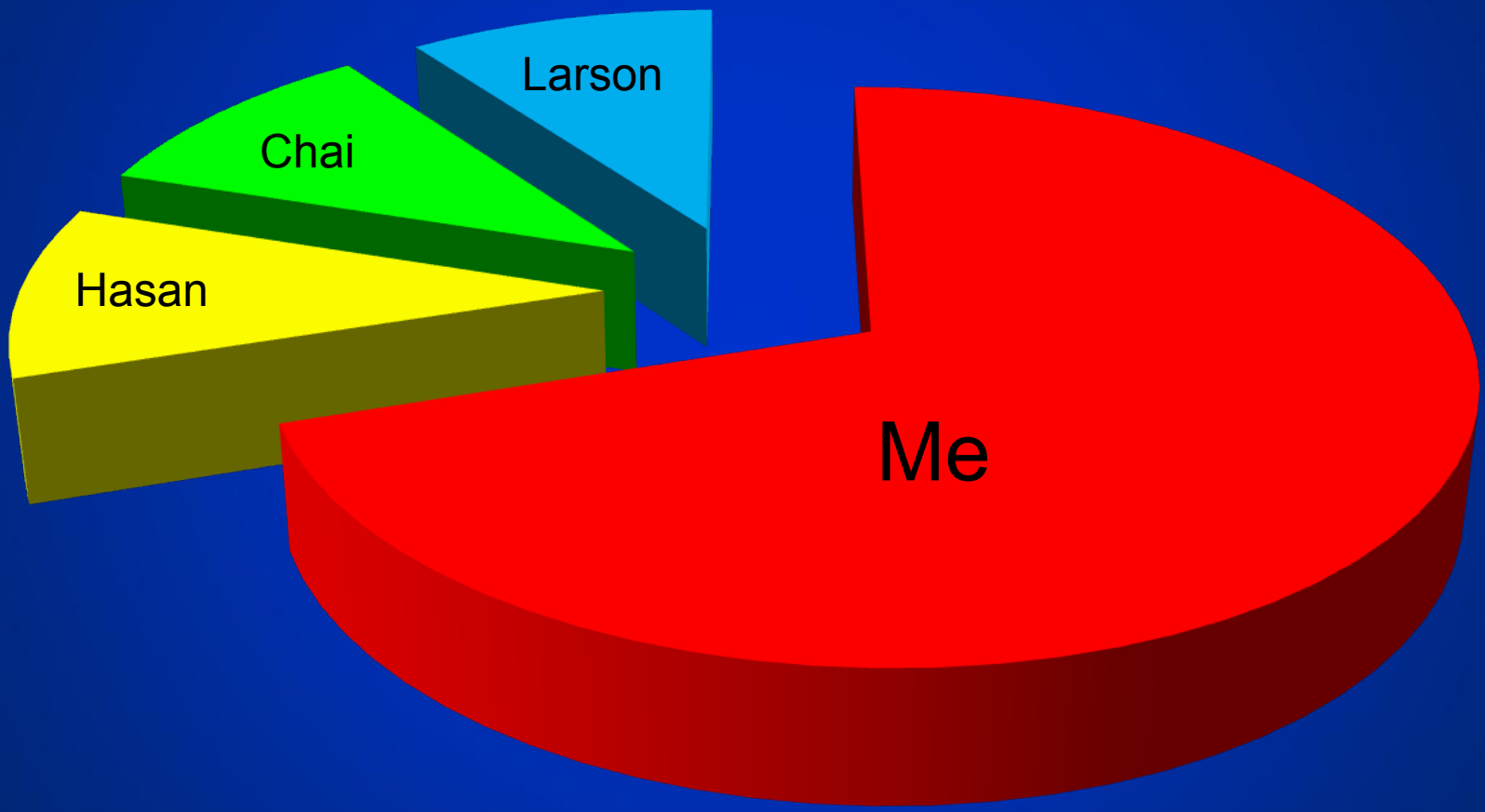
Radiation and Haematologic Neoplasms

Robert Peter Gale MD PhD DSc(hc) FACP, FRSM

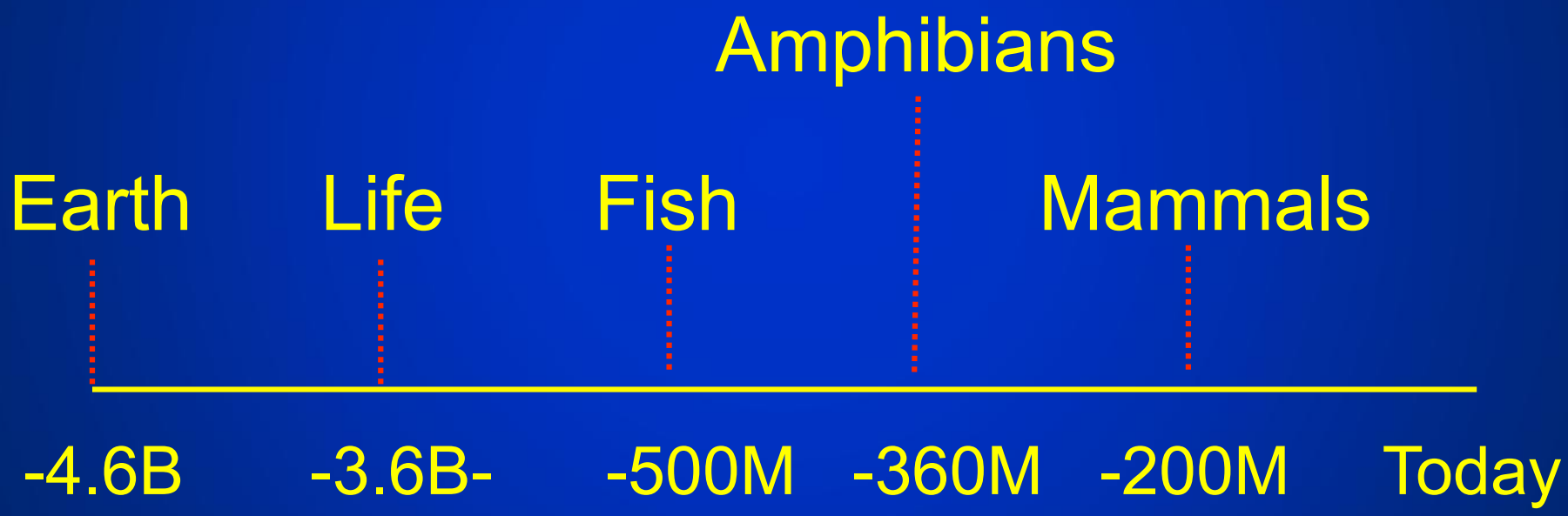
Imperial College London
UCLA Medical Center
Celgene Corp

