Performance of the Dicentric Chromosome Assay (DCA) in a recent NATO exercise of established and emerging biodosimetry methods

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Background of NATO Exercise

Organisation:

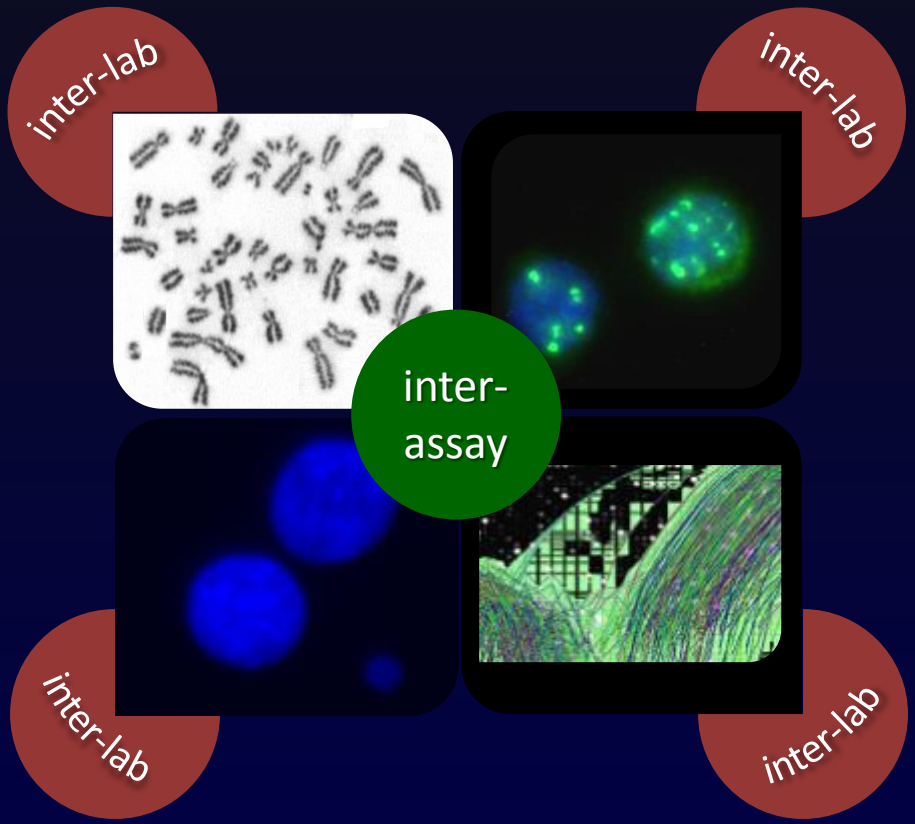
NATO RTO Research Task Group RTG-033,
"Radiation Bioeffects and Countermeasures",
in the frame of the NATO RTO
Human Factors and Medicine (HFM) panel.

NATO RTO: Research and Technology Organisation (http://www.rto.nato.int/)

Mission of HFM: „To provide the science and technology base for optimising health, human protection, well being and performance of the human in operational environments with consideration of affordability."

Aim of the Exercise

Established vs. new emerging
radiation biodosimetry methods



This presentation: Inter-laboratory Comparison of the Dicentric Chromosome Assay (DCA)

I. DCA / study design

II. Endpoints / Results

1. Time required for providing quick triage dose estimates
2. Dose estimates
3. Statistical parameters describing the assay`s precision

III. Conclusion

Other parts of NATO exercise presented as poster at IRPA 13:

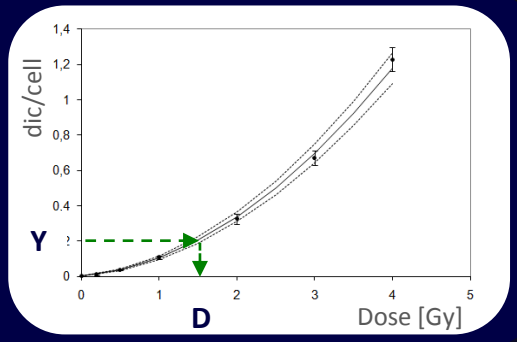
1. Automated micronucleus analysis vs. automated DCA P02.145
2. Inter-assay comparison (DCA, micronuclei, γH2AX, gene expression) P02.129

