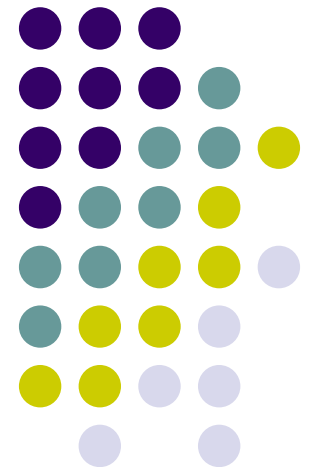


# Comparative risk assessment with ionising and non- ionising radiation

Jürgen Kiefer  
Justus-Liebig-Universität  
Giessen, Germany



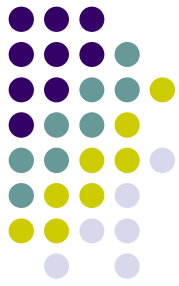
# The „Bradford-Hill Criteria“



**Strength**  
**Consistency**  
**Specificity**  
**Temporality**  
**Biological gradient**  
**Plausibility**  
**Coherence**  
**Experiment**  
**Analogy**

Hill, A.B. (1965). "The environment and disease: association or causation?". Proceedings of the Royal Society of Medicine 58: 295-300.

# Consistency



Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.

# Biological gradient



Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect.

*(Dose-effect relationship)*

# Plausibility



A plausible mechanism between cause and effect is helpful (but Hill noted that knowledge of the mechanism is limited by current knowledge)

# Coherence



Coherence between epidemiological and laboratory findings increases the likelihood of an effect.

But also: *Different agents claimed to have the same effect should display an analogous pattern of reactions, both in vivo and in vitro (JK).*

# Radiation effects in humans



## Acute Effects

### **Impairment of organ function:**

Blood forming system, alimentary tract, fertility, skin

Eye cataracts

Acute radiation syndrome and acute radiation death

### Teratogenic Effects

### **Characteristics:**

*Extent* is dose dependent

Effects are *deterministic*

There are threshold doses

## Late Effects

**Genetic Risk by germ line mutations, cancer**

### **Characteristics:**

*Probability* is dose dependent

Effects are *stochastic*

Threshold doses are not known



**Approaches  
to risk assment**

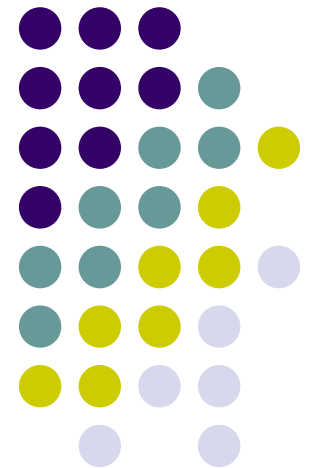
**Epidemiology**

**Animal studies**

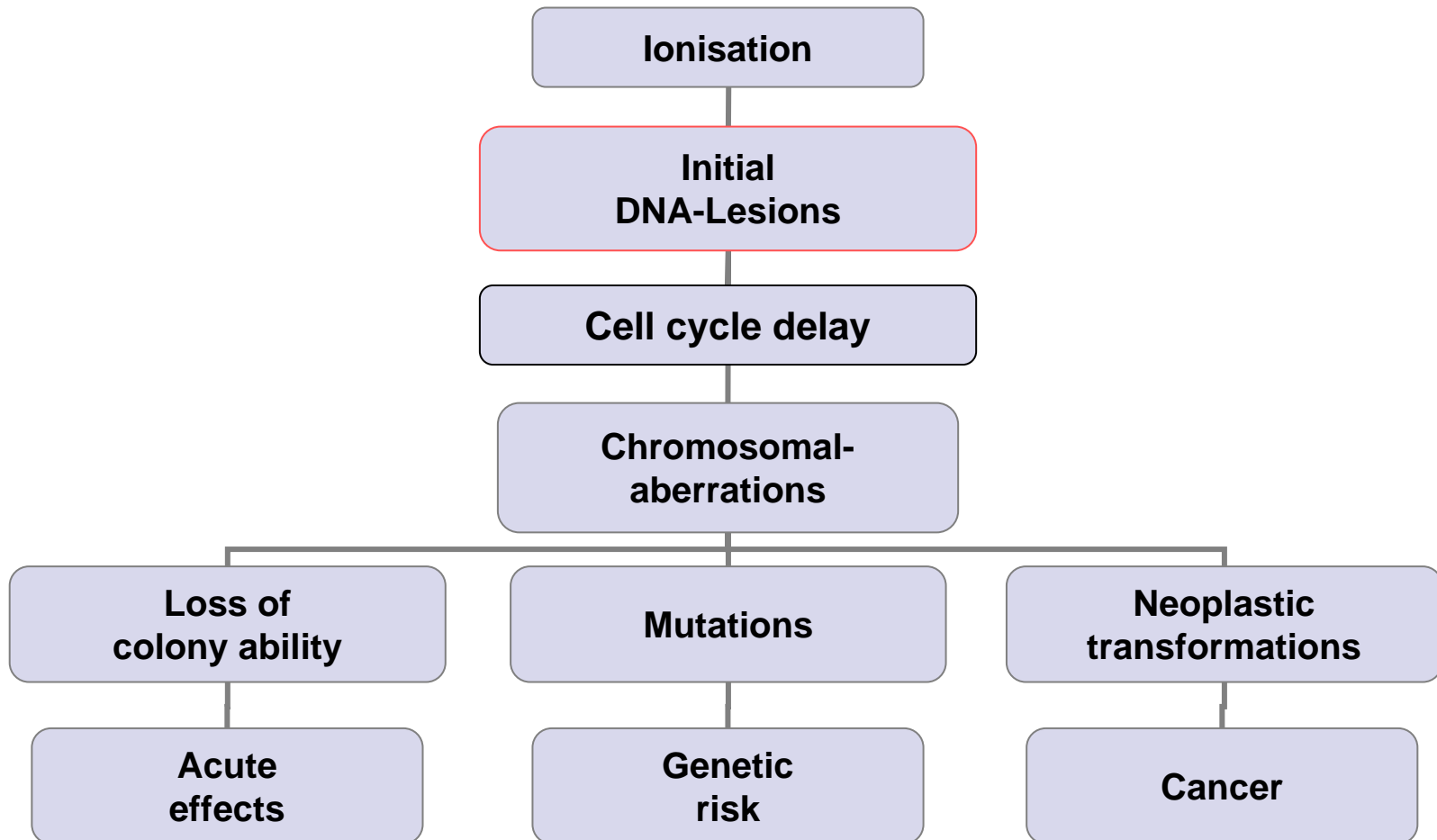
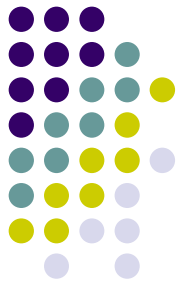
**In-vitro-  
experiments**

