Comparison of physical and biological dosimetry for internal emitters

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EURADOS Working Groups 7 (Internal Dosimetry) and 10 (Retrospective Dosimetry)

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REVIEW OF RETROSPECTIVE DOSIMETRY TECHNIQUES FOR EXTERNAL IONISING RADIATION EXPOSURES

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Objective: **Review of cases of internal exposures, where biodosimetry + internal dose evaluations where done: >60 publications + unpublished data**

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- **Task 1.- Radiotherapy – Natalie Maznyk – Kharkov, Ukraine**
- **Task 2.- Radiodiagnosis – Horst Romm – BfS, Germany**
- **Task 3.- Occupational Exposures – Paco Barquinero – IRSN, Fr**

The principle of retrospective dosimetry

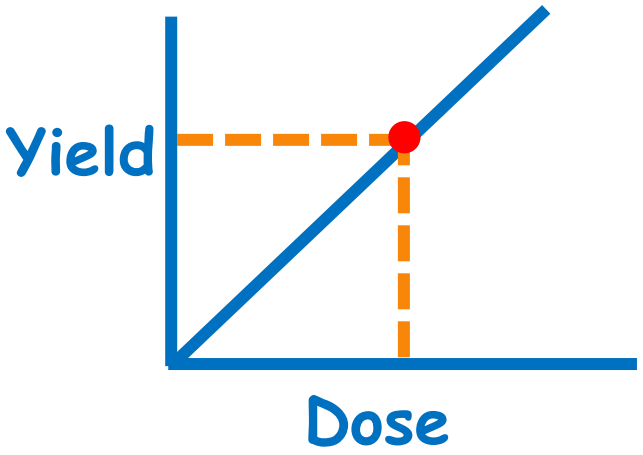
1. **Identify** potentially exposed individuals

2. Take a **sample**

3. **Measure** radiation-induced signal

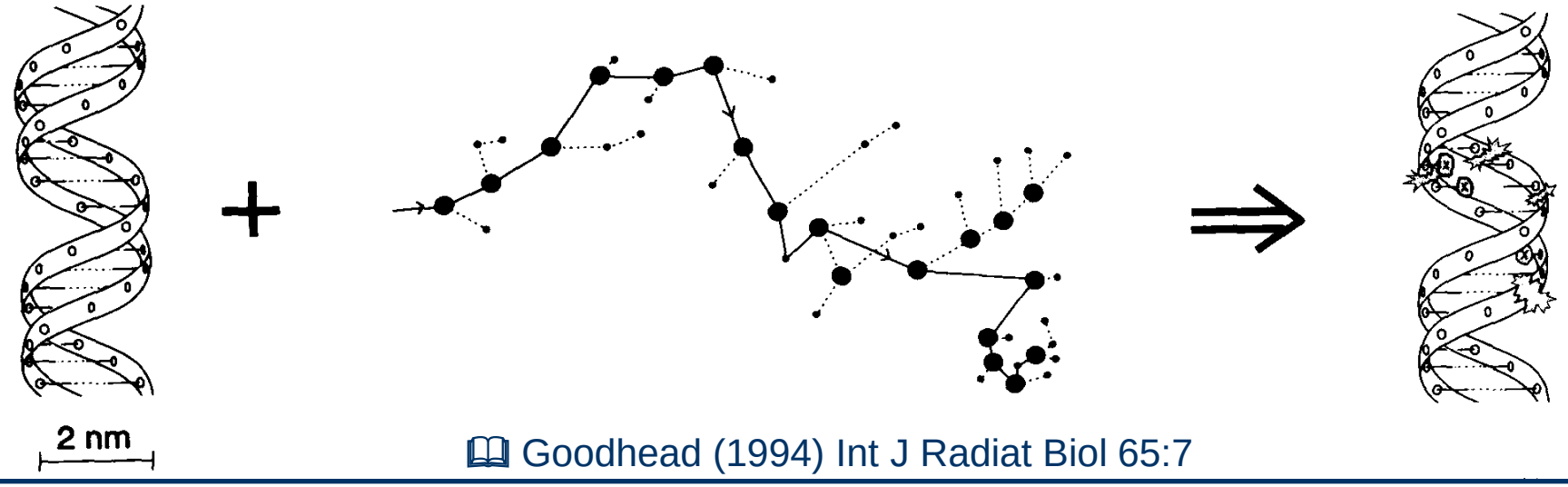
4. **Interpret**: Compare the test result with a calibration curve for dose response