DCA – State of the Art

- Most validated

dicentric frequency

Conversion into radiation dose (calibration curve)



- Largely harmonized + standardized
  - technical manual (*IAEA 2011)
  - ISO standardization (ISO 19238:2004; ISO 21243:2008)
  - method harmonization (Multibiodose 2010: IRPA: TS9b.5, TS2c.3)
- High capacity
  - triage mode (50 cells scored, Routine mode 500-1000 cells)
  - highly automatable
  - laboratory networking (**RENEB 2012: IRPA: P02.141)

* „Cytogenetic Dosimetry: Applications in Preparedness for and Response to Radiation Emergencies“
** Realizing the European Network in Biodosimetry

DCA – Inter-laboratory Comparison

(1) Establishment of calibration curve (optional)

7 known doses + control (0 Gy)

(2) Triage dose estimation (2 month later)

10 coded blood samples

6 labs

via e-mail to InstRadBioBw:

1. **quick results**
   dose estimates of coded samples (triage mode)
2. **complete results**
   a. interim results
   b. calibration curve
   c. methodical details
3. **questionnaire**
   information about laboratory

Organization of venipuncture/irradiation/shipping: InstRadBioBw, Germany
Shipping of blood samples: temperature-controlled and film dosemeter included

Questionnaire and Time for Triage Dose Estimation

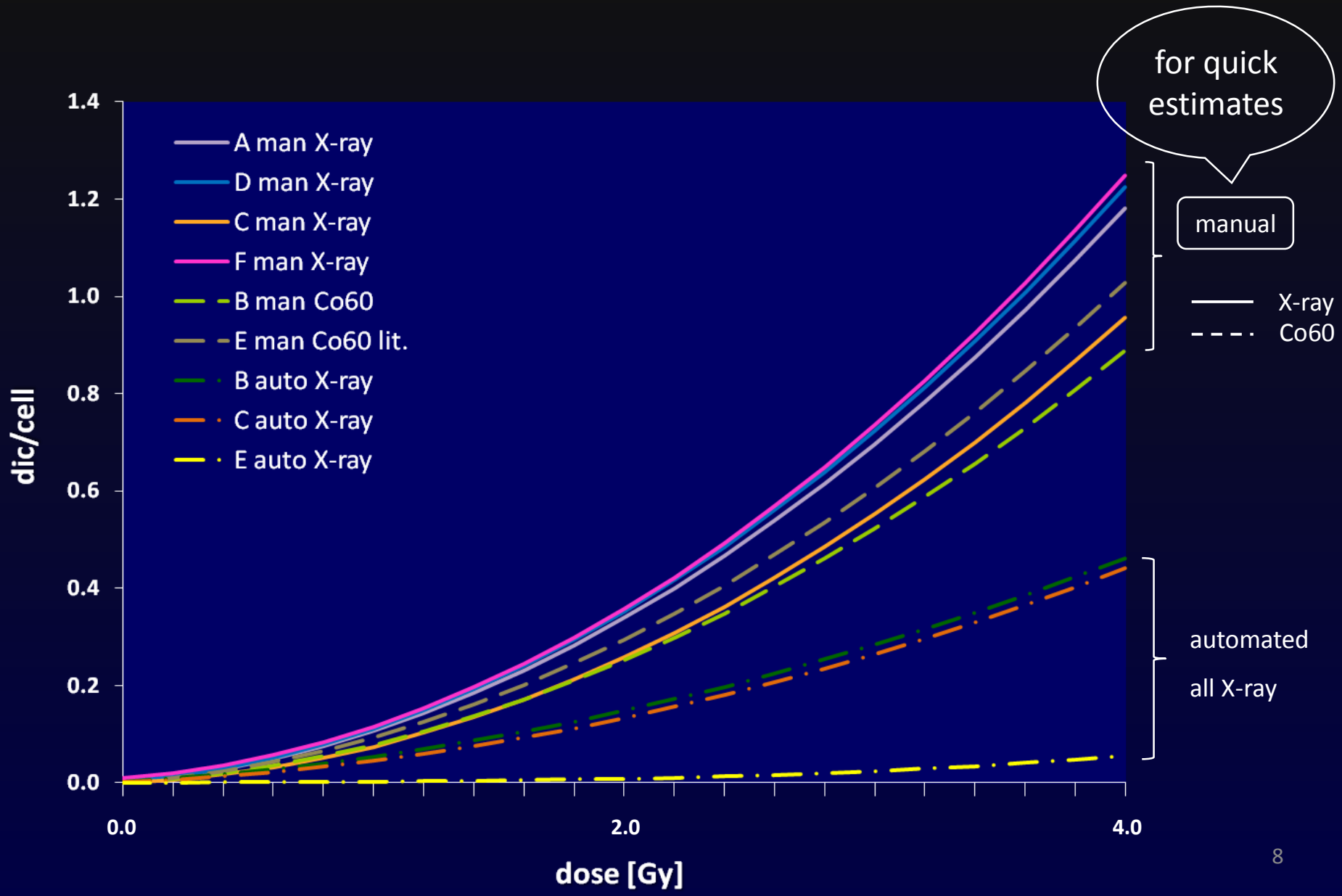
institution	calibration curve	* scoring procedure	# previous exercises	DCA established for biodosimetry purposes since… (month)	lab specialized in biodosimetry	NATO samples processed with priority?	personnel involved in scoring	quick results: time required to report dose estimates (d)
D	250 kVp X-ray	manual	6	480	yes	yes	3	2.4
E	Co-60, literature	manual	0	30	yes	yes	4	2.6
C	240 kVp X-ray	manual	0	36	yes	yes	1	4
B	Co-60	manual	5	360	yes	yes	4	4
A	240 kVp X-ray	manual	2	60	yes	yes	1	5.3
F	200 kVp X-ray	manual	9	96	yes	yes	2	6.1

