

# Chromosome Aberrations induced by the Auger Electron Emitter I-125

**Sabine Schmitz**

**Forschungszentrum Jülich GmbH**

**Department of Safety and Radiation Protection**

**Radiation Biology**

ISCA 2014

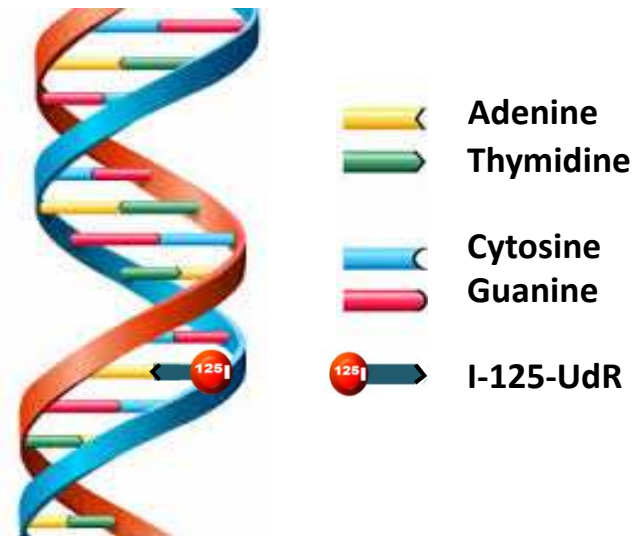
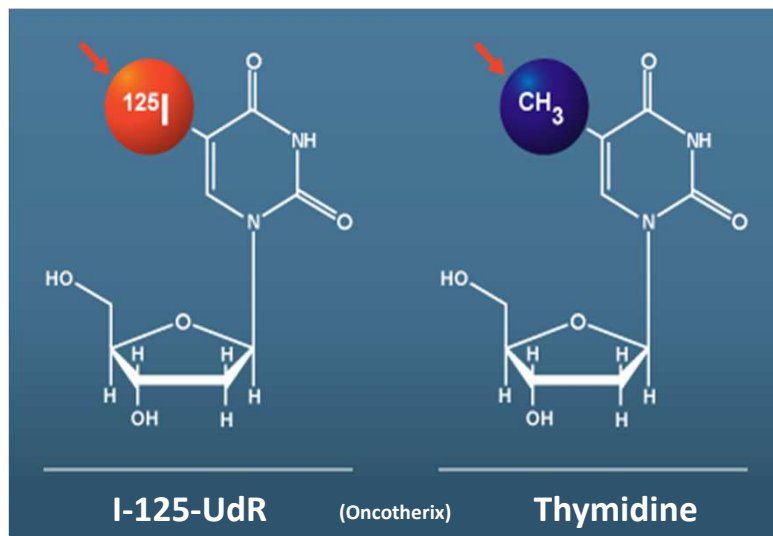
1

- **Auger Electron Emitters (AEE) induce cellular damage leading to high-LET type cell survival curves and possess enhanced relative biological effectiveness.**
- **DNA dsb induced by Iodine-125-deoxyuridine (I-125-UdR) decays are claimed to be very complex, thus efficiently leading to cell transformation, gene mutation and induction of chromosome aberrations.**
- **No general RBE can be defined for Auger electrons.**

## Aim of the study

- **To elucidate the assumed genotoxic potential of the DNA-associated Auger Electron Emitter I-125-UdR in human lymphocytes.**
- **Find out how many I-125 decays per cell are needed to induce one single chromosome aberration.**
- **To improve the dosimetry of internal emitters like I-125-UdR.**
- **Long term aim: To determine the RBE of I-125.**

