Hanns Langendorff

(2.v.r.), 1902 – 1974,
bei der Feier des 50-jährigen Bestehens des „Radiologischen Instituts“, Freiburg

im Gespräch mit
Hedi Fritz-Niggli, Zürich,
Jürgen Berndt (l.), Neuherberg,
und
Christian Streffer (r.), Essen.

Abschätzungen der Risiken kleiner Strahlendosen:

es kommt auf den Zweck an!

Herwig G. Paretzke
(HMGU - Institut für Strahlenschutz, Neuherberg
TU München - Physik Department, Garching)

Die wichtigsten Aufgaben des Strahlen-Schutzes sind:

a) Die **Gesundheit des Menschen**

und

b) die **Umwelt**

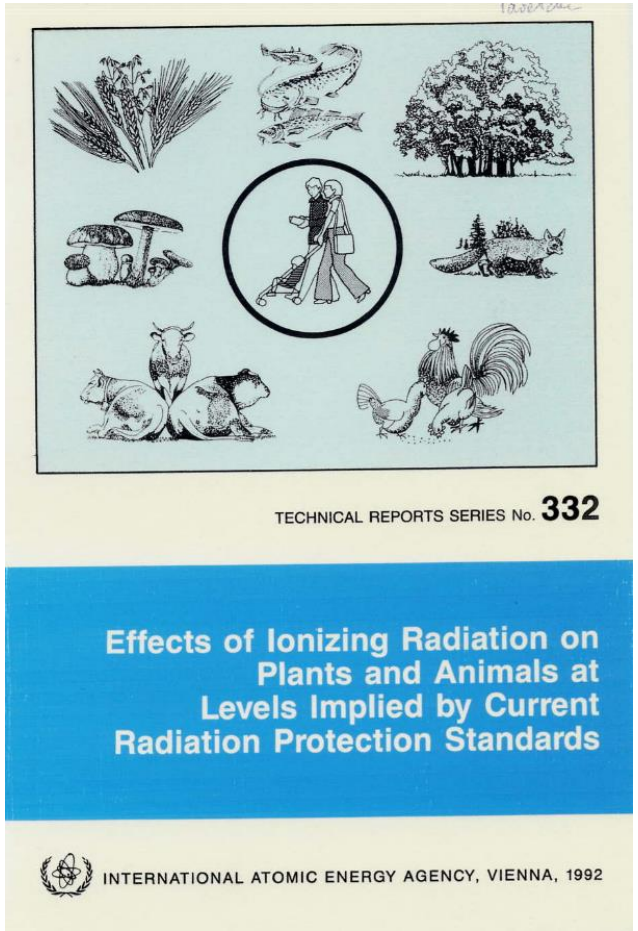
vor **schädlichen Einflüssen** durch ionisierende Strahlung
und
radioaktiven Stoffen **zu schützen**.

Zuerst „der Schutz der Umwelt“:

Es gibt viele reale Beobachtungen an Pflanzen und Tiere in der Umwelt
(viele Daten wegen Atombomben-Tests, -Herstellung,..)

No Observable Effect Level = 1 mGy / Tag = 0.365 Gy/Jahr

(NOEL-Werte x 10 in Gewässern!)



Was ist „ die Gesundheit des Menschen“?

Nach der **Definition der WHO**:

„**Gesundheit** ist der Zustand des vollständigen

1) **körperlichen**,
2) **geistigen**, und
3) **sozialen Wohlbefindens**.

Und nicht nur die Abwesenheit von Krankheit und Gebrechen“.

Praktisch alle Arbeiten in der Strahlenschutz-Forschung und in den -Regulierungen konzentrieren sich auf die

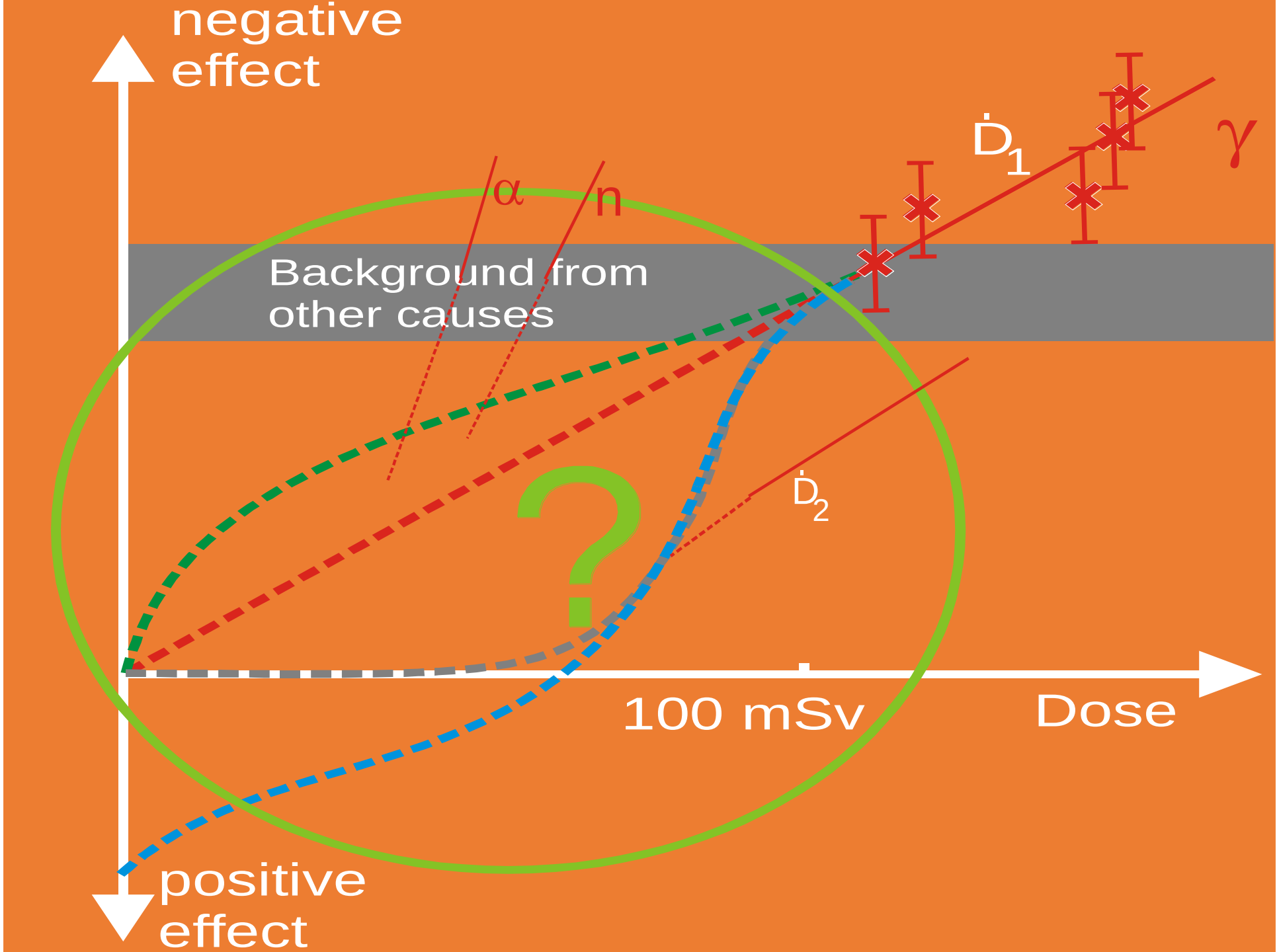
„**körperlichen**“ Gesundheits-Wirkungen,