5. Inform **clinical treatment** decisions



Spectrum of biological damage induced by ionising radiation

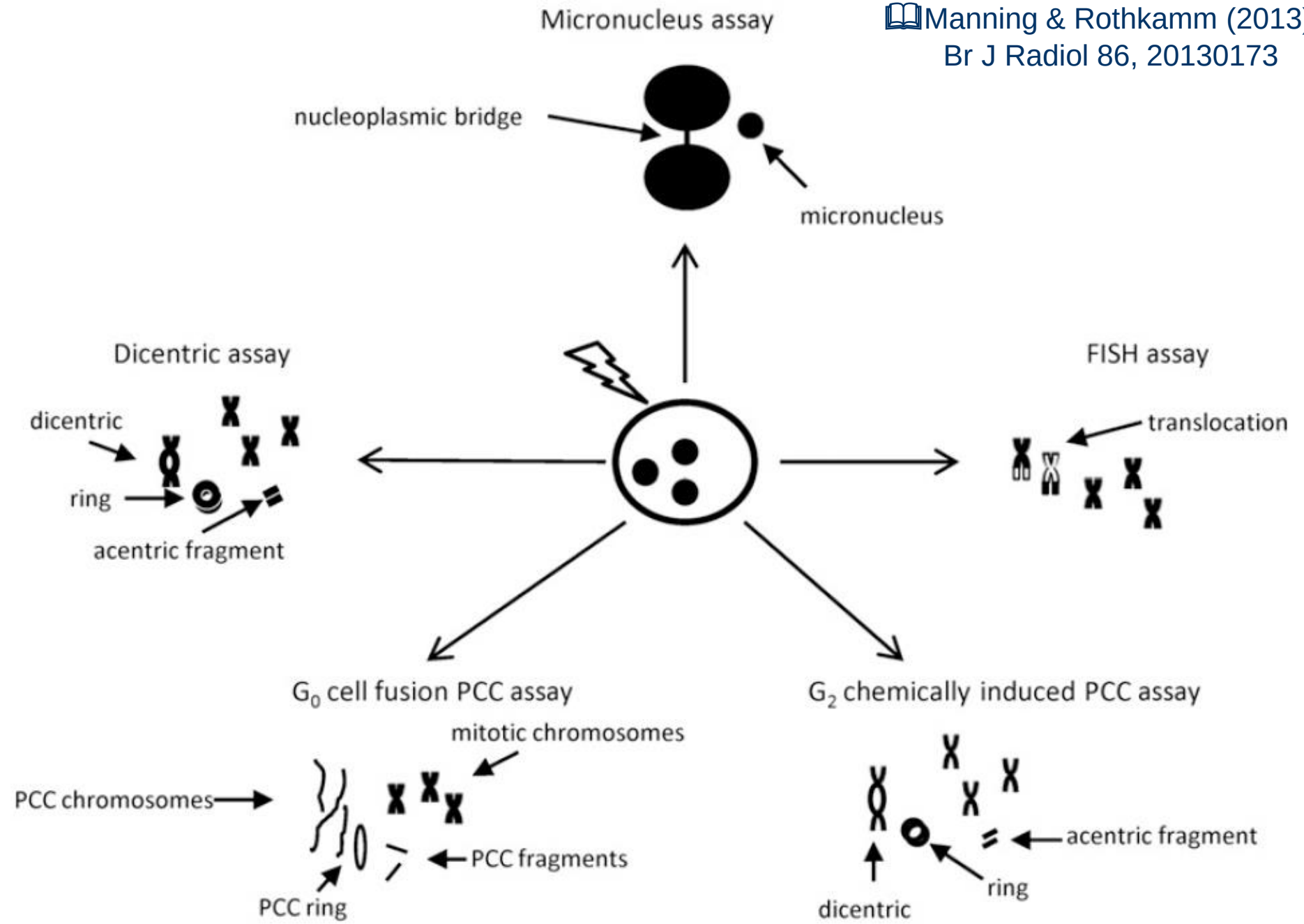
Damage induced by 1 Gy X-rays in a human cell:	**physical**	• 100,000 ionisations in the cell nucleus • 2,000 direct ionisations in the DNA
	biochemical	• 1,000 single-strand breaks • 1,000 damaged bases • 150 DNA protein crosslinks • **35 double-strand breaks**
	cellular	• **0.1 dicentrics / micronuclei** • 0.3 lethal events • 10^{-5} *hprt* mutations



📖 Goodhead (1994) Int J Radiat Biol 65:7

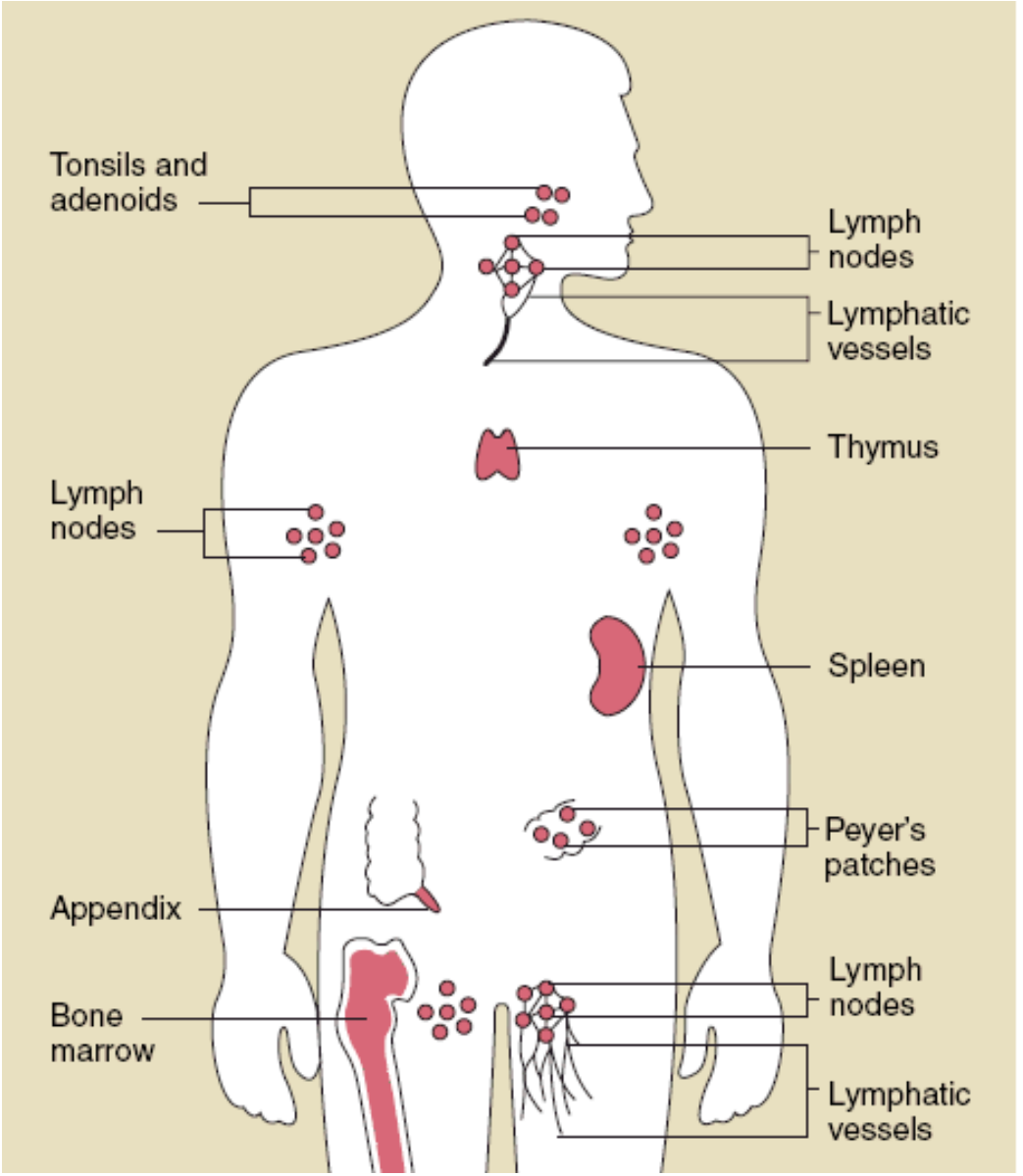
Cytogenetic biomarkers of radiation exposure

