation, mitotic (cell) cycle, dose fractionation, **inherent radiosensitivity**, biological consequences of radiation such as cell death, **chromosomal damage, recovery from radiation damage** and most importantly the **dependence of many of these effects on radiation quality**”.

INTERNATIONAL JOURNAL OF RADIATION BIOLOGY
2019, VOL. 95, NO. 7, 1029–1042
<https://doi.org/10.1080/09553002.2019.1623428>

 Taylor & Francis
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REVIEW

 Check for updates

Radiobiology at the forefront: Hanns Langendorff and two of his disciples

Source

Christian Streffer



Wo geht es denn hin...





Essen, November 1991



Juli 1990 – September 1996