Durch die „vorsichtige“ **Annahme der LNTH** hierbei werden aber gleichzeitig **große**

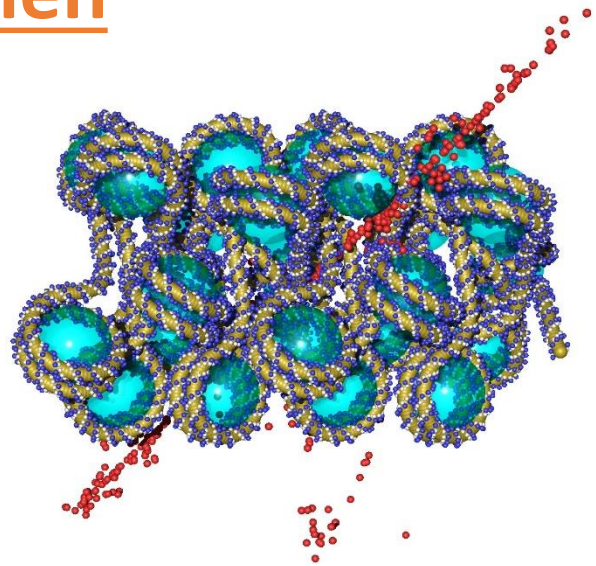
„**geistige**“ (z.B. Strahlenangst)

und „**soziale**“ (z.B. Politik gegen Kernreaktoren und Endlager)

schädliche Gesundheits-Wirkungen bewirkt!


negative effect
positive effect
α
n
γ
$\dot{D}_1$
$\dot{D}_2$
Background from other causes
?
100 mSv
Dose

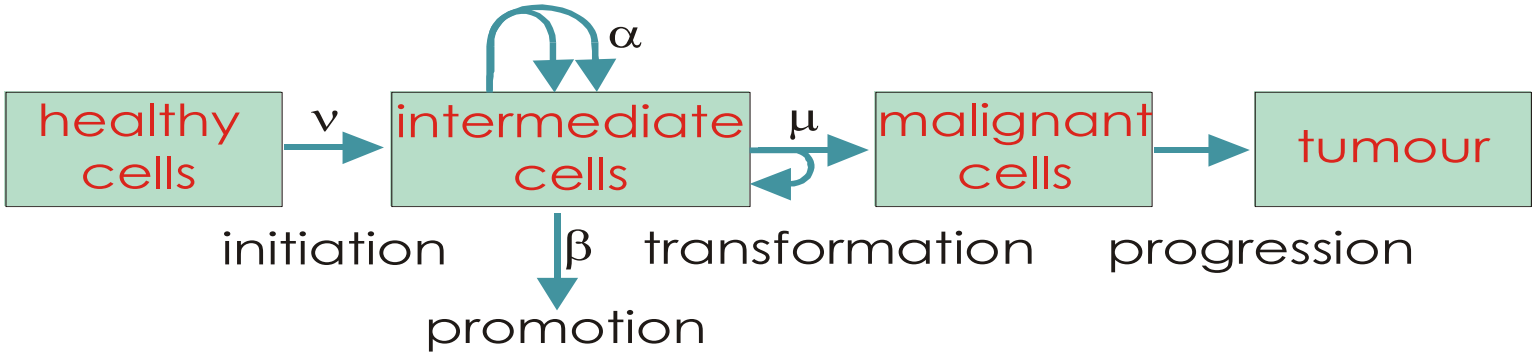
Verschiedene Ansätze, die Strahlenrisiken (Mechanismen, Quantifizierung) bei niedrigen Dosen zu erforschen



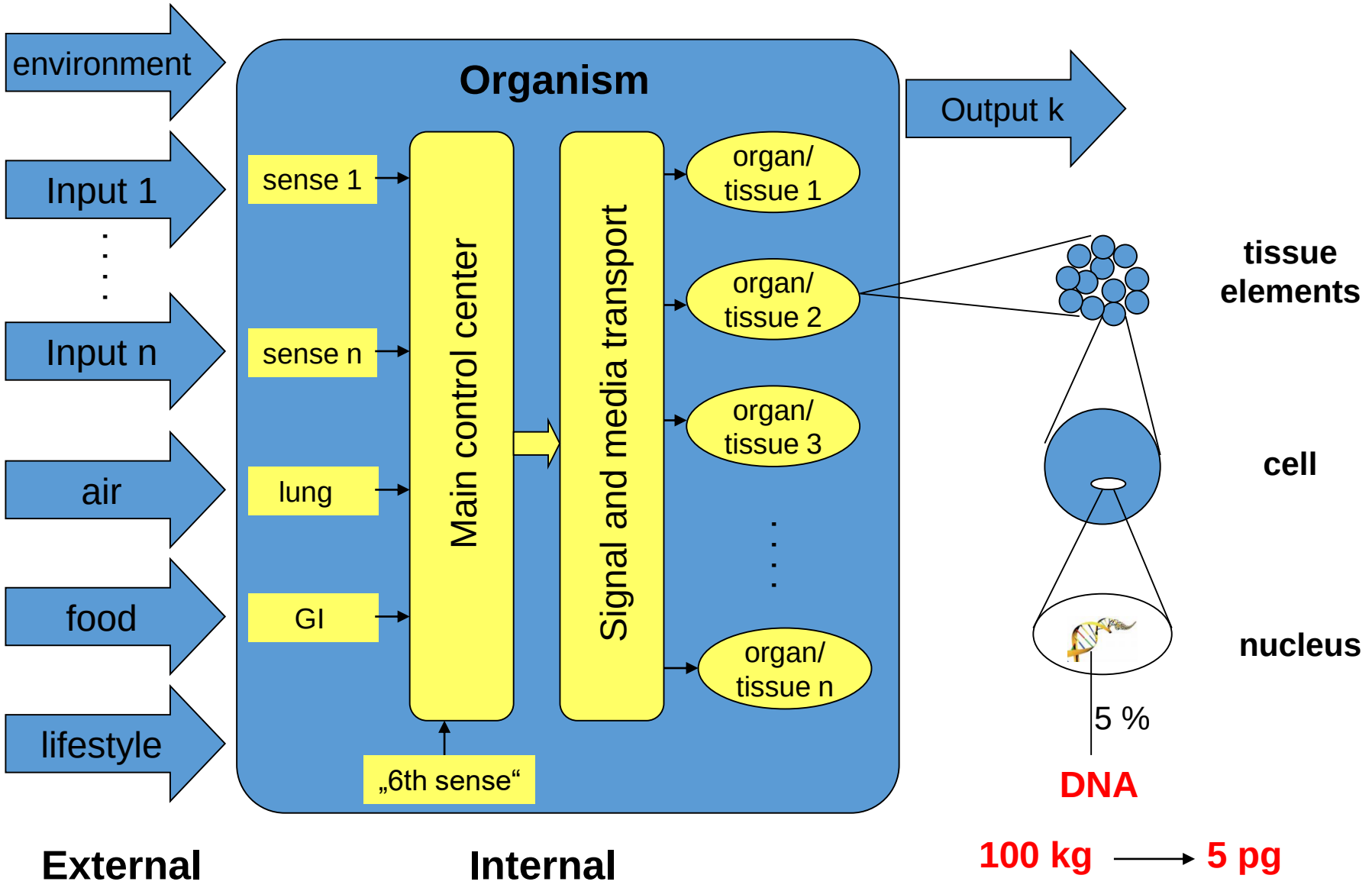
Early stages:

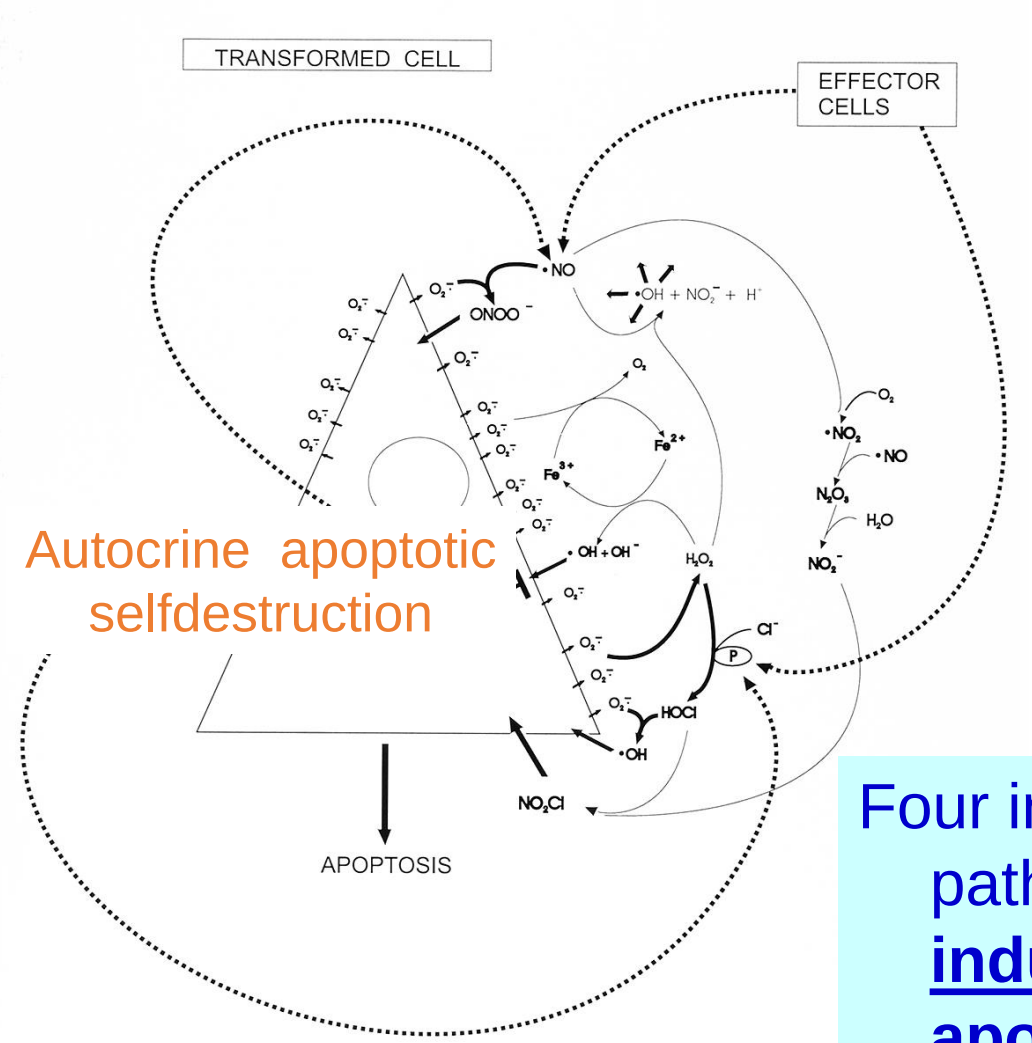
Track structure analysis of

DNA and cellular damage, and repair



Later stages: Mechanistic, quantitative modelling of low-dose radiation radiation effects, including intracellular signalling, genetic instability, individual sensitivity, microenvironment effect, etc.


environment
Input 1
Input n
air
food
lifestyle
Organism
sense 1
sense n
lung
GI
„6th sense“
Main control center
Signal and media transport
organ/ tissue 1
organ/ tissue 2
organ/ tissue 3
organ/ tissue n
Output k
tissue elements
cell
nucleus
5 %
DNA
External
Internal
100 kg
5 pg



