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Radiation Dose from Cancer Treatment

Radiation Epidemiology & Dosimetry Course

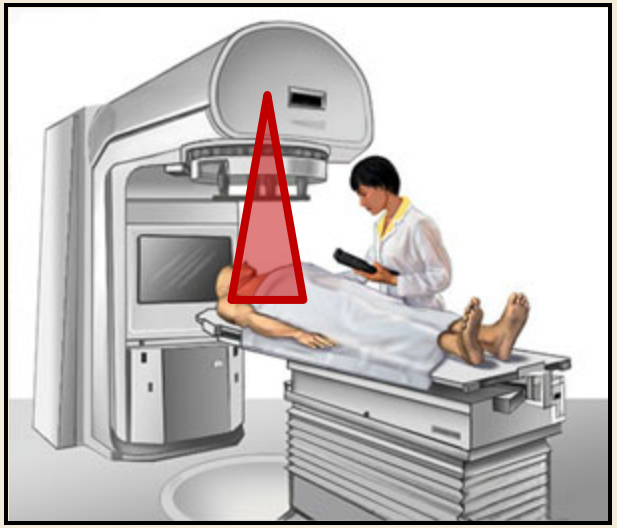
TODAY’S TOPICS

1. Types of radiotherapy
2. Components of dose *(known verses unknown)*
3. Treatment process and records
4. Dosimetry for late effects studies
5. Managing data for epidemiological studies
6. *Dosimetry challenges for modern radiotherapy (time permitting).*

Types of Radiotherapy

External Radiotherapy

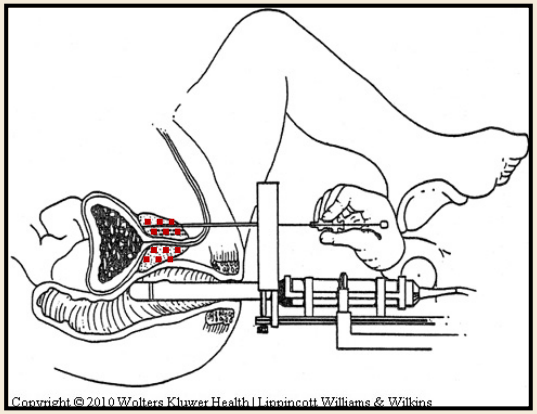
- External source of radiation aimed from outside body.
- Most common: MV photon beam therapy using linear accelerator.

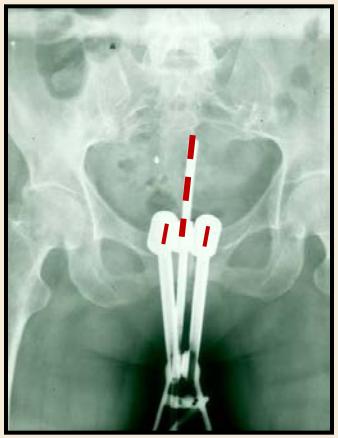


External beam figure from:
http://www.cancer.gov/cancertopics/factsheet/Therapy/radiation

Internal Radiotherapy

- Internal source of radiation implanted inside the body.
- Most common: brachytherapy with implanted radioactive source.





Prostate figure from: FM Khan. Physics of Radiation Therapy 4th ed., ISBN: 978-0-7817-8856-4, 2010

Components of Dose
Therapeutic verses Stray Radiation

- Therapeutic radiation is specifically intended to treat the target volume, i.e. intended dose → Known Dose.

- Stray radiation is radiation outside the therapeutic beam, i.e. unwanted consequence → Unknown Dose

Components of Dose Therapeutic Radiation

- Therapeutic radiation is the radiation inside the defined therapeutic treatment field.
- High dose to intended target volume.
  - Organs in close proximity to the intended target may also receive high doses.

- Unless organ is delineated, this dose is also “unknown”

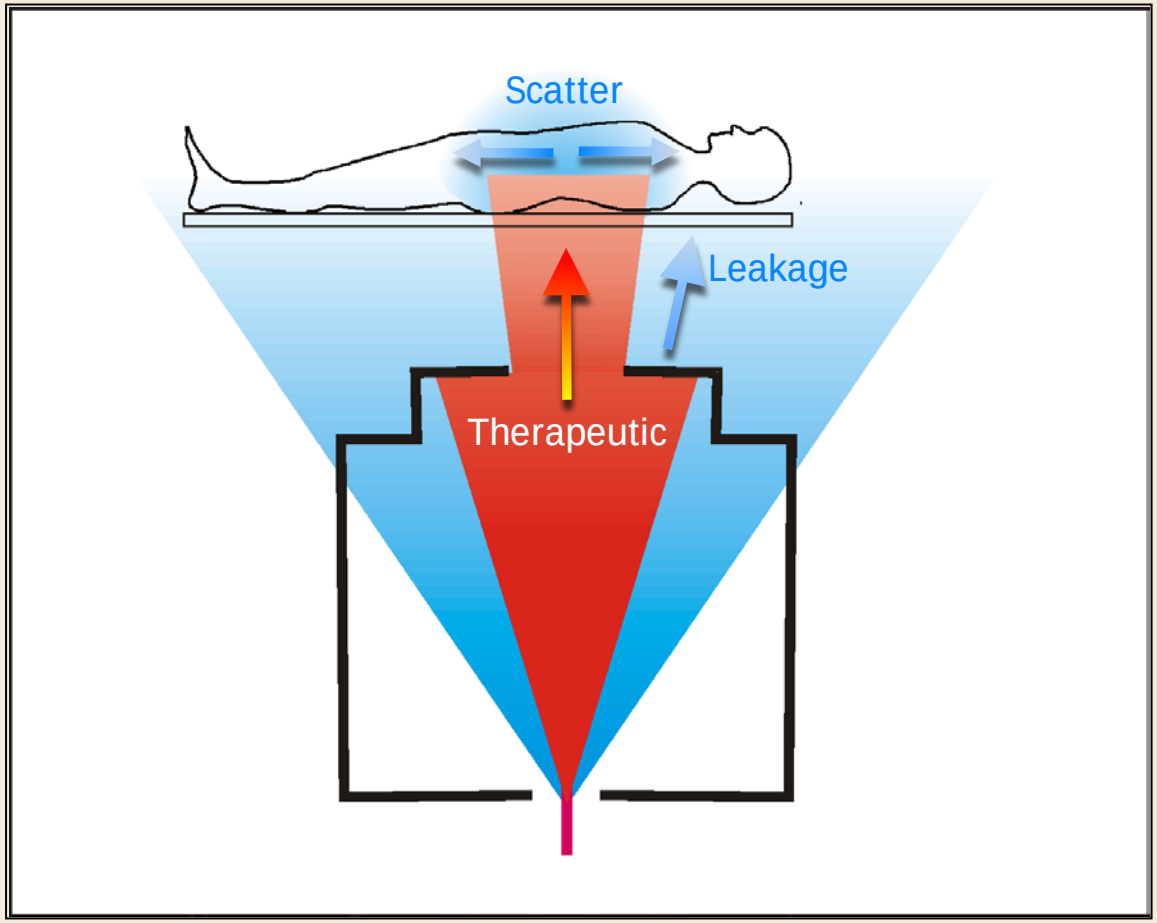
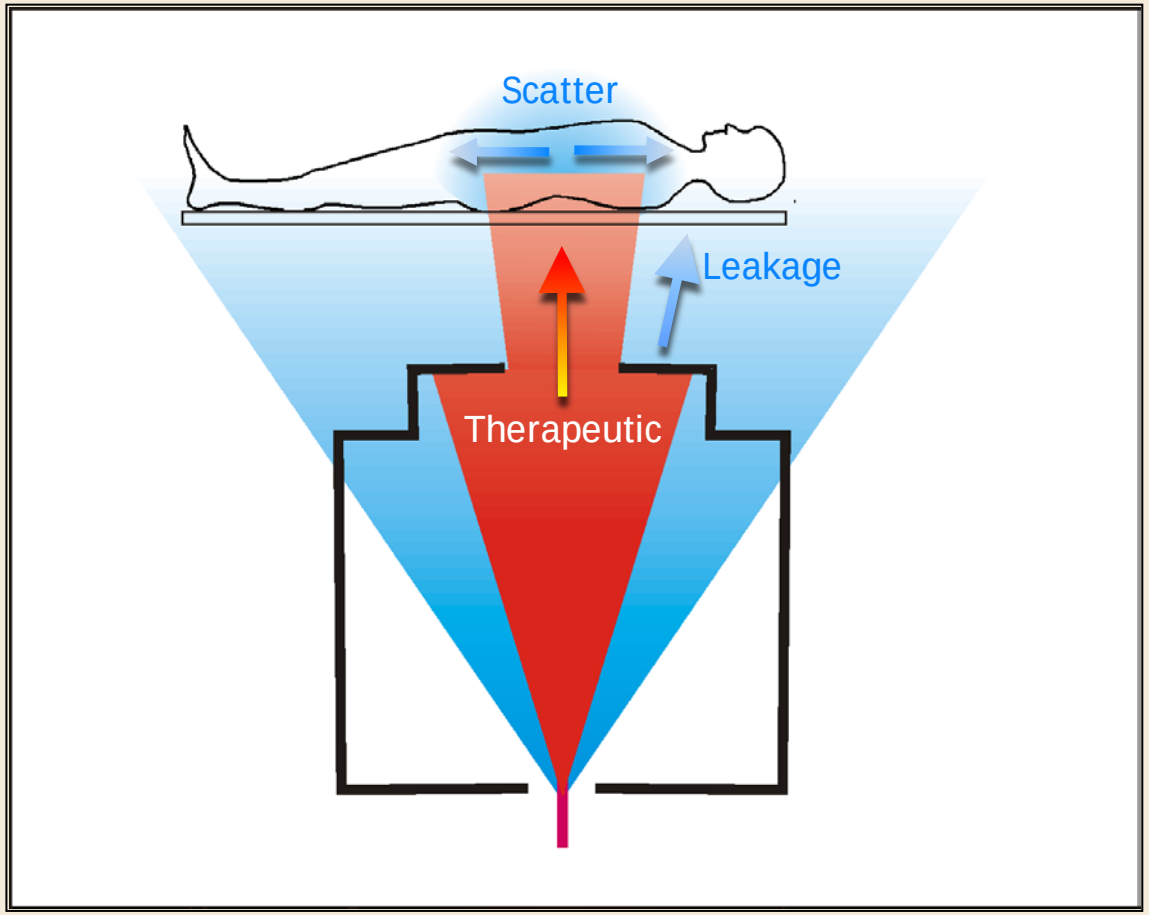


Figure from: WD Newhauser and M Durante, Nature Reviews Cancer 11 (6), 438-448

Components of Dose
Therapeutic verses Stray Radiation

- Stray radiation is radiation outside the therapeutic beam.
  - Includes scatter and leakage radiation
- Results in low dose to organs throughout the body (even those far from target volume).

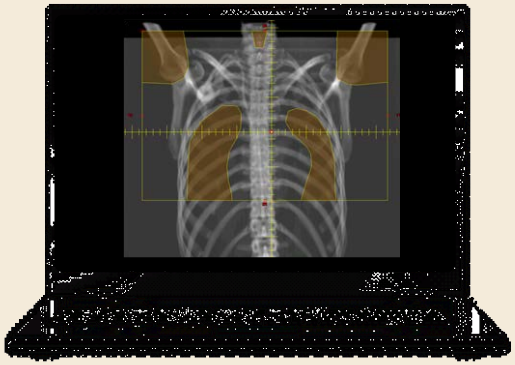


Important:

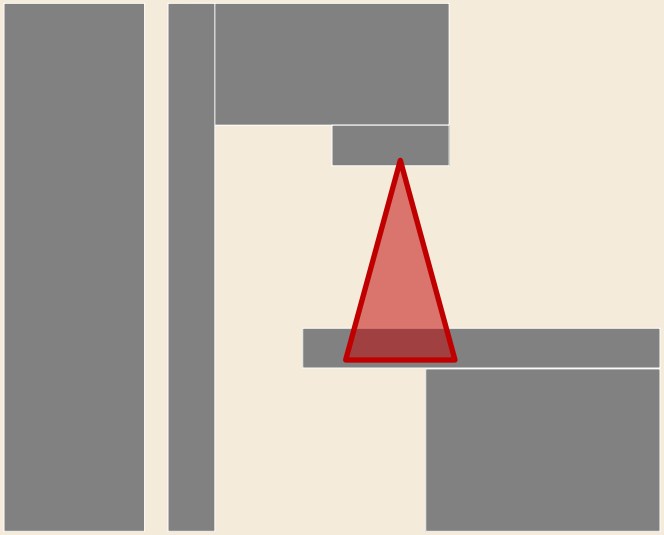
All organs receive some dose from any radiation therapy treatment field.

The Treatment Process

Imaging



Treatment Planning



Treatment

Commercial Treatment Planning Systems (TPS)

Current standard of care in radiotherapy:
TPS calculates dose to region of anatomy included in CT scan (up to 12 to 15 cm from field).

- Accurately calculate therapeutic dose.
  - Accurate up to ~ 3-5 cm beyond field edge.
- Do not accurately calculate stray dose.
  - **Dose is still reported, but is not accurate**.
  - Accuracy decreases with distance from the field edge.
  - Low doses are underestimated.

Dosimetry for Late Effects Studies

I will focus on method used by Radiation Dosimetry Services at M D Anderson and which has been used in numerous radiation epidemiology studies…
but will also briefly discuss other methodologies

Radiation Epidemiology Studies Missing Information

- Because of latency period (≥ 5 years), radiation epidemiology studies are typically carried out many years after treatment.
  - *Thus, we are often studying historic RT*.

Radiation Epidemiology Studies Challenges for Radiation Dosimetry:

RT Records

- RT records included prescription dose to target location.
- RT records do not include dose to specific organs or organ locations.
- Missing information.

CT Data

- No CT data, i.e., treated in pre-CT era of RT.
- Even if CT used for planning:
  - Typically includes only region of interest for RT
  - software limitations for accessing and reviewing.

Organ doses must be reconstructed for radiation epidemiology studies.

