Uncertainties associated with biological and physical dosimetry-based dose estimation

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Introduction

- What are uncertainties and why are they important?
- What are 'biological dosimetry' and 'physical dosimetry'
- Current framework of uncertainty estimation
- Further research and development
- Relevance for MELODI + recommendations

What are uncertainties?

- Surely that is a silly question?

    No! – many practising scientists still see uncertainties as secondary, an ‘afterthought’

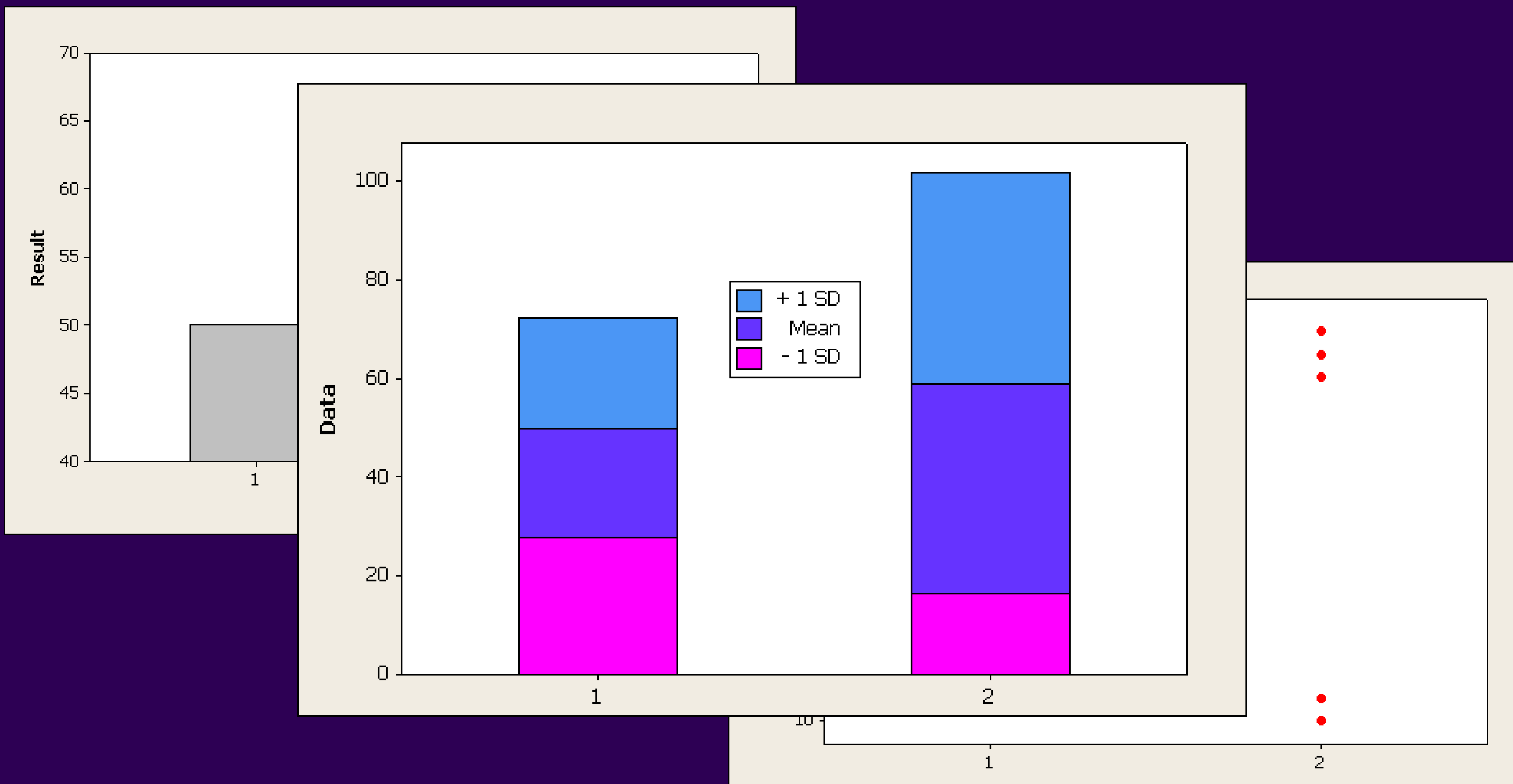
Answer:

Every experimental variable has an uncertainty associated with it

NB: This includes those that can’t be controlled!

