Workshop on
Science and Values in Radiological Protection

- Views of Researchers -

Objectives of the present Workshop is
to improve understanding in both research and policy communities

Ohtsura Niwa, Jan. 15, 2008

1. The principle of current radiation protection?
2. The research issues at this meeting?
   - non-targeted effect
   - individual sensitivity
   - circulatory diseases
3. What could these issues bring up?
   - LNT losing its position in protection?
   - personalized protection?
   - deterministic effects w/ stochastic manifestation?

   and

4. Science and values?

1. The principle of current radiation protection?
2. The issues in research at this meeting?
   non-targeted effect: fact
   individual sensitivity: fact
   circulatory diseases: fact
3. What could these issues bring up?
   LNT losing its position in protection?
   personalized protection?
   deterministic effects w/ stochastic manifestation?
   and
4. Science and values?

1. Principle of current risk evaluation systems

The current system accommodates a large uncertainty

Risk = total dose x risk coefficient x DDREF x W_R x W_T

LNT: a foundation of radiation protection

Data: A bomb survivor data

dose :	measurements + estimation (uncertain)
risk coefficient:	cross population risk transfer (uncertain)
DDREF:	a rounded value (uncertain)
W_R:	rough rounded values (uncertain)
W_T:	a rough rounded values (uncertain)

Those in blue have somewhat uncertainty

Uncertainty particularly large for low doses and dose rates

ICRP Publication 99

Two foundations of LNT
- with their limitations -

Epidemiological studies on A bomb survivors

dose → detriments

”Lacking power for low doses/dose rates”

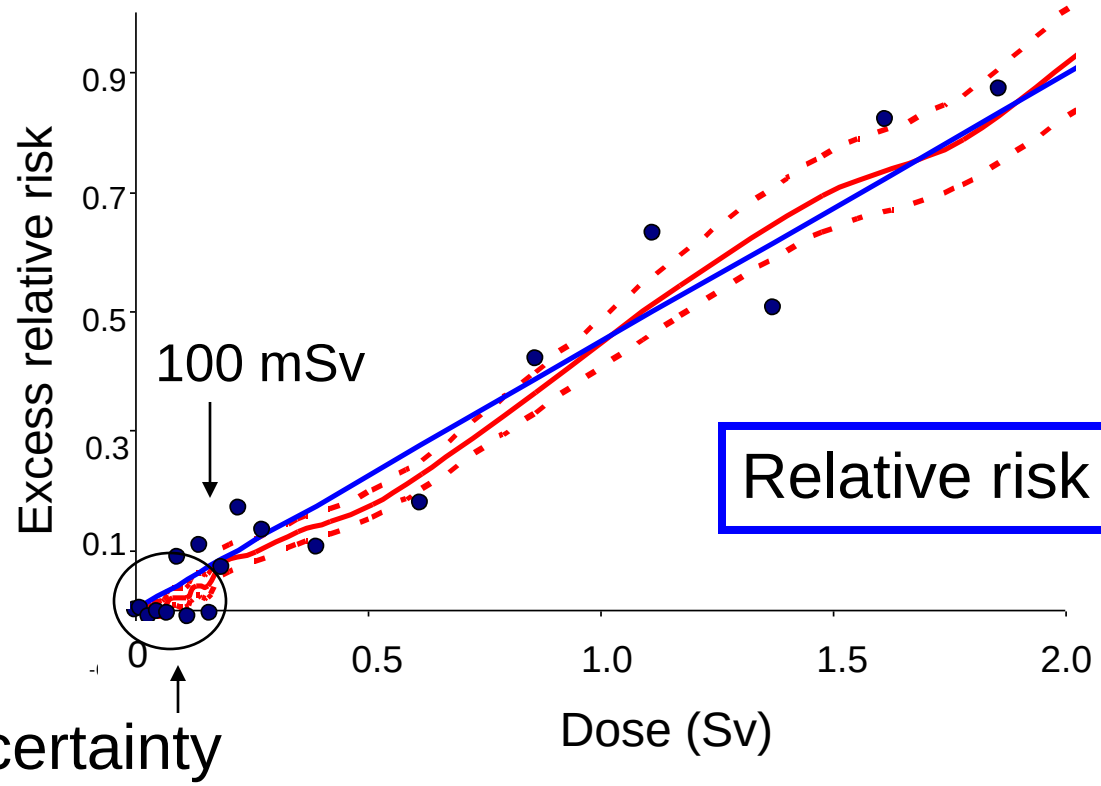
Radiation biology

dose → damage → detriments

”Too naïve a view”

“challenged by the non-targeted”

Epidemiological studies
Dose response of A bomb survivors

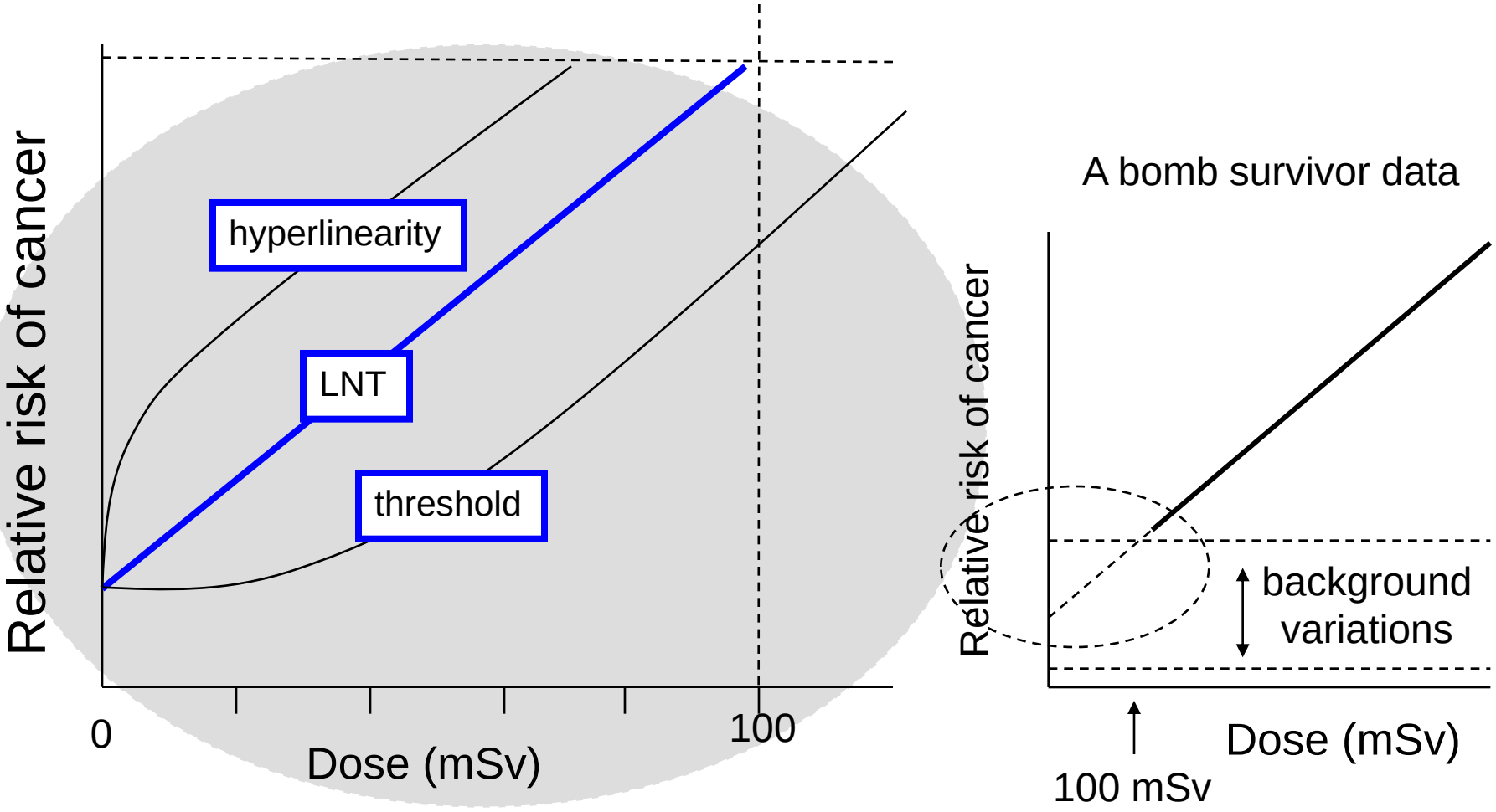


Relative risk = 1.5/ Sv

Area of uncertainty

Linear increase of the risk above 100 mSv

Current system of risk evaluation/protection



What are the dose responses in the gray zone?