Dosimetry
Late Effects Studies

Patient Data

Abstract radiotherapy records for individual patients.

Therapeutic dose is known from Rx record, stray dose is unknown. Out of field dosimetry is required.

Physics Data

Use abstracted data to measure and/or calculate organ doses for individual patients.

Out-of-Field Dosimetry for Late Effects Studies

Calculations

- Analytical dose model + mathematical phantom
  frequently used can be customized for special projects

Measurements

- Anthropomorphic phantoms - frequently used
  can be customized for special projects

- Treatment Planning Systems - not routinely used due to inaccuracy outside treatment field (UNDERESTIMATE DOSE).
- Monte Carlo simulations - not routinely used because computationally demanding.

All Dosimetry Methods Begin with RT Record Review

Goal of record review….

- Obtain enough information about the treatment so that the treatment can be reconstructed on a phantom (real or computational) and determine dose to organs of interest for particular studies.

What Data are Abstracted?

- Age at RT
- Treatment site
- Prescribed and delivered dose
- Field arrangement & orientation
- Field energy
- Field size
- Treatment depth
- Field blocking

- Field location
  - Photograph
  - Radiograph
  - Diagram
  - Text description, e.g., jaw to diaphragm or top of head to C6.

→ *Can be highly uncertain, may have multiple, may not be in agreement, trained abstractor required.*

All Dosimetry Methods Begin with RT Record Review

RT record review requires:

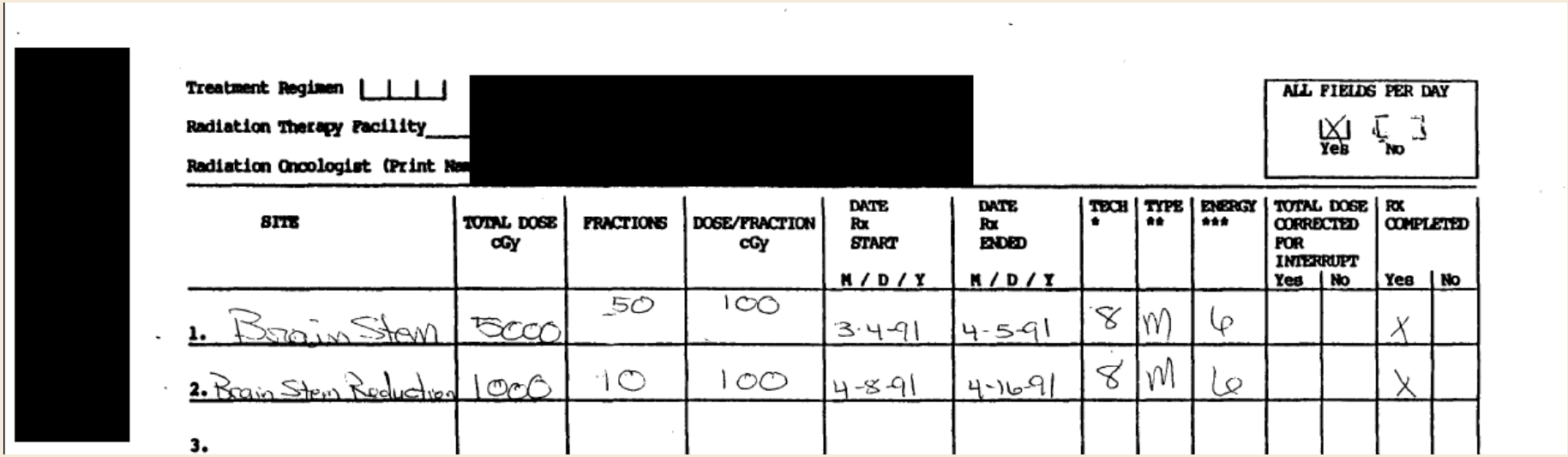
- Extensive training
- Knowledge of RT and standards of care
- Knowledge of institution specific information
- Diagram does not always translate – investigation needed.

Example: Prescription for 12 MV photon beam, trained abstractor would question correct energy. 12 does not exist – is it 10 or 15? Was it electrons?

Example: Mantle field prescription noted jaw to diagram, but radiograph shows field ending at nipple. Was this entire course of Rx? Or a boost/ conedown?

Example Record 1

- This record was only 2 pages, but had some very useful information for dose reconstruction.



[redacted]

Treatment Regimen [| | |]

Radiation Therapy Facility [redacted]

Radiation Oncologist (Print Na[redacted]

ALL FIELDS PER DAY — [X] Yes [ ] No

	SITE	TOTAL DOSE cGy	FRACTIONS	DOSE/FRACTION cGy	DATE Rx START M / D / Y	DATE Rx ENDED M / D / Y	TECH *	TYPE **	ENERGY ***	TOTAL DOSE CORRECTED FOR INTERRUPT Yes	TOTAL DOSE CORRECTED FOR INTERRUPT No	Rx COMPLETED Yes	Rx COMPLETED No
1.	Brain Stem	5000	50	100	3-4-91	4-5-91	8	M	6			X	
2.	Brain Stem Reduction	1000	10	100	4-8-91	4-16-91	8	M	6			X	
3.													

Example Record 1

[redacted] F 13 4-29-91

DIAGNOSIS: Brain stem glioma.

BRIEF CLINICAL HISTORY: In the fall of 1990 the patient developed left-handed weakness accompanied by diplopia on right-sided gaze; she was also noted to have difficulty catching a basketball properly resulting on her being on the second string basketball team only. A CT scan of the head showed a calcified mass and hydrocephalus in the region of the midbrain and pons. Given the location, it was decided not to biopsy the mass and she was started on a course of radiation therapy. She was started on CCSG protocol 9882 which consisted of hyperfractionated radiotherapy.

RESPONSE TO TREATMENT: The patient had a progression of her symptoms while on treatment. A head CT revealed the development of hydrocephalus and evidence of possible progression of the tumor as well. For this reason, the patient was admitted to the hospital and was started on intravenous steroids and a shunt was placed. While in the

EXTERNAL IRRADIATION

PHYSICAL FACTORS	ENERGY	TECHNIQUE (Rotation, Opposed, Wedged, etc.)	TREATMENT PERIOD FROM	TO
A	6x	Opposed Laterals and Vertex	3-4-91	4-5-91
B	6x	RPSO, LPSO Vertex	3-4-91	4-5-91
C	6x	Opposed Laterals and Vertex	4-8-91	4-16-91
D	6x	RPSO, LPSO, Vertex	4-8-91	4-16-91

SITE	PORTS DESCRIPTION (Ant., Post., Lateral, etc.)	FIELD SIZE AT 1 Meter	PHYS FACT	DAILY DOSE	TOTAL TUMOR DOSE	FRACTIONS	ELAPSED DAYS
Brain Stem	Rt. & Lt. Laterals & Vertex	10x10	A	100	2500	25	32
Brain Stem	RPSO, LPSO, Anterior Vertex	10x10	B	100	2500	25	32
Brain Stem	Rt. & Lt. Laterals & Vertex	10x10 9.5x9.5	C	100	500	5	8
Brain Stem	RPSO, LPSO, Anterior Vertex	10x10	D	100	500	5	8

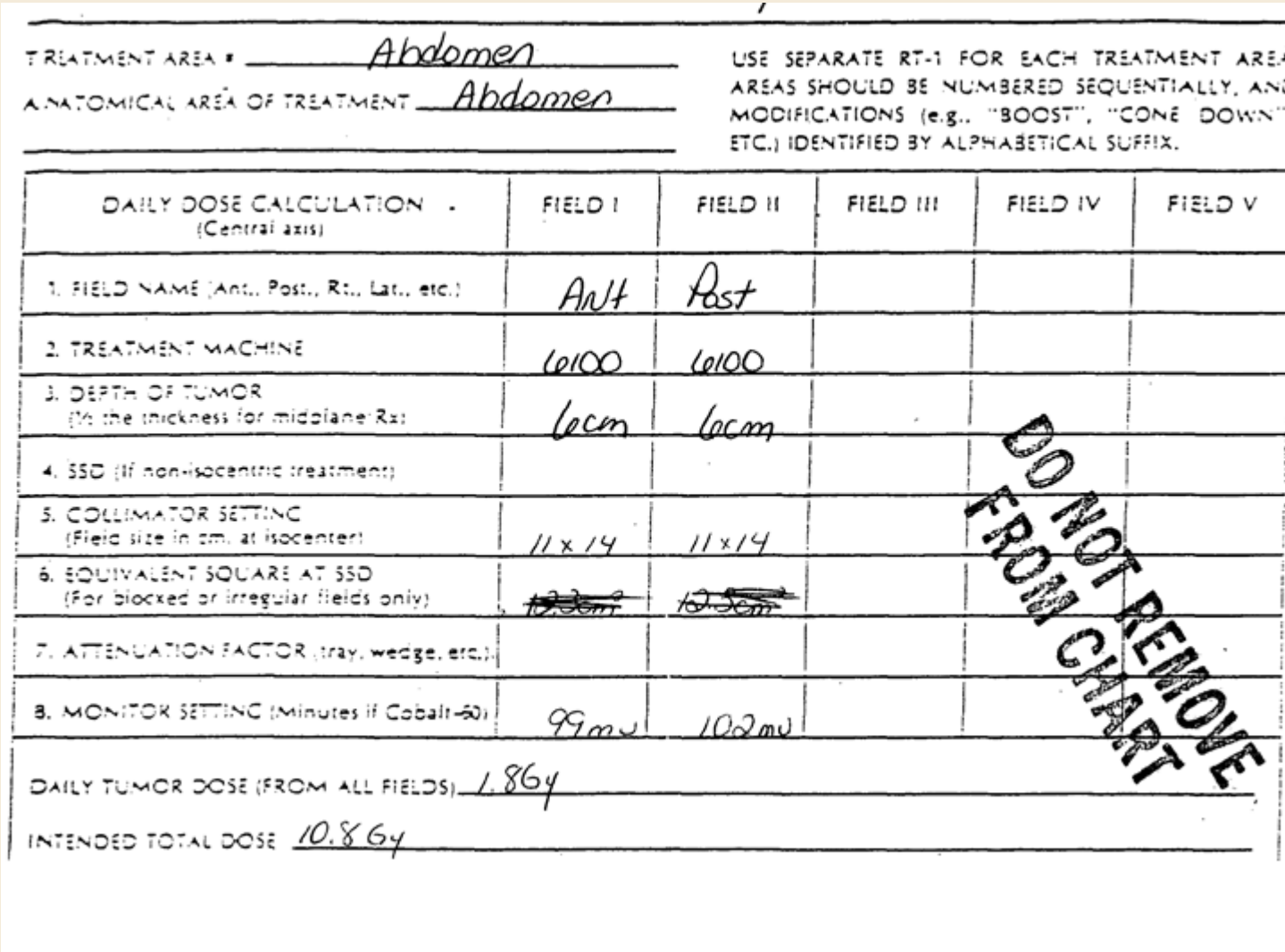
SITE	ISOTOPE	MG. RADIUM EQUIVALENT	ISODOSE PRESCRIBED	HOURS	DOSE TO SITE

TOTAL DOSE

SITE	TOTAL DOSE	FRACTIONS	ELAPSED DAYS
Brain Stem	6000	60	43

Example Record 2

- 38 page record



TREATMENT AREA # Abdomen

ANATOMICAL AREA OF TREATMENT Abdomen

USE SEPARATE RT-1 FOR EACH TREATMENT AREA
AREAS SHOULD BE NUMBERED SEQUENTIALLY, AN
MODIFICATIONS (e.g., "BOOST", "CONE DOWN"
ETC.) IDENTIFIED BY ALPHABETICAL SUFFIX.

DAILY DOSE CALCULATION (Central axis)	FIELD I	FIELD II	FIELD III	FIELD IV	FIELD V
1. FIELD NAME (Ant., Post., Rt., Lat., etc.)	Ant	Post			
2. TREATMENT MACHINE	6100	6100			
3. DEPTH OF TUMOR (½ the thickness for midplane Rx)	6cm	6cm			
4. SSD (If non-isocentric treatment)					
5. COLLIMATOR SETTING (Field size in cm. at isocenter)	11 x 14	11 x 14			
6. EQUIVALENT SQUARE AT SSD (For blocked or irregular fields only)	~~12.5cm~~	~~12.5cm~~			
7. ATTENUATION FACTOR (tray, wedge, etc.)					
8. MONITOR SETTING (Minutes if Cobalt-60)	99mu	102mu			

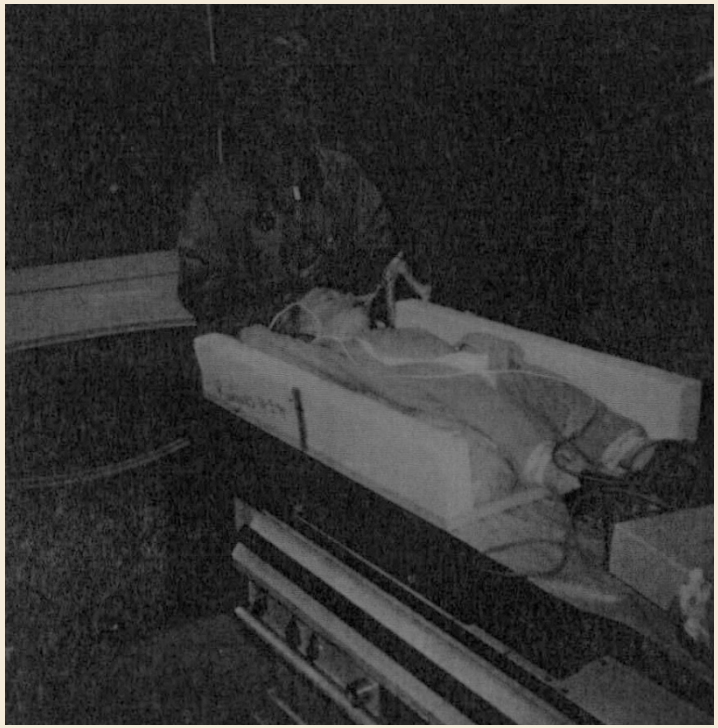
DAILY TUMOR DOSE (FROM ALL FIELDS) 1.86 Gy