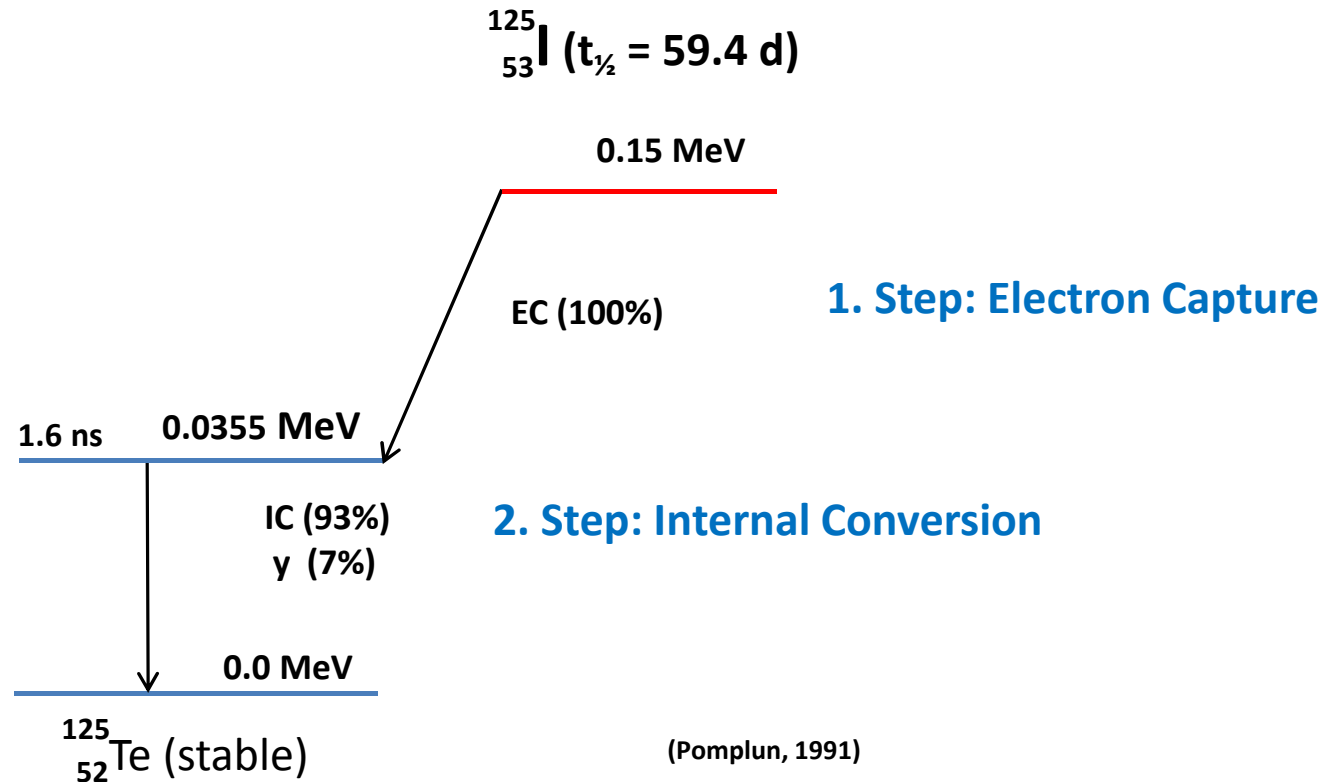
# The Trojan Horse



**It is assumed that the DNA destruction is fundamentally different than uniform low-LET radiation, as it cannot be easily repaired by the cell's DNA repair mechanisms.**

