Late Effects from Radiation Therapy
Radiation-Related Cardiac Effects
Outcome Evidence

Rebecca M. Howell
PhD, DABR

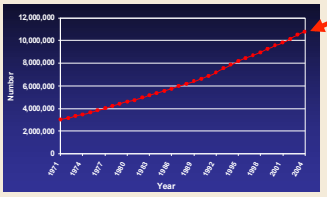
THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Overview

- Background and Significance
- Challenges of studying radiation related cardiac effects
- Effects at High Doses
- Effects at Low Doses
  - Childhood Cancer Survivors
  - Breast Cancer survivors
- Clinical Relevance
- Test Questions

Will include overview of dose reconstruction techniques used in these studies.

Significance
10 Million Cancer Survivors



10 million+

Source: Ries et al. (eds). SEER Cancer Statistics Review, 1975-2004, NCI. Bethesda. MD.http://seer.cancer.gov/1975_2004/, based on November 2006 SEER data submission, posted to the SEER website, 2007.

- **Number of cancer survivors in the U.S. has increased every year since 1971 and is now estimated to be 10 million+.**
- **This increase in cancer survivors is due to improved treatments, more frequent screening, greater life expectancy, and in some cases, increased cancer incidence rates.**

Radiation Related Late Effects

- Second Cancers
  - Most commonly reported late effect in Cancer Survivors.
- Cardiovascular Toxicity
  - Cardiovascular events are the leading non-malignant cause of death among survivors of childhood cancers.
  - Responsible for a 7-fold increase in risk of death compared with age matched peers.
- Cognitive impairments
- Sexual development
- Reproduction/fertility
- Endocrine abnormalities
- Growth/development delays

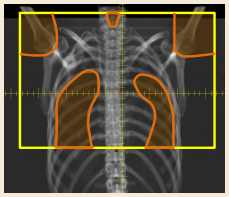
It difficult to study radiation related cardiac effects.

Why?

- Long latency
- Broad spectrum of cardiac diseases, including:
  - Coronary artery disease, congestive heart failure, myocardial infarction, pericardial disease, valvular dysfunction.
- Each type of disease may be associated with damage to particular part of the heart.
- Medical record validation of cardiac events is challenging:
  - Difficult to obtain and ensure accuracy of records for all events and deaths.

Evidence of Radiation Related Cardiac Effects at High Doses

- Until recently, there was a general belief that radiation related cardiac effects were only associated with high doses, *i.e.,* >30 Gy.
- Evidence in the literature was for patients treated for Hodgkin Lymphoma (Hancock, Tucker, and Hopp 1993).
  - Older treatment techniques, i.e., mantle field → heart in field.
  - Higher doses than current standard of care for HL.



Evidence of Radiation Related Cardiac Effects at Low Doses

- More recently, evidence is emerging that cardiac toxicity can occur at much lower doses.
  - A bomb survivors (*Preston et al.* 2003)
  - Childhood cancer survivors (*Mulroony et al.* 2009, Tukenova et al 2010)
  - Breast cancer survivors (*Taylor et al.* 2007, EBCTCG, 2005, Darby *et al.* 2010, McGale *et al.* 2011, Taylor *et al.* 2011)
  - Patients treated for peptic ulcers (*Carr et al.* 2005)

Cardiac Outcomes
Childhood Cancer Survivors

Incidence of Cardiovascular Disease
Mulrooney *et al.* BMJ 2009

- Largest analysis to date of **INCIDENCE** of cardiovascular disease among adult survivors of childhood/adolescent cancers.
  - **Design:** Retrospective cohort study
  - **Setting:** 26 Institutions that participated in CCSS
  - **Participants:** 14,358 5-year survivors of 8-different types of cancer treated between 1970 and 1986.
  - **Comparison group:** 3899 siblings of cancer survivors.
  - **Dose Reconstruction** - Mean radiation dose to the heart was estimated on the basis of detailed dosimetry calculations by Stovall (Methodology described in Stovall et al., 2006).

