National Cancer Institute

Radiation Risk Assessment

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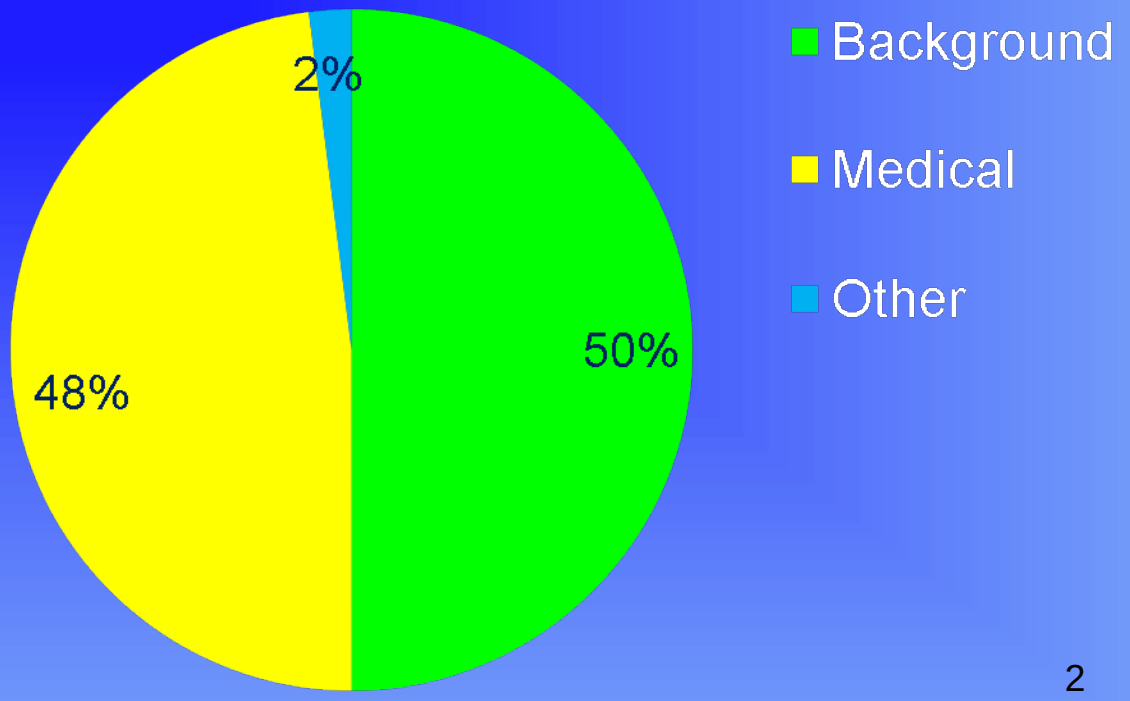
US Population Radiation Exposure 2006

Average annual exposure per capita

- **Background radiation 3.1mSv**
- **Medical radiation 3.0mSv**
- **Occupational exposure 1.1mSv**



NCRP Report 160 (2008)

Cancer Risks from Low-dose Radiation Exposures

Difficult to Quantify Risks from Low Doses Directly

- Infeasibly large sample size & lifetime follow-up

2 Mammograms at age 35
60 million women & 20 years follow-up 50% power (Land, 1981)

Estimate Indirectly using Existing Data

- Japanese atomic bomb survivors & LNT
- Provides a more timely assessment of potential risk

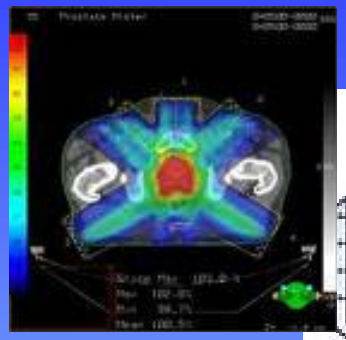
Risk Projection Studies - Examples

Medical Radiation Exposures

- Diagnostic tests – CT, cardiac stress
- Screening tests - CT colonography, mammography
- Radiotherapy – IMRT scatter dose

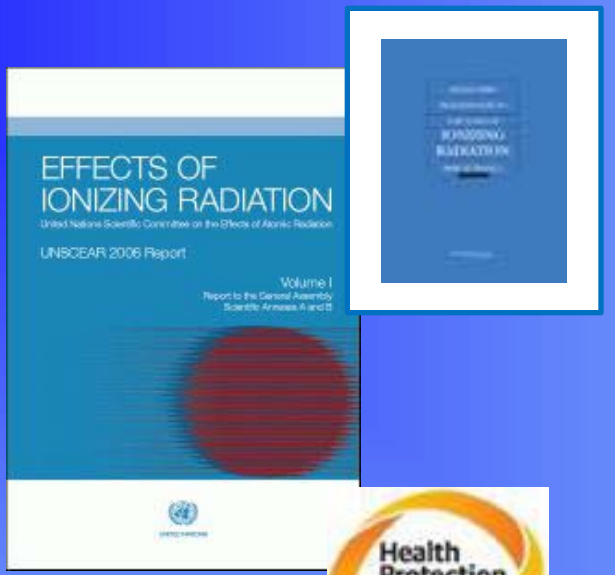
Environmental Exposures

- Lung cancers attributable to radon
- Future cancers in the Marshall Islands



Risk Assessment Reports

- **BEIR VII – US population (2006)**
- **UNSCEAR – multiple populations (2008)**
- **Health Protection Agency – UK (2011)**



Lifetable methods

- Risk of radiation-related cancer elevated indefinitely
  - Apply age-specific ERR (EAR) to obtain excess cancers occurring at each age
  - Follow the population forward in time allowing for attrition as the population ages
- Required information on population of interest
  - Age-sex composition
  - Organ-specific doses
  - Survival (life-table) data
  - Age- and sex-specific baseline rates for cancer(s) of interest (for ERR models)

