

# Late Effects: After Radiation Therapy for Childhood Cancer

Karen Goddard



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# Conflict of Interest

- None. I have no industry financial relationships.



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# Objectives

- Overview of:
  - Frequency of late effects in survivors of pediatric cancer
  - Late effects caused by:
    - Disease
    - Therapy:
      - Surgery
      - Chemotherapy
      - **Radiation Therapy (RT)**
  - Multiple different organ systems at risk
- Identify:
  - Major long term health problems in this population
  - The impact of these problems on survivor's life
  - Health care implications



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# Incidence

- 15,780 new cancer cases of childhood/adolescent cancer diagnosed in children and adolescents in 2014 in U.S.
- In Canada 1500 patients diagnosed with cancer between the ages of 0 and 19 per year.
- Over 80% of these children will be long term survivors who have been cured of their disease
- 20 to 30 years ago many children with cancer did not survive
- Improvements due to:
  - Multimodality Rx
  - Therapy intensification
- In 2014: **1 in 530** of all adults are childhood cancer survivors (CCS) in North America
- Over 375,000 childhood cancer survivors in US



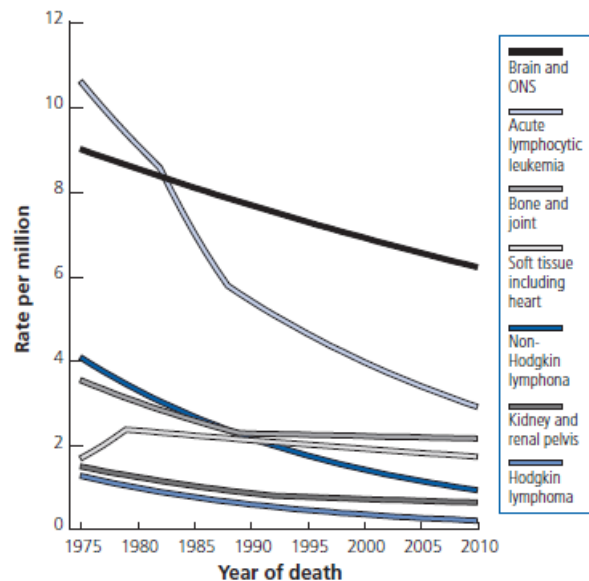
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# U.S. Mortality and Survival Rates

**Figure 3. Trends in Pediatric Cancer Mortality Rates by Site, Ages 0-19, 1975-2010**



ONS = Other nervous system.

**Note:** Lines are fitted trends based on Joinpoint analyses.

Average annual percent change (APC) for cancers with significant trends during most recent period: ALL (-3.1 during 1988-2010), brain (-1.1 during 1975-2010), NHL (-4.1 during 1975-2010), soft tissue (-1.0 during 1979-2010), kidney (-1.2 during 1992-2010), HL (-4.9 during 1975-2010).

**Source:** National Center for Health Statistics, Centers for Disease Control and Prevention.

American Cancer Society, Surveillance Research, 2014

**Table 4. Pediatric Cancer Five-year Observed Survival Rates for Two Time Periods, Ages 0-19**

	Year of Diagnosis	
	1975-79 %	2003-09* %
All ICCC sites	63	83
Leukemia	48	84
Acute lymphocytic leukemia	57	90
Acute myeloid leukemia	21	64
Lymphomas and reticuloendothelial neoplasms	72	91
Hodgkin lymphoma	87	97
Non-Hodgkin lymphoma	47	85
Brain and CNS	59	75
Ependymoma	37	81
Astrocytoma	69	85
Medulloblastoma	47	70
Neuroblastoma and ganglioneuroblastoma	54	79
Retinoblastoma	92	99
Wilms tumor	75	90
Hepatic tumors	25	74
Bone tumors	49	73
Osteosarcoma	45	71
Ewing sarcoma	42	72
Rhabdomyosarcoma	49	64
Testicular germ cell tumors	74	96
Ovarian germ cell tumors	75	94
Thyroid carcinoma	99	98
Melanoma	83	95

ICCC=International classification of childhood cancers.

CNS=Central nervous system.

\*Cases were followed through 2010.

Note: Does not include benign and borderline brain tumors.

**Source:** Surveillance, Epidemiology, and End Results (SEER) program, 9 SEER registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014



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# Late Effects

- Definition:
  - “Side effects that occur more than 5 years after diagnosis”
- Problems with definition:
  - Etoposide related AML (short latency)
- Generally takes many years for late effects to develop
- How are these problems detected?
  - Follow up
    - Surveillance programs



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# Late Effects

- Late effects include:
  - Physical problems
    - Organ damage
      - Development affected
      - High risk of late effects in adults treated for childhood cancer
    - Secondary tumors
  - Psychological problems
    - Depression, anxiety



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# Late Effects

## Clinical Ascertainment of Health Outcomes Among Adults Treated for Childhood Cancer

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**C**URATIVE THERAPY FOR PEDI-  
atric malignancies has pro-  
duced a growing population  
of adults formerly treated for

**Importance** Adult survivors of childhood cancer are known to be at risk for treatment-related adverse health outcomes. A large population of survivors has not been evaluated using a comprehensive systematic clinical assessment to determine the prevalence of chronic health conditions.

**Objective** To determine the prevalence of adverse health outcomes and the proportion associated with treatment-related exposures in a large cohort of adult survivors of childhood cancer.

**Design, Setting, and Participants** Presence of health outcomes was ascertained using systematic exposure-based medical assessments among 1713 adult (median age, 32 [range, 18-60] years) survivors of childhood cancer (median time from diagnosis, 25 [range, 10-47] years) enrolled in the St Jude Lifetime Cohort Study since October 1, 2007, and undergoing follow-up through October 31, 2012.

**Main Outcomes and Measures** Age-specific cumulative prevalence of adverse outcomes by organ system.

**Results** Using clinical criteria, the crude prevalence of adverse health outcomes was highest for pulmonary (abnormal pulmonary function, 65.2% [95% CI, 60.4%-69.8%]), auditory (hearing loss, 62.1% [95% CI, 55.8%-68.2%]), endocrine or reproductive (any endocrine condition, such as hypothalamic-pituitary axis disorders and male germ cell dysfunction, 62.0% [95% CI, 59.5%-64.6%]), cardiac (any cardiac condition, such as heart valve disorders, 56.4% [95% CI, 53.5%-59.2%]), and neurocognitive (neurocognitive impairment, 48.0% [95% CI, 44.9%-51.0%]) function,



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# Late Effects

- At age 45 years:
  - 95.5% cumulative prevalence of any chronic health condition
  - 80.5% (95% CI, 73.0%-86.6%) for a serious/disabling or life-threatening chronic condition



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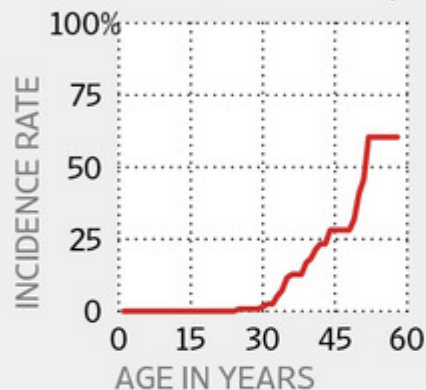
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# Survivors at Risk

Researchers followed more than 1,700 adults who had been treated for cancer as children and found that those who had received certain types of treatment were very likely to develop certain health problems later in life.