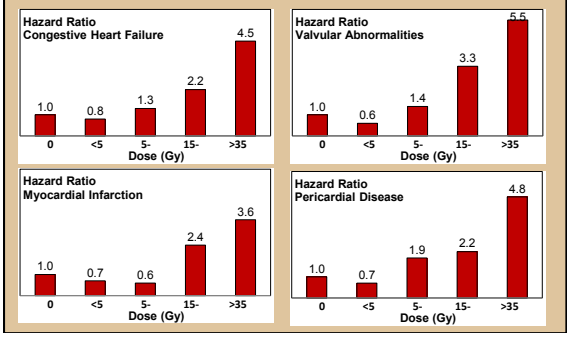
Incidence of Cardiovascular Disease
Mulrooney *et al*. BMJ 2009

- **Major Finding:** Radiation significantly increased risk for (compared with a sibling control group):
  1. congestive heart failure,
  2. myocardial infarction,
  3. pericardial disease,
  4. valvular dysfunction
- Increased risk was significantly associated with specific therapeutic exposures to
  - Anthracyclines or
  - cardiac radiation dose of more than **15 Gy.**

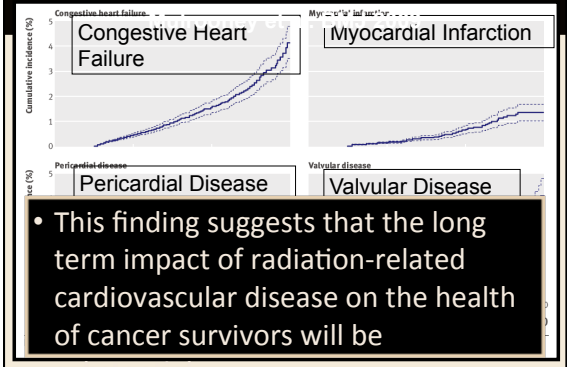
Incidence of Cardiovascular Disease
Mulrooney *et al.* BMJ 2009

- An important finding of this study was that it provided some insight into the dose-response relationship for cardiac outcomes.
- For all 4 outcomes incidence was found to increase with increasing dose.

Incidence of Cardiovascular Disease
Mulrooney *et al.* BMJ 2009



Incidence of Cardiovascular Disease



- This finding suggests that the long term impact of radiation-related cardiovascular disease on the health of cancer survivors will be

Study Strengths and Limitations
Mulrooney *et al.* BMJ 2009

Limitation
- Self reported outcomes, i.e., cardiac complications were evaluated by having survivors fill-out a questionnaire.

Strength
- Dose Reconstruction.

Dose Reconstruction – Cardiac Dose
Mulrooney *et al.* BMJ 2009

Patient Data
Abstract radiotherapy records for individual patients.

Therapeutic dose and treatment field details were obtained from Rx records, but individual organ doses were not available, patients were treated in pre-CT era.

Dose Reconstruction
- Analytical dose model + mathematical phantoms used to reconstruct the heart dose

Analytical Model of Out-of-Field Dose
Stovall *et al.* Radiat Res, 2006

- **Dose outside the treatment beam was measured in large water phantom**
  - **Various beam energies and field sizes.**

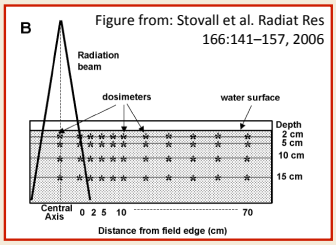
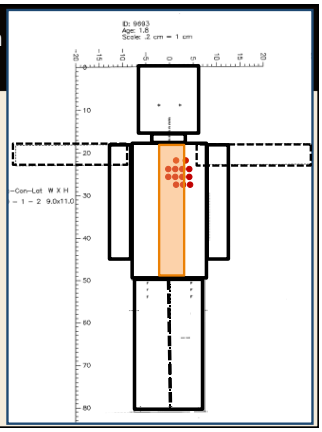


Figure from: Stovall et al. Radiat Res 166:141–157, 2006

Data were fit to analytical models to derive doses at specified distances from the field

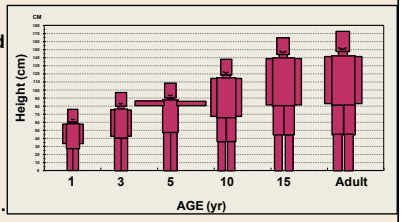
Mathematical Phantom
Stovall et al. Radiat Res, 2006

- **Organs represented by a grid of points.**
  - **Grid can moved.**
  - **Grid resolution can be ⇧ or ⇩.**
- Field can be placed in any position.
- Field geometry can be varied



Mathematical Phantom(s)
Stovall *et al.* Radiat Res, 2006

- **Phantom size can be modified to represent patient of any age.**
- **Models representing 7 age groups are shown in figure.**



- Mathematical phantoms are also inexpensive to use.