Lifetable Methods – LAR, REID & ELR

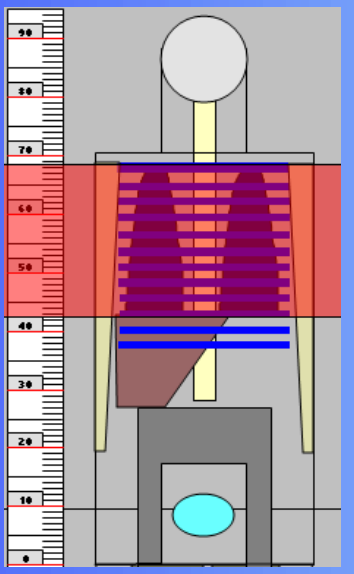
Attained age	Excess Risk	Conditional Survival probability	Adjusted excess risk
70	0.005	0.81	0.004
71	0.005	0.80	0.004
72	0.004	0.79	0.003
73	0.004	0.78	0.003
74	0.003	0.77	0.002
75	0.003	0.76	0.002
Sum	0.024		0.019

- LAR & REID Include cancers that would have occurred anyway at a later age
- REID Survival probability includes radiation-induced deaths
- ELR does not include either
- Similar results at low doses

Thomas et al (Health Phys 1992); Kellerer et al (Radiat Environ Biophysics 2001); BEIR VII (2006)

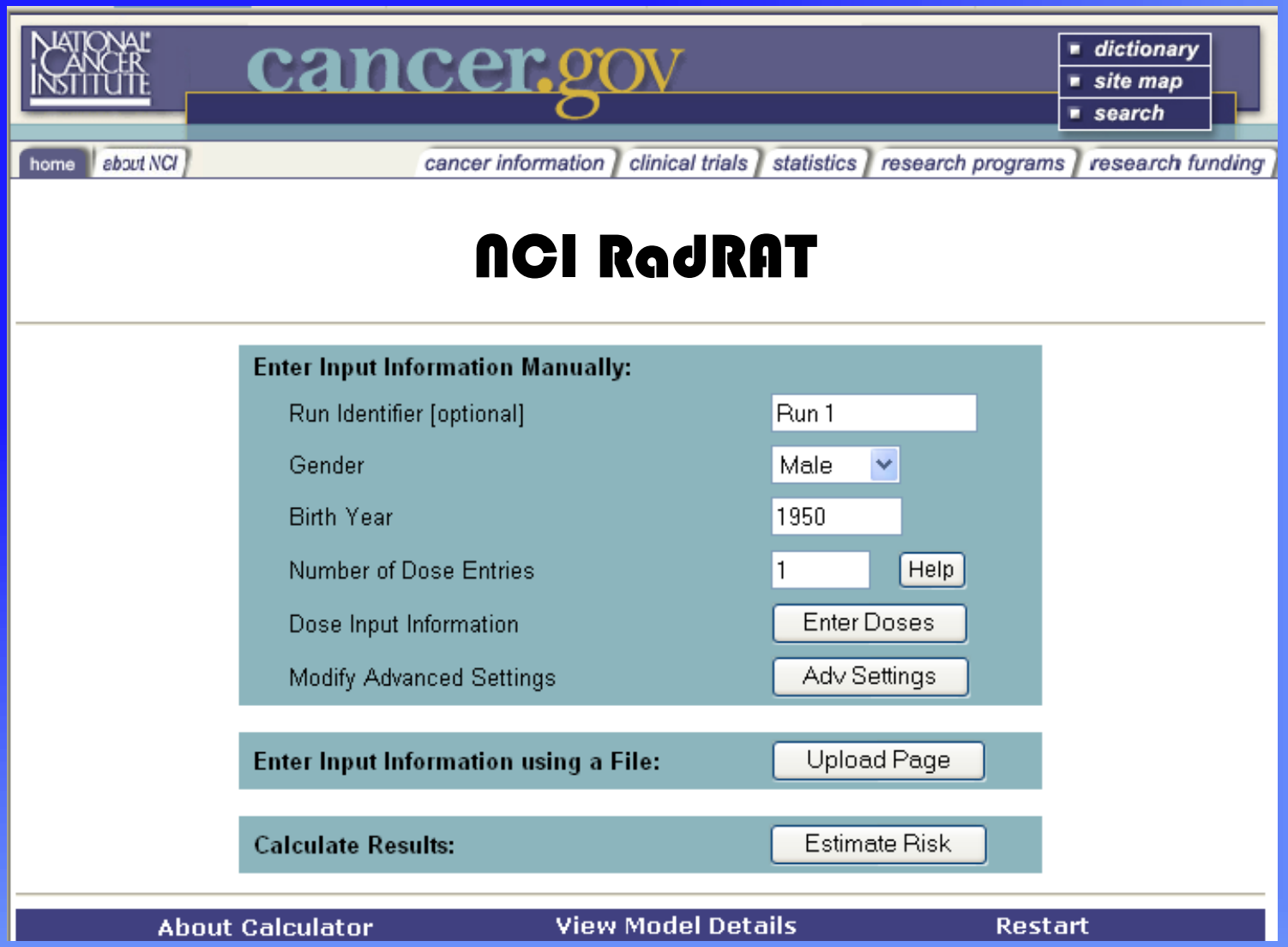
Dose Estimates

- Non-uniform exposure (eg medical radiation)
  - Organ-specific doses
  - Sum risks across exposed cancer sites
  - Effective dose & all cancers generally inappropriate



- Uniform exposure (eg cosmic radiation)
  - All solid cancers + leukemia

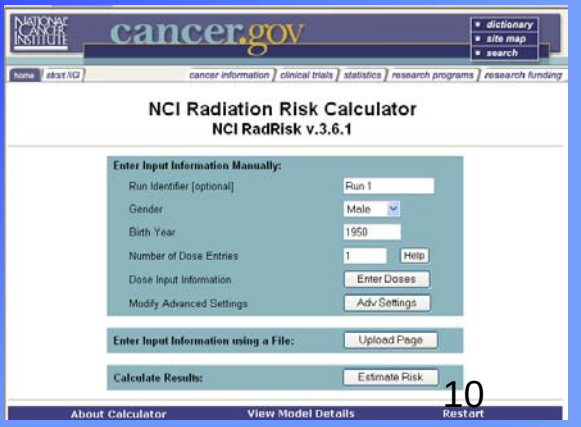
NCI Radiation Risk Assessment Tool



Berrington de Gonzalez et al (submitted)