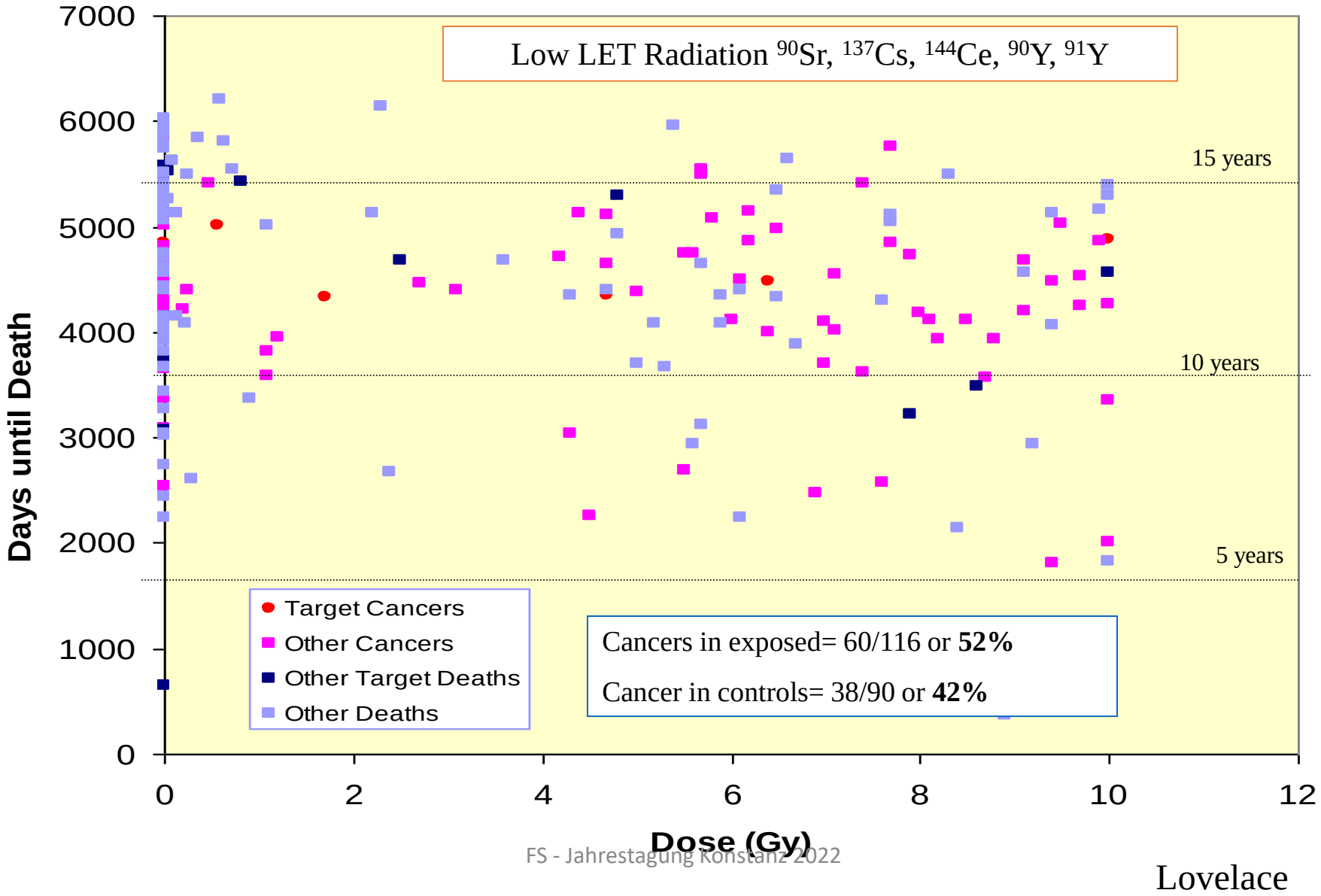
Aber: Es gibt kein „einsames“ Molekül im Festkörper und keine „einsame“ Zelle im Gewebe! Sie haben Nachbarn!

Georg Bauer et al., Univ. Freiburg:

Transformed cells can be sent into apoptosis by signalling with healthy neighbours:

Four interactive ROS-mediated signaling pathways are responsible for **intercellular induction of apoptosis and autocrine apoptotic selfdestruction**.

Tierversuche: Beagle lifespan inhalation study (c: Anthony Brooks)
Nur wenige Krebserkrankungen im "bestrahlten Organ", hohe Dosen!

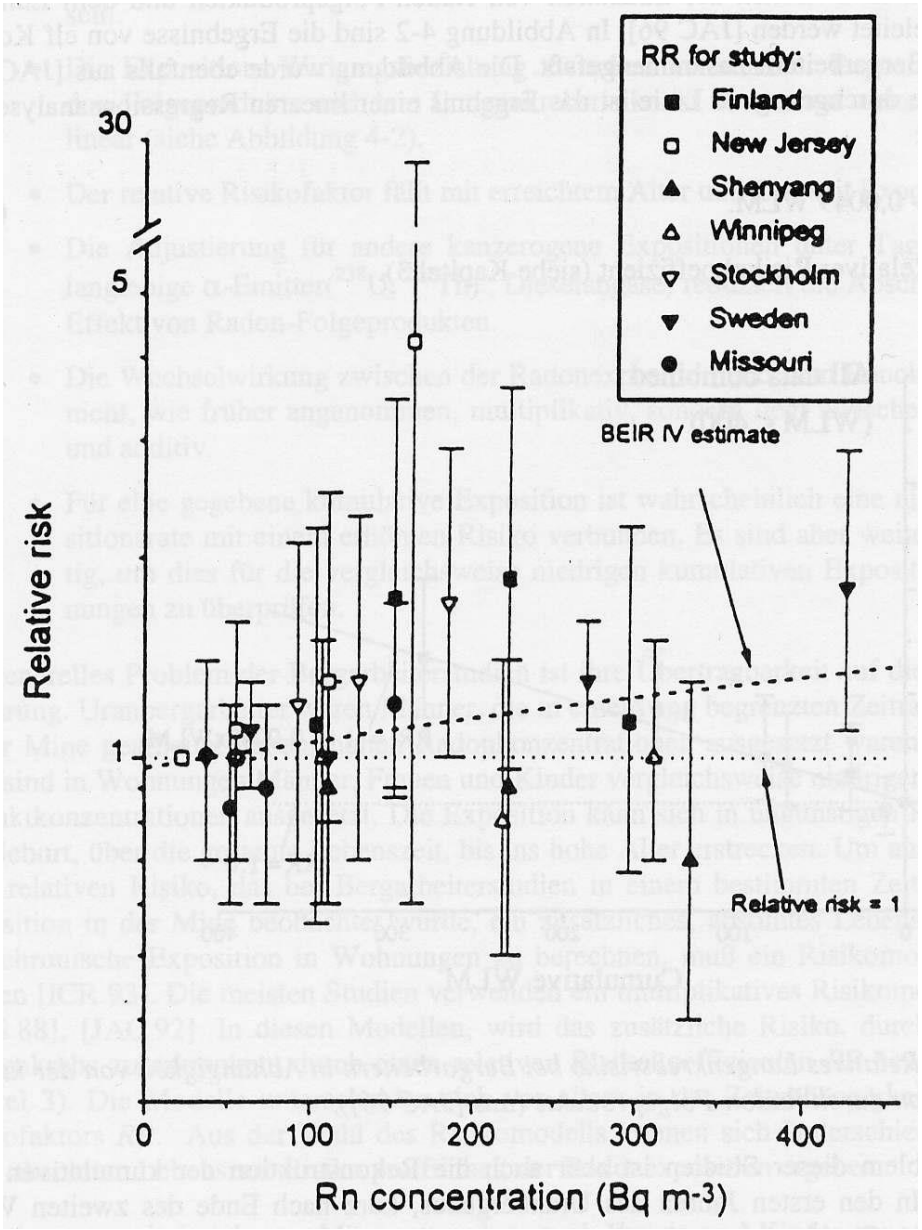


Lovelace

„Menschliche“ Epidemiologie:

Die größte Strahlenexposition der Bevölkerungs (-Lungen) geschieht durch Rn und -Zerfallsprodukte:

- keine oder geringe Effekte ?
- in welche Richtung (+-) ?