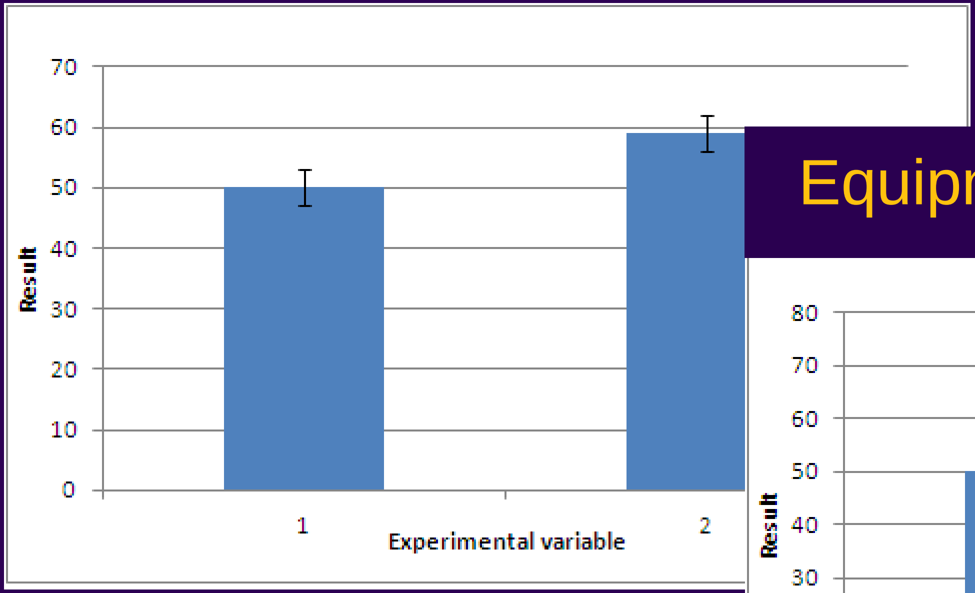
Example 1:
Measuring an effect

One experimental variable:

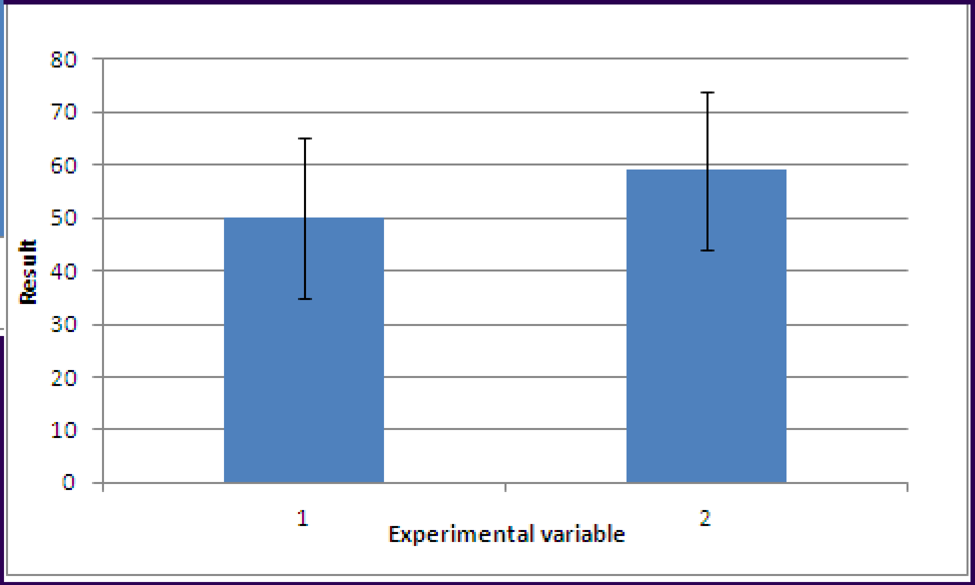


Example 2:
Equipment variability

Measurement standard deviation:



Equipment standard deviation:



Uncertainty is important because…

- **Rigorous experimental method:** In order to be able to characterise uncertainties it is necessary to understand your experiment fully, which leads to optimisation
- **Falsifiability:** If an hypothesis can't be proved false, then it is likely to be true…
- **Finally:** If we weren't uncertain about anything, we would all be out of a job!