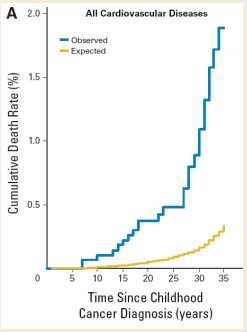
Figure from: Stovall et al. Radiat Res 166:141–157, 2006

Cardiac and Cardiovascular Mortality
Tukenova *et al.* JCO 2010

- Analysis of **Mortality from** cardiovascular disease among adult survivors of childhood/adolescent cancers.
  - **Design:** Retrospective cohort study
  - **Setting:** French-British cohort
  - **Participants:** 4,122 5-year survivors of childhood cancer (excluding leukemia) treated between 1942 and 1986.
  - **Comparison group:** Compared cardiac mortality in cohort with that of general populations of France and United Kingdom.
  - **Dose Reconstruction** - Mean radiation dose to the heart was estimated on the basis of detailed dosimetry calculations by using Dos_EG software, Gustave-Roussy Institute (Diallo et al 1996)

Cardiac and Cardiovascular Mortality
Tukenova et al. JCO 2010

- Individuals in this cohort were 5x more likely to die as a result of cardiovascular disease (compared to the general populations of France and Great Britian).
- Cumulative death rate increased with time since diagnosis.



Cardiac and Cardiovascular Mortality
Tukenova et al. JCO 2010

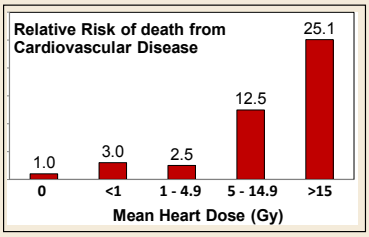
- The adjusted RR of death as a result of cardiac disease was significantly higher among patients treated with radiotherapy.

and

- **RR increased with increasing average radiation dose received by the heart** and with cumulative exposure to anthracyclines.

Cardiac and Cardiovascular Mortality
Tukenova *et al.* JCO 2010

- RR increased with increasing heart dose.



- A linear fit dose response model, with **ERR = 60%** (95% CI, 20% to 250%).

Study Strengths and Limitations
Tukenova *et al.* JCO 2010

Strengths

- Cause of death determined from death certificate.
  - more definitive than self-reported incidence information).
- Dose Reconstruction.

Limitations

- Cause of death determined from death certificates
  - only considered principal cause of death → death as result of cardiovascular disease probably underreported.
- No information regarding tobacco consumption, weight, or genetic factors → can introduce bias.

Cardiac Outcomes
Breast Cancer Survivors

Cardiac Mortality Left vs Right Breast RT
Darby *et al.* Lancet Oncology 2005

- Compared mortality ratio from heart disease in 300,000 women from SEER cancer registry that received radiation for left and right breast cancers.

Years since breast cancer diagnosis	No radiotherapy: No. of deaths left/right	No radiotherapy: Mortality ratio left versus right & 95% CI	Radiotherapy: No. of deaths left/right	Radiotherapy: Mortality ratio left versus right & 95% CI
Heart disease death				
< 5 years	2164/1972	1.03 (0.97-1.09)	700/633	1.04 (0.93-1.15)
5 - 9	1632/1479	1.05 (0.98-1.13)	521/442	1.10 (0.97-1.25)
10 - 14	806/758	1.01 (0.91-1.11)	281/197	1.37 (1.14-1.64)
15+	568/524	1.02 (0.91-1.15)	254/162	1.53 (1.25-1.86)
All other known causes				
< 5 years	14775/13522	1.04 (1.01-1.06)	6911/6516	1.01 (0.98-1.05)
5 - 9	8009/7863	0.97 (0.94-1.00)	3178/2990	1.01 (0.96-1.06)
10- 14	3472/3343	0.99 (0.94-1.04)	1165/1095	1.01 (0.93-1.10)
15+	2106/2040	0.98 (0.92-1.04)	611/560	1.04 (0.93-1.17)

Radiation Associated Cardiac Events (RACE)

Radiation Associated Cardiac Events (RACE)

- An Initiative in Denmark and Sweden to evaluate the risk of developing cardiovascular disorders in women who were treated for breast cancer.
- Project is dedicating substantial effort in establishing accurate heart doses.
- http://www.race.ki.se/.