📖Manning & Rothkamm (2013)
Br J Radiol 86, 20130173



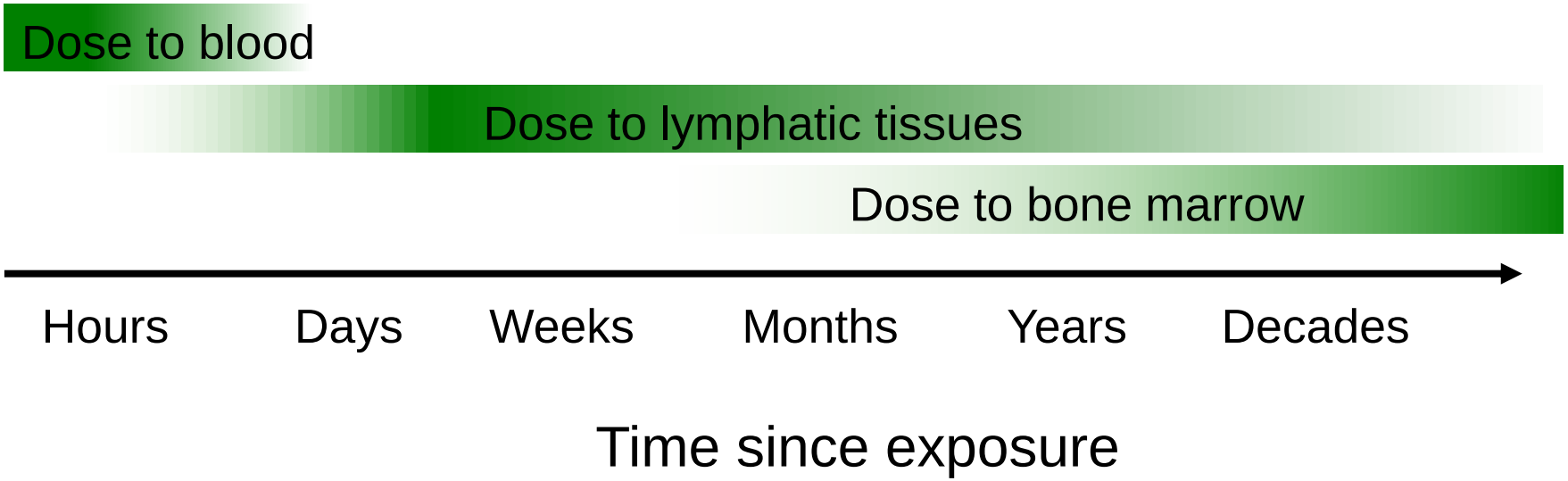
T-lymphocytes

- 2% of lymphocytes present in peripheral blood
- Others in thymus, lymph nodes, tonsils, intestines, spleen, bone marrow...
- 80% migrate between tissues and peripheral blood with a recirculation time of ~12 hrs
- Mixing of circulating blood lymphocytes takes only minutes
- Half life: ~2-3 years; renewal from HSC pool in bone marrow, maturation in thymus



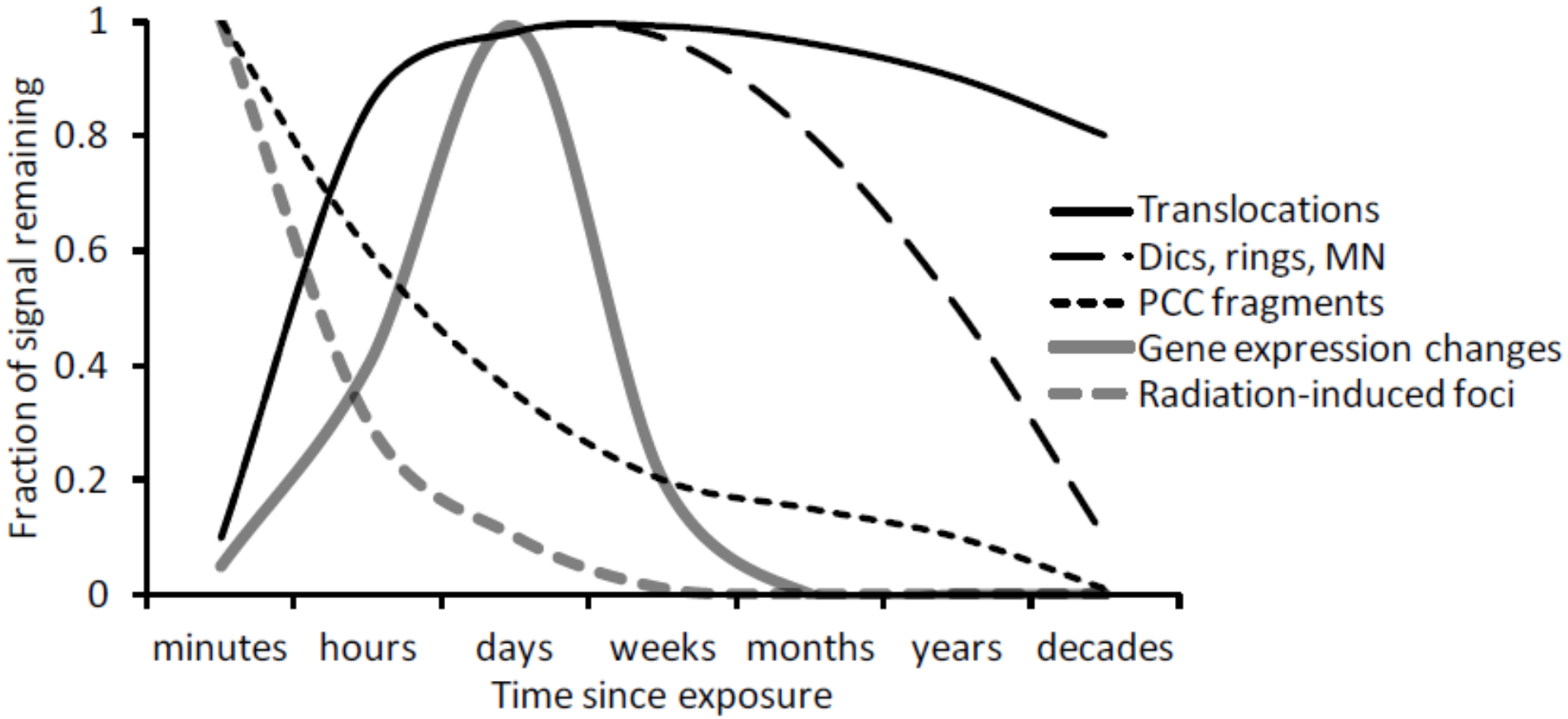
http://www.web-books.com/eLibrary/Medicine/Physiology/Immune/index.htm