Esce dalla porta e rientra dalla finestra

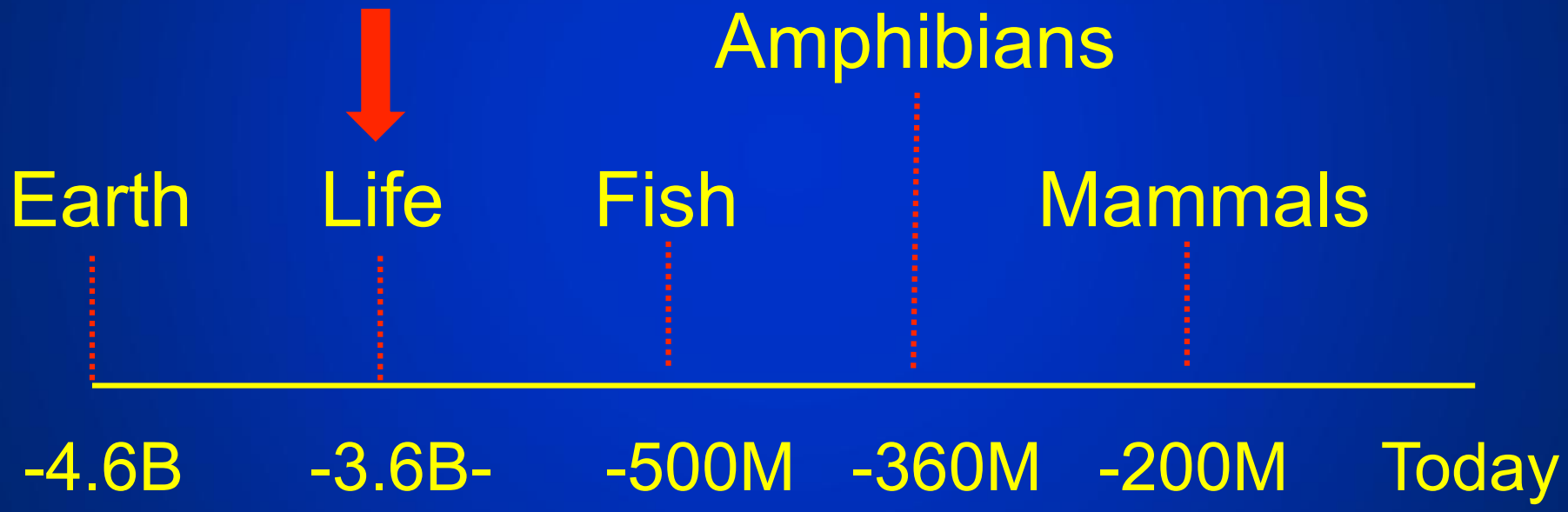
1430-1600 h CEST



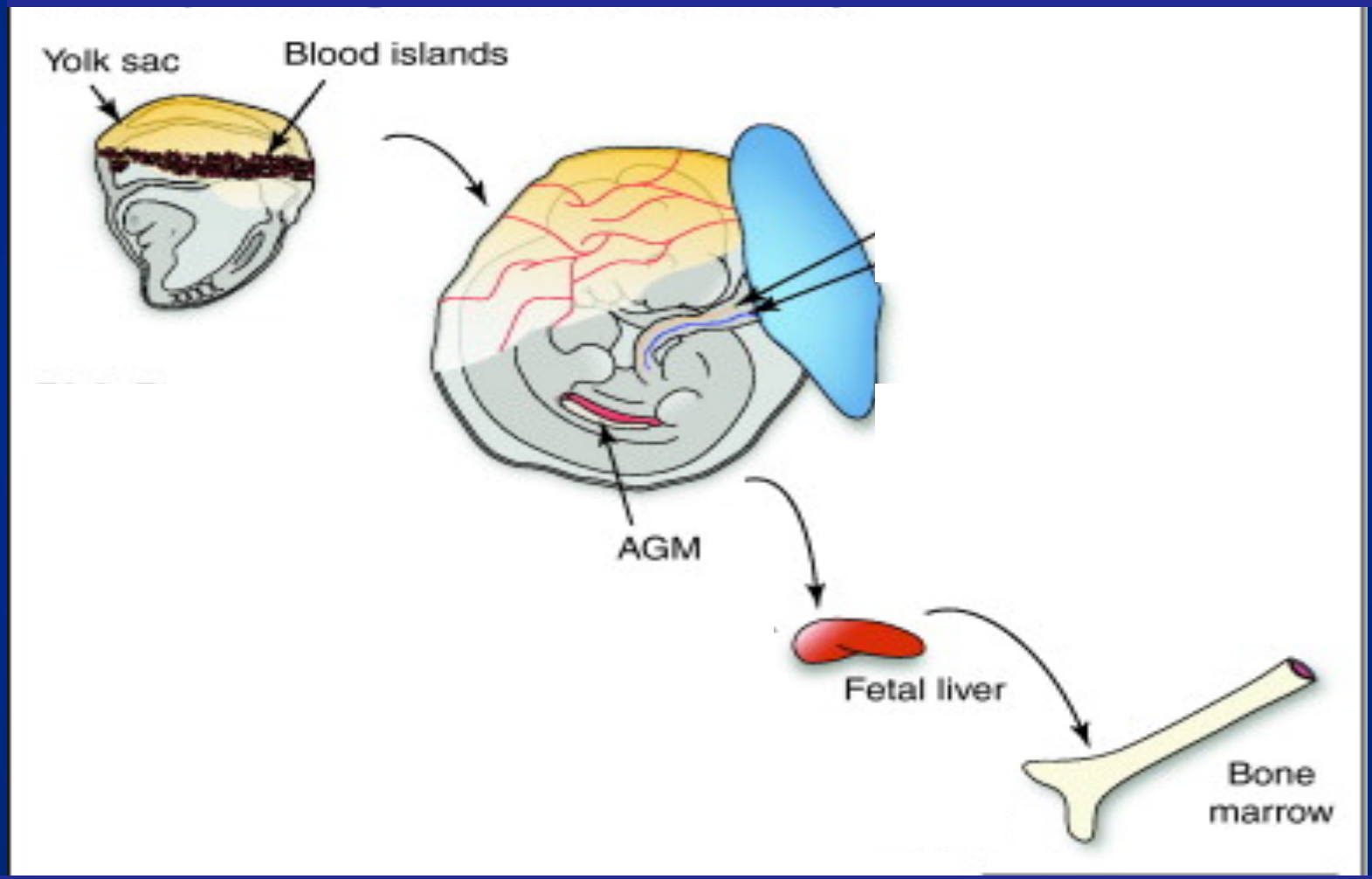
Origin of Life



Origin of Life



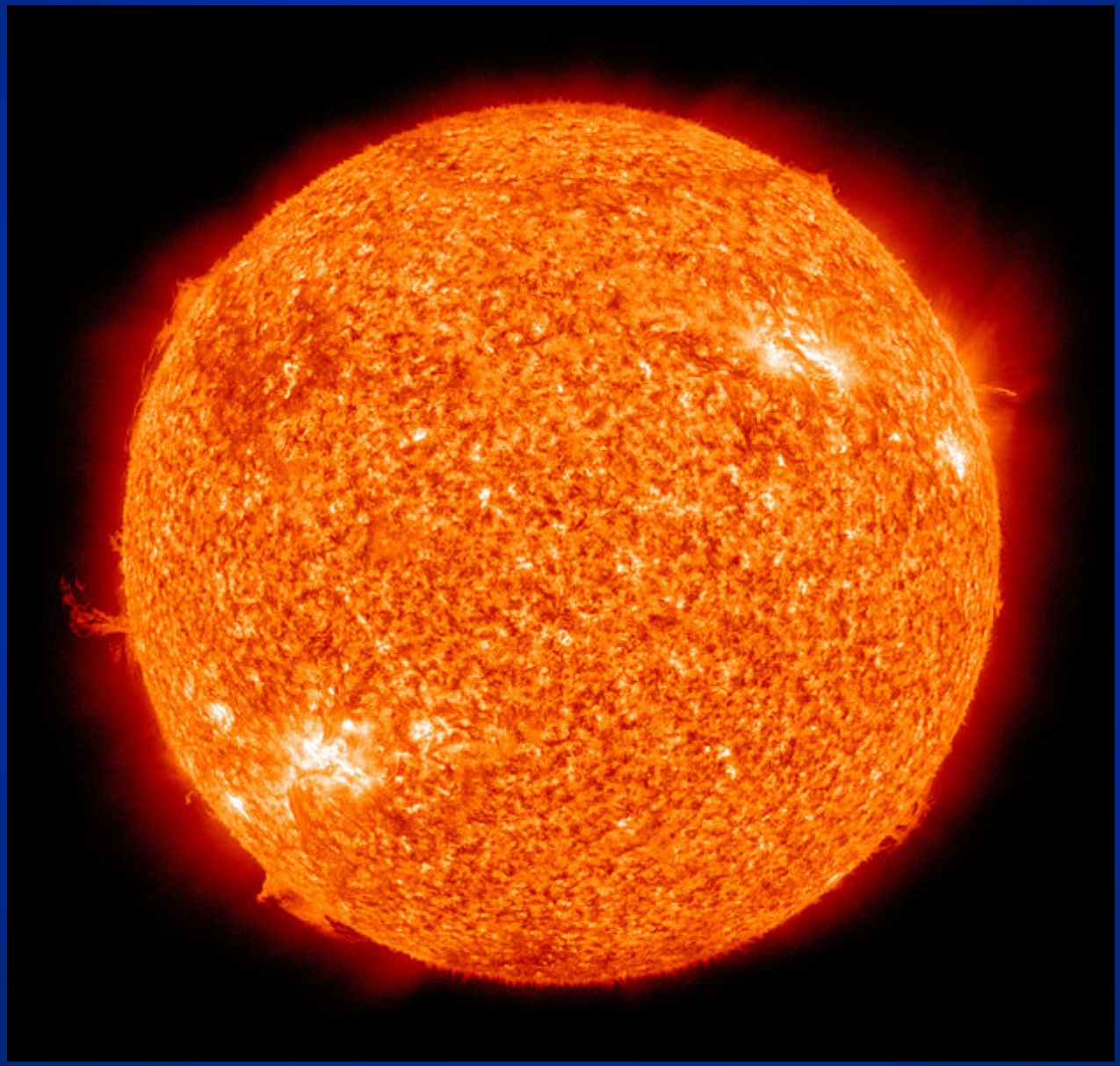
Hematopoietic Development



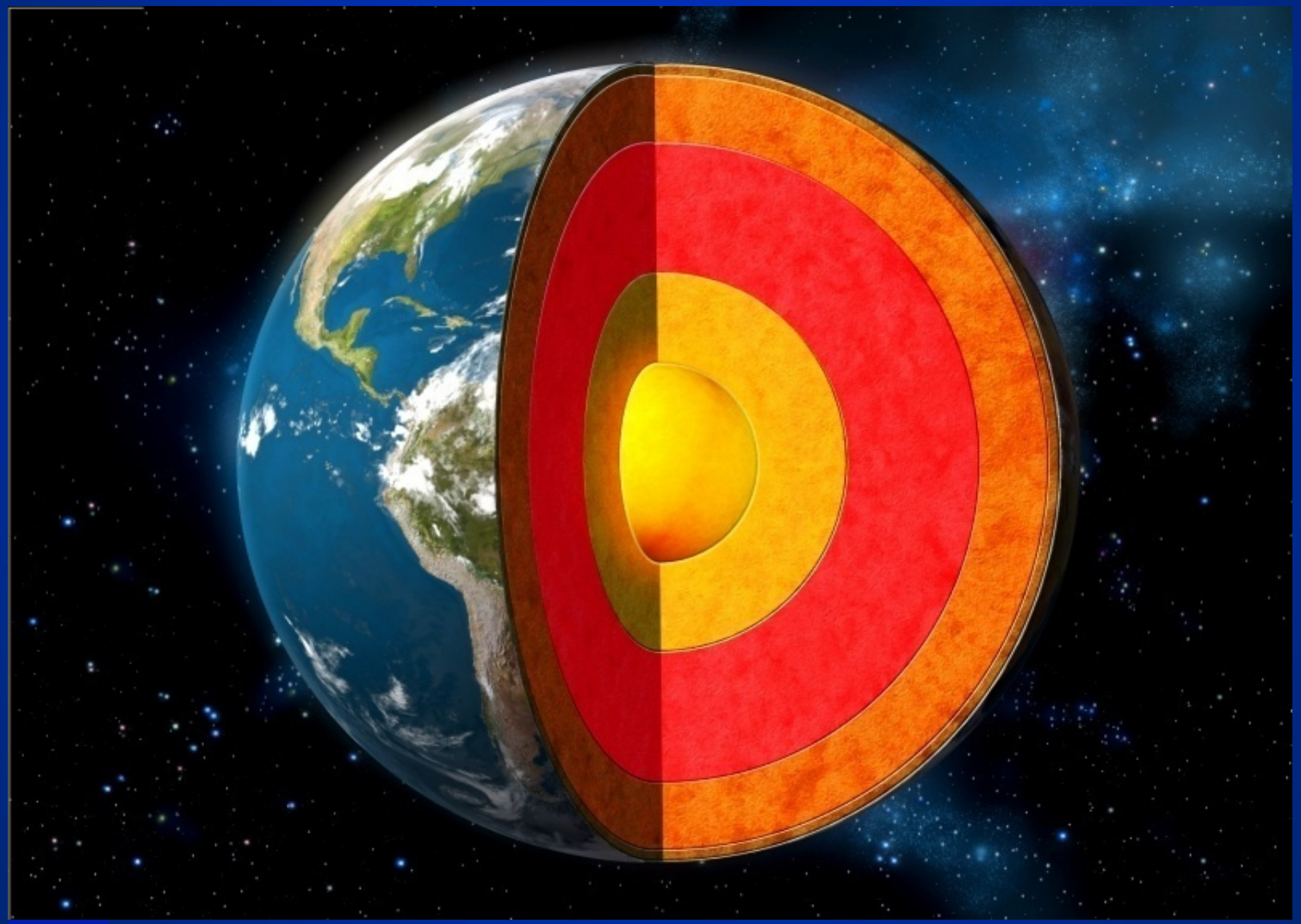
3.6 B years ago cosmic, solar and terrestrial radiation levels were much higher than today

