

The dicentric assay in triage mode as a reliable biodosimetric scoring strategy for population triage in large scale radiation accidents

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The aim of the project

After an unclear radiation exposure, the conventional chromosome analysis based on the dicentric assay is method of choice for dose reconstruction. But the method is time consuming and needs well trained scorers (One Scorer needs 1 week for a careful analysis of 1000 cells).

Strategies, to receive fast results in a large scale radiation accident :

- Network for mutual assistance, increasing capacity
- Faster scoring strategies, scoring in triage mode, quick scan, web based
- Improvement of the method, automation

Here: 8 laboratories are involved in an inter-comparison to set up a new network, first step is to validate the scoring in triage mode



Dicentric chromosome assay performed in triage mode

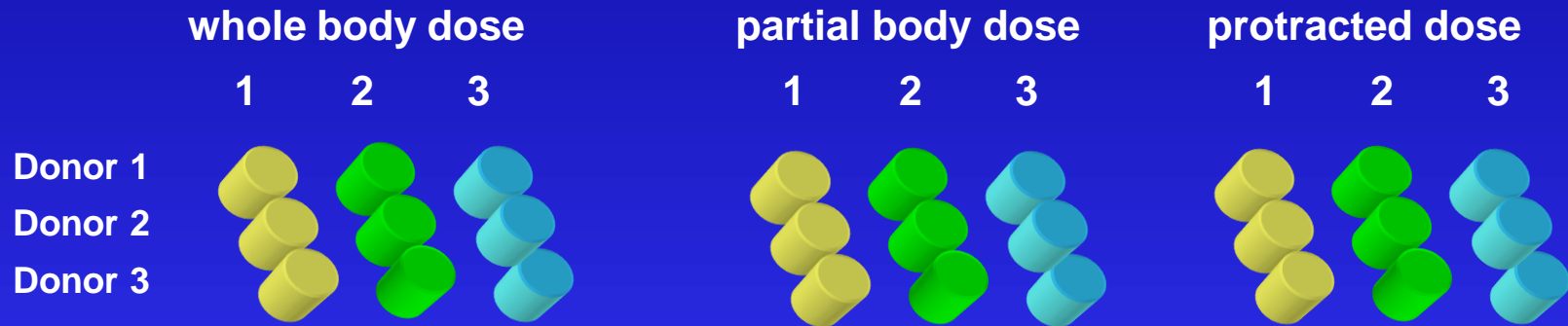


Mitosis in first cell division, Fluorescence plus Giemsa staining

Each Lab perform conventional scoring as usual

Use of standard culture conditions

Conventional scoring of 50 cells / slide, 2 slides / sample



Plus 6 shame controls

Status:

33 blood samples were distributed in total.

Scoring in triage mode (20, 30 & 50 cells) performed and doses estimated

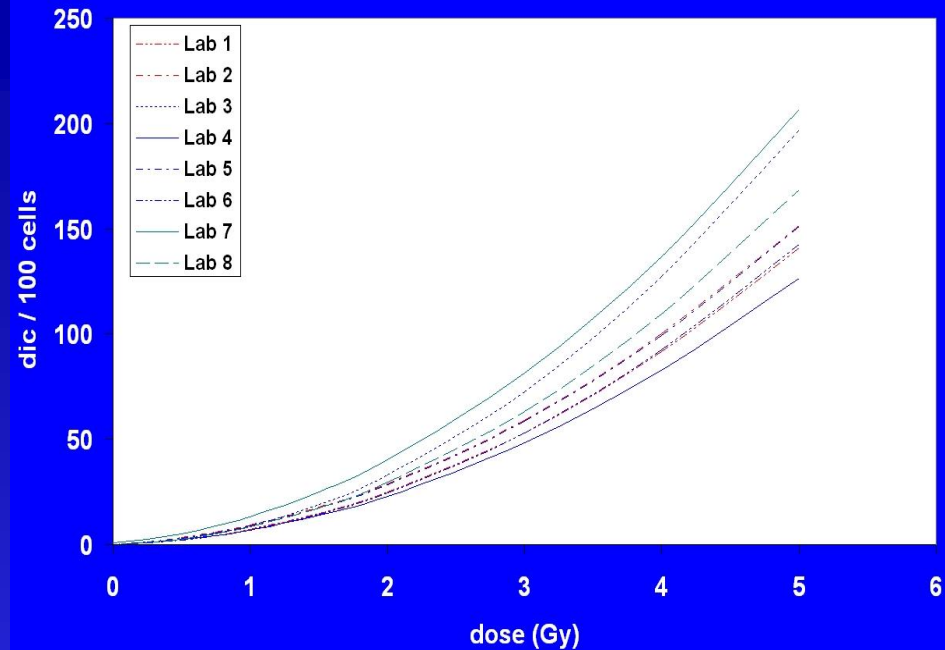
The γ -ray dose effect curves of participants used for dose estimations