1. The principle of current radiation protection?
2. Research issues at this meeting?
   non-targeted effect
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   circulatory diseases
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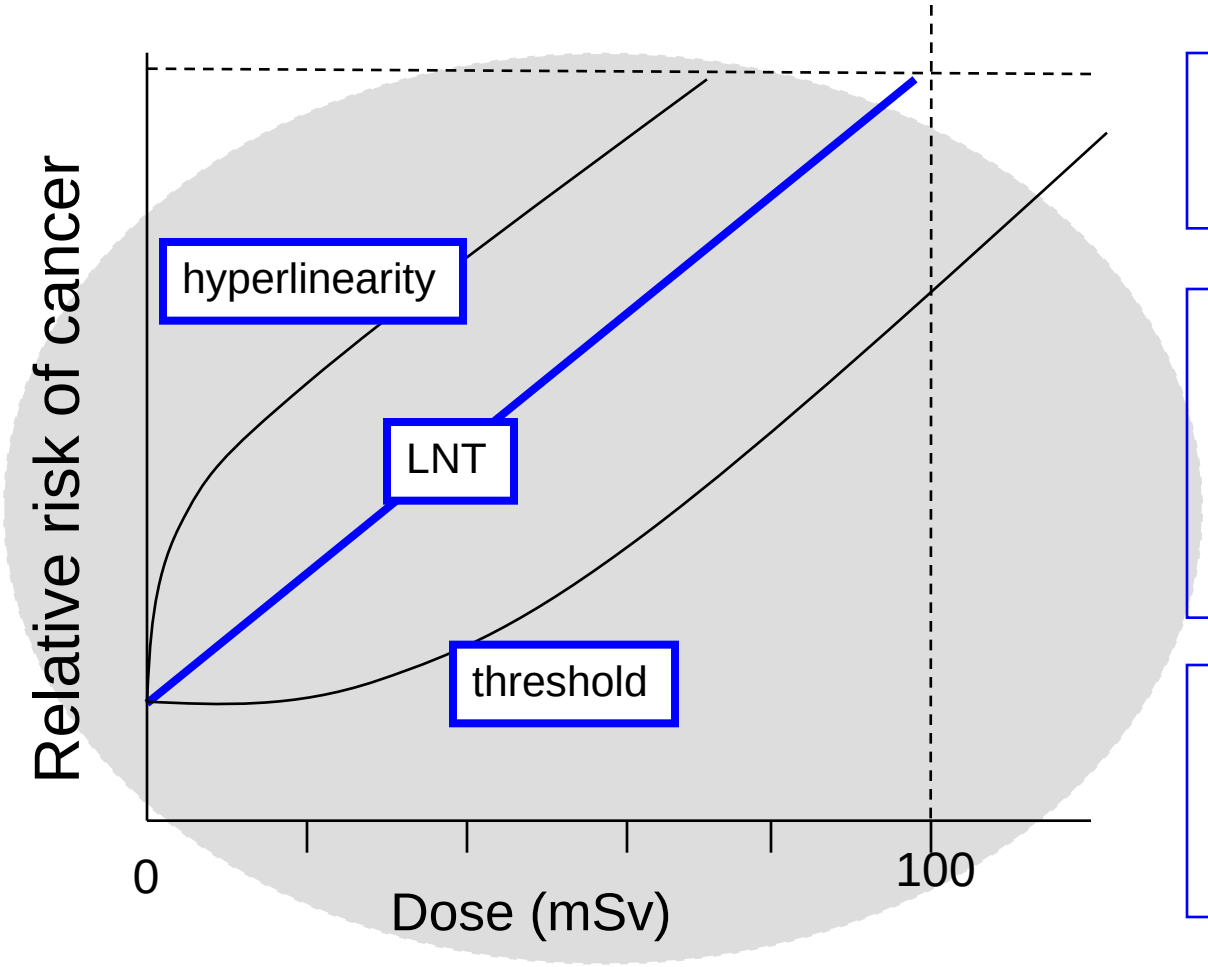
Non-targeted, individual sensitivity, and cardiovascular disease



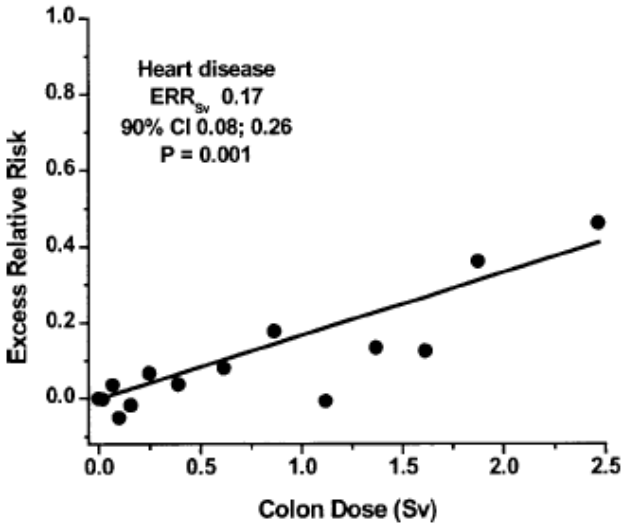
Non-targeted effects
⟶ hyper-linearity?

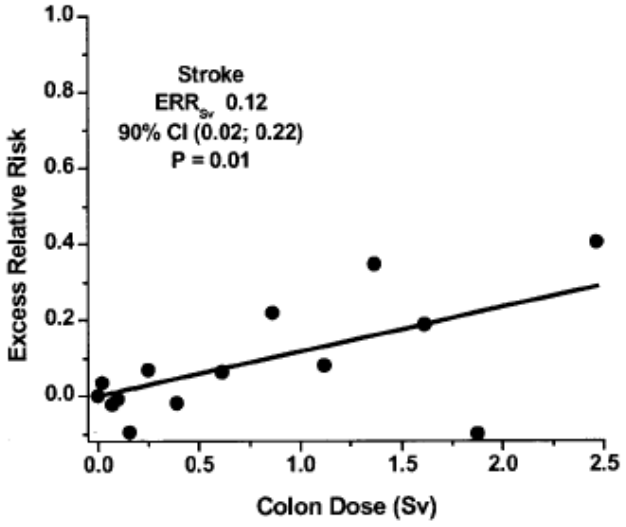
Sensitive individuals
⟶ hyper-linearity?
& personalized protection?

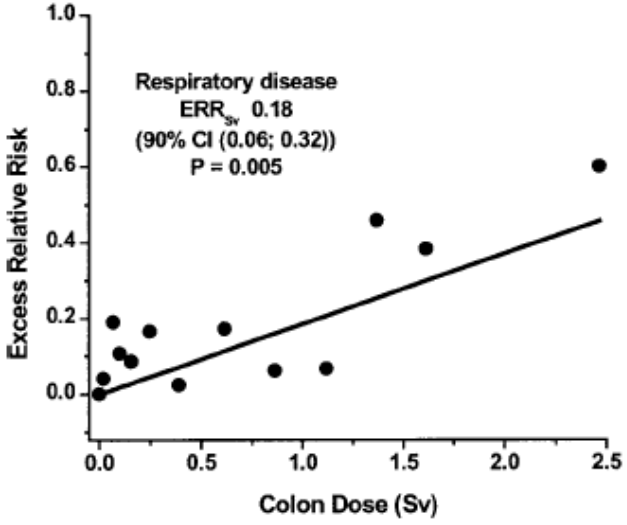
Non cancers
higher risk
⟶ coefficients?