Cosmic Radiations

Solar Radiations



Terrestrial Radiations



Water and bone are good radiation shields

Aquatic Frog

Aquatic Frog

Terrestrial Frog

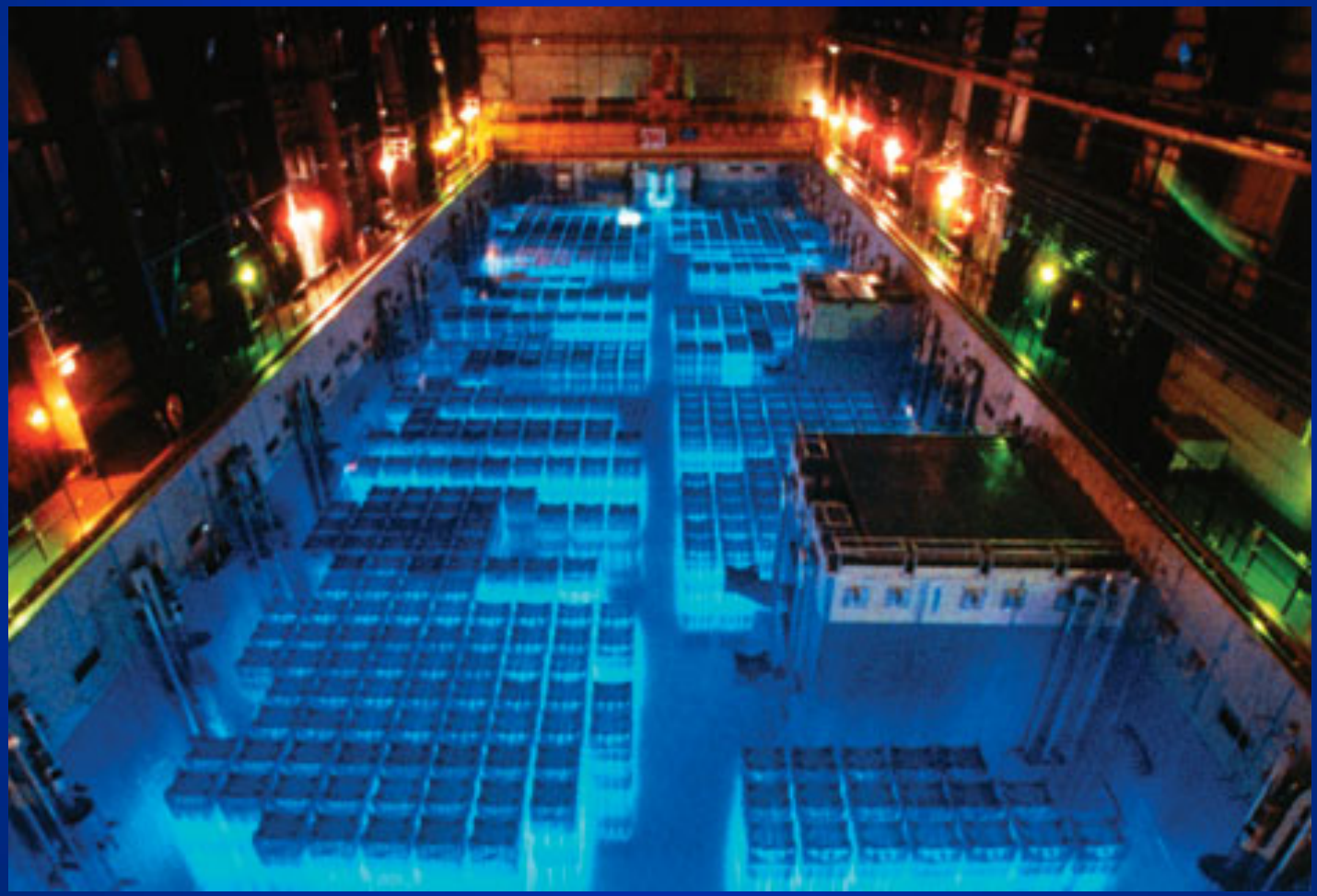
Terrestrial Frog

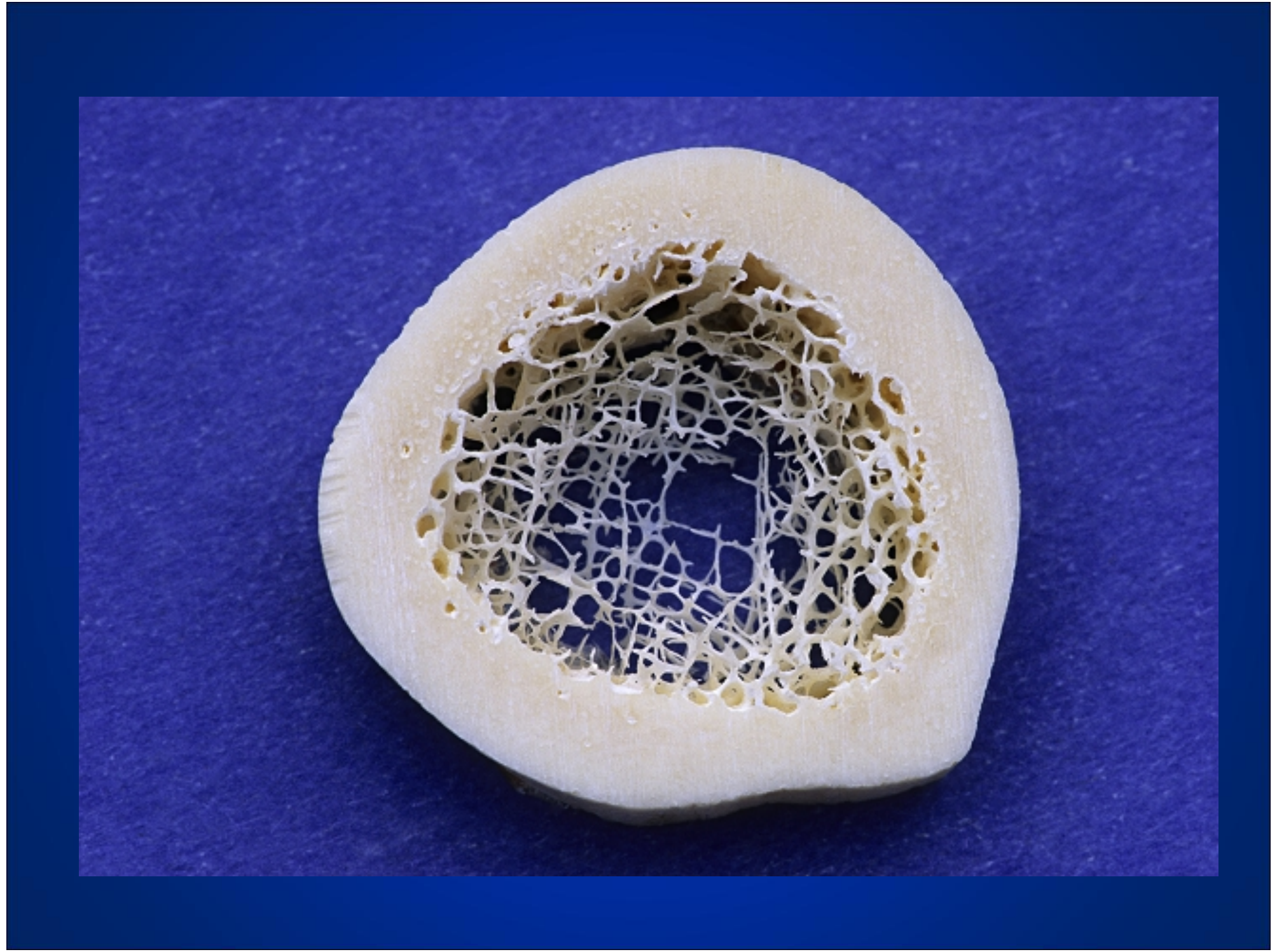
Tyrannosaurus rex

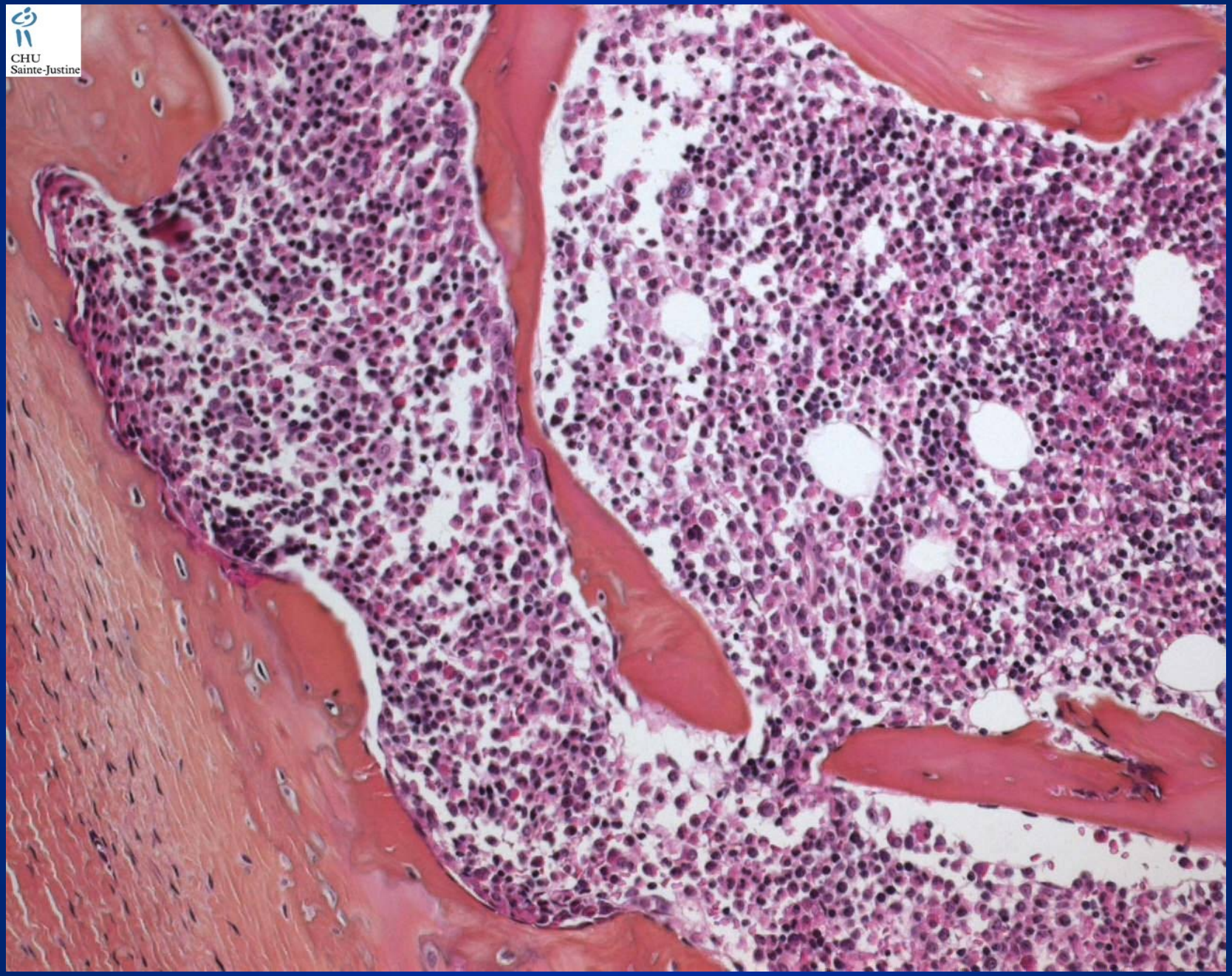
Schweitzer Science 2005

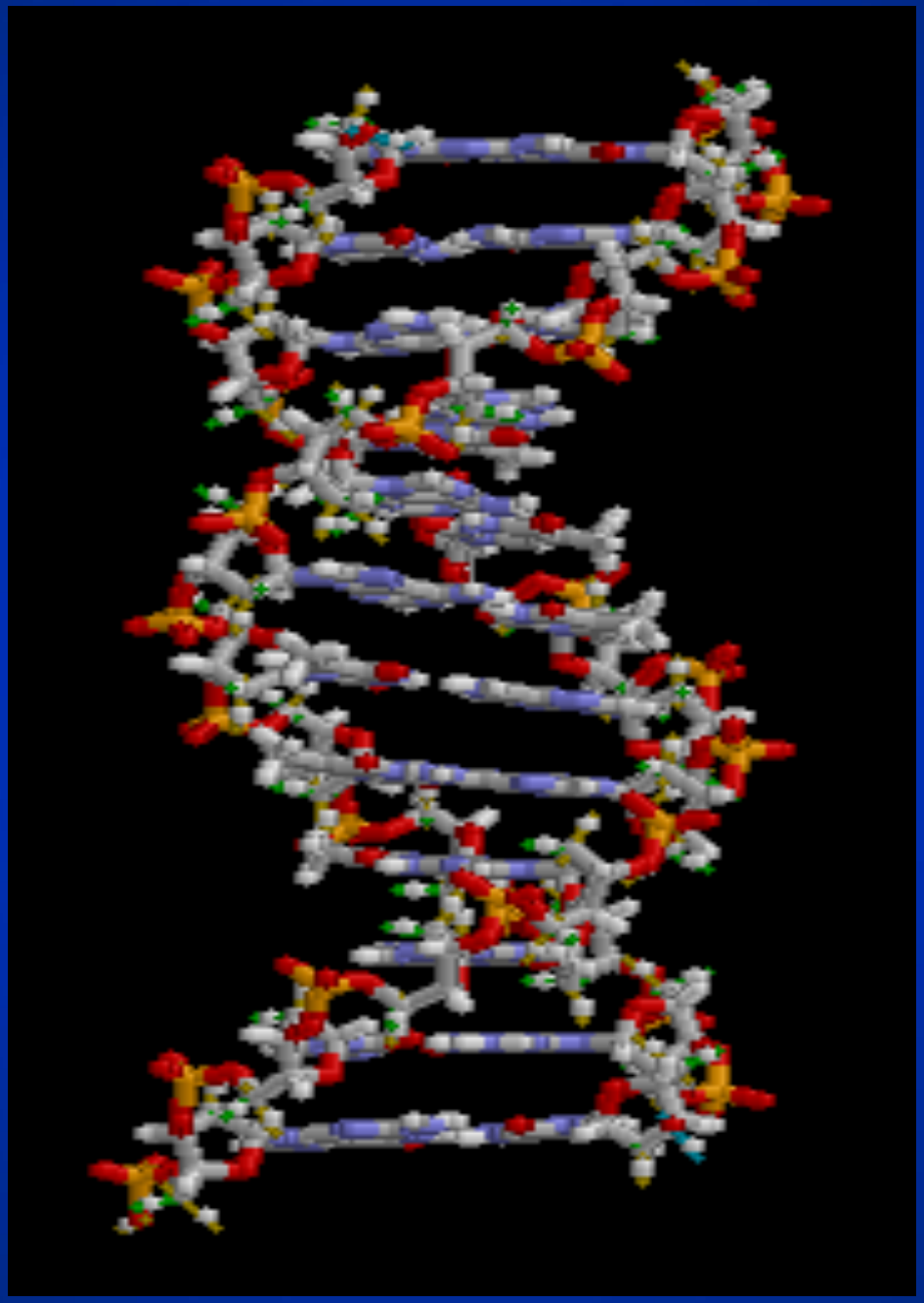
Do you have any idea how fast you were evolving?”

Spent Nuclear Fuel

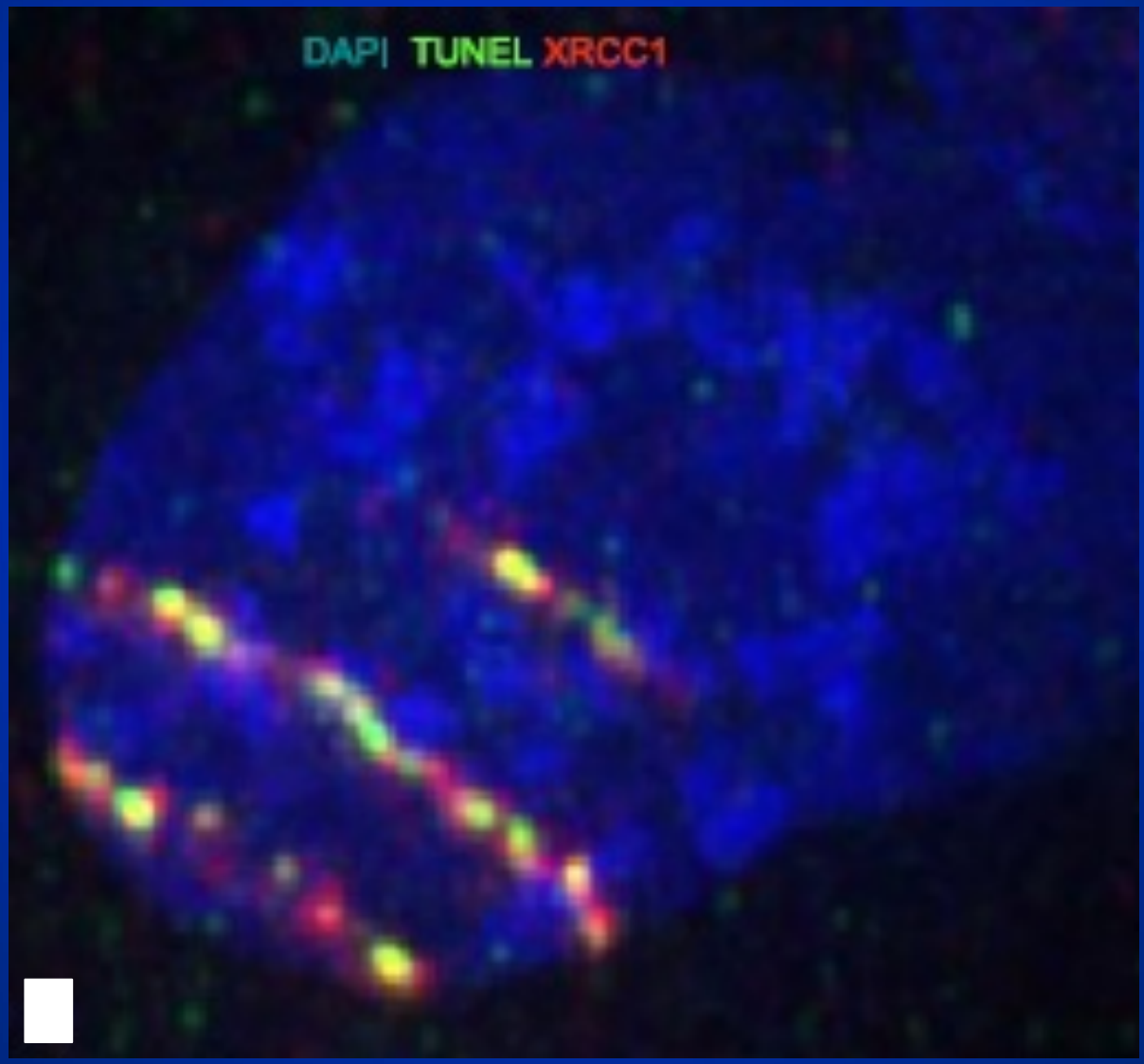





CHU
Sainte-Justine



Uranium Ion Paths

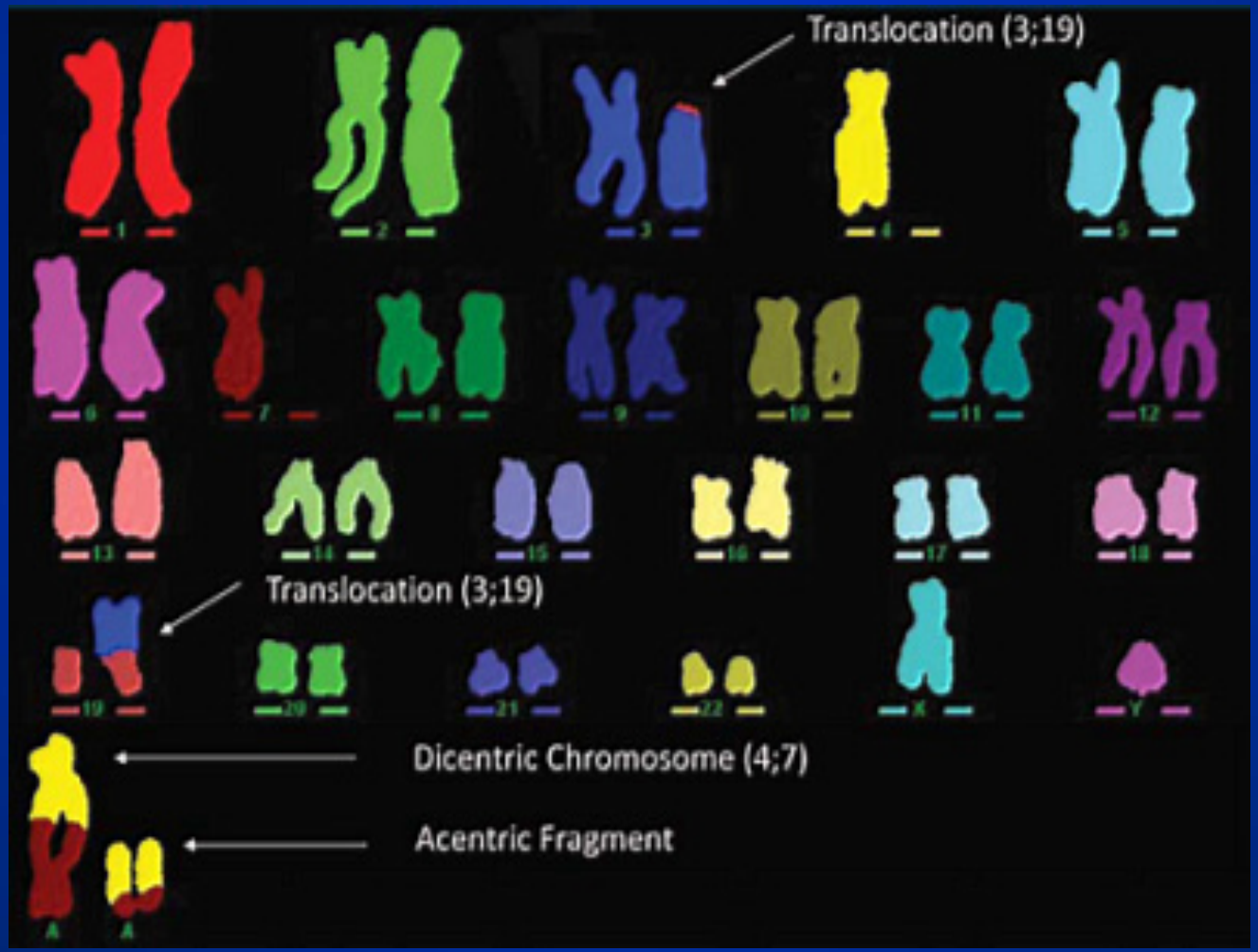


Durante Health Phy 2012

1 Gy γ or photon radiation

1000 single-strand breaks
500 damaged bases
40 double-strand breaks
150 DNA-protein cross-links