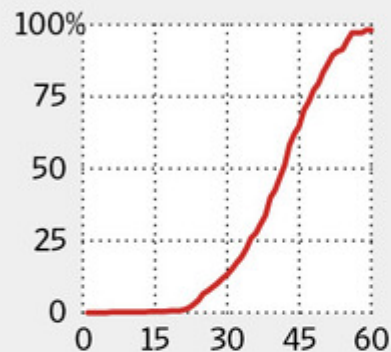
**Adult condition: Breast cancer**

**Childhood treatment:** Radiation to the breast (females only)



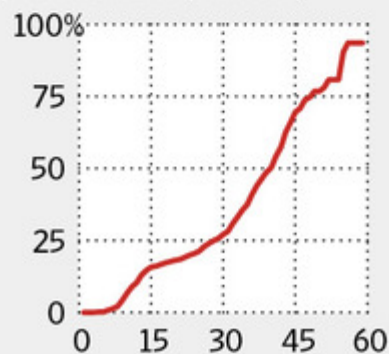
**Heart-valve disorder**

Radiation to the heart



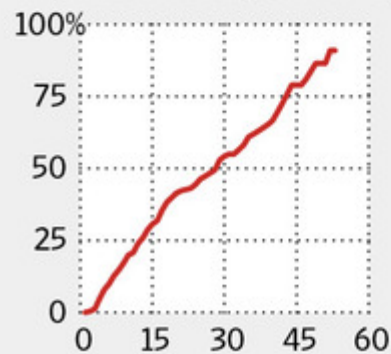
**Pituitary dysfunction**

Radiation to the hypothalamus-pituitary



**Hearing loss**

Radiation to the ear or exposure to cisplatin or carboplatin



Sources: St. Jude Children's Research Hospital; JAMA

The Wall Street Journal



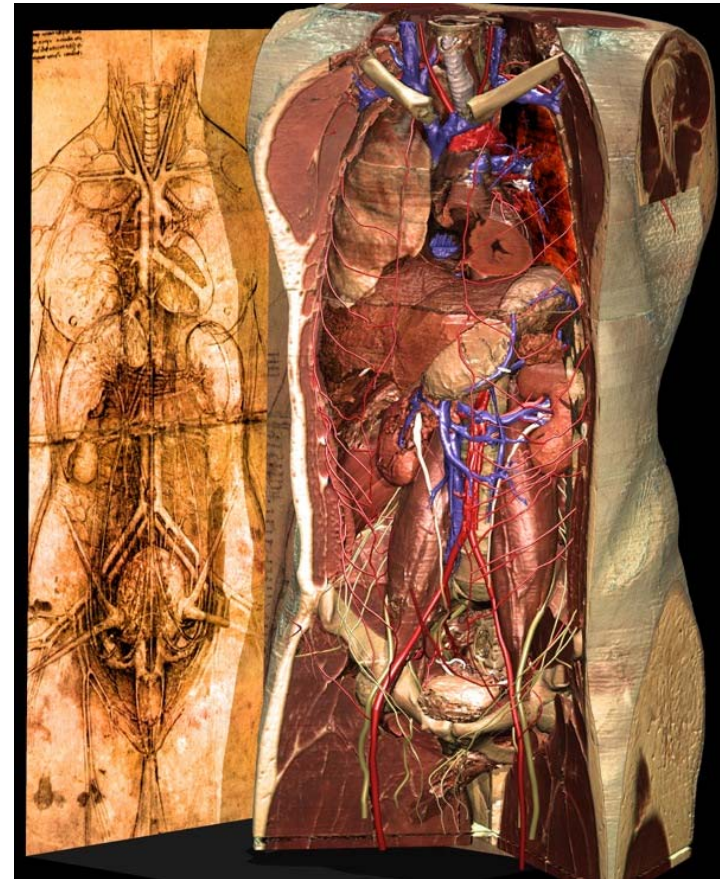
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# Organs at Risk

- Central nervous system
- Orbit
- Hearing
- Peripheral Nervous system
- Endocrine
- GU system
- Respiratory
- Gastro-intestinal
- Musculoskeletal
- Reproductive organs
- Cardiovascular
- Skin



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# Tumor Related Damage

- Invasion into and pressure on different structures
  - Wilms tumor
    - One kidney usually completely destroyed by disease and has to be removed



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# Tumor Related Damage

- Craniopharyngioma tumor growth and cyst expansion leads to compression of:
  - Optic apparatus
    - Blindness
  - Pituitary
    - Endocrinopathy



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# Surgery Related Damage

- Surgery
  - Prime modality for local control
- Lymph node dissection
  - Lymphedema
- Splenectomy
  - Life threatening infection
    - Pneumococcal vaccine
    - Medic Alert bracelet



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# Chemotherapy Related Damage

- Chemotherapy prime modality for systemic control
- Depends on agent and sensitivity of target organs
  - Adriamycin – cardiomyopathy
  - Cisplatin – nephrotoxicity and hearing loss
  - Alkylating agents – infertility and second cancers
  - Vincristine and peripheral neuropathy



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# Radiation Therapy (RT)

- In children (unlike adults) affects normal growth/development
- Toxicity depends on:
  - Age at the time of therapy
  - Total dose given
  - Fractionation
  - Region treated:
    - Some organs more sensitive and easily damaged
    - Amount of normal tissue treated
  - Concurrent chemotherapy can sensitize normal tissues
  - Underlying genetic problems:
    - Ataxia-telangiectasia
    - Radio-genomics



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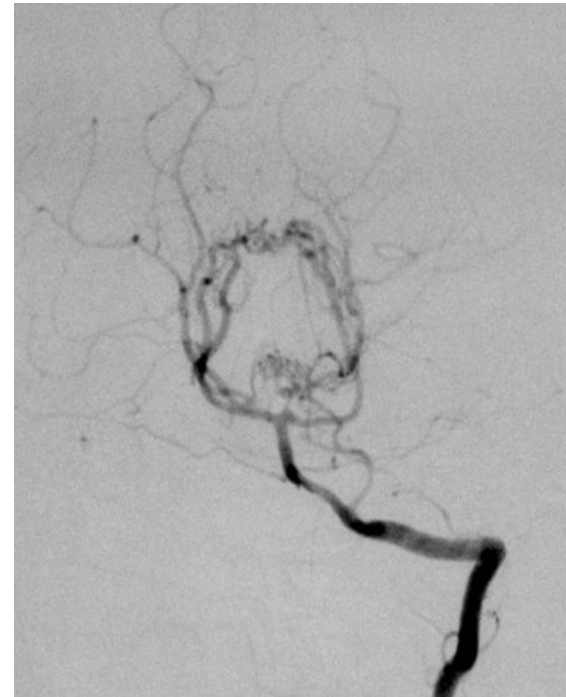
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# CNS

- Brain
  - Developmental delay
  - Poor short term memory
  - Poor executive function
  - Seizures
  - Cerebrovascular events
    - Thrombotic and haemorrhagic
- Spinal cord
  - Myelitis
- Hearing loss
- Visual loss



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# CNS: Brain Tumors

- Long term IQ in pediatric brain tumor patients depends on age at the time of therapy:
- Age at time of therapy for medulloblastoma:
  - 1–5 years:
    - Mean IQ of 72
    - 50% of patients had scores less than 80
  - 6–10 years
    - Mean IQ of 93
    - 14% had IQ scores of less than 80
  - Children 11- 15 years
    - Mean IQ of 107
    - 9% had IQ scores of less than 80



