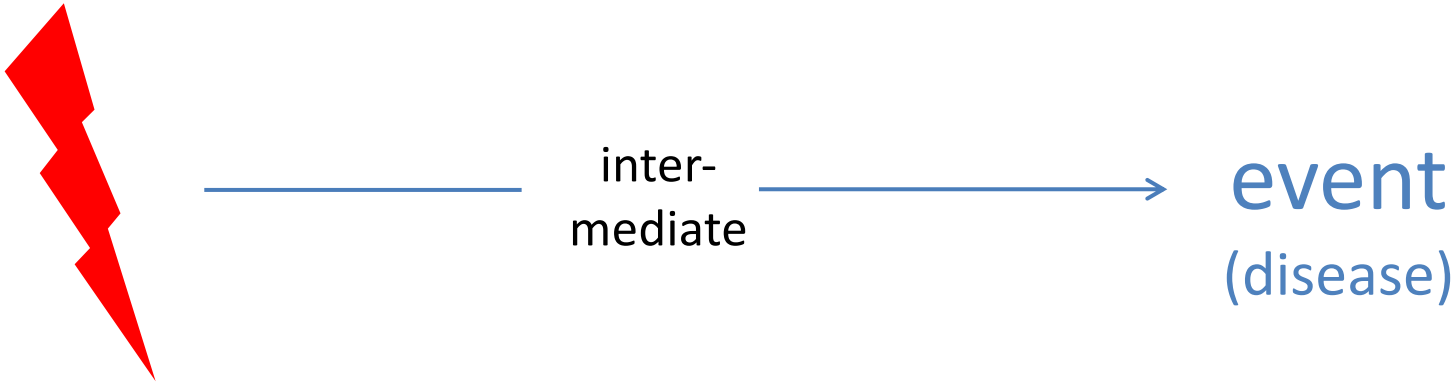
Using dose for effect prediction - a challenging task -

M. Abend

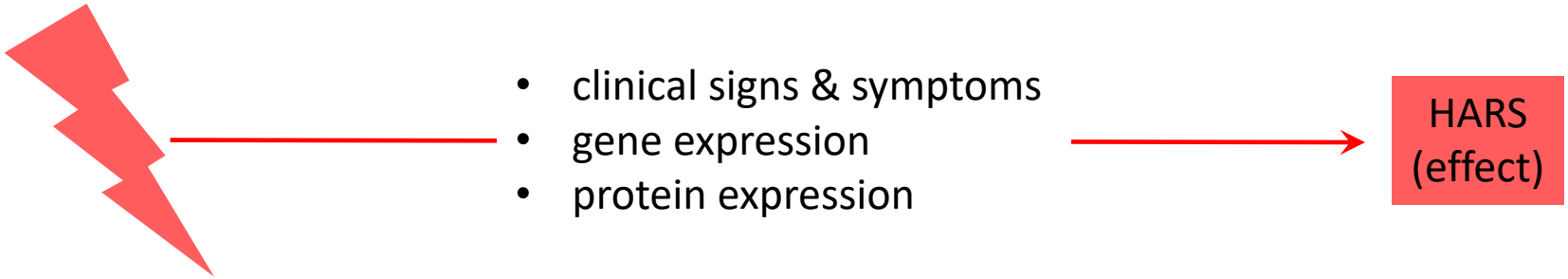
Bundeswehr Institute of Radiobiology, Munich, Germany