$$Y = C + \alpha \cdot D + \beta \cdot D^2$$

Curves are not significant different

Mean $\alpha = 0.023$, $\beta = 0.059$

SE $\alpha = 28 \pm 4 \%$, $\beta = 7 \pm 2 \%$



Lab	C	SE	alpha	SE	beta	SE	radiation quality	dose rate (Gy / min)
Lab 1	0.0002	0.0001	0.0187	0.0047	0.0527	0.0039	Caesium 137	0.42
Lab 2	0.0007	0.0004	0.0375	0.0085	0.0531	0.0054	Cobalt 60	0.30
Lab 3	0.0005	0.0005	0.0142	0.0044	0.0759	0.0027	Cobalt 60	0.50
Lab 4	0.0011	0.0008	0.0228	0.0048	0.0460	0.0020	Cobalt 60	0.28
Lab 5	0.0010	0.0004	0.0338	0.0101	0.0536	0.0044	Cobalt 60	0.50
Lab 6	0.0006	0.0003	0.0135	0.0043	0.0544	0.0034	Cobalt 60	0.25
Lab 7	0.0072	0.0063	0.0538	0.0310	0.0716	0.0163	Caesium 137	0.40
Lab 8	0.0013	0.0005	0.0210	0.0052	0.0631	0.0040	Cobalt 60	1.07