Lymphocyte biomarkers: target organs change over time

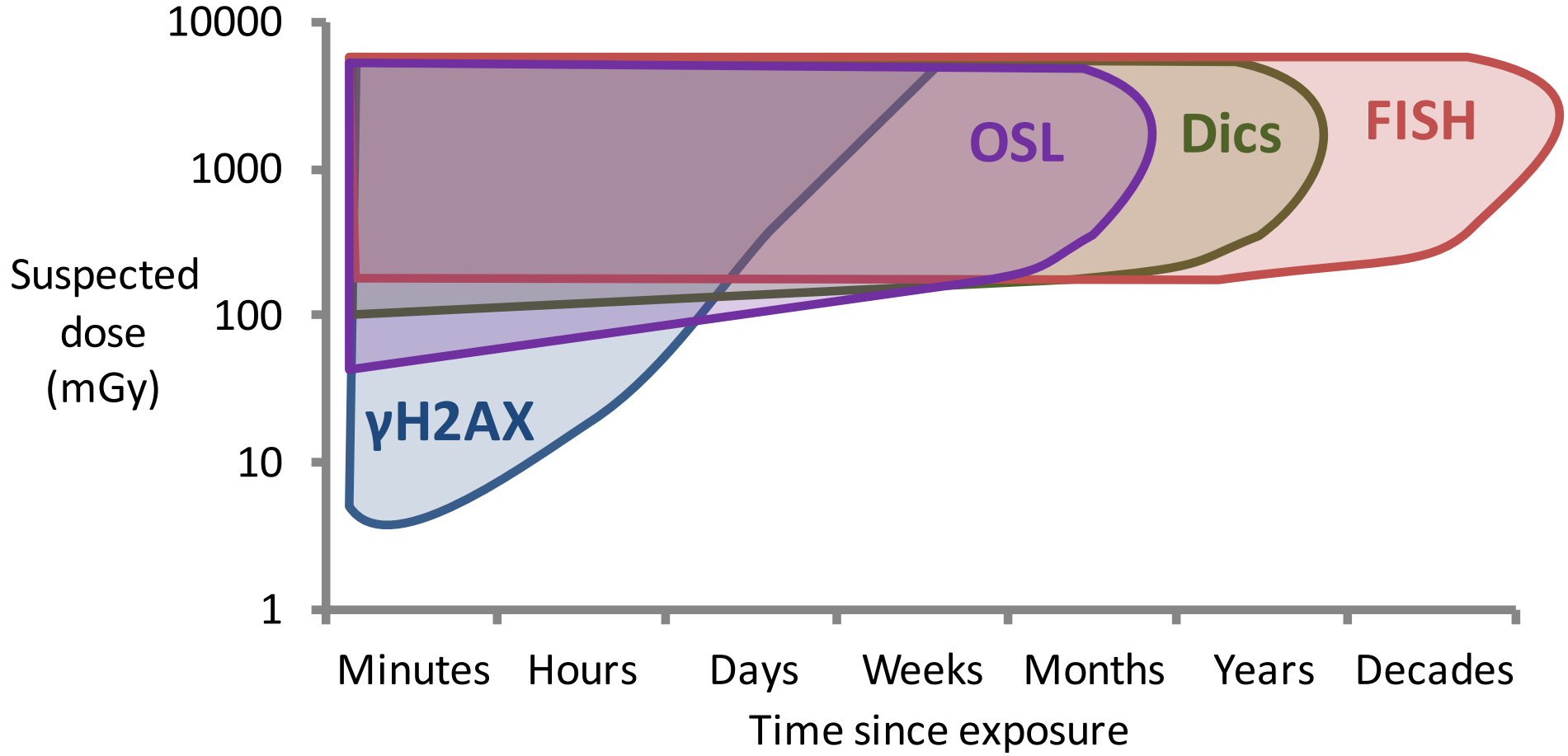


Biodosimetry markers are not stable over time

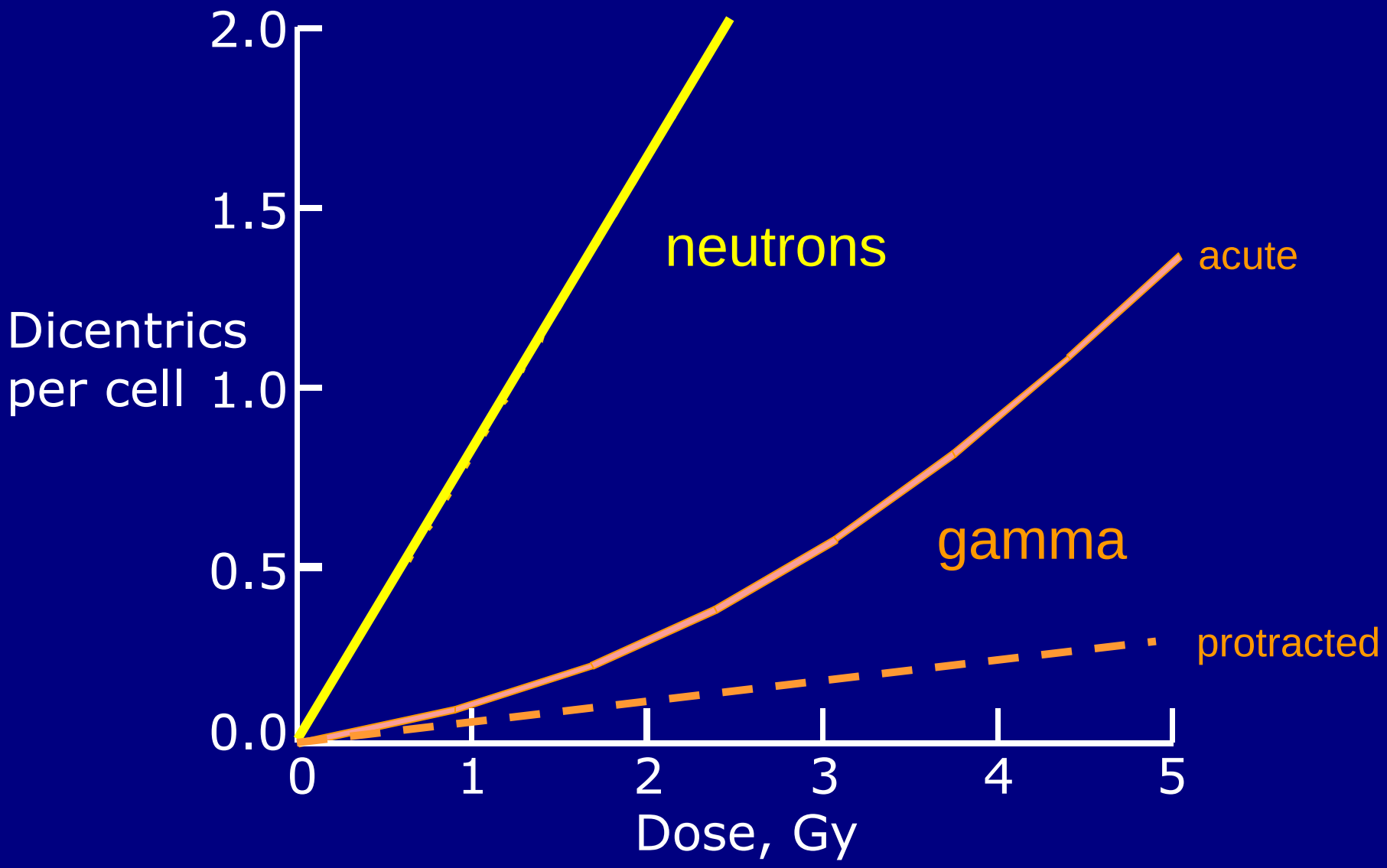
Manning & Rothkamm (2013) Br J Radiol 86, 20130173