Dose – effect prediction

Dose – effect prediction

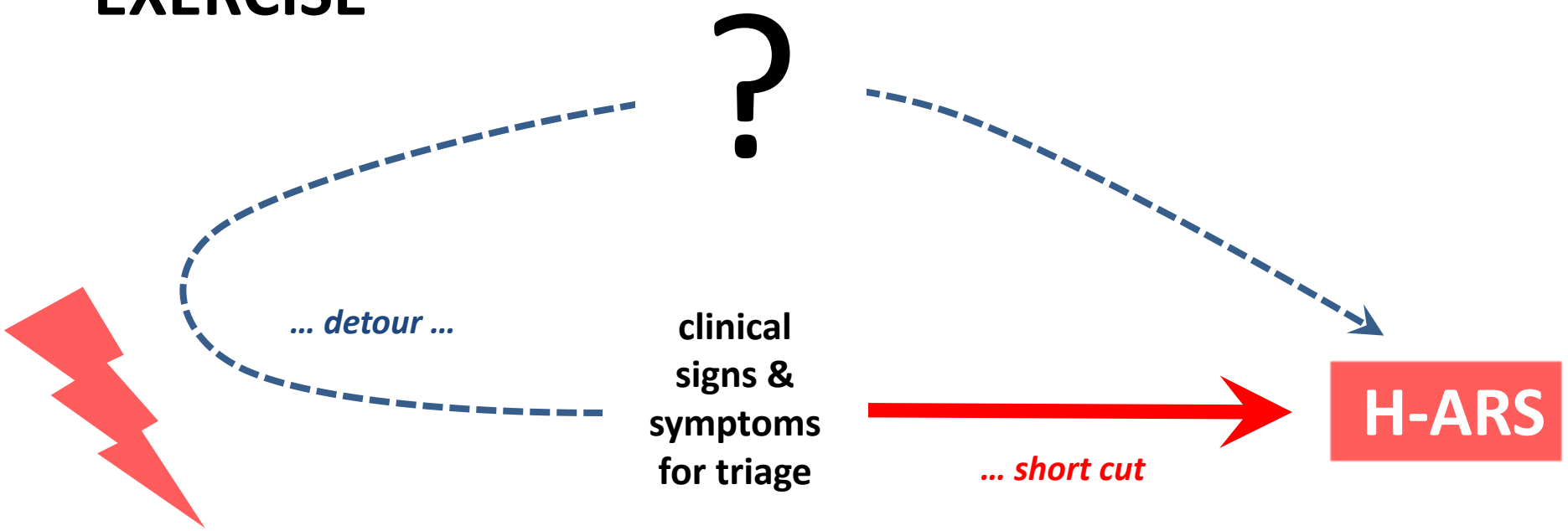


Dose – effect prediction



Early diagnosis of deterministic effects

2015 EXERCISE



Doerr et al. RadRes, 2017

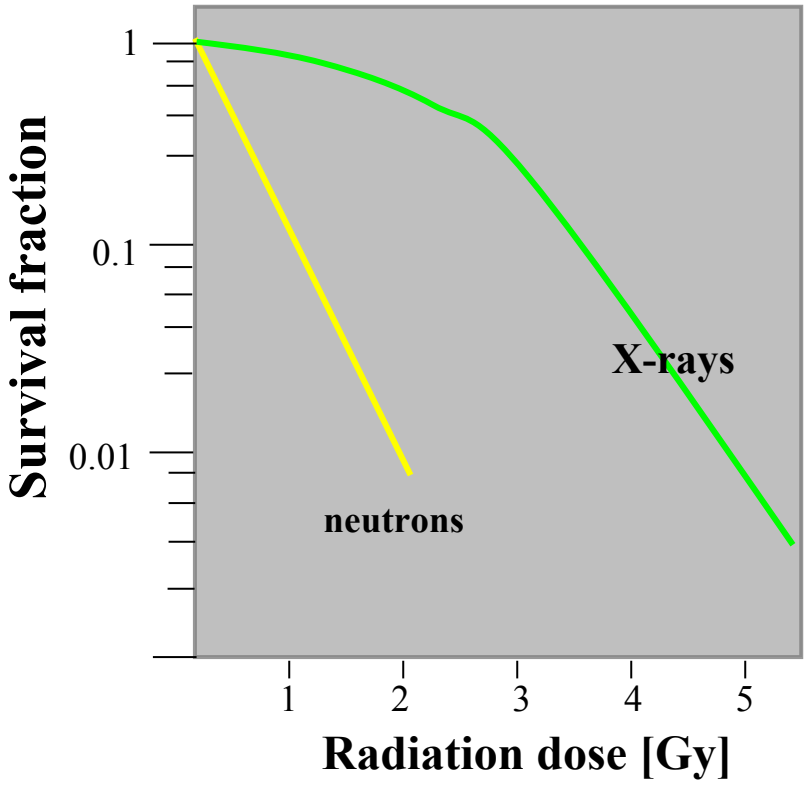
Dose-effect relationship

… known modifier
related to
EXPOSURE

Dose-effect relationship

… known modifier related to **EXPOSURE**

Radiation quality

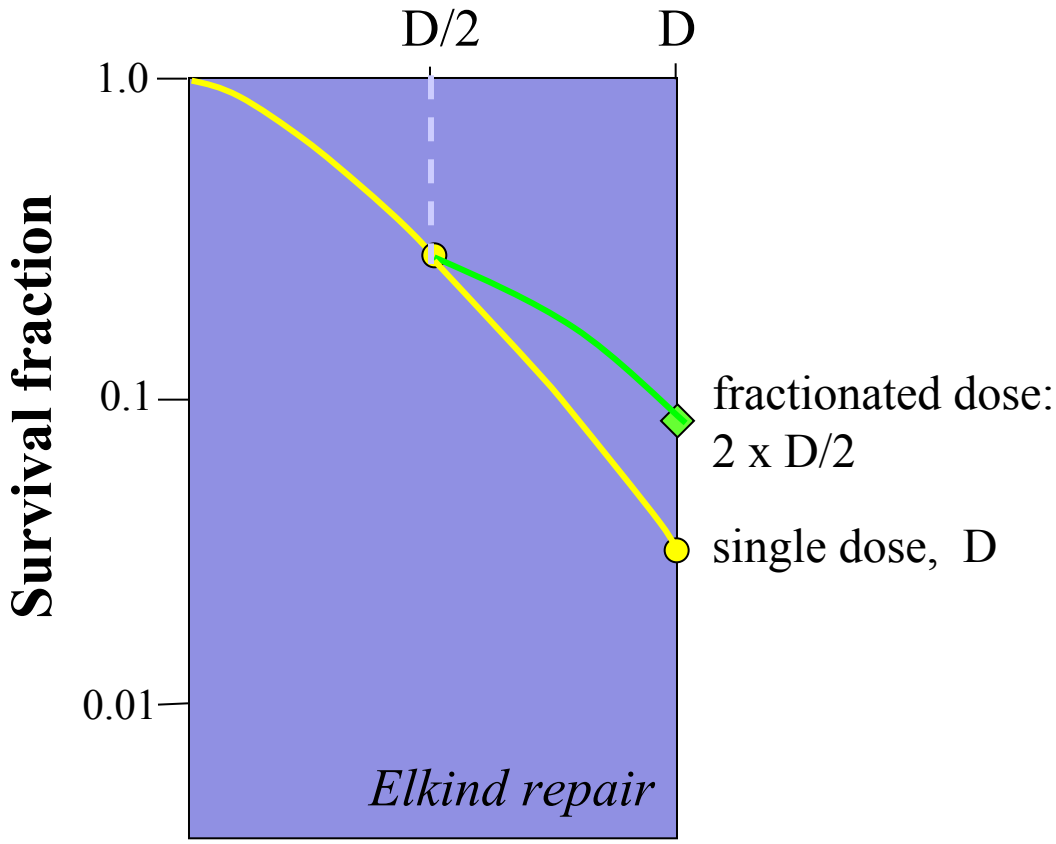


E. Hall, Radiobiology for the Radiologist, 5th edition, 2000

Dose-effect relationship

… known modifier related to **EXPOSURE**

