Out-of-field dose reconstructions for studies of health risks following photon radiotherapy when DICOM-RT are NOT available

NIH NATIONAL CANCER INSTITUTE

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Agenda

1. *Kaiser Breast cancer survivors study*
   - *Overview of cohort*
   - *Radiogenic health risks of interest*
2. *Exposure assessment goals*
3. *Obstacles…*

Kaiser case-control study of breast cancer patients

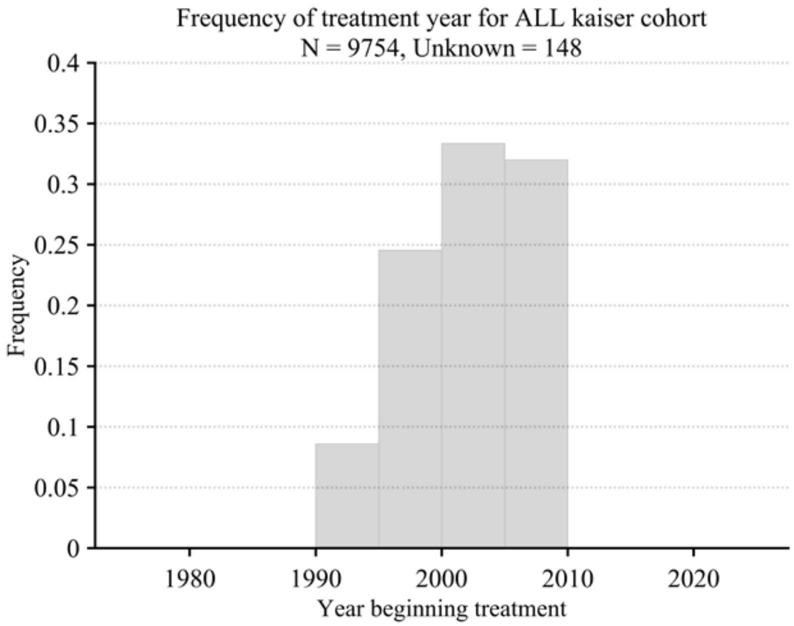
- Substantial improvements in breast cancer survival, combined with increasing incidence rates have resulted in **3 million breast cancer survivors in the US**; 20% of all cancer survivors.
- The long-term health of these women is a clinical and public health concern, with an estimated **10% developing a second cancer by ten years after diagnosis.**

- Radiotherapy results in a reduction of breast cancer mortality 15 years after treatment; However, studies also demonstrated that **radiotherapy increases cardiovascular mortality and second cancer risks**, particularly for women with left-sided breast cancer.

Kaiser case-control study of breast cancer patients

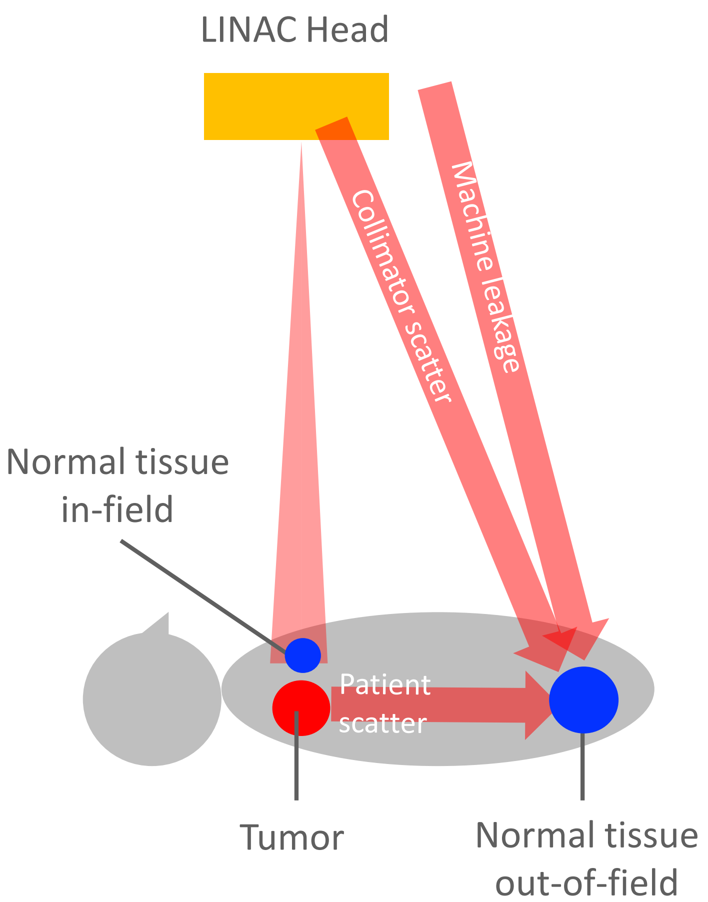
- We aim to examine the relationship between **radiotherapy techniques and risks for 2nd cancers and cardiovascular events** using an established cohort.