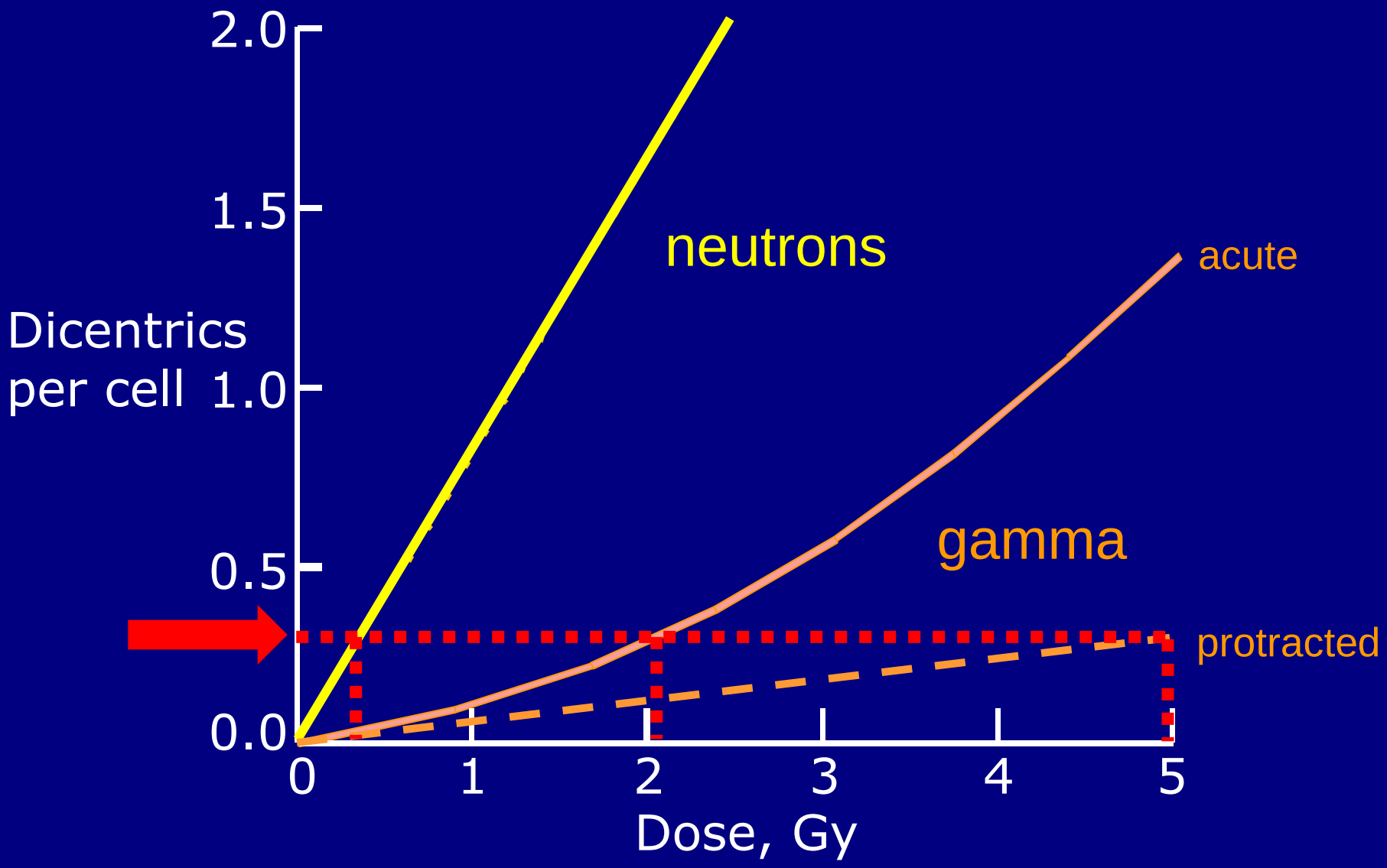
Sensitivity ~100 mGy whole body dose for cytogenetic markers