dose fractionation

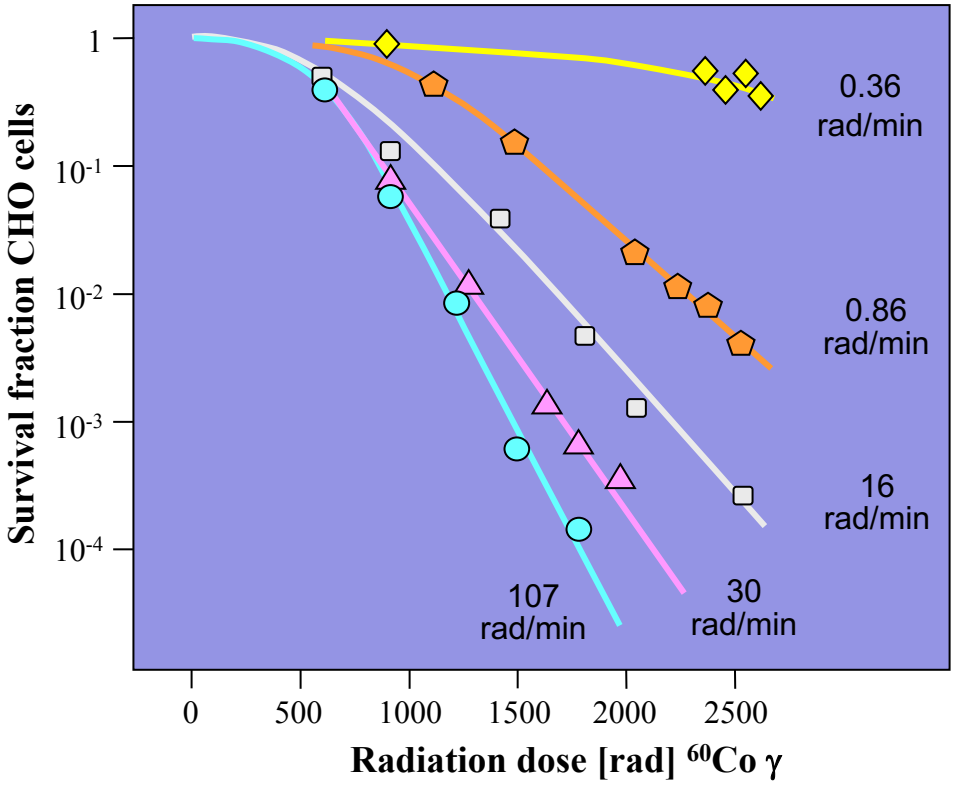


modified after Elkind and Sutton, 1960

Dose-effect relationship

… known modifier related to **EXPOSURE**

dose rate



↓ dose rate

↓

↑ exposure time

↓

↓ biolog. effect

(due to SLD repair)

↓

↑ survival

modified after Bedford and Mitchell, 1973

Dose-effect relationship

… known modifier related to **EXPOSURE**

- radiation quality
- fractionated exposure
- dose rate
- partial/total body irradiation
- homogenous/inhomogenous exposure
- external/internal contamination

Chain of events

physical phase:	absorbed energy (excitation + ionization)	10^{-18}-10^{-14} s
chemical phase:	hydrolysis, formation of radicals	10^{-6} s
biochemical phase:	direct and indirect action on target molecules (breakage of chemical bonds) ⇓ biochemical changes on macromolecules (nucleid acids, proteins, lipids; altered 3D confirmation and function)	10^{-2} s s - h
biological phase:	- chromosomal changes, gene aberration - morphological changes + cell cycle alterations - cell death, mutagenesis - death of the organism - epigenetic modification, cancerogenesis	h - d y

