Ionizing Radiation and Cancer Risk

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DCEG Radiation Epidemiology and Dosimetry Course 2019
Objectives

- Provide a broad overview of the current understanding of ionizing radiation and cancer risk from epidemiological studies
  
- Features of high-quality studies for providing evidence
Chapter 13: Ionizing Radiation

Amy Berrington de González
André Bouville
Preetha Rajaraman
Mary Schubauer-Berigan
Introduction and Key Concepts
Ionizing radiation

Universal carcinogen

• Can cause cancer in most organs
• Can cause cancer at any age (including in utero)

Variation in the magnitude of risk

Large risks from childhood exposure

• Leukemia, breast, thyroid, CNS tumors

UNSCEAR 2006, BEIR VII 2006
Established carcinogen... fundamental questions

- Magnitude of risk at very low doses
- Risk from different types of radiation
- Modifiers of risk
  - Joint effects
- Impact of rate (timing) of exposure
- Mechanisms of radiation-induced carcinogenesis
- Risk from emerging medical technologies

... and more!
Key concepts related to the exposure

- Types of radiation
- Modes and patterns of exposure
- Sources of exposure
Types of Ionizing Radiation

• All types can cause cancer in humans
  ➢ *sufficient evidence* - IARC Group 1

• Varying energies and ability to penetrate
  ➢ potential variation in cancer risk


IARC Monograph 100D 2012
Internal vs external exposure

• Internal – Source within the body
  ➢ Ingestion, inhalation, injection of radioactive particles

• External – Source outside the body
  ➢ Proximity to photon-emitting source
## Rate of exposure

<table>
<thead>
<tr>
<th>Type</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Delivered within seconds</td>
</tr>
<tr>
<td>Fractionated</td>
<td>Multiple acute or short-term exposures delivered at intervals</td>
</tr>
<tr>
<td>Protracted</td>
<td>• Continuous, over relatively long time</td>
</tr>
<tr>
<td></td>
<td>• Fairly constant rate</td>
</tr>
</tbody>
</table>
Full- or partial-body

• Full-body – (relatively) uniform exposure over the body

• Partial-body – only part of the body exposed
### Patterns of exposure: Examples

<table>
<thead>
<tr>
<th>Exposure/Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atomic bomb survivors</td>
<td>• External&lt;br&gt;• Acute&lt;br&gt;• Whole-body</td>
</tr>
<tr>
<td>Diagnostic x-rays</td>
<td>• External&lt;br&gt;• Fractionated&lt;br&gt;• Partial-body</td>
</tr>
<tr>
<td>I^{131} from fallout</td>
<td>• Internal&lt;br&gt;• Protracted&lt;br&gt;• Largest exposure to thyroid, smaller exposures elsewhere</td>
</tr>
</tbody>
</table>
Units of exposure

Absorbed dose
- radiation energy absorbed per unit mass of organ or tissue
- Unit: Gray (Gy)
- Primary unit for epidemiologic studies

Equivalent dose
- mean absorbed dose to organ/tissue weighted by type and energy of radiation
- Unit: Sievert (Sv)

Effective dose
- sum of absorbed dose to organs multiplied by radiation and tissue weighting factors
- Unit: Sievert (Sv)
- Primary unit for regulatory purposes
Sources of exposure

Environmental  Medical  Occupational
Main sources of exposure – general population

• Medical (diagnostic)
• Low-level environmental

• Historic
  • Atomic bombs in Japan
  • Chernobyl accident
  • Therapeutic radiation for benign conditions

Figure 13–1. Comparison of current estimated annual per capita radiation exposure (mSv) for countries with a similar health-care level.
## Environmental Exposures

<table>
<thead>
<tr>
<th>Natural background radiation</th>
<th>Man-made environmental exposures</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Radon</td>
<td>• Atomic bombs, nuclear weapons testing</td>
<td>• Industrial activities, security inspection systems, medical facilities, educational/research institutions</td>
</tr>
<tr>
<td>• Cosmic radiation</td>
<td>• Nuclear accidents</td>
<td></td>
</tr>
<tr>
<td>• Radionuclides in food and earth</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Medical Exposures

- Primarily fractionated, partial-body

Diagnostic
X-rays, CT scans
Nuclear Medicine

Interventional Radiology

Radiotherapy

Images: https://lab.research.sickkids.ca/qbict/what-is-a-ct-scan/
https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam
Increasing medical radiation exposure in the U.S.