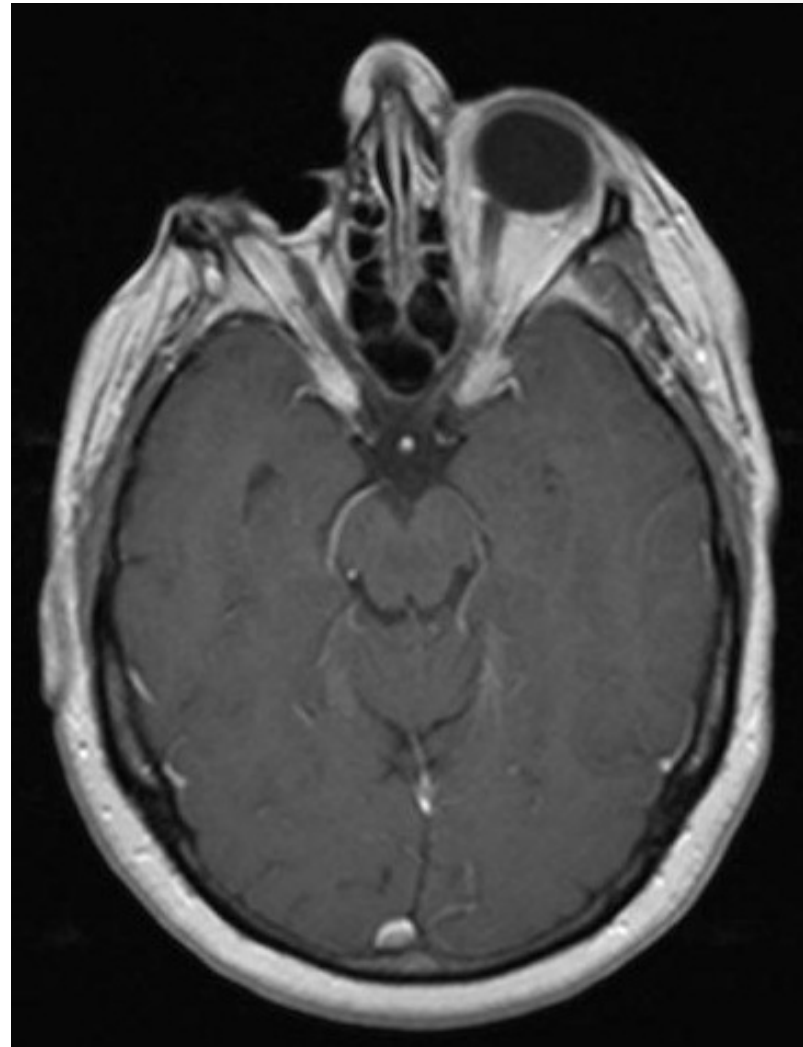
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# Orbit

- Visual loss
  - High dose RT:
    - Anterior chamber damage
    - Acute glaucoma
    - Painful red eye
    - Treated by enucleation
  - Low dose RT:
    - Cataracts



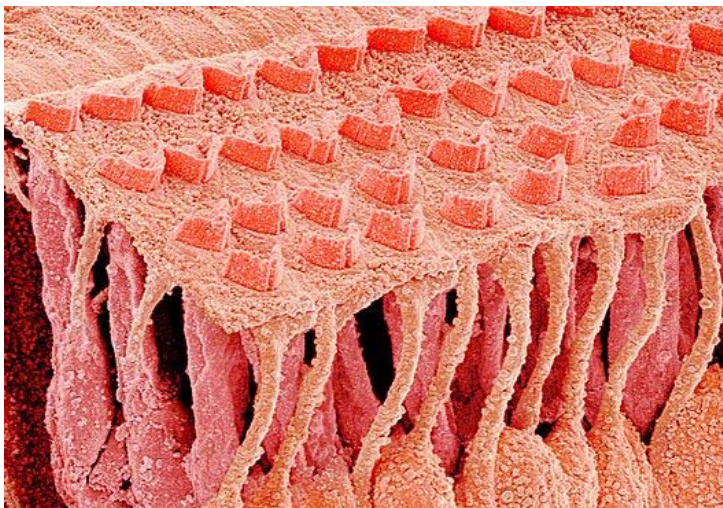
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# Hearing loss

- Radiation Therapy:
  - Conductive: wax build up
  - Sensorineural: direct damage to cochlea
- Chemotherapy:
  - Sensorineural
  - Cisplatin causes high frequency hearing loss
    - Sensory hair cells in the cochlea



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# Musculoskeletal

- Bone/Muscle/soft tissues
  - “Hypoplasia” – reduced growth within the RT field

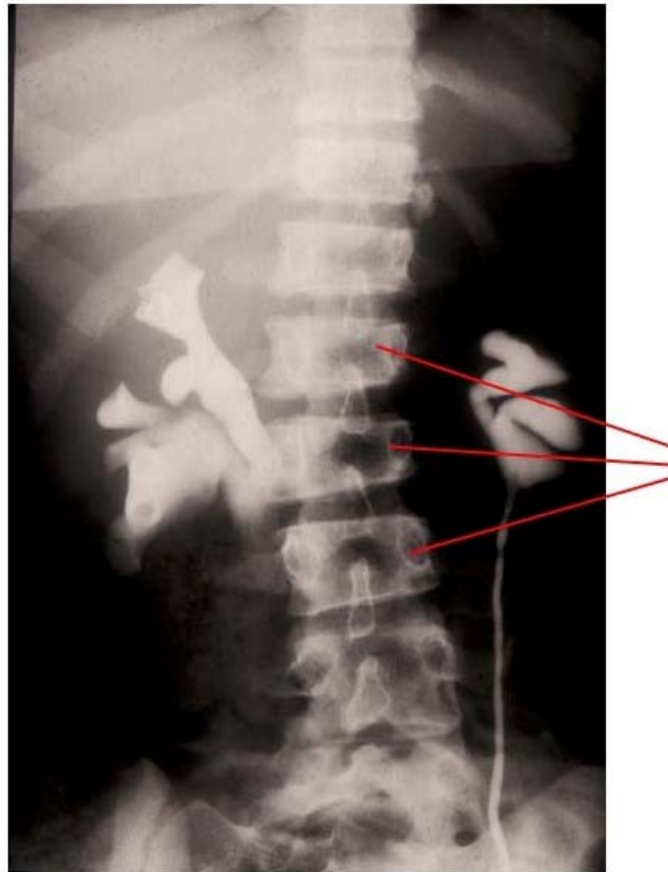


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# Musculoskeletal



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# Facial Hypoplasia

- Lucy Greal “Autobiography of a face”



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# Musculoskeletal

- Bone/Muscle/soft tissues
  - Hypoplasia – reduced growth within the RT field
  - Endocrinopathy



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# Endocrinopathy

- Pituitary dysfunction
  - GH
  - TSH
  - FSH & LH
  - ACTH
- Thyroid damage
  - Primary Hypothyroidism



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# Metabolic Syndrome

- Associated with treatment for childhood cancer
- Cranial radiation therapy and TBI (whole body RT prior to transplant) significantly increase the risk
- Etiology
  - Poorly understood post chemotherapy alone
  - Radiation therapy:
    - Hypothalamic effect
    - RT to pancreas
- Characterized by:
  - Central obesity
  - Hypertension
  - Hyperlipidemia
  - Diabetes



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# Cardiovascular disease

- Etiology: Adriamycin and RT
  - Adriamycin:
    - Dose related cardiomyopathy
  - Mediastinal RT for Hodgkin lymphoma (HL): 5% of patients have symptomatic heart disease 10 years later
    - Cardiomyopathy
    - Coronary artery disease
    - Pericarditis
    - Valvular disease
    - Conduction system problems
      - AV and bundle branch block
  - Neck RT: Vascular problems
    - Carotid artery disease
- Hypertension