Incidence of Cardiovascular Disease
McGale *et al. Radiother Oncol* 2011

- Analysis of **INCIDENCE** of cardiovascular disease among breast cancer survivors in Sweden and Denmark.
  - **Design:** Retrospective cohort study
  - **Setting:** used the population-based disease registries in Denmark and Sweden, included 34,828 patients that had received RT
  - **Study design:** Radiation-related risk was evaluated by comparing patients treated with left verses right sided breast cancer.
  - **Dose Reconstruction:** Mean cardiac doses were estimated using dose-volume histograms (Methodology described in **Taylor et al., 2007 and 2011**).

Dose Reconstruction – Cardiac Dose

McGale et al. Radiother Oncol 2011 (Taylor et al 2011, 2007)

- Radiotherapy treatment charts were obtained and categorized according to regimen:
  - laterality, target dose(s), dose/fx, and ± supraclav or axillary RT.

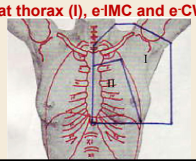
Dose Reconstruction – Cardiac Dose

McGale *et al. Radiother Oncol* 2011 (Taylor et al 2011, 2007)

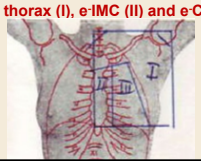
Wide Tangential Pair

Tangential Pair to Midline

Lat thorax (I), e-IMC and e-CW (II)



Lat thorax (I), e-IMC (II) and e-CW (III)

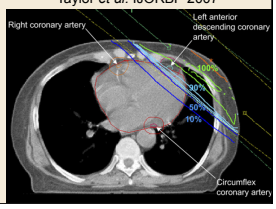


Dose Reconstruction – Cardiac Dose

McGale *et al. Radiother Oncol* 2011 (Taylor et al 2011, 2007)

- 22 different RT regimens(11 left & 11 right) were reconstructed on a CT scan of typical patient of average build.

Taylor *et al.* IJORBP 2007

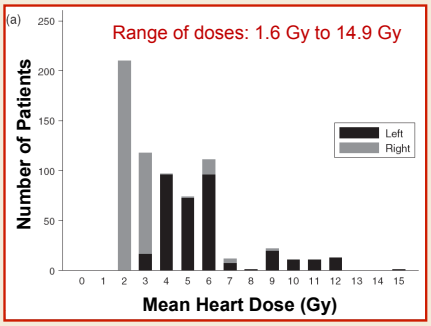


- Heart and Coronary arteries were contoured
- DVH were used to determine mean heart dose for each regimen.

Dose Reconstruction – Cardiac Dose

McGale *et al.* Radiother Oncol 2011 (Taylor et al 2011)

- Low doses dominated by RIGHT breast patients
- High Doses dominated by LEFT Breast Patients



Incidence of Cardiovascular Disease

***McGale et al. . Radiother Oncol* 2011**

Results

- Left and right sided breast tumors: mean heart dose = 6.3 Gy and 2.7 Gy, respectively
- **Incidence ratios for cardiac effects were higher in patients treated left verses right:**
  - Myocardial infarction: 1.22
  - Angina: 1.25
  - Pericarditis: 1.61
  - Valvular heart disease: 1.54

Study Strengths and Limitations

McGale *et al.* . *Radiother Oncol* 2011

- Strength: Heart disease was defined using **hospital discharge codes**.
  - Scandinavian countries have detailed medical records that follow individuals for entire lifespan.
  - More definitive than self-reported incidence information.
- Strength: Unbiased compared to studies that use unirradiated patients as control group.
  - Such studies often underestimate cardiac effects as patients with left sided disease are frequently selected for therapy without radiation due to concerns regarding cardiac effects.

