

ARRO Case

Inflammatory Breast

Cancer

Laura E. G. Warren, MD, EdM

Faculty Advisor: Jennifer R. Bellon, MD

Brigham and Women's Hospital

Dana-Farber Cancer Institute

History

- **49 year-old post-menopausal female presenting with acute onset right breast erythema and skin thickening**
- **Right breast mammogram showed skin thickening and right axillary adenopathy**
- **A 1-week course of antibiotics was recommended, after which the erythema improved**
- **She received an additional 2 weeks of antibiotics after which the erythema was entirely resolved but the induration remained present**

History

- **In-office ultrasound demonstrated persistent mixed echogenicity at the 9 o'clock position**
- **She was told to follow-up in 1 month, at which point given the lack of resolution of ultrasound changes, a skin punch biopsy and core needle biopsy were performed**



Physical examination approximately 1 month following completion of final course of antibiotics

History

PMH/PSH: Negative

Reproductive History: Menarche age 10

G2P2 (First birth: 23 years)

LMP: 1 year prior

No hormone exposure

Medications: None

Allergies: Keflex, Sulfa

**Social History: Works as a hairdresser. Never smoker.
2-3 drinks/week.**

ROS: +Fullness of right breast. No headaches, changes in vision, SOB, cough, nausea, vomiting, diarrhea or bone pain.

History

Family History: No Ashkenazi Jewish ancestry.

- **Mother – Lung cancer (Age 71).**
- **Maternal Aunt – Breast cancer (Age 70s).**
- **Father – Melanoma (Age 60).**
- **Paternal Aunt – Breast cancer (Age 44).**
- **Paternal First Cousin – Breast cancer (Age 30).**
- **Second Paternal First Cousin – Breast cancer (38).**
- **Third Paternal First Cousin – Breast cancer (age 33).**
- **Fourth Paternal First Cousin – Lung cancer (Age 53).**

Imaging: Mammography



Skin thickening



Enlarged axillary lymph nodes

Differential Diagnosis

- **Inflammatory breast cancer**
- **Infectious Mastitis**
- **Breast abscess**
- **Ductal ectasia**
- **Locally advanced breast cancer**
- **Lymphoma of the breast**
- **Leukemia of the breast**

Pathology

- **Core Needle Biopsy: Invasive ductal carcinoma, poorly differentiated (modified Bloom-Richardson grade III/III), measuring at least 0.6 cm. No lymphovascular invasion is identified.**
 - **Estrogen receptor: Positive (>95%, strong)**
 - **Progesterone receptor: Positive (5%, moderate to strong)**
 - **HER2/NEU: Negative (1+)**
- **Skin, Punch Biopsy: High-grade carcinoma present within dermal lymphatics**

Definition of IBC

- **International Expert Panel Diagnostic Features:**
 1. **Rapid onset of breast erythema, edema and/or peau d'orange and/or warm breast**
 2. **Duration of history of no more than 6 months**
 3. **Erythema occupying at least one-third of the breast**
 4. **Pathologic confirmation of invasive carcinoma**
- **Derma lymphatic invasion is neither required nor sufficient by itself for a diagnosis of IBC**

Clinical Presentation

- **Ipsilateral axillary disease is common (50-90%).¹⁻³**
- **30% Stage IV at initial presentation.**
- **Contralateral axillary nodal disease in 38/177 (22%) patients in MDACC study; only site of M1 disease in 47% of them.⁴**
 - **For those treated with chemotherapy, surgery (bilateral mastectomy and ALND), and RT, 4/13 durable NED**

1. Rueth, *J Clin Oncol*. 2014;32:2018-24.

2. Tsai, *Am J Clin Oncol*. 2013.

3. Rehman, *Int J Radiat Oncol Biol Phys*. 2012;84:619-24.

4. Woodward, *Breast Cancer Manage*. 2014; 3:43-52.

Characteristics of IBC

- **1-5% of all breast cancers in the United States**
- **Younger age at diagnosis and increased likelihood of being estrogen receptor negative compared to locally-advanced breast cancer**
- **Less favorable outcome compared to locally-advanced or early-stage breast cancer**
 - **LRR: 10-27% versus 7-10%**
 - **OS5: 40-60% versus 40-86%**
- **Hypothesis that IBC is not a unique biologic entity but rather is a subset of the non-IBC tumors**

