

Ductal Carcinoma In-Situ

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Case Presentation

- 53-year-old female underwent routine bilateral screening mammogram
 - Findings: architectural distortion and coarse, clumped calcifications in the retroareolar left breast. Right breast normal.
- PMH
 - Otherwise healthy

Case Presentation

- OB/Gyn History
 - G0P0
 - Age at menarche: 13
 - Menopause at 46
 - No history of oral contraceptives
 - No history of hormone replacement therapy
- Family History
 - Mother with ovarian cancer at 79
 - No family history of breast cancer
- Social History
 - Non-smoker
 - 2-3 alcoholic drinks/week

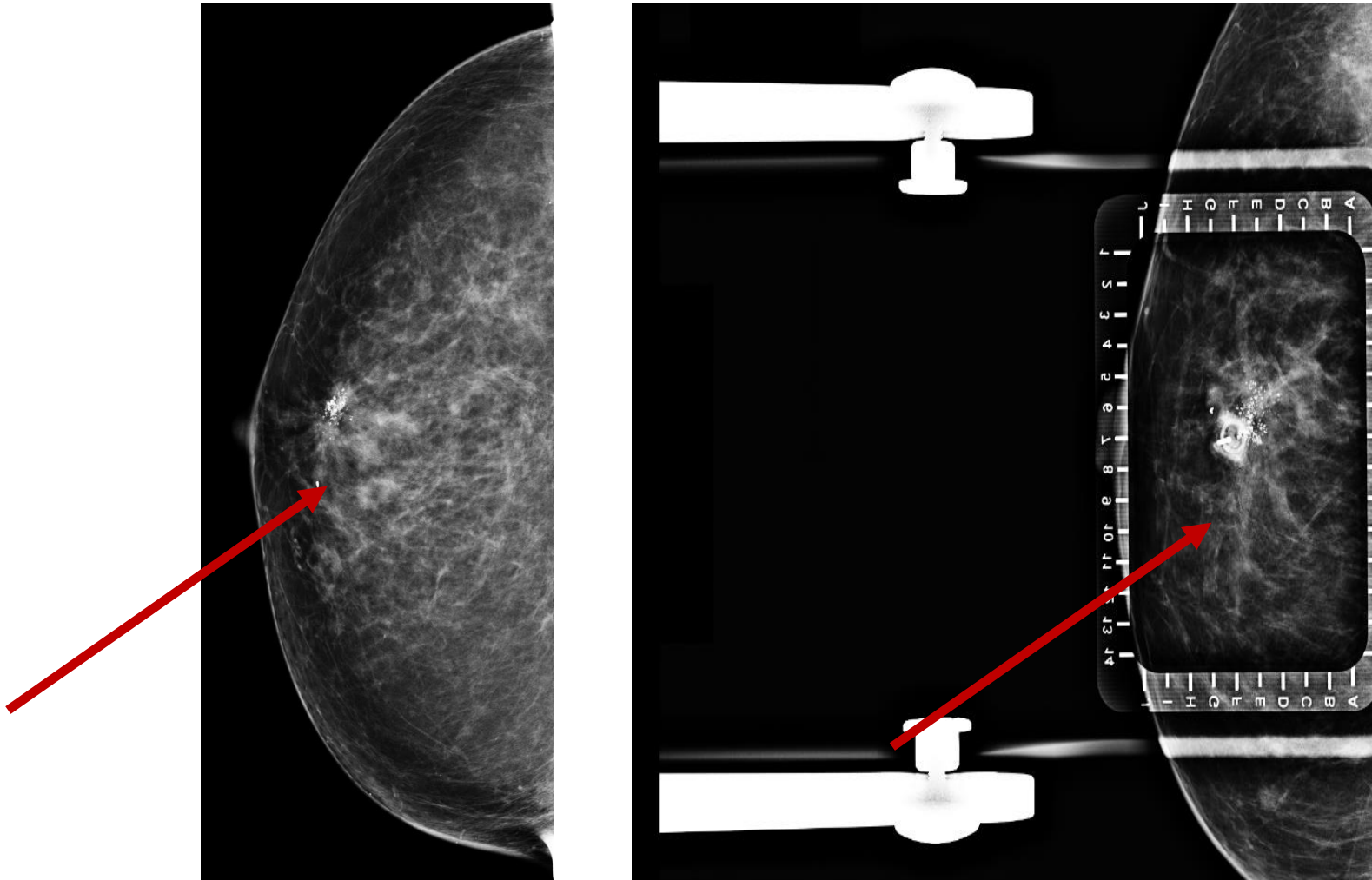
Physical Exam

- General: Well appearing Caucasian female in no acute distress
- HEENT: PERRLA, EOMI. Sclerae anicteric. No thyromegaly
- Lymphatic: No palpable cervical, supraclavicular, infraclavicular or axillary lymphadenopathy
