RENEB BIOLOGICAL AND PHYSICAL DOSIMETRY STUDY
LABORATORY INTER-COMPARISON OF EIGHT DOSIMETRY ASSAYS

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INTRODUCTION

- Tools for radiation exposure reconstruction are required to support the medical management of radiation victims in radiological or nuclear incidents. In 2021, we conducted an international laboratory inter-comparison of eight established biological dosimetry assays. (fig. 1)

MATERIAL AND METHOD

- Three coded blood samples were exposed to 0, 1.2 and 3.5 Gy X-ray doses (240 kVp, 1 Gy/min).
- These exposures roughly correspond to clinically relevant groups of unexposed, lower exposed (no severe acute health effects expected) and high exposed individuals requiring early intensive medical health care.
- Samples were sent to 89 specialized teams from 27 nations
- Endpoints: report time + dose estimates (absolute difference (AD), 0.5 Gy triage dosimetry interval) + identifying clinically relevant groups per assay

RESULTS

- 512 dose estimates reported: **5-10 h** for GE, gH2AX, LUM, EPR, **2-3 days** for DCA, CBMN and estimated to be available within **6-7 days** for TRANS assay (fig. 2).
- Variance in reported dose estimates differed among teams.
- 0 Gy irradiated sample ≈ all assays
- 1.2 + 3.5 Gy irradiated sample: e.g. ADs EPR or OSL < DCA (fig. 3).
- all samples: ≈ 40-60 % correctly reported (+/- 0.5 Gy) employing DCA, CBMN, OSL and EPR assays.
- Clinically significant categories (unexposed or highly exposed samples) correctly identified with all assays (NPV & PPV 100%, table 1).

CONCLUSION

- Early local physical dose estimation by EPR und LUM confirmed.
- Mean whole-body exposure by DCA and CBMN confirmed.
- All eight assays comparably applicable for identification of unexposed and highly exposed individuals.

Acknowledgment

This work would have not been possible without the 89 teams involved, which could not be cited here due to space restrictions

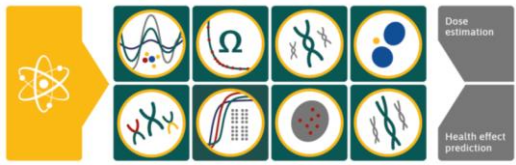

Figure 1: RENEB - established and emerging assays employed for retrospective dosimetry and medical management support. Symbols refer to physical dosimetry based assays (electron paramagnetic resonance [EPR] and optically stimulated or thermoluminescence [LUM]), cytogenetic assays (dicentric chromosome assay [DCA], cytokinesis-block micronucleus assay [CBMN], stable chromosomal translocation assay [TRANS], and premature chromosome condensation assay [PCC]) and emerging biological dosimetry assays (gamma-H2AX foci [gH2AX] and gene expression assays [GE]). Abbreviations are shown in figure 2.

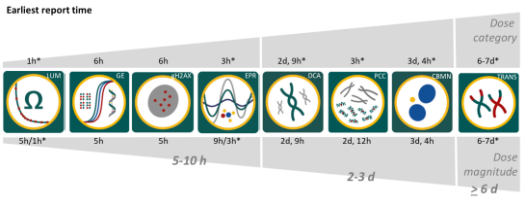

Figure 2: Earliest report times of dose categories (low, medium, high, upper part) as well as dose estimates (dose magnitude, lower part) are provided for all assays. Three categories in report time were defined and expressed in bold grey letters. Asterisks refer to estimated dose estimates and are not reported dose estimates. Assays are ordered over report time of dose estimates. Abbreviations: see figure legend 1.

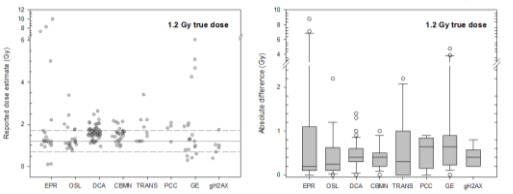

Figure 3: Descriptive statistics of absolute differences (AD) calculated between reported dose estimates and true doses. Quantiles were calculated using SAS and are shown for the 1.2 Gy irradiated sample only.