- A nested CC study from ~12,000 breast patients treated at three Kaiser centers
  - Over 9k treatment summaries abstracted thus far from NW, CO
  - Treated between 1990 to 2010



Dosimetry for epidemiologic purposes

- Radiation doses received by individuals from medical exposures are often not recorded and must be reconstructed from exposure information
- Radiation doses must be **specific to each organ under study**
  - Contralateral breast, lung, heart, and esophagus
- To make realistic estimates of organ doses requires an understanding of the clinical exposure, radiologic technology and the physics it is based on



Dosimetry for epidemiologic purposes

- **Individualized dosimetry is not possible** due to limited resources and a lack of information in the medical records

GROUP HEALTH HOSPITAL

OUTPATIENT MEDICAL RECORD

NAME [redacted] MEDICAL HISTORY NUMBER [redacted]

RADIATION ONCOLOGY TREATMENT SUMMARY

This is a 42-year-old lady with T2 N0 breast carcinoma involving the left side. The primary tumor was about 2.5 cm in size while all the lymph nodes were not involved. She received concurrent chemotherapy and radiation therapy.

From [redacted] through [redacted] she received 6,480 cGy to the tumor bed, 5,040 cGy to the entire left breast. The tumor bed was boosted with photon beam with the dose calculiated at a 2 cm depth.

This patient tolerated the treatment well with some skin reaction, as expected. I intend to check her again in early [redacted] In the meantime, she will continue her chemotherapy with Dr. [redacted]

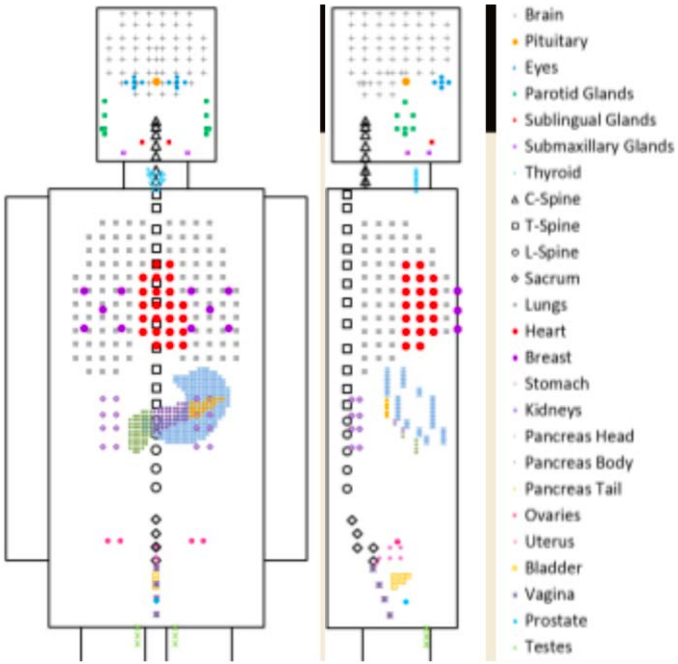
Dosimetry for epidemiologic purposes

- **Individualized dosimetry is not possible** due to limited resources and a lack of information in the medical records

- We must therefore use **averaged imaging parameters** that are collectively defined from measurement data, computational modeling, literature, and RT treatment summaries (no DICOM-RT)

Existing dosimetry methods for radiotherapy patients

- MD Anderson Cancer Center method[1]
  - Comprehensive 3D dose measurements within a water phantom
  - Age-specific computational phantoms superimposed on the dose matrices
  - Structure of the phantoms based on anatomy textbooks
  - **Limited to conventional radiotherapy techniques**