- CV: Regular rate and rhythm. No murmurs, rubs or gallops
- Lungs: Clear to auscultation. No wheezes, rhonchi or rales
- Abdomen: Soft, non-tender and non-distended
- Breast: Inspection and palpation of the bilateral breasts demonstrates no erythema, edema, peau d'orange, nipple inversion, nipple discharge, or palpable masses. No axillary or supraclavicular lymphadenopathy.
- Extremities: No clubbing, edema or cyanosis
- Neurological Exam: CN II-XII grossly intact. Motor strength 5/5 in the upper and lower extremities. Sensation grossly intact. No focal neurologic deficits.

Workup

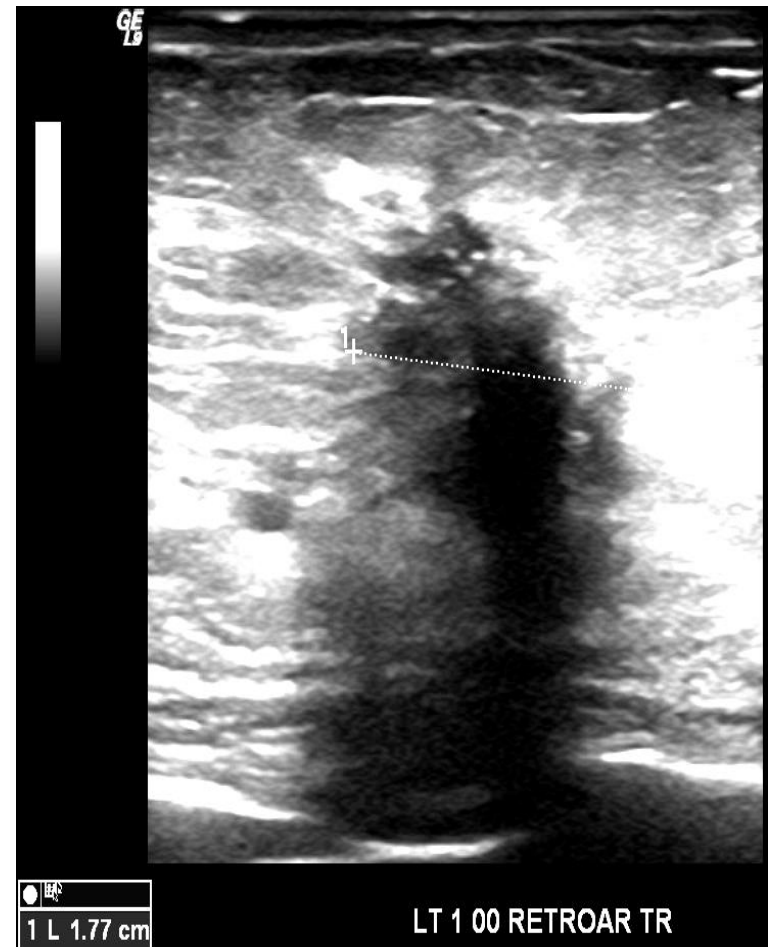
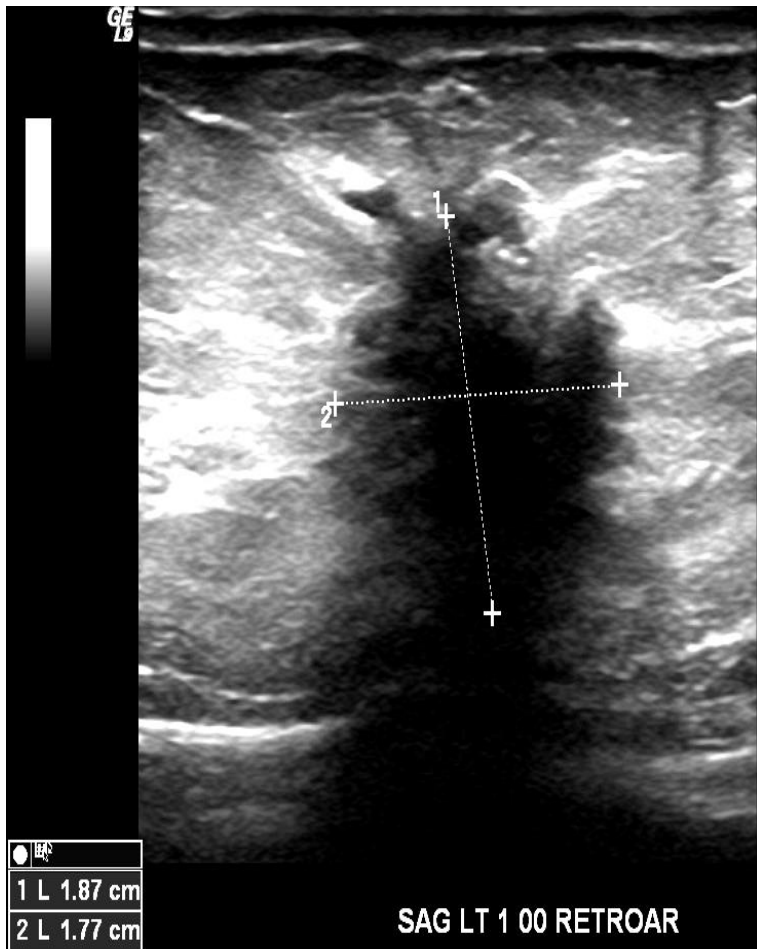
- Diagnostic bilateral mammogram
 - Magnification views of left breast show clustered pleomorphic calcification in the retroareolar region
- Bilateral breast ultrasound
 - 1.9 x 1.8 x 1.8 cm irregular, hypoechoic mass in the left retroareolar region at the 1:00 position