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# Ionising radiations

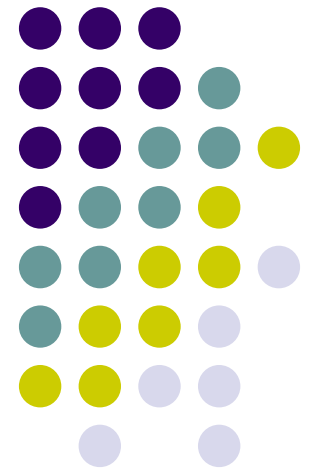


# Pathway of radiation effects (ionising radiations)



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# Ionising radiation



# Fundamental Studies on Radiation Carcinogenesis

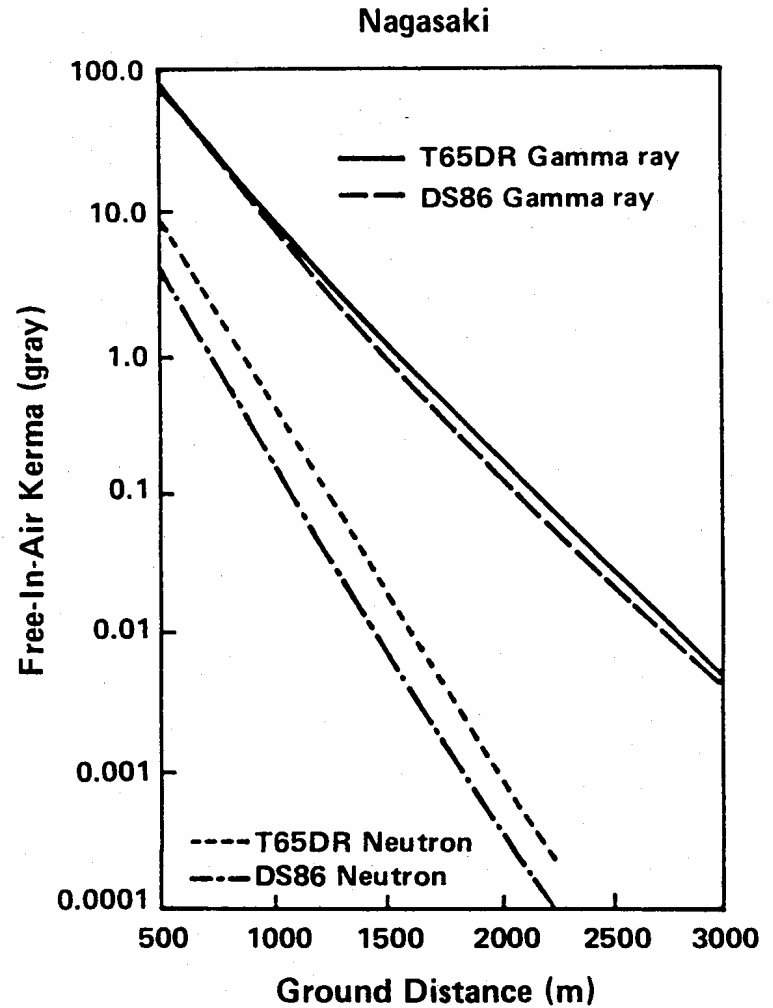
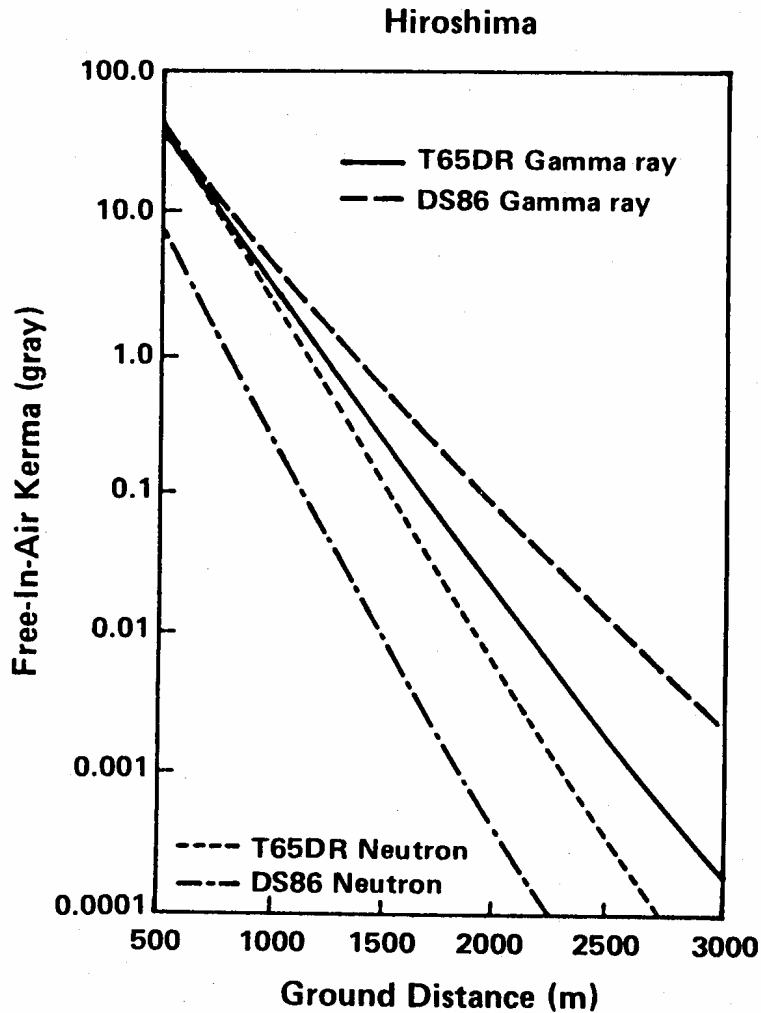


- **Japanese Mortality Study 1950-1990:**  
86 572 persons, 2 812 863 person years,  
mean dose (exposed) : 0,21 Sv  
*D. A. Pierce et al., Radiat. Res. 146, 1–27 (1996).*
- **Japanese Mortality Study 1950-1997:**  
86 572 persons, 2 812 863 person years,  
mean dose (exposed) : 0,21 Sv  
*D. L.. Preston, D. Let al., Radiat. Res. 160, 381–407 (2003).*
- **Japanese Incidence Study 1958-1998:**  
105 427 persons,  
*D. L. Preston et al., Radiat. Res. 168, 1-64 (2007).*
- **Occupationally Exposed People (mortality):**  
407 391 persons, 5 200 000 person years,  
mean dose (exposed): 0,0194 Sv  
*E. Cardis et al., Brit. Med J. 331, 77-82 (2005)*