NCI RadRAT Methodology

- Cumulative lifetime risk of radiation-related cancer
- Organ-specific risk models
  - Based on NAS BEIR VII models
  - 11 site-specific cancer models
  - Japanese atomic bomb survivors
  - Medical exposure studies (breast and thyroid cancer)
- 7 Additional models
  - Oral, esophagus, rectum, pancreas, gallbladder, kidney, brain/CNS
- Web-based version 2011



Methodology cont

- Risk models formulation
- Transfer to US population
- Low doses and low-dose rates (DDREF)
- Lag/latency period
- Relative Biological Effectiveness
- Uncertainty assessment

BEIR VII risk models

- LSS data (Preston et al, 2007)
- Standard formulation for ERR & EAR models

$$\beta D \exp(-0.03e) (a/60)^{-1.4}$$

- D - dose e - age at exposure a – attained age
- Test for departure from standard parameters
- 11 site-specific risk models
- Leukemia linear-quadratic (+ time since exposure)
- Breast, thyroid models from pooled analyses (Preston et al, 2002; Ron et al, 1995)

Transfer from Japanese

	Annual Cancer Incidence Rates (Females ASR per 100,000)	
	Japan	United States
All cancers	185	280
Stomach	34	3.5
Colon	17	22
Liver	9.8	1.3
Breast	30	89

Source: Cancer Incidence in Five Continents, 1997

Model for transporting risks: How do we decide?

- Compare epidemiologic data on non-Japanese populations and A-bomb survivors
- Evaluate interaction of radiation and factors that contribute to differences in baseline risks
  - Multiplicative ERR
  - Additive EAR
- Biological considerations (initiation/promotion)

Transfer from Japanese cont

- Weighted average of ERR and EAR estimates
- BEIR VII Subjective weights
  - ERR 0.7 & EAR 0.3
  - Lung cancer ERR 0.3 & EAR 0.7
  - Breast cancer EAR
  - Thyroid cancer ERR
- Weights varied in uncertainty analysis
- UNSCEAR approach – present EAR & ERR separately

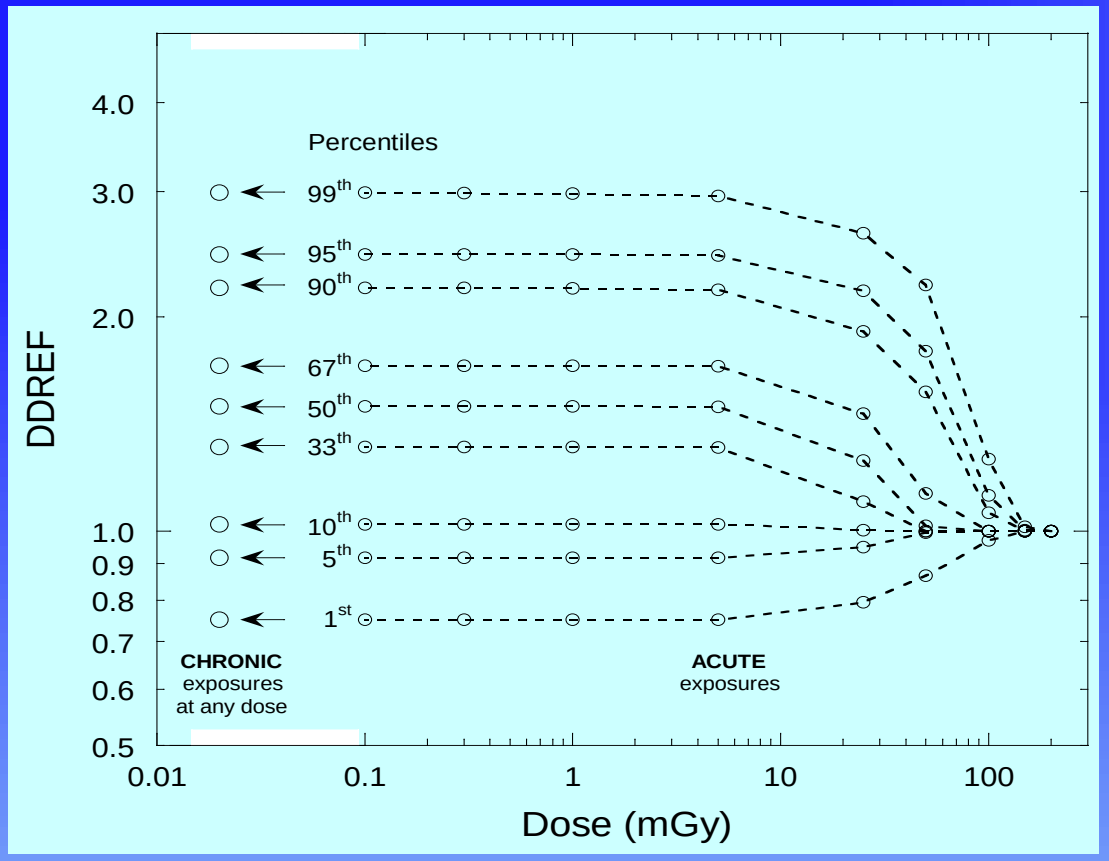
Example: Lifetime Risk of Stomach Cancer Incidence in Males