Initial Evaluation

- **Multi-disciplinary evaluation**
- **Biopsy for confirmation of diagnosis and receptor studies**
- **Bilateral diagnostic mammograms (ultrasound if necessary for biopsy)**
- **CT C/A/P and bone scan *or* PET-CT**

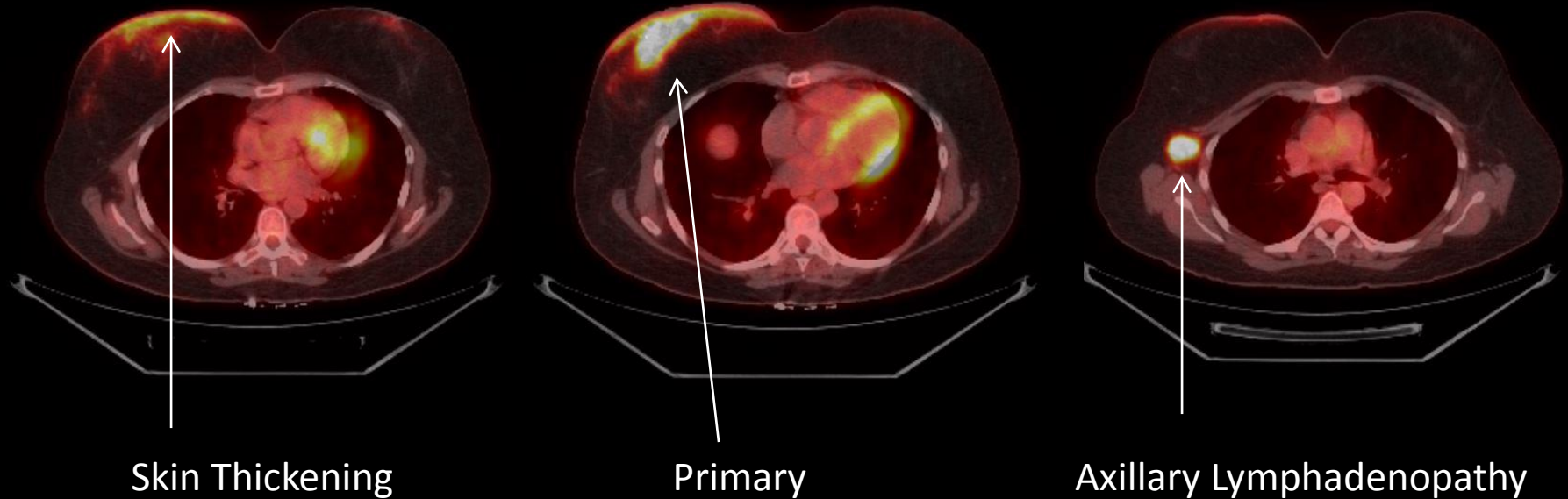
Recommended Treatment

- **Pre-operative chemotherapy including anthracycline and taxane; HER2-directed therapy if HER2-positive**
- **If adequate response, then total mastectomy and Level I/II axillary dissection, then radiation therapy, including comprehensive regional nodal radiotherapy**
- **If inadequate response, consider additional chemotherapy and/or pre-op radiation therapy**

Case Management

- **PET-CT performed: Showed skin thickening of the right breast, multiple FDG-avid right axillary lymph nodes. No evidence of distant disease.**
- **Diagnosis: T4dN1M0 (Stage IIIB)
ER+/PR+/HER2- Inflammatory Breast Cancer**
- **Genetic counseling and testing revealed a BRCA2 mutation**

Imaging: PET-CT



No evidence of FDG-avid distant metastatic disease.