Biological dosimetry

Definition:

Biological dosimetry relies on the proportional relationship between the frequency of radiation induced damage and radiation dose

Key techniques:

- Dicentric assay (Dics)
- Cytokinesis-blocked micronucleus assay (MN)
- Protein biomarkers (e.g. gamma-H2AX)
- Gene expression
- Metabolomic markers...

Physical dosimetry

Key techniques:

- Electron paramagnetic resonance spectroscopy (EPR) which detects stable radicals induced by the ionisation process in biological or inert materials (e.g. teeth, glass)
- Thermally or optically stimulated luminescence (TL/OSL) which detects luminescence emitted by crystalline materials (e.g. ceramics, quartz, glass) following exposure to ionising radiation

Current status of uncertainty analysis

- ISO/IEC 98-3 - Guide to the Expression of Uncertainty in Measurement (1998)
- ISO 5725-5 - Accuracy (Trueness and Precision) of Measurement Methods and Results (1998)
- ISO 13528 - Statistical Methods for Use in Proficiency Testing by Interlaboratory Comparisons (2005)
- IAEA EPR-Biodosimetry manual 2011 - Cytogenetic Dosimetry: Applications in Preparedness for and Response to Radiation Emergencies

MULTIBIODOSE (1): Multi-disciplinary biodosimetric tools to manage high scale radiological casualties

Participant no. *	Participant organisation name	Country
1 (Coordinator)	Stockholm University (SU)	Sweden
2	Bundesamt für Strahlenschutz (BfS)	Germany
3	Universiteit Gent (UGent)	Belgium
4	Health Protection Agency (HPA)	UK
5	Institut de Radioprotection et de Sûreté Nucléaire (IRSN)	France
6	Istituto Superiore di Sanità (ISS)	Italy
7	Norwegian Radiation Protection Authority (NRPA)	Norway
8	Radiation and Nuclear Safety Authority (STUK)	Finland
9	Universitat Autonoma de Barcelona (UAB)	Spain
10	Institute of Nuclear Chemistry and Technology (INCT)	Poland
11	Helmholtz Zentrum München (HMGU)	Germany
12	Bundeswehr Institut für Radiobiologie in Verbindung mit der Universität Ulm (BIR)	Germany
13	Gray Institute for Radiation Oncology and Biology, University of Oxford (UOXF)	UK
14	EURADOS	Germany

MULTIBIODOSE (2)