Radiation-Induced Translocations



RUNX1/AML1

blood®

NEOPLASIA

Implications of somatic mutations in the *AML1* gene in radiation-associated and therapy-related myelodysplastic syndrome/acute myeloid leukemia

Hironori Harada, Yuka Harada, Hideo Tanaka, Akiro Kimura, and Toshiya Inaba

Radiation and Haematologic Neoplasms

Atomic bomb

Occupational exposures

Medical exposures

Terrestrial radiations

Radiation and Leukemia

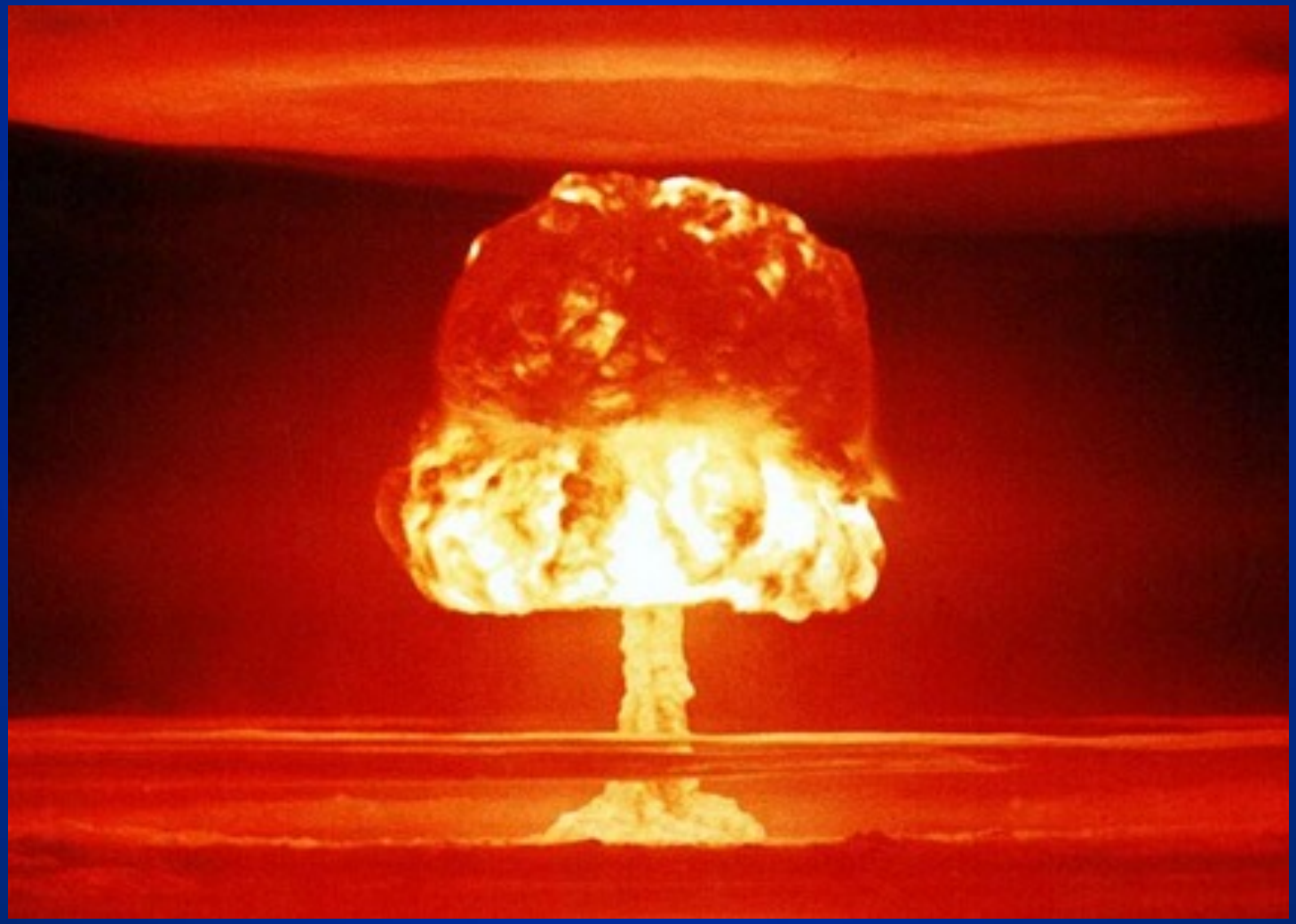
Atomic bomb

Occupational exposures

Medical exposures

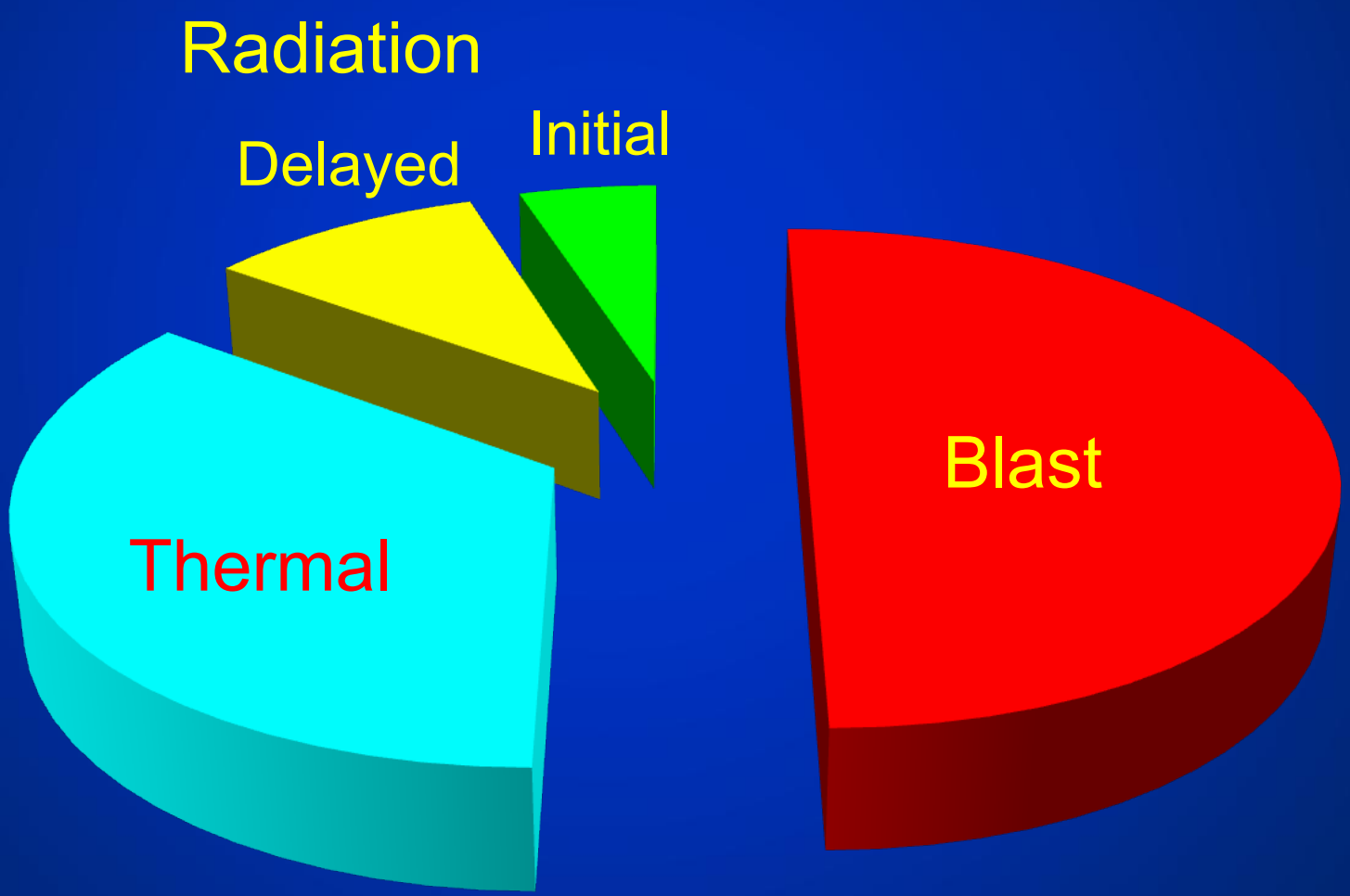
Terrestrial radiations

A-Bombs