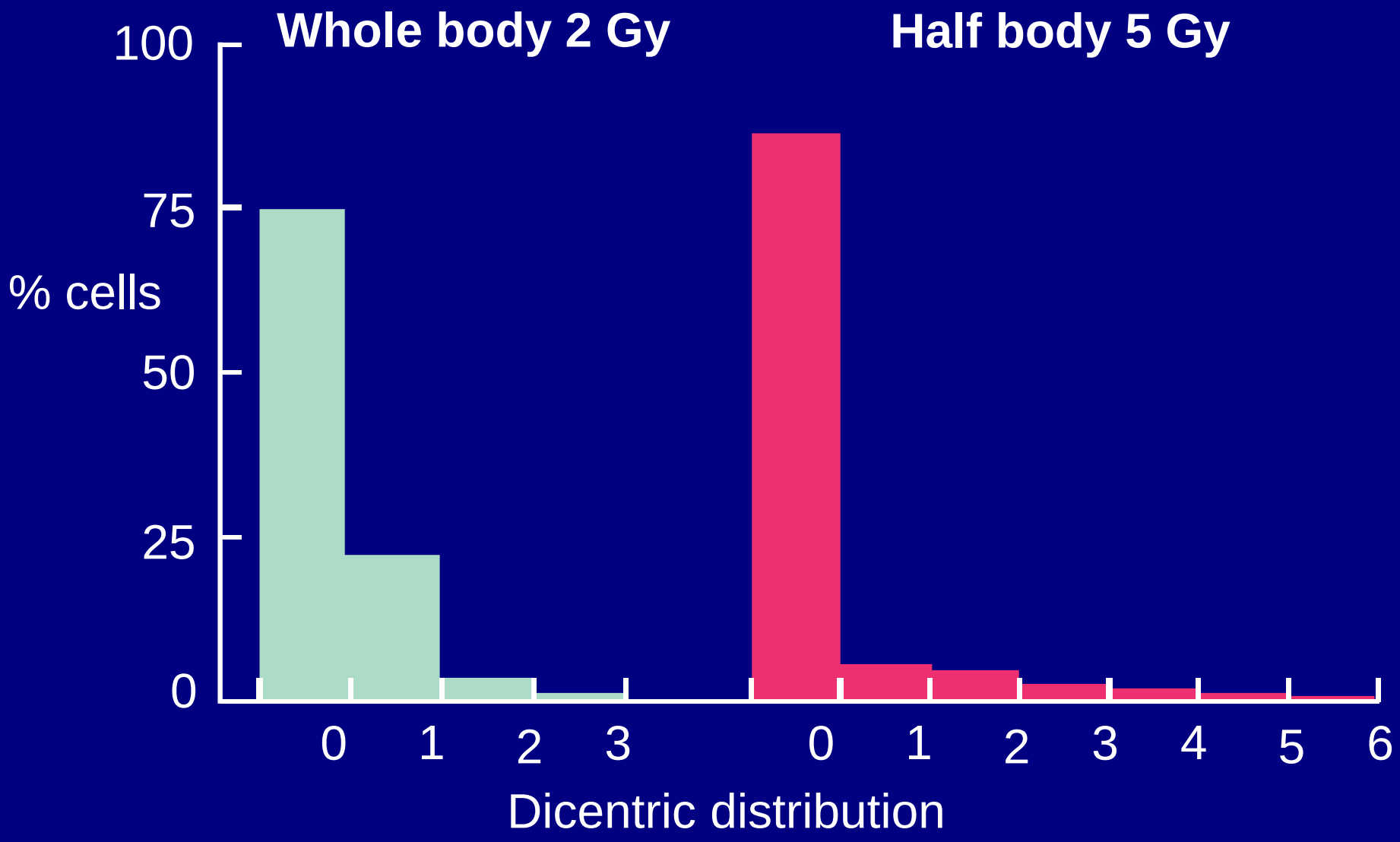
Yields affected by radiation quality & dose rate



Yields affected by radiation quality & dose rate



0.3 Dicentrics per Cell



Why are internal exposures ‘complicated’ for biological dosimetry?

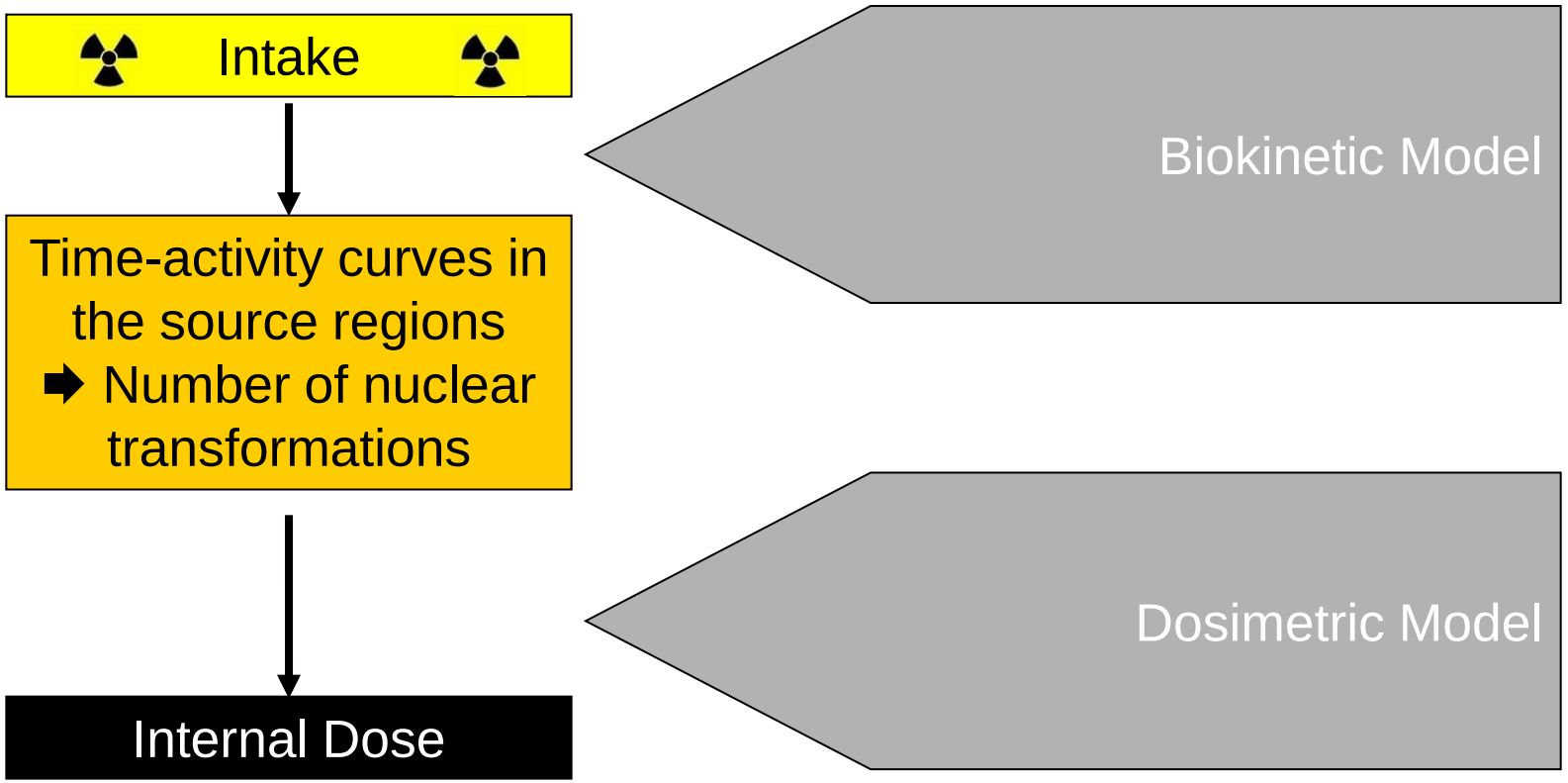
- Protracted exposures with changing dose rate
- Non-uniform dose distributions
- Range of radiation qualities
- Often accompanied by external exposures
- Doses typically quite low