INTENDED TOTAL DOSE 10.86 Gy

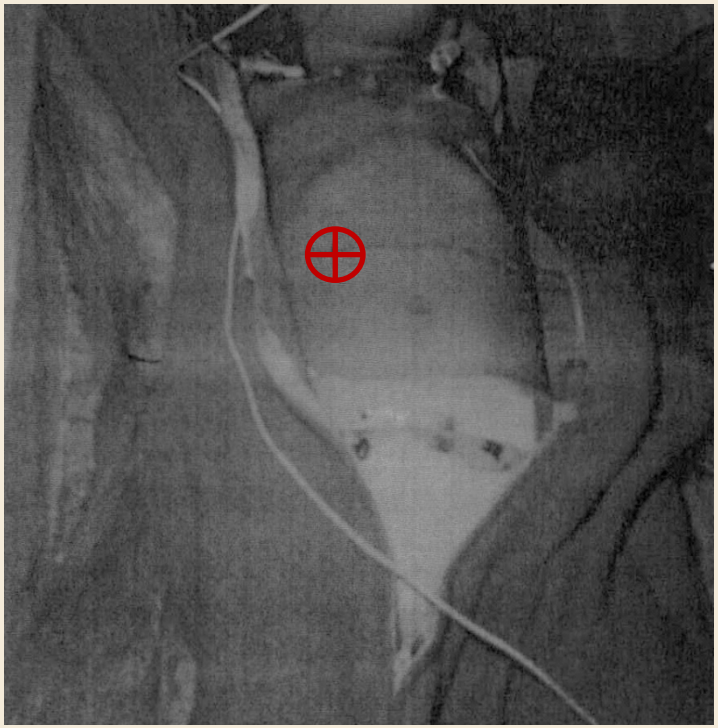
DO NOT REMOVE FROM CHART

Example Record 2

- Photographs are sometimes in the charts and can be useful for determining field borders or isocenter



Not a very useful photo

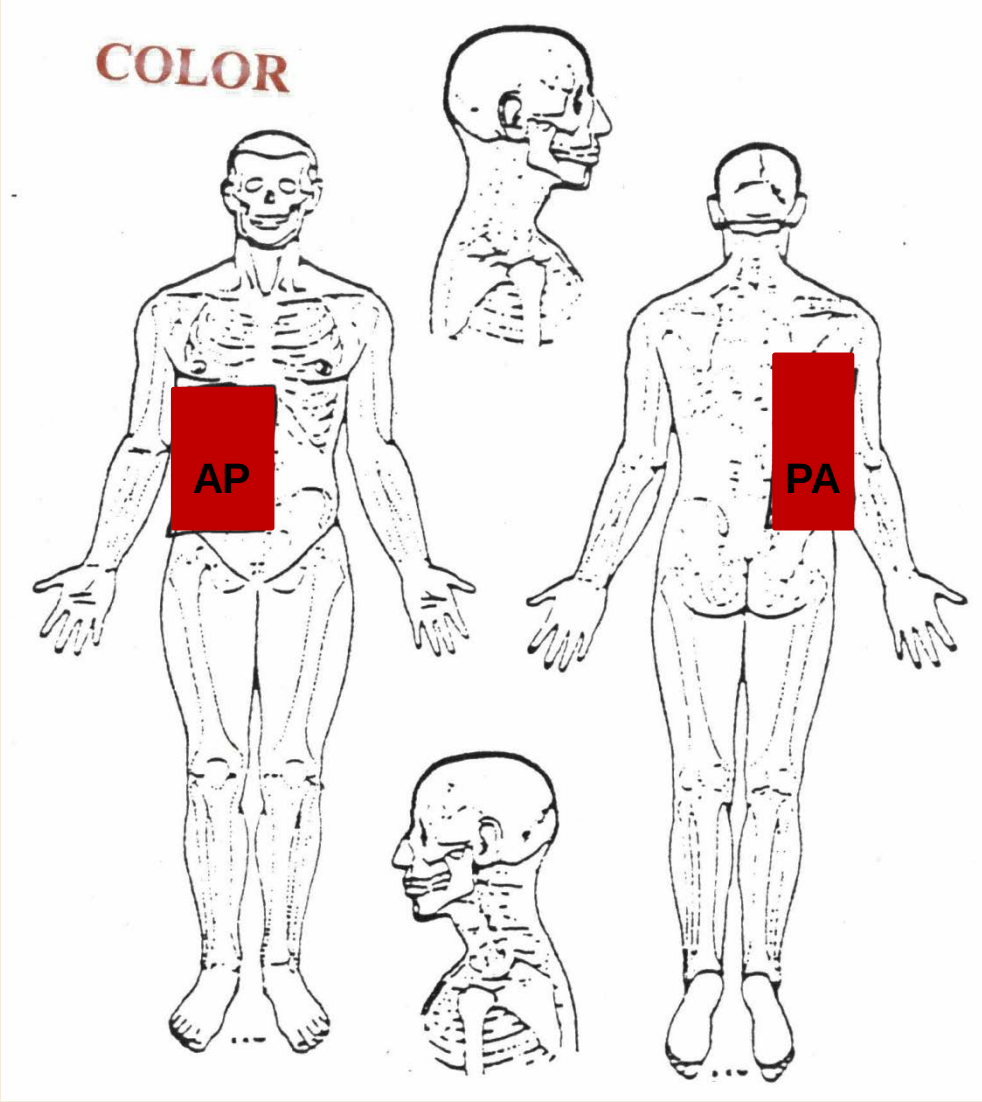


Field isocenter is visible

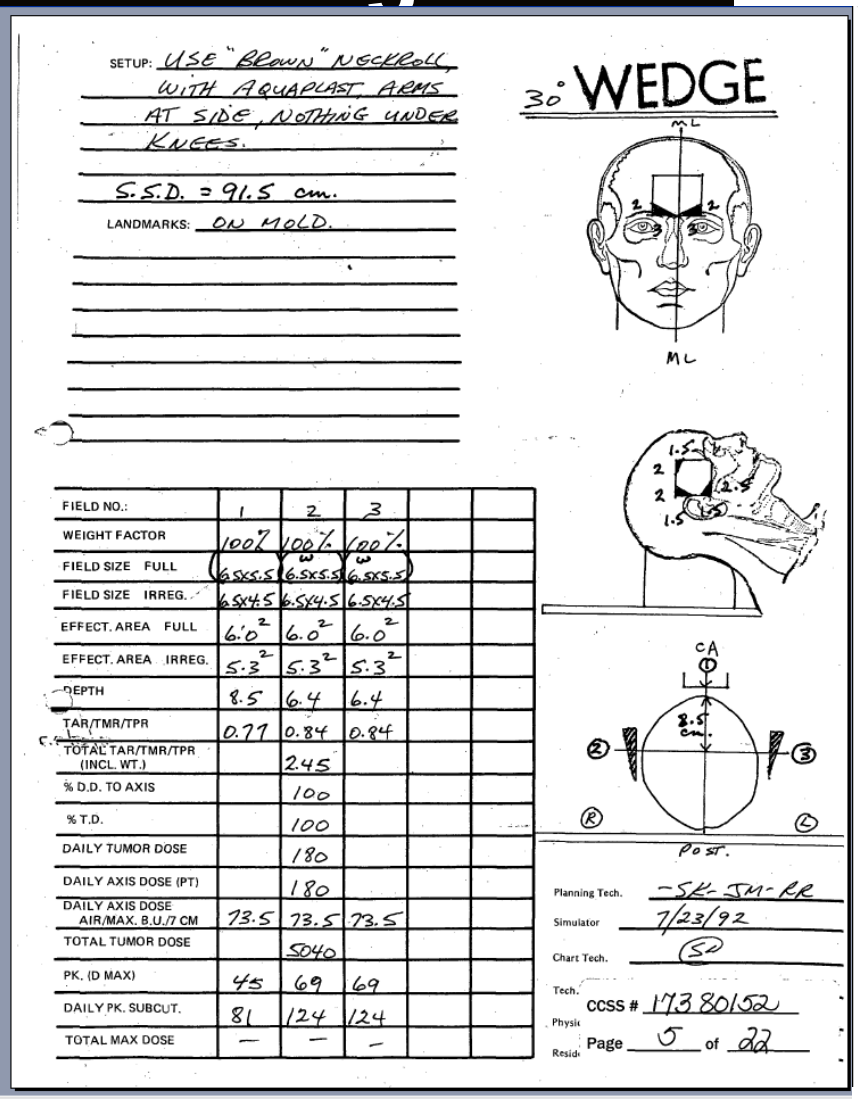
Example Record 2

- Diagrams provide very useful information for field placement on the generic phantom for dose reconstruction.
- Some uncertainty in field position relative to midline
  - AP drawn to midline
  - PA not quite to midline

These sorts of discrepancies can sometimes be sorted out based on a photo or the physicians' notes.



More examples of diagrams



SETUP: USE "BROWN" NECKROLL, WITH AQUAPLAST. ARMS AT SIDE, NOTHING UNDER KNEES.

S.S.D. = 91.5 cm.

LANDMARKS: ON MOLD.

30° WEDGE

ML

ML

FIELD NO.:	1	2	3		
WEIGHT FACTOR	100%	100%	100%		
FIELD SIZE FULL	6.5x5.5	6.5x5.5	6.5x5.5		
FIELD SIZE IRREG.	6.5x4.5	6.5x4.5	6.5x4.5		
EFFECT. AREA FULL	6.0 ^{2}	6.0 ^{2}	6.0 ^{2}		
EFFECT. AREA IRREG.	5.3 ^{2}	5.3 ^{2}	5.3 ^{2}		
DEPTH	8.5	6.4	6.4		
TAR/TMR/TPR	0.77	0.84	0.84		
TOTAL TAR/TMR/TPR (INCL. WT.)		2.45			
% D.D. TO AXIS		100			
% T.D.		100			
DAILY TUMOR DOSE		180			
DAILY AXIS DOSE (PT)		180			
DAILY AXIS DOSE AIR/MAX. B.U./7 CM	73.5	73.5	73.5		
TOTAL TUMOR DOSE		5040			
PK. (D MAX)	45	69	69		
DAILY PK. SUBCUT.	81	124	124		
TOTAL MAX DOSE	—	—	—		

Planning Tech. -SK-JM-RR

Simulator 7/23/92

Chart Tech. (S2)

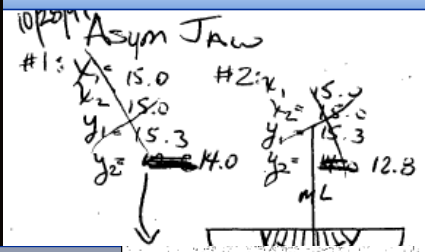
Tech.

Physi

Resid

CCSS # 17380152

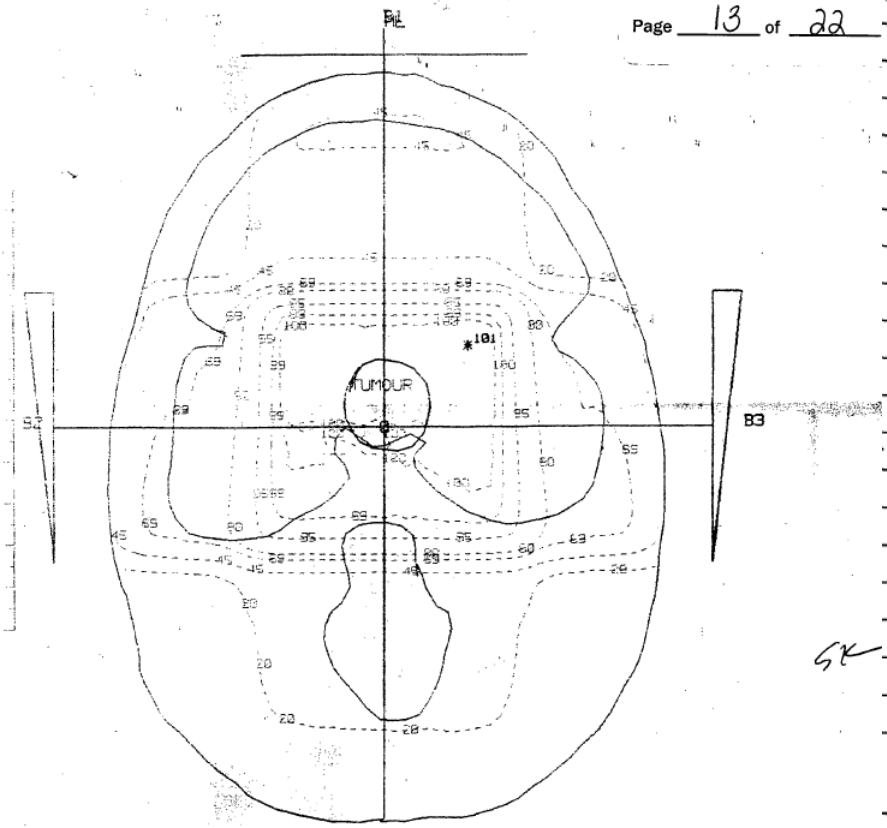
Page 5 of 22



"C" "D" NECKROLL, ARMS AKIMBO, Δ UNDER KNEES.