Number of cases per 100,000 persons exposed to 0.1 Gy

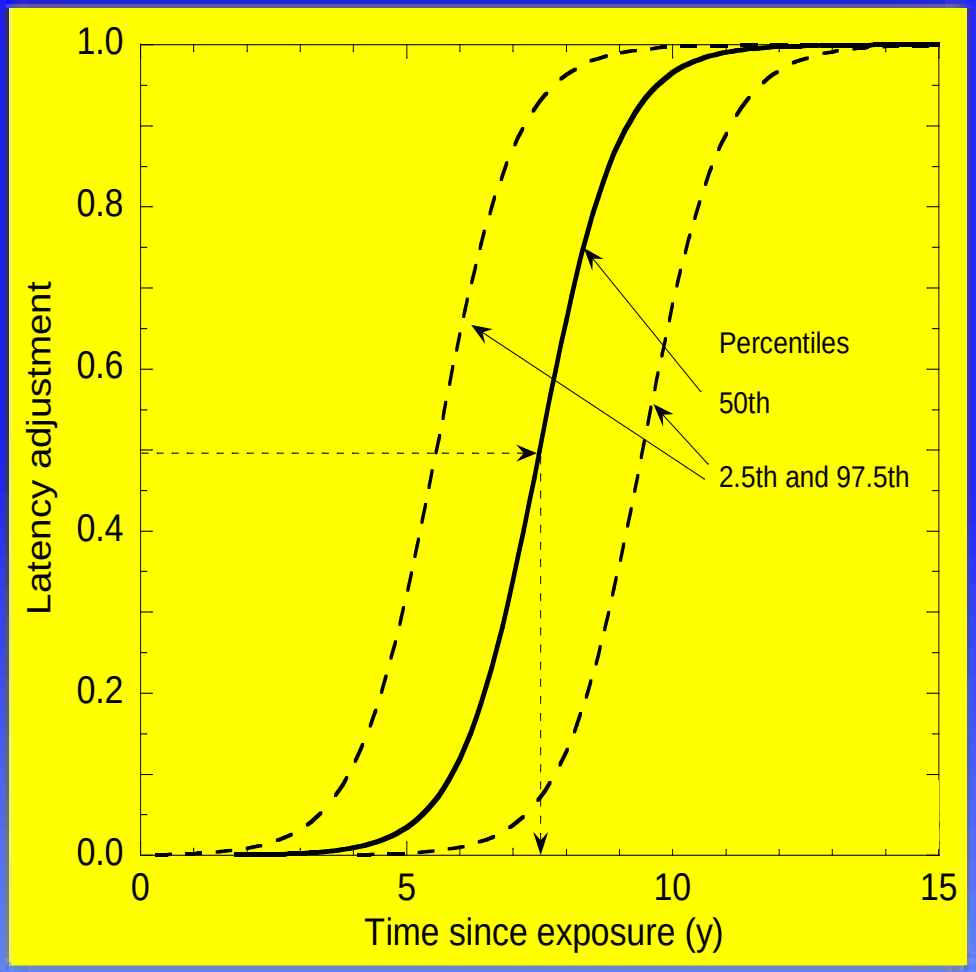
Estimate based on ERR:	25
Estimate based on EAR:	280
Weighted mean:	52
Apply DDREF of 1.5:	34

DDREF

- **BEIR VII Solid cancer LSS DDREF Median 1.5**
  - **Based on LSS data and experimental data (mice)**
  - **Leukemia linear-quadratic model**
- **UNSCEAR Linear-quadratic models all cancers**



Latency period

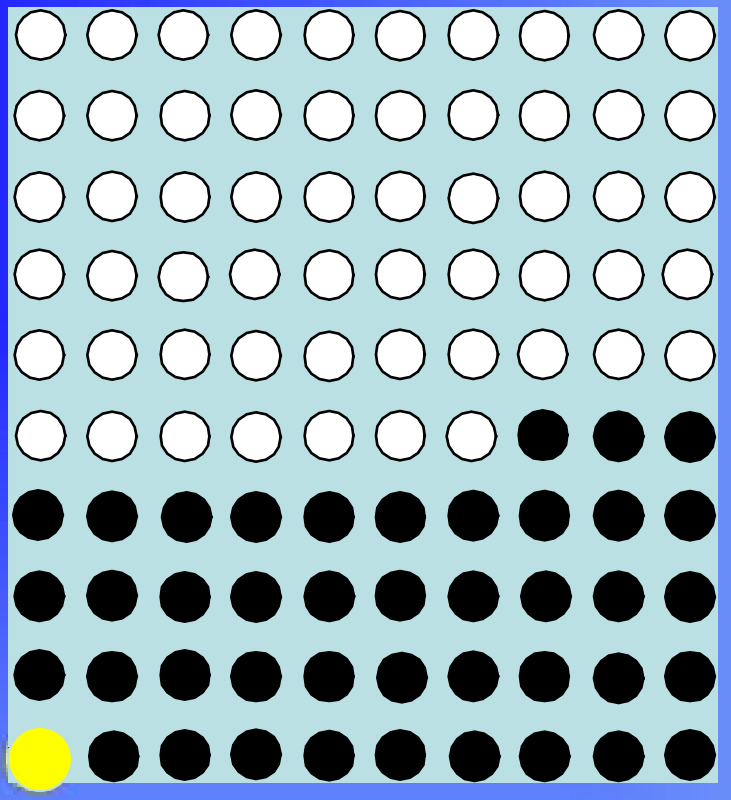


BEIR VII:
Leukemia 2yrs
Solid cancers 5 yrs

Lifetime risk for incidence of solid cancer and leukemia

If 100 people exposed to 0.1 Gy (100 mGy), expect

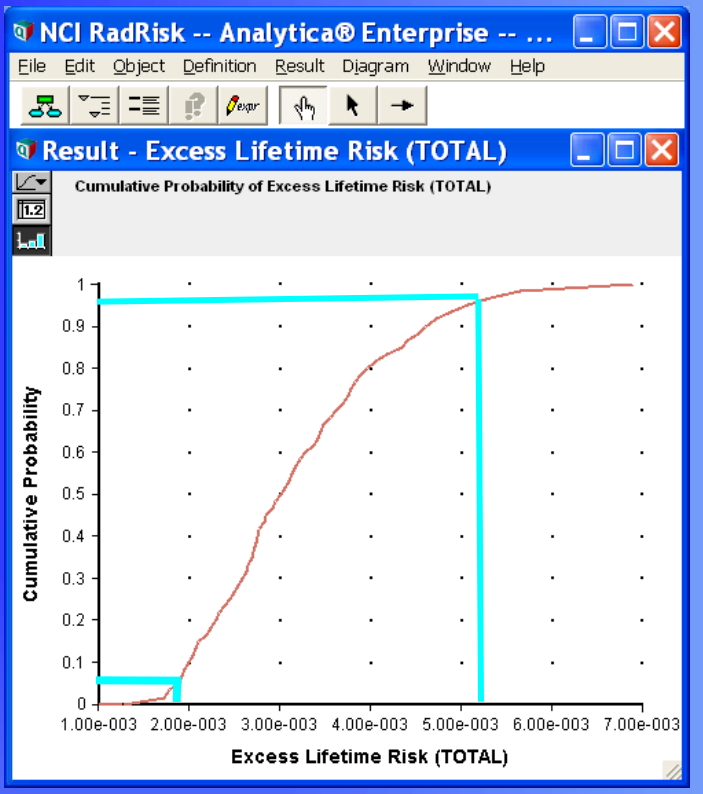
- 1 cancer from this exposure
- 42 cancers from other causes