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# GU/Renal disease

- Kidneys especially vulnerable
- Chemotherapy
  - Cisplatin
    - Magnesium-wasting tubulopathy
  - Ifosfamide
    - Proximal tubular dysfunction and less frequently decreased GFR
  - Methotrexate
    - Acute renal dysfunction
- RT
  - Doses greater than 20 Gy result in significant nephropathy
- Surgery
  - Reduction in renal tissue
- Hypertension



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# Pulmonary disease

- Lungs very sensitive to both RT and chemotherapy
- Bleomycin:
  - Intra-alveolar exudates with subsequent organization
  - Hyaline membrane formation
  - Interstitial fibrosis
  - Atypical proliferation of alveolar cells
- RT :
  - Pneumonitis
  - Chest wall deformity – restrictive defect

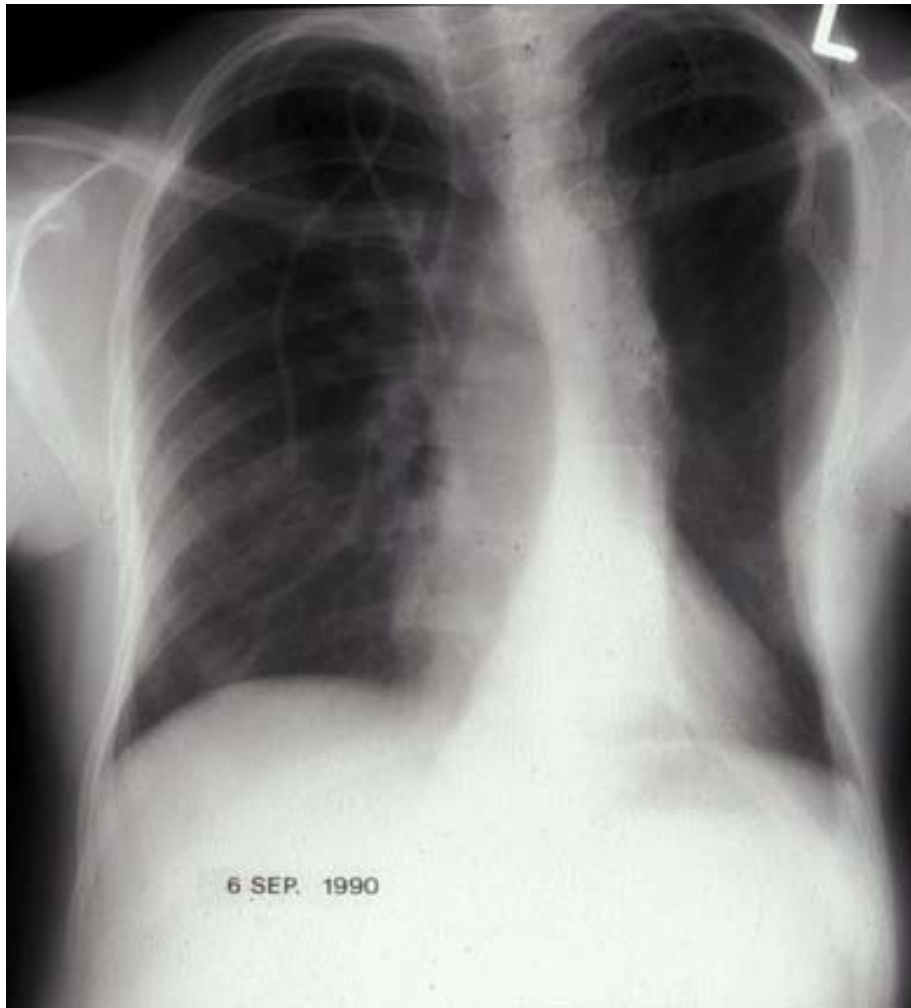


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# Chest wall deformity:



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# GI disease

- Intestines very sensitive to RT:
  - Malabsorption
  - Strictures
  - Adhesions and obstruction
  - Fistula
- Previous surgery increases risk



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# Reproductive system

- Gonads very sensitive to both RT and chemotherapy
  - Alkylating agents
  - RT to ovaries:
    - The dose of RT needed to destroy 50% of the oocytes = LD50
    - Oocytes are very sensitive with an LD<sub>50</sub> of < 200 cGy
- Damage to developing uterus



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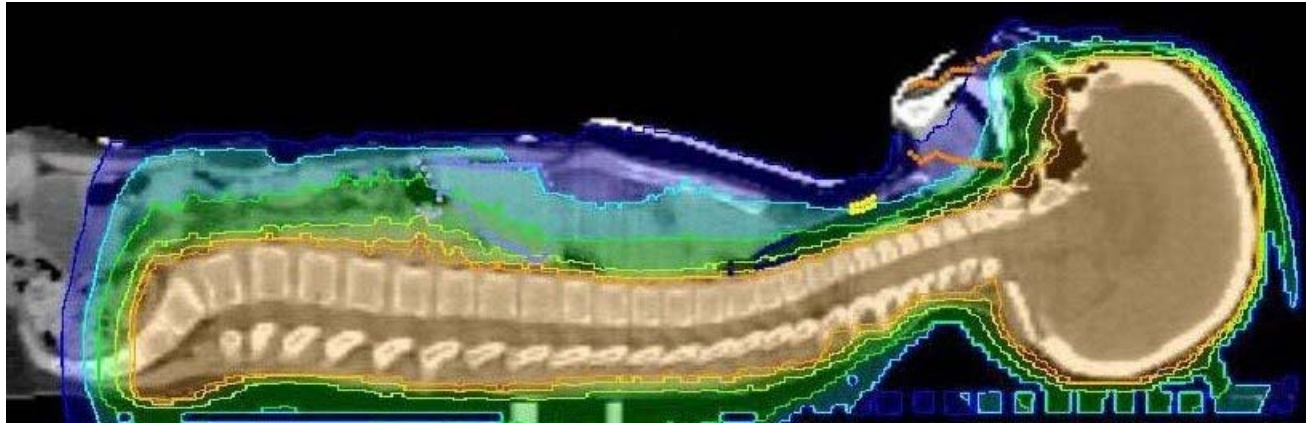
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# Craniospinal RT:

- Multiple late effects:



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# Psychosocial

- Many brain tumor survivors:
  - Need very modified school curriculum
  - Rely on permanent disability pension:
    - Differences across the province and between different provinces regarding available programs
      - Access to vocational/recreational rehab
  - Drug costs covered by parents benefits plan
  - Other costs not covered:
    - Hearing aids



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# Impact on Life

- Huge range of late effects:
  - Low risk:
    - Many (but not all) previous lymphoma and leukemia patients
    - Function very well
    - Minimal risk for long-term health problems
  - High risk:
    - Any RT, high dose chemotherapy including alkylating agents and anthracyclines
    - Some leukemia patients, brain tumors and solid tumors (e.g. sarcomas)
    - Lives may be “devastated”
  - Long term health care:
    - Counseling
    - Screening/Surveillance for late effects



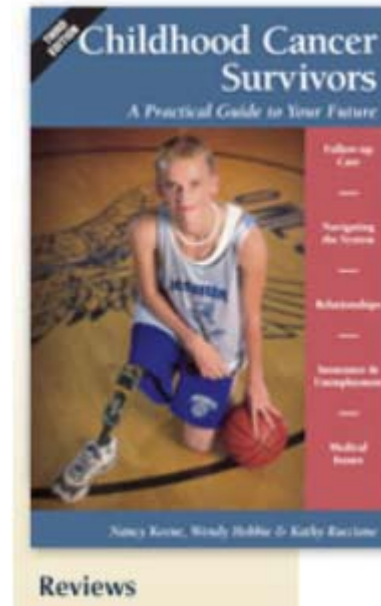
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# Reducing the Risk