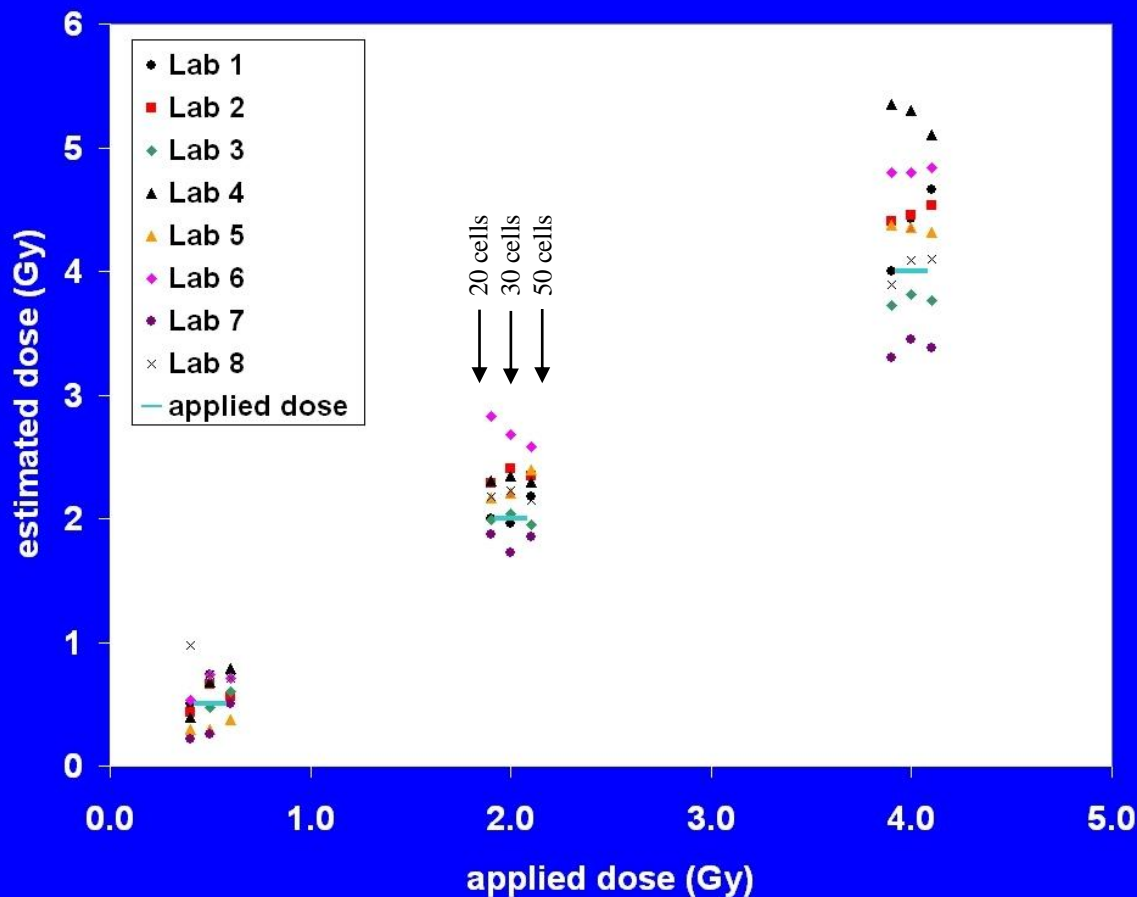
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Dose estimates based on 20, 30 and 50 cells