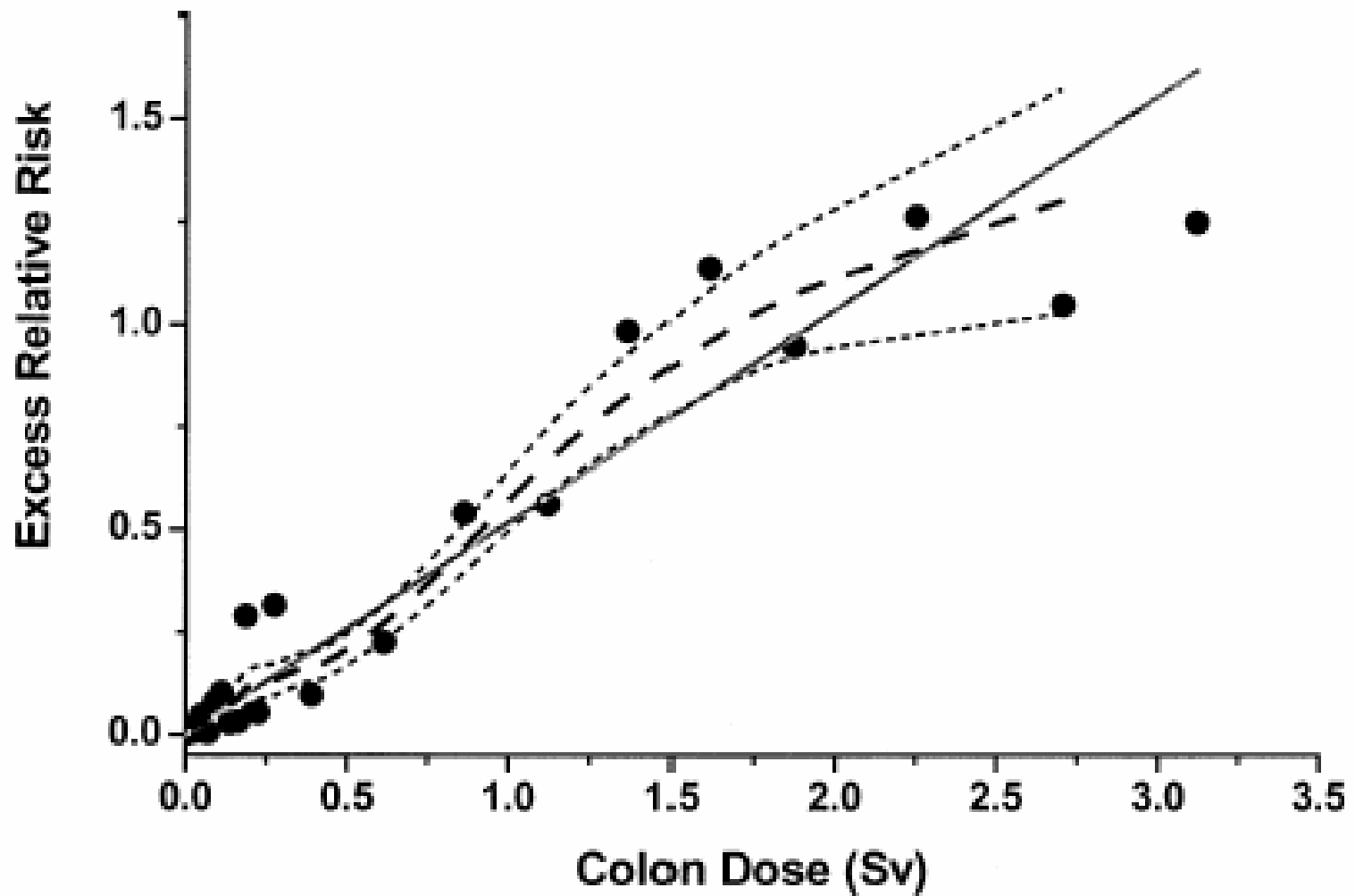
# Atomic bomb survivors: Dosimetry



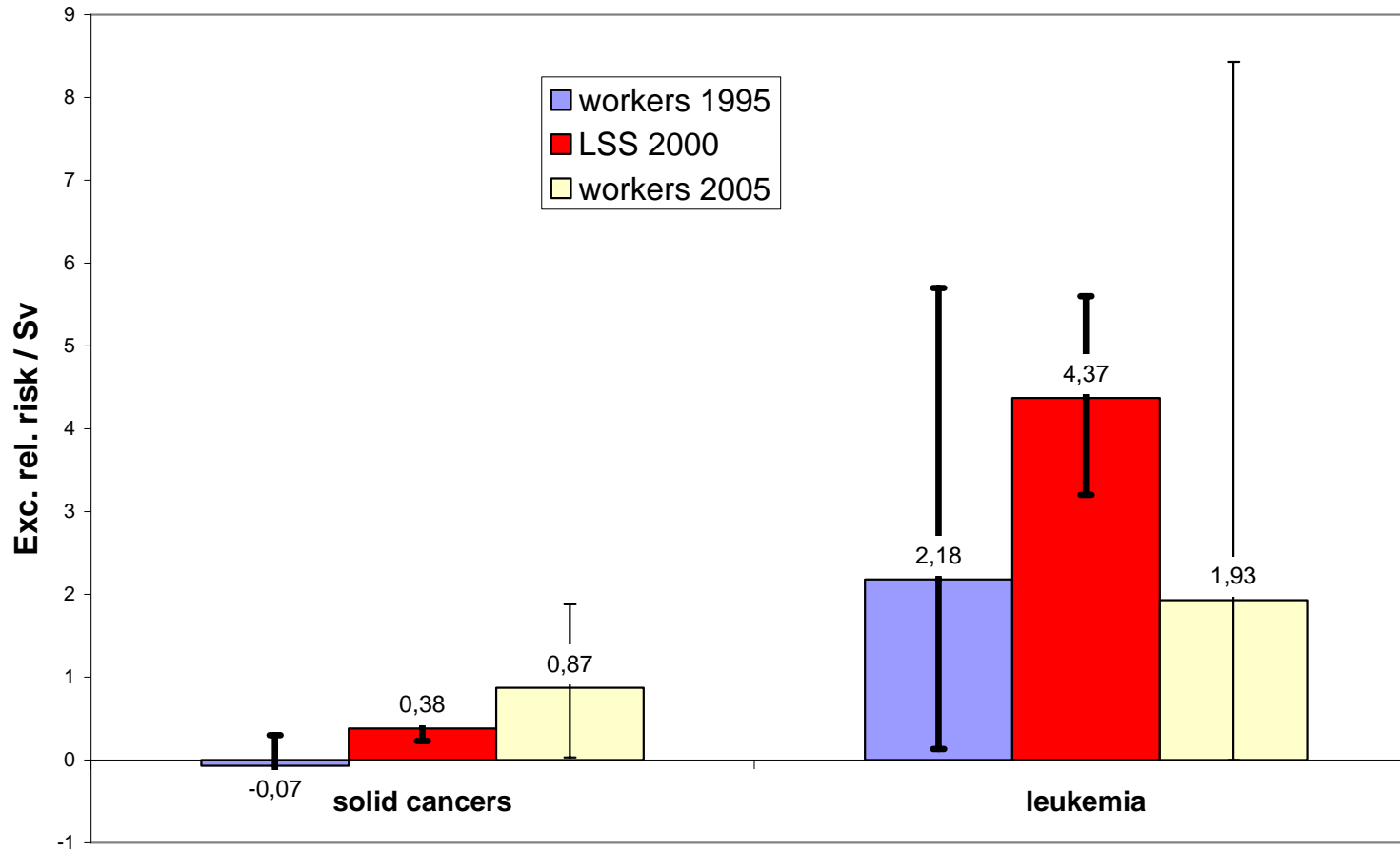
System 1965  
o?



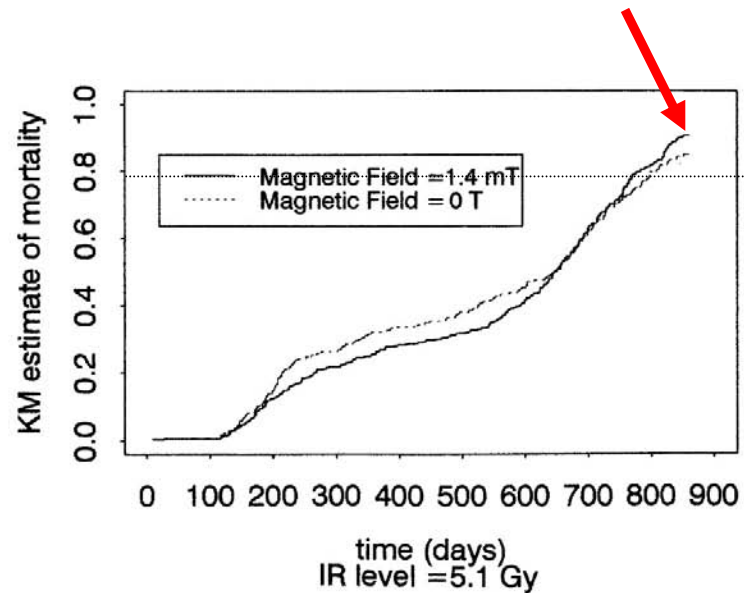
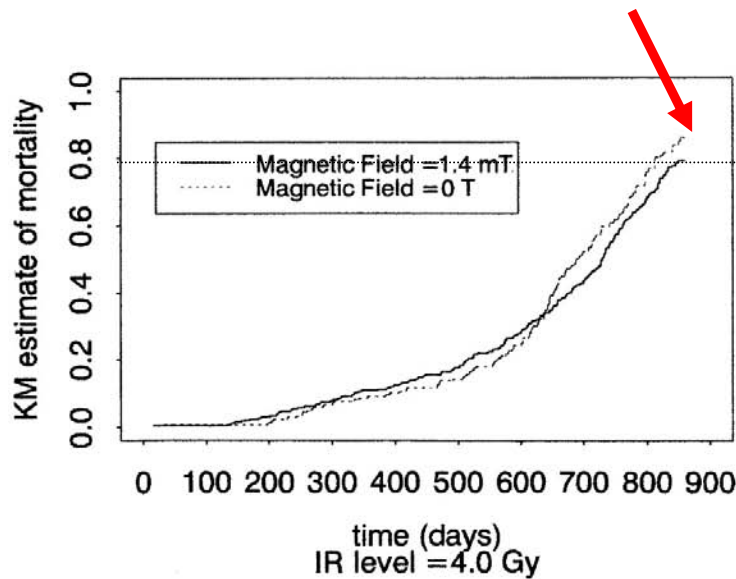
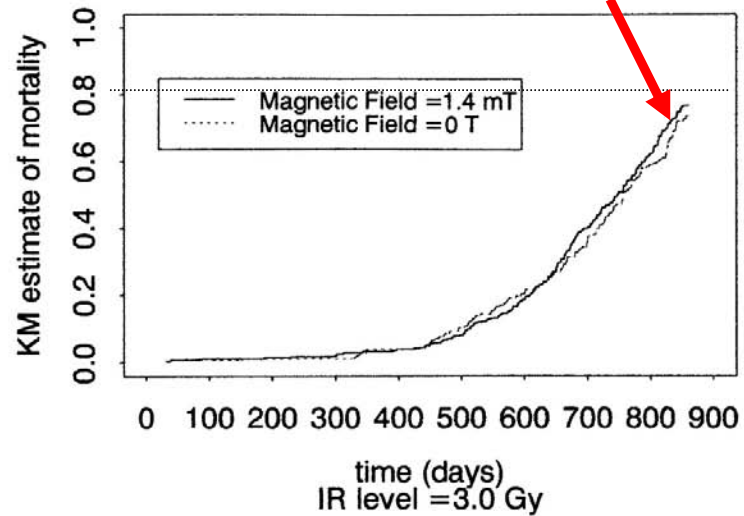
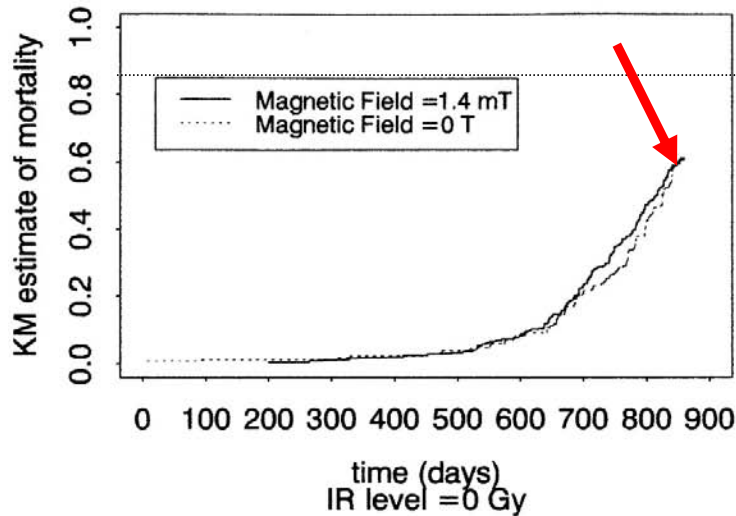
# Solid Tumours (atomic bomb survivors 1950-1990)