Case Management

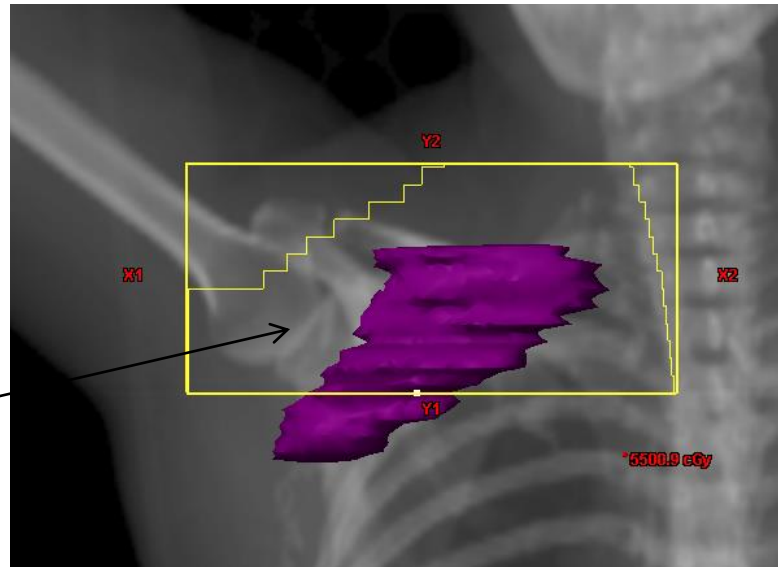
- **The patient completed four cycles of dose-dense Adriamycin, Cytosin followed by four cycles of dose-dense Taxol**
- **She went on to modified radical mastectomy with pathology as follows:**
 - **Residual invasive ductal carcinoma, spanning a 1.4 x 1.0 cm zone of fibrosis**
 - **Lymphatic invasion focally present**
 - **Deep margin free of invasive carcinoma**
 - **Metastatic ductal carcinoma in 7 of 20 lymph nodes, largest foci 11.0 mm, without extranodal extension**
 - **Miller-Payne response grade 3; residual cancer burden = 3.434 (RCB class III)**

Radiation Therapy

- **Adjuvant radiotherapy was recommended**
 - **CT Sim: Supine, breast board**
 - **Wires placed at midline, mastectomy scar**
 - **Radiation delivered to the chest wall, supraclavicular and axillary lymph nodes**
 - **50 Gy in 25 fractions to chest wall, supraclavicular and axillary lymph nodes**
 - **1.0 cm bolus every other day during CW+regional lymph nodes, including to inferior anterior supraclavicular field**
 - **10 Gy chest wall boost (Total Dose: 60 Gy)**
 - **1.0 cm daily bolus during CW boost**
 - **Full Axilla (including levels I-III) targeted 2/2 bulk of axillary disease and incomplete response to systemic therapy**
 - **Adequate margin on medial disease pre-chemotherapy required some extension across midline**

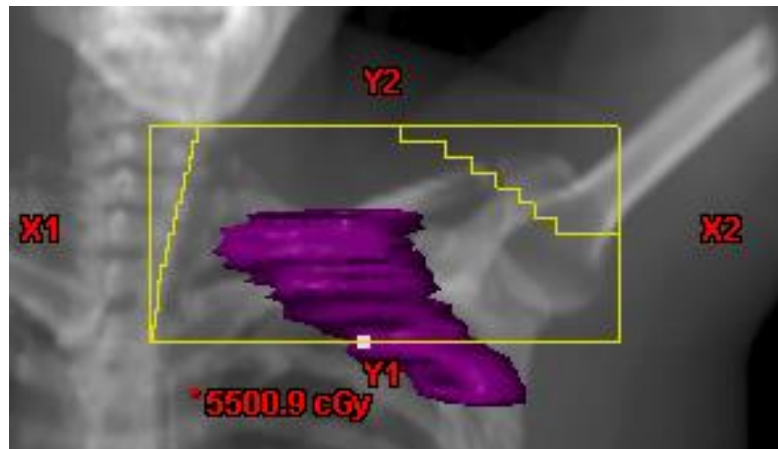
Radiation Therapy: Supraclavicular and Full Axilla