NCI RadRAT - Uncertainty Intervals

Monte Carlo simulations

- Subjective uncertainties
  - Transfer risks (Japanese to US)
  - Low dose risks (DDREF)
- Statistical uncertainties
  - Model parameters
  - Doses



Relative Biological Effectiveness

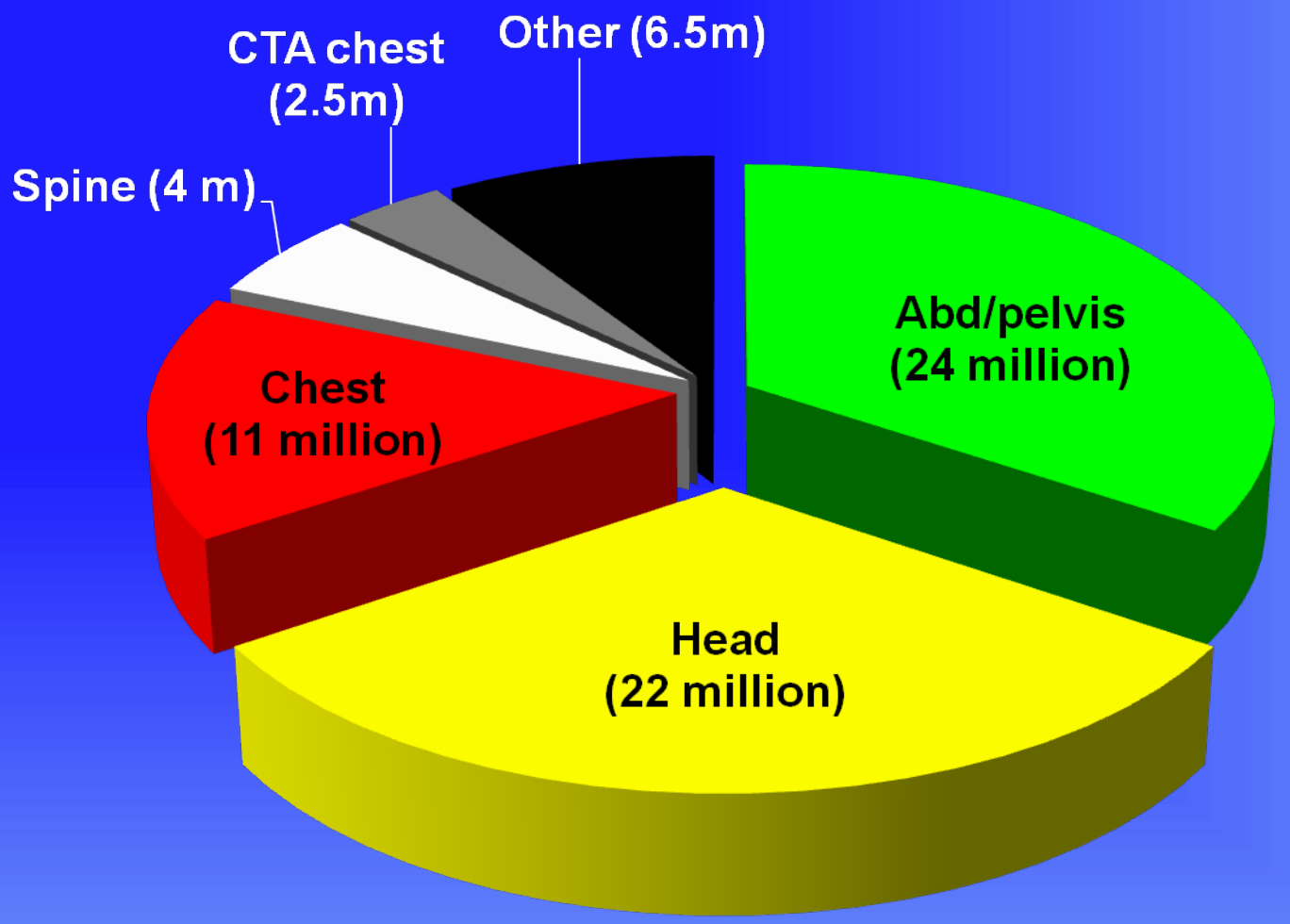
Radiation Type	Weighting Factor
X-rays & Gamma-rays	1
Protons	2
Neutrons	5-20 (according to energy)
Alpha particles	20

- In vitro data suggest X-rays RBE > gamma-rays
  - Difficult to assess in epidemiological studies

ICRP Report 90 (2003); Hunter & Muirhead (J Radiol Protect 2009)