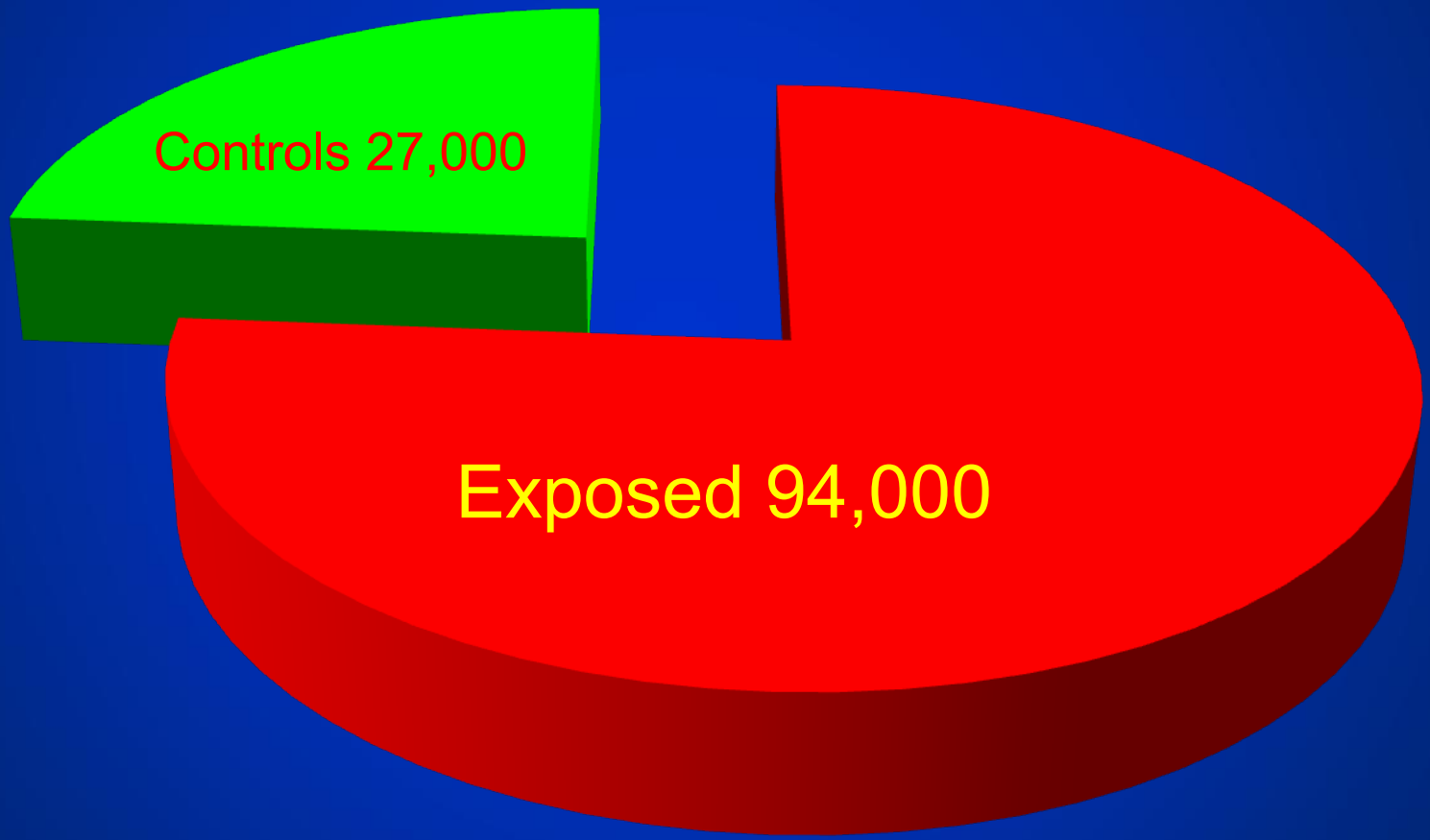


Hiroshima

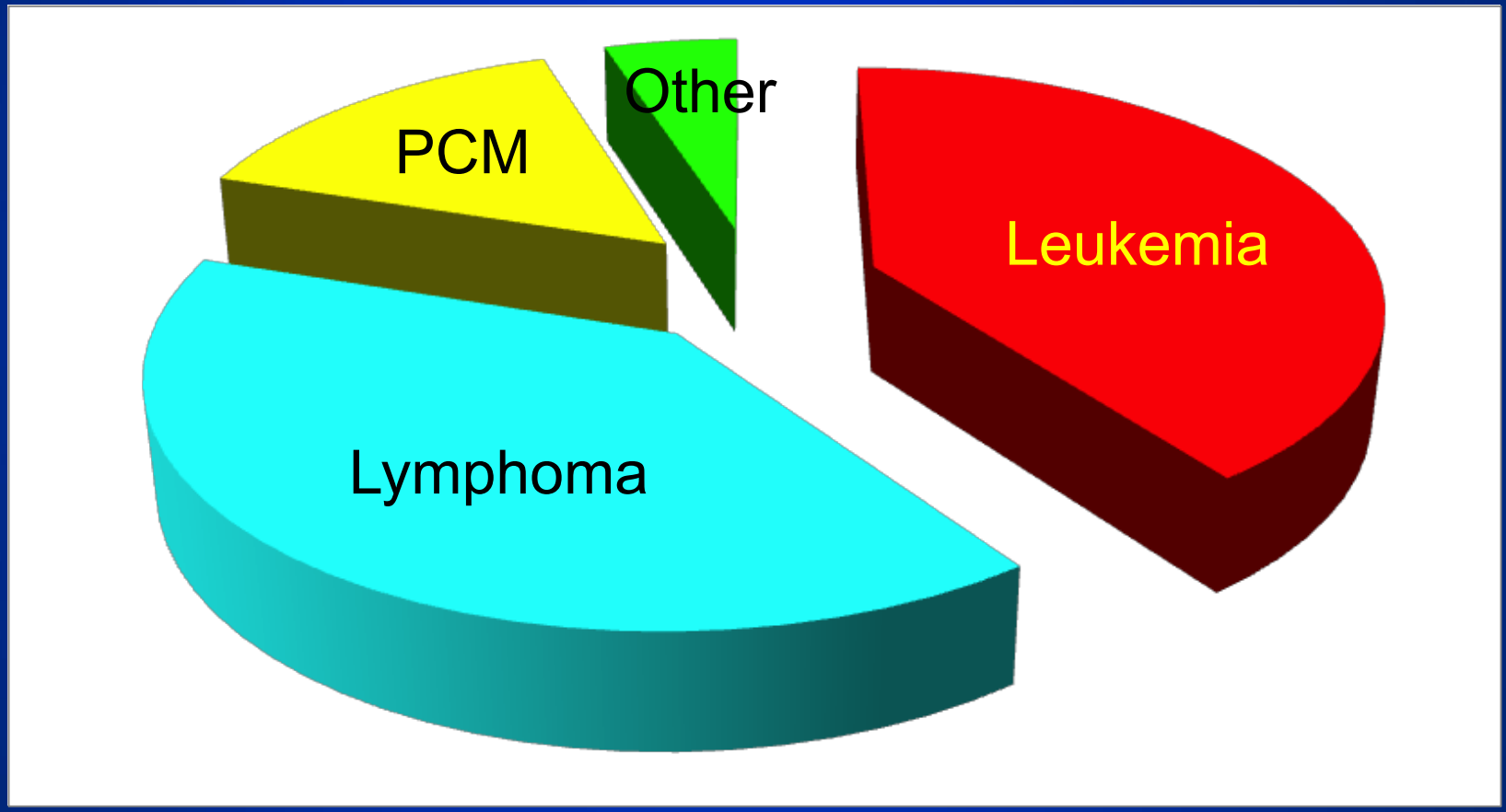
Energy Released



A-Bomb Life-Span Study



A-Bomb Lifespan Cohort



A-Bomb Lifespan Cohort

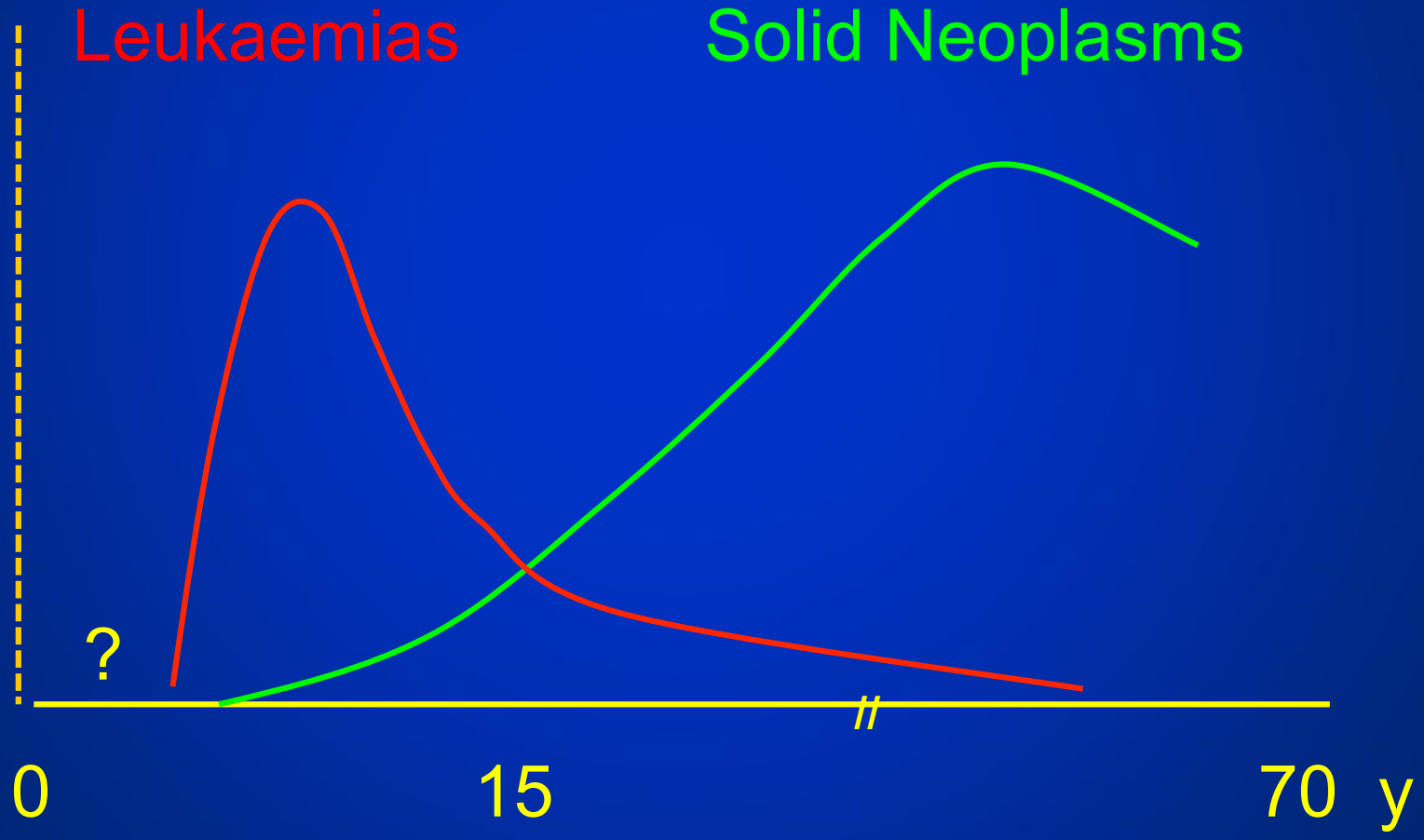
All	944
Leukemia	371
Lymphoma	437
PCM	76

Hsu Rad Res 2013

A-Bomb Lifespan Cohort

ALL	43
AML	176
CML	75
CLL	12
ATL*	47
NHL	402
HD	35
PCM	136

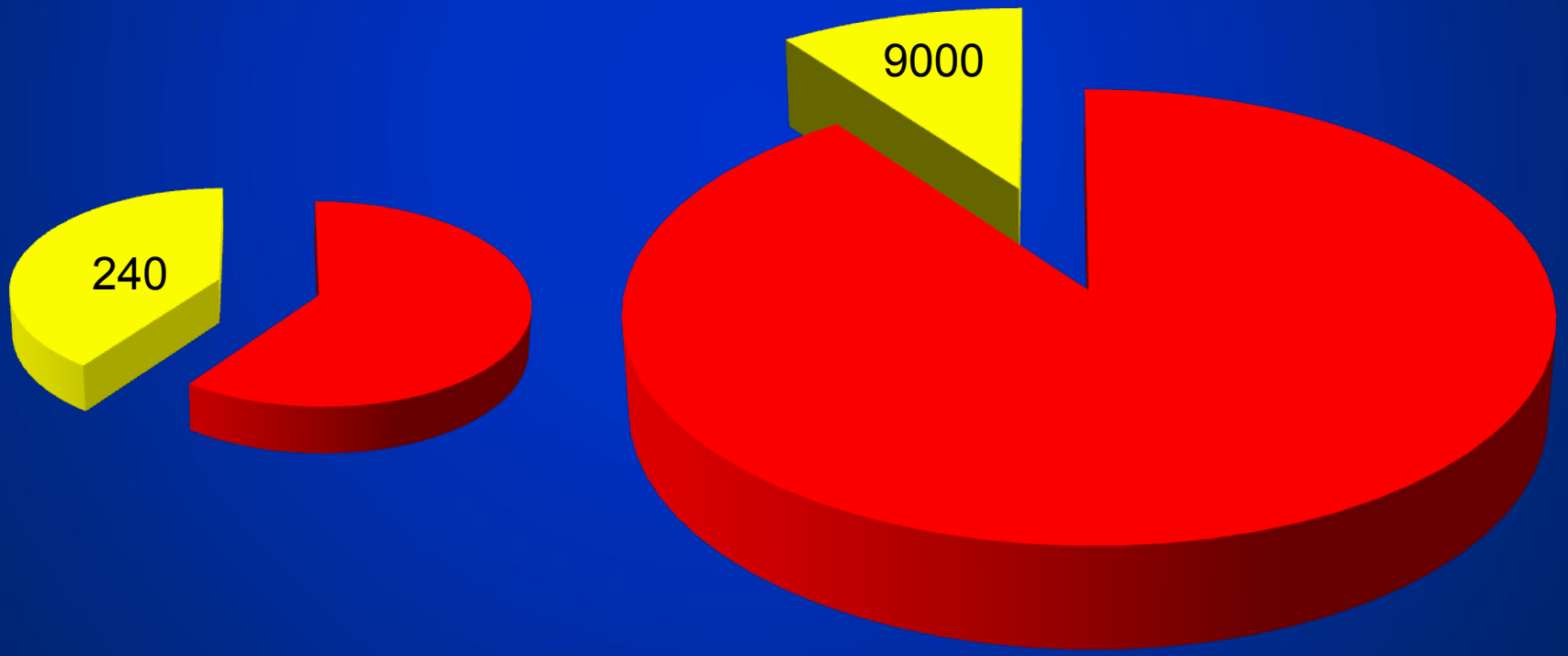
Time after A-Bombs



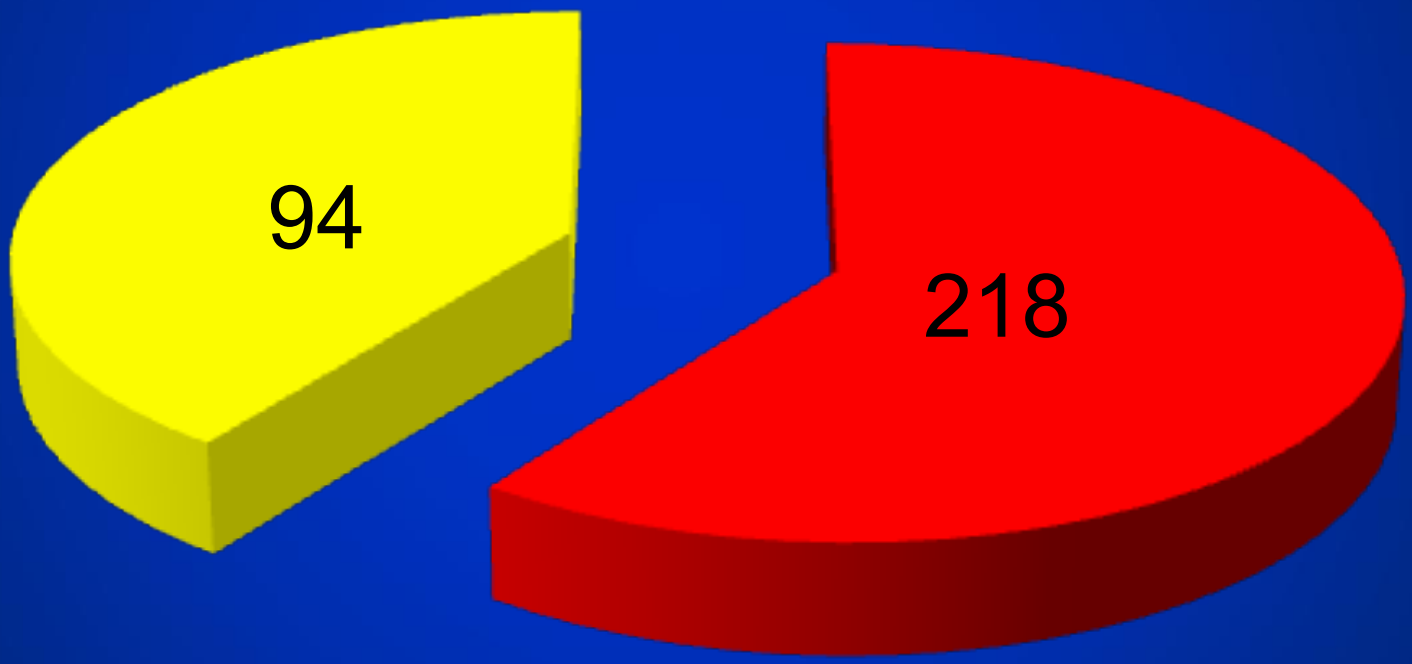
Cancers After A-Bombs

Leukaemias

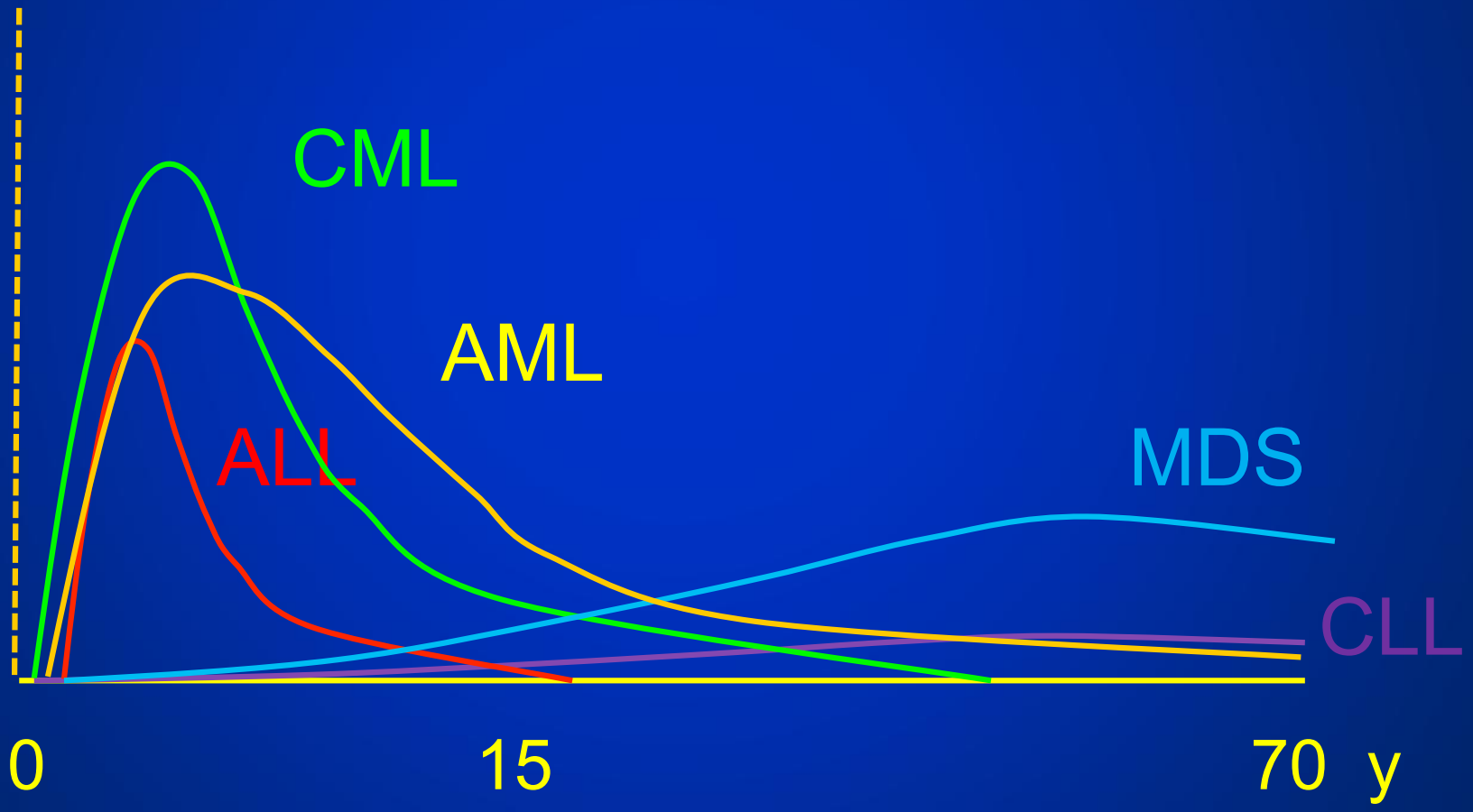
Solid Neoplasms



Leukaemias from A-Bombs (N=312)