- How can we reduce the risk of late effects?
  - Initial treatment modality
    - Avoid RT
    - Lower RT doses
  - Patient selection
  - Radio-protectant
    - Amifostine
  - Awareness of long term health risks:
    - Patients
      - Life style choices – smoking, diet, exercise
      - Screening
    - Health care professionals
      - Do the correct investigations



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# Second Cancers: After Radiation Therapy for Childhood Cancer

Karen Goddard



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# Objectives

- Overview of:
  - Frequency and etiology of second neoplasms in survivors of pediatric cancer
  - Common secondary tumors:
    - Associated therapy
    - Incidence
    - Prognosis
- Strategies for prevention



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# Definition

- A second cancer or second malignant neoplasm (SMN) is defined as a histologically distinct second cancer that develops after the first.
- Definition: (According to ICD-O)
  - Neoplasm in new location and not from direct spread or metastasis of the primary cancer
  - Neoplasm in the same location as the primary cancer but of different histological type



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# Etiology

- Factors associated with a risk of second neoplasm
  - Patient related
  - Disease related
  - Treatment related



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# Etiology

- Patient related:
  - Age
    - Increased risk if young at diagnosis
    - Time since Rx
  - Lifestyle and environment
    - Smoking
  - Underlying genetic condition
    - Clearly defined:
      - [Bilateral retinoblastoma](#)
      - [NF1](#)
      - [Li-Fraumeni](#)
        - Germ line mutation in tumor suppressor genes
    - More complex genetic factors
      - Radiogenomics



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# Etiology

- Disease related:
  - Hodgkin lymphoma
  - Ewing sarcoma
- Therapy related:
  - Chemotherapy alone
    - Alkylating agents
    - VP-16
  - **Radiation therapy (RT)**
  - Combined RT and chemotherapy



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# Etiology

- Proposed mechanisms for RT induced SMN:
  - DNA damage and gene mutations:
    - Rearrangements within the genome place proto-oncogenes within regions with high rates of translation
    - Double strand DNA breaks and imperfect repair
    - Tumour suppressor gene deactivation
  - Radiation-induced genomic instability



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# Incidence

- Significant long term risk for any child who has RT
  - 8-10% risk of second malignancies within 20 years
  - 5-20 X greater than general population (Friedman et al. Pediatr Clin North Am 2002)
- Childhood Cancer Survivor Study
- 30-year cumulative incidence rates for all CCS:
  - All second neoplasm
    - 20.5% (95% CI, 19.1%–21.8%).
  - Malignant second neoplasms (excluding non-melanoma skin cancer)
    - 7.9% (95% CI, 7.2%–8.5%).
  - Non Malignant second neoplasms
    - 9.1% (95% CI, 8.1%–10.1%).
    - Meningioma
      - 3.1% (95% CI, 2.5%–3.8%).
- This is a 6X increased risk of secondary neoplasms among cancer survivors, compared with the general population.



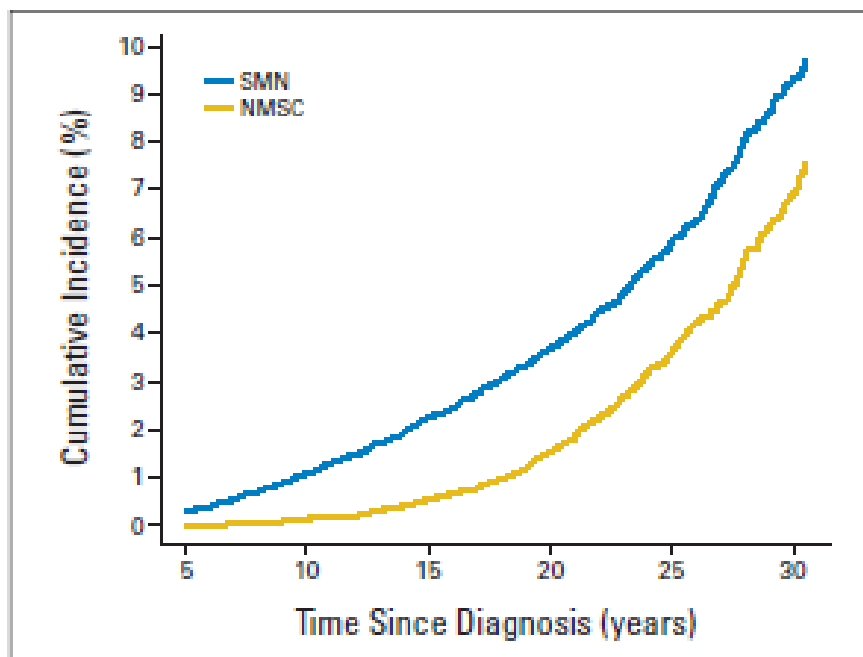
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# Incidence

- Childhood Cancer Survivor Study
  - 30 year cumulative incidence of second malignancy = 9%



**Fig 1.** Cumulative incidence of second malignant neoplasms (SMNs) and nonmelanoma skin cancer (NMSC) in childhood cancer survivors. At the 30-year follow-up, the cumulative incidence of SMNs and NMSC continues to increase with time since 5 years after diagnosis of primary childhood cancer.



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# Types of Secondary Tumors

- Most common:
  - RT induced meningioma
  - Thyroid carcinoma
  - Skin cancers
    - Basal cell
    - Melanoma
  - Breast carcinoma
  - Colorectal carcinoma
  - Sarcomas (bone)
  - Myelodysplastic syndrome (MDS) and AML



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# SMN after Rx for HL

- Breast
  - 15-55 X increased risk of secondary breast cancer
  - De Bruin et al: 1122 female HL survivors
    - SIR 5.6
    - AER 57/10,000 person-years
    - Cumulative incidence at 30 years: 19%
      - If < 21 yrs at treatment: 26%
- Thyroid
  - 10-35 X increased risk
  - SIR of 3.03 (SEER data)
- Sarcoma
  - SIR 6.28 (soft tissue) and 8.44 (bone) – (SEER data)
- Also CRC, lung, gastric



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# RT induced Meningioma

- Incidence:
  - High incidence after even low dose RT
- Banerjee et al (University Hospital of Oulu, Finland) reported on a group (60 patients consecutively treated) of long term survivors treated with cranial RT for leukemia as children between the ages of 1 and 8 years:
  - Overall incidence of meningiomas: 22%
  - No other types of brain tumors were seen in these survivors



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# RT induced Meningioma

- Factors which did NOT affect the risk of development of meningiomas:
  - Age at the time of RT
  - Gender
  - Chemotherapy (intensity/Rx regime)
  - Dose of RT
- Risk of meningiomas strongly linked with the length of follow up:
  - Long latency period (mean, 25 years; range, 14-34 years)
  - Increasing incidence with time after therapy
  - 20 years after the treatment the incidence was 47%