AP



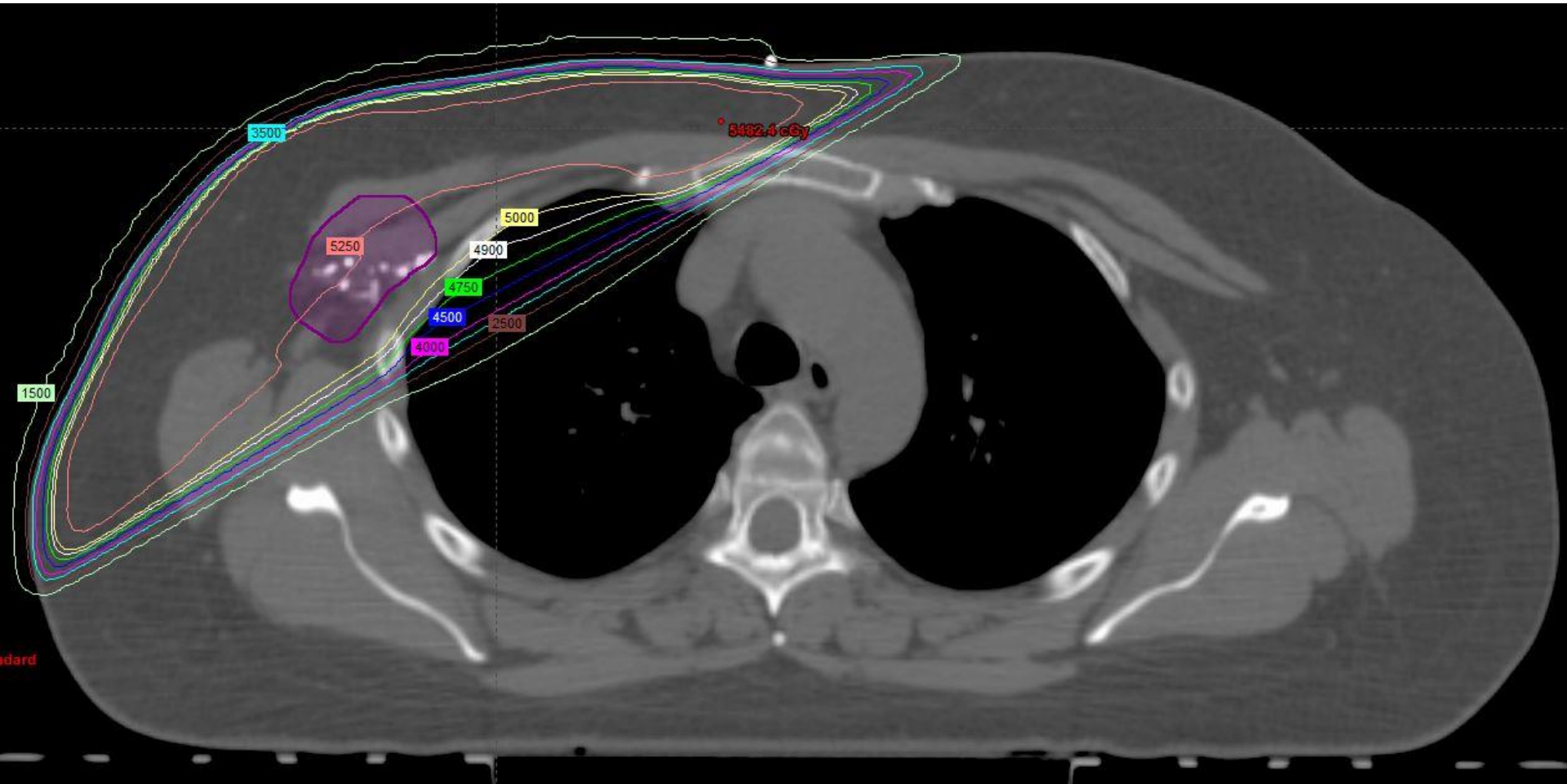
Levels I-III and supraclavicular lymph nodes contoured based on RTOG Atlas