Left Breast Mammogram



Magnification views show clustered pleomorphic calcification in the retroareolar region

Left Breast Ultrasound



1.9 x 1.8 x 1.8 cm irregular, hypoechoic mass in the left retroareolar region at the 1:00 position

Workup

- Core needle biopsy
 - Ductal carcinoma in situ, solid type
 - ER- 95% positive; PR- 85% positive; HER-2 not obtained
 - Intermediate nuclear grade

Overview of DCIS

- Noninvasive malignant epithelial cell proliferation limited to the ductal system
 - No basement membrane invasion
 - May be limited to few or several duct tubules
- With the introduction of routine screening mammography it now constitutes 15-20% of all breast cancers
 - Represented only 1-5% of breast cancers in the pre-mammography era (Parker et al)
- 30% of DCIS cases may be multicentric (Fonseca et al)
- Classification according to:
 - Architecture: solid, comedo, cribriform, papillary, and micropapillary
 - Grade: high, intermediate, and low (grades 1-3)
 - Comedo Necrosis: Yes or No

Treatment Options

DCIS (Tis N0 M0)

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graph TD; A[DCIS (Tis N0 M0)] --> B[Lumpectomy]; A --> C[Total Mastectomy +/- SLN biopsy]; B --> D["+/- Radiotherapy *"]; D --- E["RT reduces risk of local recurrence. Older patients with small, low-grade tumors excised with widely negative margins benefit less from radiation. (Silverstein et al)"]; C --- F["Consider for diffuse malignant microcalcifications, multicentric disease, persistently positive margins or patient preference"];
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Lumpectomy



+/- Radiotherapy *

*RT reduces risk of local recurrence.
Older patients with small, low-grade
tumors excised with widely negative
margins benefit less from radiation.
(Silverstein et al)*

Total Mastectomy
+/- SLN biopsy

*Consider for diffuse
malignant
microcalcifications,
multicentric disease,
persistently positive margins
or patient preference*

* Lumpectomy + RT = Breast Conserving Therapy (BCT)