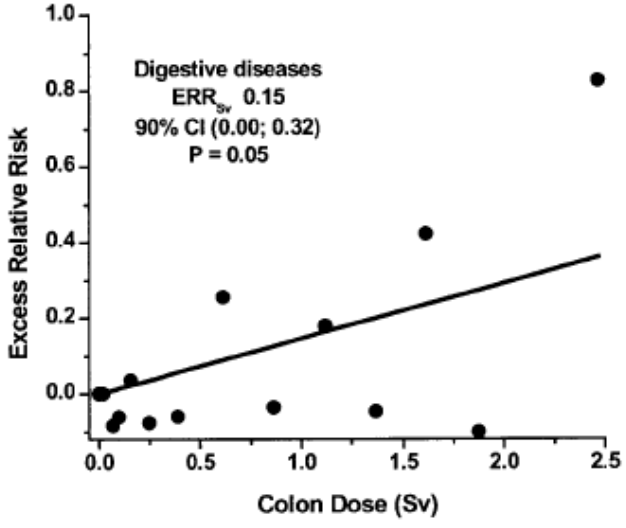
All discussion in the gray zone

Non cancer diseases among A bomb survivors





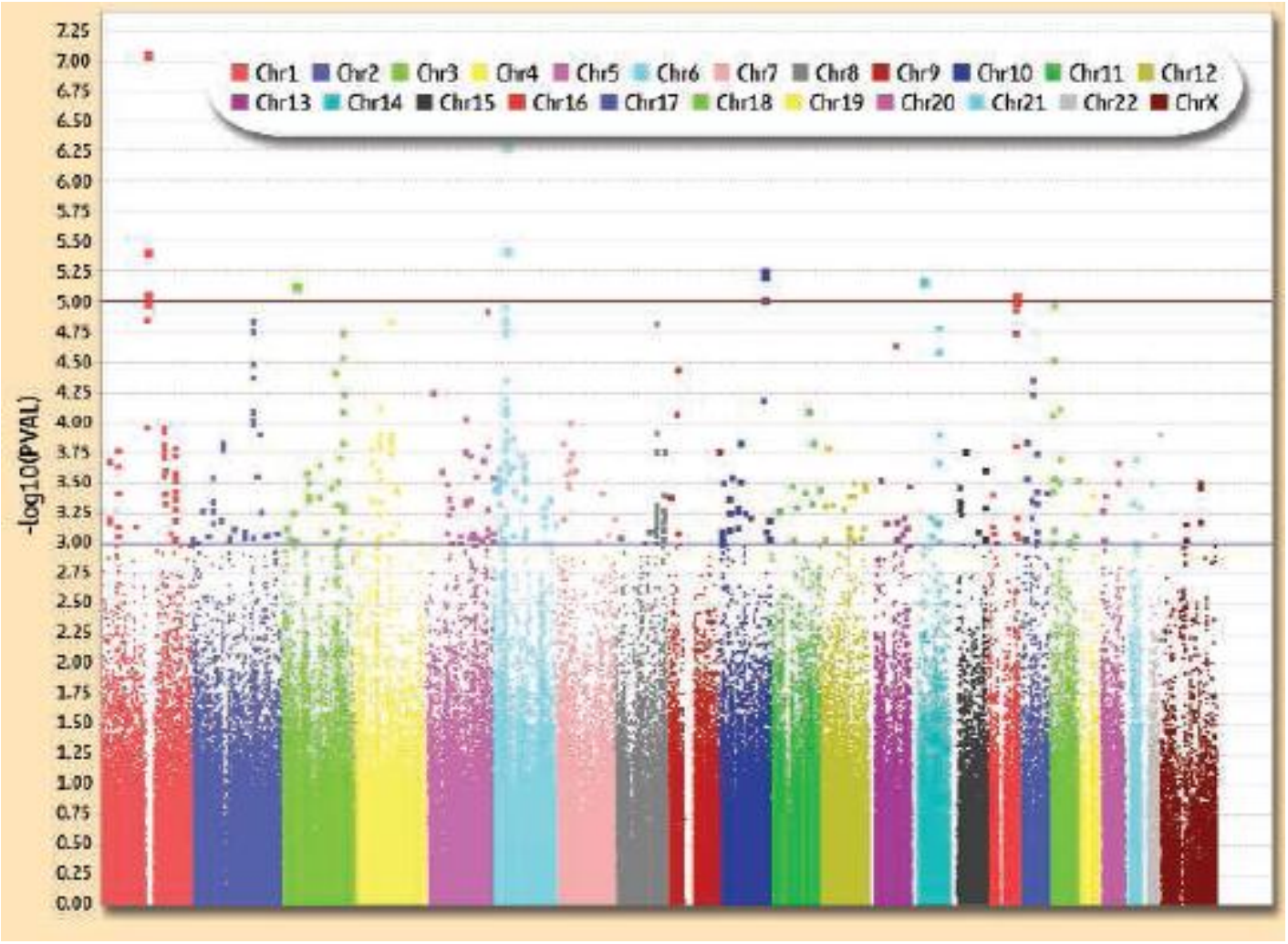




Have to lessen the low dose uncertainty !!