Study Strengths and Limitations
McGale *et al. . Radiother Oncol* 2011

- Strength: Dose reconstruction was completed using real patient anatomy for 22 different treatment regimes and TPS.

Limitations

- All data are for a single "typical" patient, study does not take anatomical variations between patients into account.
- All MV photon plans were for 6 MV (actual was 6-25 MV)
- All electron plans were calculated for 10 MeV (actual 6-18 MeV)
- commercial TPSs underestimate stray photon doses.
- Stray dose from neutrons not considered

Incidence of Cardiovascular Disease
***McGale et al. . Radiother Oncol* 2011**

- The work by McGale et al. did not report dose response model…
- However such data will likely be published in future manuscript…
- Until then, we have glimpse of results from 2010 ASTRO presentation by *Darby et al.*
  - In case control study of patients that received breast radiation therapy, *compared*
    - those who developed heart disease
    - those who had not developed heart disease

Incidence of Cardiovascular Disease
***Darby et al. IJORBP* 2010**

- Risk of heart disease increased linearly with dose.
- **On average, there was a 4% increase in heart disease risk per 1 Gy increase in mean heart dose** (95% CI, 2-6%).

These data are very interesting. When the full manuscript is published, it will fill an important gap in our present knowledge regarding the details of the dose response relationship for breast cancer patients.

Summary

Cardiac Outcome Studies

Summary
and
Applications to Clinical Practice

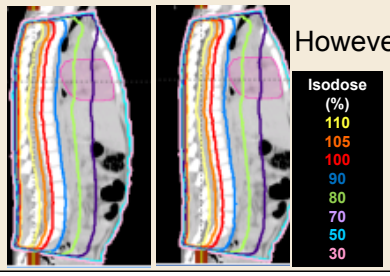
- There remains uncertainty in the exact details of the dose response models for radiation related cardiac effects,
  - but as discussed today, there is increasing evidence that points toward a linear dose response model.
- While more research is needed in this area, efforts should be made to keep the cardiac dose as low as possible for individual patients.

How can we incorporate information on cardiac effects in to clinical practice?

Pediatric CSI Example

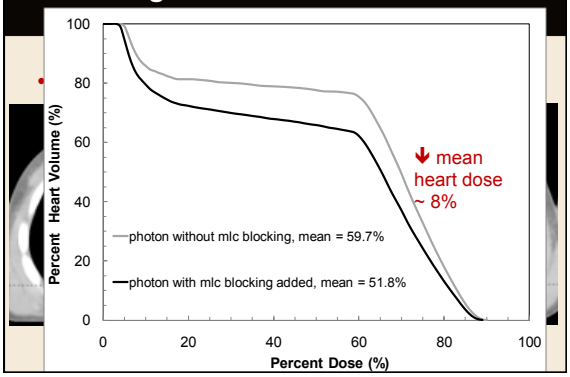
Reducing Cardiac Dose in Clinical Practice

- **Two different 6MV FIF CSI treatment plans, appear identical in sagittal view.**