Category/ Assay	# data sets	TN	TP	FN	FP	TN (%)	TP (%)	FN (%)	FP (%)	Specificity (%)	Sensitivity (%)	accuracy (%)	NPV (%)	PPV (%)
Identification of unexposed individuals (0 vs >0 Gy)														
gH2AX	18	6	12	0	0	33,3	66,7	0,0	0,0	100,0	100,0	100,0	100,0	100,0
DCA	151	42	104	0	5	27,8	68,9	0,0	3,3	89,4	100,0	96,7	100,0	95,4
OSL	67	18	44	0	5	26,9	65,7	0,0	7,5	78,3	100,0	92,5	100,0	89,8
PCC	10	3	6	0	1	30,0	60,0	0,0	10,0	75,0	100,0	90,0	100,0	85,7
TRANS	30	7	20	0	3	23,3	66,7	0,0	10,0	70,0	100,0	90,0	100,0	87,0
GE	50	15	30	0	5	30,0	60,0	0,0	10,0	75,0	100,0	90,0	100,0	85,7
CBMN	81	18	54	0	9	22,2	66,7	0,0	11,1	66,7	100,0	88,9	100,0	85,7
EPR	66	14	44	0	8	21,2	66,7	0,0	12,1	63,6	100,0	87,9	100,0	84,6
Identification of individuals requiring hospitalization and discrimination from low exposed (1.2 vs >=3.5 Gy)														
TRANS	21	10	11	0	0	47,6	52,4	0,0	0,0	100,0	100,0	100,0	100,0	100,0
DCA	104	53	47	4	0	51,0	45,2	3,8	0,0	100,0	92,2	96,2	93,0	100,0
PCC	8	4	3	1	0	50,0	37,5	12,5	0,0	100,0	75,0	87,5	80,0	100,0
CBMN	54	27	18	9	0	50,0	33,3	16,7	0,0	100,0	66,7	83,3	75,0	100,0
GE	40	16	14	6	4	40,0	35,0	15,0	10,0	80,0	70,0	75,0	72,7	77,8
OSL	43	22	9	12	0	51,2	20,9	27,9	0,0	100,0	42,9	72,1	64,7	100,0
EPR	42	17	11	9	5	40,5	26,2	21,4	11,9	77,3	55,0	66,7	65,4	68,8
gH2AX	12	6	1	5	0	50,0	8,3	41,7	0,0	100,0	16,7	58,3	54,5	100,0
Identification of individuals requiring hospitalization and discrimination from unexposed (0 vs >=3.5 Gy)														
TRANS	20	10	10	0	0	50,0	50,0	0,0	0,0	100,0	100,0	100,0	100,0	100,0
DCA	104	53	47	4	0	51,0	45,2	3,8	0,0	100,0	92,2	96,2	93,0	100,0
PCC	8	4	3	1	0	50,0	37,5	12,5	0,0	100,0	75,0	87,5	80,0	100,0
GE	39	20	13	6	0	51,3	33,3	15,4	0,0	100,0	68,4	84,6	76,9	100,0
CBMN	55	27	19	9	0	49,1	34,5	16,4	0,0	100,0	67,9	83,6	75,0	100,0
EPR	41	22	10	9	0	53,7	24,4	22,0	0,0	100,0	52,6	78,0	71,0	100,0
OSL	44	23	9	12	0	52,3	20,5	27,3	0,0	100,0	42,9	72,7	65,7	100,0
gH2AX	12	6	1	5	0	50,0	8,3	41,7	0,0	100,0	16,7	58,3	54,5	100,0

Table 1: Preliminary results for sensitivity, specificity, accuracy, as well as positive (PPV) and negative predictive values (NPV) of triage classifications are shown for each assay and binary categories of clinical significance (provided as subtitle). General features identified in all assays are marked in grey. Abbreviations: true positive =TP, true negative =TN, false positive =FP and false negative =FN.

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