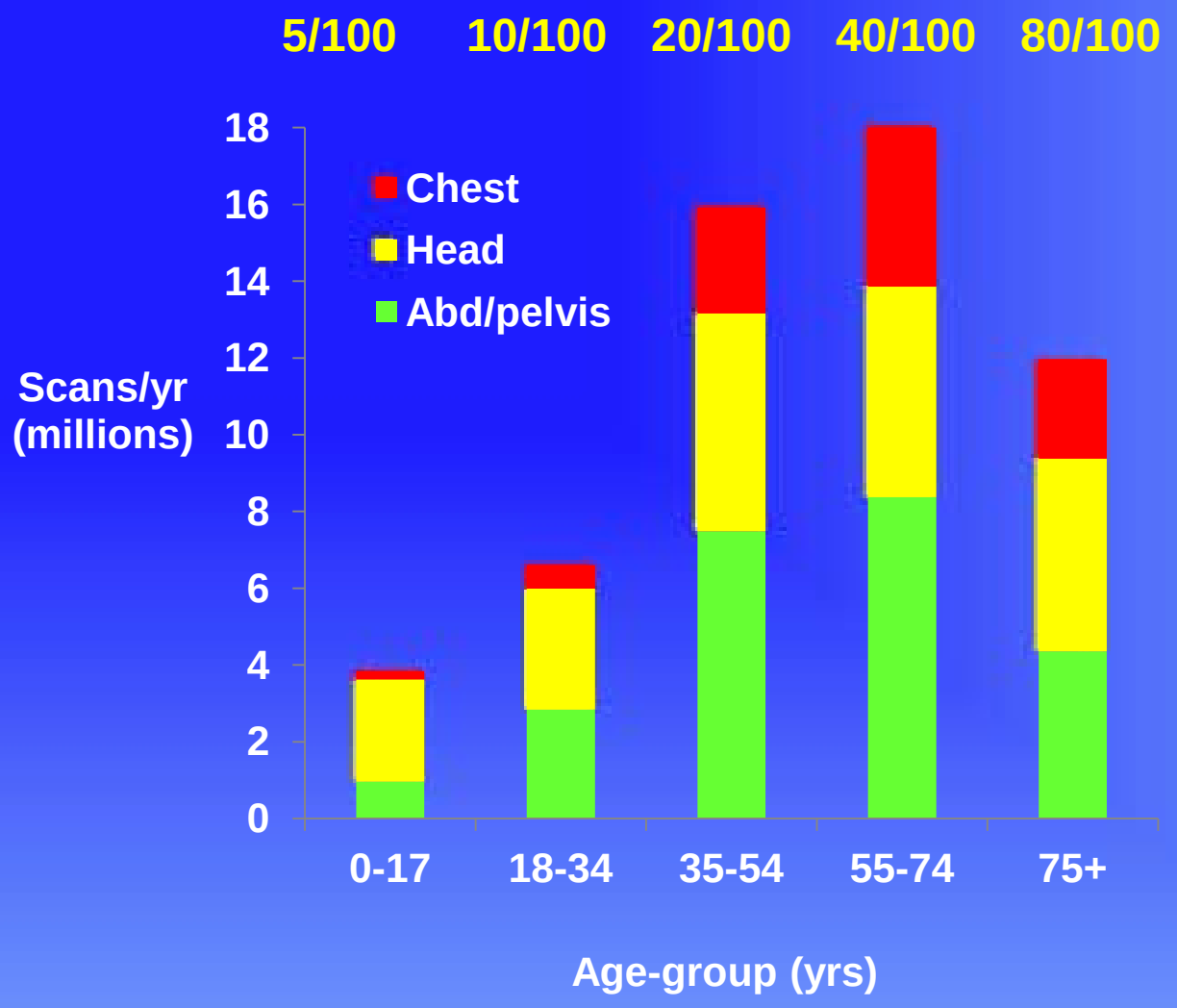
Applications

70 Million CT scans U.S. 2007



Mettler et al (Radiology 2008); IMV 2008

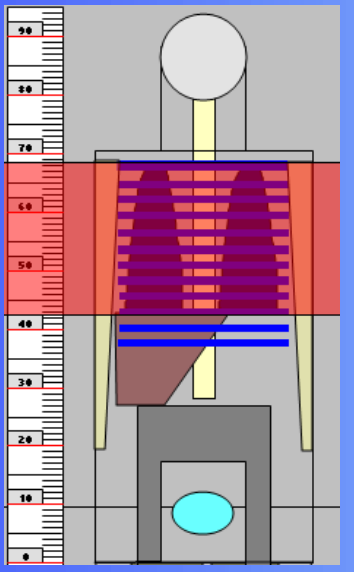
Scans Per Year by Age (U.S. 2007)