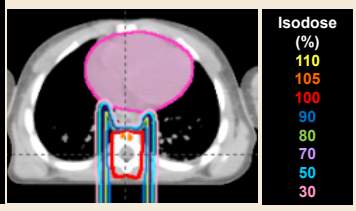
However, …

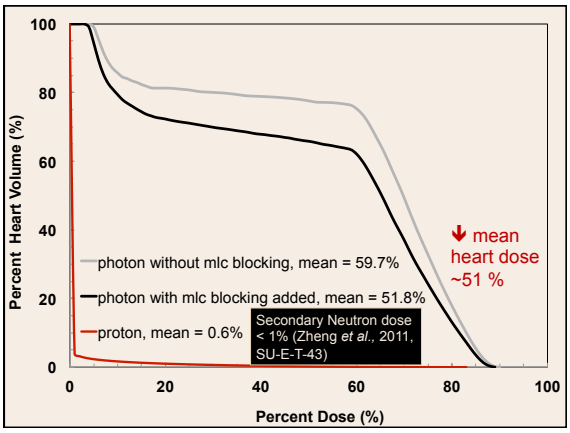
Reducing Cardiac Dose



Reducing Cardiac Dose in Clinical Practice

- Proton CSI treatment plan, very low exit dose.
- **Low heart dose.**

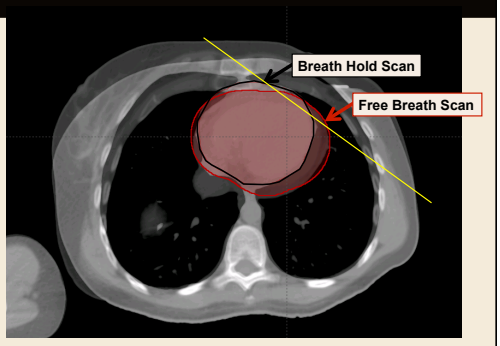


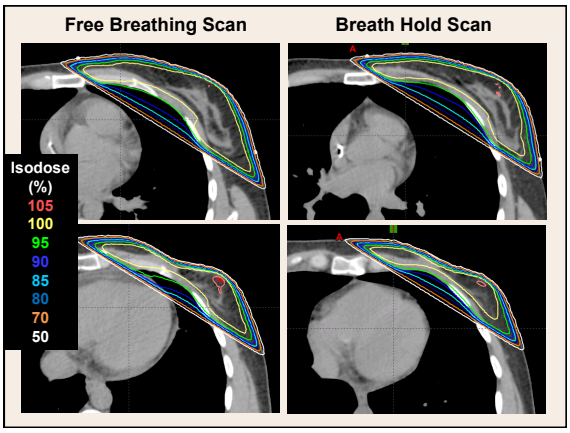


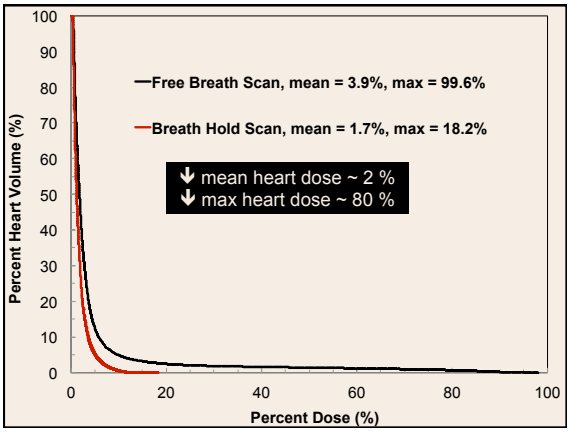
How can we incorporate information on cardiac effects in to clinical practice?

Breast Cancer Example

Free Breath verses Breath Hold







Concluding Remarks…… Important Questions Remain

- **What are the effects of non-uniform irradiation?**
  - Such effects are particularly important in the era on contemporary radiotherapy where IMRT is often the standard of care.
- **What are the effects associated with dose to various parts of heart.**
  - Evidence exists that certain parts of the heart are more radiosensitive than others Adams et al., 2003; Stewart et al., 1995, but more research is needed.

References (1)

- Darby SC, Bronnum D, Correa C, Ewertz M, Gagliardi G, Gigante B, McGale P, Nisbet A, Taylor C and Hall P 2010a A dose-response relationship for the incidence of radiation-related heart disease International Journal of Radiation Oncology Biology Physics 78 S49-S50
- Darby SC, Cutter DJ, Boerma M, Constine LS, Fajardo LF, Kodama K, Mabuchi K, Marks L B, Mettler F A, Pierce LJ, Trott KR, Yeh ETH and Shore R E 2010b Radiation-related heart disease: Current knowledge and future prospects International Journal of Radiation Oncology Biology Physics 76 656-65
- Darby SC, McGale P, Taylor C W and Peto R 2005 Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: Prospective cohort study of about 300 000 women in us seer cancer registries Lancet Oncology 6 557-65
- Hancock L, Tucker MA and Hoppe RT 1993 Factors affecting late mortality from heart-disease after treatment of hodgkins-disease Jama-Journal of the American Medical Association 270 1949-55
- Mulrooney A, Yeazel M W, Kawashima T, Mertens AC, Mitby P, Stovall M, Donaldson SS, Green DM, Sklar CA, Robison LL and Leisenring W M 2009 Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: Retrospective analysis of the childhood cancer survivor study cohort British Medical Journal 339