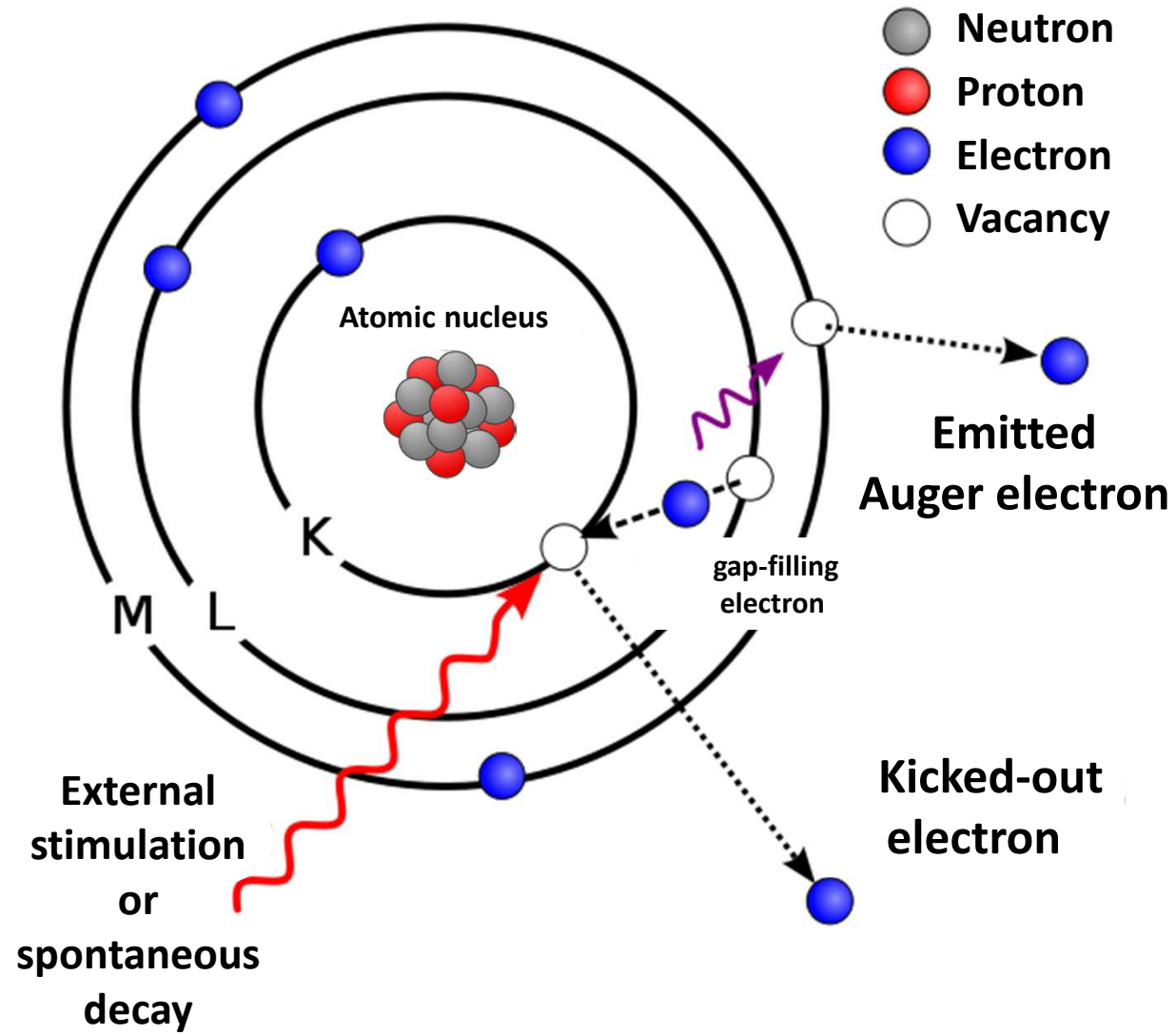
# Decay scheme of I-125

(Daten nach Lederer, 1978)



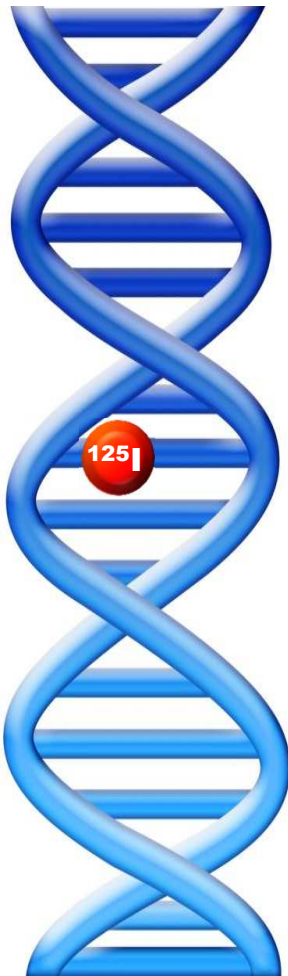
The decay of an I-125 atom leads to a deposition of approximately 2 keV in a 20-nm sphere from a cascade of about 13 Auger electrons. The energy range of Auger electrons can vary between 50 – 500 eV.

# The Auger-Process



# Biological consequences

## Incorporated <sup>125</sup>I-UdR



I-125

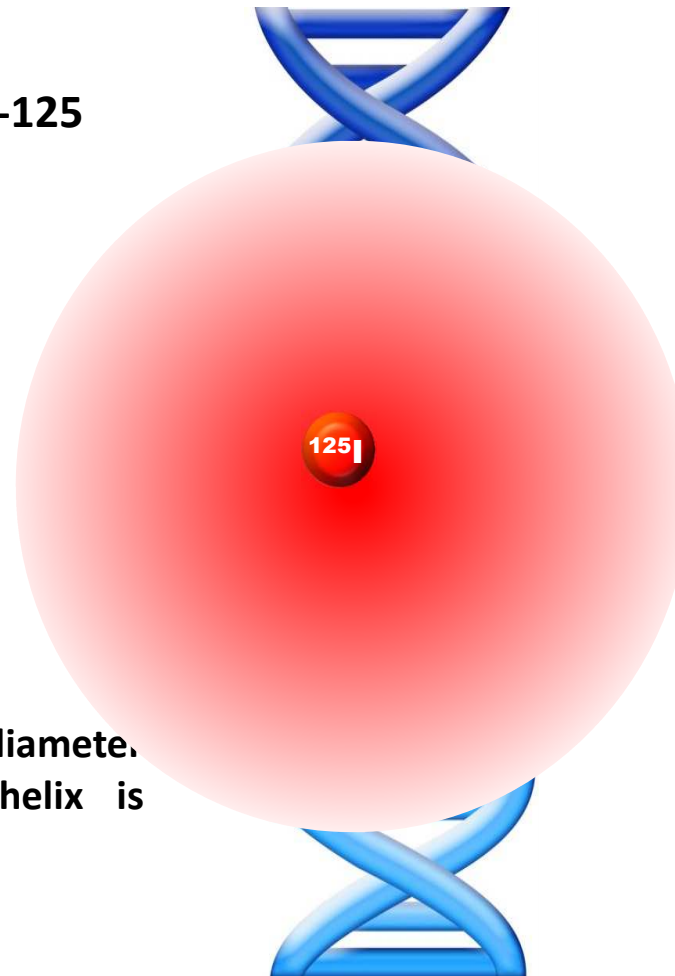


Te-125

The small range over which the AEE travel and induce biological effects is 10-100 nm.