Intake assessment:

- ✓ EXPERIMENTAL TECHNIQUES IN PHYSICAL/INTERNAL DOSIMETRY:
  - Monitoring Data from (I) In-vivo or/ and (II) In-vitro monitoring

- ✓ CALCULATION OF DOSES DUE TO INTERNAL EXPOSURES FROM MONITORING DATA

Internal dose is evaluated with mathematical models



Internal dosimetry

ICRP Publications give dose coefficients and bioassay curves and tables for REFERENCE PERSONS.

For individual dose estimates (e.g., nuclear medicine patients) biokinetic and dosimetric models should be adapted to the individual characteristics:
THE SAME INTAKE PRODUCES DIFFERENT DOSES

Dose to blood:

ICRP currently does not have blood as target tissue.

There is a methodology developed for nuclear medicine (EANM Dosimetry Group):

1. M.Lassmann et al. Eur. J. Nucl. Med. Mol. Imaging 35:1405-1412, 2008.

Scenarios reviewed

Scenario	Radionuclides Internal Doses	WG7	WG10
Goiania Accident	Cs-137	G. Etherington M. Youngman	C Lindholm
Techa River (Mayak)	Sr-90	A. Giussani	JF Barquinero, A Testa
Plutonium Workers	Pu-239, Am-241	S. McComish	H Romm
Tritium intakes	HTO	M.A. Lopez	E Gregoire
Radioiodine-Medical	I-131, I-125	A.Rojo, A. Giussani	O Gil, H Romm
Thorotrast patients	Th-232	I. Malatova	
Thorium workers	Ra-224, Bi-212	M.A. Lopez	I Guclu
Chernobyl area	Cs-137	J. Marsh, D. Gregoratto	A Jaworska, N Maznyk
Semipalatinsk	Pu, Cs, Sr	S. Tolmachev	Testa, Lindholm, Jaworska
Others (medical,…)	Ra-224,…	Kuba Osko	JF Barquinero, E Gregoire

Example of localised irradiation: Pu-239

- **Mayak workers: Plutonium production, 1948 onwards**
- **Pu-239:**
  - $t_{½}$ ~ 24,000 y
  - Alpha emitter ~ 5.2 MeV
  - Soft tissue penetration ~ 50 µm
- **Retention: ~ 40-50%**

- **Deposition on bone surface -> ~ continuous irradiation of shallow layer near marrow**

Plutonium workers: 16 papers reviewed

- Mayak (6)
- Sellafield (4)
- Rocky Flats (2)
- Manhattan Project – UPPU (1)
- UKAEA (1)
- Semipalatinsk (1)
- Russian Nuclear Workers (1)

Types of Assays

- Dicentric assay
- G-banding
- FISH
- mFISH
- mBAND

Asymmetrical Aberrations

	Was an excess observed?	
Asymmetrical	Y - Tawn (1985, G-banding)	N - Whitehouse (1998, G-banding)
Unstable	Y - Okladnikova (2005, Romanovsky-Gimsa stain)	N - Whitehouse (2001, solid Giemsa stain)[a] N - Tawn (2006, FISH)
Dicentrics	Y - Tawn (2006, FISH) Y - Livingston (2008, FISH)	N - Dolphin (1971)
Acentrics	Y - Livingston (2008, FISH)	
Rings		N - Livingston (2008, FISH)

[a] External dose not accounted for.

Symmetrical Aberrations

	Was an excess observed?	
Symmetrical	Y - Tawn (1985, G-banding) Y - Whitehouse (1998, G-banding)	
Stable	Y - Okladnikova (2005, Romanovsky-Gimsa stain)	N - Tawn (2006, FISH)
Translocations	Y - Livingston (2008, FISH)	N - Salissidis (1998, FISH) N - Tawn (2006, FISH)

Handling External Dose

- **Significant external doses in most Pu-exposed workers**
  - Median: 290 mSv Max: 3,300 mSv
- **Most common : "external only" vs. "Pu + external"**
  - Ideally, each group had the same level of external dose
  - Sometimes the "Pu + external" group had a higher external dose.
- **Linear Regression**
  - Regress the number of chromosome aberrations against body burden, red bone marrow dose, and/or external dose.

Regression Results

	External Dose	Body Burden (BB)	Red Bone Marrow (RBM)	Average Pu			Average External Dose		Comments
				BB (kBq)	RBM Dose				
Salissidis et al. (1998)	Y	N		9.1[a]			3,300	mSv	
Burak et al. (2001)	Y	N		2.0			340	mGy	
Livingston et al. (2006)	N		Y		168	mSv[b]	280	mSv[b]	
Okladnikova et al. (2005)	Y	Y	Y	7.99			90	mGy	External correlation not found for stable aberrations.
Sotnik et al. (2011)	Y	Y	Y	2.05	120	mGy	1,000 860	mGy WB mGy RBM	External correlation not found for intra-chromosomal aberrations.