Role of Radiotherapy after BCS

- No randomized trials compare BCT to mastectomy for DCIS, but comparisons of BCT to historic mastectomy controls suggest no OS difference
- 4 published randomized trials demonstrate benefit in local control with addition of whole breast RT compared to lumpectomy alone in DCIS:
 - NSABP B-17
 - EORTC 10853
 - UK/Australia/New Zealand cooperative trial (UK/ANZ)
 - Swedish Trial

Role of Radiotherapy after BCS

- Adjuvant RT after lumpectomy reduces the risk of ipsilateral breast tumor recurrence at 15 years by 52% versus lumpectomy alone (Wapnir et al)
 - Lumpectomy alone: 19.4%
 - Lumpectomy + RT: 8.9% (B-17)
 - Lumpectomy + RT: 10.0% (B-24)
 - Lumpectomy + RT + Tamoxifen: 8.5% (B-24)
- Approximately half of recurrences are invasive breast cancer and half are DCIS

Role of Tamoxifen after Lumpectomy

- NSABP B-24: The addition of tamoxifen to RT reduces overall cancer events at 5 years (Fisher et al. Lancet 1999)
 - Decreased breast cancer events from 13.4% to 8.2%
 - Ipsilateral 9.5% vs. 6.0%
 - Contralateral 3.4 vs. 2.0%
 - No difference in regional or distant mets
- In ER positive as opposed to ER negative tumors, the benefit of Tamoxifen is greater (Allred et al)
 - ER positive → 59% reduction of all breast cancer events
 - ER-negative → no significant benefit was observed

Margin Status in DCIS

- The definition of a negative margin is controversial
- Margins of 10 mm are accepted as negative
- Margins <1 mm are considered inadequate and re-excision should be performed
- Close margins (<1 mm) at the chest wall or skin do not mandate surgical re-excision, but may warrant higher doses of radiation (i.e. a boost)

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Case Treatment

- Lumpectomy
 - Pathology showed a 2.0 cm focus of DCIS, solid type, nuclear grade 2
 - All margins were negative with the closest margin being 2.2 mm superiorly.
 - ER (95%), PR (85%)
- Post-lumpectomy mammogram showed no residual calcifications
- Whole breast radiation therapy was delivered in the supine position (typically delivered 4-8 weeks after surgery)
 - Prescribed dose was 5000 cGy in 25 fractions to the whole breast using IMRT and 6 MV photons
 - Tumor bed received an additional 1000 cGy in 5 fractions using mini-tangents and 6 MV photons
- Systemic therapy
 - Aromatase inhibitor was started after completion of radiation

Boost for DCIS

- No prospective randomized trials examining a boost for DCIS
 - Institutional preference
 - Retrospective, institutional experiences demonstrate varied outcomes
- EORTC 22881/10882 demonstrated reduction in local recurrence in patients with invasive breast cancer receiving a 16 Gy tumor cavity boost after BCS
 - Greatest benefit in women < 50 years old, however all patients benefitted
 - Data often extrapolated to DCIS
- DCIS Collaborative Group Study
 - One of the largest, landmark trials showing a reduction in local recurrence with radiation for DCIS
 - 72% of patients on this trial received a boost

