

Text of the presentation C.Knüsli 15.9.2017 (Slide numbers refer to visual presentation, see congress homepage)

Ionizing Radiation: Medical Risks – New Aspects

Intl. Congress on Human Rights, Future Generations and Crimes in the Nuclear Age

Basel University, Switzerland 14. – 17. 9. 2017

Ladies and Gentlemen, dear guests, good morning !

I am invited to speak to you about the profound effects by ionising radiation on human health.

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We start with a few basics. We will then discuss health effects in Japanese A-bomb survivors. Considerable knowledge has accrued since the start of this millennium so we will look at the new studies on **low dose** irradiation health effects. I will conclude calling for a revision of the radiation protection standards.

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Ionising radiation is a form of physical energy. „**ionising**“ means that this energy changes living cells mainly at the nuclear or nonnuclear DNA level. This is crucial for steering cell metabolism especially for cell replication. Cells also may not directly be hit by irradiation, but in some way „contaminated“ by neighbour hit cells. This is called „bystander effect“. The induced cellular changes may result in a simple skin erythema, but also in cancer, cardiovascular, neurological, ocular and endocrine diseases as well as malformations and genetic effects.

Lung cancer in German uranium miners is known since more than 100 years. And many radiologists have suffered from severe radioinduced diseases.

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Ionizing radiation is occurring spontaneously in **nature**. In addition, human technologies allow to fabricate **artificial** radioactive elements or devices such as CT-scans which produce irradiation. This leads to all the situations listed on this slide.

Lets make it clear: When we are speaking about late radiation effects such as cancer or non-cancer diseases in Japanese A-bomb victims, when we describe these diseases in nuclear industry workers or when we discuss the induction of blood cancer in patients after CT-diagnostics in their childhood – **it is always the exposure to ionizing radiation** which is the common ground for these pathologies.

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The first systematic study on radiodiagnostic risks was published in 1956 by Prof. Alice Stewart, an eminent British epidemiologist. She investigated the longterm outcome of children born by mothers who had been x-rayed during pregnancy. Stewart found a 40% elevation of cancer risk in these children. However, physicians only reluctantly implemented radiation protection standards which were the logical consequence of this new scientifically based knowledge.

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Cancer is the most frequently cited disease induced by ionising radiation. Cancer is by definition a malignant disease based on dysregulated cell proliferation leading to locally infiltrating or distant (metastatic) destructive pathological tissue growth. On the left, we see the endoscopic view of an esophageal cancer (as an example of a solid organ cancer) as well as its microscopical appearance. On the right side, a blood smear of a patient with white cell blood cancer is demonstrated.

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We will speak during this presentation of ten of thousands of patients. Let me just mention one name – one name of a child who died at the age of 12 years from leukemia in 1955, it's the Japanese girl Sasaki Sadako. She lived in Hiroshima at the time of the A-bomb explosion. Sadako remains in our memory for folding of more than thousand coloured paper cranes in hope of overcoming her deadly disease.

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The story of Sadako remembers us of the suffering of so many persons due to nuclear war. The folding of origami cranes today is a worldwide inspiring symbol of peace.

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How dangerous is radiation really ?

The Life Span Study LSS has studied the health effects in 120 000 Japanese A-bomb survivors. It is an important study because of the long follow up. Nearly half of the survivors were still alive after 60 years. Actual ionising radiation risk calculations are mainly based on the LSS: The Excess Absolute Risk factor (EAR) for cancer mortality given by the ICRP is **5.5 % / Sievert (Sv)**. Similarly, elevated risks for leukemia and noncancer death have been described.

These risk calculations are based on a «collective effective irradiation dose» which means adding all individual doses of exposed persons.

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This figure from Pearce and Preston published in 2000 clearly shows, that there is a statistically significant excess of cancer deaths in nuclear bomb survivors. There is no threshold. Every ionizing radiation dose is a risk. The curve demonstrates, that there is a linear risk according to the dose to which a person is exposed. The doses at a level below 100mSv (...the blue line) are called „low doses“.

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Low dose ionising radiation will keep us occupied from now on, because it is the most frequent situation we will encounter. Chronic intake of contaminated food by cesium 137 after Chernobyl as well as living in irradiated regions around Fukushima *is* exposure to low doses of ionising radiation. „Low dose“ as opposed to „high dose“ above 100mSv is a highly questionable, arbitrary classification. It suggests „low risk“. But both low and high doses can kill !