CCSS # 17380152

Page 13 of 22



SK

'S

2H (187)

11/15/99

y_2 = 0.0

#4: Release V

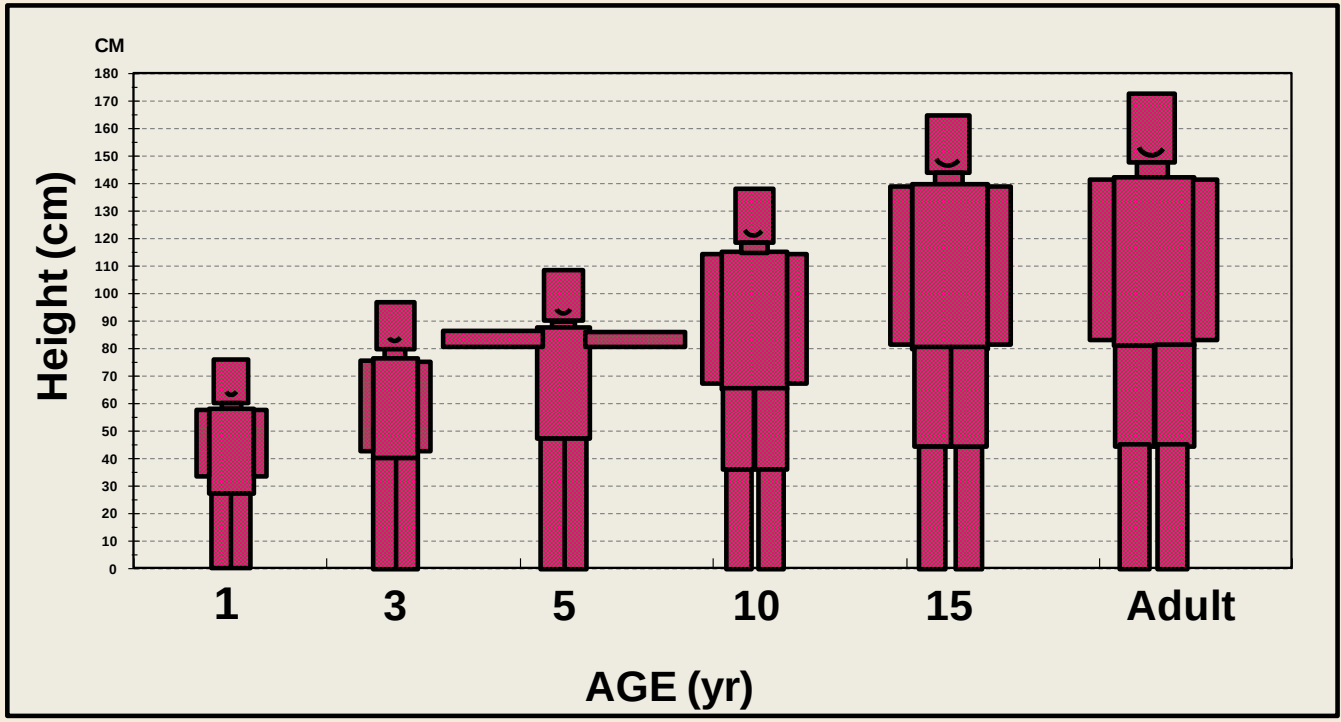
#6 11/17/94 RR Physics Checked mBP 10/18/55, 11/15/55 hd 11/12/94 11/17/55

How do we use abstracted data?

- To “reconstruct” the treatments using a library of average-size-for-age (infant through adult) generic phantoms and analytical calculation models (Stovall et al. 2006; NCRP 2011).

Mathematical Phantom(s)

- Phantom size can be modified to represent patient of any age.
- Models representing 6 age groups are shown in figure.

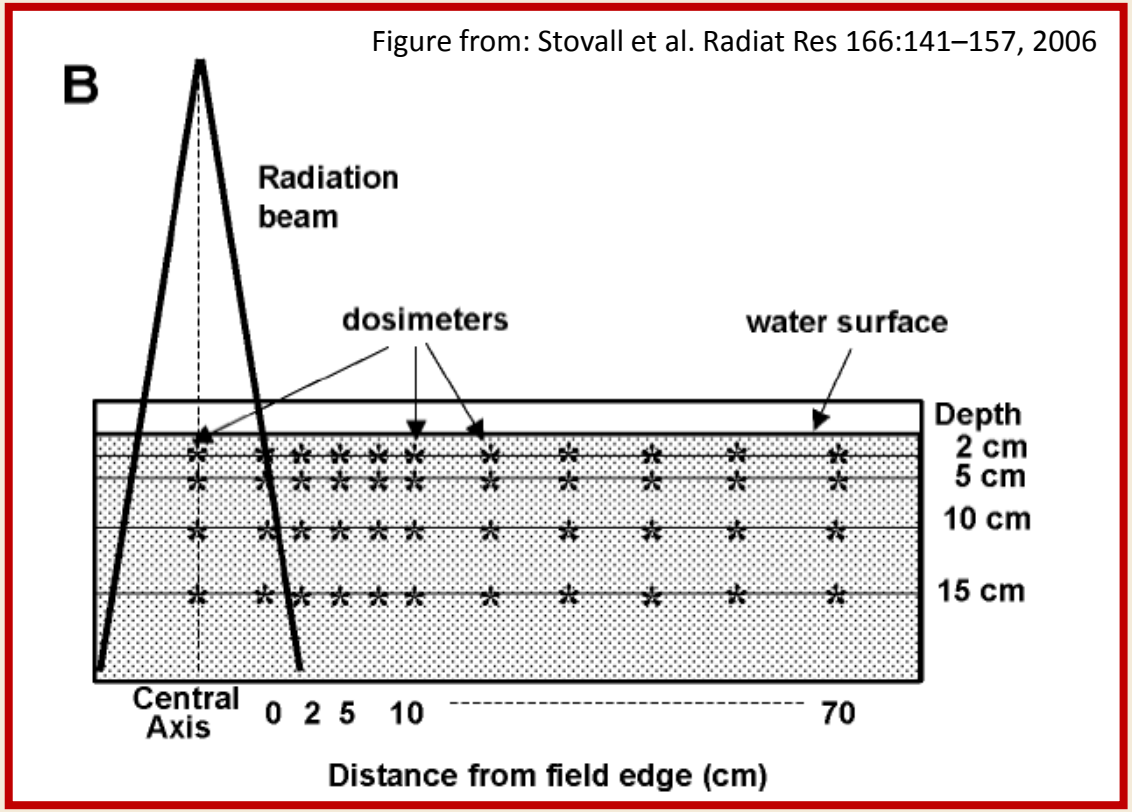


- Mathematical phantoms are also inexpensive to use.

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

Analytical Model of Out-of-Field Dose

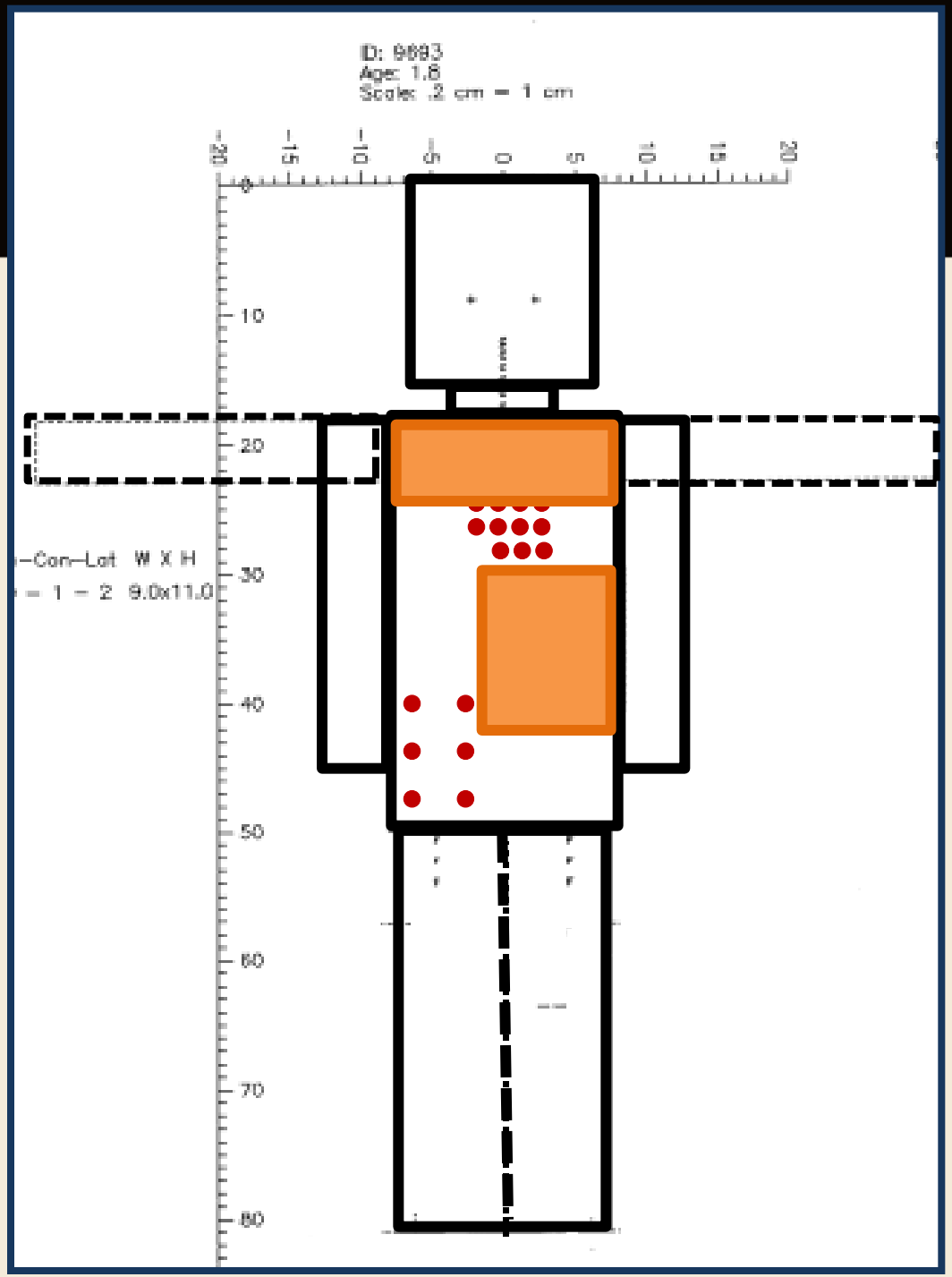
- Dose within/outside the treatment beam was measured in large water phantom
  - Various beam energies and field sizes.



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

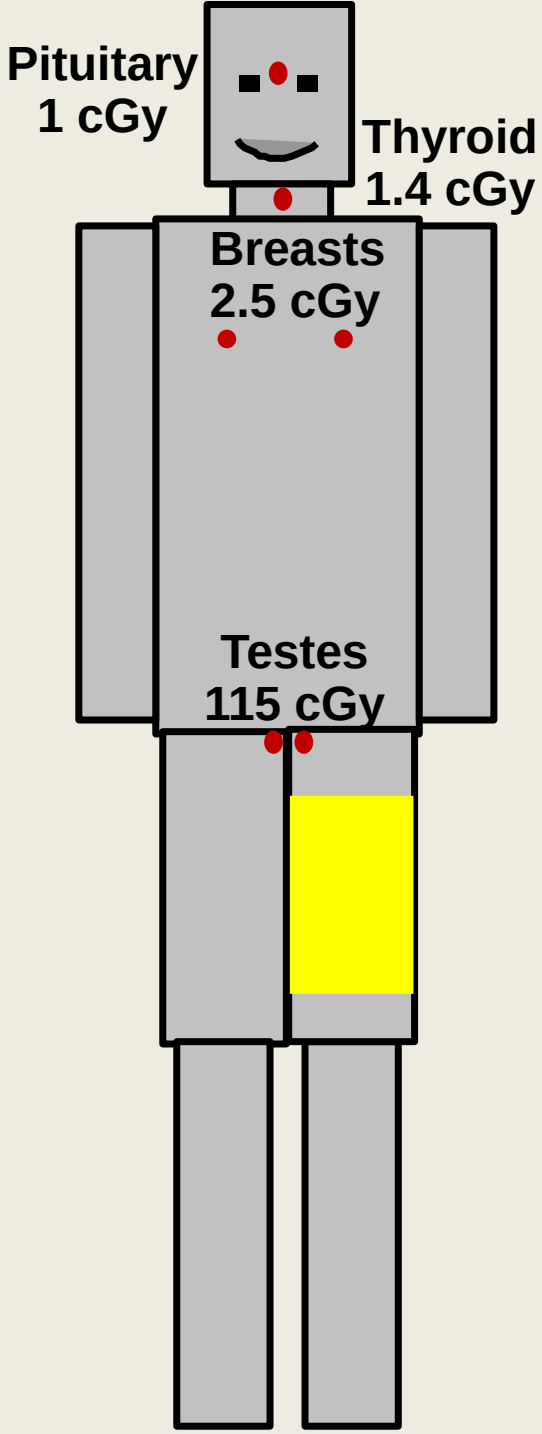
Mathematical Phantom

- 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



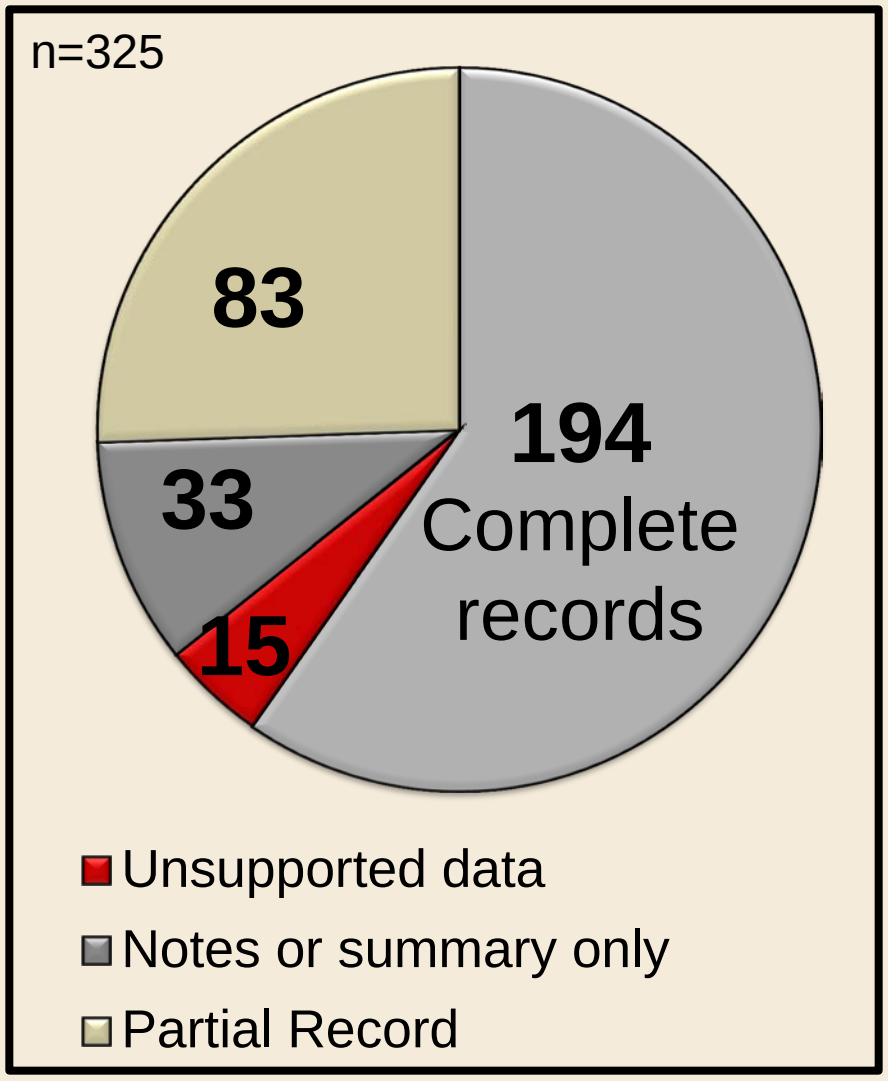
Mathematical Phantom Example

- **Details from RT record**
  - 16 year-old male treated for an osteosarcoma in the left thigh.
  - Field size: 12x17 cm^2
  - Field orientation: AP/PA
  - Target dose: 55 Gy
  - Beam type/energy: 6 MV photons
- Mathematical phantom + analytical model used to calculate dose to out-of-field organs.