Assays: Dics, MN, gamma-H2AX, TL/OSL, SPA, SSA

+ WP6 – statistics

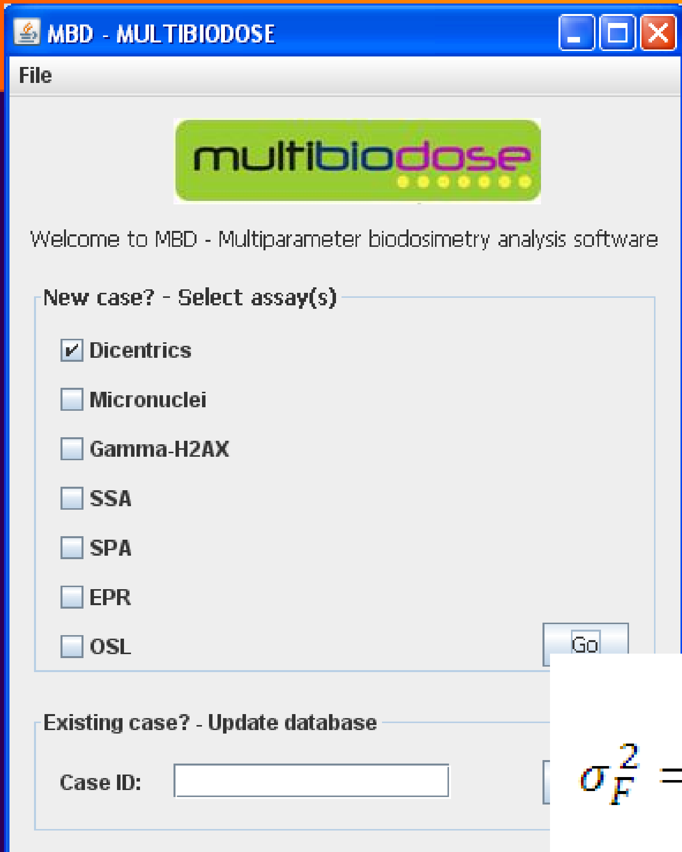
+ WP7 – dissemination

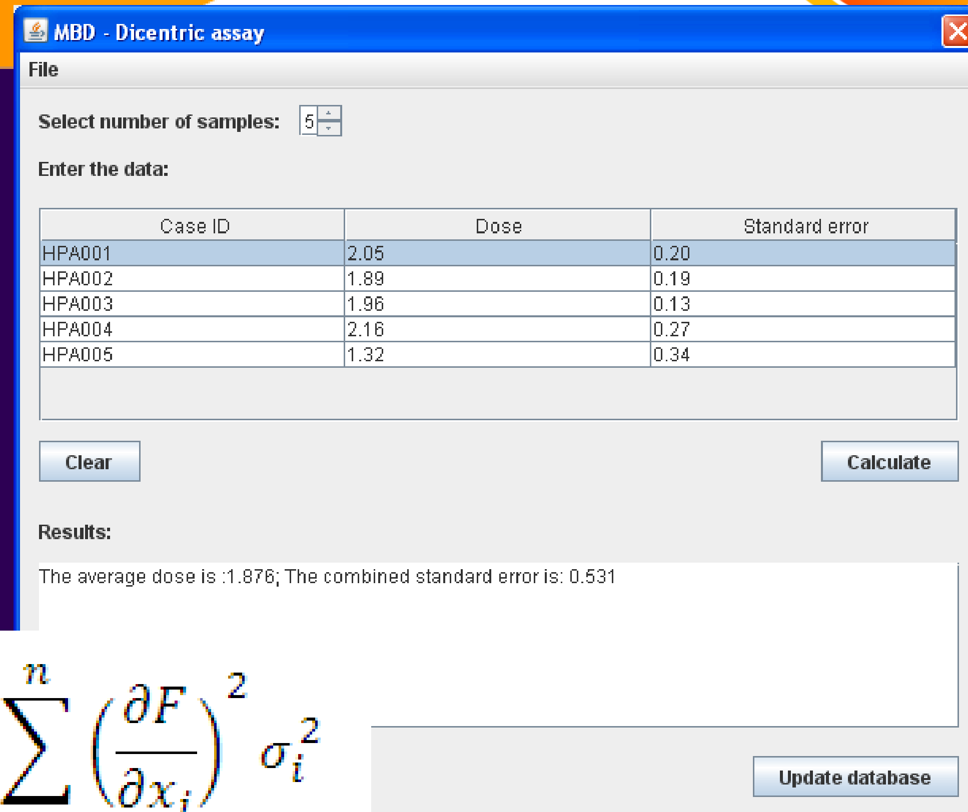
+ WP8 - management

WP6: "To produce a freeware software package for integrated statistical analysis of data from each of the assays described in WP 1 to 5."

Main tasks: Robust statistical analyses for individual assays; inter-lab comparisons; inter-assay comparisons; implement statistical methodology into a sharable 'decision making' software

MULTIBIODOSE (3)





$$\sigma_F^2 = \sum_{i=1}^{n} \left(\frac{\partial F}{\partial x_i}\right)^2 \sigma_i^2$$

$$\sigma_D{}^2 = \left(\frac{\partial D}{\partial \alpha}\right)^2 \sigma_\alpha{}^2 + \left(\frac{\partial D}{\partial \beta}\right)^2 \sigma_\beta{}^2 + \left(\frac{\partial D}{\partial y}\right)^2 \sigma_y{}^2 + \left(\frac{\partial D}{\partial t}\right)^2 \sigma_t{}^2 + \left(\frac{\partial D}{\partial t0}\right)^2 \sigma_{t0}{}^2$$