- CT scans: 3 to 80 million
- NM procedures: 6 to 18 million

NCRP Report 160 2009
Occupational Exposures

- Nuclear workers
- Miners
- Medical workers

- Trend towards decreasing exposures
- Exceptions - Interventional radiology physicians & nuclear medicine radiologic technologists
Exposure assessment and study design
Exposure assessment: Common sources

- Questionnaires
- Measurements
- Medical records
- Badge dose
Exposure assessment: Considerations

Strength - Dose can be measured

Challenges – quality, detail varies across studies

• From “exposed” vs. “unexposed” to individual organ dose estimates
• (Often) rely on historical information to reconstruct dose long after exposure
• (Often) need multiple sources of information
Sources and consideratinos: Environmental studies

• Questionnaires:
  • level of detail
  • timing relative to exposure

• Measurements:
  • number of measurements
  • timing relative to exposure
  • coverage

• Challenge: Uncontrolled, unexpected exposure
Sources and considerations: Medical studies

- Treatment records:
  - detail about patient and treatment
  - accuracy of treatment parameters
  - availability of treatment-planning images

- Medical records from diagnostic procedures:
  - detail about patient
  - types of machines
  - settings - individual vs typical protocols

- Questionnaires: Complement records (or be only source)
Sources and considerations: Occupational studies

• Badge dose measurements
  • Usage
  • Location, limit of detection
  • Not used < 1960s

• Bioassay measurements (internal exposures)
  • Coverage

• Questionnaires on work history
  • Level of detail
Quality of individual doses for epidemiologic studies

Lack human-based measurements
Sparse data
Based on retrospective interviews

Human-based measurements
• Reliable
• Available for all participants
• Representative of organ of interest

Lowest

Highest
Features of high-quality studies

- Individual level data
- Organ doses - estimate dose-response relation
- Completeness of follow-up
- Availability of covariate data
- Incident vs mortality data
- Appropriate comparison groups
- Exposure and outcome independent, reliable
- Long-term follow-up
- Adequate statistical power

UNSCER 2000; BEIR VII 2006
Exposure collected independently of outcome

Follow-up

Prospective cohort
- Select participants
- Data collection designed specifically for study
- Requires long follow-up
  - Challenging given long latency radiation and solid cancers

Retrospective cohort
- Select participants
- Use existing records, measurements, etc… to determine exposure and outcome status

Possible from both prospective and retrospective cohort designs
Completeness of follow-up

- Improper censoring - immortal person-time
- Completeness of follow-up related to exposure or risk of disease *but not both*
  - underestimate rates, cumulative incidence but internal comparison can still be valid
- Completeness of follow-up related to both exposure and outcome
  - Bias risk estimates
Appropriate comparison groups

Internal comparison
- Dose-response analyses
- Improve comparability of groups although not immune to bias

Compare exposed versus unexposed
- Challenging due to underlying differences in these groups
- “Healthy worker effect”, confounding by indication
## Incidence vs mortality

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Often have national data</td>
<td>• Ideal: population-based registries</td>
</tr>
<tr>
<td>• Under-reporting of cancer on death certificates</td>
<td>• Often rely on self-report with subsequent validation</td>
</tr>
<tr>
<td>• Less informative for non-fatal outcomes</td>
<td>• Informative for non-fatal outcomes</td>
</tr>
<tr>
<td>• Reflects factors related to survival as well as risk</td>
<td>• More informative for evaluating latency period</td>
</tr>
</tbody>
</table>
Life Span Study (LSS) of Japanese Atomic Bomb Survivors

“Gold Standard” of radiation epidemiology

- Large, unselected population
- Males and females
- Wide range of age at exposure
- Long-term, comprehensive follow-up
- Well-characterized doses across range