Time after A-Bombs



Temporal Patters of Leukaemia Risk

Cohort	ALL	AML	CML
1950-1960	28%	25%	48%
1961-1980	3%	50%	28%
1981-2001	1%	73%	15%

Variables Associate with Leukaemia-Risk

Dose

Quality

Field

Dose-rate

Fractionation

Physical-chemical form

Variables Associate with Leukaemia-Risk

Dose

Quality

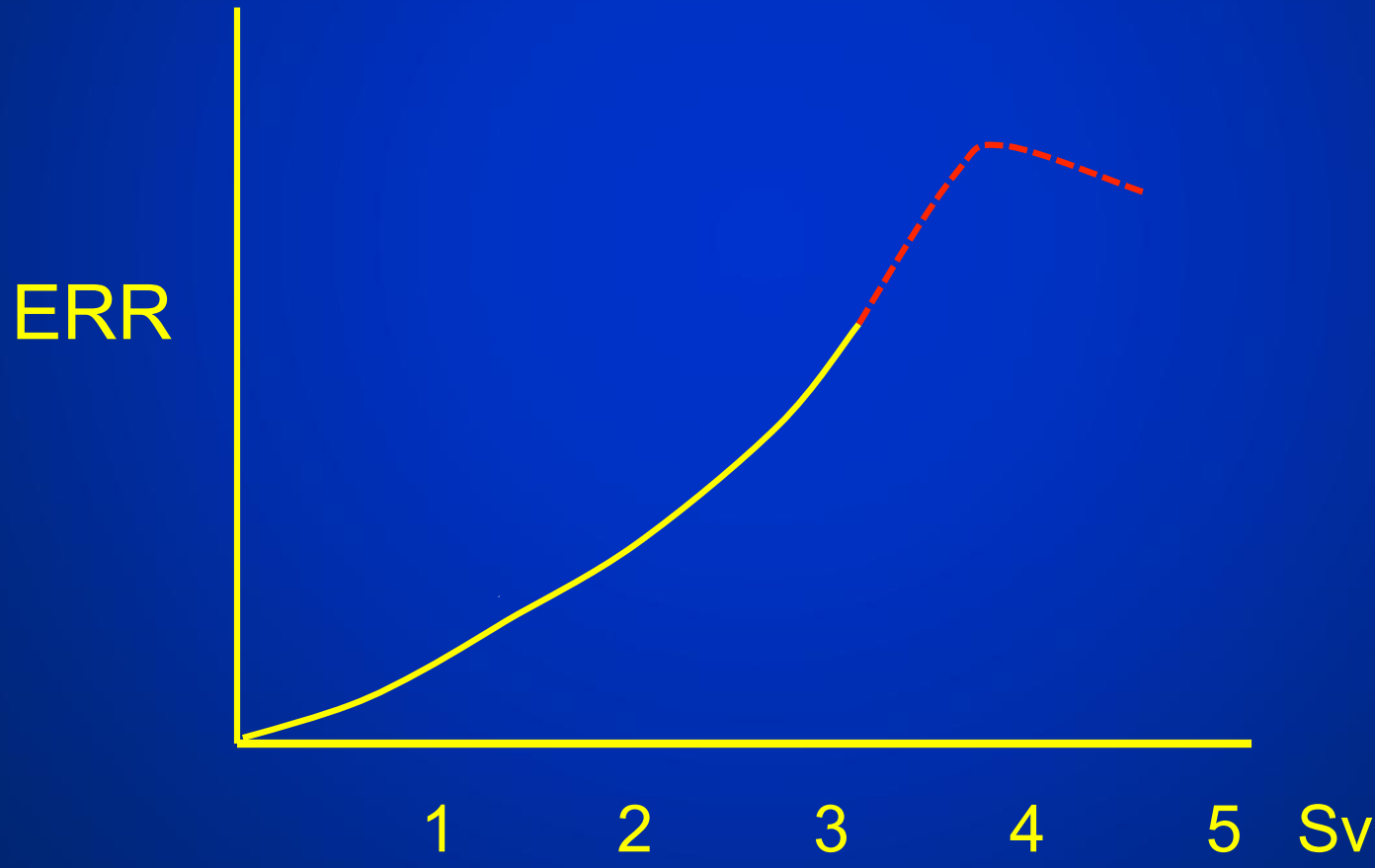
Field

Dose-rate

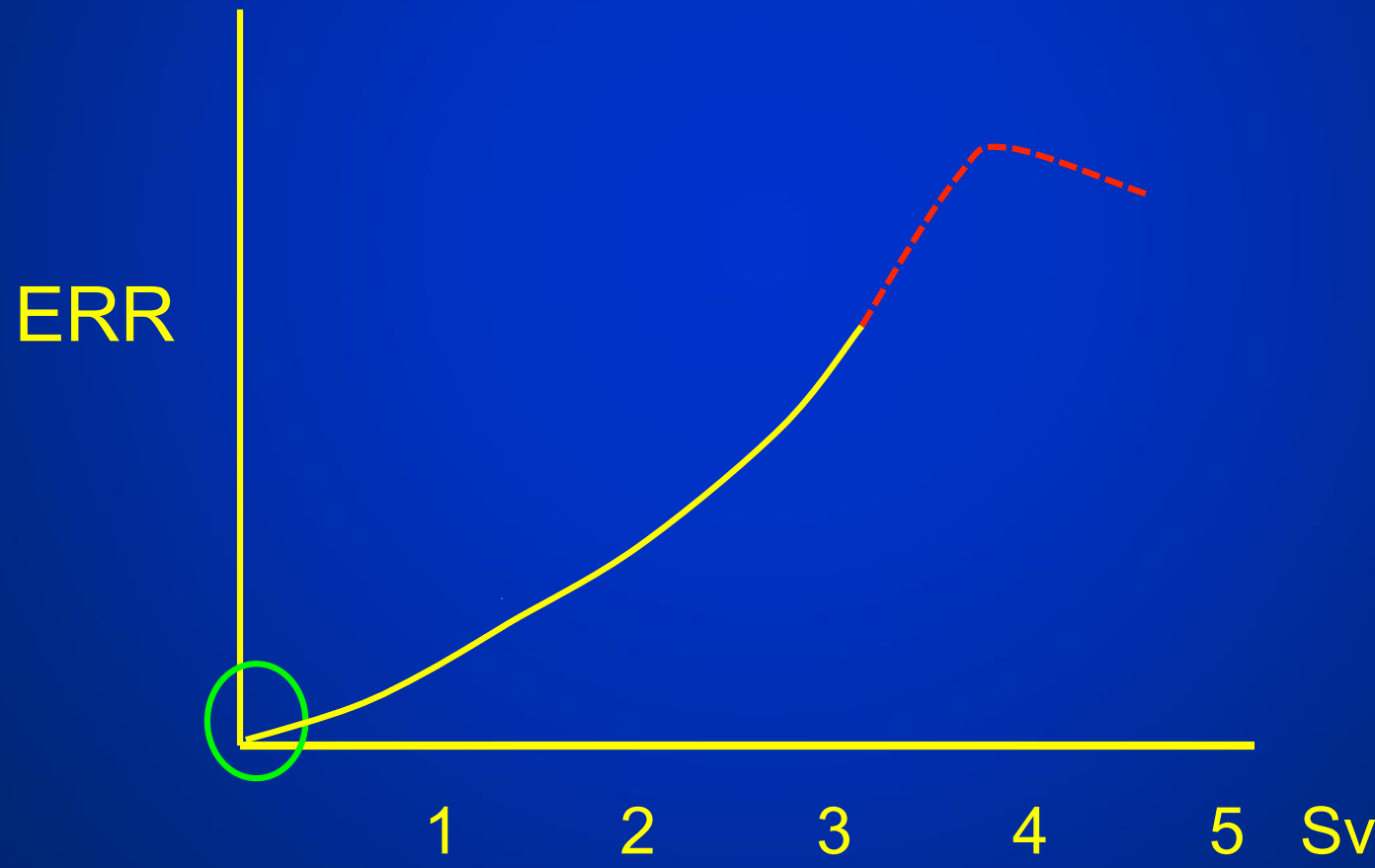
Fractionation

Physical-chemical form

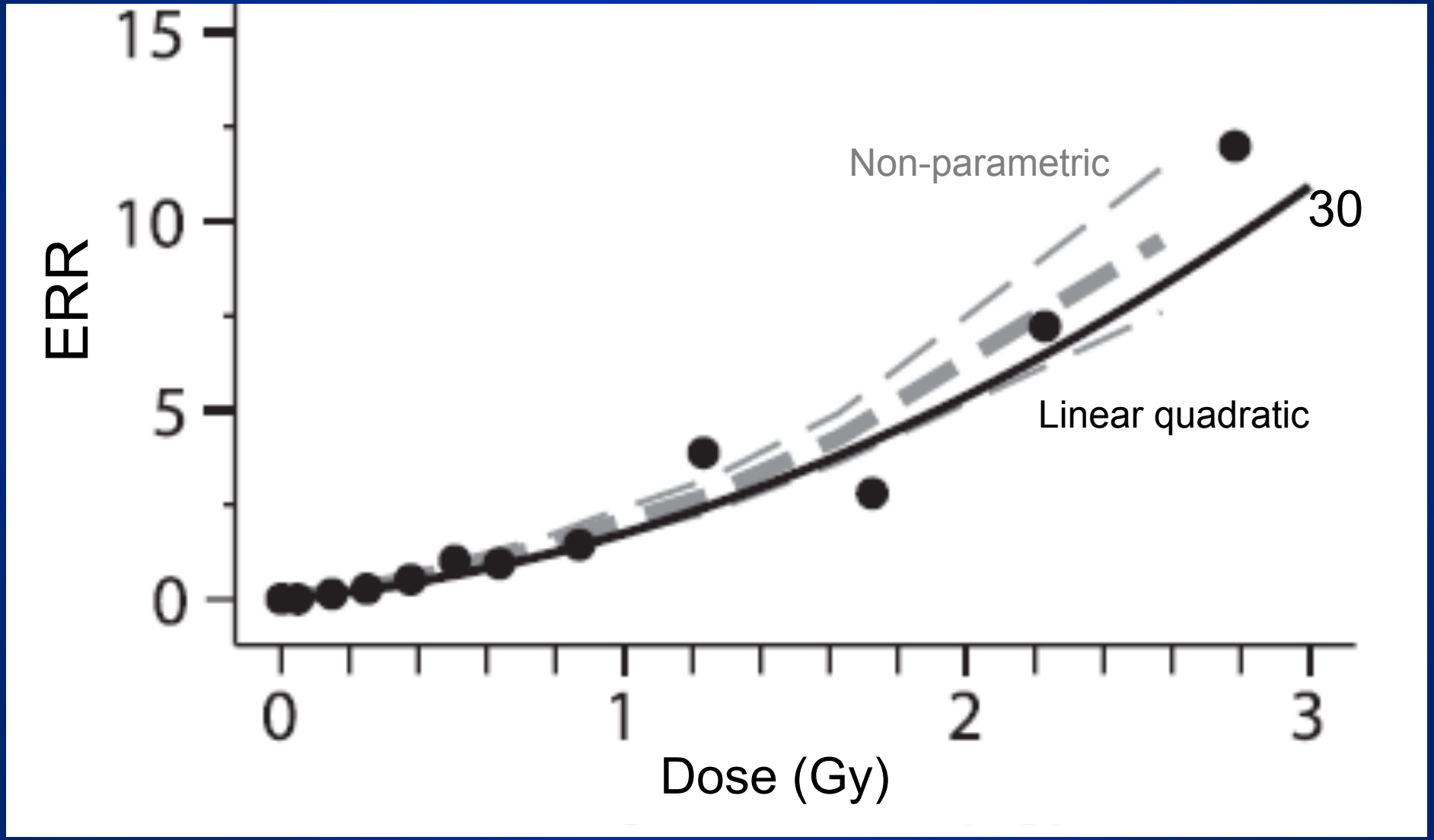
Dose-Response Curve for Leukaemia in A-Bomb Survivors



Dose-Response Curve for Leukaemia in A-Bomb Survivors



Leukaemia Dose Response



Fitted Cases of Leukaemia

Dose (Gy)	Background	Excess
<0.005	117	0.1
0.1	61	4
0.2	14	4
0.5	14	11
1	8	18
2	4	28
>2	2	29