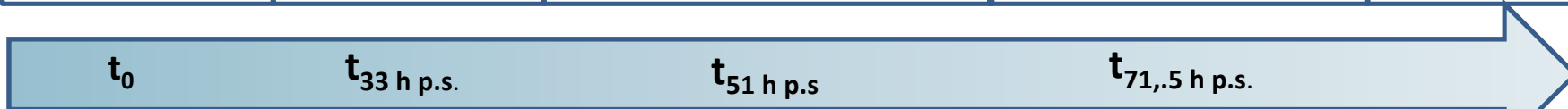
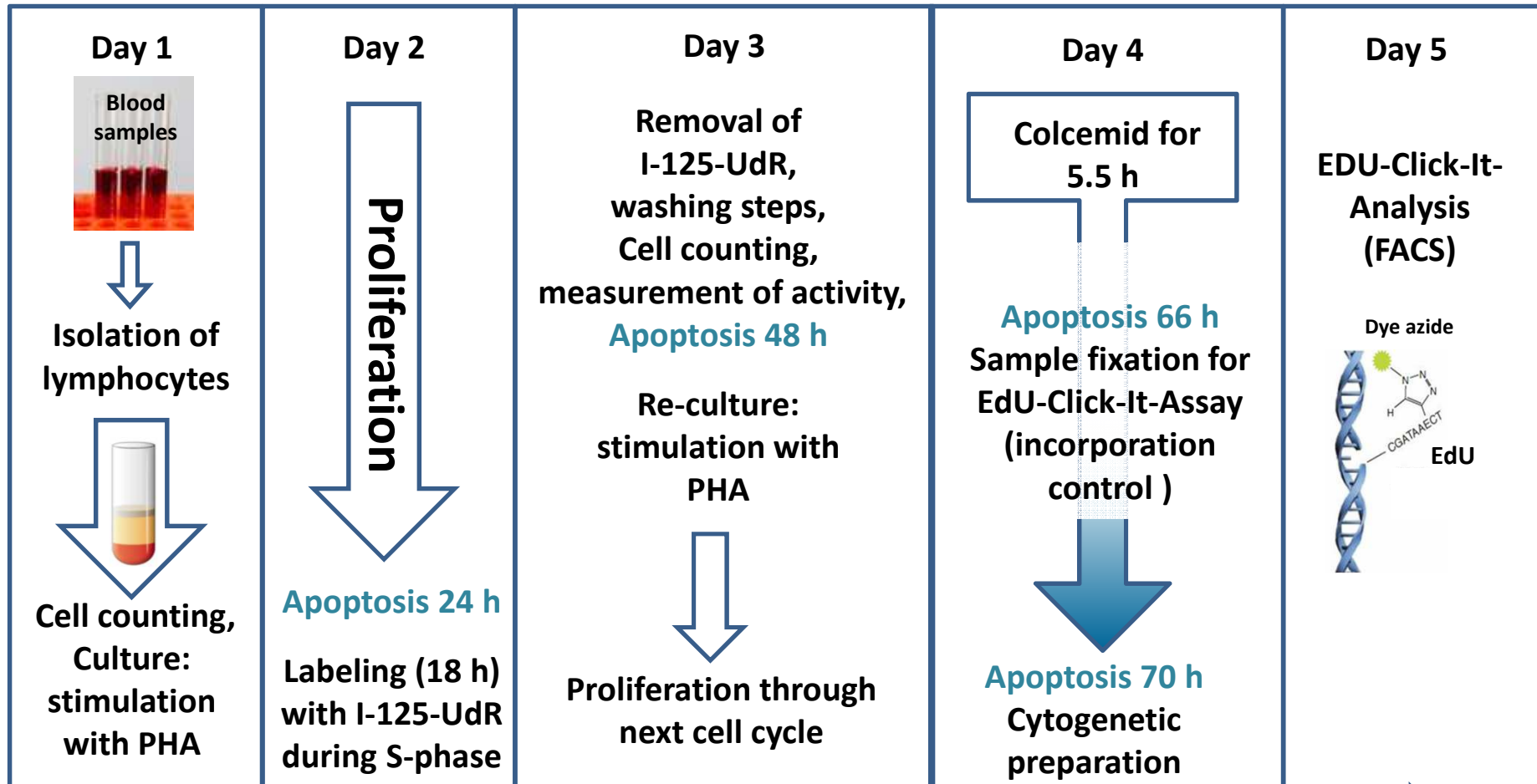
For perspective, the diameter of a DNA double helix is approximately 2 nm.

## DNA damage after decay



Each cascade produces the disruption of ~5 bp on both sides of the decaying atom.