“Tierische” Epidemiologie:

Gibt es positive Strahleneffekte bei niedrigen Dosen?

Plot of 50% survival age for all deaths competing with fatal lung cancer for all rat groups, and their 95% confidence bounds:

W.F. Heidenreich, F.T. Cross, and H.G. Paretzke, Math. Comp.Modelling 41: 689-95 (2005)

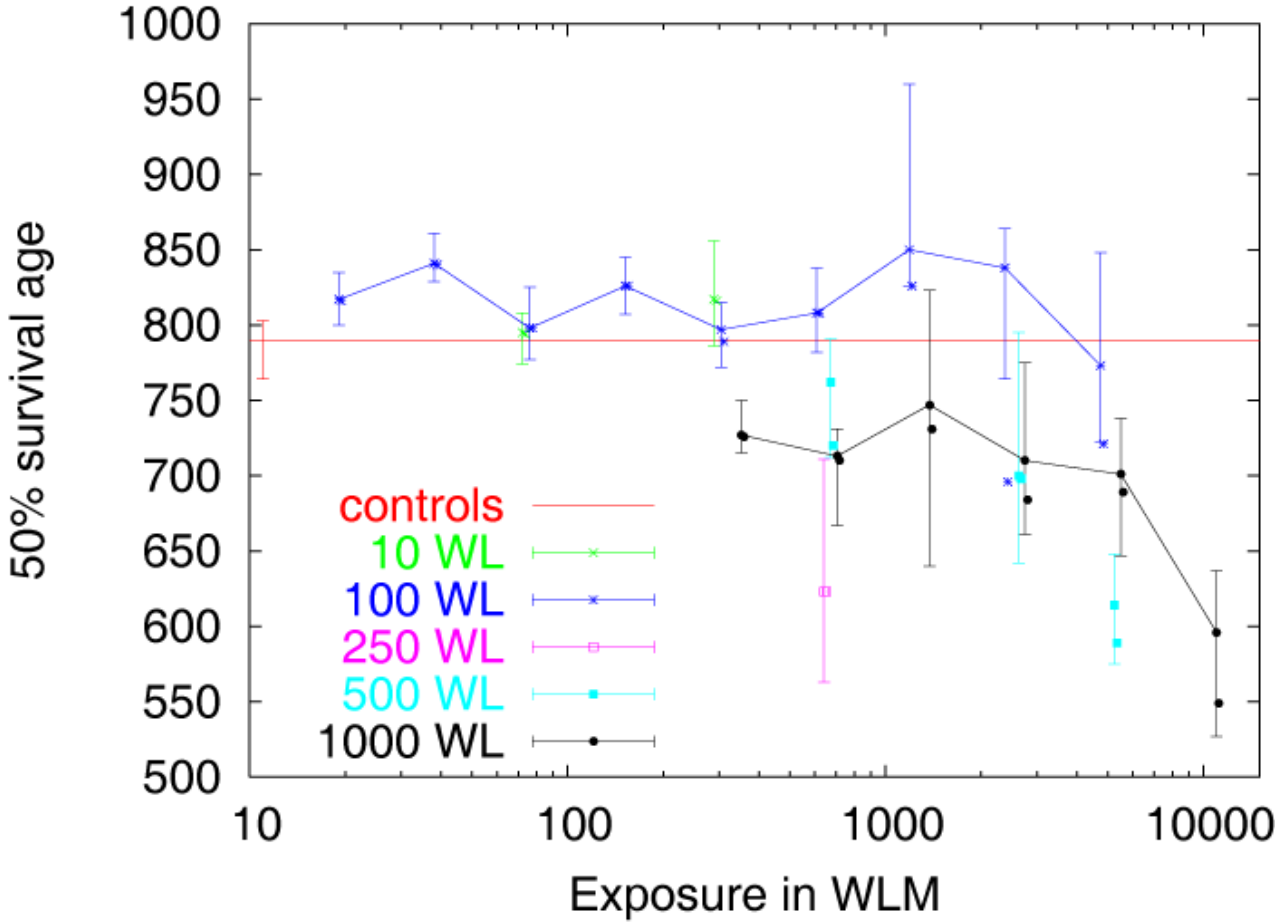
Different health effects of radiation on different individuals?:

Those many, who do not die from Rn-induced lung cancer, might live longer! **(Rn = red wine?)**

A nice problem for future RP:

How to 1) „justify“ rad.exp. in RP,

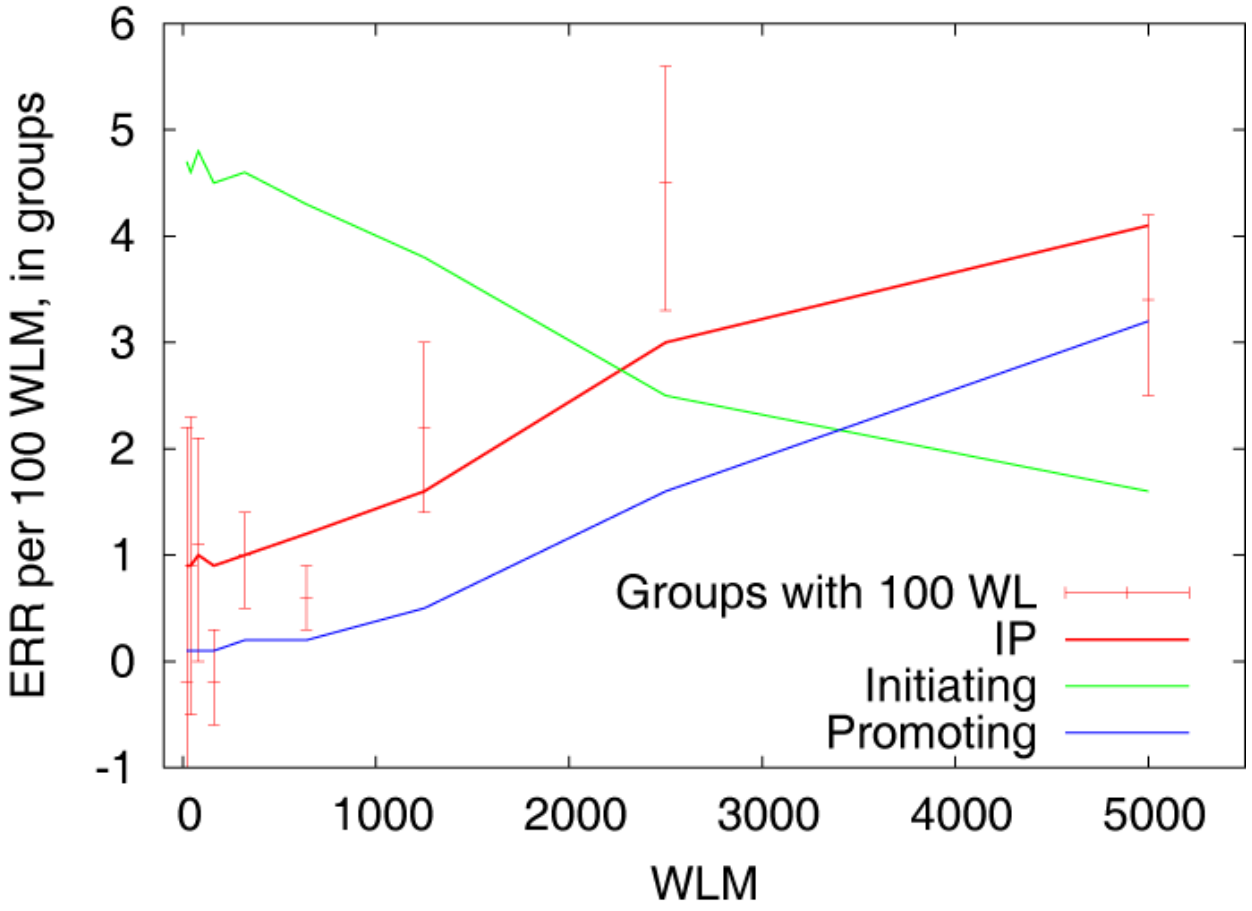
2) with which limits?



Die Analyse von Tierdaten zeigt:

There might be more **promoting** than **initiating action** of radiation

(contrary to LNTH!)

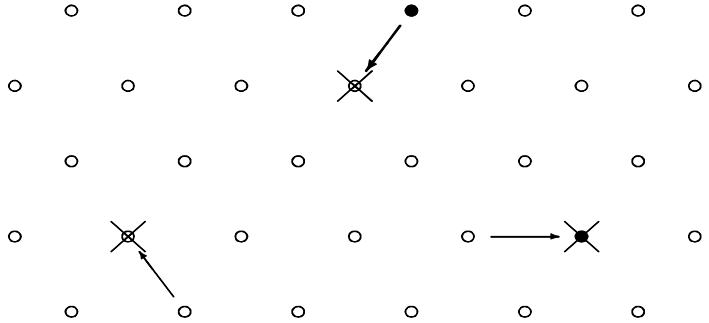


ERR per 100 WLM for these groups, based on the fitted background for fatal lung tumors. Duration of exposure with a rate of 100 WL of radon in the PNNL- rat range from 2 to 700 days. (TSCE-Model)

W.F. Heidenreich, P. Jacob, H.G. Paretzke, F.T. Cross and G.E. Dagle, Rad.Res. 151:209-217 (1999)

How would we explain this obvious contradiction to everything we now teach (initiation action only, "dead = good" cells)?

One possible mechanism of **promotion by irradiation**:



Normal cell nuclei in a lung tissue (open circles) and initiated cell nuclei (filled circles) form a 2-dim pattern.

IR inactivates cells (X).

Three possibilities of subsequent **replacement** are shown:

1) A normal cell replaces an inactivated normal (left)

2) or a previously initiated cell (right).

3) **A previously initiated cell (with growth advantage) replaces an inactivated normal cell (top).**

Then a "dead cell is a bad cell"!

This model elegantly explains why a) **no fingerprints** of previous irradiation are found in tumors,
b) the "**relative** risk" model is often observed in experimental data.

Heidenreich, Atkinson, Paretzke, Rad. Res. 155:870-2 (2001)

Bislang haben wir keinerlei Hinweise auf die Gültigkeit der LNTH gefunden:

„Jede Strahleneinwirkung kann eine Mutation/Veränderung im Genom/in der DNS hervorrufen, die Jahre später zu einer Krebserkrankung der bestrahlten Person führen kann“.

Diese Annahme scheint nicht zu stimmen für „der Gesundheit schädliche“ Wirkungen!

Wie gehen wir dann bei Risikoabschätzungen in der Praxis vor?

Abschätzung von Strahlenrisiken **zum Zweck der Begutachtung im Berufskrankheitenrecht:**

- Verursachung einer gegebenen Erkrankung ist **nicht identifizierbar**:
  daher: **Wahrscheinlichkeitsbetrachtungen** „Spontan“ / „Strahlung“

- Auf **individuelle** Person bezogen statt über Alter und Geschlecht gemittelt

- **Inzidenz** bezogen statt auf **letale** Erkrankungen

- **Zeitlicher** Expositionsverlauf wird berücksichtigt

- Positiver Wahrscheinlichkeitsbeweis vor Gericht **nur bei > 50 %:**

dazu sind Dosen **oberhalb einiger Zehntel Sv** nötig = viel **bessere Datenlage**

Verwendet werden dabei „Best-Estimate“ Strahlenrisiko-Funktionen:

SSK - Empfehlung 1995 basierend auf GSF-„Strahlenepidemiologische Tabellen“, Chmelevsky, Nekolla, Barcley.