Acute, whole body exposures

Foundation of radiation protection standards
7 nested case-control studies of second GI cancers

- Nested within registry-based cohorts
  - Denmark, Finland, Iowa, Netherlands, Norway, Ontario, Sweden
- Detailed treatment data from medical records
- Dose reconstruction from RT records
- Dose-response relationship
- Joint effects – radiation and chemotherapy

<table>
<thead>
<tr>
<th>First cancer</th>
<th>Second Cancer</th>
<th>Esophagus</th>
<th>Stomach</th>
<th>Pancreas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Thyroid Cancer in Children in Ukraine

• Key source of information about long-term risk of thyroid cancer from I-131
  • One of several studies in exposed areas
• Cohort of 12,514 children screened regularly for thyroid cancer
• Resident in 3 contaminated areas
• Dose estimates:
  • individual radioactivity measures
  • dietary/lifestyle patterns reported on questionnaires
  • environmental measurements

Brenner et al. *Environ Health Perspect* 2011
Cancer risks
Cancer risks observed

- **Natural background**: Low, protracted
- **Nuclear Workers**: Low to moderate
- **A-bomb**: Moderate acute
- **Diagnostic**: Low to high fractionated
- **Therapeutic**: High frequency
Classification of radiation-related cancers

“Yes”
Significant dose-response relationship from robust epi studies

“Possibly”
Some evidence for dose-response relationship
Questions about biases, potential confounding

“Unclear”
Lack of adequately powered, high-quality studies
Inconsistent findings across studies

Berrington de González et al. Cancer Epidemiology and Prevention
Cancers caused by radiation

Yes
Bladder, Breast, Lung, Leukemia (non-CLL), Brain/CNS, Ovary, Thyroid, Colon, Esophagus, Oral (salivary gland), Stomach, Liver, NMSC, Bone, Soft tissue, Pancreas, Rectum

Possibly
Endometrial, Multiple Myeloma, CLL

Unclear
Non-Hodgkin Lymphoma, Prostate, Renal cell, Cervix, Gallbladder, Melanoma

Berrington de González et al. Cancer Epidemiology and Prevention
“Possibly related”

**Uterine corpus (endometrial)**

- Increased risk for certain ages at exposure?
- ERR greater when account for probability of hysterectomy

**CLL**

- Long thought to be unrelated to radiation
- Excess risk observed among Chernobyl clean-up workers

Utada et al. *JNCI Cancer Spec* 2018
Zablotska et al. *Environ Health Perspect.* 2013
Excess relative risks appear to vary by site

Berrington de González et al. Cancer Epidemiology and Prevention
Preston et al., *Rad Res* 2007
Questions

Why might magnitude of risk vary?

What can this variation teach us in terms of mechanisms?

What can we learn from sites with no apparent association?
Linear model

- Most parsimonious
- Good representation for most sites
  - Acute low to moderate doses – LSS
  - Fractionated, high-dose (> 5 Gy) RT
- Power often limited to detect departure from linearity – even at high-doses

BEIR VII 2006; Preston et al. Rad Res 2007
Berrington de Gonzalez et al Red Journal 2013
Non-linear relationships

• Leukemia (non CLL)

Hsu et al. *Rad Res* 2013

• Thyroid

Bhatti et al. *Rad Res* 2010
Why is shape important?

Radiation protection standards primarily based on extrapolation from LSS (low-to-moderate dose, high dose-rate)

Most exposures to workers and the general population at low(<100 mGy) dose, low dose-rate

What about risks from high-dose fractionated exposure (cancer survivors)?