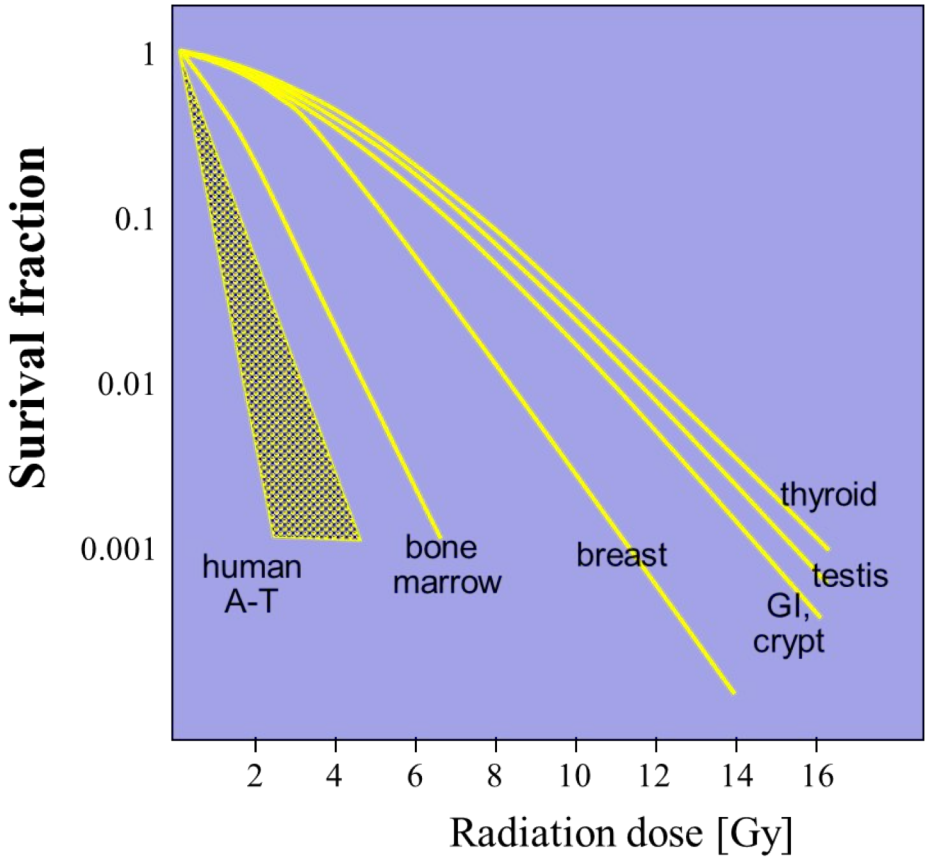
Dose-effect relationship

… known modifier
related to
BIOLOGICAL PROCESSES

Dose-effect relationship

… known modifier related to **biological processes**

radio-sensitivity



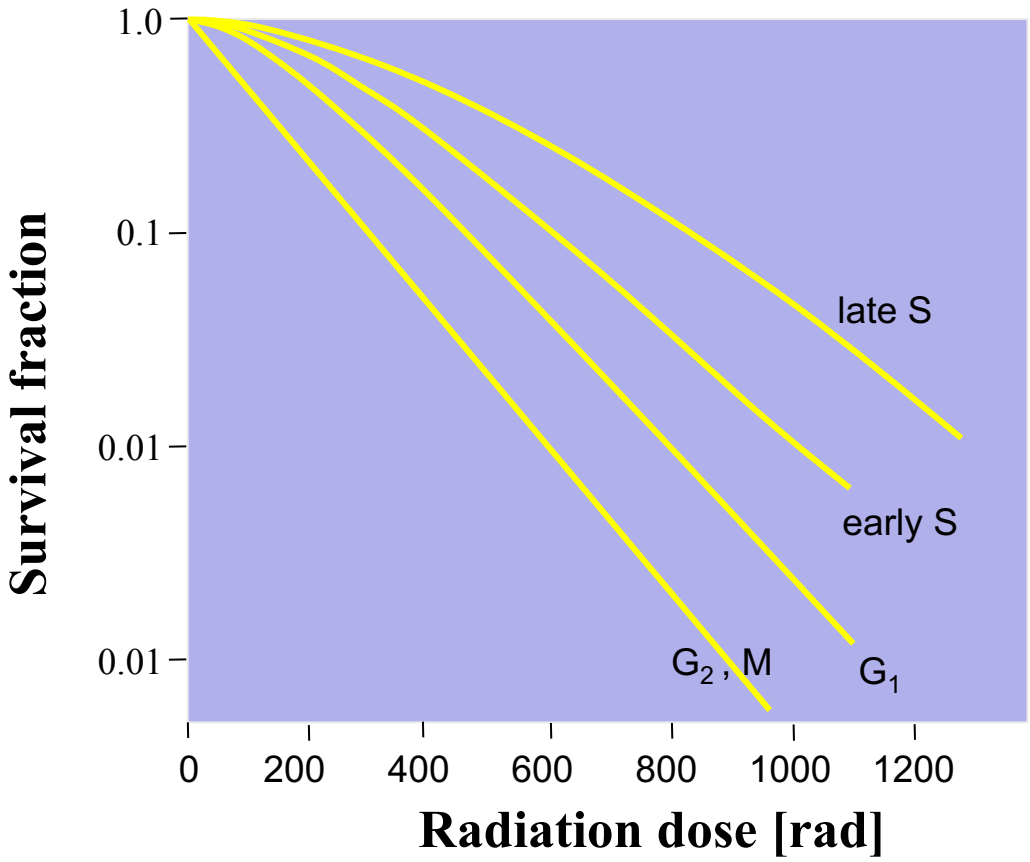
A-T: Ataxia teleangiectasia
GI, gastrointestinal tract