References (2)

- Taylor CW, Nisbet A, Mcgale P and Darby SC 2007 Cardiac exposures in breast cancer radiotherapy: 1950s-1990s International Journal of Radiation Oncology Biology Physics 69 1484-95
- Tukenova M 2010 Role of cancer treatment in long-term overall and cardiovascular mortality after childhood cancer (vol 28, pg 1308, 2010) Journal of Clinical Oncology 28 3205-
- Zhang Z, Howel RM, Giebeler A, Taddei PJ, Mahajan A, and Newhauser WD. SU-E-T-43: Calculation of the Risks of Second Cancer and Cardiac Toxicities for a Pediatric Patient Treated with Photon and Proton Radiotherapies. Med. Phys. 38, 3495 (2011)
- Adams MJ, Hardenbergh PH, Constine LS and Lipshultz SE 2003 Radiation-associated cardiovascular disease Critical Reviews in Oncology Hematology 45 55-75
- Stewart JR, Fajardo LF, Gillette M and Constine LS 1995 Radiation-Injury to the Heart *International Journal of Radiation Oncology Biology Physics* 31 1205-11
- McGale P, Darby SC, Hall P, et al. Incidence of heart disease in 35,000 women treated with radiotherapy for breast cancer in Denmark and Sweden. Radiotherapy and Oncology 2011;100:167-175.
- Taylor CW, Bronnum D, Darby SC, et al. Cardiac dose estimates from Danish and Swedish breast cancer radiotherapy during 1977-2001. Radiotherapy and Oncology 2011;100:176-183.

Question Set for Radiation-Related Cardiac Effects

_____are the leading non-malignant cause of death among survivors of childhood cancers

93% 1. **Cardiovascular events.**
0% 2. **Reproduction/fertility events.**
2% 3. **Endocrine abnormalities.**
5% 4. **Growth/development delays.**
0% 5. **skin cancers.**

Correct answer: 1

Armstrong G T, Liu Q, Yasui Y, Neglia J P, Leisenring W, Robison L L and Mertens A C, Late mortality among 5 -year survivors of childhood cancer: A summary from the childhood cancer survivor study Journal of Clinical Oncology 27 2328-38 (2009).

_____are the leading non-malignant cause of death among survivors of childhood cancers

1. **Cardiovascular events.**
2. **Reproduction/fertility events.**
3. **Endocrine abnormalities.**
4. **Growth/development delays.**
5. **skin cancers.**

Correct answer: 1

Armstrong G T, Liu Q, Yasui Y, Neglia J P, Leisenring W, Robison L L and Mertens A C, Late mortality among 5 -year survivors of childhood cancer: A summary from the childhood cancer survivor study Journal of Clinical Oncology 27 2328-38 (2009).

_____It is difficult to study radiation related cardiac events for all of the following reasons *EXCEPT:*

11% 1. **Long latency**
5% 2. **Broad spectrum of cardiac diseases.**
23% 3. **Medical record validation is challenging.**
48% 4. **Cardiac events are rare in cancer survivors.**
13% 5. **Each type of disease may be associated with damage to particular parts of the heart.**

Correct answer: 4

Darby S C, Cutter D J, Boerma M, Constine L S, Fajardo L F, Kodama K, Mabuchi K, Marks L B, Mettler F A, Pierce L J, Trott K R, Yeh E T H and Shore R E, Radiation-related heart disease: Current knowledge and future prospects International Journal of Radiation Oncology Biology Physics 76 656-65 (2010).

_____It is difficult to study radiation related cardiac events for all of the following reasons EXCEPT:

1. Long latency
2. Broad spectrum of cardiac diseases.
3. Medical record validation is challenging.
4. Cardiac events are rare in cancer survivors.
5. Each type of disease may be associated with damage to particular parts of the heart.

Correct answer: 4

Darby S C, Cutter D J, Boerma M, Constine L S, Fajardo L F, Kodama K, Mabuchi K, Marks L B, Mettler F A, Pierce L J, Trott K R, Yeh E T H and Shore R E, Radiation-related heart disease: Current knowledge and future prospects International Journal of Radiation Oncology Biology Physics 76 656-65 (2010).

