The selected aspects of low doses influence on organisms

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Influence of radiation - overview

- DNA damages
  - Repair
  - Cell death
  - Mutation $\rightarrow$ cancer

- System of DNA repair
  $\rightarrow$ non-radiation damages
  also repaired

- Number of DNA damages
  is usually linear with the dose

- Adaptive response

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Adaptive response

HIGH DOSE
- Chromosomal aberrations
- Mutations
- Genetic instability
- Cells death

LOW DOSE
HIGH DOSE
No disturbances or weaker ones
Low doses of ionizing radiation

- Below 150-200 mSv per year
- Three major hypotheses:
  - Linear no-threshold (LNT)
  - Threshold
  - Hormetic (J-shape or U-shape)
Which hypothesis?

- Difficulties in low dose region
- Data are usually not precise (statistically nonsignificant or no data at all)
- New important researches all over the world
- Radiation protection standards based on LNT hypothesis
Main goal of the Thesis

- Researching many different aspects of low dose radiation influence on organisms
- Testing which model (linear, threshold or hormetic) fits best to the presented data

Methodology:
- Statistical analysis of existing and recently collected data
- Simulation and modelling
- Experiment on plants
First example

Statistical analysis of cancer cases among nuclear workers

Statistical analysis

- Bayesian methods of analysis
- Nuclear workers from 15 countries (excluding Poland)
  - Nuclear workers from Świerk will be analyzed later
- One observes statistically significant decrease of deaths among irradiated workers
Cancer deaths from 15 countries

24,000 workers
Average dose-rate: 2 mSv/year

SMR [%]

controls  nuclear workers

all causes  cancers only
Results

- SMR for cancers equals 19%
- Average annual excess dose 2 mSv per worker
- However the SMR for all causes is not equal 100%
- Healthy worker effect?
- Need for future studies
Second example

Pooled analysis of 28 studies on radon induced lung cancers

Fornalski K.W., Dobrzyński L. 'Pooled Bayesian analysis of 28 studies on radon induced lung cancers'. Health Physics, September 2011 (in press)
Radon and lung cancers

- Radon – alpha radioactive gas
- Bayesian analysis of data from 28 popular radon studies
- Unified data through UNSCEAR commission recommendations
- Conversion factor:

\[ 1 \text{ Bq m}^{-3} = 0.179 \text{ mSv/year to lungs} \]
28 studies (without uncertainties)
Pooled Bayesian analysis

- 7 models fitted to data and tested:
  - Dose-independent
  - Linear models (including LNT)
  - Quadratic models

- Model selection algorithm shows that the most likely model is the one which states that the mortality due to lungs cancer is independent of the dose (within observed range of doses)
Third example

Standard mortality ratios of cancer in higher radiation areas in Poland

High radiation areas in Poland

- Radiation from natural origin:
  - Radon concentration
  - Gamma rays (mostly from the ground)
  - Others (cosmics, in-body elements etc.)

- The lowest dose-rate
  in Świnoujście: 1.06 mSv/year

- The highest dose-rate
  in Jelenia Góra: 4.75 mSv/year

- Doses from man-made sources not included!

- All data taken from National Cancer Registry and radioecological maps and studies
Natural gamma radiation in Poland
6 sets of data
The increase of cancer mortality [%]

Polish study
controls
LNT assumption

Excess effective dose from natural origin [mSv/year]
Results

- All six sets show the regular decrease of cancer deaths
- No confounding factors included!
- Many explanations of such decrease
- One of them can be hormetic effect of ionizing radiation
- Congruity with many other data
Fourth example

Author’s stochastic Markov model of cellular response to radiation

The new model

- A group of virtual cells and its response to some dose of radiation
- The new point of view – completely stochastic approach instead of deterministic ones
- Markov Chain Monte Carlo techniques
- Dozens of input parameters – physics and biology of cells’ radiation
second loop over cells - one by one

1st step

healthy cell  healthy cell  healthy cell  healthy cell  healthy cell  ...  ...
nothing  mutation  death  multiplication

2nd step

healthy cell  mutated cell  dead cell  healthy cell  healthy cell  ...  ...
mutation  multiplication  nothing  death

3rd step

mutated cell  mutated cell  mutated cell  healthy cell  dead cell  ...  ...
repair  transformation  multiplication  nothing

4th step

healthy cell  cancer. cell  mutated cell  mutated cell  healthy cell  ...  ...

...  ...  ...  ...  ...  ...  ...

...  ...  ...  ...  ...  ...

stochastic trees

stochastic trees

stochastic trees

stochastic trees
\[ P_{\text{hit}} = 1 - \exp(-\text{const}_1 \cdot D) \]
An example of one branch

A healthy cell is hit by radiation (see Fig. 2)

- $P_D + P_{RD}$: death
  - $P_{RC}$: transformation into a cancerous cell
  - $1 - P_{RC}$: no transformation

- $P_M$: spontaneous mutation

- $P_S$: natural multiplication

- $P_B$: bystander effect - signal to a nearby cell
  - $P_{RC}$: transformation into a cancerous cell
  - $1 - P_{RC}$: no transformation

- $P_{RM}$: radiation-induced mutation
  - remaining probability
  - no change
Results of modelling

- An influence of many biological mechanisms of single cells
- Results with and without adaptive response
- All results are consistent with many experiments
- Threshold appears in very natural way
- Model can be easy applied to any types of cells or tissues
Low doses

- **mutated cells**
- **cancer cells**

![Graph showing the fraction of cells as a function of dose per step (mGy).]
Medium doses

![Graph showing fraction of cells vs. dose per step (mGy) for mutated cells and cancer cells.](image-url)
High doses
Fifth example

Irradiation of cress

Irradiation of plants

- Plants are much more resistant to radiation than humans
- The main goal: find the possible threshold (and/or hormetic period) in the case of irradiated cress
- Cress (*lepidium sativum* L., Pol. *rzeżucha ogrodowa*) – the popular & fast growing plant
Cress (*Lepidium sativum* L.)

- Gamma irradiation during growth
  - Up to 4 Gy

- Gamma irradiation of dry seeds
  - Up to 100 Gy

- Growing in phytotron chambers (IBB PAN)
Experiment
Results of dry seeds irradiation

- Relative ratios – comparison with the control group

- Statistically non significant hormetic effect in relative number of formed plants after 7 days
For higher doses
Final conclusions

All presented data show that LNT hypothesis cannot be generally valid.
All statistical analysis shows sometimes the threshold model and sometimes the horbetic one.
The one possible compromise: the threshold model (?)
THANK YOU

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