Preston et al. Radiat Res 160, 381-407, 2003

Sensitive individuals:
386,731 genetic markers for type 2 diabetes



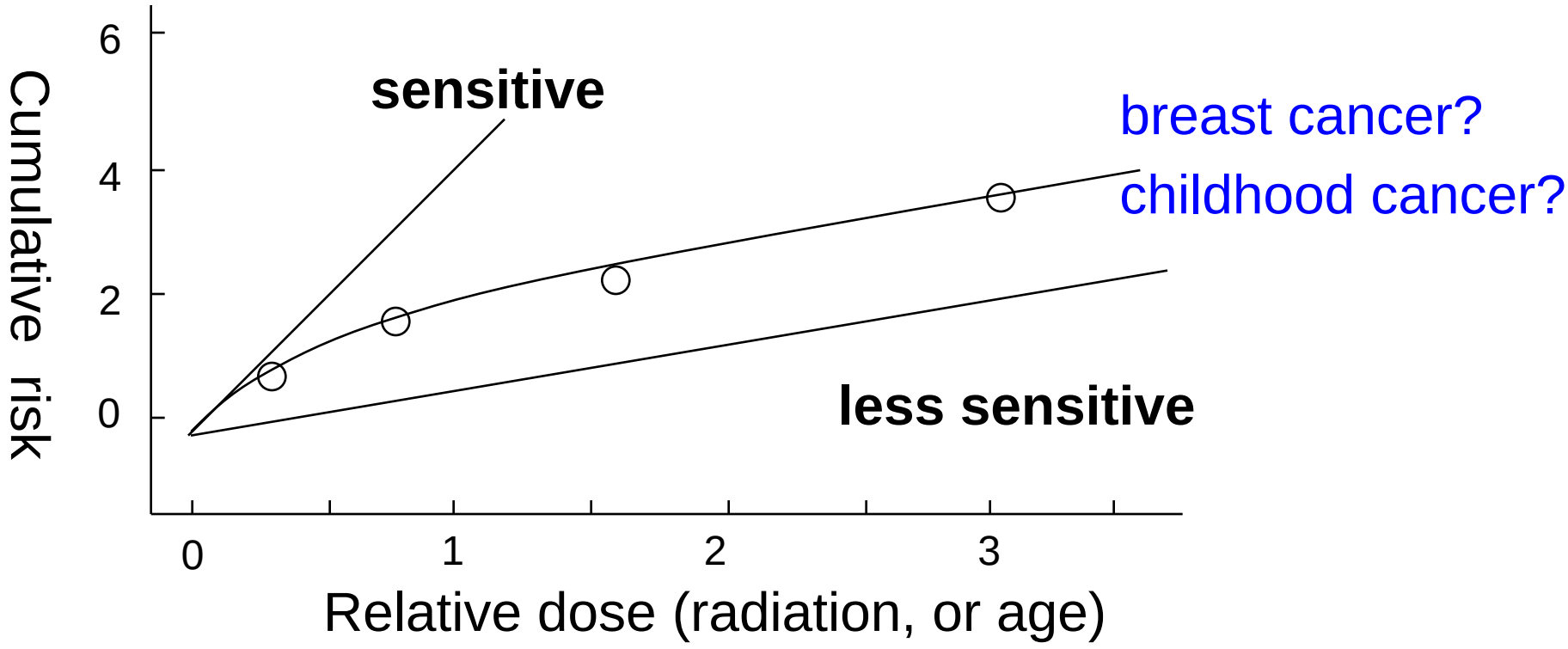
Association with the disease

For most of SNP, 50% or so increase in the rate

More to be studied on radio-sensitivity

Science 316, 820, 2005

A population with varying sensitivities



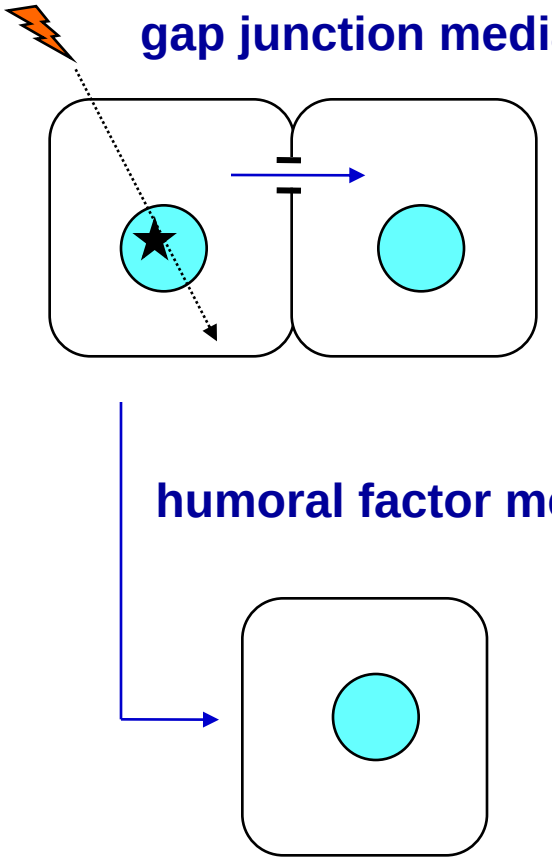
Non-targeted effects, but their relevance?

A bomb epidemiology (above 100 mSv) includes non-targeted effects

Relevance to low dose radiation risks?

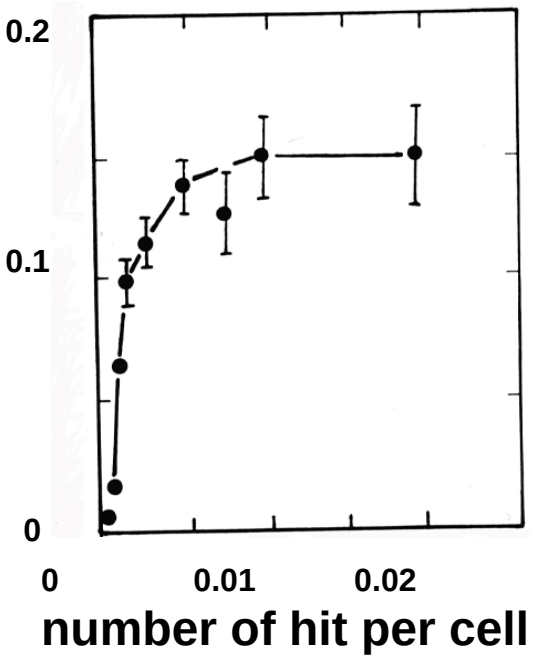
Bystander effects studied in vitro (20% O_2)

α particle



1 hit cell ⇨ over 100 bystander cells
SCE, gene mutations
chromosome instability
and cell killing

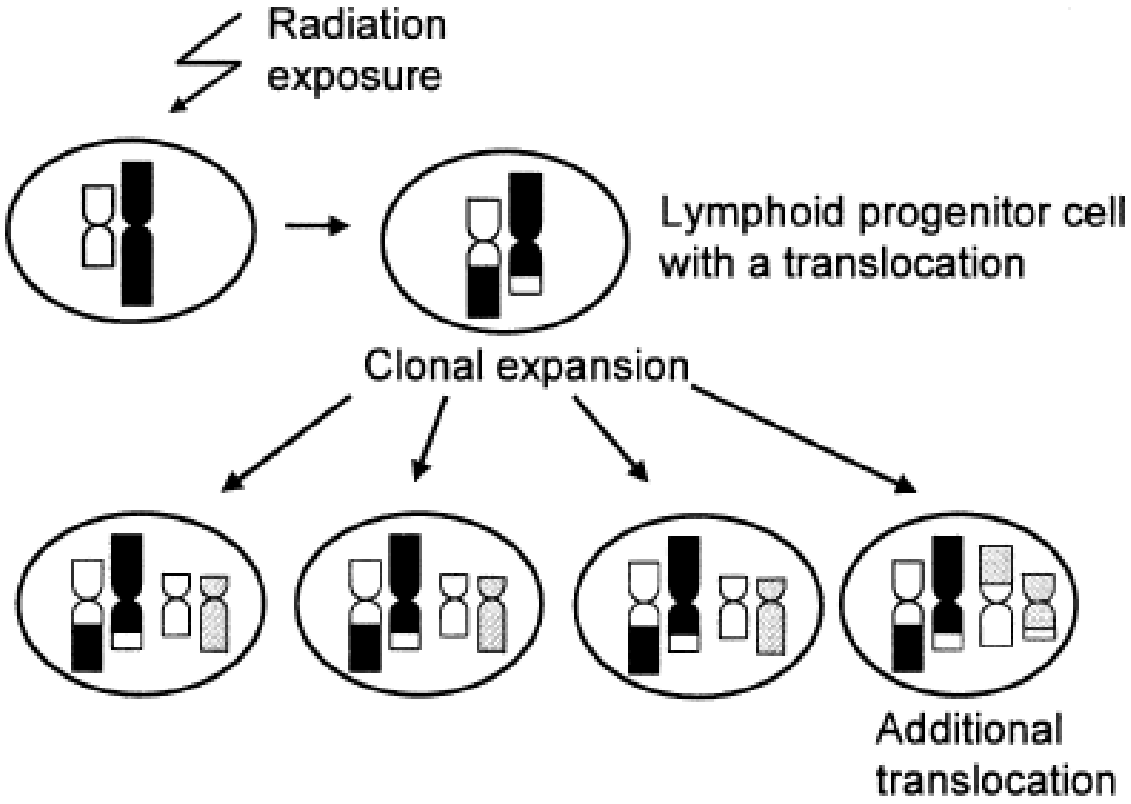
SCE per chromosome



ROS related bystander factors

Cancer Res. 52, 6394, 1992

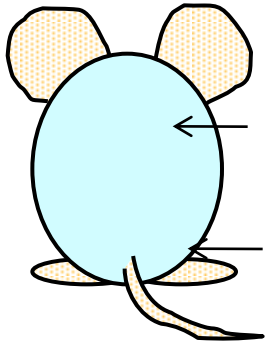
No chromosome instability in survivors (5% O_2 or less)



Translocation type	frequency by G banding
Spontaneous translocation	219/17,878 cells (1.22 %)
Additional translocation	6/936 cells (0.6%)