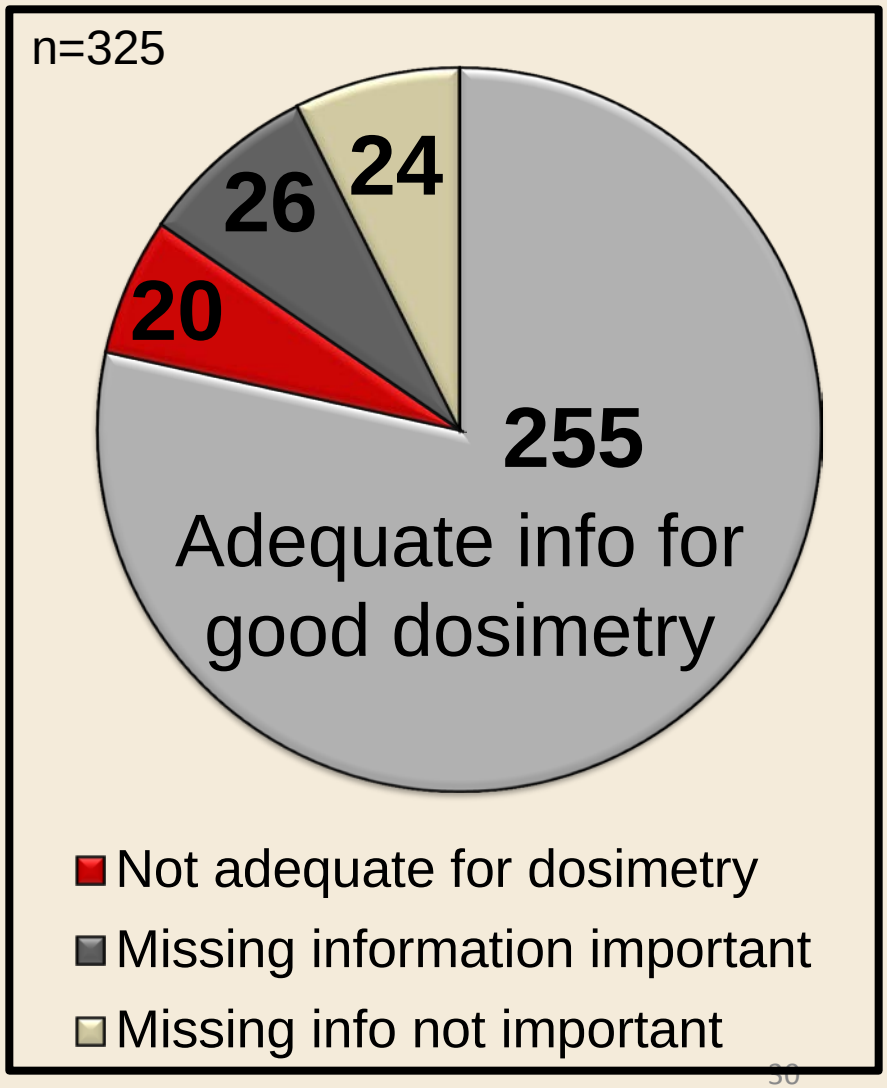


What is the relationship between the quality of the radiotherapy record and adequate dosimetry for epidemiologic studies?

Radiation Therapy Data Received



Radiation Therapy Information Quality



Uncertainties
Out-of-Beam Dosimetry

Source	Magnitude
Organ near field	Large
Treatment record incomplete	Variable
Patient age surrogate for size	Small
Measurement system	Very Small

Consistency is Essential

- **Within a Study**
  - No systematic differences between cases and controls or you may bias a study.
  - Maintain same quality of documentation for cases and controls.
- **Across Studies**
  - Important to be able to compare data, pool patients, etc. in studies many years apart.
  - If you change dosimetry method, do it deliberately, with full understanding of the impact on results.

Organ Doses from Typical Pediatric Radiation Therapy

Disease Treated	Age (yrs) at XRT	Regions Treated	Tumor Dose Range (cGy)	Average Dose Range (cGy)		
				Heart	Lungs	Kidneys
Cranio-spinal Tumors	7	Brain only	4500 - 5500	15 – 55	15 - 65	5 – 30
Leukemia	4	Brain only	1800 - 2500	9 – 35	10 – 40	4 – 20
Hodgkin Lymphoma	15	Chest only	3500 - 4500	2800 – 3650	620 – 900	40 – 100
		Chest and Abdomen	3500 - 4500	3500 – 4500	1000 – 1500	950 – 1600
Wilms (Kidney)	4	Abdomen only	1500 - 2500	145 – 330	105 – 265	85 – 210 untreated side
		Abdomen & Chest	1500 - 2500 1200 - 2000	1300 – 2240	1200 – 2100	115 – 300
Neuroblastoma	2	Chest (right)	1200 - 2500	800 – 1850	600 – 1300	15 – 90

Dosimetry for Late Effects Studies

- *Other Dosimetry methodologies used in retrospective radiation epidemiology studies…..*
  - Measurements in anthropomorphic phantoms.
  - Commercial TPS with representative patients or phantoms.
  - Monte Carlo with representative patients or phantoms.

Measurements with Anthropomorphic Phantoms

Advantages

- They most nearly simulate a real person.
- Commercially available from several manufacturers.

Disadvantages

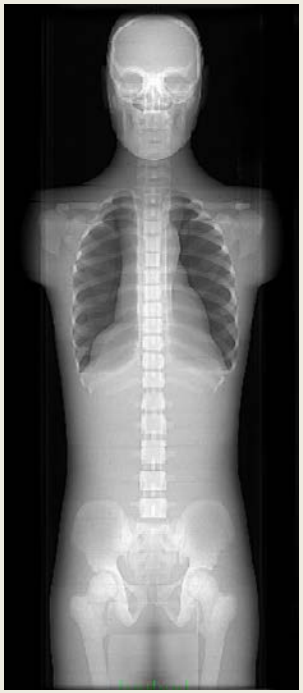
- Only available limited sizes.
- Expensive to buy and use.
- Internal organs are in a fixed position.

Anthropomorphic Phantoms

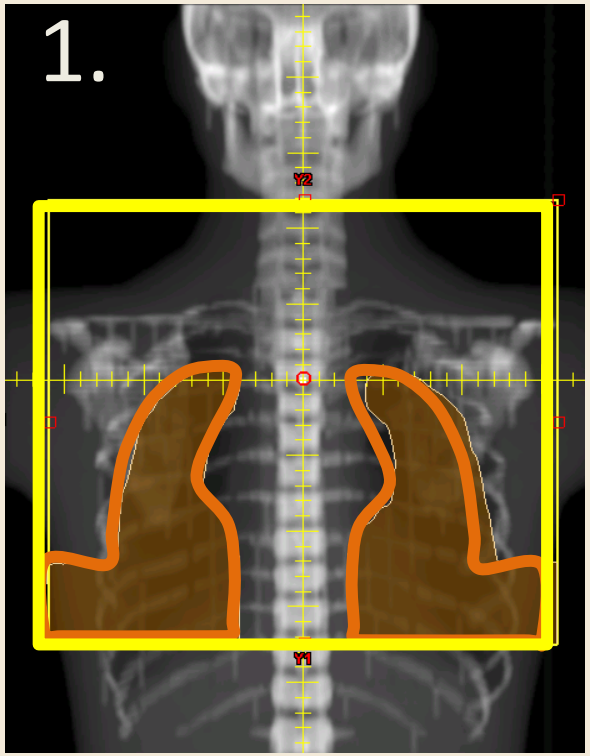
- Available sizes: newborn, 1-year old, 5-year old, 10-year old, adult male, adult female.
- The size of each model is based on ICRP 23, ICRU 48

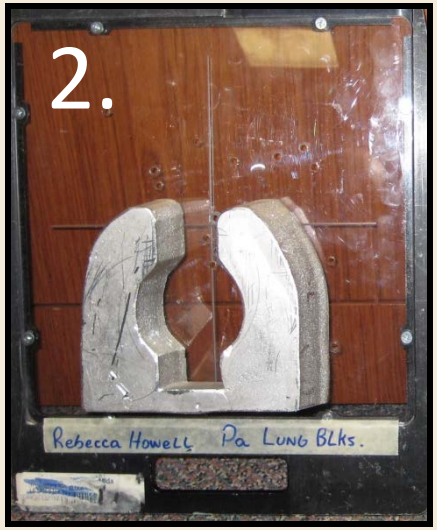
- **Tissue equivalent materials:**
  - Soft tissue, bone, cartilage, spinal cord, spinal disks, lung, brain, sinus, trachea and bronchial cavities (ICRP-23).
- Simulated bone tissue for pediatric models matches age related density.