E. Hall, Radiobiology for the Radiologist, 5th edition, 2000

Dose-effect relationship

… known modifier related to **biological processes**

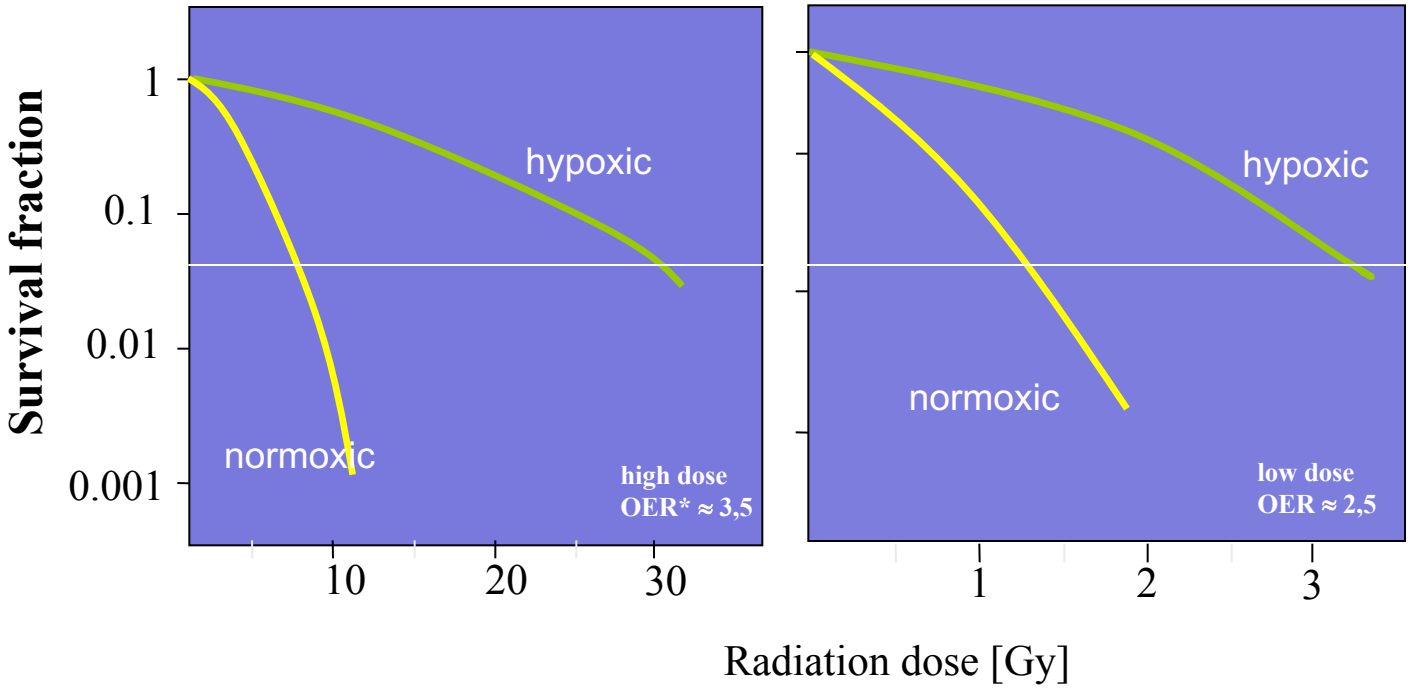
Cell cycle dependency



Sinclair, 1968, modified

Dose-effect relationship

… known modifier related to **biological processes**



oxygenation

Palcic and Skarsgard, 1984, modified
**OER, oxygen enhancement ratio*

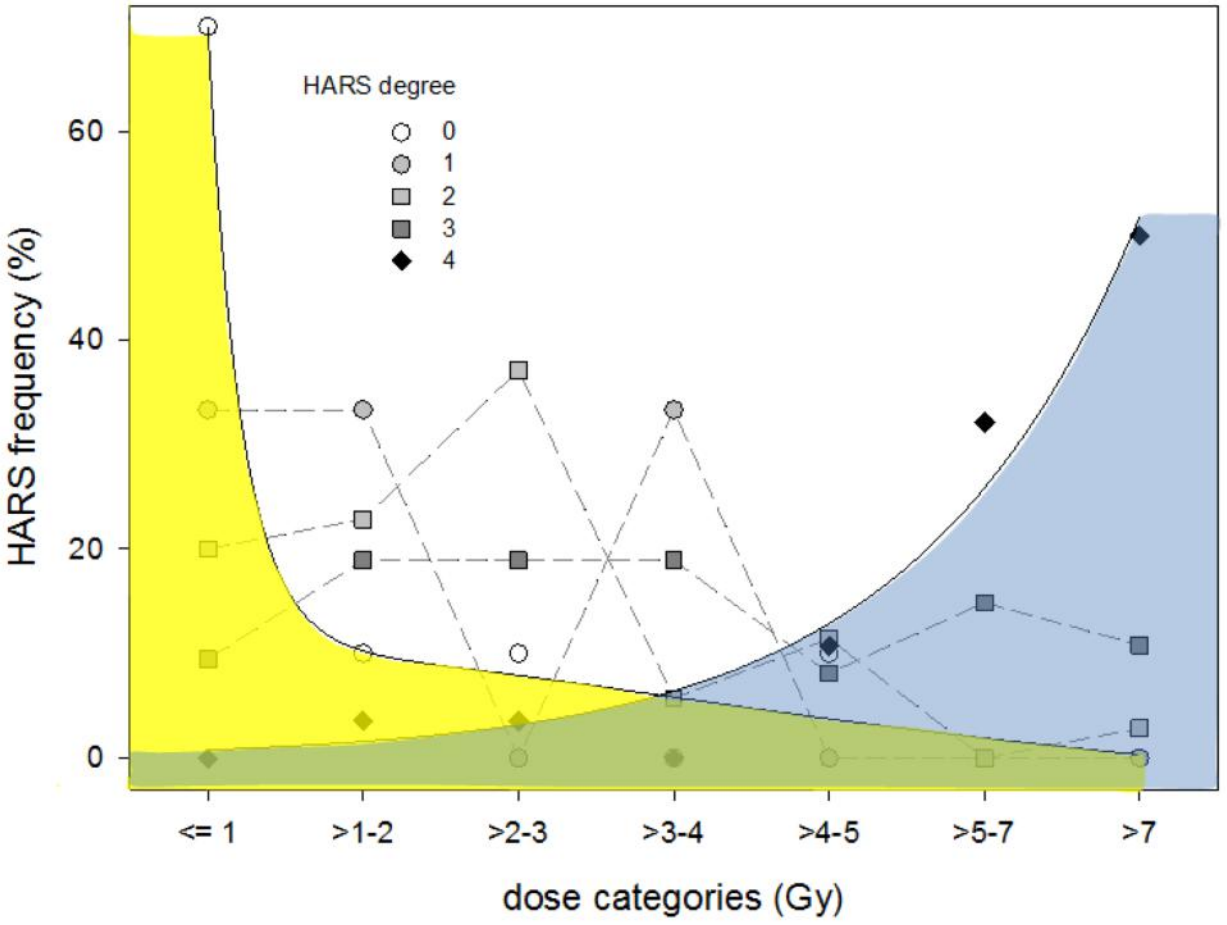
Dose-effect relationship

… known modifier related to
EXPOSURE & BIOLOGICAL PROCESSES

1. radiation quality