Kodama et al. Radiat Res 164, 618-626, 2005

Hematopoietic stem cells in extreme hypoxia



pimonidazole

↓ 3 hr

Ho-33342

↓ 5 & 10 min

bone marrow

↓

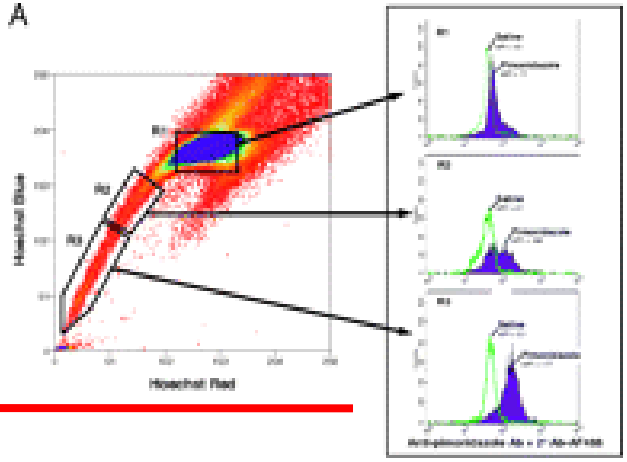
FACS analysis of stemcells

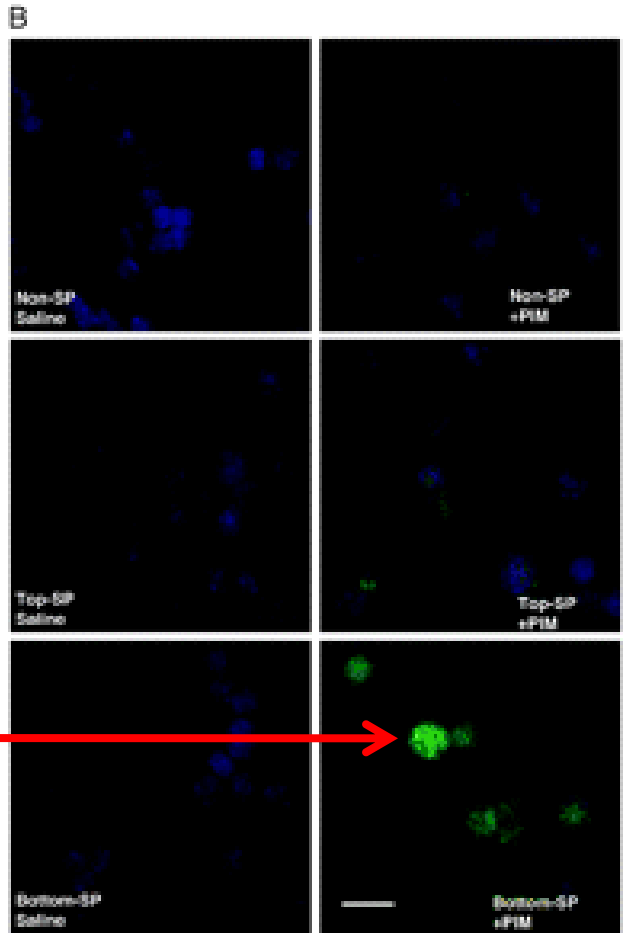
↓

Stem cells stained with **pimonidazole** meaning 1% O2 or less

Parmar et al. PNAS 104, 5431, 2007

Pimo-positive Cell





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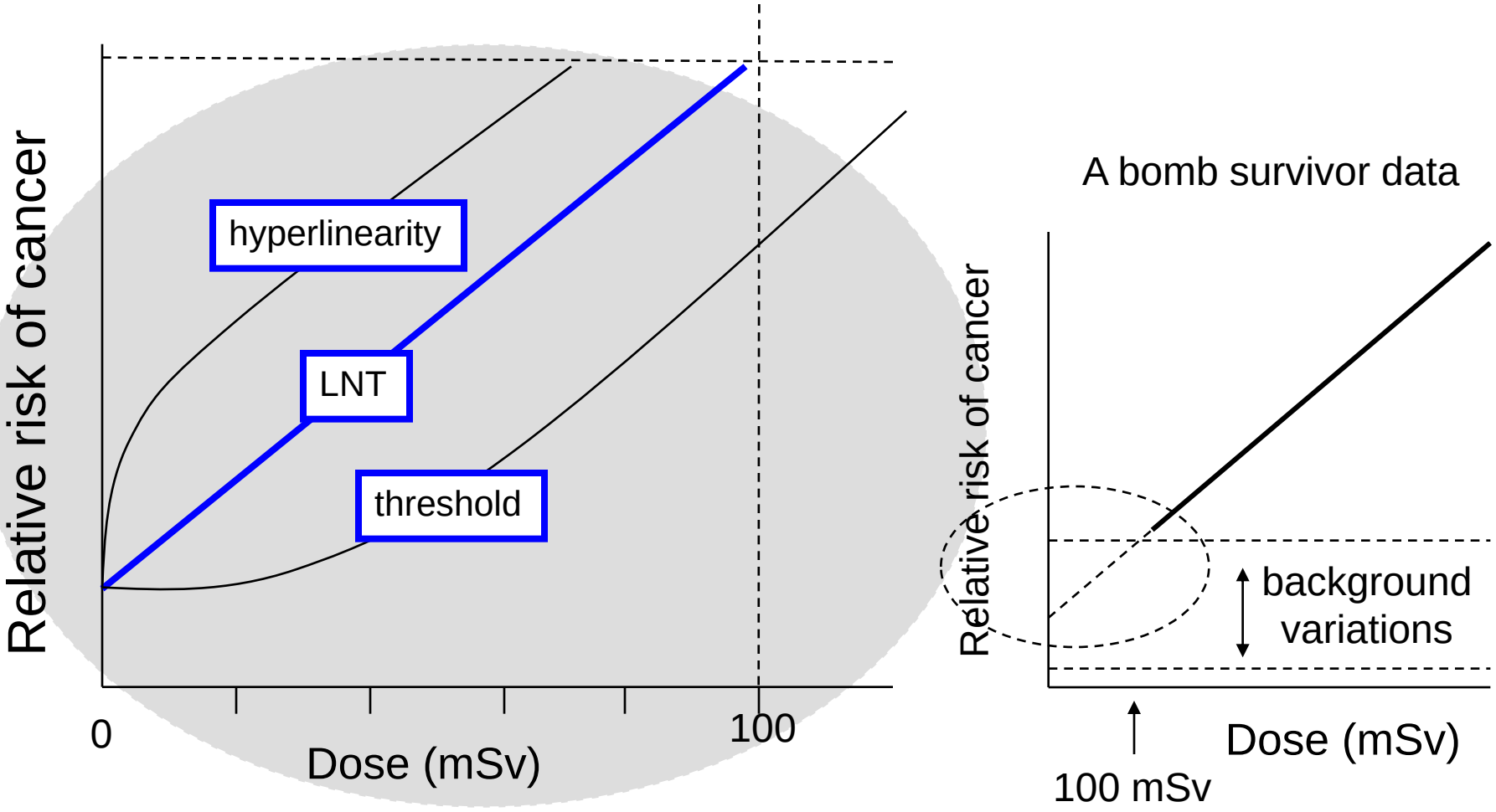
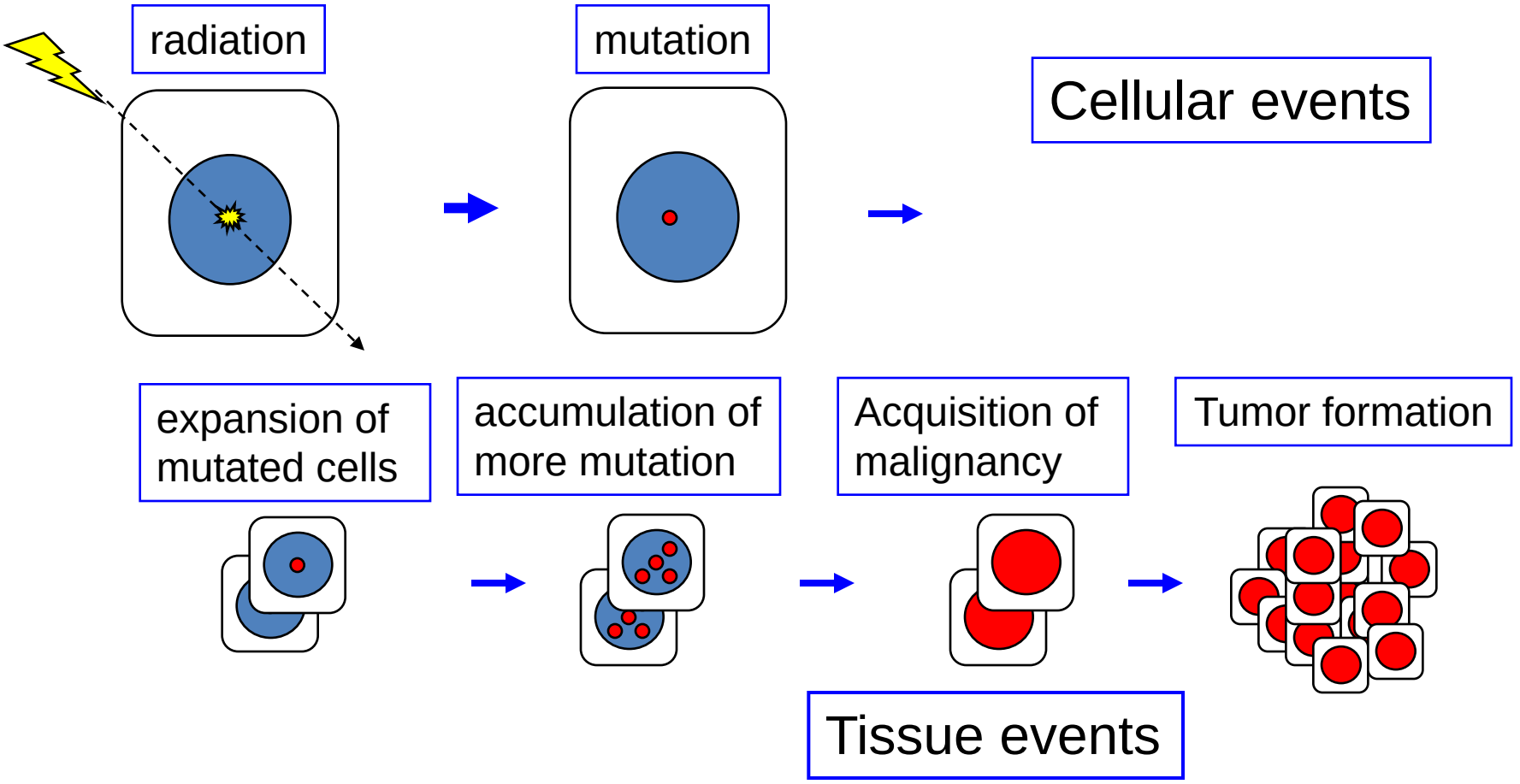
Too early to change the system of protection since we still do not know much