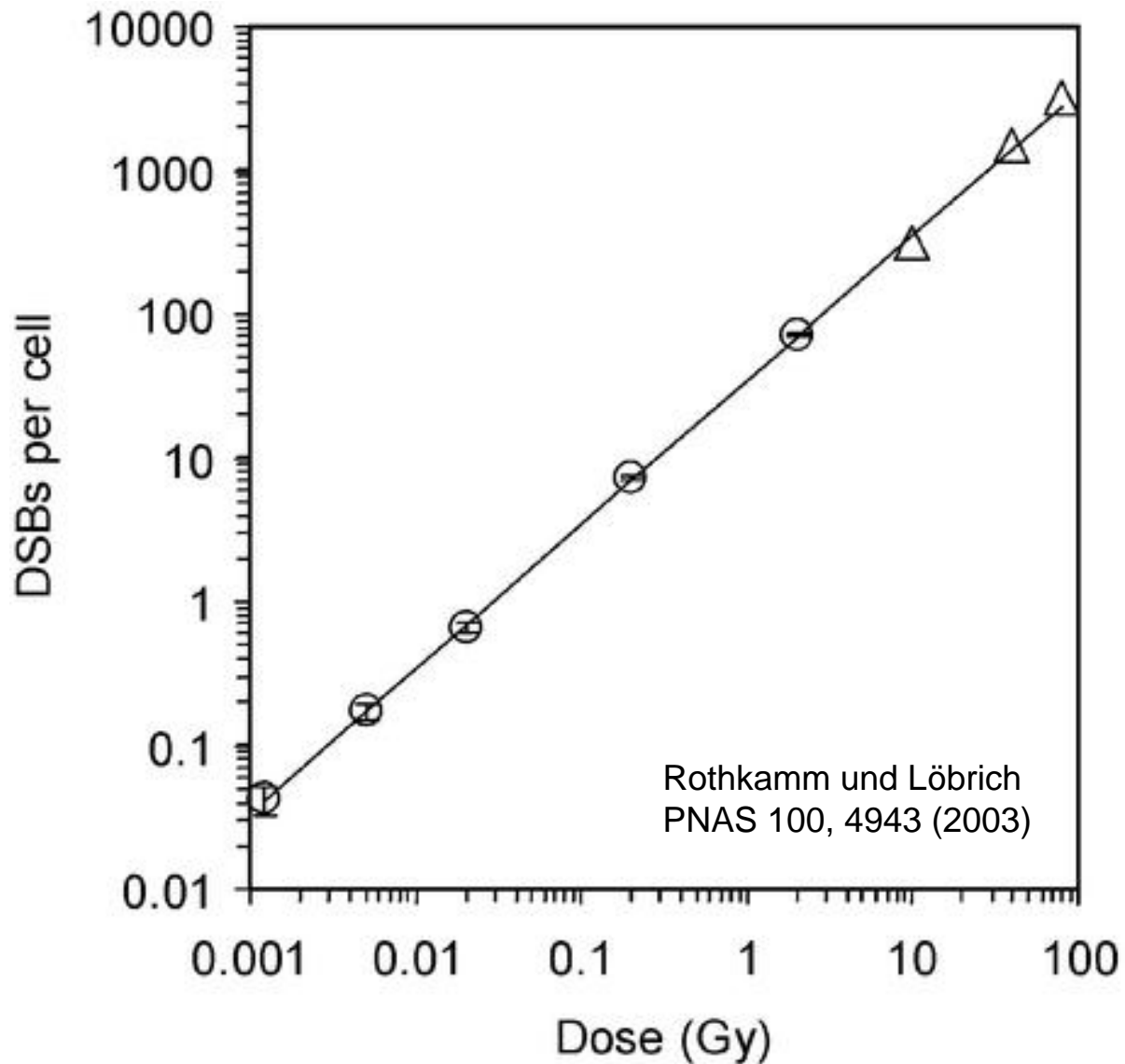
# Risk comparison: Consistency

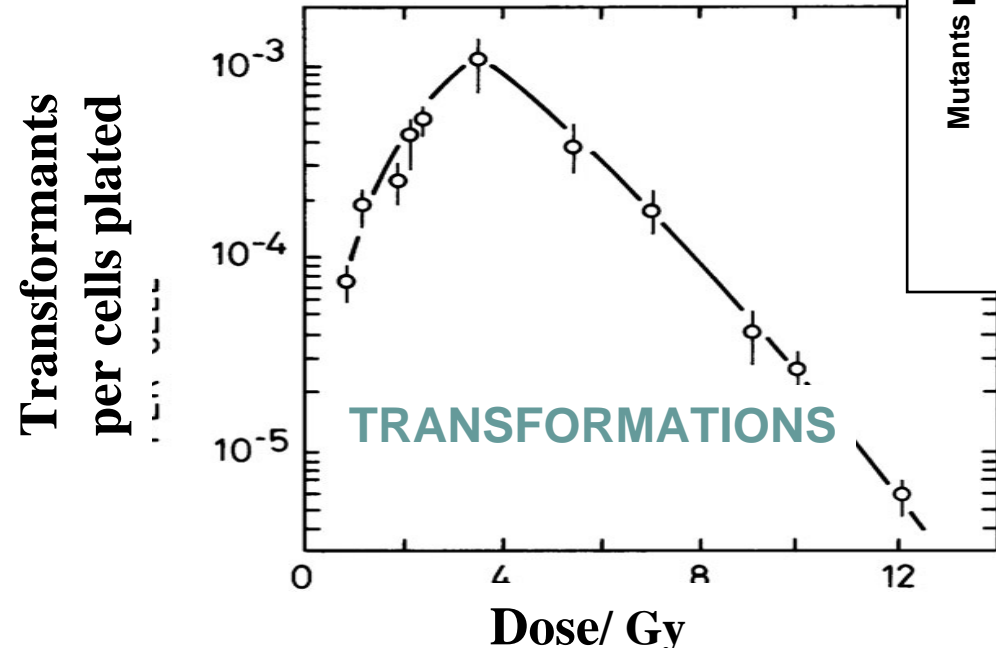
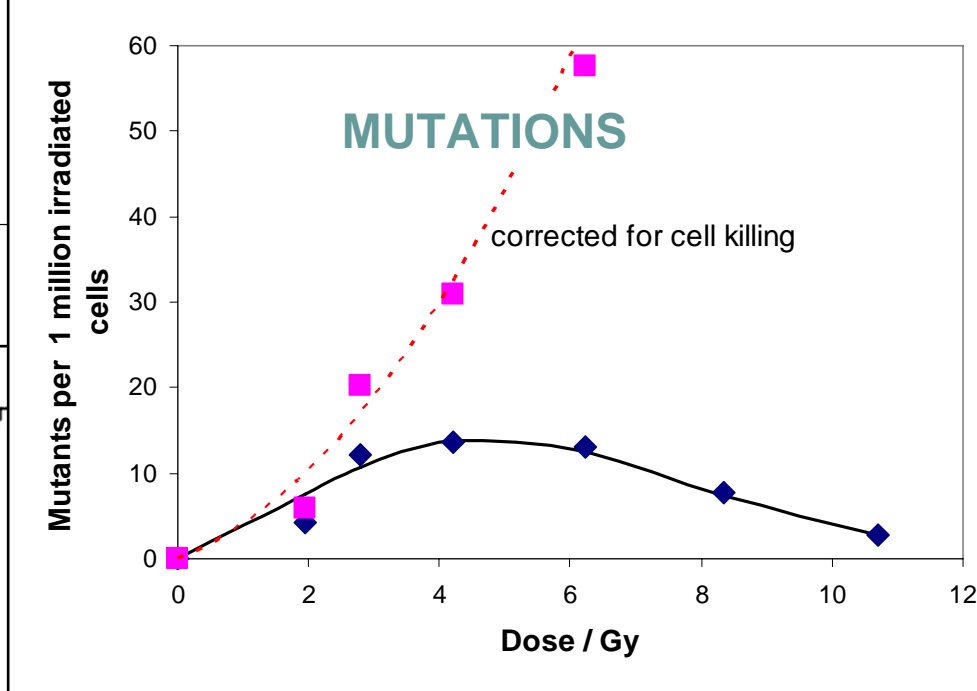
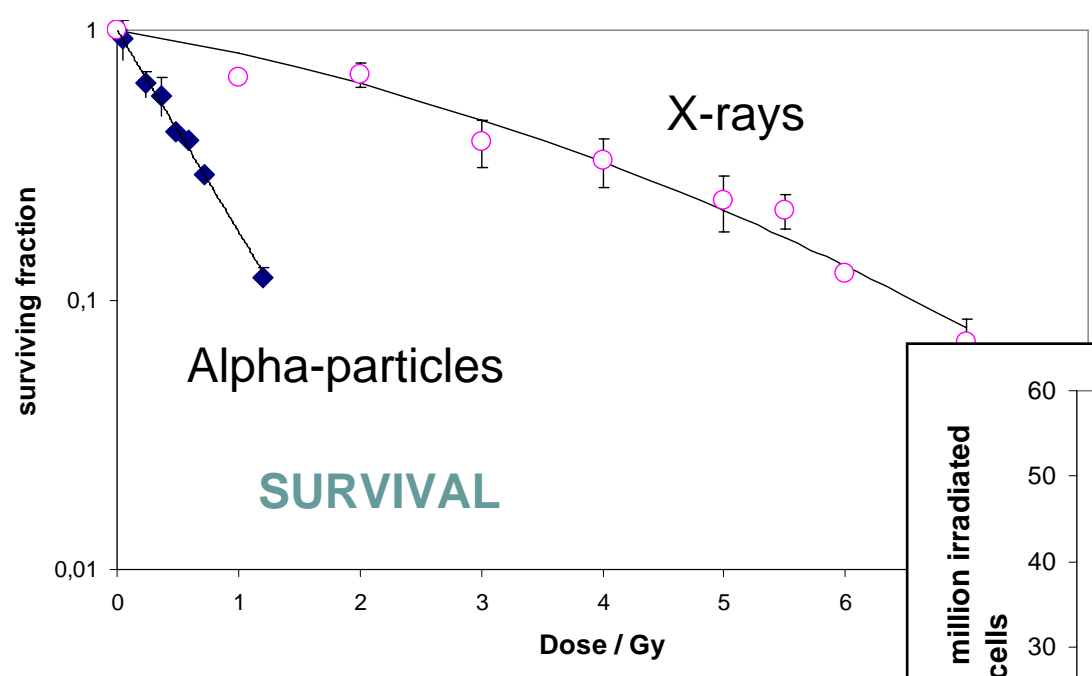