Treatment Planning

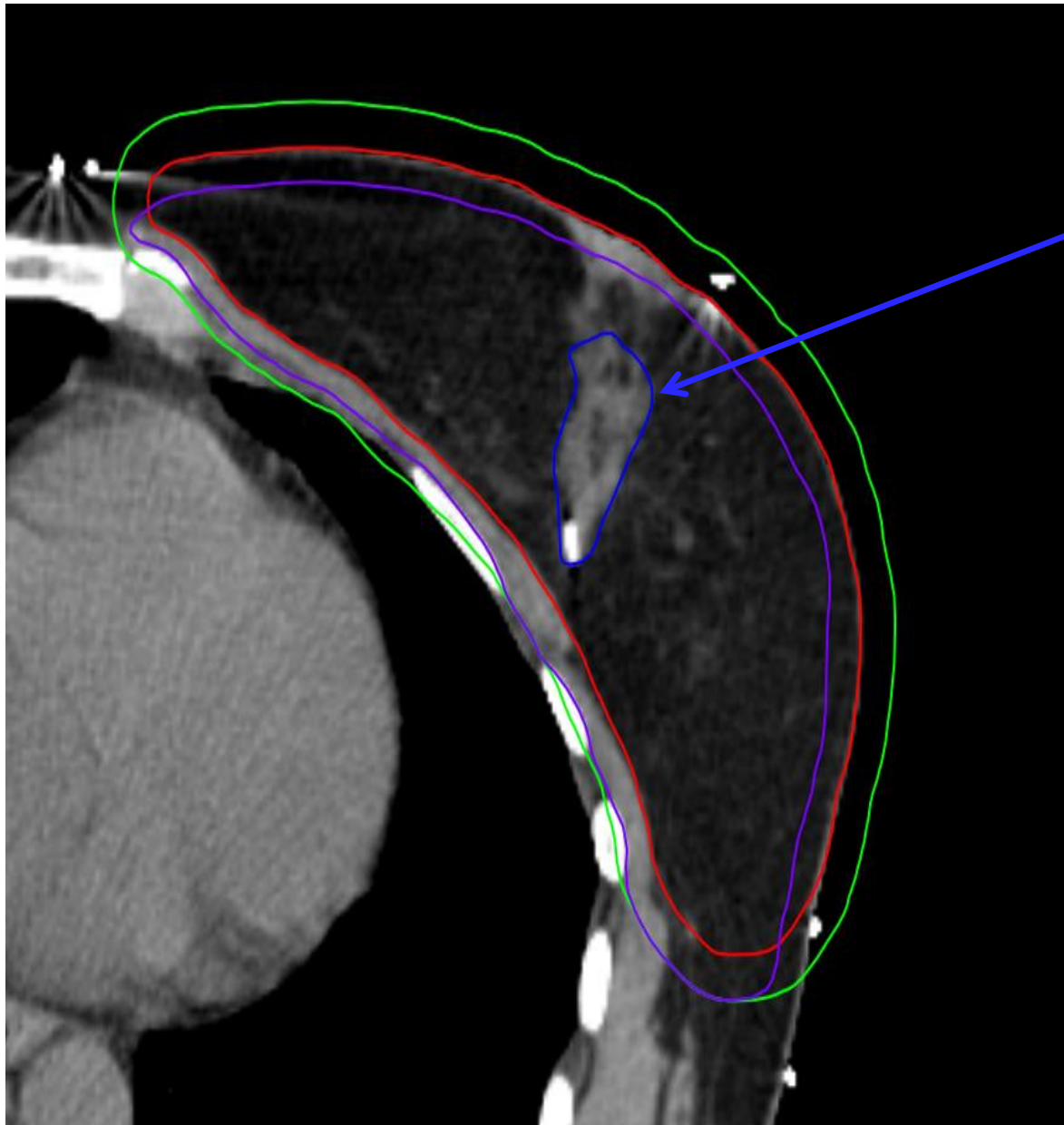
- 2D Treatment Planning
 - Uses plain x-rays for generating the plan
 - Assessment of treatment plan done by evaluating dose distribution at midplane of breast
 - Wedges used to compensate for differences in tissue thickness
 - Significant dose heterogeneity on off axis regions (IM fold, axilla)
- 3D/IMRT Treatment Planning
 - Uses CT scan for generating the plan
 - allows for better evaluation of target coverage, hot spots and dose to normal tissues
 - IMRT improves dose homogeneity
 - decreases acute and chronic skin toxicity
 - Improves dose conformality
 - better sparing of heart for left-sided cancers and lung
 - Many different techniques utilized
 - field in field AKA fluence planning AKA forward planned IMRT
 - inverse planning AKA traditional IMRT