[1] Stovall, M., Weathers, R., Kasper, C., Smith, S. A., Travis, L., Ron, E., & Kleinerman, R. (2006). Dose reconstruction for therapeutic and diagnostic radiation exposures: use in epidemiological studies. *Radiat Res*, *166*(1 Pt 2), 141–157. http://doi.org/10.1667/RR3525.1

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MEASUREMENTS IN ANTHROPOMORPHIC PHANTOMS (continued)

Body Region Treated	Phantom used	Field Configuration	Field size (w-cm x h-cm)	Radiation Beams
Chest/ Breast	Alderson phantom female #225 with breast attached (size medium)	AP/PA supraclav	16 x 12	Orthovoltage 3.0 mm Cu HVL Cobalt-60 6 MV photons
		Anterior supraclav	16 x 12 20 x 20	6 MV photons
		Medial and lateral tangentials (various wedge combinations)	19 x 9	Orthovoltage 3.0 mm Cu HVL Cobalt-60 6 MV photons
		Medial and lateral tangentials with field-in- field technique	17 x 9	6 MV photons
		Medial and lateral tangentials with beam splitter	20 x 6	Cobalt-60
		Anterior internal mammary chain	6 x 15	Cobalt-60 6 MV photons
		Anterior breast (rt.)	20 x 20 10 x 10 (with cut out)	9 MeV electrons
		Anterior chest (rt.)	16 x 16	Orthovoltage 0.3 mm Cu HVL
		AP/PA mantle	31 x 29	6 MV photons
	CIRS ATOM Adult Male	AP/PA mantle	15 x 27	6 MV photons
	Phantom Laboratory Adult Female	Supraclav Medial and Lateral Tangentials	15 x 8 9 x 20	6 MV photons
	[illegible] phantom	Anterior Thymus	5 x 5	Orthovoltage 0.3 mm Cu HVL

- **Limited to conventional radiotherapy techniques**

[1] Stovall, M., Weathers, R., Kasper, C., Smith, S. A., Travis, L., Ron, E., & Kleinerman, R. (2006). Dose reconstruction for therapeutic and diagnostic radiation exposures: use in epidemiological studies. *Radiat Res*, *166*(1 Pt 2), 141–157. http://doi.org/10.1667/RR3525.1

Dosimetry of Kaiser case-control study

- In this study, **CT images are not retrievable** from the hospitals and we know dose distribution and treatment planning to be highly affected by patient morphometry.
- We established a **surrogate patient cohort for dosimetry** with the University of Michigan
- We will then use that information in conjunction with the radiotherapy summaries as the basis for our calculations using NCIRT

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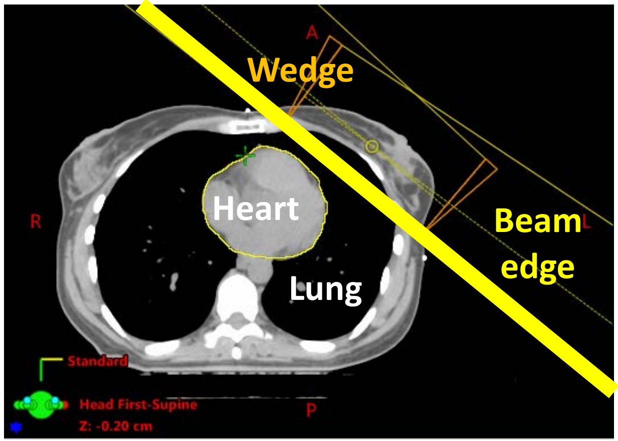
Dosimetry Plan	
Patient anatomy	Surrogate CT library with anatomy extension
Treatment plans	Reconstruct based on radiation summary
Dosimetry method	NCIRT Monte Carlo