PA

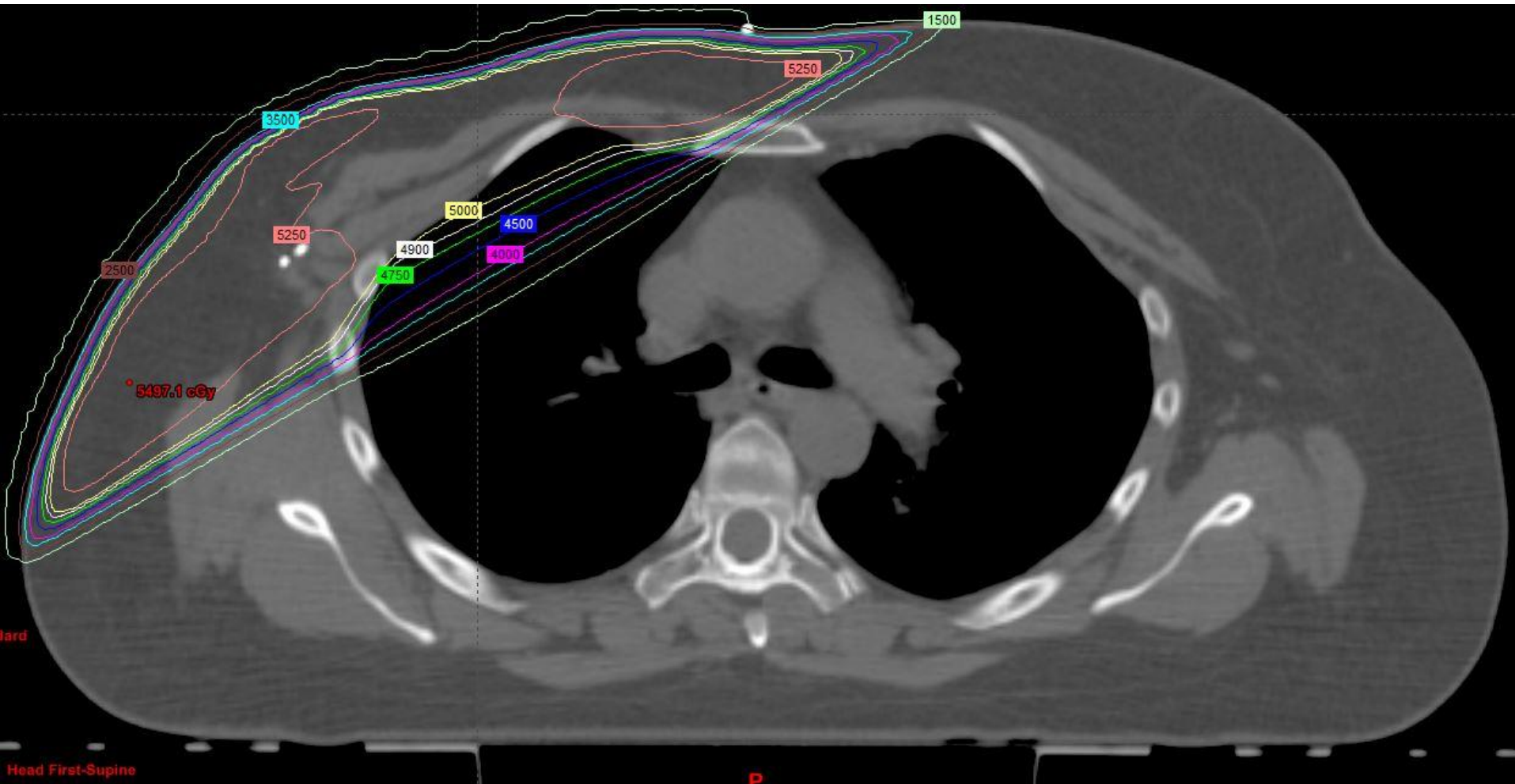


Teaching Point:
Lateral border of the AP and PA fields set to include adequate margin on levels I-III lymph nodes when treating full axilla