3D/IMRT

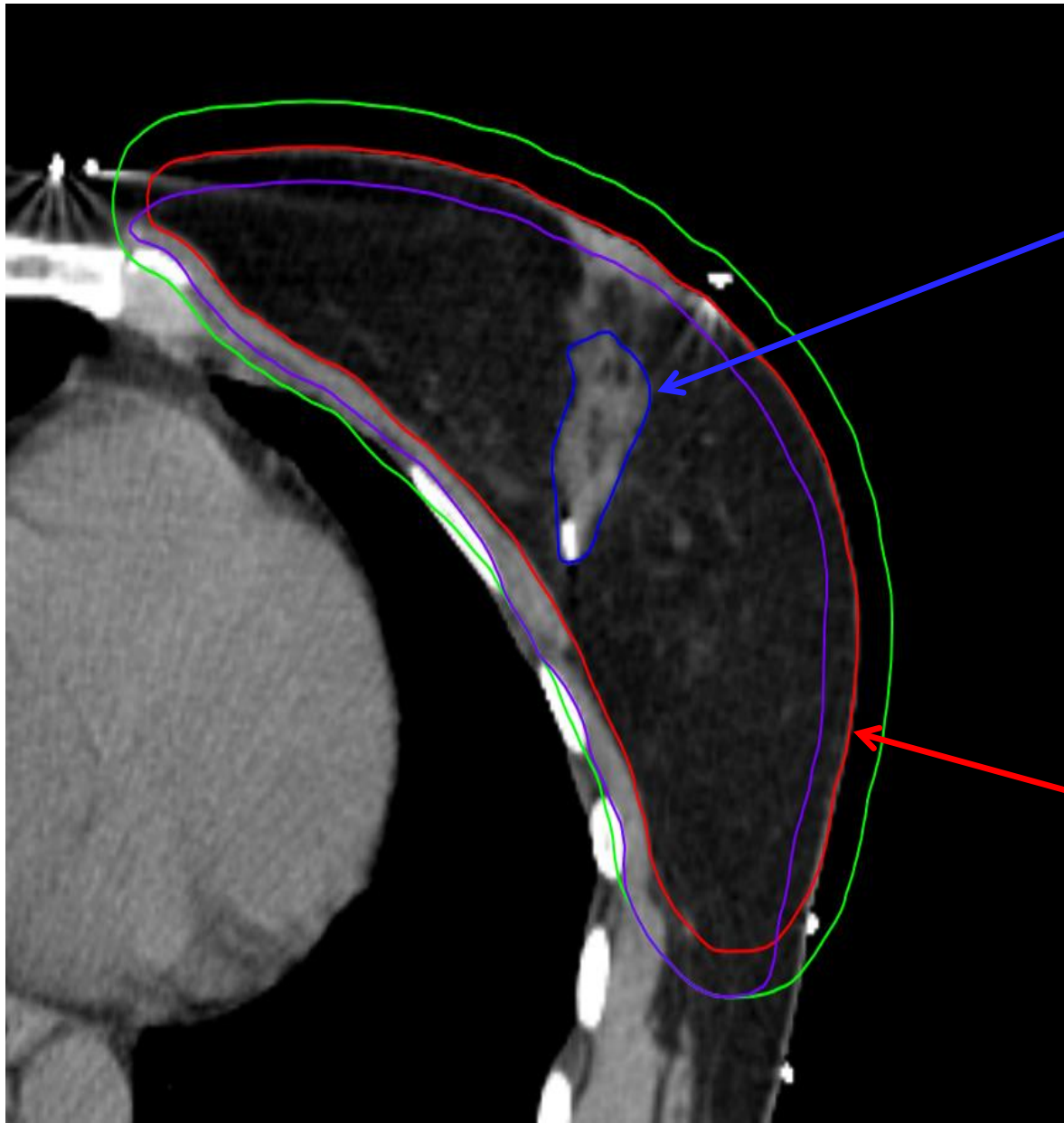
- Field in Field (Forward Planned)
 - Open medial and lateral tangents + segmental fields added manually to attenuate beam in higher dose areas
 - MLCs used to improve homogeneity and to shield critical structures
- IMRT (Inverse Planned)
 - Computerized algorithm used to reduce hot spots
 - Multiple weighted segments and beam angles can be used to achieve optimal conformality
 - May result in more low dose spread
 - Minimized by restricting beam angles to normal tangential arrangement

Treatment Planning

- CT Simulation
 - Supine with arms up on a 15-20 degree breast board
 - Goal is to bring sternum parallel to the table
 - Wire palpable breast tissue, clinical breast borders and lumpectomy incision
 - Medial border → mid sternum
 - Lateral border → 2 cm lateral to palpable breast tissue (mid axillary line)
 - Inferior border → 2 cm below the inframammary fold
 - Superior border → head of the clavicle or 2nd intercostal space



GTV
Surgical cavity;
includes seroma
and surgical clips
when present.