# Experimental set-up



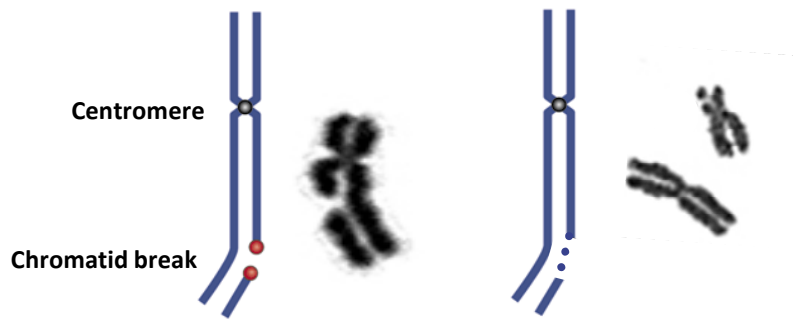
Timescale



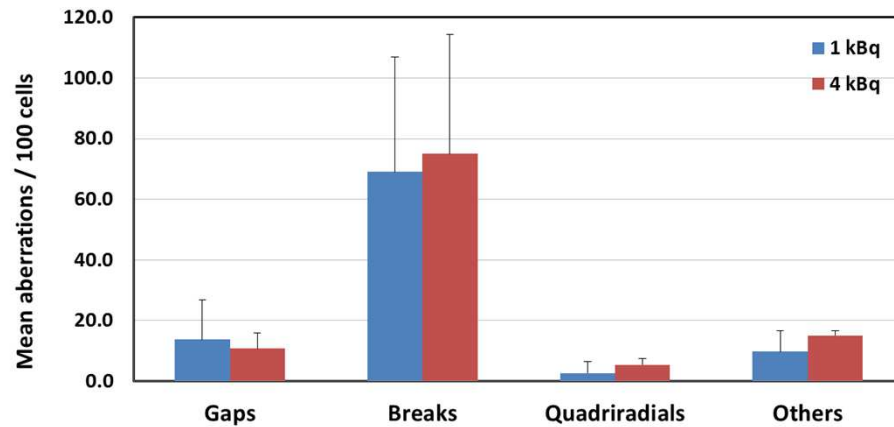
## Chromosome aberrations

### Simple aberrations

Chromatid break    Chromatid gap

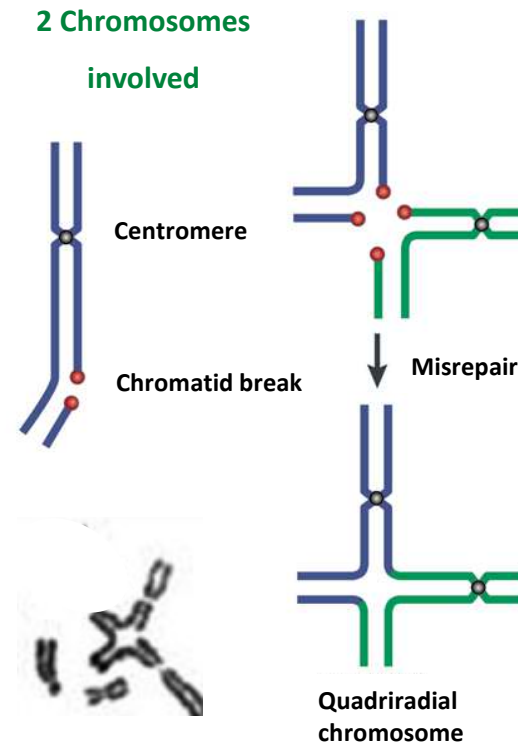


Frequency of Aberrations



### Complex aberration

Asymmetrical chromatid interchange



(Nature Reviews / Genetics)