How does variation in dose and dose-rate impact the risk?
Dose and dose-rate effectiveness factor (DDREF)

• Factor by which radiation effect changes at low doses, dose-rates compared with high dose, dose-rate

• BEIR VII: 1.5
  • Based on animal and epidemiological studies
  • Risk per unit dose reduced by 1/3 for protracted dose or total dose <100 mGy

• Use: risk projection, estimation of lifetime risks

BEIV VII 2006
Recent low dose, dose-rate studies

• Report risk estimates comparable to the LSS
  ➢ Suggests similar risk from protracted or fractionated low-dose exposures

• Challenge to compare across study populations that differ beyond dose and dose-rate characteristics
## Low dose, dose-rate studies: Two examples

<table>
<thead>
<tr>
<th>Study</th>
<th>ERR/Gy (95% CI)</th>
<th>Reference</th>
<th>Age exposure</th>
<th>LSS Age at exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leukemia (non-CLL)</strong></td>
<td></td>
<td>Pearce et al. <em>Lancet</em> 2012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK Childhood CT - Fractionated</td>
<td>36 (5-120)</td>
<td></td>
<td>&lt;15</td>
<td>45 (16-188)</td>
</tr>
<tr>
<td><strong>Solid cancer mortality</strong></td>
<td></td>
<td>Richardson et al. <em>BMJ</em> 2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INWORKS - Protracted</td>
<td>0.47 (0.18-0.79)</td>
<td></td>
<td>20-60</td>
<td>0.32 (0.01-0.50)</td>
</tr>
</tbody>
</table>
High-dose fractionated studies

• Therapeutic (high-dose) fractionated exposures
  • Risk estimates < LSS (5- to 10-fold)
  • Dose-response linear (exception thyroid) – unexpected

• Importance: Second cancer risks, inform risk/benefit assessment

Berrington de Gonzalez et al. Red Journal 2013
High-dose fractionated studies: Two examples

……. Fitted dose-response
- - - - For similar age (exposure, attained), BEIR VII model

How does risk per unit of dose vary by type?

Estimates of relative biological effectiveness (RBE) largely from animal and laboratory studies

Lack of data from epidemiologic studies

Implications for newer types of radiotherapies?

• Neutron scatter from proton - Neutrons 20 x > X-rays?
Radiation-related risks by age - illustrated for thyroid cancer (1)

- Relative and absolute risks tend to be higher at earlier age at exposure
  - Especially breast, leukemia, thyroid, brain
  - Exceptions: Lung?
  - Thyroid, brain – no apparent increase for exposure >20 y

Furukawa et al. *IJC* 2013
Radiation-related risks by age - illustrated for thyroid cancer (2)

- ERR – decreases with attained age
- EAR – increases with attained age

Furukawa et al. IJC 2013
Age at exposure and solid cancer incidence in LSS

- Suggestion of upturn in ERR at older ages observed earlier
- Most recent study shows this was driven by inclusion of autopsy-only cases

Grant et al. *Rad Res* 2017
Higher risk among females vs males?

- Observed in number of studies
- Differences in radiosensitivity?
- Modification by other factors?
- Differences in background rates?

Grant et al. *Rad Res* 2017
Time since exposure

• Minimum latency
  • ~ 2 years for leukemia
  • ~ 5 years for solid cancers

  ➢ Need for long-term follow-up and value of retrospective design

• Risks persist long-term
  • Do not return to baseline
  • Important for estimating cumulative risk, screening of high-risk populations

BEIR VII 2006
Joint effect of radiation and smoking

• Modification of radiation dose-response relationship by smoking observed across number of studies
• Nature of the interaction unclear

<table>
<thead>
<tr>
<th>LSS</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{ERR}_{\text{non-smokers}} )</td>
<td>&gt;</td>
</tr>
<tr>
<td>( \text{ERR}_{\text{light-moderate smokers}} )</td>
<td>&gt;</td>
</tr>
<tr>
<td>( \text{ERR}_{\text{heavy-smokers}} )</td>
<td></td>
</tr>
</tbody>
</table>

(Cahoon et al. *Rad Res* 2017)

<table>
<thead>
<tr>
<th>Radiotherapy</th>
<th>Lung after HL</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{ERR}_{\text{smokers}} )</td>
<td>&gt;</td>
</tr>
<tr>
<td>( \text{ERR}_{\text{nonsmokers}} )</td>
<td></td>
</tr>
</tbody>
</table>

(Gilbert et al. *Rad Res* 2003)
Variation in breast dose-response by age at menarche?