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Surgical cavity;
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CTV:

*Posteriorly -
Excludes pec
major/minor
Anterior - Skin
Cranial/Caudal
- Per clinical
breast borders
Medial -
Sternal/rib
junction
Lateral - Mid
axilla per
clinical
reference*

PTV

Breast CTV + 7 mm expansion (excluding heart and not crossing midline)



GTV

Surgical cavity; includes seroma and surgical clips when present.

CTV:

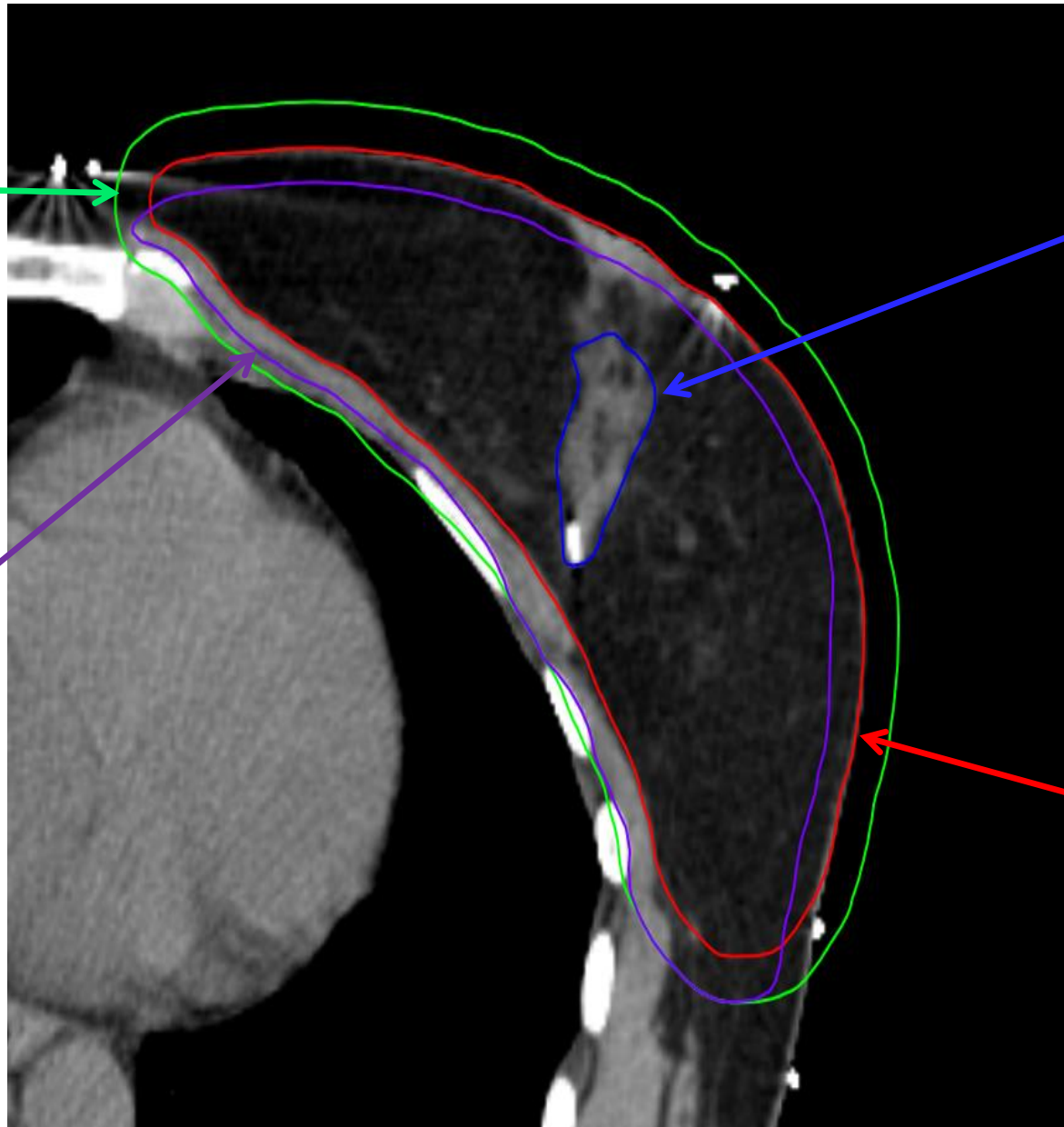
Posteriorly - Excludes pec major/minor
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PTV