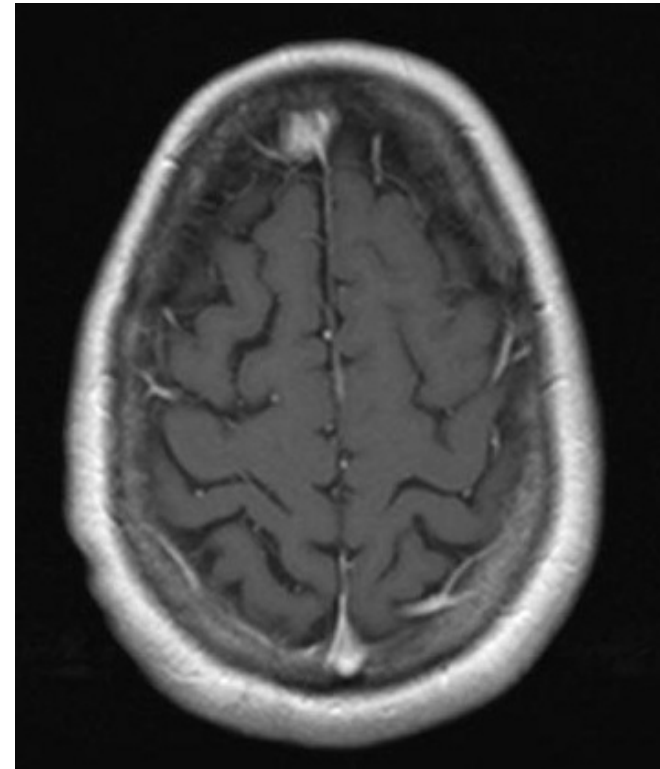
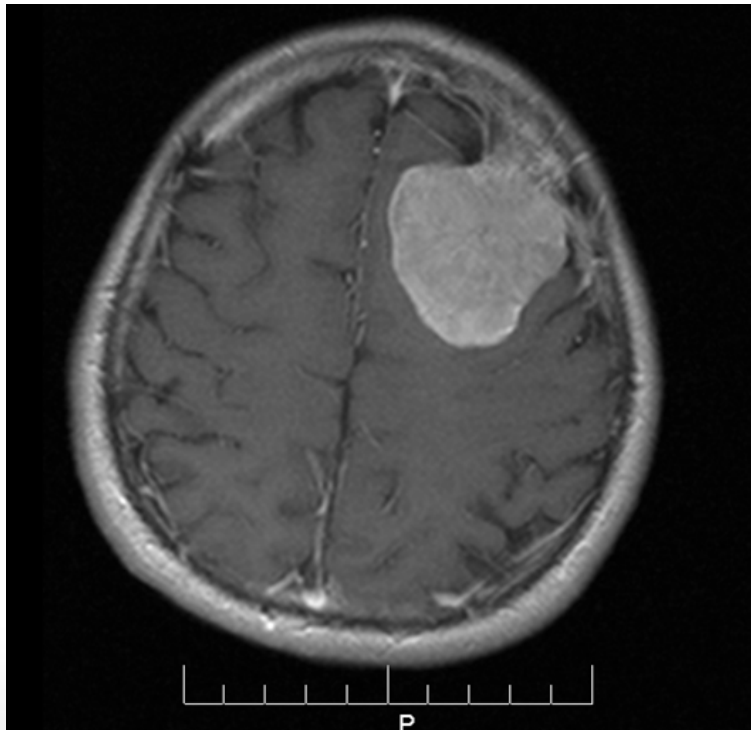
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# RT induced Meningioma

- RT induced meningioma
  - Multiple
  - Atypical
  - More likely to recur after surgery



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# Skin Cancer

- Increased risk of cancers in previous RT field
  - Basal cell carcinoma
  - Melanoma

## Skin Cancer Information



### What Is Skin Cancer?

Skin cancer is the uncontrolled growth of abnormal skin cells. It occurs when unrepaired DNA damage to skin cells (most often caused by ultraviolet radiation from sunshine or tanning beds) triggers mutations, or genetic defects, that lead the skin cells to multiply rapidly and form malignant tumors.

### What to Look for



Actinic Keratosis



Basal Cell



Dysplastic Nevi



Melanoma



Squamous Cell



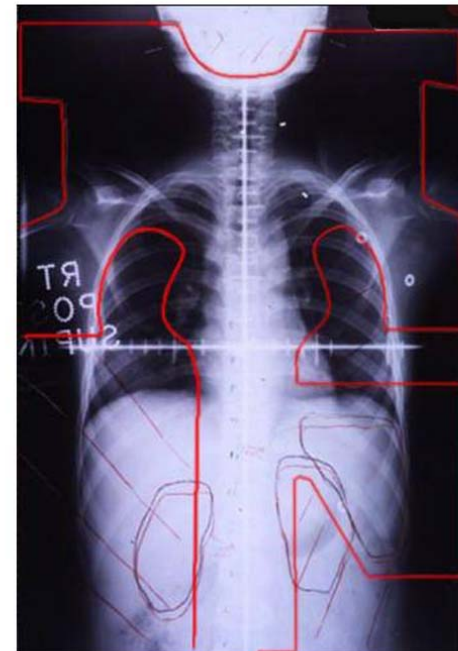
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# Breast Cancer

- Commonest solid tumor among female survivors of Hodgkin lymphoma
- Moderately high-dose mediastinal RT
  - Scatter to adjacent (breast) tissue
- Adolescent girls most at risk
- Any chest RT increases risk
  - Upper border of flank field for WT



The NEW ENGLAND  
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## ORIGINAL ARTICLE

### Breast Cancer and Other Second Neoplasms after Childhood Hodgkin's Disease

Smita Bhatia, M.D., M.P.H., Leslie L. Robison, Ph.D., Odile Oberlin, M.D., Mark Greenberg, M.B., Ch.B., Greta Bunin, Ph.D., Franca Fossati-Bellani, M.D., and Anna T. Meadows, M.D.

N Engl J Med 1996; 334:745-751 | March 21, 1996 | DOI: 10.1056/NEJM199603213341201

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# Breast Cancer

- After RT for Hodgkin lymphoma in adolescence
  - 37X risk of breast cancer
  - Bilateral disease more common
  - Increased risk:
    - Over 12 years of age at diagnosis
    - Higher dose of RT

Unilateral and bilateral breast cancer in women surviving pediatric Hodgkin's disease.

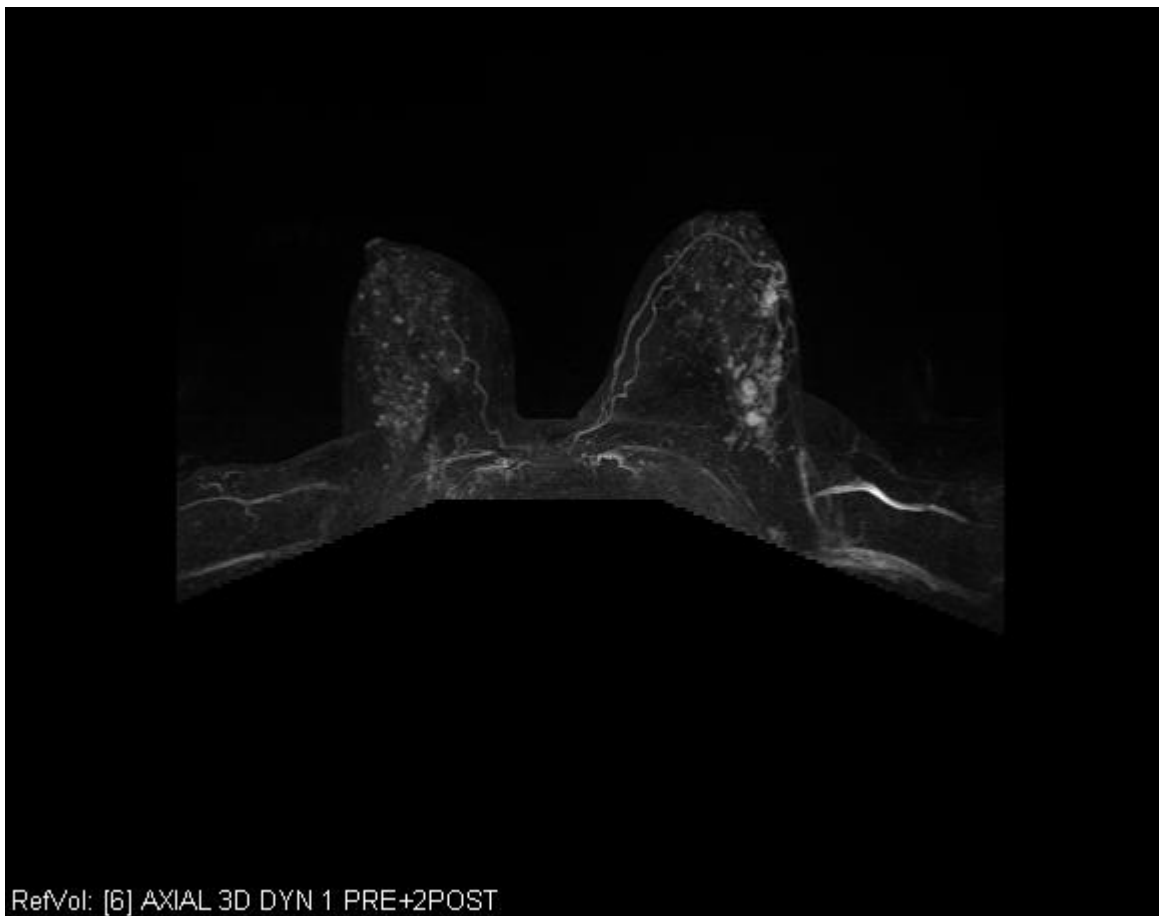
Basu SK<sup>1</sup>, Schwartz C, Fisher SG, Hudson MM, Tarbell N, Muhs A, Marcus KJ, Mendenhall N, Mauch P, Kun LE, Constine LS.