Fitted Cases of Leukaemia

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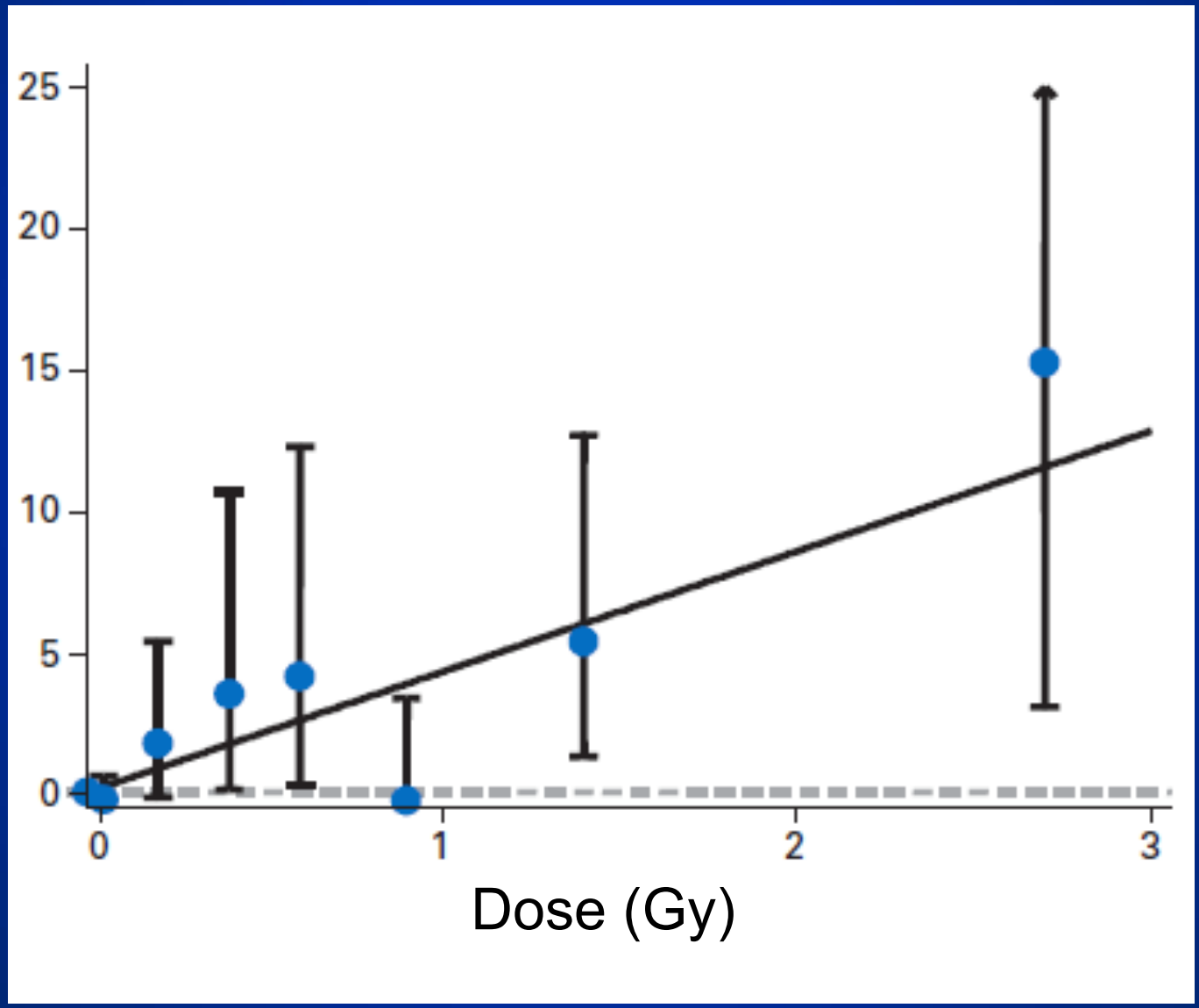
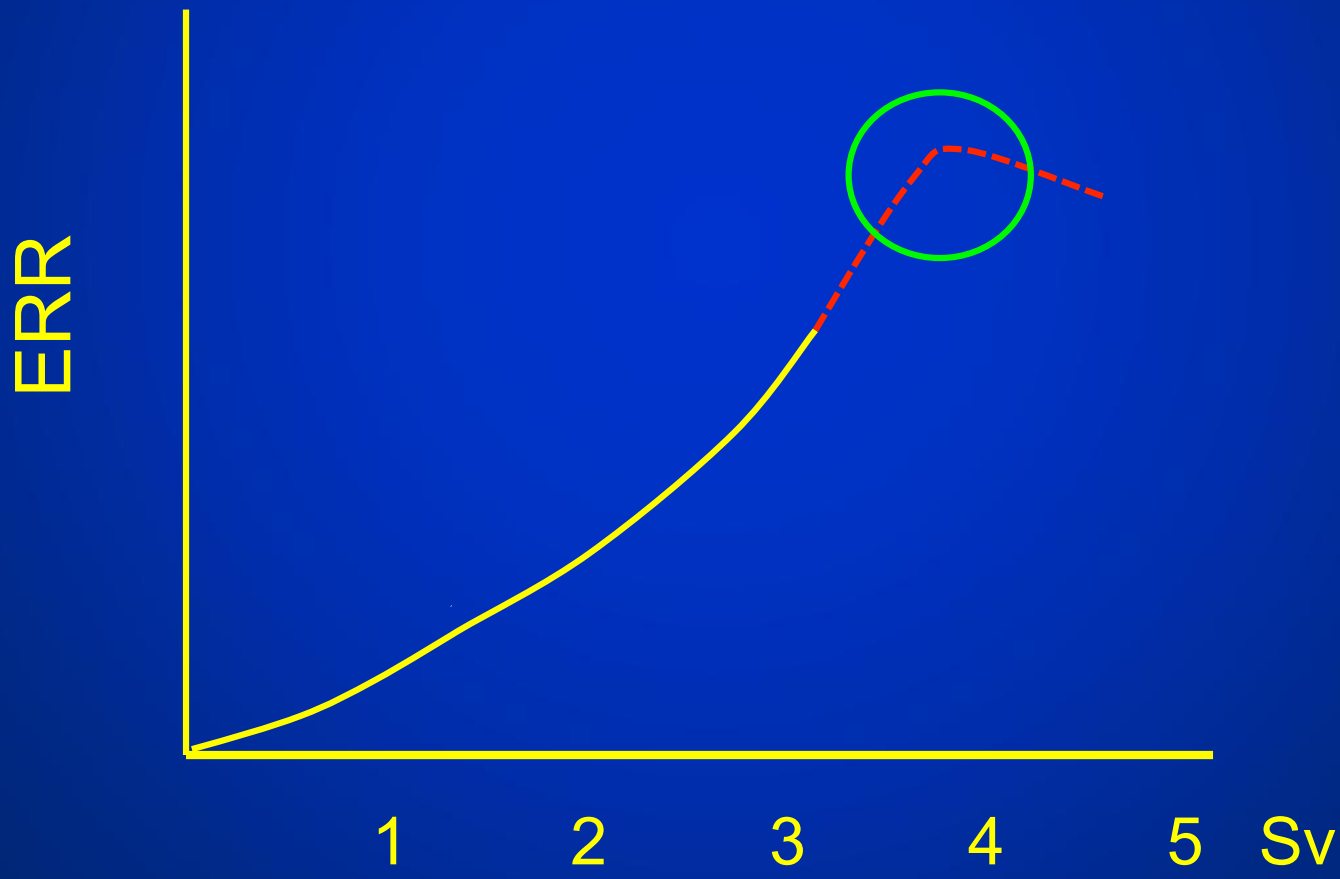
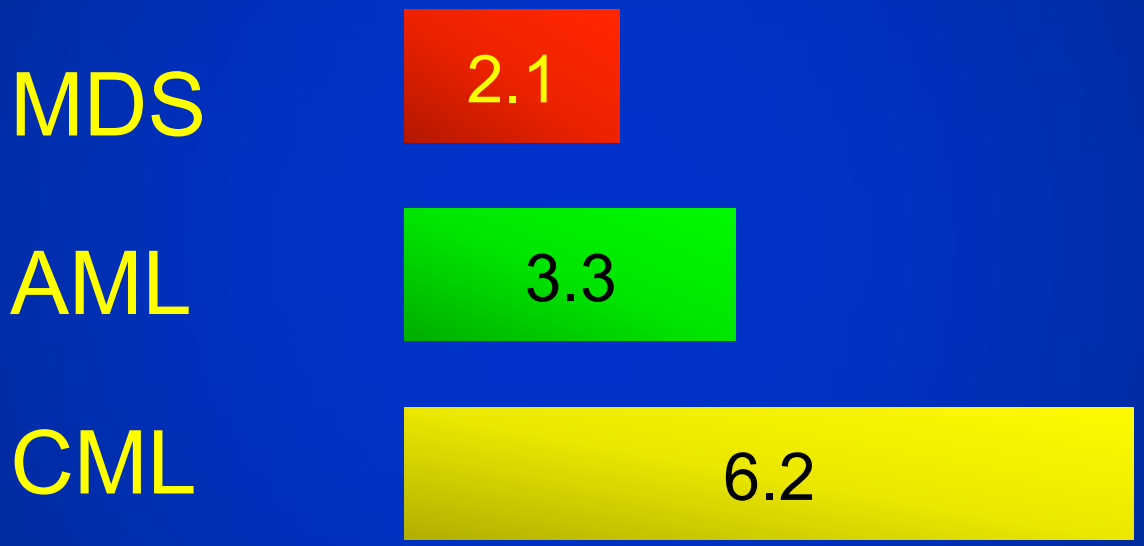
MDS Dose-Response