2. fractionated exposure
3. dose rate
4. partial/total body irradiation
5. homogenous/inhomogenous exposure
6. external/internal contamination

7. radiosensitivity
8. cell cycle dependency
9. oxygenation

Dose – effect prediction, real case histories (whole body, single dose)



≤ 1 Gy, predominantly H0

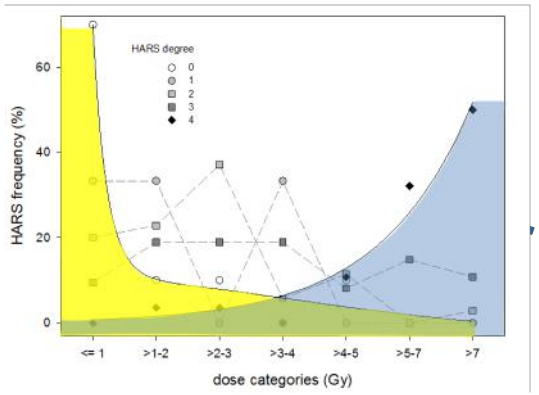
> 5 Gy predominantly H3/4

> 1-5 Gy either H1, H2 or H3

Limited significance of dose for clinical outcome prediction

Port et al. RadRes 2018

Early diagnosis of deterministic effects



... detour ...