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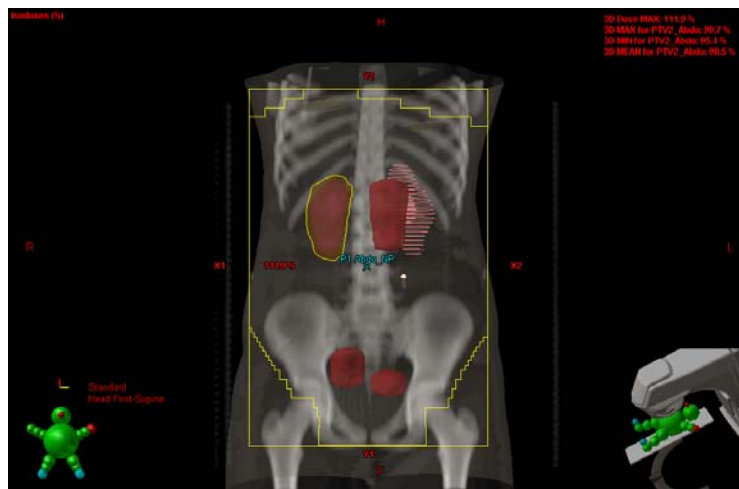
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# Colorectal Cancer (CRC)

- 2- 3% risk of CRC 30 – 40 years after Rx for childhood cancer and increasing.
- Associated with abdominal RT
  - Wilms tumor
  - Childhood sarcomas
  - Hodgkin lymphoma
  - Lower end of craniospinal RT field



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# Colorectal Cancer (CRC)

- RT and alkylating agents associated with increased risk of secondary CRC.
- Risk is proportional to dose and volume of RT
  - Increased by 70% with each 10-Gy increase in RT dose.
  - Increased RT volume increased risk (group 1 OR, 1.5; P .001; group 2 OR, 1.8; P .001).
- Alkylating agent exposure associated with 8.8X increased risk of secondary CRC.

VOLUME 30 • NUMBER 20 • JULY 10 2012

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

## Secondary Colorectal Carcinoma After Childhood Cancer

Kerri Nottage, Joshua McFarlane, Matthew J. Krasin, Chenghong Li, Deokumar Srivastava, Julie L. Robison,  
and Melissa M. Hudson



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# Sarcomas

**The New York Times**

**Books**


WORLDU.S.N.Y. / REGIONBUSINESSTECHNOLOGYSCIENCEHEALTHART & DESIGNBOOKS Sunday Book ReviewBest SellersDANCE

## David Rakoff, 47, Comic Essayist, Dies

By MARGALIT FOX  
Published: August 10, 2012

David Rakoff, a prizewinning humorist whose mordant, neurotic essays examined everything from his surreal stint portraying Sigmund Freud in a Christmastime shop window display to his all-too-real battles with cancer, died on Thursday in Manhattan. He was 47.

[Enlarge This Image](#)



Louis Lanzano/Associated Press

David Rakoff in Central Park in 2001. His most recent collection of comic essays, "Half Empty," was published in 2010.

### Related

ArtsBeat: David Rakoff

His death was announced by his mother, Gina Shochat-Rakoff. Mr. Rakoff's cancer had first appeared when he was 22 and recently reappeared as a tumor in his left shoulder.

The return of his cancer, and the possibility that his arm and shoulder would have to be amputated, were the subjects of the concluding essay in Mr.

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# Sarcomas

- RT induced SMN after Rx for Ewing sarcoma
  - German Ewing sarcoma studies
  - CESS 81 & 86
    - Retrospective
    - 674 pts.
    - Median FU 5.1 yrs
  - Cumulative risk of SM was
    - 0.7% after 5 yrs
    - 2.9% after 10 yrs
    - 4.7% after 15 yrs



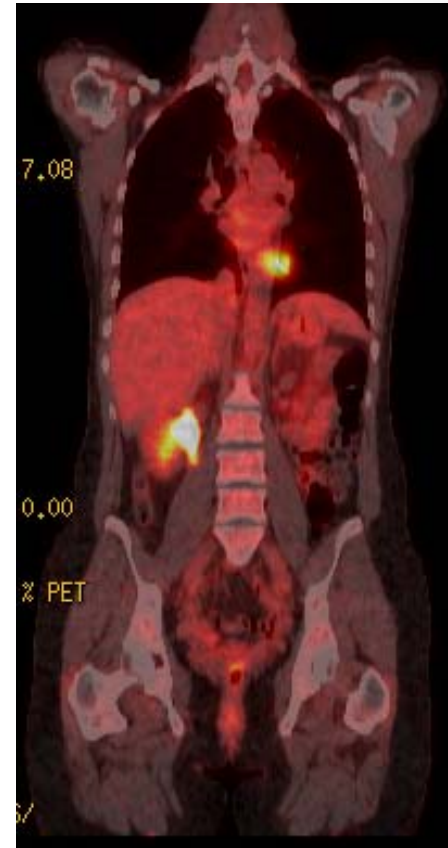
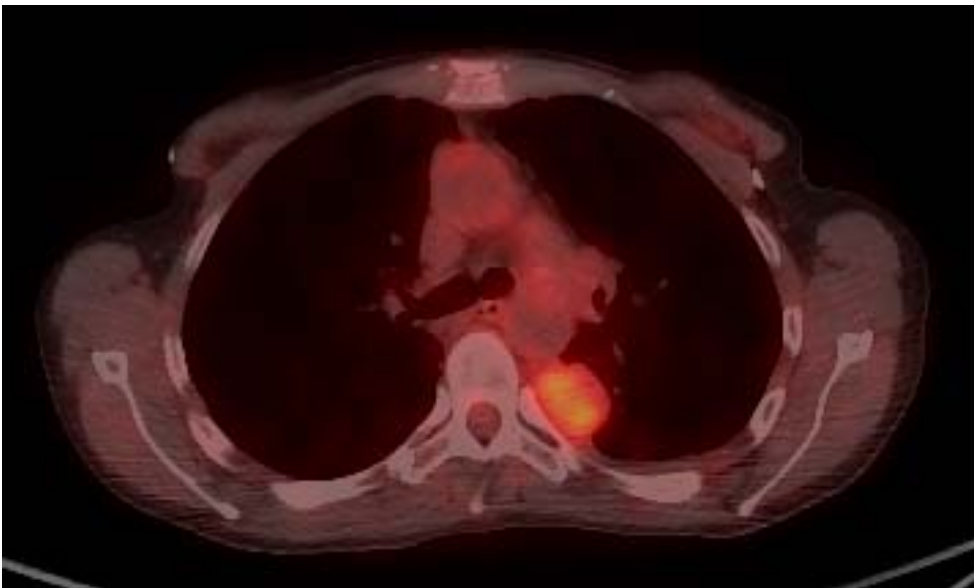
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# Sarcomas