Analytic calculation methods for dose reconstruction (in epidemiological studies) using generic phantoms typically include all of the following EXCEPT:

2%	1. Leakage photon radiation.
4%	2. Primary (in-field) photon radiation.
0%	3. Patient (photon) scatter radiation.
91%	4. Neutron contamination.
4%	5. Collimator scatter radiation.

Correct answer: 4

Stovall M, Weathers R, Kasper C, Smith S A, Travis L, Ron E and Kleinerman R,, Dose reconstruction for therapeutic and diagnostic radiation exposures: Use in epidemiological studies Radiation Research 166 141-57 (2006)

Analytic calculation methods for dose reconstruction (in epidemiological studies) using generic phantoms typically include all of the following EXCEPT:

1. Leakage photon radiation.
2. Primary (in-field) photon radiation.
3. Patient (photon) scatter radiation.
4. Neutron contamination.
5. Collimator scatter radiation.

Correct answer: 4

Stovall M, Weathers R, Kasper C, Smith S A, Travis L, Ron E and Kleinerman R,, Dose reconstruction for therapeutic and diagnostic radiation exposures: Use in epidemiological studies Radiation Research 166 141-57 (2006)

In the studies of incidence and mortality of radiation related cardiac events in survivors of childhood cancer, cardiac events were found to:

17% 1. Increase with doses > 30 Gy.
80% 2. Increase with increasing dose.
3% 3. Follow a linear plateau dose response model.
0% 4. No pattern was observed.
0% 5. Increase only if chemotherapy was also part of the patient's therapy.

Correct answer: 2

Mulrooney D A, Yeazel M W, Kawashima T, Mertens A C, Mitby P, Stovall M, Donaldson S S, Green D M, Sklar C A, Robison L L and Leisenring W M, Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: Retrospective

In the studies of incidence and mortality of radiation related cardiac events in survivors of childhood cancer, cardiac events were found to:

1. Increase with doses > 30 Gy.
2. Increase with increasing dose.
3. Follow a linear plateau dose response model.
4. No pattern was observed.
5. Increase only if chemotherapy was also part o the patient's therapy.

Correct answer: 2

Mulrooney D A, Yeazel M W, Kawashima T, Mertens A C, Mitby P, Stovall M, Donaldson S S, Green D M, Sklar C A, Robison L L and Leisenring W M, Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: Retrospective

The mortality ratio from heart disease in patients who received radiotherapy for left verses right breast was approximately _____at 15 years after treatment.

6% 1. 1.0
3% 2. 0.5
6% 3. 5
10% 4. 2
74% 5. 1.5

Correct answer: 5

Darby S C, McGale P, Taylor C W and Peto R , Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: Prospective cohort study of about 300 000 women in us seer cancer registries Lancet Oncology 6 557-65 (2005).

The incidence of cardiac events in patients who received radiation therapy for breast cancer was found to _____.

70% 1. To have a linear dose response, 4%/Gy
7% 2. To have a linear dose response, 14%/Gy
10% 3. Increase with dose above 30 Gy.
0% 4. No pattern was observed
13% 5. Dosimetry data was insufficient to establish a dose response model

Correct answer: 1

Darby S C, Bronnum D, Correa C, Ewertz M, Gagliardi G, Gigante B, McGale P, Nisbet A, Taylor C and Hall P, A dose - response relationship for the incidence of radiation-related heart disease International Journal of Radiation Oncology Biology Physics 78 S49-S50 (2010).

The incidence of cardiac events in patients who received radiation therapy for breast cancer was found to _____.

1. To have a linear dose response, 4%/Gy
2. To have a linear dose response, 14%/Gy
3. Increase with dose above 30 Gy.
4. No pattern was observed
5. Dosimetry data was insufficient to establish a dose response model

Correct answer: 1

Darby S C, Bronnum D, Correa C, Ewertz M, Gagliardi G, Gigante B, McGale P, Nisbet A, Taylor C and Hall P, A dose - response relationship for the incidence of radiation-related heart disease International Journal of Radiation Oncology Biology Physics 78 S49-S50 (2010).

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Thank you.

Questions?