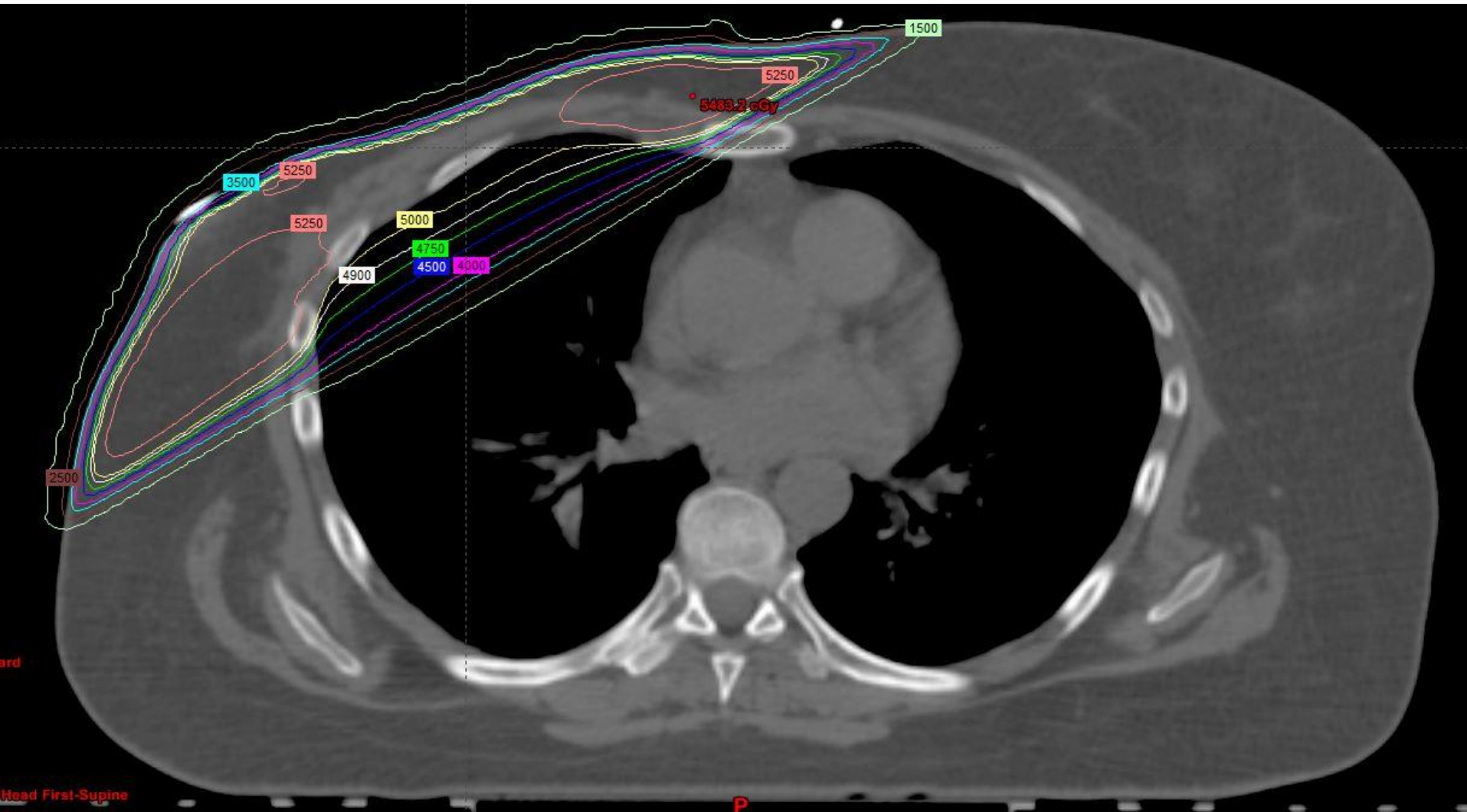
Radiation Therapy: CW Tangents



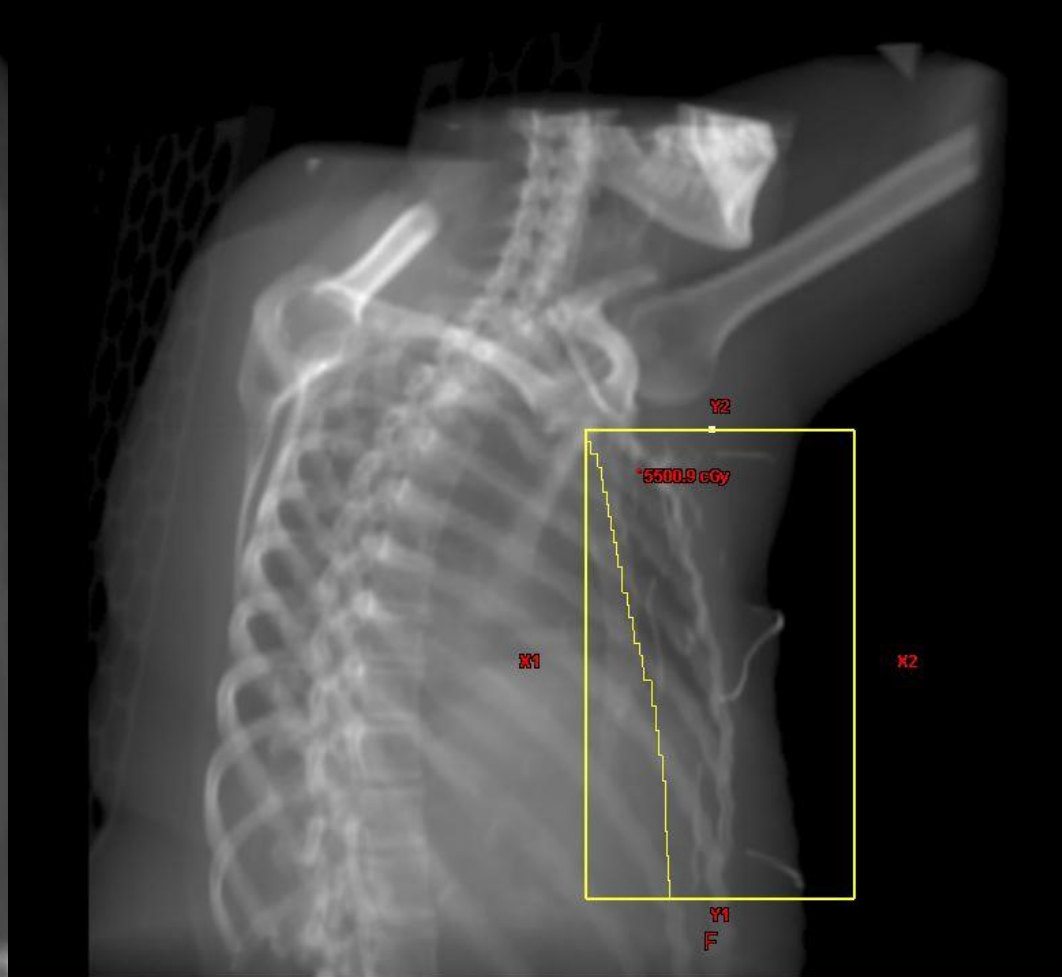