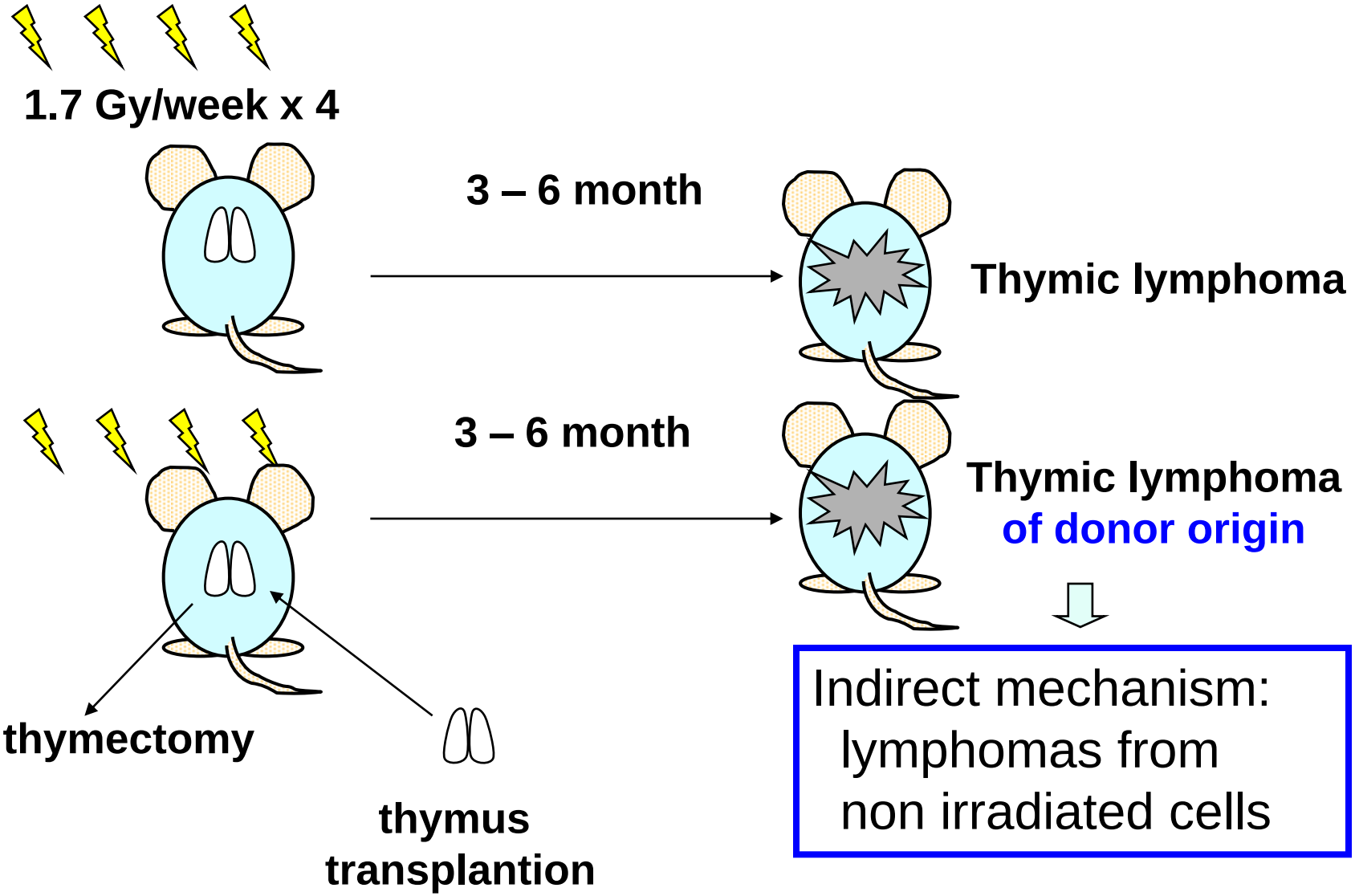
ICRP Publication 99, with uncertainty analysis

What do we know?
Current paradigm of radiation carcinogenesis
- Too naïve a view -