After low dose irradiation – either on one single occasion or by protracted repeated exposure –, there is no immediate health effect. The longterm health effects of low dose irradiation are called **stochastic** which means „occurring by chance“. The linear no threshold model – LNT – best describes the risk which is proportional according to the dose.

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The results of the LSS are still important, however, they are **outdated for risk calculations** for several reasons:

- The short exposure to high energy gamma-radiation is not comparable to chronic alpha-, beta-, gamma-irradiation or x-rays
- The low dose radiation range is not reliably covered. There was no dosimetry but only dose estimates. The studies began in 1950 only and therefore diseases with short latency periods were missed.
- There was a substantial selection bias with many early, traumatic casualties which led to the „survival of the fittest“. Finally the family histories of Japanese A-bomb survivors are not very adequate because they have been ostracised.

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What are the difficulties of studies on ionising radiation health effects in general? It is mainly the lack of straight forward proof. Nobody probably would doubt, that this cat has killed this mouse, but with lethal radiation effects, it is not that simple. We don't have smoking colts, nor do we have specific tags on a cancer which would help for the identification of its cause.

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The fact of indirect proof with **epidemiological studies** leaves us even in big studies with some uncertainty: Is there only a statistical association - or do we have a causal role of radiation for observed health problems? Nevertheless not laboratory research but **epidemiological studies** give the strongest information. They are based mainly on temporal and geographical criteria.

Long induction periods of up to several decades between radiation and following diseases are challenging logistical aspects.

And there are many other difficulties as confounders like smoking, drinking, social problems and migration, as insufficient radiation dose information and selection bias or statistical fallacies (e.g. lack of statistical power in small study populations).

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For all these reasons, we need new modern epidemiological studies for reliable risk calculations.

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In this reference list you find some of the most relevant studies of the last 15 years. I'll call them „new studies“ in comparison to the Life Span Study. These are new epidemiological studies which have found statistically significant health effects associated to ionising radiation for the following 4 criteria: solid cancer, leukaemia, non-cancer disease and here especially cardiovascular disease.

Slide 18. **(Table)**

On this coloured table, which was distributed as a hardcopy and which is also available on the congress homepage, details of these studies have been compiled.

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Horizontal lines refer to the publication, to the size of the studied populations, to the observed health effects and finally to the exposure data.

Here I looked at the question, if there is **a dose response**. This was the case in nearly all of these new studies.

The bottom line explores if the observed health effects are associated with **low** radiation doses. You see that the doses in all new studies are clearly below 100mSv (or mGy). These are therefore low dose studies by definition.

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Colour coded columns refer to the different radiation exposure situations.

Yellow stands for the Life Span Study.

The next four columns refer in **blue** to nuclear workers and in **green** to the two studies on children under the age of 5 years living within 5 km distance from a nuclear power plant. Both the German KiKK-Study and the Metaanalysis from children in France, Great Britain, Germany and Switzerland by Koerblein and Fairlie showed a significant increase of childhood leukemia. For this the most likely explanation are the high isotope emission peaks during the periodical exchange of nuclear fuel elements.

Orangebrown is for populations exposed to radiation by Tschernobyl or Fukushima. For both catastrophies a huge number of detrimental health effects have been described. They are best summarized by a publication of the German IPPNW. Here we must mention the extremely high risks for thyroid cancer in children and in adults due to contamination by radioiodine.

Finally **pink** stands for radon and natural background radiation studies - and **purple** for patients exposed to diagnostic medical radiation in their childhood.

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This slide gives you the overall **summary of the results** from these new studies.

1. About 10 studies since 2005 found a statistically significant association of exposure to **low dose** and also a **dose-response** of ionising radiation and mortality (or incidence) by solid cancer, leukemia or non-malignant diseases such as cardiovascular diseases.

2. **I'd like to emphasize that dose-response is a strong argument for causality**

3. Severe health effects were found even at **very low levels** in two studies on background radiation by Kendall from Great Britain and Spycher from Switzerland. Here, doses of about 1mSv/year were associated with significant elevated risk for malignancies.