Acute whole body exposure (HDR) with 0.5, 2.0 and 4.0 Gy



Mean dose (Gy)

20 – 30 – 50 cells

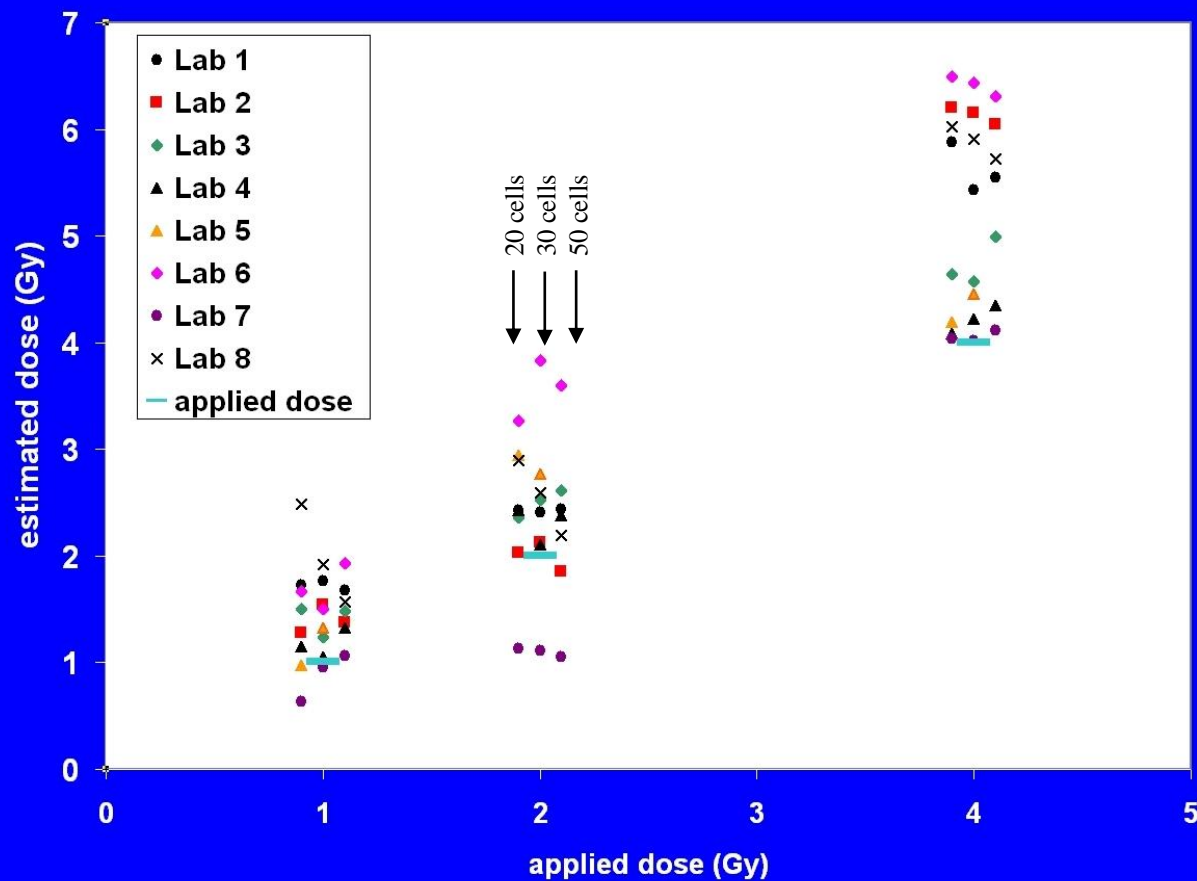
0.5 Gy: 0.51, 0.57, 0.60 Gy (p=0.74)