Brenner et al. Rad Res 2018
RT - dose-response attenuated by ovary dose

Breast cancer after RT CCSS
Genetic susceptibility

- Most knowledge to date based on rare mutations
  - Cancer-prone families
  - Highly-sensitive population
- Advances in technology
  - New opportunities to broaden the research
Absolute Risk & Attributable Fraction
Excess lifetime risk from pediatric CT: UK

Journy et al. BJC 2017
Cumulative breast cancer risk after chest RT

Moskowitz et al. JCO 2014
Estimated Attributable Fraction (AF)

• What proportion of cancers are caused by radiation?

• Contributing factors
  • exposure characteristics - dose and age at exposure distributions
  • population characteristics (age, sex, etc…)
  • distribution of cancers types
AF: Environmental Radiation Exposure

<table>
<thead>
<tr>
<th>Source</th>
<th>Population</th>
<th>Outcome</th>
<th>Estimated AF</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background radiation</td>
<td>England – all ages (&lt;15)</td>
<td>Leukemia</td>
<td>5% (15%)</td>
<td>Kendall et al. <em>Leuk Res</em> 2011</td>
</tr>
<tr>
<td>Residential radon</td>
<td>UK</td>
<td>Lung cancers</td>
<td>3%</td>
<td>Parkin and Darby <em>BJC</em> 2011</td>
</tr>
<tr>
<td>Chernobyl accident</td>
<td>Cleanup workers, residents, evacuees at highest exposure levels</td>
<td>Cancer deaths</td>
<td>3%-4%</td>
<td>WHO 2006</td>
</tr>
<tr>
<td>Japanese atomic bomb</td>
<td>Survivors</td>
<td>Solid cancers</td>
<td>10%</td>
<td>Grant et al. <em>Rad Res</em> 2017</td>
</tr>
</tbody>
</table>
AF: (up to age 75) from diagnostic medical radiation

Berrington and Darby *Lancet* 2004
<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome</th>
<th>Estimated AF</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>US adults treated for 15 cancers typically with RT</td>
<td>Solid cancers</td>
<td>8%</td>
<td>Berrington de Gonzalez et al. <em>Lancet</em> 2011</td>
</tr>
<tr>
<td>UK all ages treated for 13 cancers typically treated with RT</td>
<td>All cancers excluding NMSC</td>
<td>Males: 6%</td>
<td>Parkin and Darby <em>BJC</em> 2011</td>
</tr>
<tr>
<td>Female Hodgkin lymphoma survivors</td>
<td>All cancers excluding NMSC</td>
<td>19%</td>
<td>Parkin and Darby <em>BJC</em> 2011</td>
</tr>
<tr>
<td>Male Hodgkin lymphoma survivors</td>
<td>All cancers excluding NMSC</td>
<td>16%</td>
<td>Parkin and Darby <em>BJC</em> 2011</td>
</tr>
</tbody>
</table>
Opportunities for reducing exposures and risks

Radon remediation
- Careful clinical justification
- Using lowest reasonable dose
- Increase awareness
- Technologies to monitor and control dose

Diagnostic
- Treatment-planning systems to optimize tumor treatment, minimize dose to surrounding tissue

Radiotherapy
- Monitoring
- Improving protective gear to encourage use

Berrington de González et al. Cancer Epidemiology and Prevention
A few “classic studies”
Radiologists: First evidence that radiation can cause leukemia

**Leukemia in Radiologists**

HERMAN C. MARCH, M.D.
Philadelphia, Penna.