# X-rays: Tumours in animals



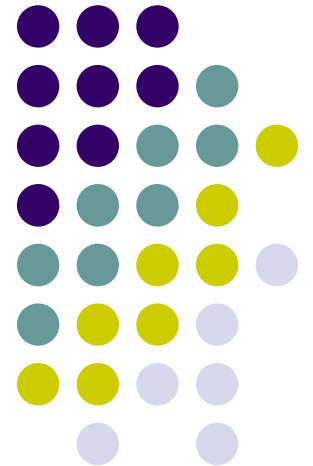
# X-rays: Linear induction of double strand breaks



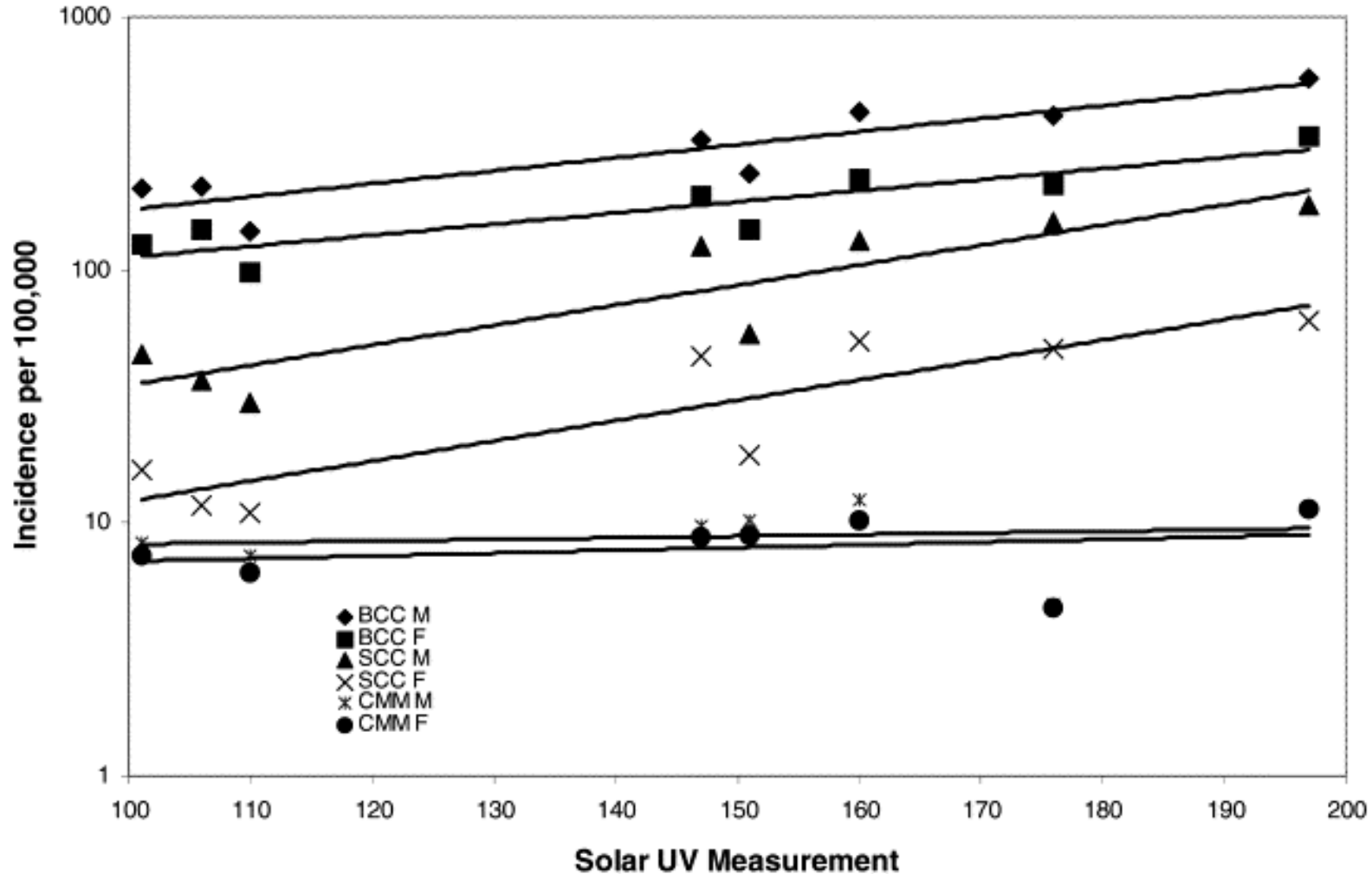


**Cellular radiation effects**

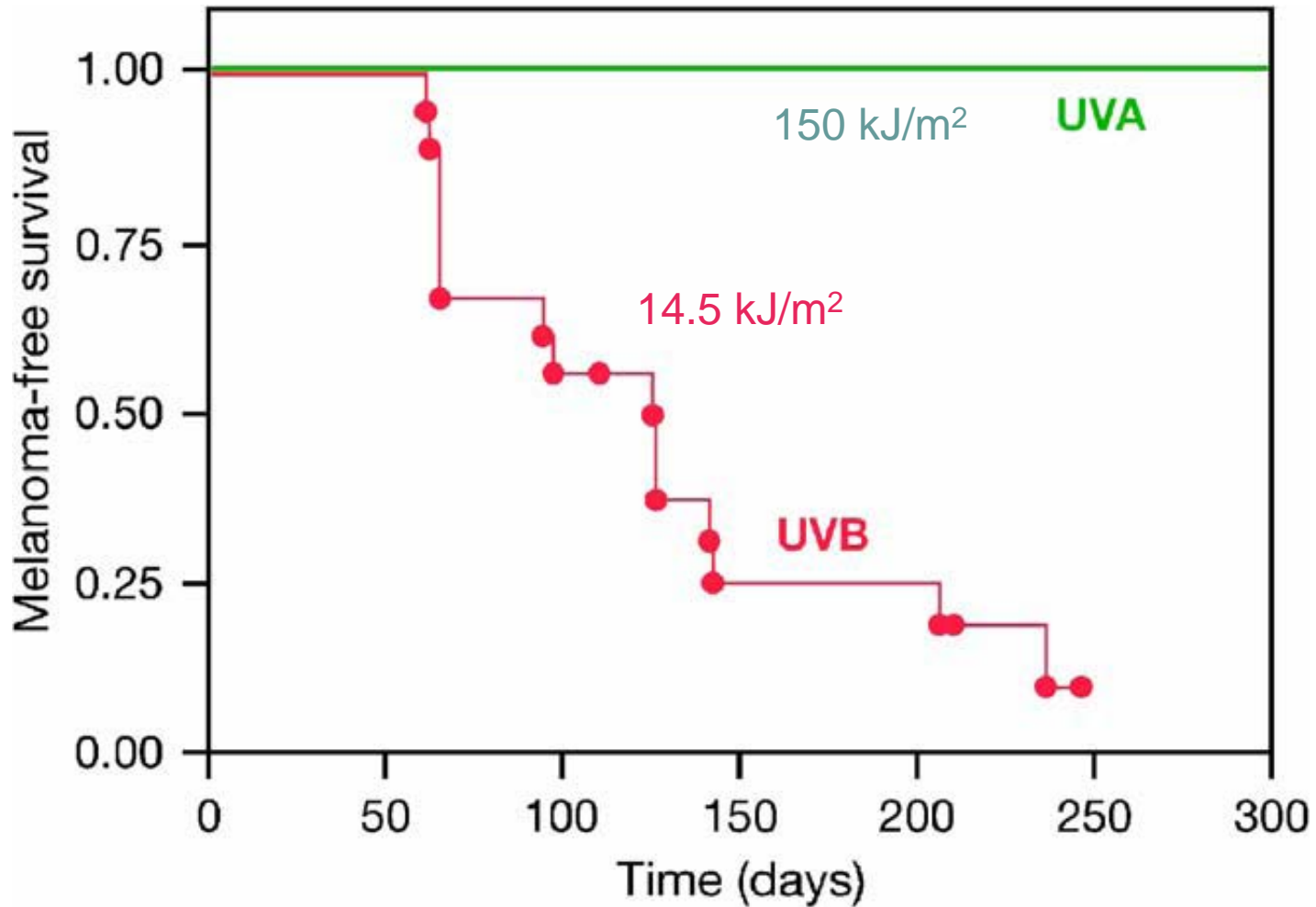
# Ultraviolet



# UV: Epidemiological evidence

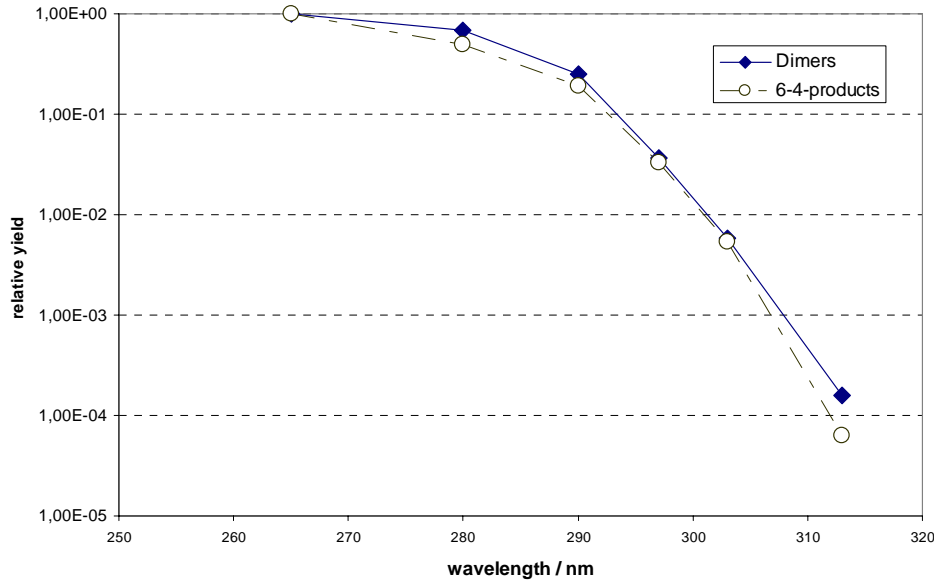


# UV: Melanoma in mice





# UV-photoproducts

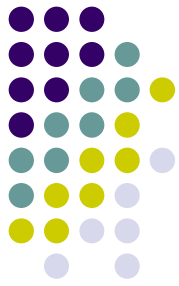


Action spectrum

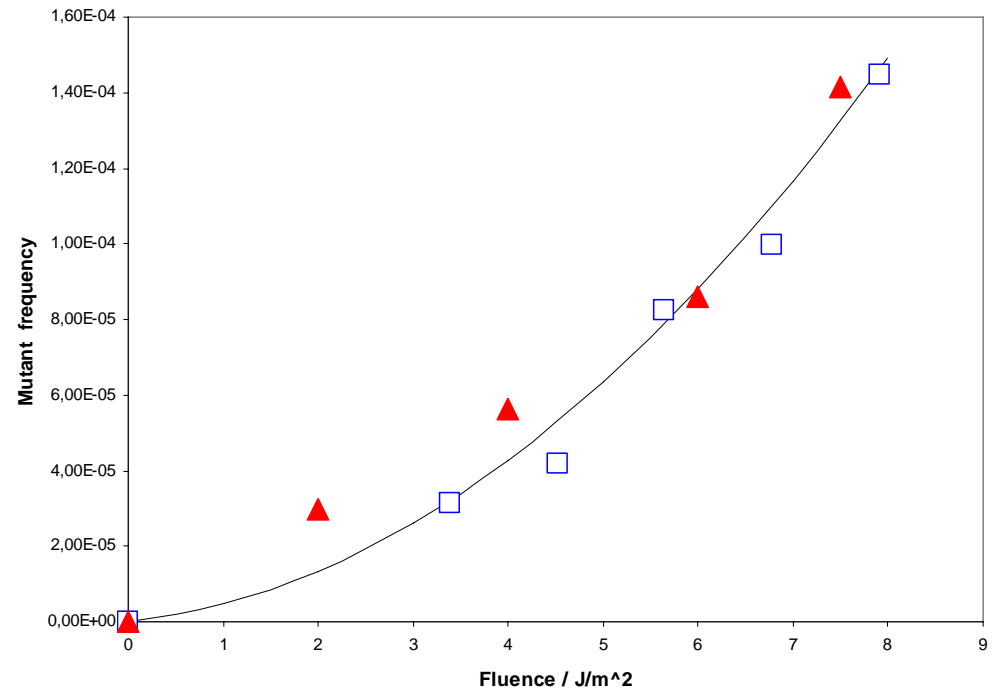
Product	Yield ( $10^8 \text{ u}^{-1}$ ( $\text{Jm}^{-2}$ ) $^{-1}$ )	Relative yield	Reference
CPD	2.0	1	Rosenstein and Mitchell 1987
6-4 product	0.4	0.2	Rosenstein and Mitchell 1987
DNA-protein crosslinks	$1.3 \times 10^{-4}$	$6.6 \times 10^{-5}$	Peak et al. 1985
DNA single strand breaks	$4.1 \times 10^{-4}$	$2 \times 10^{-4}$	Rosenstein and Ducore 1983

Product yields in mammalian cells with 254 nm

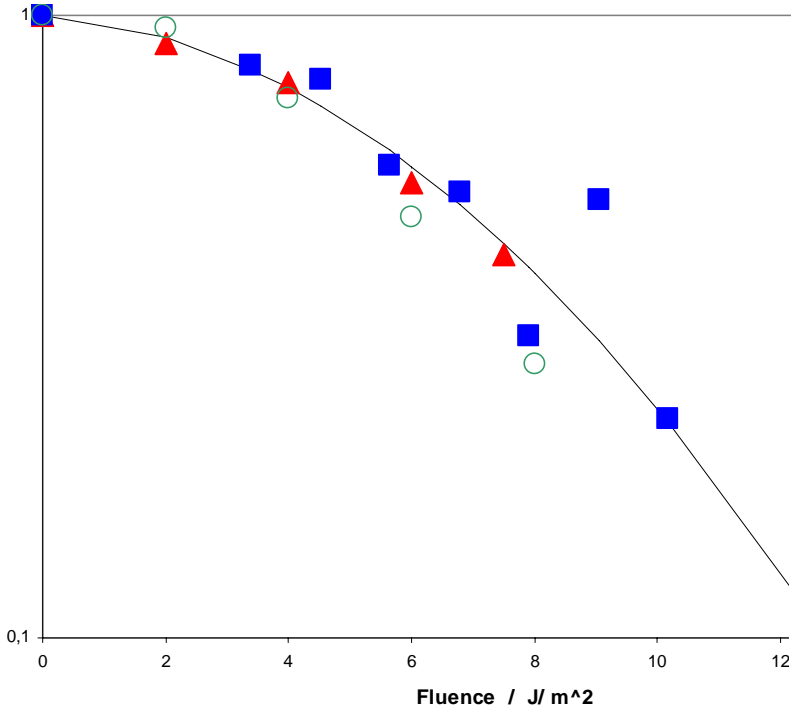
# UV: Cellular effects



## Mutations

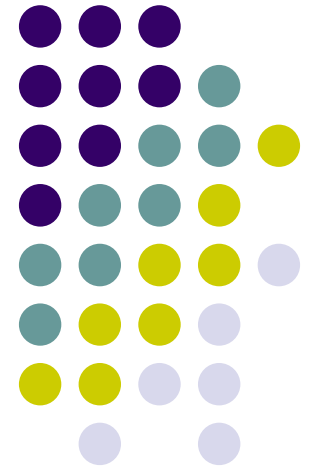


## Survival



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# Radiofrequency



# RF: Epidemiological evidence

(INTERPHONE study: IARC update February 2008)



- The study includes approximately 2600 gliomas, 2300 meningiomas, 1100 acoustic neurinomas, 400 parotid gland tumours and their respective controls.
- In most studies, the OR related to ever having been a regular mobile phone user was below 1.
- For **glioma**,.... pooling of data from Nordic countries and part of the UK yielded a significantly increased risk of glioma related to use of mobile phones for a period of 10 years or more on the side of the head where the tumour developed. This finding could either be causal or artifactual, related to differential recall between cases and controls.
- For **meningioma** and **acoustic neurinoma**, most national studies provided little evidence of an increased risk.
- For **parotid gland tumours**, no increased risk was observed overall for any measure of exposure investigated.