clinical signs & symptoms for triage

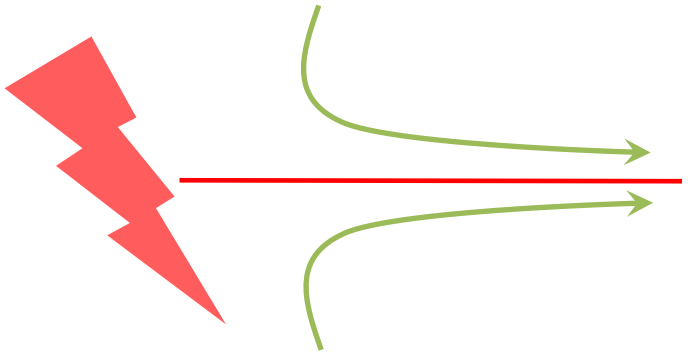
... short cut

H-ARS

Doerr et al. RadRes, 2017

~~Dose~~ – effect prediction

radiation quality
fractionated exposure
dose rate
partial/total body irradiation
homogenous/inhomogenous exposure
external/internal contamination



- clinical signs & symptoms*
- gene expression*
- protein expression*

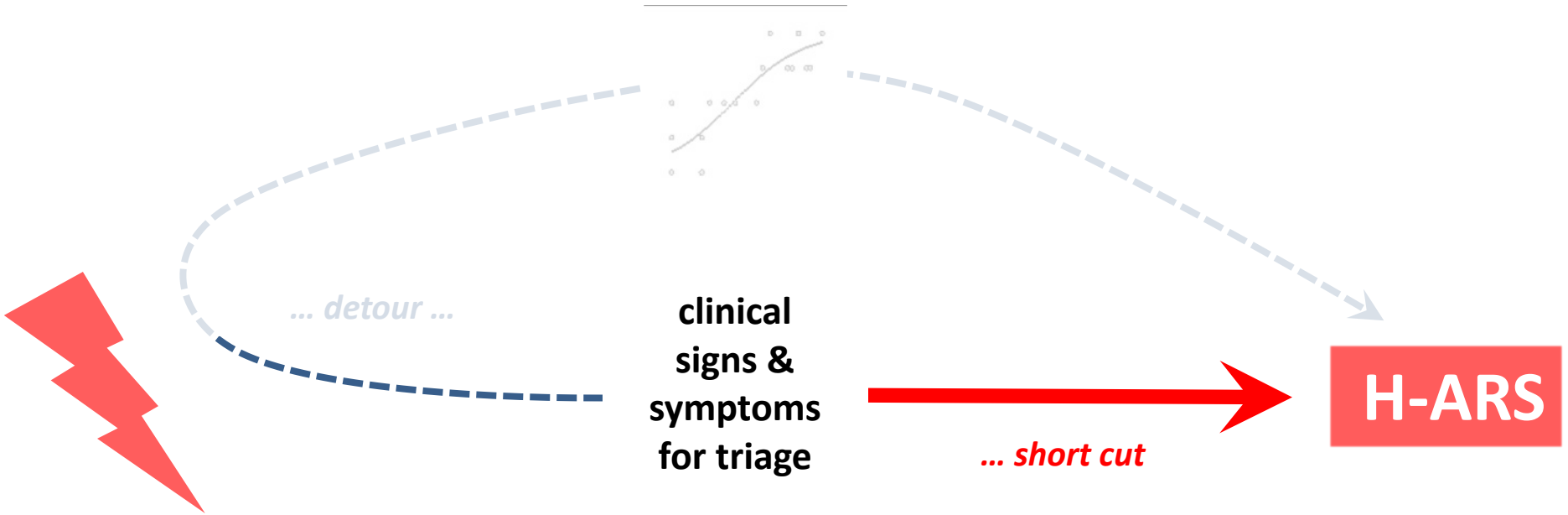
→ HARS (effect)

radiosensitivity
cell cycle dependency
oxygenation
.....

**bioindicators of effect*

Early diagnosis of deterministic effects

2015 EXERCISE



…integrating modifiers of exposure and biological processes for effect prediction