# Results

## Chromosome aberrations

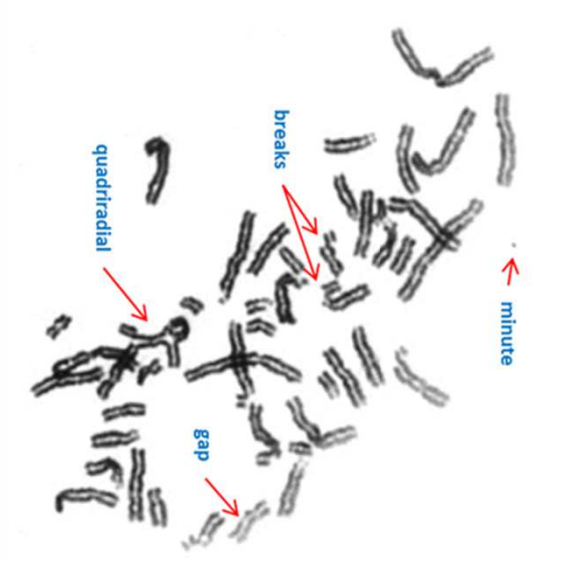
A



B



C



D



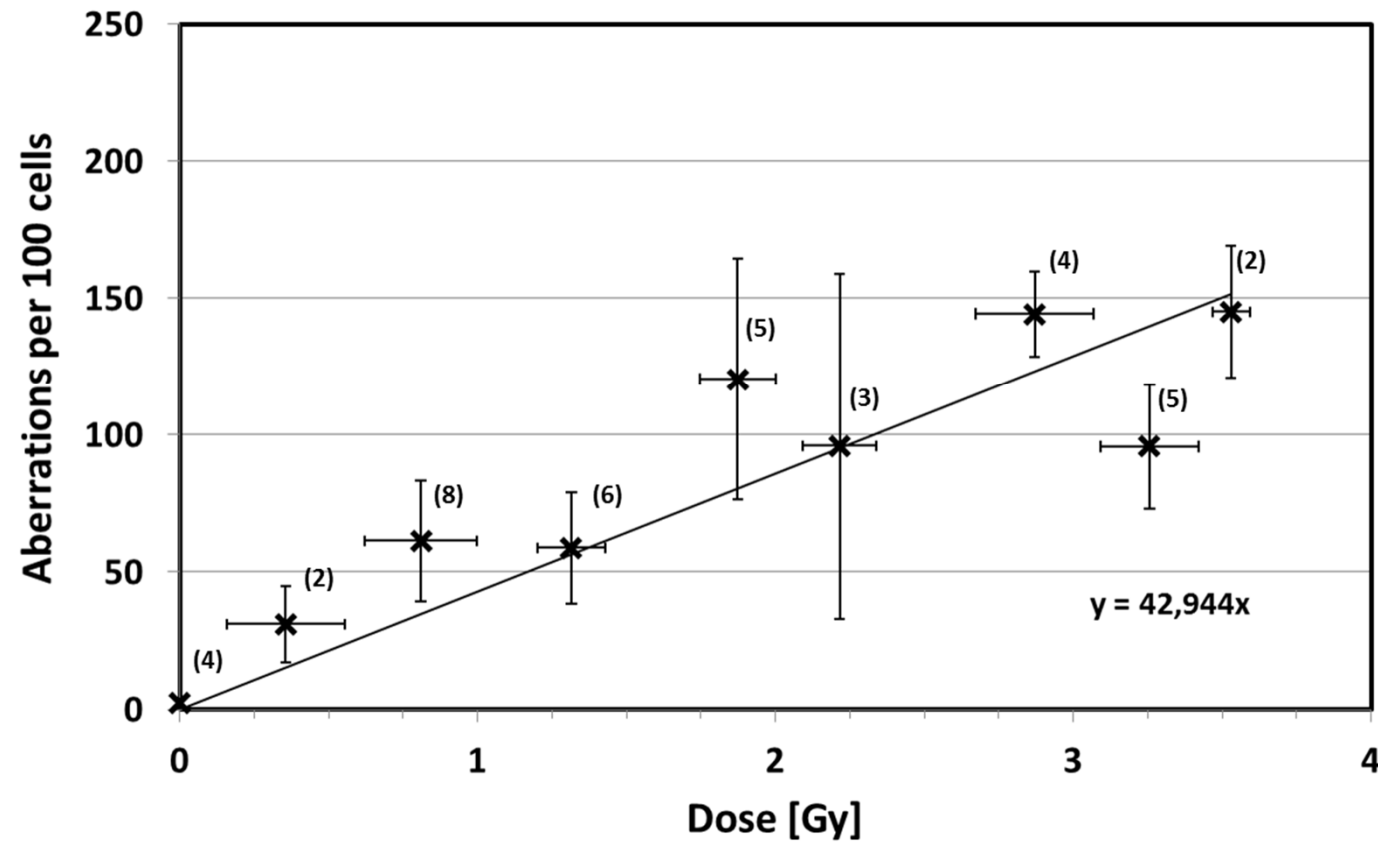
Multiple complex damages

# Results

## Dose-Response-Relationship

Linear ...