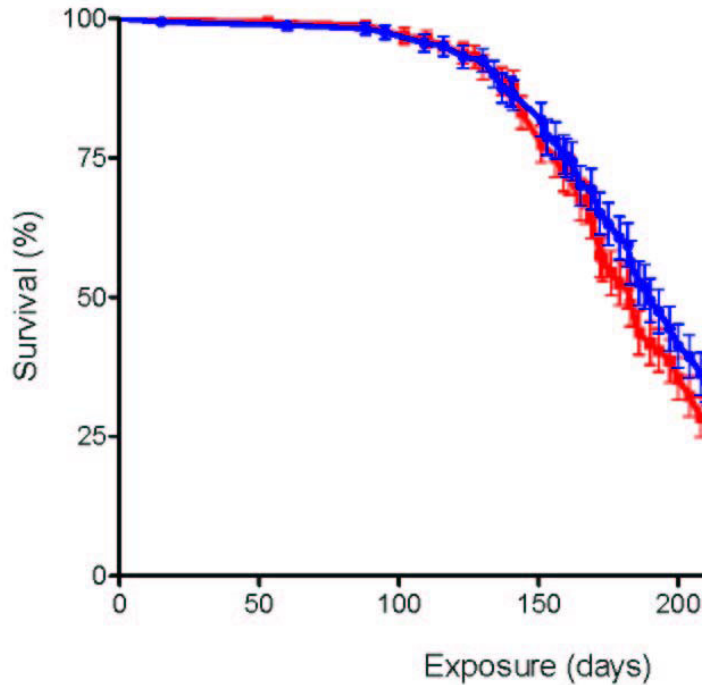
# Radiofrequency: Cancer studies in animals



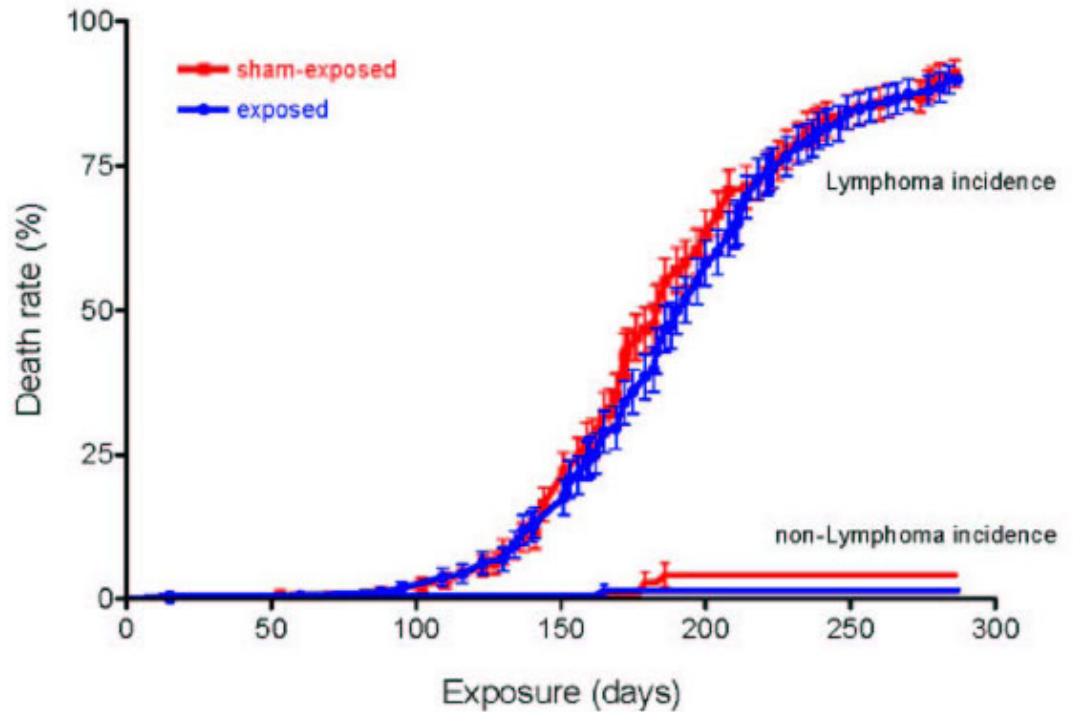
„Under the described experimental circumstances and with the shortcomings listed below, the animal cancer studies reviewed and published until now did not show a significant tumor-promoting or co-carcinogenic effect due to mobile phone-relevant rf radiation. The only exception was Repacholi’s study of 1997...“

C. Dasenbrock, Toxicol Appl Pharmacol.207:342-346 (2005).

# RF: Leukemia in mice



sham-exposed  
exposed



Sommer, A. et al.,  
BMC Cancer 4: 77 (2004)

# RF: Cellular effects



## Survival:

There are no studies on colony forming ability.

## Mutations:

There is only one study on mutation induction in mammalian cells:

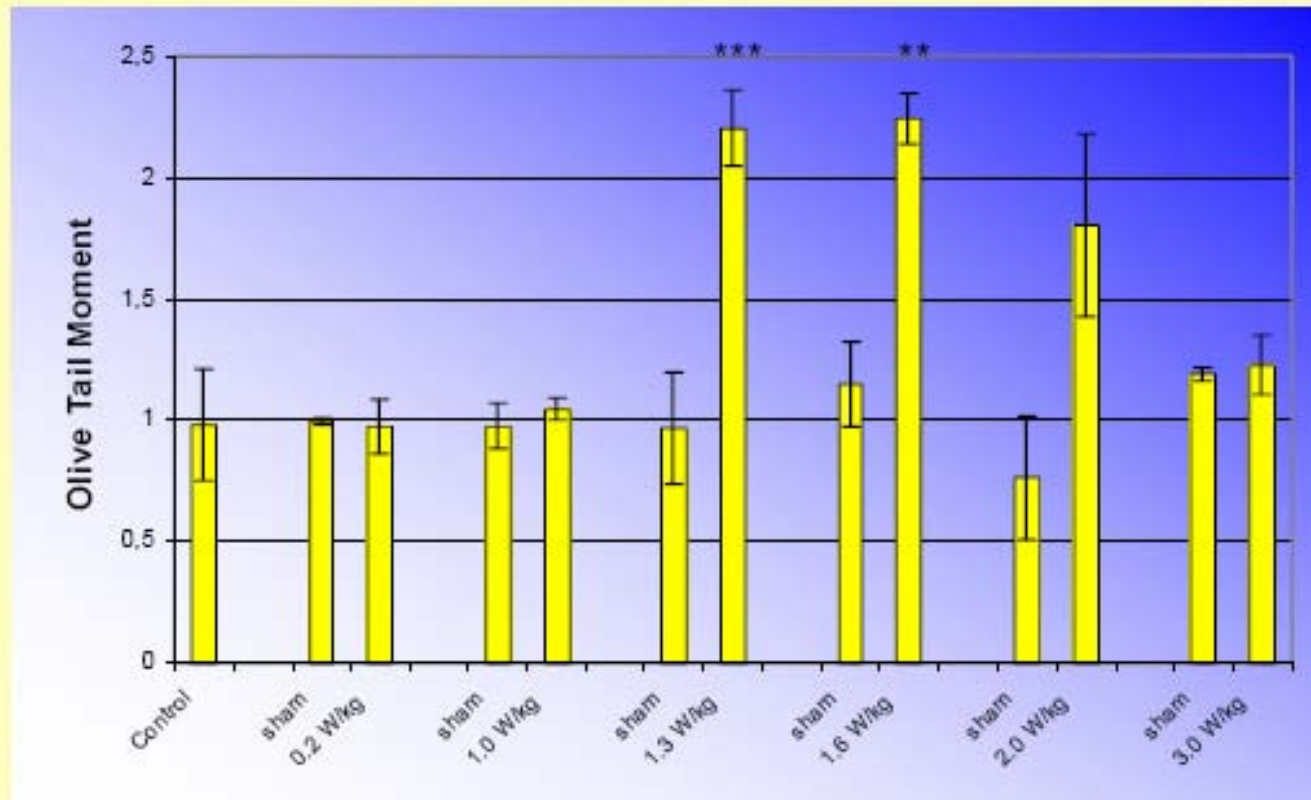
*„Chinese hamster ovary (CHO)-K1 cells were exposed to HFEMF for 2 h at SARs from **5 to 200 W/kg**. We detected a combination effect of simultaneous exposure to HFEMF and bleomycin at the respective SARs. A statistically significant difference was observed between the cells exposed to HFEMF at the **SAR of 200 W/kg**.“*