* scoring of 50 cells or 30 dic

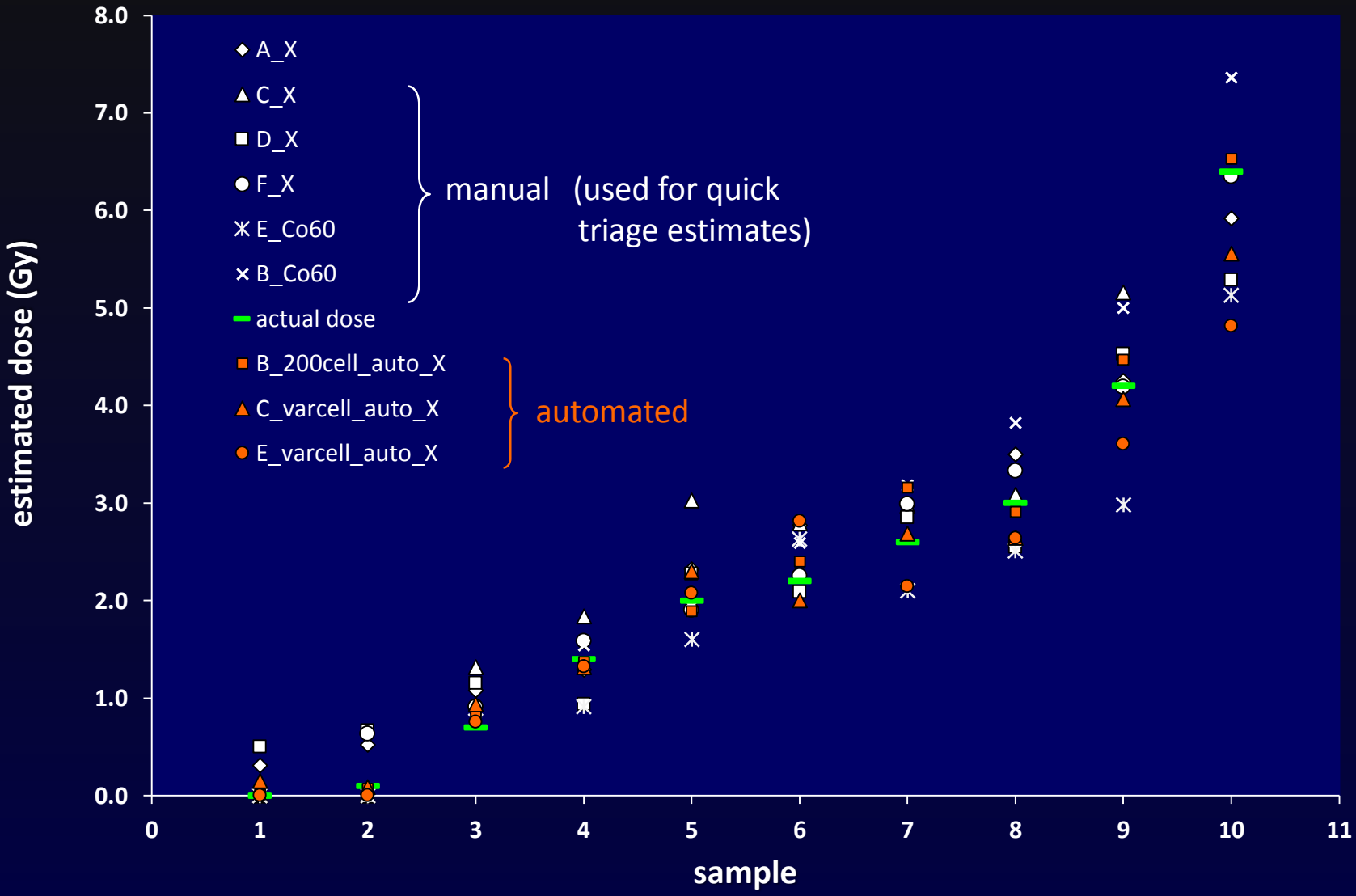
wide range:

- calibration curves based on different radiation qualities
- degree of experience/expertise
- no. personnel involved in scoring

Calibration Curves



Dose Estimates (1)



Dose Estimates (2)

institution_cell no_ scoring_cal curve:		true (actual) dose [Gy] 0	0.1	0.7	1.4	2	2.2	2.6	3	4.2	6.4	MAD	lower than true dose	higher than true dose	Time
F_50cell_man_X	estimated dose [Gy]	0.0	0.6	0.9	1.6	1.9	2.3	3.0	3.3	4.2	6.4	0.19	4	6	
A_50cell_man_X		0.3	0.5	1.1	1.3	2.3	2.8	3.0	3.5	4.3	5.9	0.35	2	8	
B_50cell_man_Co		0.0	0.0	0.9	1.5	1.9	2.6	3.2	3.8	5.0	7.4	0.40	3	7	
C_50cell_man_X		0.0	0.0	1.3	1.8	3.0	2.8	3.0	3.1	5.2	nd**	0.42	2	7	
D_50cell_man_X		0.5	0.7	1.2	0.9	2.3	2.1	2.9	2.5	4.5	5.3	0.45	4	6	
E_50cell_man_Co		0.0	0.0	0.8	0.9	1.6	2.6	2.1	2.5	3.0	5.1	0.50	8	2	
MAD		0.10	0.21	0.25	0.27	0.33	0.34	0.43	0.42	0.58	0.79				
lower or equal		4	3	0	3	3	1	1	2	1	4				
higher than true dose		2	3	6	3	3	5	5	4	5	1				

MAD: mean absolute deviation from true dose

MAD and time needed are opposed, each in a range up to the 2.5 fold of the minimum. From 0 to 4 estimates fall out of the ±0.5 Gy interval accepted for triage (**blue**; Lloyd 2000).

Conclusion

- **laboratory** and **actually applied dose** influence **variation of dose estimates**
- **DCA: reliable diagnostic triage tool suitable for lab networking nevertheless: potential for optimization existing in terms of time needed for and precision of triage dose estimates**

Identification of laboratory conditions requiring improvement
(methodological procedures, quality assurance…)

- implementation of optimized protocols into the laboratory's organization and operation procedures
- compliance with existing recommendations (e.g. choice of calibration curve)
- gain of practical expertise (ring trials, continuous training)