We do not know the mechanism of radiation carcinogenesis

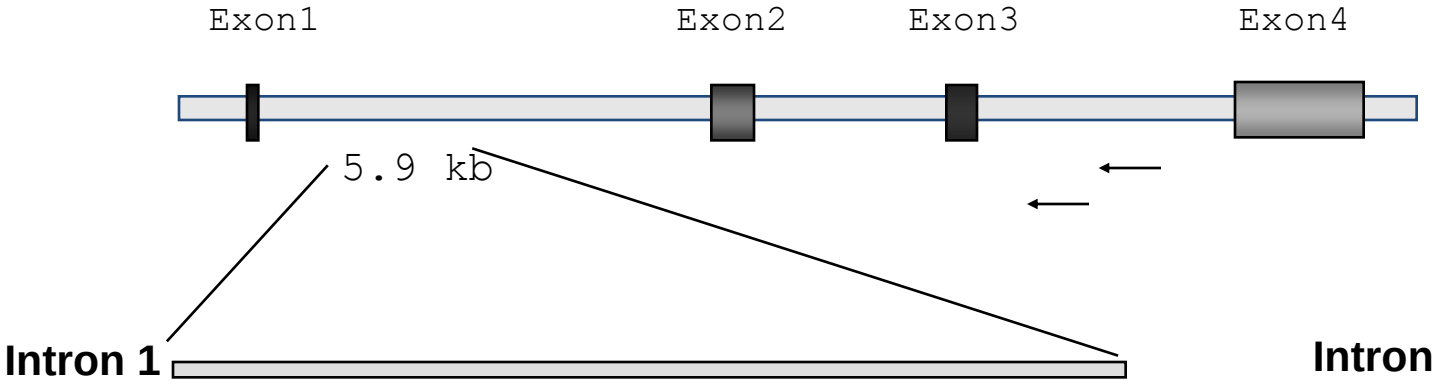
A case of mouse thymic lymphomas



Indirect mechanism:
lymphomas from
non irradiated cells

HS Kaplan, 1953

Rit1/Bcl11 deletion mutation occurs through erroneous T cell receptor rearrangement



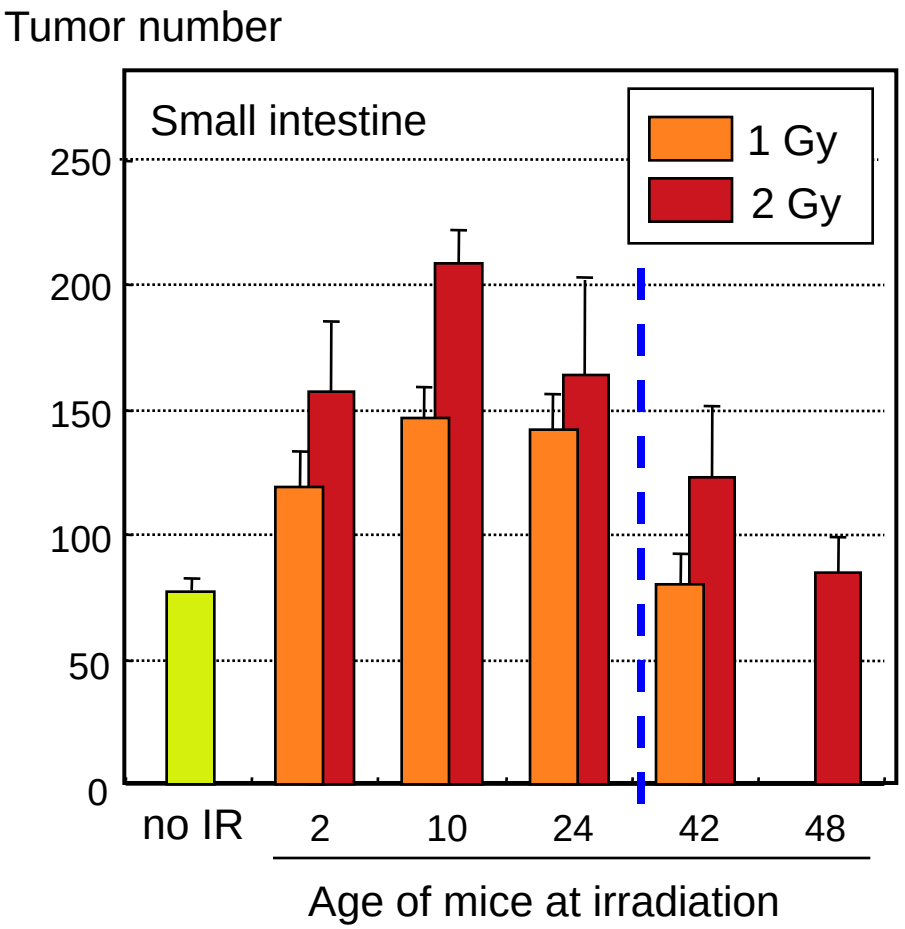
GGGACACACAGACACACAGACACACACACACACA **CACTGTGTGAGATTAATTTCTTTCCTTG**

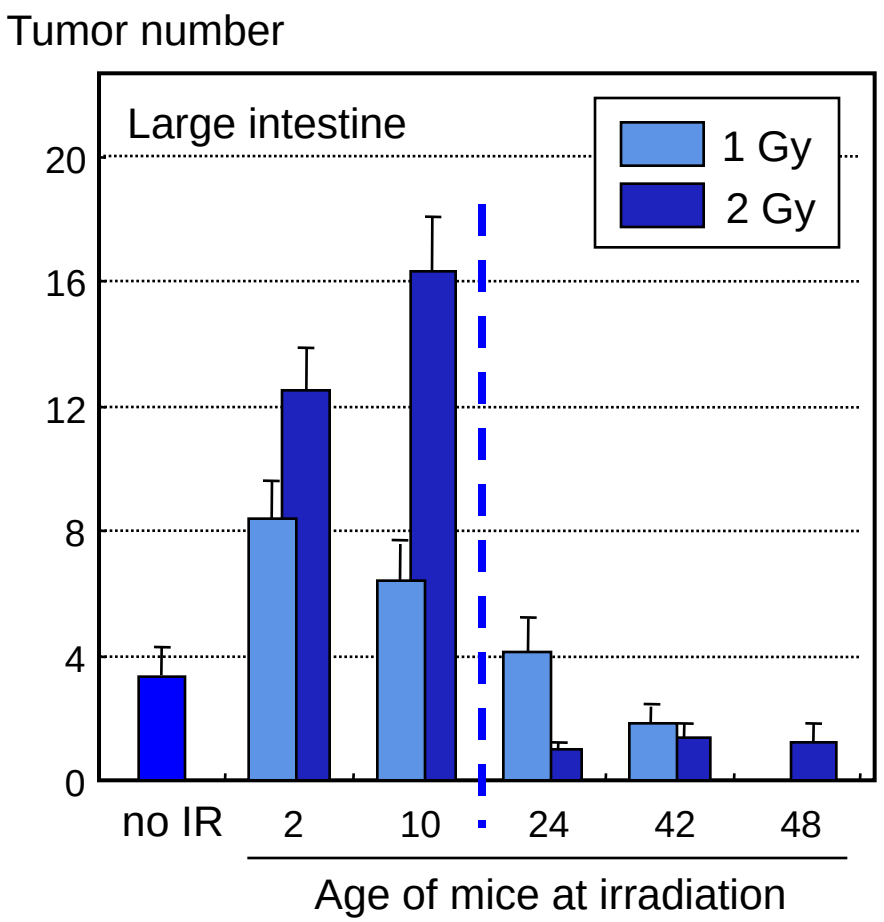
GGGACACACAGACACACAGACAC	CC	GATTAATTTCTTTCCTTG
GGGACACACAGACACACAGACACAC		GAGATTAATTTCTTTCCTTG
GGGACACACAGACACACAGACACA	GTATGGGGCC	TTAATTTCTTTCCTTG
GGGACACACAGACACACAGACACAC	GGGAAG	AATTTCTTTCCTTG
GGGACACACAGACACACAGACACAC	G	GATTAATTTCTTTCCTTG

Deletion by the erroneous TCR rearrangement
Radiation provides microenvironment for tumor growth

Sakata et al., Carcinogenesis 25, 1069, 2004

A case of Min mouse tumors





Strong age dependency !!