Koyama, S. et al., **Journal of Radiation Research**l. 48 (2007) , 69-75

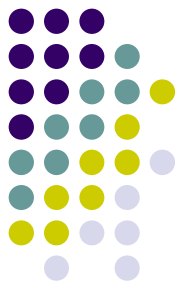
# RF: Strand breaks (Comet assay) (1)



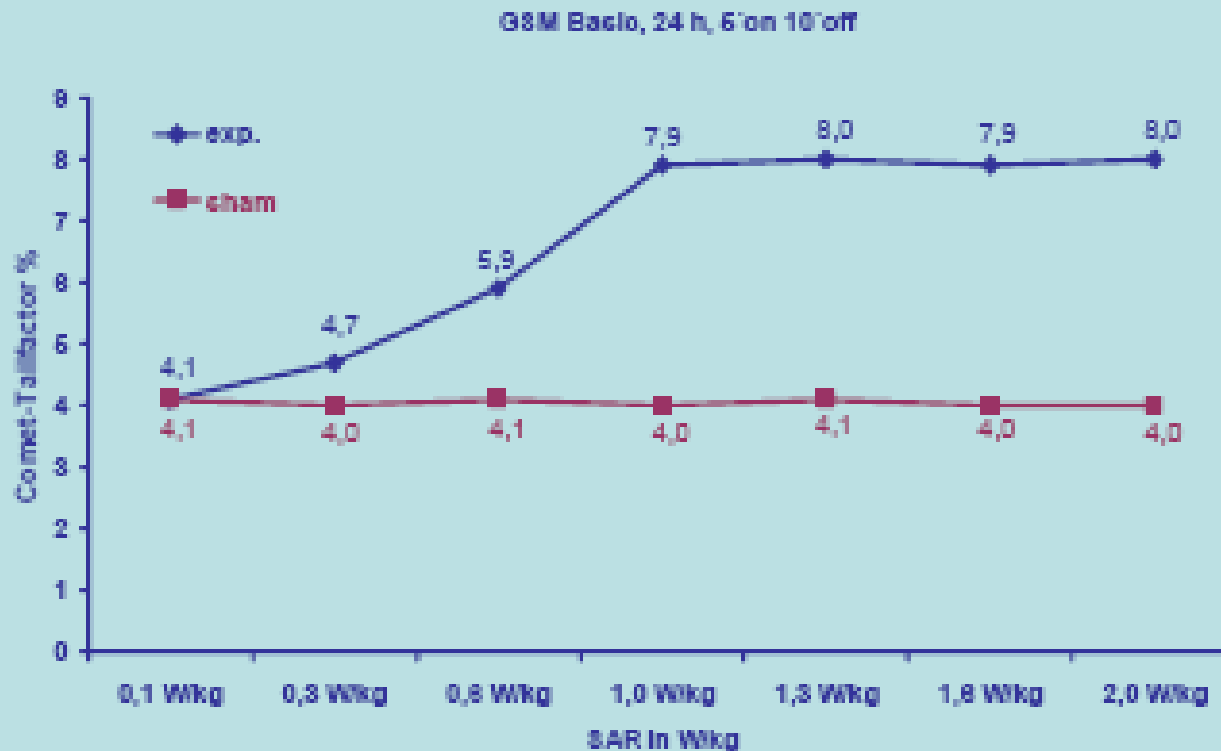
RF-EMF exposure (1800 MHz, C.W., 24 h) at different SARs led to induction of DNA strand breaks



# RF: Strand breaks (Comet assay) (2)



## SAR dependent effect of RF- EMF 1950 MHz in the alkaline comet assay



# A

## FORSCHUNGSSCHWINDEL

**Studien über Gefahren der Handystrahlung gefälscht  
Zwei aufsehenerregende Studien über Erbgutschäden durch  
Mobilfunk sind offenbar das Werk einer Schwindlerin.  
Nach SPIEGEL-Informationen hat eine Labortechnikerin einer  
Wiener Universität die Daten manipuliert.**

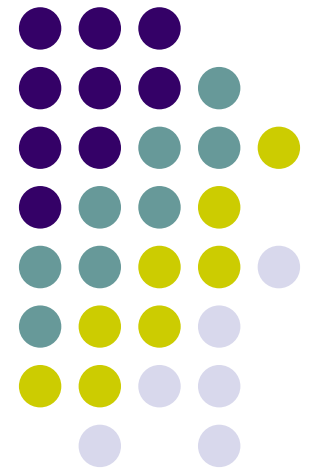
Beide Studien, durchgeführt an der Medizinischen Universität Wien und veröffentlicht in den Jahren 2005 und 2008, hatten schon bei geringer Mobilfunkdosis Brüche im Erbgut von Zellen festgestellt. In Wahrheit hat eine Labortechnikerin die Daten einfach erfunden. Das ergab die Untersuchung einer von der Universität eingesetzten Kommission. Die Angestellte, die ihre Manipulationen offenbar über Jahre hinweg fortsetzte, wurde auf frischer Tat beim Fabrizieren von Daten ertappt. Nach Auskunft des Rektors Wolfgang Schütz war sie sofort geständig:  
"Wir haben das Arbeitsverhältnis beendet."

Als Nächstes werde untersucht, so Schütz, wie es geschehen konnte, dass die leitenden Professoren sich von einer einfachen Laborkraft hinters Licht führen ließen. Die Universität fordert, dass beide Studien zurückgezogen werden



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# Resumé





# Ionising radiations

- Epidemiological cohort studies show consistently a relationship between dose and cancer risk.
- This is substantiated by many animal studies
- In-vitro experiments allow to delineate a plausible mechanism.

These findings allow to give an estimate of the dose-related cancer risk



# Ionising Rad.: Nominal risk factors (% lethal tumours per Sv) (ICRP 1990)

<b>Bone marrow</b>	<b>0.50</b>
<b>Colon</b>	<b>0.85</b>
<b>Lung</b>	<b>0.85</b>
<b>Stomach</b>	<b>1.10</b>
<b>Urinary bladder</b>	<b>0.30</b>
<b>Breast</b>	<b>0.20</b>
<b>Liver</b>	<b>0.15</b>
<b>Oesophagus</b>	<b>0.30</b>
<b>Thyroid</b>	<b>0.08</b>
<b>Skint</b>	<b>0.02</b>
<b>Bone lining</b>	<b>0.05</b>
<b>Ovaries</b>	<b>0.10</b>
<b>Remainder</b>	<b>0.50</b>
<b>Total</b>	<b>5.00</b>

# Ultraviolet



- Ecological epidemiological studies indicate a relationship between UV-exposure and skin cancer
- Skin cancer is found in suitable animal models after UV-exposure
- In-vitro experiments demonstrate that events critical for carcinogenesis are caused by ultraviolet.

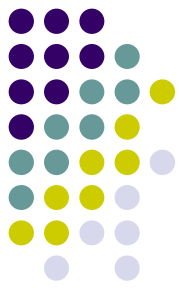
It is not possible at present to give a quantitative relationship between cancer risk and UV exposure



# Radiofrequency

- No association between mobile phone use was demonstrated in the overwhelming majority of epidemiological case-control studies.
- Animal experiments do not demonstrate cancer induction or promotion by mobile phone fields
- There is no consistent and reproduced in-vitro study demonstrating the initiating or promoting ability of mobilephone fields

There is presently no consistent, plausible and reproducible demonstration that RF-fields may initiate or promote tumour formation.



# Conclusions

- The carcinogenic action of ionising radiations is well proven. Dose related risk can be estimated with some certainty.
- The carcinogenic action of ultraviolet is well proven. A quantitative estimate of dose-related risk is not yet possible.
- The carcinogenic action of RF-fields is not proven. A plausible mechanism has not been suggested. The existence of a carcinogenic risk is highly doubtful.