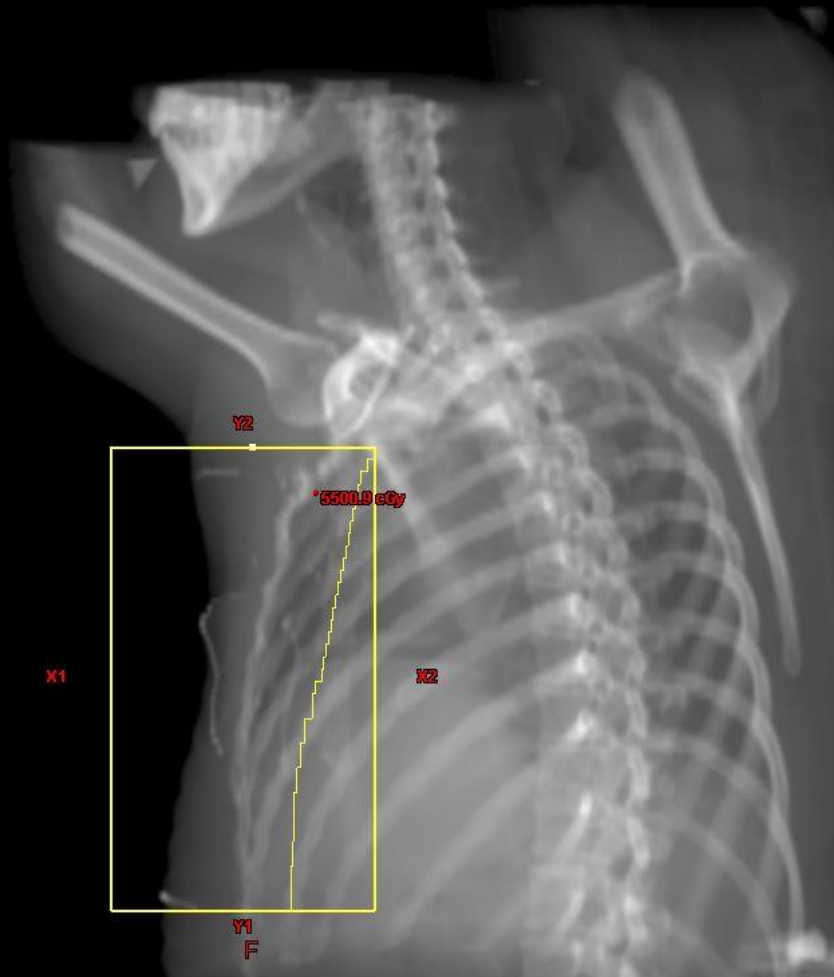
Radiation Therapy: CW Tangents