M. Okamoto and H.Yonekawa
J Radiat. Res. 46, 83-91, 2005

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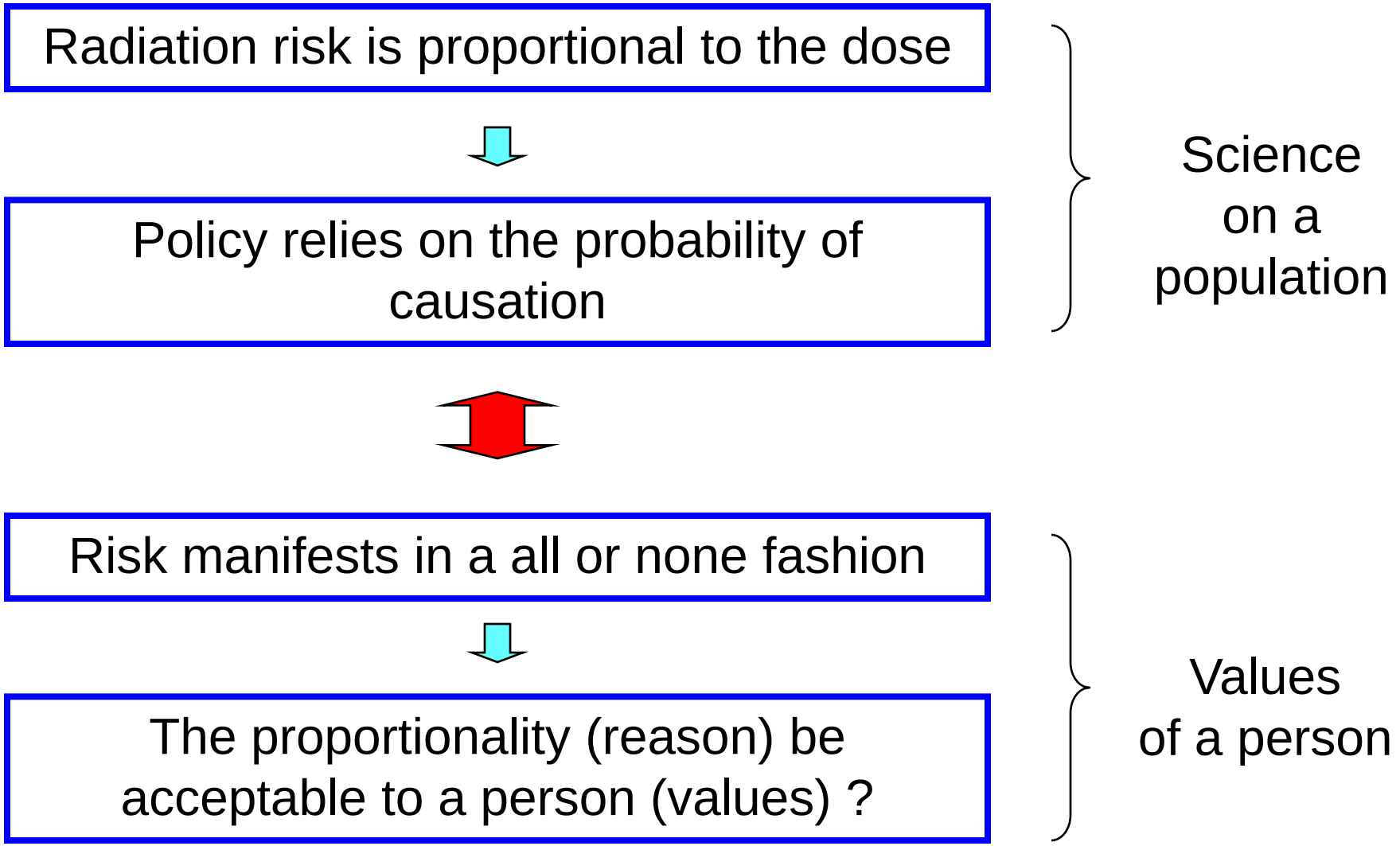
   Needs to balance reason and heart

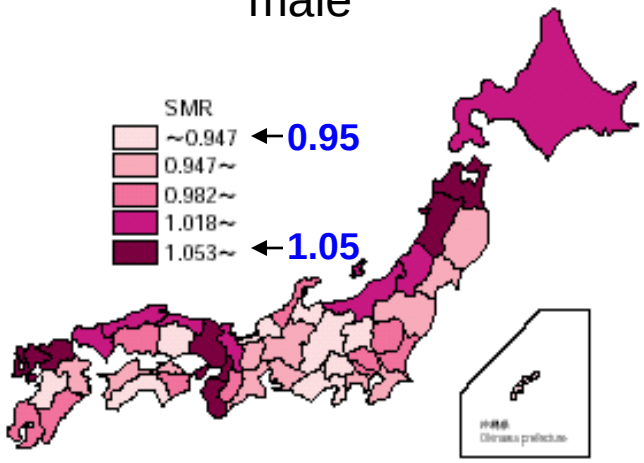
A deep cleft separating science and values



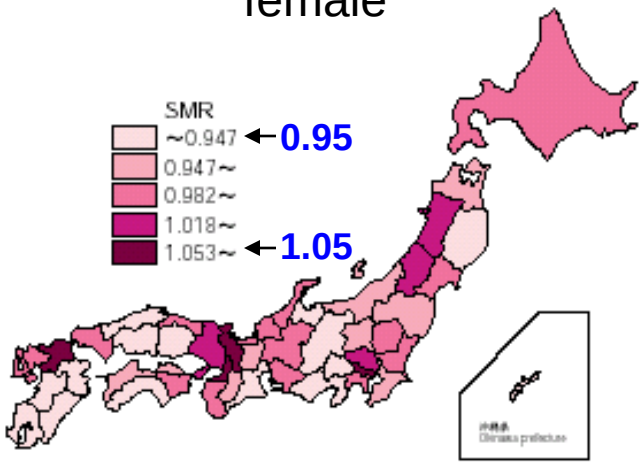
In our real world, we are living in a large variations in risks

Total

male

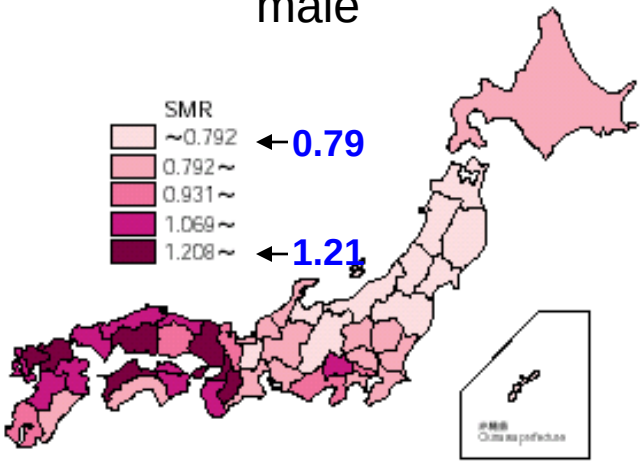


female

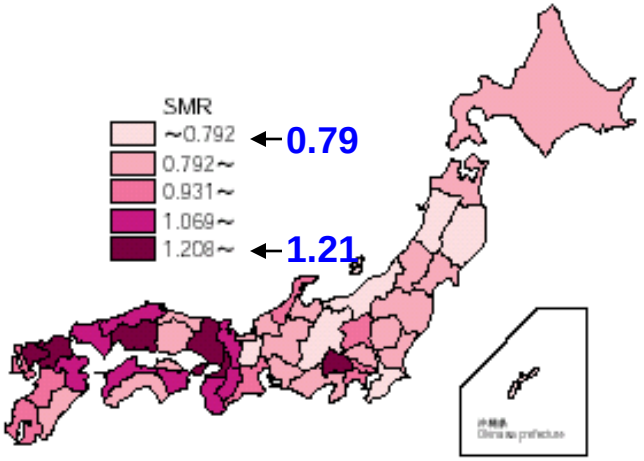


Liver cancer

male



female



Regional variations in cancer mortality Over 10 %

⇩

Accepted by people