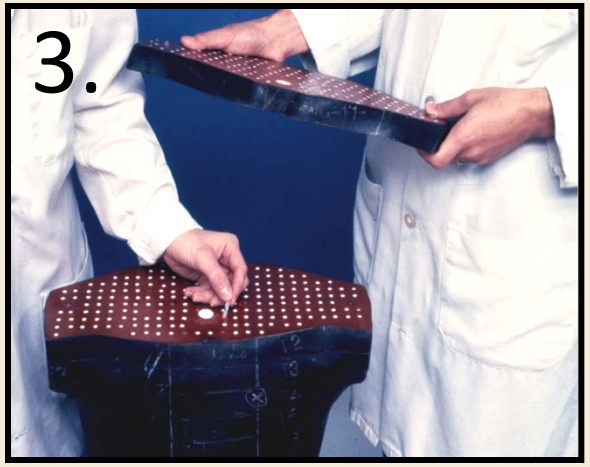
http://www.cirsinc.com/700_ct_xray.html

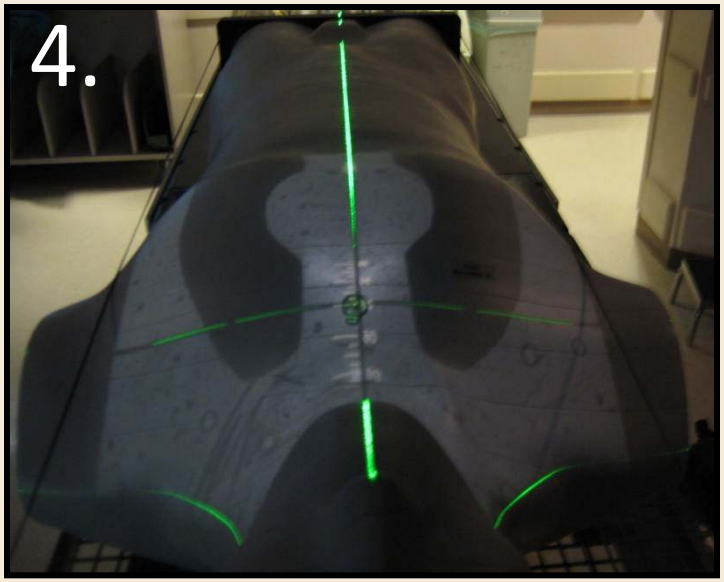


Procedure for Measurements with Anthropomorphic Phantoms



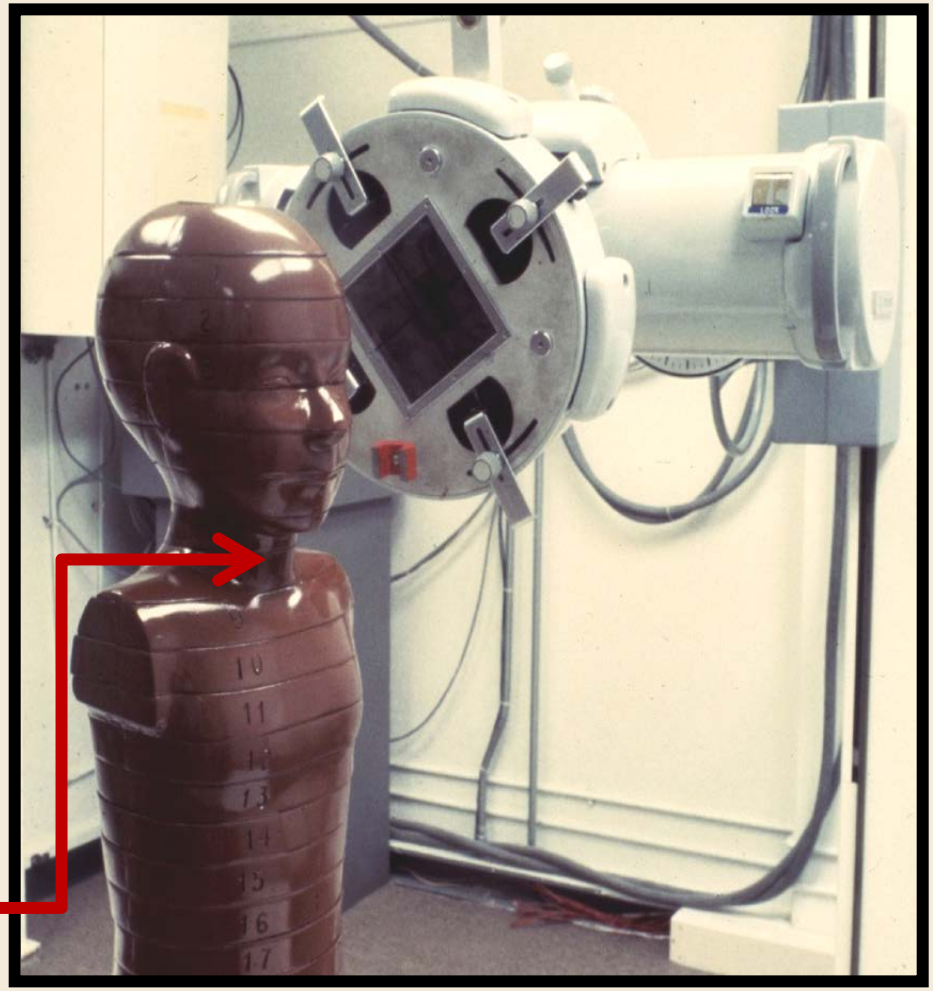






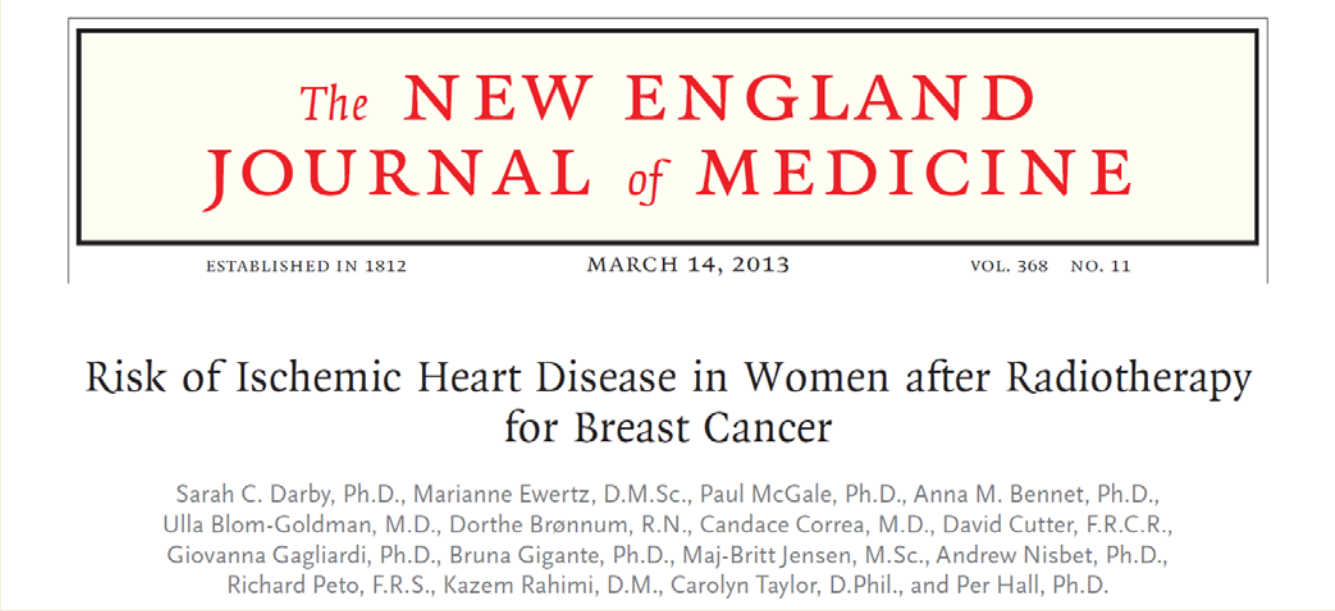
Example of “6-year old” Phantom for Pediatric Study

- Planned radiation fields for treatment of benign tonsil lesion were delivered.
- Measure dose in the phantom at positions corresponding to location of thyroid.



Dosimeters placed in this region of phantom.

Example of Study that used commercial TPS for dose reconstruction



The NEW ENGLAND JOURNAL of MEDICINE

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Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D., Ulla Blom-Goldman, M.D., Dorthe Brønnum, R.N., Candace Correa, M.D., David Cutter, F.R.C.R., Giovanna Gagliardi, Ph.D., Bruna Gigante, Ph.D., Maj-Britt Jensen, M.Sc., Andrew Nisbet, Ph.D., Richard Peto, F.R.S., Kazem Rahimi, D.M., Carolyn Taylor, D.Phil., and Per Hall, Ph.D.

RT for breast cancer increases rate of ischemic heart disease: proportional to the **mean heart dose.**

How was mean heart dose determined for thousands of women?

Dose Reconstruction – Cardiac Dose

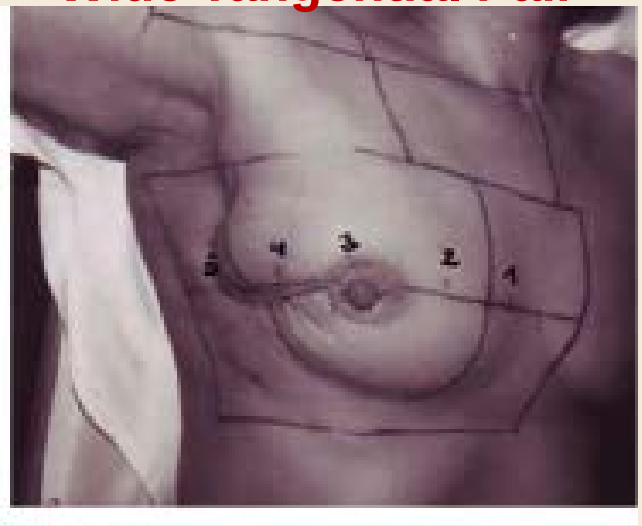
(Previously described in Taylor *et al.* 2011, 2009, 2007)

- RT charts were obtained and categorized according to regimen:
  - laterality, field arrangement, prescription dose(s), dose/fx.
- 22 standard treatment regimens were identified.
  - Each patient was classified to a particular regimen based on data in treatment chart.

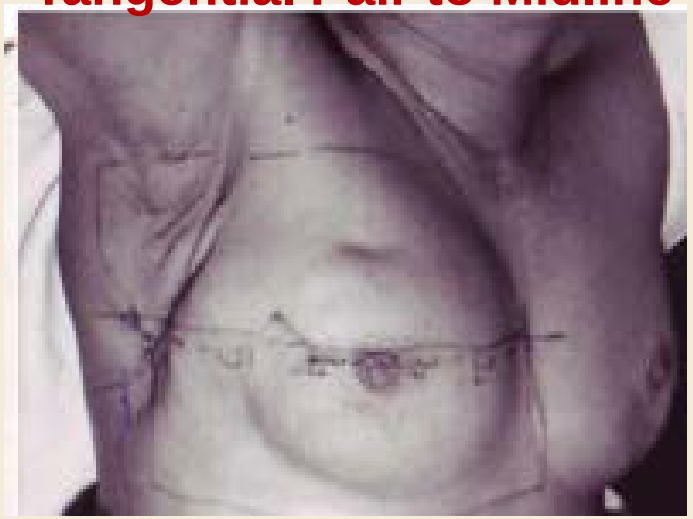
Dose Reconstruction – Cardiac Dose

(Previously described in Taylor et al. 2011, 2009, 2007)

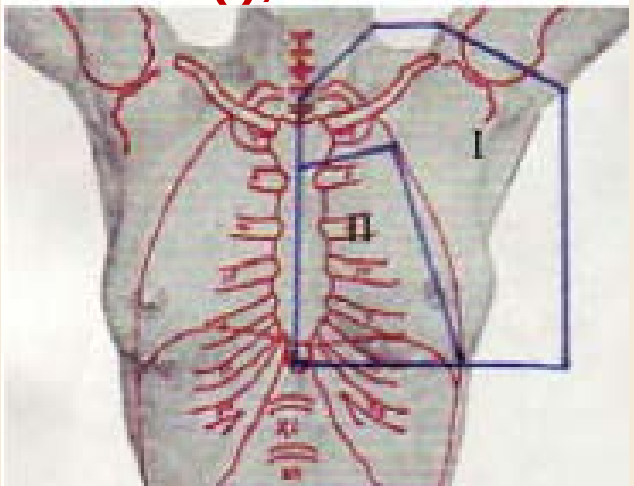
Wide Tangential Pair



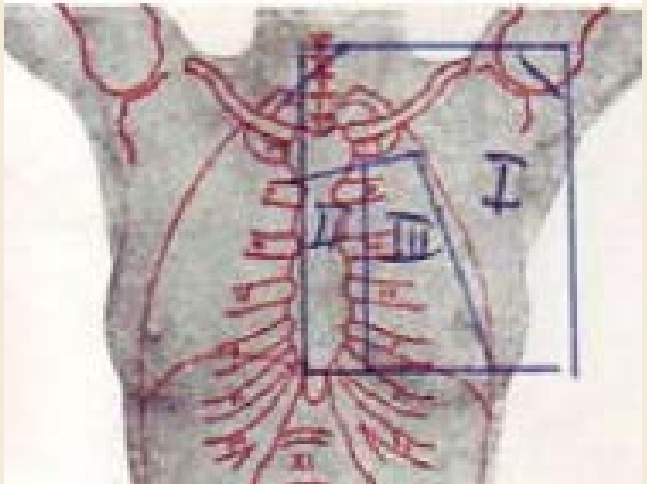
Tangential Pair to Midline



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



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

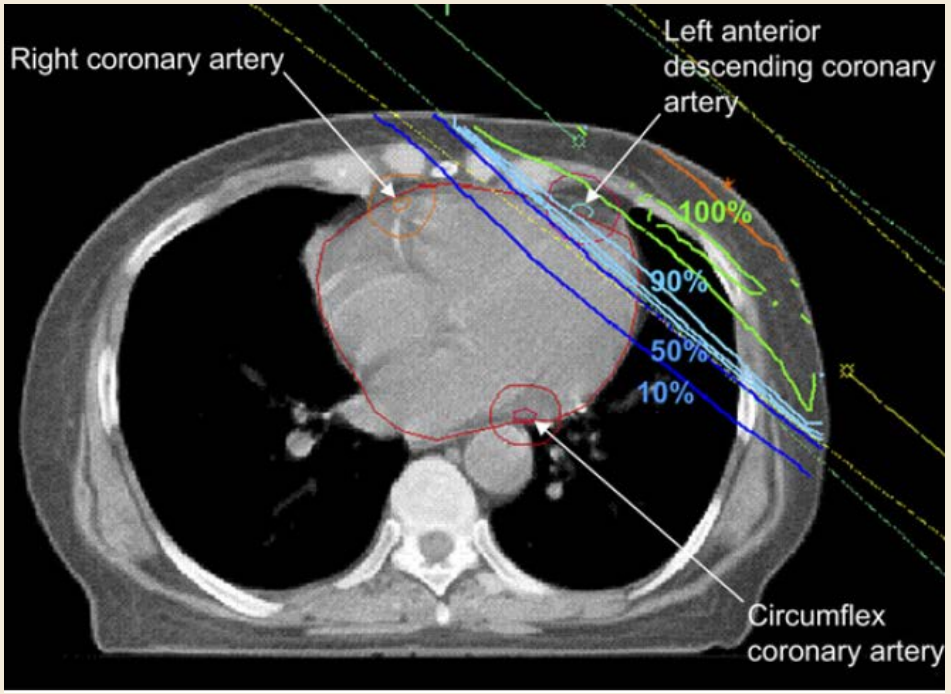


Taylor *et al.*
RO 2011

Dose Reconstruction – Cardiac Dose

(Previously described in Taylor et al. 2011, 2009, 2007)

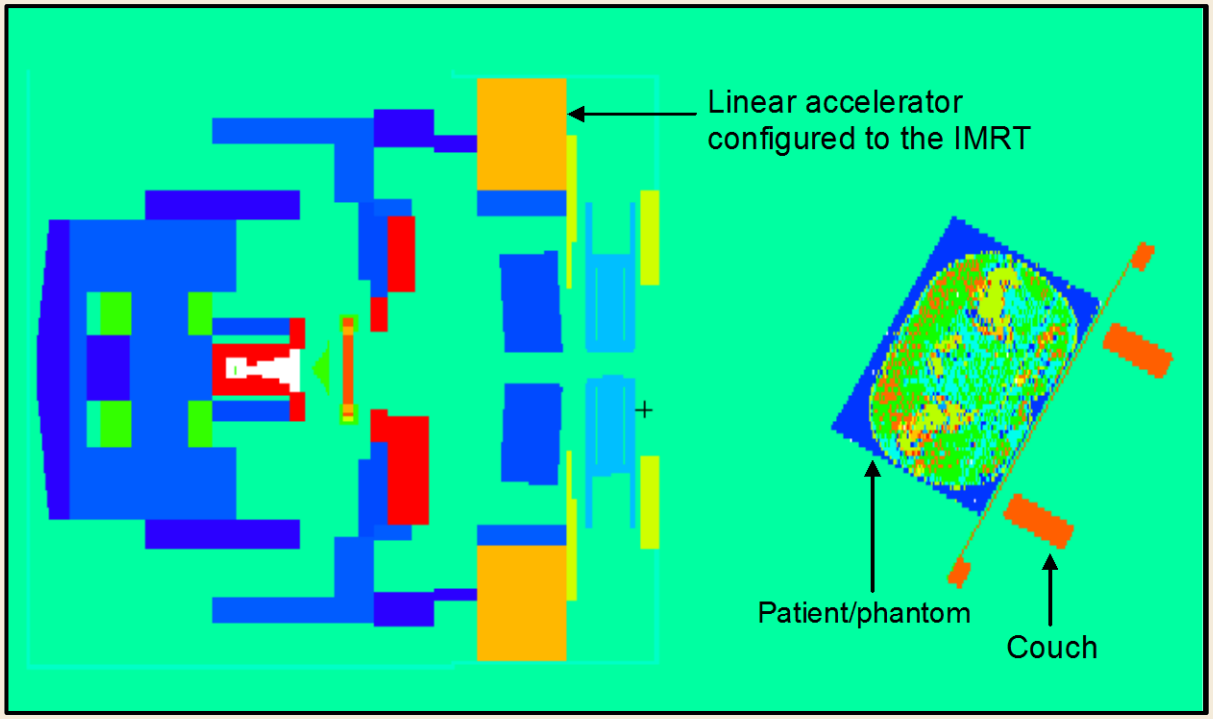
- The different RT regimes were reconstructed on a CT scan of typical patient of average build.
  - Heart and Coronary arteries were contoured
  - DVH were used to determine mean heart dose for each regime.
  - Heart doses were “assigned” to individual patients according to regimen classification



Taylor *et al.* IJORBP 2007

Monte Carlo (MC) Techniques

- MC techniques can accurately determine stray dose to organs outside the treatment field because it relies on 1st principles of radiation transport physics.