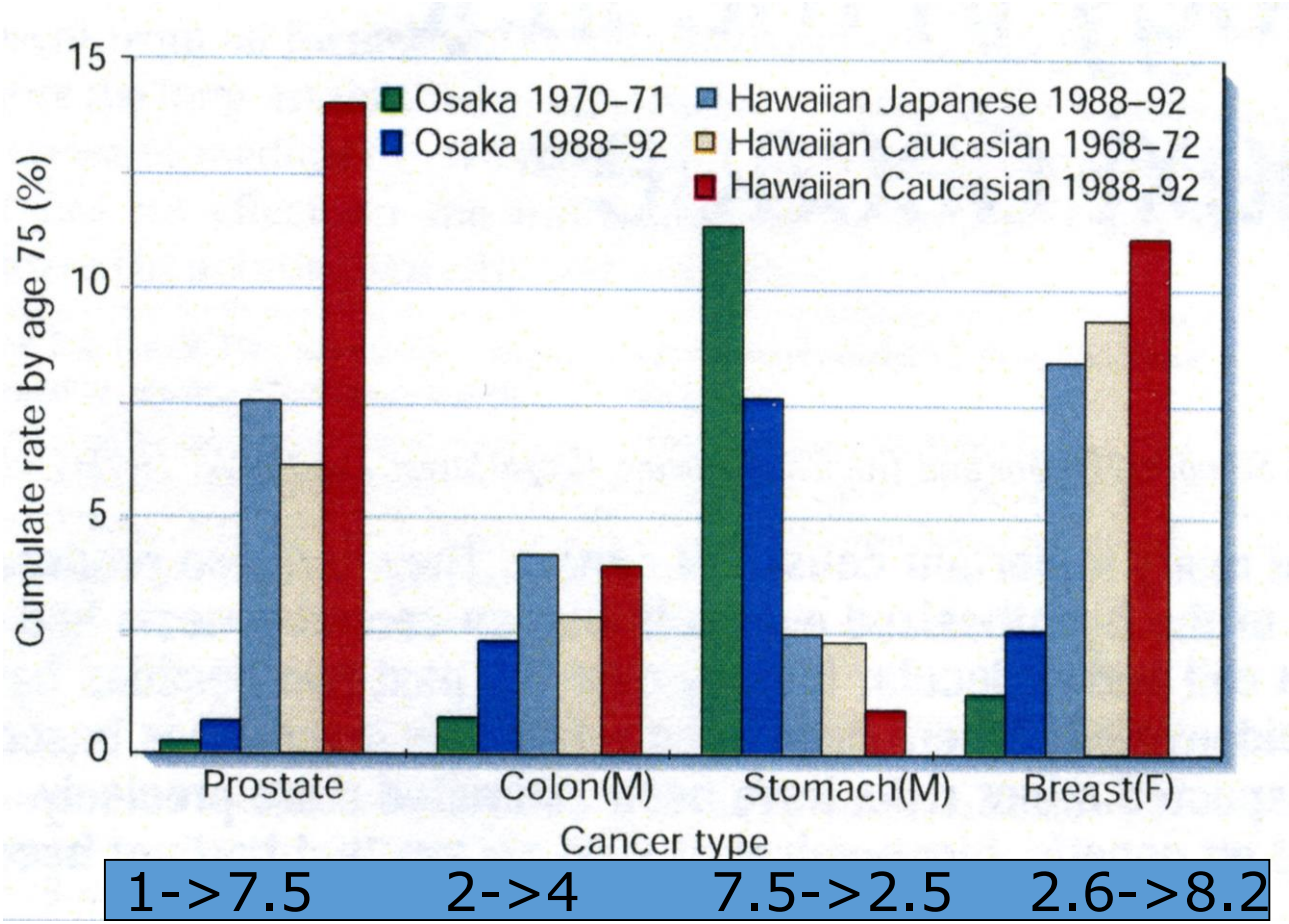
SSK – Empfehlung 2015 basierend auf dem interaktiven Programm ProZES (Programm zur Berechnung der Zusammenhangs-wahrscheinlichkeit einer Erkrankung und einer Strahlenexpostition)

Probleme sind bei der Erstellung dieser Tabellen u.a.
die Annahmen zum Transport von Strahlen-Risikofunktionen
(z.B. RR, AR, etc.)
von einer Bevölkerung (-Gruppe) zu einer anderen.

Human epidemiological data on importances of life style and environment on carcinogenesis (epigenetics!):

Julian Peto, „Cancer epidemiology in the last century and the next decade“, Nature 411,390-395:

„The convergence towards local cancer rates seen among immigrants excludes a genetic explanation of these differences.“



Das Spektrum der Krebserkrankungen ändert sich zeitlich und regional!
Die Summe bleibt etwa gleich!

Jeder Mensch trägt auch bei der Migration sein angeborenes Genom in allen Zellen mit sich!

Initiation vs. Promotion!?

Abschätzung der Strahlenrisiken zum Zweck des Strahlenschutzes (ICRP Report 103, 2007) :

Annahme der Linear No Threshold – Hypothese

Letale Endpunkte, Alters- und Geschlechtsmittelung, „Detriment“

Rechtfertigung (LNTH, positiver Nettonutzen)

Optimierung (LNTH, ALARA)

Begrenzung (LNTH, Dosisgrenzwerte, Allg. Berufsrisiken Vergleich)

Die Benutzung der LNTH ist der Hauptgrund für unsere Situation bezüglich unserer großen Probleme beim fehlenden

- **geistigen** (Strahlenphobie allerorten)
- und
- **sozialen** (Kerntechnik, Endlagerung, etc.: „viel zu gefährlich“)
- „Wohlbefinden“.

- Es wurden weltweit **mehrere hundert Millionen EUR und $** ausgegeben, um hier Klarheit zu bekommen:
- **Es gelang kein mechanistischer, noch ein epidemiologischer Nachweis der Korrektheit der LNTH- Annahme!**

Dies ist auch in dem **Abschlussbericht einer großen EU-weiten Studie** zu diesem Thema formuliert:

SCIENCE AND SOCIETY

Assessing cancer risks of low-dose radiation

Leon Mullenders, Mike Atkinson, Herwig Paretzke, Laure Sabatier and Simon Bouffler

Abstract | Ionizing radiation is considered a non-threshold carcinogen. However, quantifying the risk of the more commonly encountered low and/or protracted radiation exposures remains problematic and subject to uncertainty. Therefore, a major challenge lies in providing a sound mechanistic understanding of low-dose radiation carcinogenesis. This Perspective article considers whether differences exist between the effects mediated by high- and low-dose radiation exposure and how this affects the assessment of low-dose cancer risk.

Despite the considerable benefits obtained from the use of radiation (such as medical uses, energy production and other industrial uses (BOX 1)), it is clear that there are health risks to humans exposed to radiation. Radiation has several well-established, and some more recently identified, effects on human health (BOX 2), and cancer is considered the major long-term contributor to health risk at levels below those causing acute tissue injury. For the purposes of this article, low doses are defined as those less than 100 mSv and low dose rates are defined as those below 0.1 mSv min^{-1}.