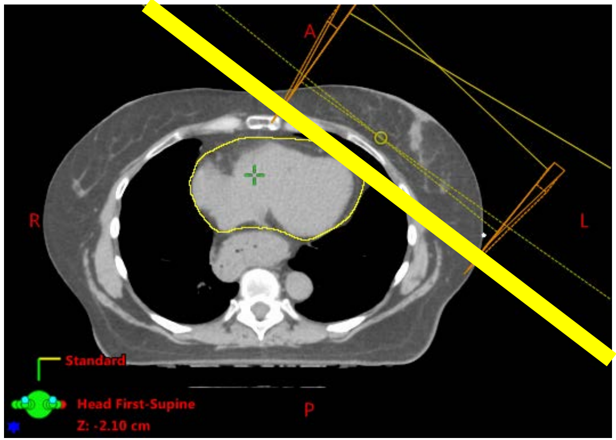
Dosimetry of Kaiser case-control study

- 200 Female breast cancer patients (100 left breast, 100 right breast) – stratified by BMI
- Treated at the University of Michigan, Ann Arbor, MI
- Between 2014 – 2015

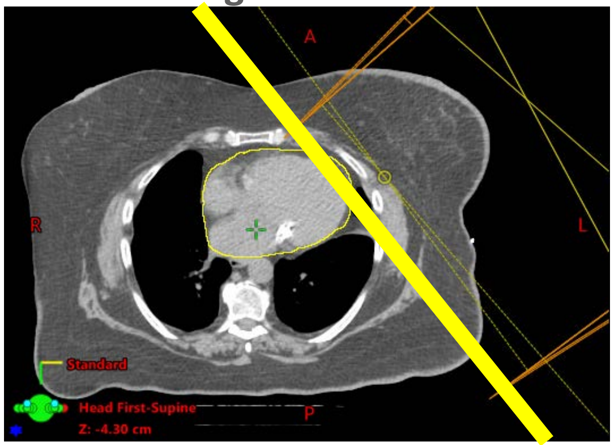
Small breast



Medium breast

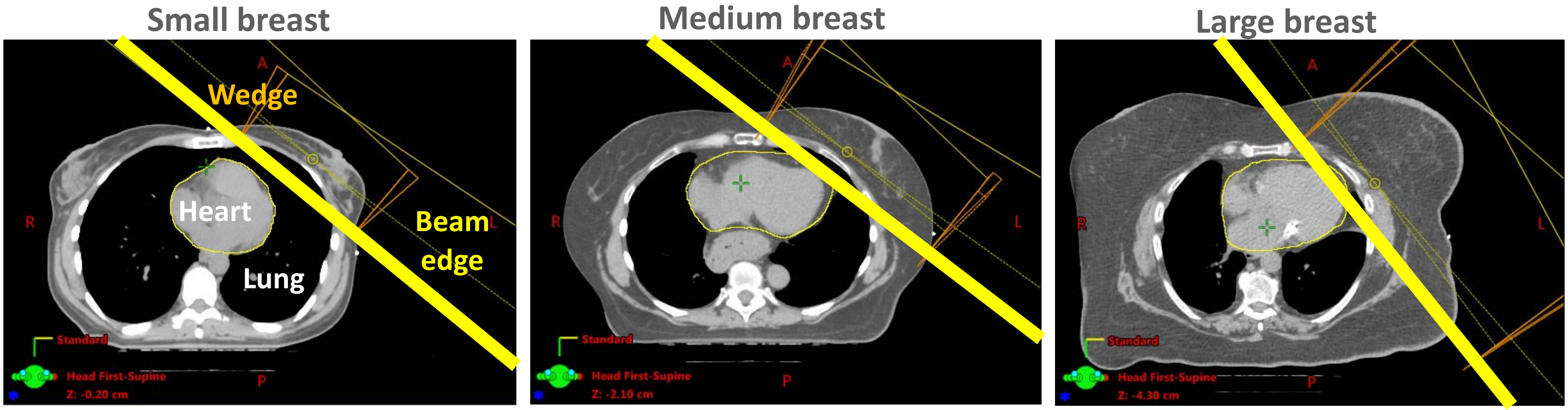


Large breast



Dosimetry of Kaiser case-control study

- Treatment planning data (beam energy, prescriptions, gantry angle, collimator angle and sizes, MLC block shapes, 3D dose distribution)