4. Most studies are published in peer reviewed journals.

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This presentation of 20 minutes allows for only a few highlights.

INWORKS is one of the most important epidemiological studies. Its mature results have been published in several portions during the last 2 years.

INWORKS investigated over 300 000 nuclear workers in USA, GB and F. After a follow-up of 8.2 million person-years, 22% of the workers had died. The mean radiation dose was 20.9 Milli-Gray in the publication of Richardson in 2015. His study focuses on **death from solid cancer**. He found an estimated rate of mortality from all cancers of **48% per Gy**. These results suggest a linear increase of the cancer death rate with increasing radiation exposure.

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This figure from Richardsons work shows - even at low radiation doses - a significant elevated risk for cancer death. There is no threshold – even a very low must be considered a risk.

Similarly Leuraud and coworkers showed in 2015 a significant dose dependent elevation of the death rate due to *leukemia* in the INWORKS population.

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The most recent publication on INWORKS stems from Gillies from July 2017. A statistically significant excess of deaths after low irradiation doses was found with an Excess Relative Risk of 50% per Sievert for cerebrovascular disease and of 18% / Sv for ischemic heart disease.

The authors conclude that the estimates of associations between radiation dose and non-cancer mortality are comparable with those observed in A-bomb survivor studies. However their wording about causality is very conservative.

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We also must speak about radon - a naturally occurring noble gas - and its decay products which emit alpha-radiation. The mean yearly dose attributable to radon amounts to 1.1 mSv per person. (Germany) .

A statistically significant dose response effect of low dose ionizing radiation from indoor radon exposure and lung cancer has been demonstrated by Darby. The risk factor is 8.4 % / 100 Bq / m³ .

In Europe, 9 % of lung cancer deaths and 2% of all cancer deaths are attributed to indoor radon radiation . This means for Switzerland that every year +/- 240 persons are dying from radon induced cancer.

Since 2005 international experts understand low dose ionising irradiation by indoor radon as a severe health risk. Building legislation has implemented standards which aim at reducing radon exposure for inhabitants.

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For Switzerland this looks like that: Since 2006 our Federal Office of Health warns with this leaflet about the radon related cancer risks.

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What is most striking for me as a physician is the wording *radon “causes” lung cancer* (which is by the way absolutely true) and the wording *“legal”* which gives us the link between health experts and lawyers.

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With all this scientifically based knowledge on health effects by low doses of ionizing radiation in mind, we wonder how the leading international bodies involved in radiation protection handle this subject.

In its recommendations in force since 2007 the ICRP - which is most relevant for the WHO and the IAEA - does not accept epidemiologically based risk estimations for low dose ionizing radiation.

The wording of this widely respected document is scientifically inappropriate in 2017.

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I would like to conclude

- Modern scientific studies confirm the linear no threshold (LNT) model. They support the validity of epidemiological risk calculations for severe health effects due to ionising radiation at doses far below 100mSv (i.e. «low dose ionising radiation» ; Ref. 20).
- The LNT forms the basis for radiation protection of the public exposed to low dose ionising radiation, e.g. after nuclear accidents.
- The risk factor (EAR = Excess Absolute Risk) for cancer death due to ionising radiation has to be adapted from 5.5% to 20% / Sv.
- Significant increase of mortality related **to non-cancer deaths** in the order of **cancer-related** mortality due to low dose ionising radiation has been documented. This must be officially acknowledged
- Therefore the ICRP 103 recommendations (2007) must be revised

(Slide 30 → %)

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Ladies and Gentleman,

During this congress we will hear much more about health problems of irradiated populations

- by uranium mining,

- from exposure to fallout from A-bomb tests, in A-bomb survivors and people
exposed to depleted uranium DU

- from regular and accidental exposure by nuclear power plants and also in the context of NPP decommissioning and nuclear waste management.

In future, we should think in an **integrative way** when it comes to discussions on radiation protection. For sure, there are on the one hand already established regulations for workers in nuclear facilities, in the medical field and in the building legislation with respect to radon.

But also in all other situations, where populations are exposed to low doses of ionising radiation without nowadays being protected by the mentioned standards, the Precautionary Principle in view of the unalienable Human Right of Health should be respected.

Thank you.



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