2.0 Gy: 2.21, 2.20, 2.22 Gy (p=0.64)

4.0 Gy: 4.26, 4.33, 4.34 Gy (p=0.53)

Dose estimates based on 20, 30 and 50 cells

Protracted exposure (LDR) with 1.0, 2.0 and 4.0 Gy



Mean dose (Gy)

20 – 30 – 50 cells

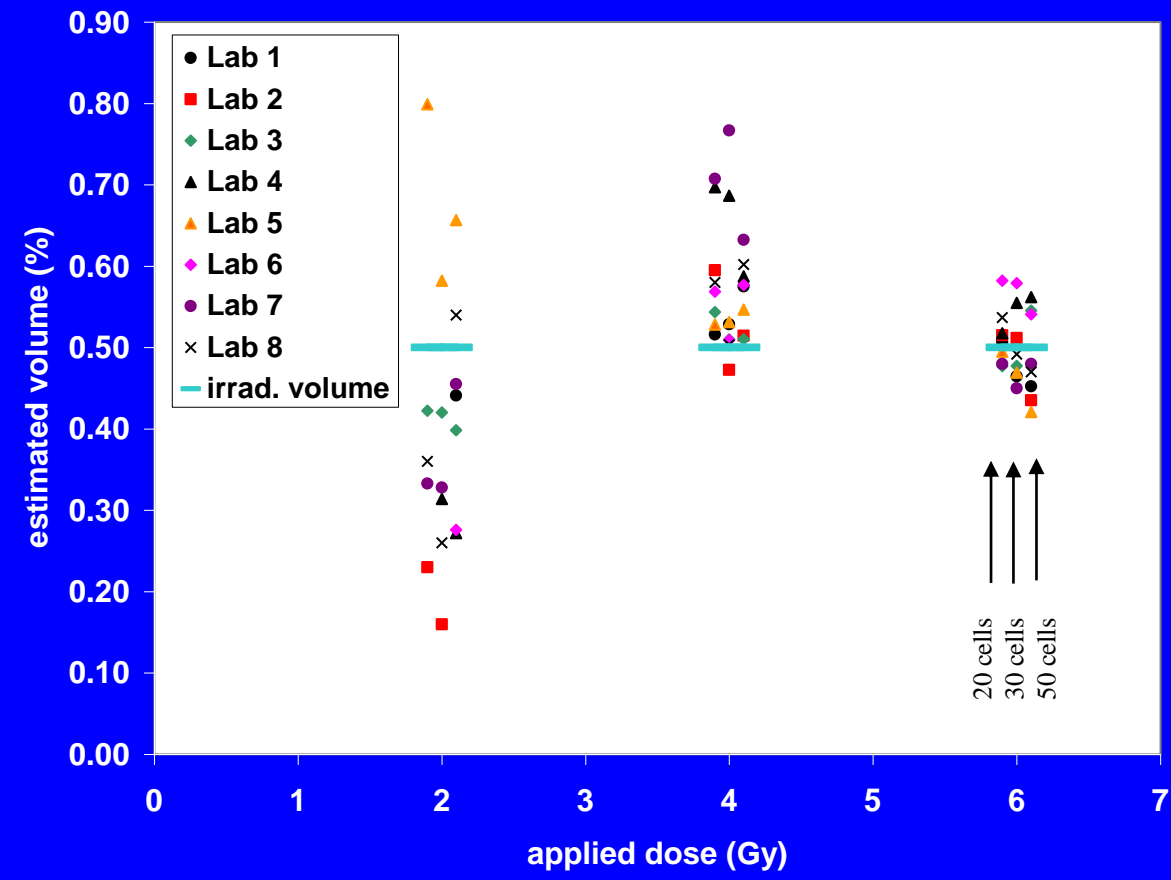
1.0 Gy: 1.37, 1.41, 1.45 Gy ($p=0.24$)