Dose Range 0.5 Gy

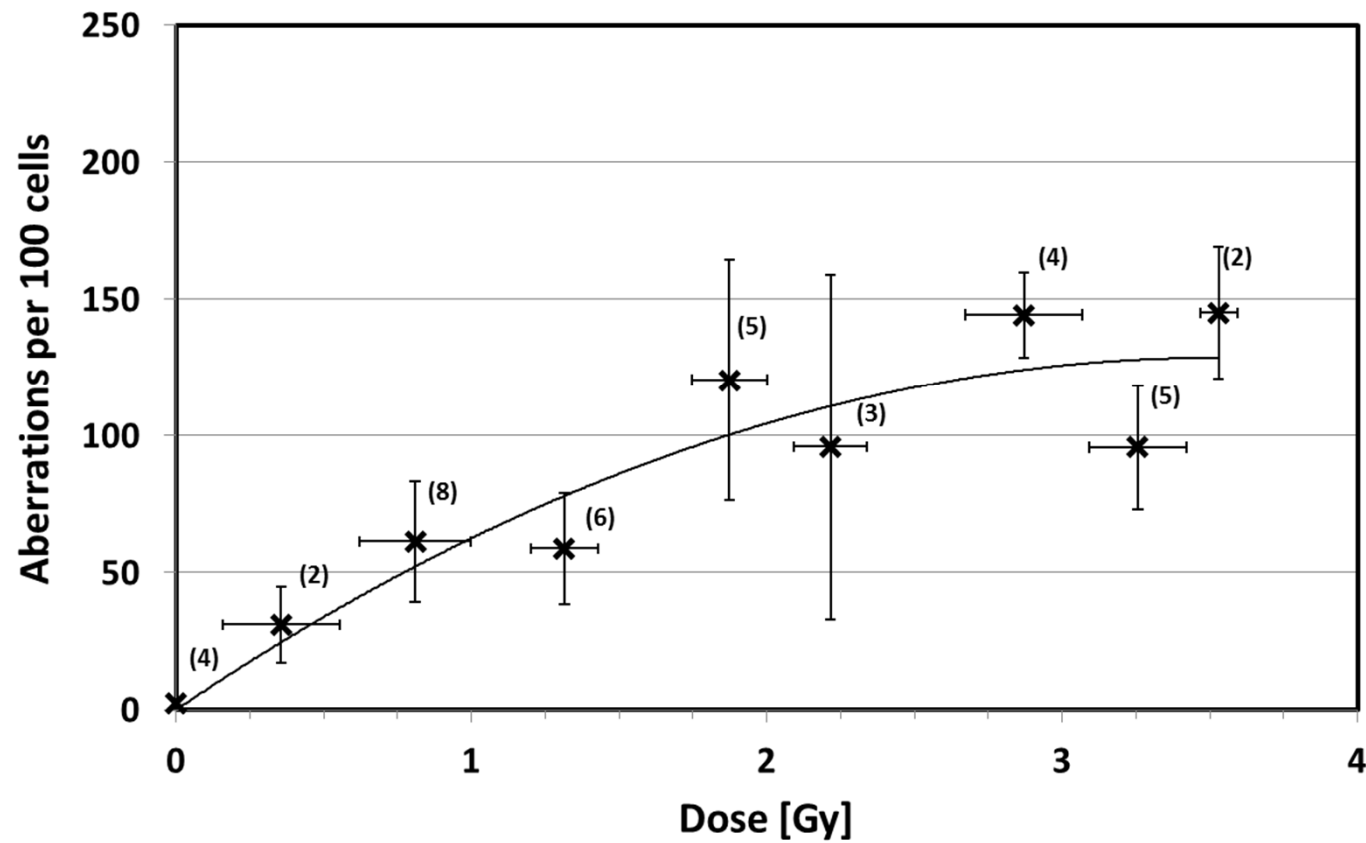


# Results

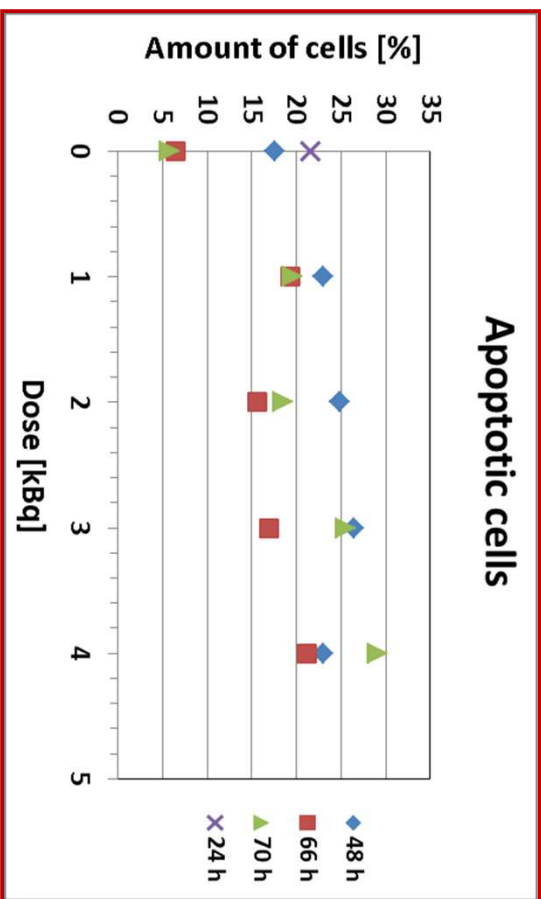
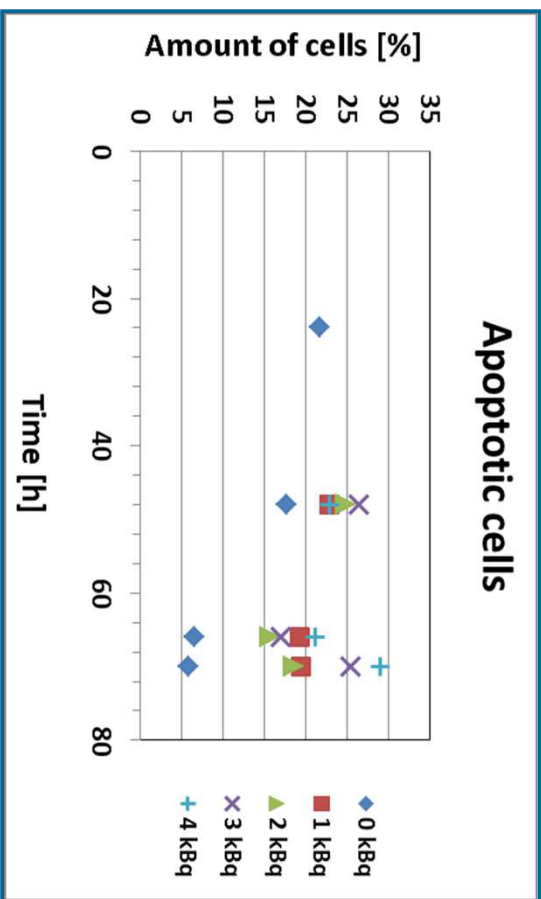
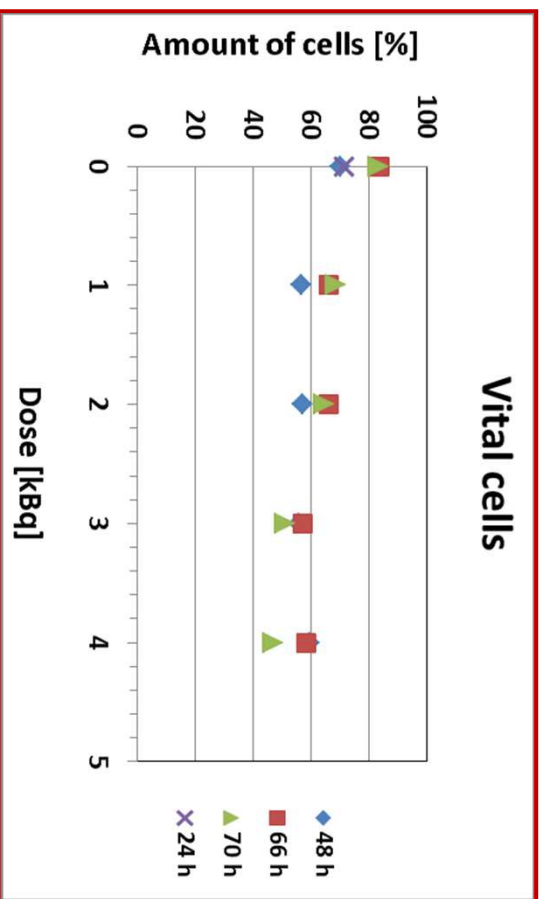
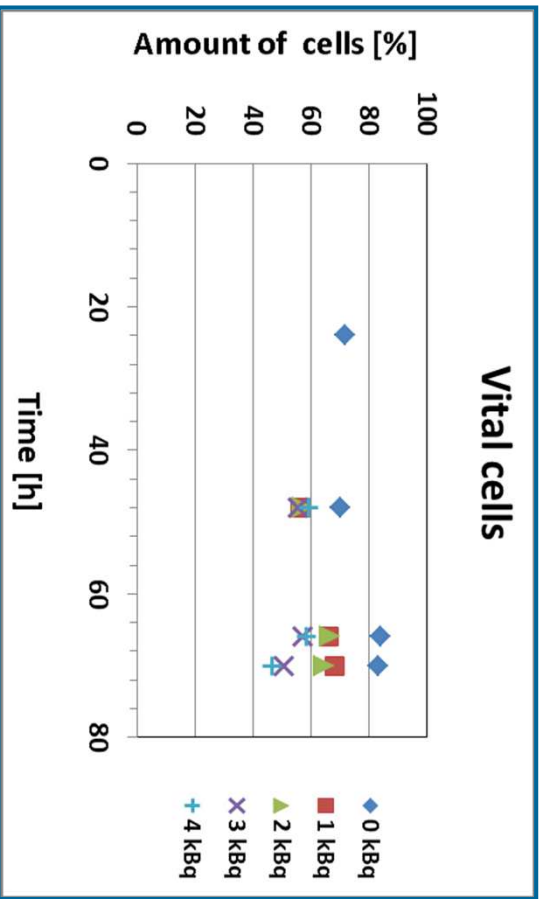
## Dose-Response-Relationship

... or polynomial?

Dose Range 0.5 Gy



# Results - Apoptosis



## Summary/Conclusions

- **I-125-UdR has a very strong genotoxic capacity in human lymphocytes even at very low doses.**
- **Efficiently labelled cells displaying a prolonged cell cycle compared to moderate labelled cells, and cell death contribute substantially to the desynchronisation of the cell cycle.**
- **One out of four intracellular I-125 decays give rise to a single chromosome aberration in human lymphocytes.**
- **Our data contradict former results (1 decay = 1 chromosome aberration) which overestimate the biological effectiveness of the AEE I-125.**

- **More data are needed, especially in the very low activity range, to decide which dose-response-relationship fits best for chromosome aberrations induced by the AEE I-125-UdR.**

Thank you for your attention...



## Acknowledgments

- Dominik Oskamp (Apoptosis assay)
- Marcel von Ameln (Chromosome aberrations)
- Ekkehard Pomplun (Dose calculations)