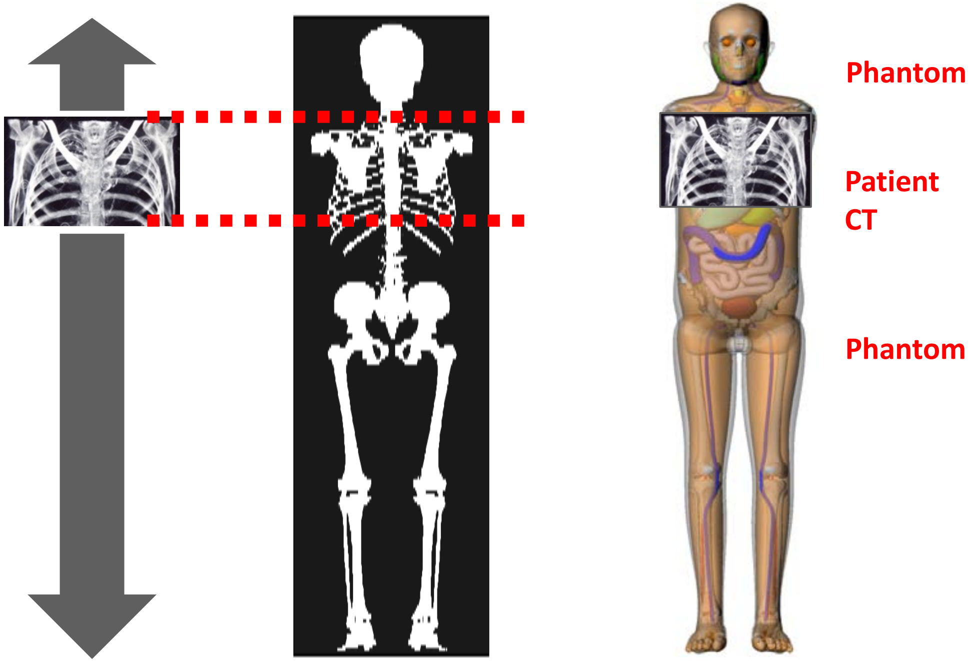
Dosimetry of Kaiser case-control study

- Radiation doses must be **specific to each organ under study**
- Other organs (out-of-field) of based on second cancers reported in cohort:
  - Colon
  - Ovaries
  - Corpus uteri
  - And pancreas… for now

Skeleton map from patient CTs

Skeleton map of phantoms

Patient-Phantom merged model[1]



[1]Kuzmin, G. A., Mille, M. M., Jung, J. W., Lee, C., Pelletier, C., Akabani, G., & Lee, C. (2018). A Novel Method to Extend a Partial-Body CT for the Reconstruction of Dose to Organs beyond the Scan Range. *Radiation Research*, *189*(6), 618–626. http://doi.org/10.1667/RR14999.1

Dosimetry of Kaiser case-control study

- Varian Clinac LINAC: 6MV, 16(15)MV
  - Two field tangents w/ MLC heart-blocks
  - Field-in-field technique (instead of physical wedges)
  - Dose calculations were done with Varian AAA v13.6 algorithm
- Treatment Planning System (Varian AAA v13.6 algorithm)
  - Several papers indicating TPS not accurate for **out-of-field** and **heterogeneous** regions
  - TPS reported to underestimate measurements or Monte Carlo dose[1,2]

[1]Howell, R. M. *et al.* (2010). Methodology for determining doses to in-field, out-of-field and partially in-field organs for late effects studies in photon radiotherapy. *Physics in Medicine and Biology*, *55*(23), 7009–7023. http://doi.org/10.1088/0031-9155/55/23/S04
[2]Joosten, A. *et al.* (2013). Evaluation of organ-specific peripheral doses after 2-dimensional, 3-dimensional and hybrid intensity modulated radiation therapy for breast cancer based on Monte Carlo and convolution/superposition algorithms: Implications for secondary cancer risk assessment. *Radiotherapy and Oncology*, *106*(1), 33–41. http://doi.org/10.1016/j.radonc.2012.11.012

Needs of Kaiser case-control study

- Clinical beam data and measurements to validate and implement a virtual source model of clinical accelerators
  - Among the CC cohort, ~30% of patients treated with 4 MV and ~10% at 23 MV
  - Phase-space data files (IAEA-compliant phase space calculations)
- Modeling of radiotherapy compensators and wedges
  - Used in ~50% of cohort and of these we have wedge information for 75%
  - Physical wedges, enhanced dynamic wedges, virtual wedge (Siemens)
- Special treatment techniques (*e.g.*, IMRT in later years)

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