---

**Table II: Deaths from Leukemia in Radiologists, 1929-1943**

<table>
<thead>
<tr>
<th>Date of Death</th>
<th>Type of Leukemia Recorded</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct. 17, 1943</td>
<td>Lymphatic</td>
<td>54</td>
</tr>
<tr>
<td>July 15, 1943</td>
<td>Acute</td>
<td>43</td>
</tr>
<tr>
<td>April 23, 1943</td>
<td>Acute myelogenous</td>
<td>42</td>
</tr>
<tr>
<td>Feb. 22, 1942</td>
<td>Acute myelogenous</td>
<td>63</td>
</tr>
<tr>
<td>July 10, 1940</td>
<td>Leukemia</td>
<td>48</td>
</tr>
<tr>
<td>Jan. 23, 1939</td>
<td>Chronic lymphatic</td>
<td>65</td>
</tr>
<tr>
<td>June 24, 1938</td>
<td>Leukemia</td>
<td>52</td>
</tr>
<tr>
<td>Feb. 23, 1933</td>
<td>Lymphatic</td>
<td>69</td>
</tr>
</tbody>
</table>

Source: death notices in *JAMA*, 1929-1943

Comparison: radiologists and non-radiological physicians
Radium dial and clock painters

Early sources of data on cancer risk from high-let radiation

Excess risk of sarcoma and head carcinomas among female radium dial painters

Decades of research investigating:

| Dose-response analyses | latency | age at exposure |
Israeli study of radiotherapy for tinea capitis

- Large cohort of patients who underwent radiotherapy for tinea capitis, matched unexposed groups
- Linkage with pathology and cancer registry data
- Radiotherapy treatment records
- Excess risks of thyroid, brain/CNS and skin cancer
- Refining of dosimetry over time
- Low-dose external exposure to thyroid

Sources: UNSCEAR 2000; Ron et al. *Rad Res* 1989
Bone sarcoma after treatment for childhood cancer

- Cohort study with nested case-control component
- One of the first studies to quantify risk using estimated dose to bone tumor site
- Quantified joint effects radiation and chemotherapy
- Evaluated risks by type of radiotherapy

Tucker et al., NEJM 1987
## Moving forward

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Opportunities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer risks from low doses</td>
<td>Electronic medical record linkages</td>
</tr>
<tr>
<td>• Large sample size</td>
<td>• Pooled studies</td>
</tr>
<tr>
<td>• Long-term follow-up</td>
<td>• Biological samples – leveraging advances in genomics</td>
</tr>
<tr>
<td>• Minimize measurement error</td>
<td>• Availability of potential confounders?</td>
</tr>
</tbody>
</table>
Summary of ionizing radiation and cancer

- **Universal carcinogen**
  - Not “weak”

- Increasing evidence for risks at low dose, low dose-rate

- **Magnitude of risk appears to vary by site**

- **Age - modifier of radiation-related risk**
  - More research needed to understand the many other potential modifiers
Long history of radiation epidemiology

Radiation Exposure and Cancer: Case Study

Genevieve M. Metaxaski, John D. Boice, Jr., Stephen L. Brown, Ethel S. Gilbert, Jerome S. Puskin, and Tara O'Toole


Ionising radiation and cancer risks: What have we learned from epidemiology?

ETHEL S. GILBERT

Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland, USA

NATIONAL CANCER INSTITUTE
Question #1: Which of the following is not clearly associated with radiation?

a. Breast cancer
b. Leukemia
c. Thyroid cancer
d. Prostate cancer
Question #1: Which of the following is not clearly associated with radiation?

a. Breast cancer  
b. Leukemia  
c. Thyroid cancer  
d. Prostate cancer
Question #2: Studies of radiotherapy teach us about cancer risk from fractionated, high-dose exposures?

• a. True
• b. False
Question #2: Studies of radiotherapy teach us about cancer risk from fractionated, high-dose exposures?

• a. True

• b. False
Question #3: Which of the following are correct?

• a. Radiation-related relative risks tend to decrease with increasing age at exposure.

• b. Radiation-related absolute risks tend to increase with increasing attained age.

• c. Radiation-related risks do not tend to vary by age at exposure or attained age.

• d. Age effects have not been studied.
Question #3: Which of the following are correct?

• a. Radiation-related relative risks tend to decrease with increasing age at exposure.
• b. Radiation-related absolute risks tend to increase with increasing attained age.
• c. Radiation-related risks do not tend to vary by age at exposure or attained age.
• d. Age effects have not been studied.