Radiation Therapy: CW Tangents



Radiation Therapy: CW Tangents



Radiation Therapy: DVH

Plan Sum - Dose Volume Histogram



| Structure | Structure Status | Coverage [%/ %] | Volume | Min Dose | Max Dose | Mean Dose | Modal Dose | Median Dose | Std Dev |
|------------|------------------|-----------------|--------------------------|------------|------------|------------|------------|-------------|------------|
| Cord | Approved | 100.0 / 100.0 | 24.3 [cm ³] | 73.6 cGy | 1420.9 cGy | 212.8 cGy | 183.4 cGy | 189.2 cGy | 109.3 cGy |
| nodes | Approved | 100.0 / 100.1 | 83.0 [cm ³] | 4843.4 cGy | 5443.1 cGy | 5179.0 cGy | 5242.6 cGy | 5190.5 cGy | 95.4 cGy |
| Heart | Approved | 100.0 / 100.0 | 394.7 [cm ³] | 3.9 cGy | 800.8 cGy | 89.2 cGy | 32.5 cGy | 67.7 cGy | 75.6 cGy |
| right_lung | Approved | 100.0 / 100.0 | 927.4 [cm ³] | 31.5 cGy | 5215.9 cGy | 1621.0 cGy | 106.7 cGy | 600.7 cGy | 1808.2 cGy |

Radiation Therapy Approaches

- Dose acceleration, bolus, and/or total dose escalation have been utilized in an attempt to improve local control
- Selected Approaches:
 - MD Anderson: If age <45, positive margins, or poor chemo response → 66 Gy BID (1.5 Gy/fx). Otherwise 60-66 Gy (2Gy/fx) PRN Bolus.
 - Cleveland Clinic and University of Florida retrospectively showed better control with doses (CW + boost) higher than 60 Gy (1.8-2Gy/fx)
 - MSKCC: 50.4 Gy (1.8 Gy/fx) and daily bolus (0.5-1.0 cm)
 - DFCI: 50 Gy to chest wall with every other day bolus + 10 Gy to scar with daily bolus

Radiation Therapy Approaches

- **International Expert Panel:**
 - **No “standard” dose**
 - **However, consider dose escalation to 66 Gy in:**
 - **Women age <45**
 - **Close or positive surgical margins**
 - **4 or more positive LN following pre-op chemo**
 - **Poor response to pre-op systemic treatment**

Teaching Points

- **Data on dose-escalation are variable and unlikely to be definitively proven by a randomized trial given rarity of the disease**
- **Risk of distant disease in this population is very high so escalation of local therapy needs to be considered in this context**
- **At our institution, coverage of the full axilla and internal mammary nodes determined on a case-by-case basis based on extent of disease and individual anatomy**

References

- Dawood, *Ann Oncol.* 2011;22:515-23.
- Robertson, *SpringerPlus.* 2013; 2:497.
- Rueth, *J Clin Oncol.* 2014;32:2018-24.
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