Mettler et al (Radiology 2008); IMV 2008; Large National Employer Insurance Plan

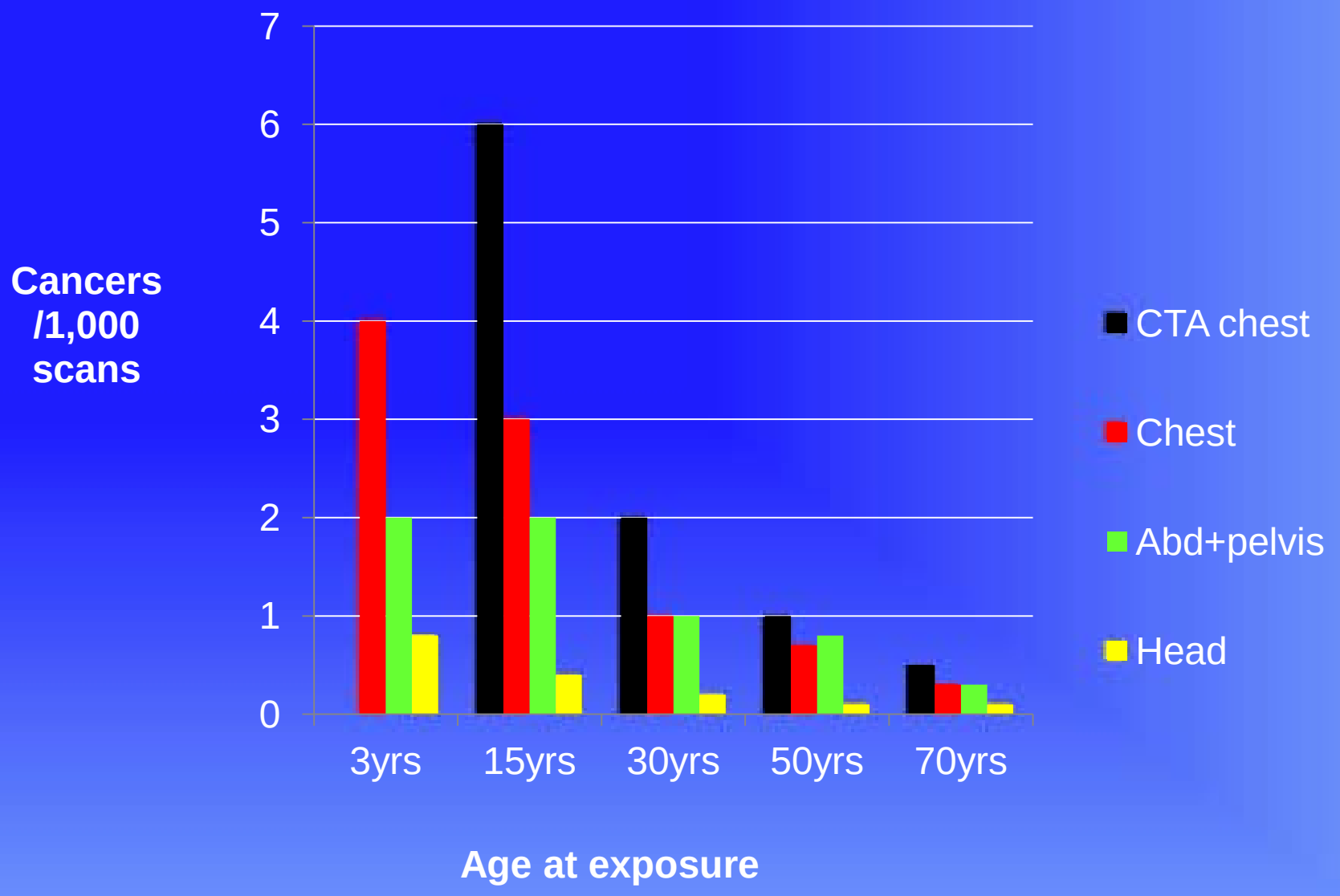
Typical Organ Doses

	CT chest	CTA chest
Effective dose	7 mSv	16 mSv
Breast	20 mGy	40 mGy
Lung	20 mGy	30 mGy
Esophagus	20 mGy	30 mGy
Red bone marrow	5 mGy	10 mGy



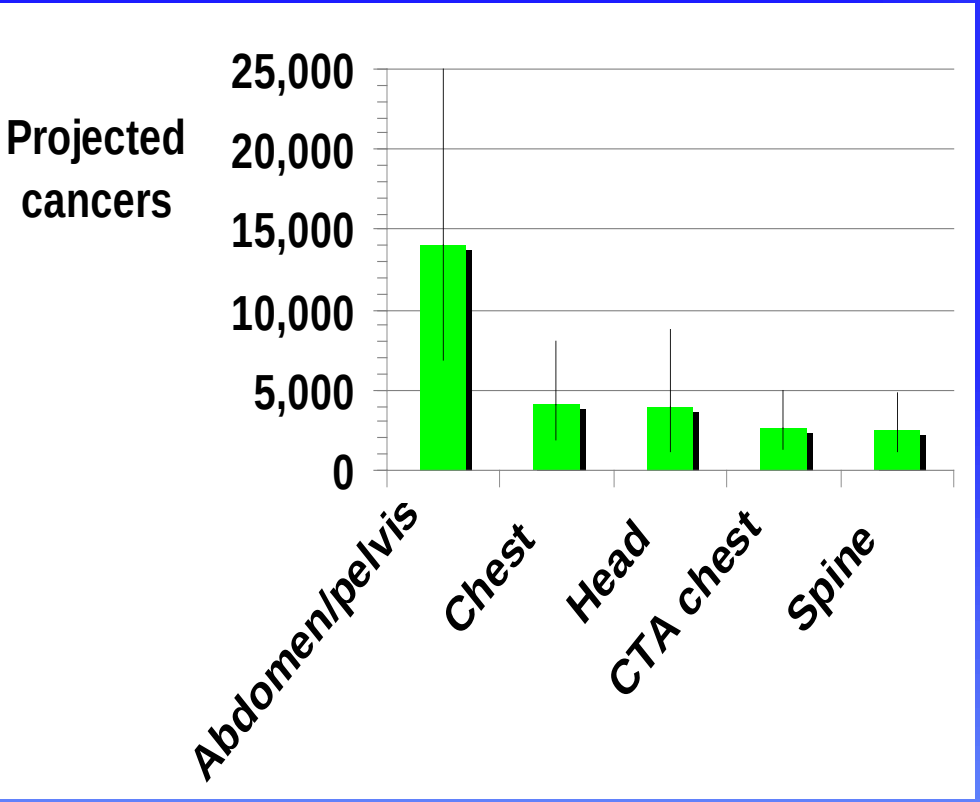
Mettler et al (Radiology 2008); CT-Expo; FDA NEXT (2005)

Projected cancers per 1,000 scans - females



Projected Cancers From CT scans (U.S. 2007)