Model of treatment field from Varian 2100 incident on patient CT

Limitations of MC for Retrospective Radiation Epidemiology Studies

- Different models are required for different external beam RT machines or sources (brachytherapy).
- Models must be benchmarked for both in-field and out-of-field dosimetry with measured data.
- Computationally demanding.
- Patient/treatment specific geometries must be defined in MC format.

Can be overcome: e.g., reference libraries, automated geometry creation, high speed processors, etc.

- **No CT for patients in study or CT only includes RT treatment region.**

Patients' anatomy remains uncertain!

Dosimetry for Late Effects Studies

Challenges of Modern Radiation Therapy

Late effects studies require a fairly long latent periods and for that reason they have focused on older conventional radiation techniques.

However, in a few years late effects studies will also include contemporary radiation techniques.

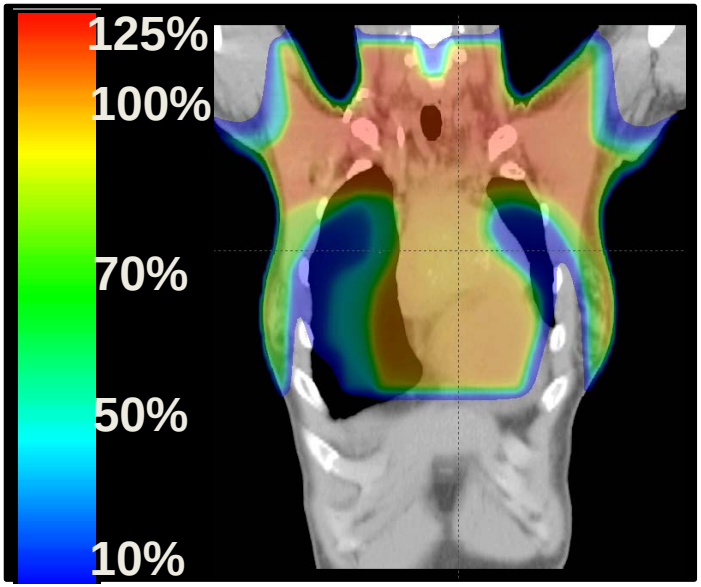
- Intensity modulated radiation therapy, IMRT

  Uses dynamically moving shielding to vary beam intensity based on individual patient anatomy (defined on CT).
  - No standardized field borders
  - More beams are used
  - Beam-on time to deliver specified dose is much longer.

Let’s compare an example of dose reconstruction for conventional RT and IMRT.

- Conventional beam therapy - Static beam with shielding blocks.
  - Standardized field borders based on anatomical borders
- Example: Hodgkin lymphoma.
  - Superior field border: ear/jaw
  - Inferior field border: T10
  - Lateral borders - cover ribcage

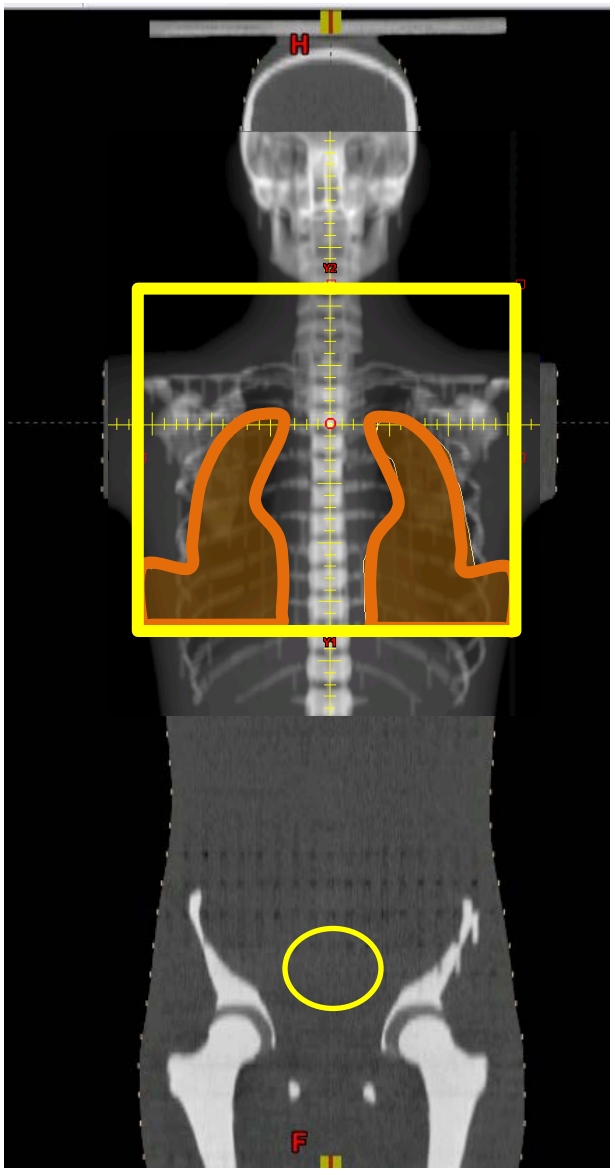
Anatomical field borders (from individual RT records) can be used to reconstruct organ doses in phantom.



- Dose distribution for patient treated with conventional mantle field.

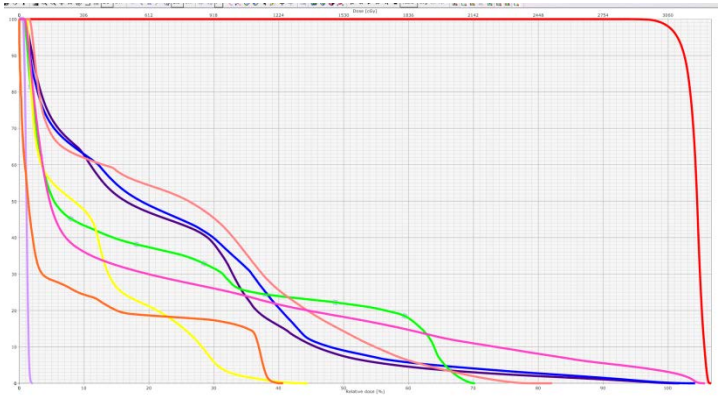
- Treatment field dimensions (and blocking information) from RT record.

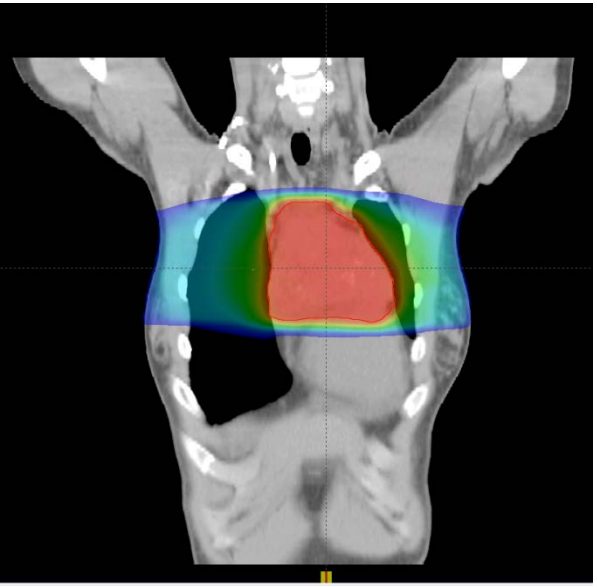
- Treatment field of same dimensions superimposed on phantom (approximately same size/age as patient).
- Dose measured or calculated in phantom (mathematical or anthropomorphic).
- Organ doses can be obtained at defined locations.

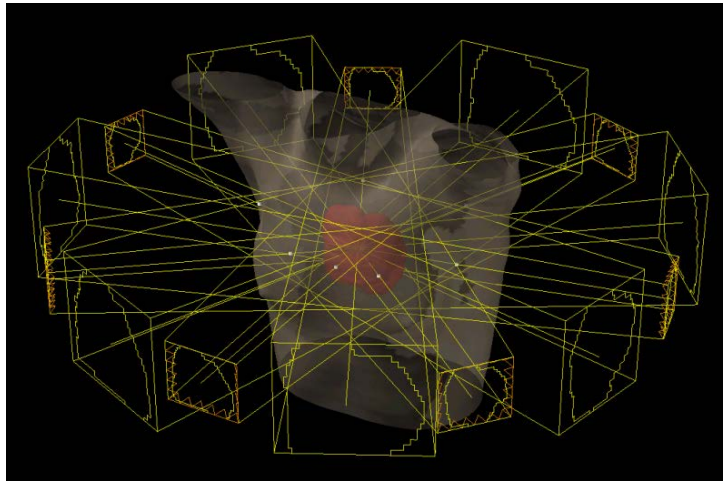


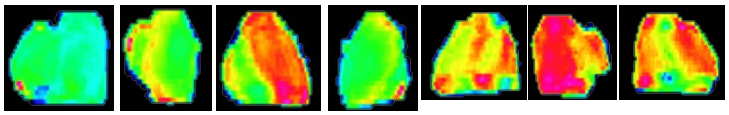
Typical information in IMRT record:

- PTV dose(s), # fx, isodose distributions in various planes, dose volume histograms, number of fields (and maybe intensity maps).









- From these data, difficult to reconstruct dose in phantom to obtain organ doses outside the field(s).

Summary

- Many methods to reconstruct organ doses from historic RT and can give very reasonable data.
- Greatest uncertainty is often not from the actual calculation or measurements but…

  from lack of or missing information in RT record, e.g., organ positions, field borders, Rx dose, etc.

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- TaShun Thomas
- Leah Richards
- Sharon McCallister,
- Ferrell Munson

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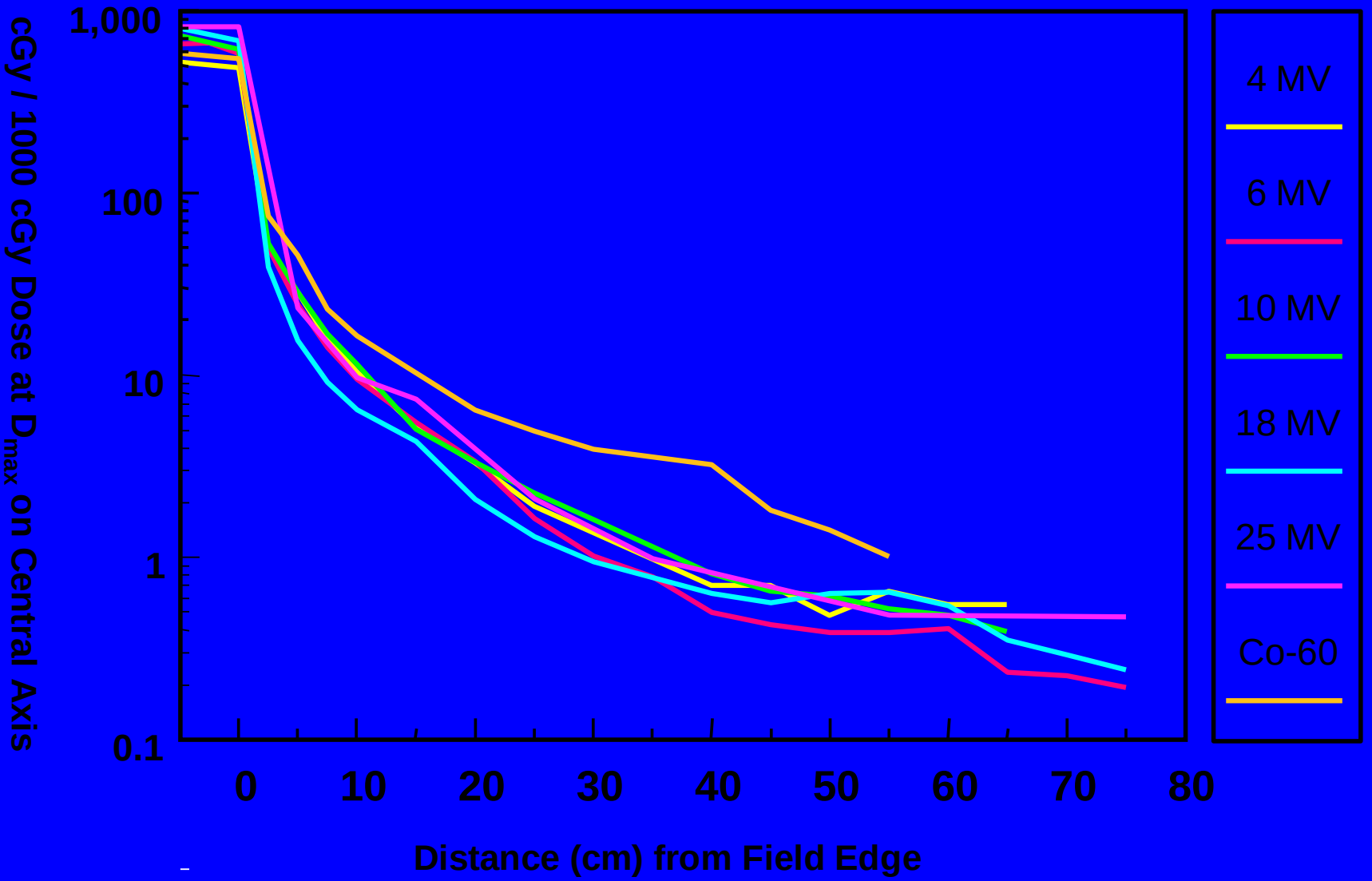
Questions and Answers