[a] midpoint of range
[b] median

Note: Body burden and dose data are for the plutonium-exposed group (1-3) or the most highly exposed plutonium group (4-5)

Techa river population: Sr-90 intakes

- **1949 -1956: release of ~ 10^{17} Bq of uranium fission products Techa River (Deposited on river bank/flood areas; Absorbed into sediment and into the food chain; Ingested with river water)**

- **Sr-90 - Internal doses:**
  - $t_{½}$ ~ 28.8 y; Beta emitter ~ 0.2 MeV and 1 MeV
  - Soft tissue penetration ~ 2 – 10 mm

- **Incorporation: Into bone volume (replaces Ca)**

- **Retention : ~ 20-30 % at 0 y; ~10 – 15% at 2-3 y; ~ 2-3 % at 30 y**

- **Incorporation into bone volume -> ~ continuous irradiation bone marrow**

Dose conversion (Techa)

- **Edwards *et al.*:**
  - Little direct research for Sr calibration
  - No evidence different RBE - Sr beta vs external gamma
  - Use external gamma for protracted exposures:

$$y = 0.015\ D^{RBM}_{Ext}$$

  – Limitations: Large uncertainty; Exposure energies unknown?

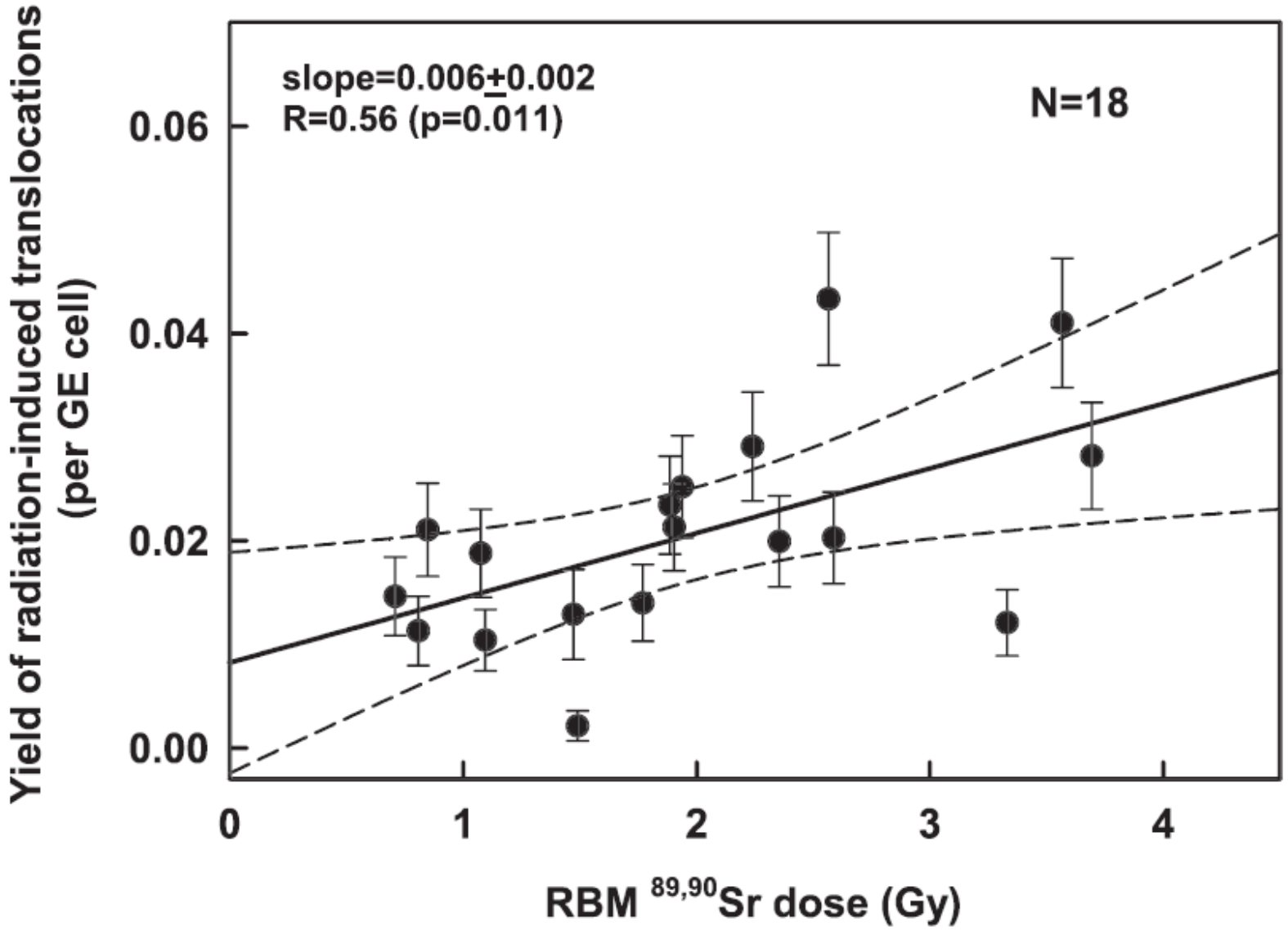
- **Vozilova *et al.* (2012):**
  - TRDS: Significant linear dependence of RBM dose and Sr doses
  - In vivo separation of Sr contribution to translocation frequency

    -> in vivo Sr-90 calibration curve:

$$y = 0.006\ (\pm\ 0.002) * D_{Int}$$

  - Limitations: Small data set; Lack of baseline data; Pooling data

Dose conversion (Techa)



Open issues:

- Calibration curves of Biological Dosimetry techniques:
  - In vitro curves often not valid for internal exposures
  - Validation requires in vivo exposures
  - What is the lowest detectable dose?
- Biodosimetry:
  - Effect of changing dose-rate on CA yields
  - Lymphocyte distribution and turnover, location of precursor cells for historic doses
  - How to compare biological dose (to blood, etc.) with physical/internal dosimetry results (ICRP)?
  - Also biological dose estimate vs. “administrated dose to patient in the radiotherapy protocol”
- Time scale, intake route and chemical composition of contaminants define the distribution of the radionuclides in the body
- Difficult to manage cases with internal+external exposures (Goiania accident)

Summary

***Aim**:*

To establish the usefulness and limitations of cytogenetic dosimetry in cases of internal and mixed internal/external exposures and compare results with internal dosimetry data

***Challenges**:*

- Spatio-temporal radionuclide distribution in the body – depending on chemical characteristics and intake route
- Lymphocyte distribution and turnover, location of precursor cells for historic doses
- Protracted exposures with dose-rate gradients
- *In vitro* calibration curves unsuitable

Summary

Results so far:

Good agreement of biological and internal dosimetry for some specific scenarios (high tritium intakes, ^{131}I treatment of patients w/o thyroid, some ^{137}Cs intakes at Goiania)

More complicated scenarios:

High LET, heterogenous distribution in the body, mixed internal & external exposures

^{90}Sr *in vivo* calibration curve for translocations established & being refined

THANK YOU!