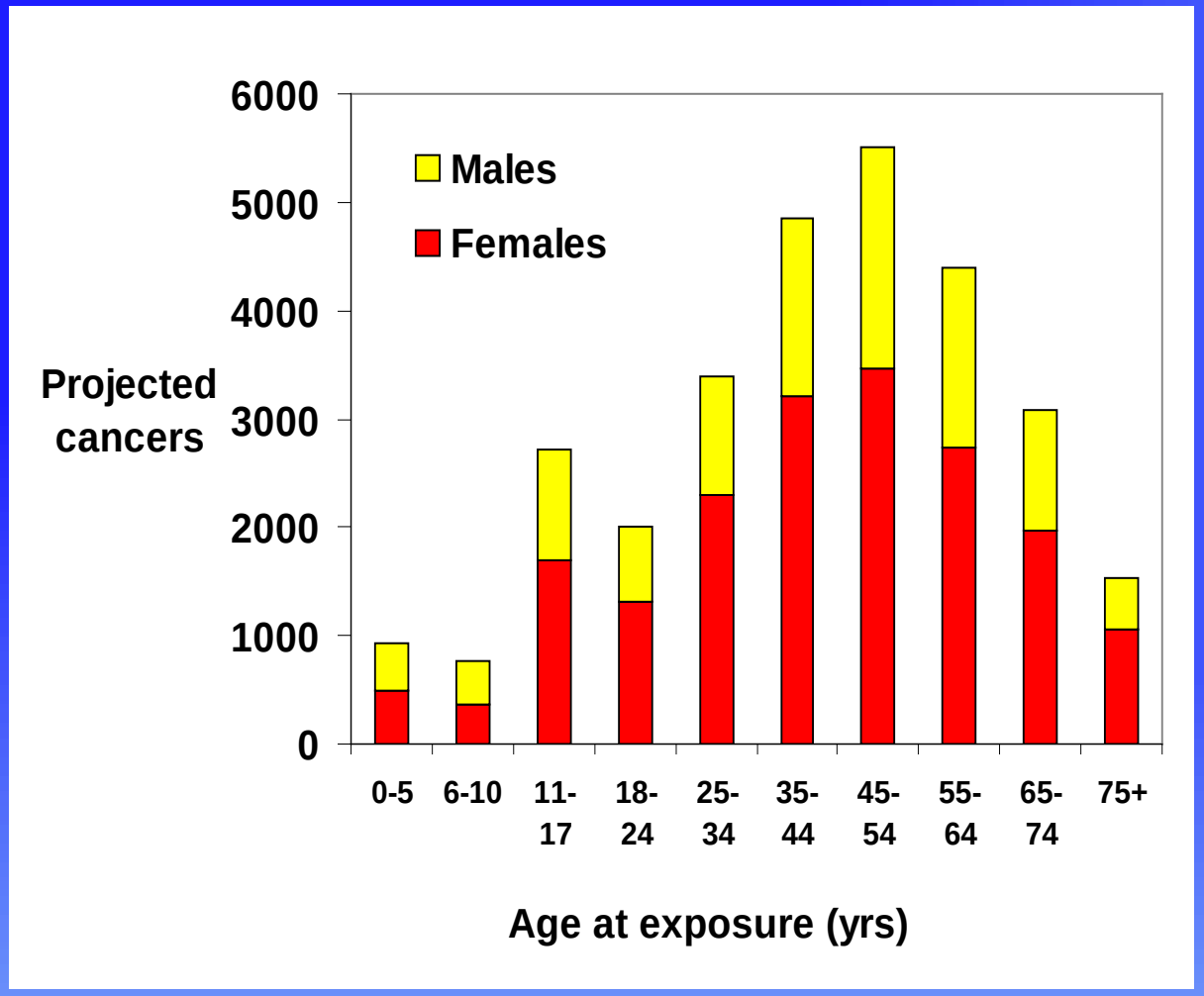
29,000 cancers (95% Uncertainty limits: 15,000 – 45,000)



Abd/pelvis	6 – 12 mSv
Chest	7 mSv
Head	2 mSv
CTA chest	16 mSv
Spine	5 – 9 mSv

Berrington de González et al (Arch Int Med 2009)

CT scans: projected cancers by age at exposure



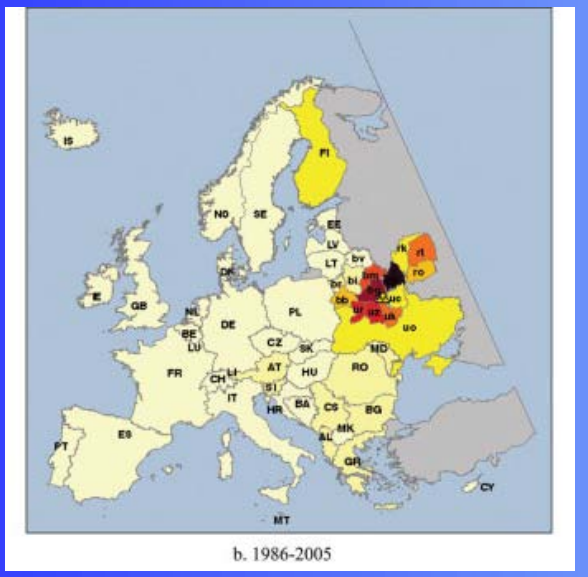
66% Females

33% Age 35-54

15% <Age 18

Berrington de González et al (Arch Int Med 2009)

Fallout from Chernobyl in Europe



- By 2006
- 1000 thyroid cancers
- 4000 other cancers
- 0.2% cancer incidence

- By 2065
- 16,000 (3400-7200) thyroid cancers
- 25,000 (11,000-59,000) other cancers
- Several hundred million from other causes

Cardis et al (Int J Cancer 2006)

Virtual Colonoscopy

- Alternative colorectal cancer screening tool
- Concern about potential radiation risks
- Effective dose 8mSv per screen
- Screening 50-80 every 5 yrs
  - 8 to 28 radiation-related cancers per 10,000 screened
  - 360 to 520 cancers prevented per 10,000 screened

Berrington de González et al (Am R Roentgenol 2011)

Childhood Leukemia & Background Radiation

- Natural background radiation estimates for UK
  - 0.7 mSv to 1.6 mSv per year
- Leukemia risk models from BEIR VII & UNSCEAR
- Estimated radiation-related cases 1991-2000
  - UNSCEAR 900
  - BEIR VII 650
- Proportion of cases diagnosed 1991-2000
  - UNSCEAR 19%
  - BEIR VII 15%
- Risks higher at younger ages (<5) in UNSCEAR
- EAR model 5% ERR model 24%

Little et al (R Radiol Prot 2009)

Summary

- Timely estimates of potential risks from low-doses
- Recognition of limitations of epidemiological studies
- Uncertainties
  - Transfer from Japanese
  - DDREF
  - RBE
- Improvements to modeling
  - Pooling studies incorporating non-Japanese data
  - Joint effect of radiation & other risk factors

RadRAT Collaborators

- Julian Apostoaei (SENES)
- Ethel Gilbert (NCI)
- Lene Veiga (IRD Brazil)
- Preetha Rajaraman (NCI)
- Owen Hoffman (SENES)
- Brian Thomas (SENES)
- Charles Land (NCI)