Dose-Response Curve for Leukaemia in A-Bomb Survivors



Excess Relative Risk per Sv



Host Variables Associated with Leukaemia-Risk

Age

Sex

Genetic susceptibility

Intrinsic risk

Host Variables Associated with Leukaemia-Risk

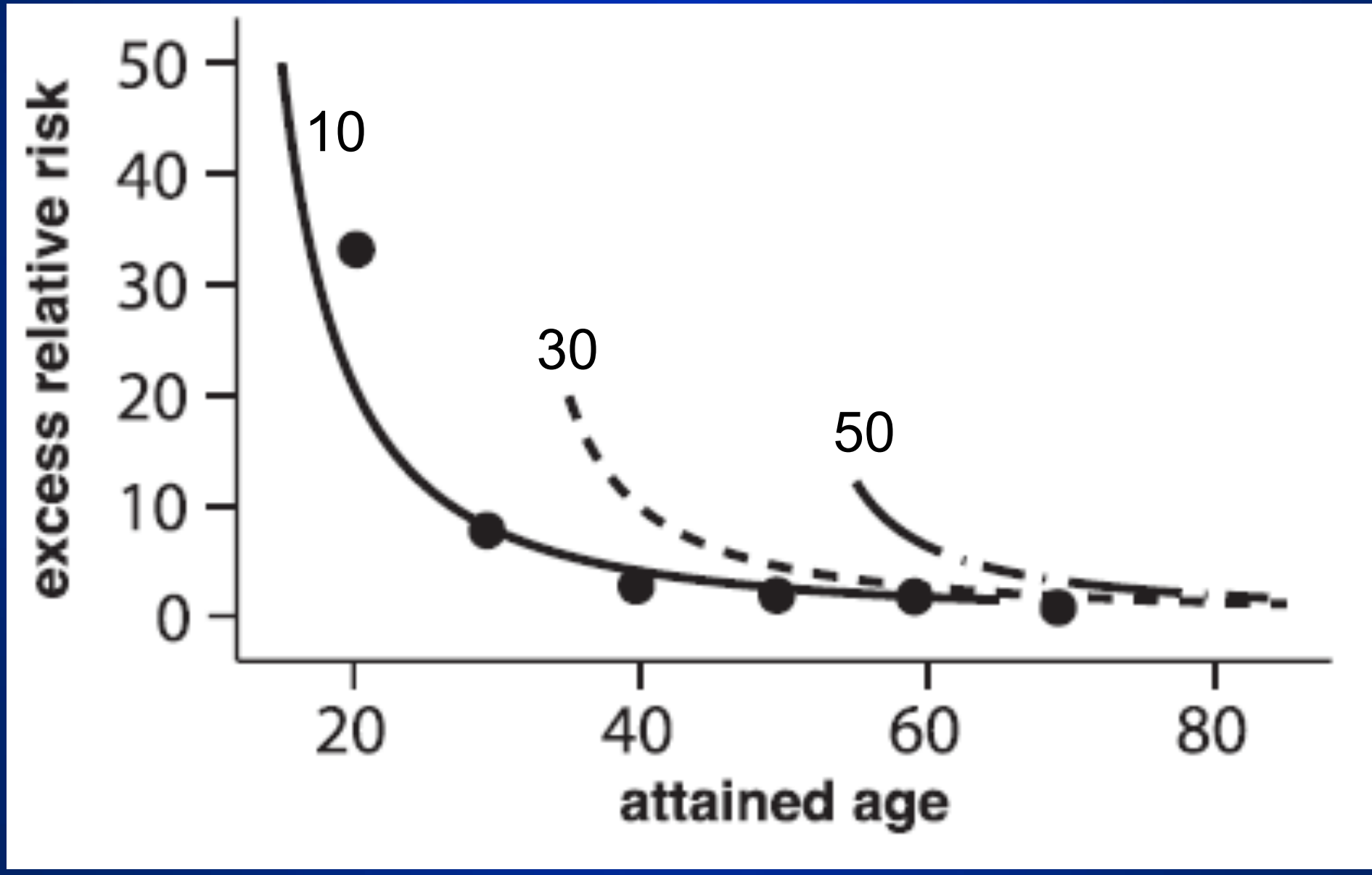
Age

Sex

Genetic susceptibility

Intrinsic risk

ERR at 1 Gy *vs* Age



Host Variables Associated with Leukaemia-Risk

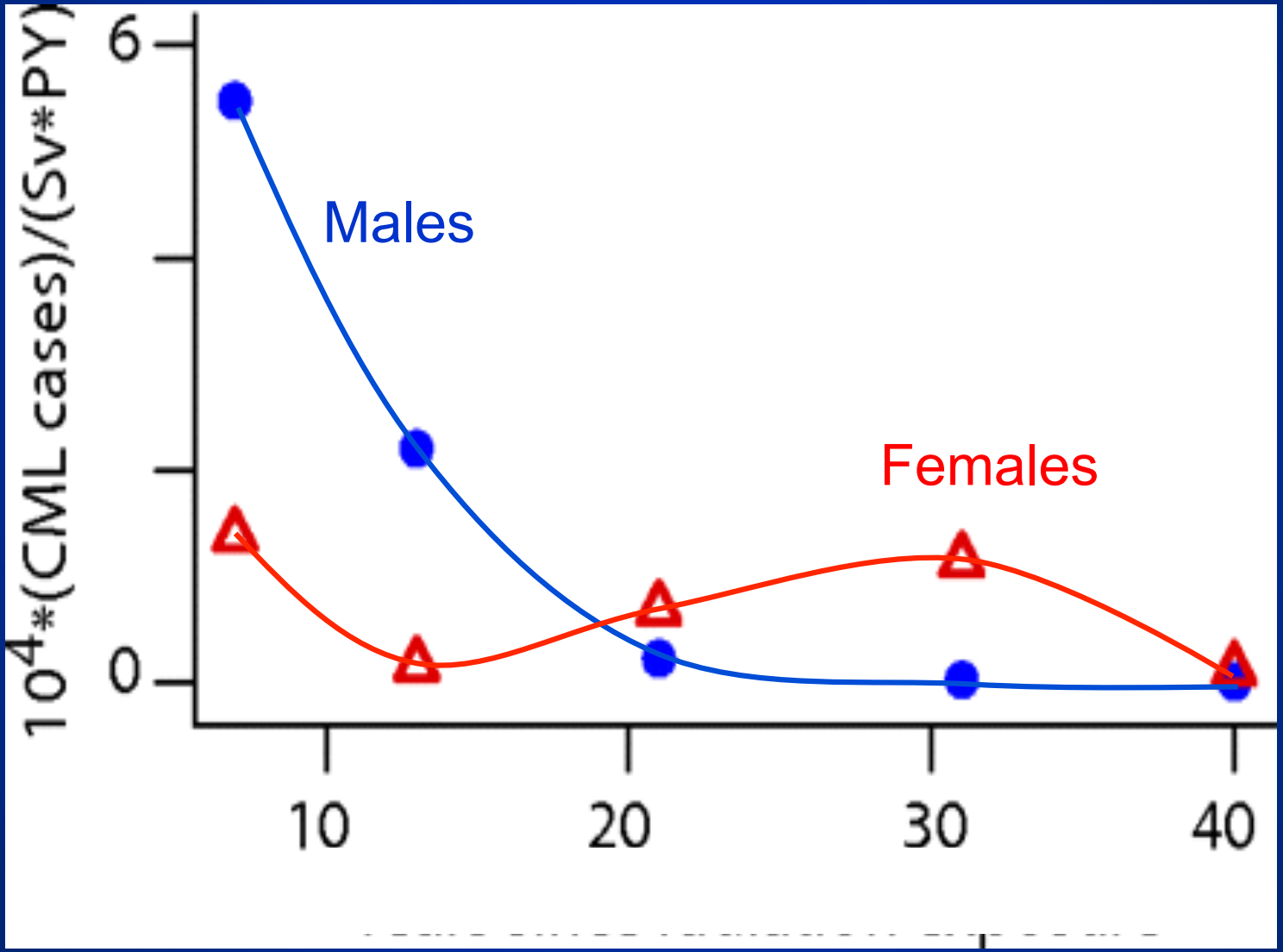
Age

Gender

Genetic susceptibility

Intrinsic risk

CML after A-Bombs



Host Variables Associated with Leukaemia-Risk

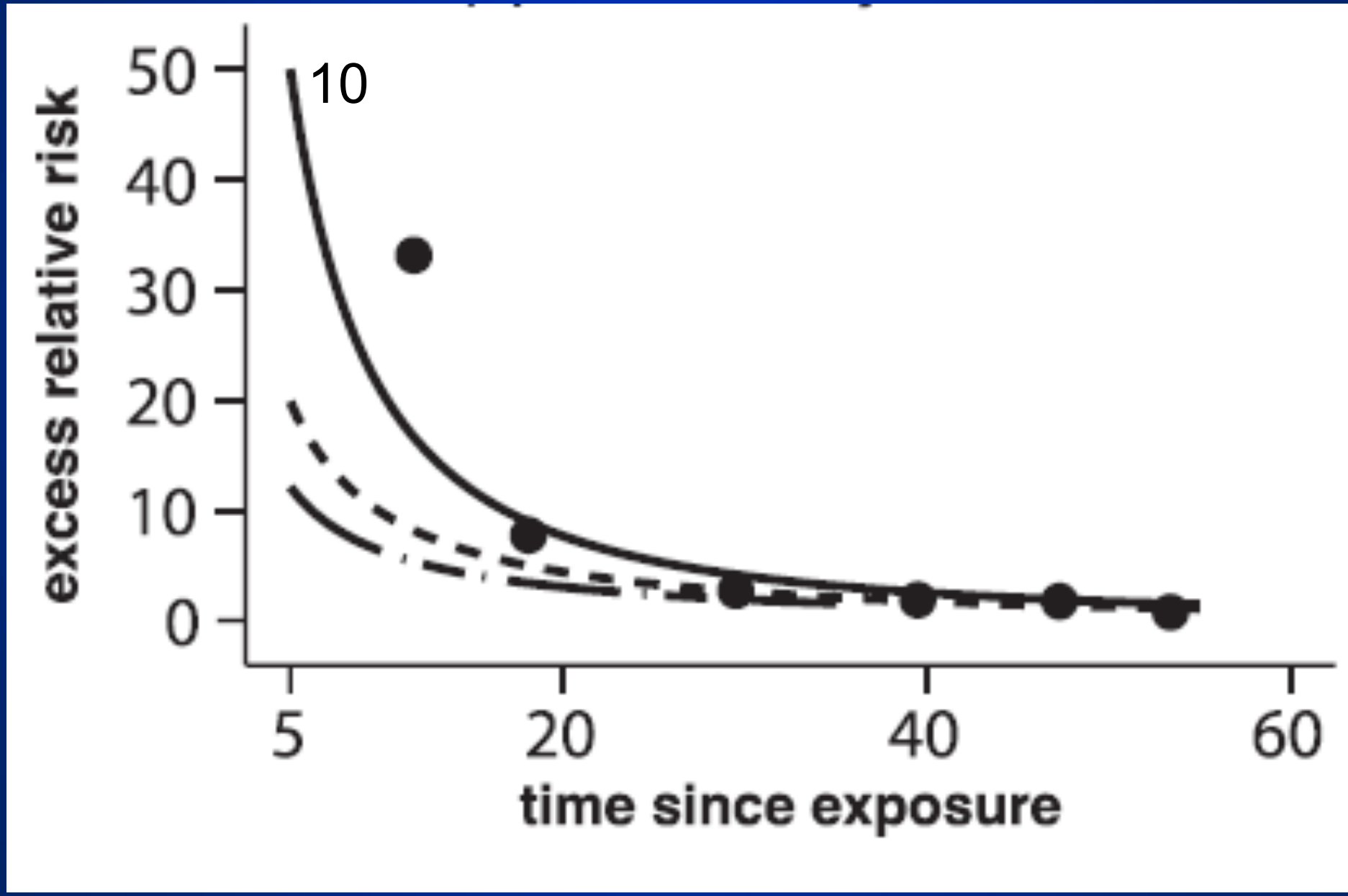
Age

Sex

Genetic susceptibility

Intrinsic risk

ERR at 1 Gy *vs* Time



A-Bomb Exposures & Other Haematologic Cancers

CLL	Yes
ATL	No
NHL Males	Weak
NHL Females	No
HD	No
PCM	No
MDS	Yes

Radiation and Leukaemia

Occupational exposures

Occupational Exposures

Radiologists

Radium dial workers

Uranium miners

Nuclear workers

Chernobyl

Occupational Exposures

AML

CML

CLL*

Radiation and Leukaemia

Medical exposures

Medical Exposures

Ankylosing spondylitis

Lymphomas

Cervical cancer

Breast cancer

Childhood cancers

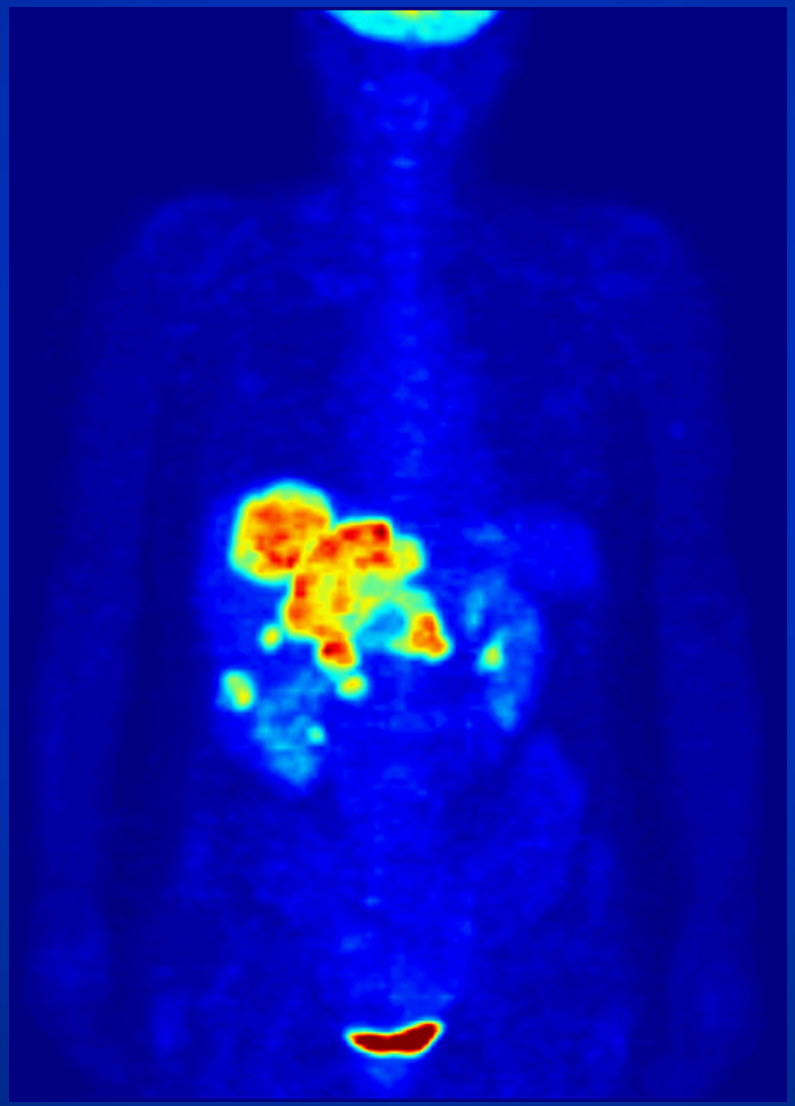
Diagnostic procedures

Radiation Therapy

Ankylosing Spondylitis	AML, CML
HD	AML
NHL	AML
Breast cancer	AML
Ovary cancer	AML
Cervix cancer	AML
Transplants	AML

Computer Tomographic (CT) Scan

PET Scan



CT Scans

Head 2 mSv

Chest 7 mSv

Abdomen 10 mSv

Angiography (heart) 20 mSv

Whole Body 10 mSv

CT/PET 30 mSv

CT Scans

Head 2 mSv

Chest 7 mSv

Abdomen 10 mSv

Angiography (heart) 20 mSv

Whole Body 10 mSv

CT/PET 30 mSv

Hiroshima 200 mSv

Radiation and Leukaemia

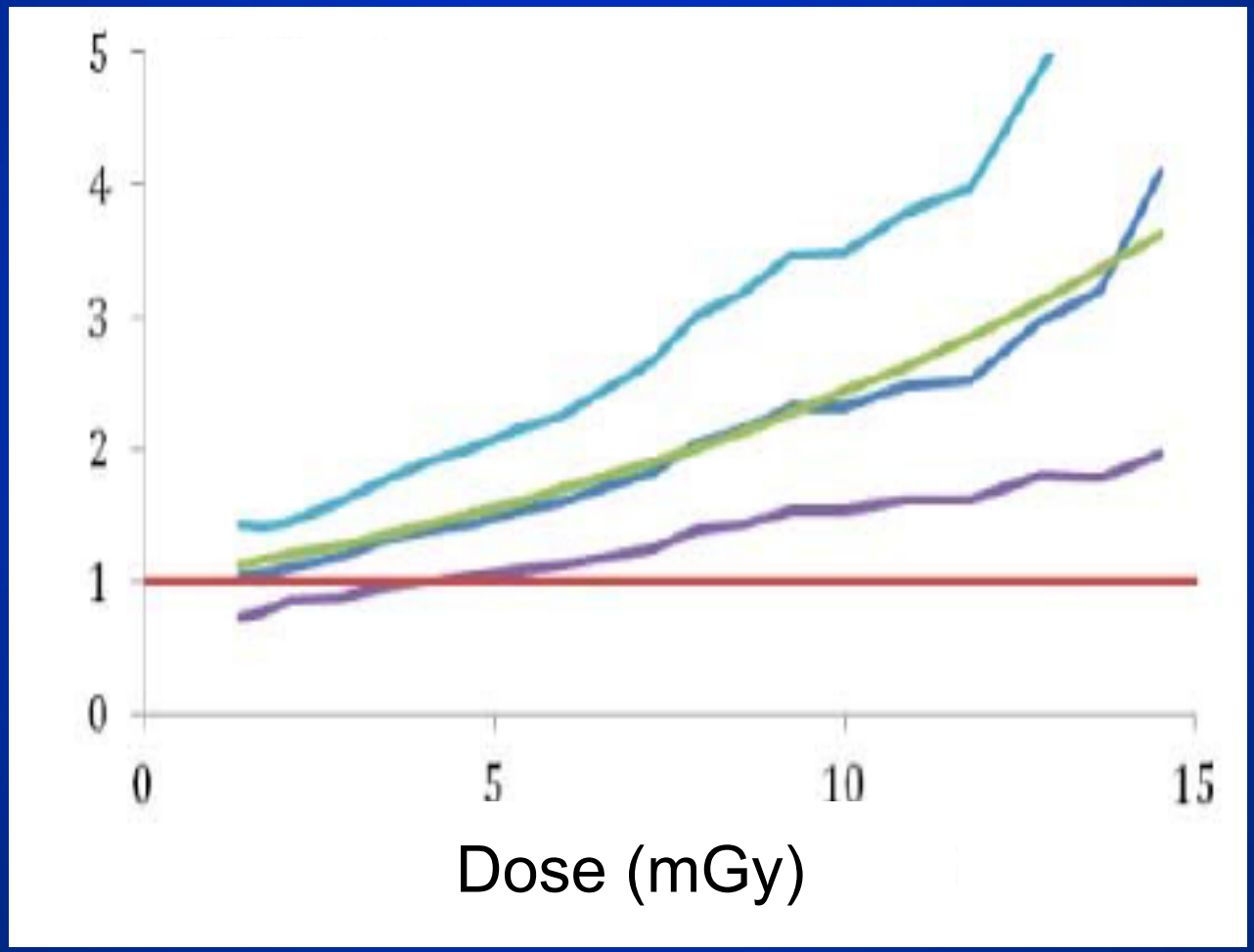
Atomic bomb

Occupational exposures

Medical exposures

Terrestrial radiations

AML and ALL in Children from Background γ-Rays



Kendall Leukemia 2012

Radiation-Related Leukaemia Increases

Chernobyl	Cs^{137}	CLL*
Persian Gulf Balkan Wars	U^{238}	No
Fukushima	Cs^{137}	No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