2.0 Gy: 2.43, 2.43, 2.28 Gy ($p=0.48$)

4.0 Gy: 5.19, 5.15, 5.26 Gy ($p=0.02$)

% irr. body volume estimates based on 20, 30 and 50 cells

Partial body exposure (PAR) with 1.0, 2.0 and 6.0 Gy



Estimated irr. body volume (%)

20 – 30 – 50 cells

2.0 Gy: 42.9, 34.4, 43.4 %

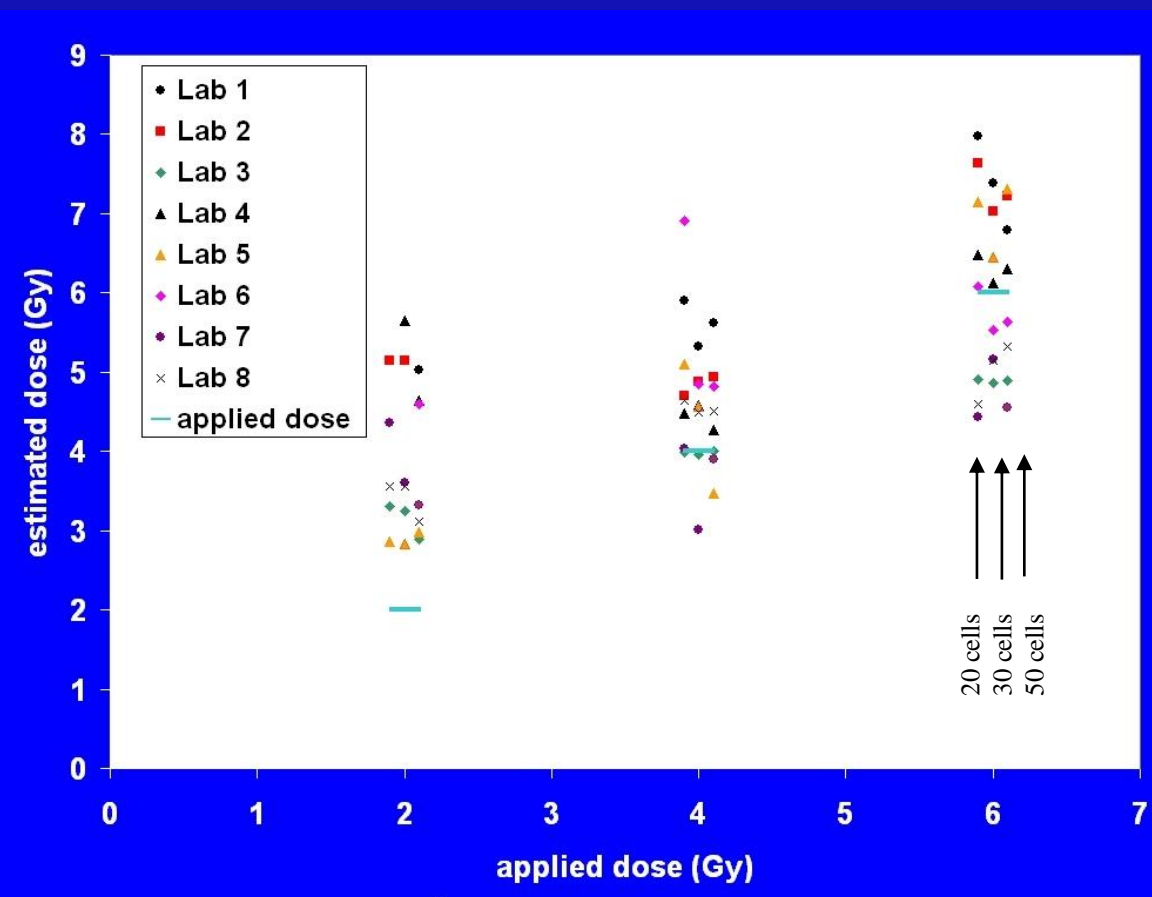
4.0 Gy: 59.2, 56.3, 56.8 %

6.0 Gy: 51.4, 50.0, 48.8 %



Dose estimates based on 20, 30 and 50 cells

Partial body exposure (PAR) with 1.0, 2.0 and 6.0 Gy



Mean dose (Gy)

20 – 30 – 50 cells

2.0 Gy: 1.67, 1.36, 2.33 Gy (p=0.02)

4.0 Gy: 3.71, 3.63, 4.18 Gy (p=0.54)

6.0 Gy: 5.16, 5.78, 5.88 Gy (p=0.84)

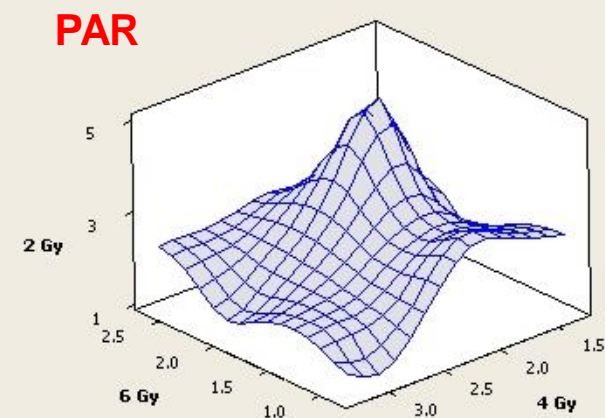
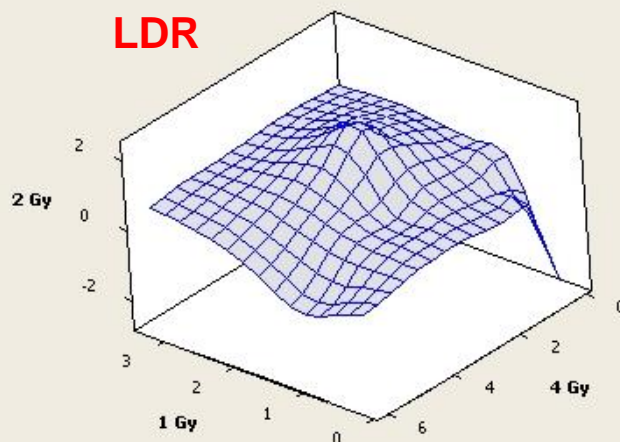
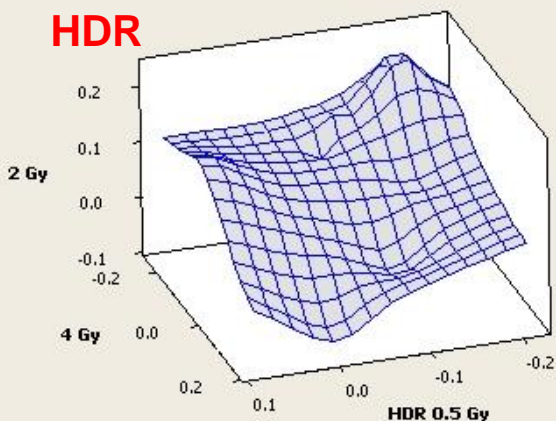
Youden plots showing the uncertainties caused by random and systematic errors