U.S. Department of Health and Human Services
National Institutes of Health | National Cancer Institute
www.dceg.cancer.gov/RadEpiCourse
1-800-4-CANCER
Produced May 2015

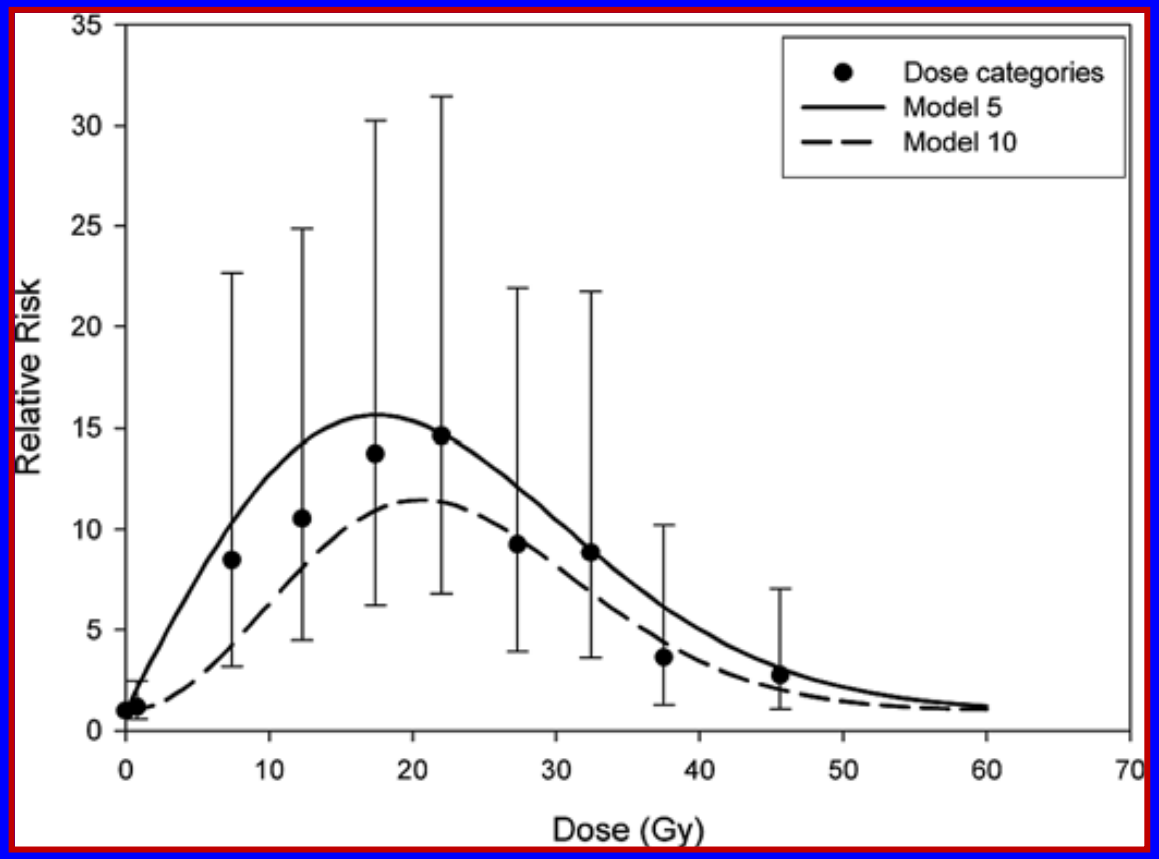
Total Absorbed Dose from Treatment Beams

6 MV Photon - 10x10 cm² Field Size - Various Energies



Second Primary Thyroid Cancer after RT
Bhatti *et al.* RadRes 2010

- Major Finding: SIR and RR of developing 2nd thyroid SPC increased steadily with dose up to the 20 to <25 Gy and then declined at higher doses.

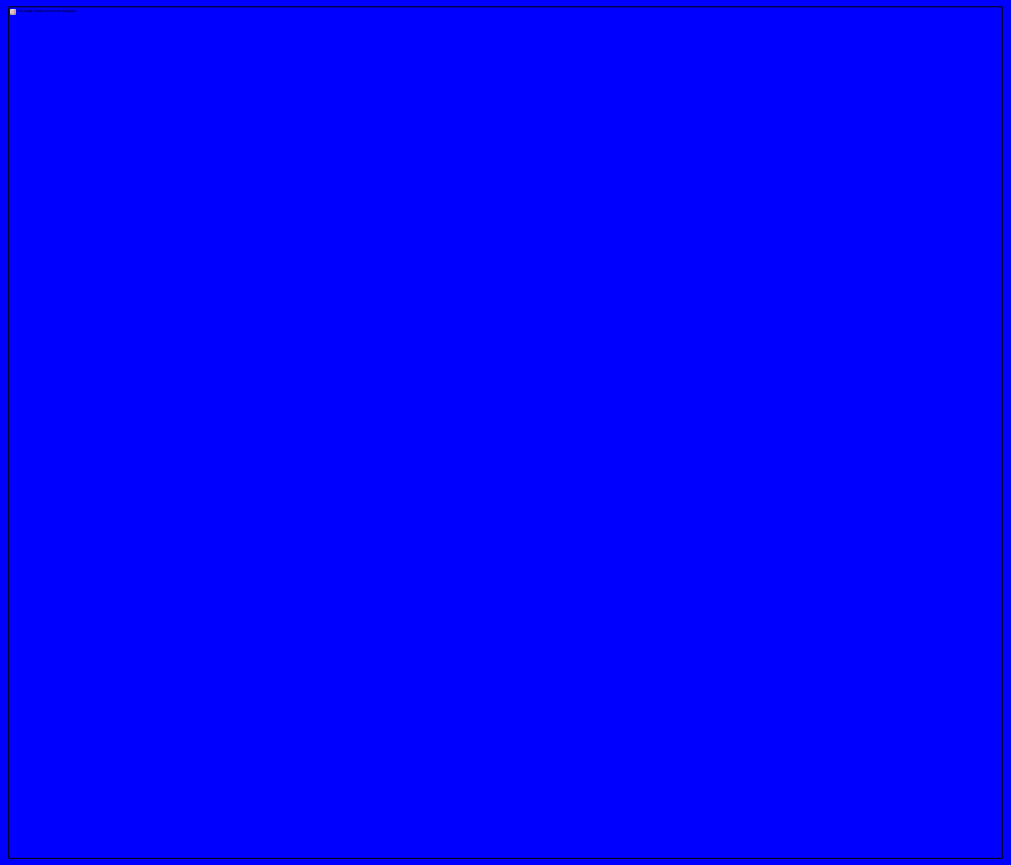


RR of thyroid cancer as a function of mean RT dose to the thyroid gland

- Two different were fit data reasonably well.
- Model 5 was
  - better fit,
  - more consistent with radiobiological theory of linear dose response at low doses.

The Treatment Record

- Type of radiotherapy
- Total therapeutic dose
- Dose per fraction
- Number of beams
- Beam orientation
- Beam energy
- Radiograph with field geometry(s)

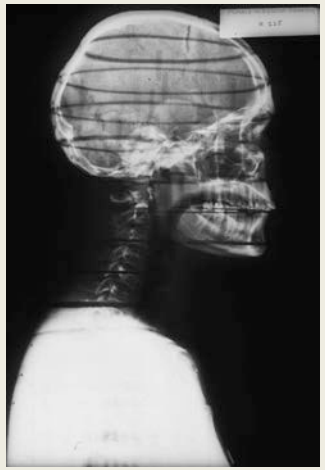


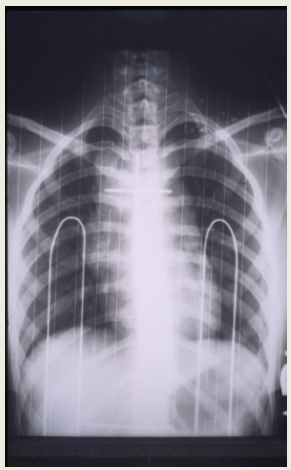
- What's not in the treatment record? **Stray radiation dose.**

Anthropomorphic Phantoms

- Available sizes:
  6-yr old child, adult male, and adult female

- They are made of 3 materials:
  - Natural human skeletons
  - Tissue-equivalent lungs
  - Tissue-equivalent soft tissue

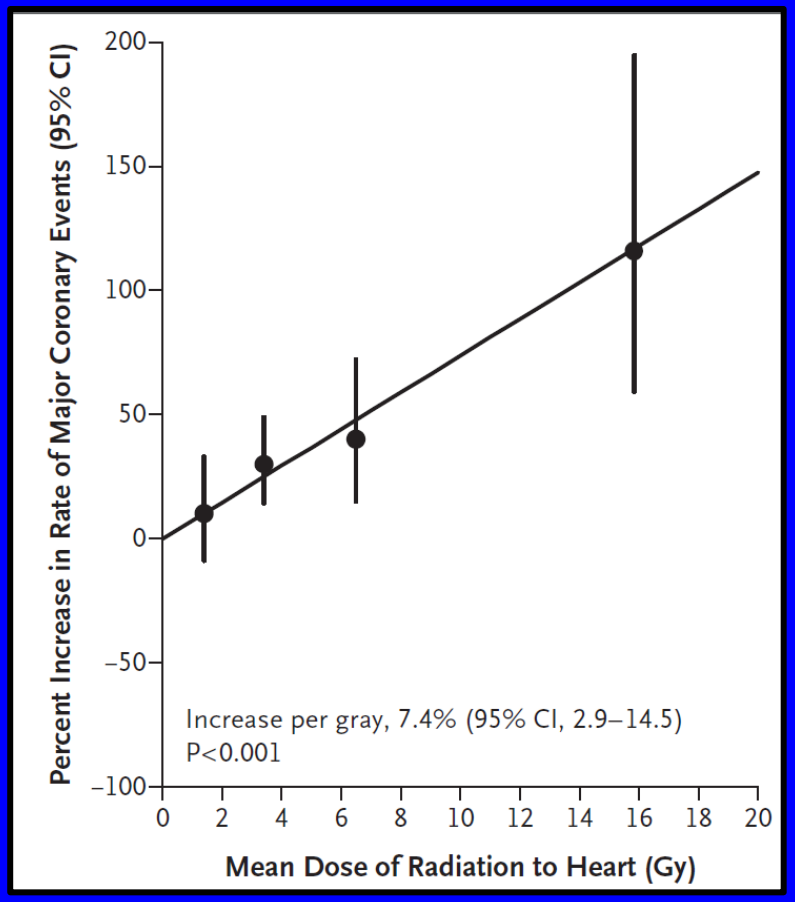


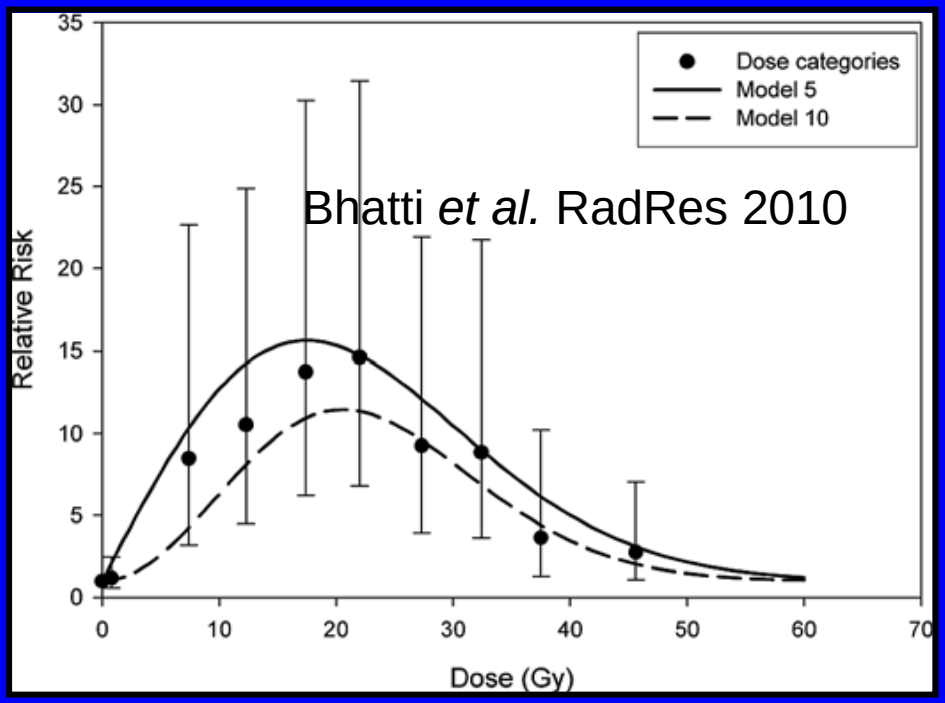


Radiographs of Rando phantoms

http://www.pnwx.com/Accessories/Phantoms/Radiology/PhantomLab/WholeBody/Rando/

Uncertainty vs. Dose Bins in Dose Response Models



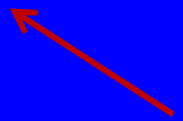


Bhatti *et al.* RadRes 2010

Inskip *et al.* JCO 2009

Dose Response Model

- Dosimetric uncertainty in this method:
  - Commercial TPS underestimates low doses, e.g., below 5%..
  - For 50Gy Rx, this would be 2.5 Gy.
- Organ position uncertainty:
  - How well does the representative patient anatomy represent individual patients to which dose was assigned?



Lowest dose value is 2Gy

Darby *et al.* NEJM 2012