- Presentation:
  - Swelling in region of previous RT
  - Pain – not necessarily

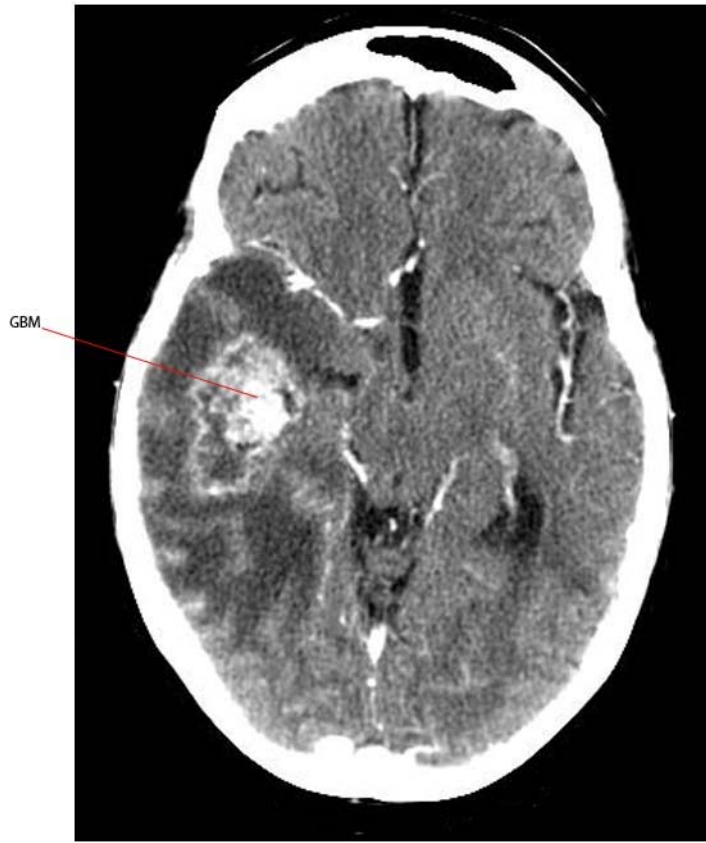


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# GBM



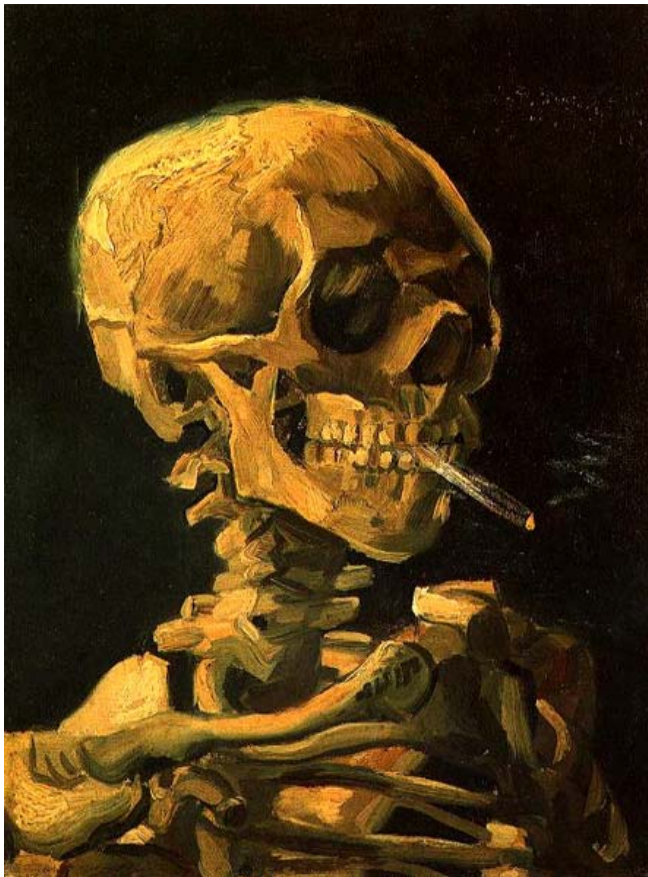
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# Lung cancer

- Smoking after therapy for Hodgkin lymphoma



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# Resources

- National Cancer Institute: [Late Effects of Treatment for Childhood Cancer](#)

The screenshot shows the National Cancer Institute (NCI) website. At the top, the NCI logo is displayed in red, followed by the text 'at the National Institutes of Health'. Below this is a navigation bar with links: 'NCI Home', 'Cancer Topics', 'Clinical Trials', 'Cancer Statistics', and 'Research'. The main heading is 'Late Effects of Treatment for Childhood Cancer (PDQ®)'. Below the heading are three tabs: 'Patient Version', 'Health Professional Version', and 'En español'. On the left side, there is a sidebar with a list of topics under the heading 'Late Effects of Treatment for Childhood Cancer (PDQ®)': 'General Information', 'Subsequent Neoplasms', and 'Late Effects of the Cardiovascular'. On the right side, under the heading 'General Information', there are four links: 'Mortality', 'Monitoring for Late Effects', 'Resources to Support Survivor Care', and 'Transition of Survivor Care'.

**National Cancer Institute**  
at the National Institutes of Health

NCI Home Cancer Topics Clinical Trials Cancer Statistics Research

**Late Effects of Treatment for Childhood Cancer (PDQ®)**

Patient Version Health Professional Version En español

**Late Effects of Treatment for Childhood Cancer (PDQ®)**

- ▶ General Information
- ▶ Subsequent Neoplasms
- ▶ Late Effects of the Cardiovascular

**General Information**

- [Mortality](#)
- [Monitoring for Late Effects](#)
- [Resources to Support Survivor Care](#)
- [Transition of Survivor Care](#)



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# Resources

- COG: [Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers](#)

**CHILDREN'S  
ONCOLOGY  
GROUP**

The world's childhood cancer experts

What is Cancer?

Types of Children's Cancer

**Late Effects of Treatment for Children's Cancer**



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# Resources

## Pediatric Oncology Education Materials

### Late Effects▼

#### General Overview

**Introduction**  
**Resources**  
**References**

CNS

Orbit

Peripheral NS

Hearing

Cardiac

Respiratory

Musculoskeletal

Bone Marrow

Skin

### Late Effects

#### General Overview



[print \[printer friendly\]](#) | [email](#)

On average approximately 10,400 North American children (between birth and 14 years of age) develop childhood cancer each year and these numbers seemingly increase annually<sup>1</sup>.

More than 80% of these children will be long term survivors who have been cured of their disease. This was very different 20 to 30 years ago, when many children did not survive.<sup>2</sup>

In general, cure rates have been improved by using:

- Multiple treatment modalities
  - Radiation therapy (RT)
  - Chemotherapy
  - Surgery
- Therapy intensification (using higher total doses of chemotherapy over a shorter period of time)<sup>3</sup>
- Improved supportive care



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# Late Effects Case



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Thank you!