Epidemiological studies of the survivors of the Hiroshima and Nagasaki atomic bombings provide strong evidence of increased risk of developing both solid cancers and leukaemias from high doses and high dose rates of radiation[1,2]. However, significantly increased cancer risk is also observed in atomic bomb survivors exposed to lower doses (5–150 mSv) of radiation[1,3,4]. Increased risk has also been demonstrated in cohorts of radiation workers who have been exposed to lower doses of radiation generally and over extended periods of time. A major international study following more than 400,000 nuclear industry radiation workers exposed to an average dose of radiation of ~20 mSv reported a significant association between radiation dose and cancer mortality even when restricted to cumulative doses of <150 mSv[5]. However, some caution is needed in interpreting this study as smoking may remain a confounding factor, and data from one country disproportionately contribute to the estimates of risk (for example, see REF. 6). More recently, further analysis of cancer incidence and mortality risks in UK nuclear industry workers has been published[7]. This analysis does not suffer to the same extent from the confounding factors that affected the international study. The UK study identifies cancer risks in line with those derived from atomic bomb survivor studies and is consistent with a linear extrapolation of low-dose risk from high-dose data. Lung cancer risks are increased in those exposed to chronic levels (<200 Bq m^{-3}, equating to an estimated 4 mSv annual effective dose (1–8 mSv range)) of radon gas in their homes[8]; however, radon dosimetry is complex and individual behaviour will affect exposure[9].

Epidemiological studies provide evidence for increased cancer risk after exposure to low doses of radiation and therefore sound evidence of risk to adults is available at 50–100 mSv delivered over a short period of less than 1 day[10]. Furthermore, the radon and nuclear industry radiation worker studies provide evidence of risk from protracted, low dose rate exposures. Epidemiological studies also provide evidence for increased risk at the 10–15 mSv level when exposures occur *in utero*[11], although such findings have remained controversial over many years (for example, see REF. 12). However, epidemiological studies are reaching their limit of detection of risk at low doses and so further understanding of the effects of doses 100 mSv and below is required to ensure adequate protection of those that are exposed.

The current generally accepted pragmatic approach to low-dose risk estimation recommended for the regulation of radiation exposures and endorsed by the *Biological effects of ionizing radiations (BEIR) VII* report of the US National Academy of Sciences[12] and the International Commission on Radiological Protection (ICRP)[13] is that a linear non-threshold (LNT) extrapolation of cancer risk from high-dose data is most appropriate (FIG. 1). The LNT model implies that there is an increase in risk to health proportionate to the radiation dose received down to the very lowest levels. The model indicates that there is no safe level of exposure — that is, there is no threshold dose below which no increase in risk to health is posed. The ICRP recommends maximum occupational dose limits of 20 mSv per year averaged over 5 years with no single year exceeding 50 mSv[13]. However, in practice most exposures do not approach these limits. In radiotherapy, significant doses of radiation are delivered to humans but in these cases there is a clear benefit of radiotherapy that outweighs the risk of exposure and this is recognized as the case for all medical exposures[13]. However, diagnostic uses of radiation are becoming a more prominent source of exposure, with some computed tomography scans delivering doses of several tens of mSv, and perhaps up to 100 mSv, each. The risk/benefit ratio for such exposures is not always clear[14], particularly when applied to asymptomatic individuals[15]. With the increasing use of interventional radiology for the treatment of various conditions, including heart disease and liver cancer, concern is growing that the low doses to which patients and staff are exposed may pose significant health risks[16–18].

The LNT model is based on an unproven assumption, albeit one supported by several biological arguments that are discussed in detail in several reviews[10,12,19,20]. Ionizing radiation damages DNA through direct biophysical and physicochemical interactions and so it is therefore assumed that the extent of DNA damage to cells is proportionate to the radiation dose received. There is a clear relationship between DNA damage, mutations and cancer development[21]. Therefore, there is a finite probability that even the lowest possible radiation doses can increase the probability of developing cancer. The LNT model is regularly challenged as being overprotective and it is argued that low-level radiation exposure may have health benefits[22,23]. By contrast, some more recently characterized effects of radiation, such as persistent transmissible genomic instability and bystander phenomena, could increase cancer risk above extrapolations based on the LNT model if such processes do in fact contribute to radiation carcinogenesis (for example, see REF. 24).

Clearly, accurate assessment of radiation risk is important for regulators and governments worldwide and an interdisciplinary

Zusammenfassung – meine Empfehlungen, hinsichtlich „ICRP103 neu“

- 100 Jahre Forschung konnten keine Hinweise auf die Gültigkeit der LNTH erbringen.

Daher: „man begrabe sie“! **Diese Annahme war offensichtlich falsch**!

- Ändere die Bezeichnung „Grenzwerte“ in

„Werte, unterhalb denen keine schädlichen Gesundheitseffekte beobachtet wurden (NOAEL)“

- Damit sind auch „Rechtfertigung“ und „Optimierung“ zu begraben, da dann unbegründet.

- Belasse die neuen NOAELs numerisch bei ihren gegenwärtigen Grenzwertzahlen und die
- Strahlenrisikoberechnungen oberhalb der G. (ca. 0,02 Sv/a) so, wie sie sind.
- Belasse die Messverfahren (damit sichergestellt wird, dass Exp. im analysierten Rahmen)
- Fördere die großen, positiven Konsequenzen hinsichtlich des

„geistigen“ und des „sozialen“ Wohlbefindens!

Schon der große Wissenschaftstheoretiker
Thomas Kuhn "The Structure of Scientific Revolutions" (1962)
(1922-1996, Physicist, Science Theoretician,Harvard,Princeton,UoC Berkeley,MIT)
hat erkannt:

- science does not progress towards truth with each new discovery,
- but instead undergoes periodic **revolutions.**
- These revolutions are called "**Paradigm Shift**", in which the research strategy within a field is suddenly and significantly changed.

- "**Normal science**" is the routine, day-to-day work of scientists **within a paradigm (set of explicit or implicite working hypotheses)** collecting data and ordering them within the usually applied frameworks, refining the paradigms used to solve problems.

- During periods of „*normal* science ", scientists try to enlarge the central paradigm by "puzzle-solving".
- "**In learning a paradigm the scientist acquires theory, methods and standards together, usually in an inextricable mixture".**

- ...If contradictions and difficulties arise by new facts, conflicts and discussions follow.
- **Only relatively late, the possibility of wrong assumptions in the prevailing paradigm is considered**.
- Thus, the failure of a result to conform to the paradigm is seen not as refuting the paradigm, but as the mistake of the researcher (contra Karl Popper‘s refutability criterion)!
-

- „As anomalous results build up impressingly,
- **science reaches a *crisis***, at which point a ***new paradigm***,
- **which subsumes the old results along with the anomalous results into one new framework, is accepted**.

- This is termed ***revolutionary science.“***
- ***LNTH: RIP!***

„Der Kopf ist rund, damit das Denken leicht seine Richtung ändern kann!“

(Pablo Picasso)