RENEB (1): Realizing the European Network in Biodosimetry

Partici-pant no.	Participant organisation name		Country
1. (Coord.)	BfS	Bundesamt für Strahlenschutz	Germany
2.	BIR/UULM	Bundeswehr Institut für Radiobiologie in Verbindung mit der Universität Ulm	Germany
3.	CEA	Commissariat à l´Énergie Atomique	France
4	ENEA	Agenzia Nazionale per le Nuove Tecnologie, L´Energia e lo Sviluppo Economico Sostenibile	Italy
5.	HGUGM	Hospital General Universitario Gregorio Marañón	Spain
6	HMGU	Helmholtz Centre Munich	Germany
7.	HPA	Health Protection Agency	UK
8.	ICHTJ	Institut Chemii i Techniki Jadrowej	Poland
9.	INSP	Institut National de Sanatate Publica	Romania
10.	IRSN	Institut de Radioprotection et de Sûreté Nucléaire	France
11.	ISS	Instituto Superiore di Sanità	Italy
12.	ITN	Instituto Tecnológico e Nuclear	Portugal
13.	LAFE	Fundacion para la Investigation del Hospital Universitario la fe de la Comunidad Valenciana	Spain
14.	LUMC	Leiden University Medical Center	The Netherlands
15.	NCRRP	National Center for Radiobiology and Radiation Protection	Bulgaria
16.	NCSR D	National Centre for Scientific Research "Demokritos"	Greece
17.	NRIRR	National Research Institute for Radiobiology & Radiohygiene	Hungary
18.	NRPA	Norwegian Radiation Protection Authority	Norway
19.	STUK	Radiation and Nuclear Safety Authority	Finland
20.	SU	Stockholm University	Sweden
21.	UAB	Universitat Autonoma de Barcelona	Spain
22.	UGent	Universiteit Gent	Belgium
23.	UNITUS	University of Tuscia	Italy

RENEB (2)

- **WP 1: "Operational Basis of the Network"**

  Includes comparison, standardisation, harmonization of techniques

- **WP2: "Basis to Develop the Network"**

  Includes developing techniques to identify, verify and integrate new technologies and members into the existing network

- **WP3: "Education, training and quality"**

  A Quality Assurance & Quality Management (QA&QM) programme

EURADOS WG10 TG6

"To survey, compare and assess techniques of uncertainty analysis for physical and biological retrospective dosimetry"

*** Full TG member list available at: http://www.eurados.org/en/Working_groups ***

To date:

- Survey of uncertainty estimation techniques carried out February 2012
- Paper reviewing techniques is currently being prepared
- Manual/guidelines for best practice planned 2013
- Summer school and/or e-learning module being planned 2013/2014

Royal Society International Joint Project (1): Statistical methods for chromosomal biodosimetry

Objective: To develop practical improvements to statistical methods for cytogenetic radiation dosimetry and to implement the methods into a software tool to enable use within the community

Aims:

1. Literature review to identify limitations in the current statistical methodology
2. Categorize and test improved statistical methods
3. Produce a practical software tool to facilitate use of the most appropriate methods

Royal Society International Joint Project (2)

Outcomes:

- Literature review detailing statistical limitations
- Identification of ‘difficult scenarios’
- Review of Bayesian methods in the literature
- Testing of methods against ‘difficult’ cytogenetic data
- Development of novel methods
- Implementation of methods into user-friendly software tool

Hypothesis, shown to be true: Bayesian statistical techniques are more applicable to cytogenetic data

Why are uncertainties important for MELODI?

Conclusion: The <u>best science</u> **always** incorporates a *sophisticated* consideration of uncertainties

MELODI

- "Low dose"
- Higher uncertainties
- Statistically harder to demonstrate significant results

In English: "The bar is raised"

‘Take home’ messages

Health Protection Agency

Sophisticated, high level, statistical analysis should:

- Be an intrinsic part of the strategic research agenda
- Be a focus of all future work under MELODI
- Be a focus of all training and education under MELODI

This will:

- Facilitate true, multidisciplinary work
- Inform research directions and priorities
- Aid policy making for radiation protection

Acknowledgements

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- **Paola Fattibene,** Istituto Superiore di Sanità, ITALY and on behalf of the collaborators of EURADOS WG10; TG6
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- **Ulrike Kulka**, Bundesamt für Strahlenschutz, GERMANY and on behalf of the RENEB project participants

Thank you for listening!

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