z - values on the straight surface but far from the origin indicate large systematic errors, z - values far from the origin and not on the surface indicate large random errors.

HDR: This figure nicely illustrates the spread of dose estimates across the labs, which increases with increasing dose, but decreases with increasing numbers of cells scored.

LDR is fairly flat, but the higher z-values are related to the systematic trend of dose over-estimation with increasing protracted dose.

PAR: The increased z-values indicate systematic errors and the bumps indicate random errors, highlighting the need to score more cells when assessing partial body exposures.

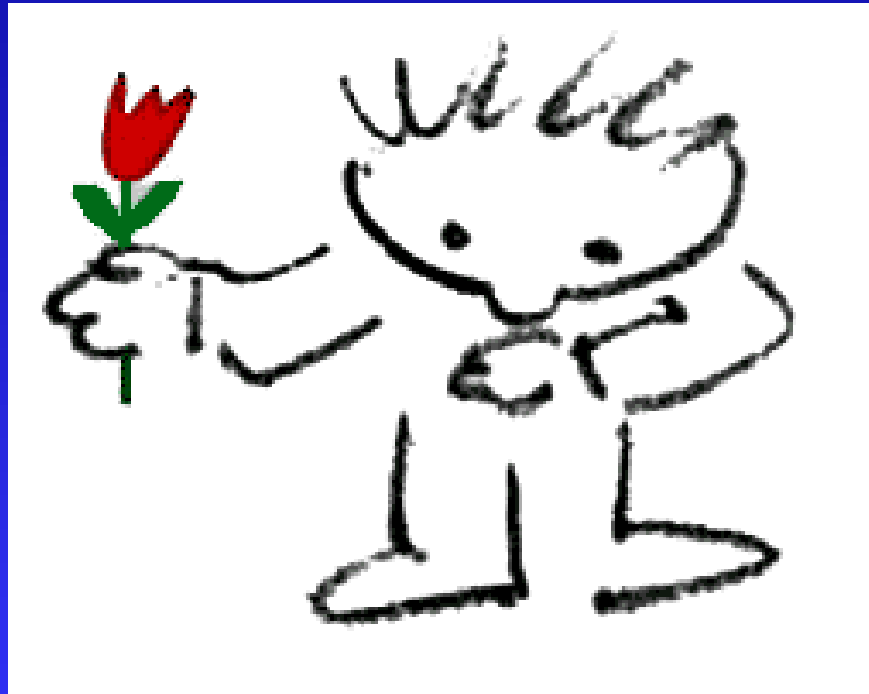


Summary

- All labs were well trained during this exercise, using the tools for the different scenarios
- 20 cells can give a rough indication of dose, 50 cells are more accurate, but not different
- The results after acute exposure were good
- There was an unexpected trend to dose overestimations after protracted exposure, may be explained by uncertainties in the alpha term
- Limitations of scoring in triage mode after partial body exposure were observed, therefore we recommend to increase the cell number in cases, where there are signs of potential inhomogeneous exposure in order to obtain more reliable data
- With respect to the homogeneity of the conventional scoring results, each lab was able to manage the challenges in biological dosimetry
- In the frame of the MULTIBIODOSE project, further investigations with these samples will be performed to improve the automated scoring procedure and to validate new scoring strategies



Thank you for your attention



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