Breast CTV + 7 mm expansion (excluding heart and not crossing midline)

PTV-EVAL

Excludes chest wall & pectoralis muscles; Extends to 5 mm from skin



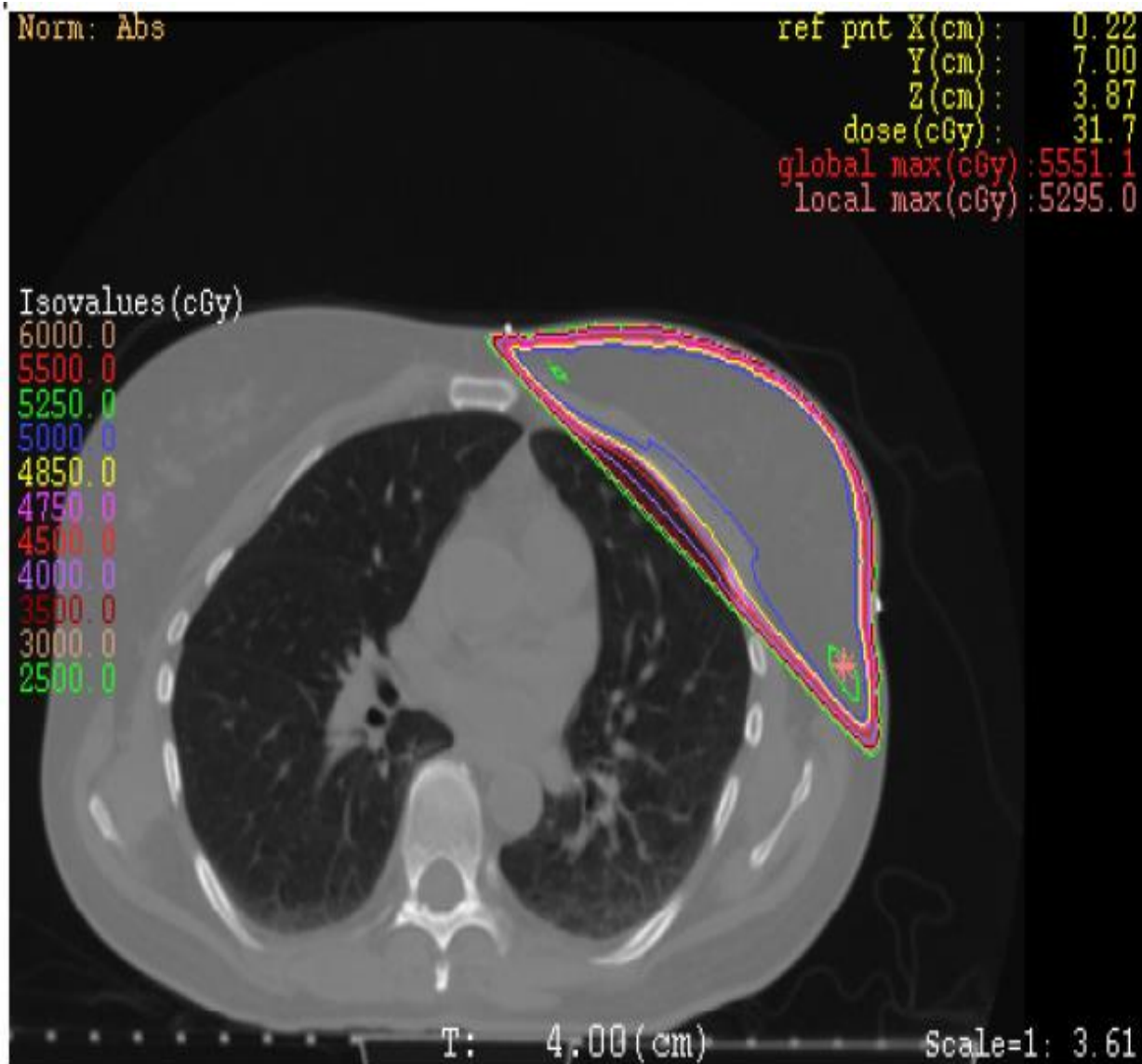
GTV

Surgical cavity; includes seroma and surgical clips when present.

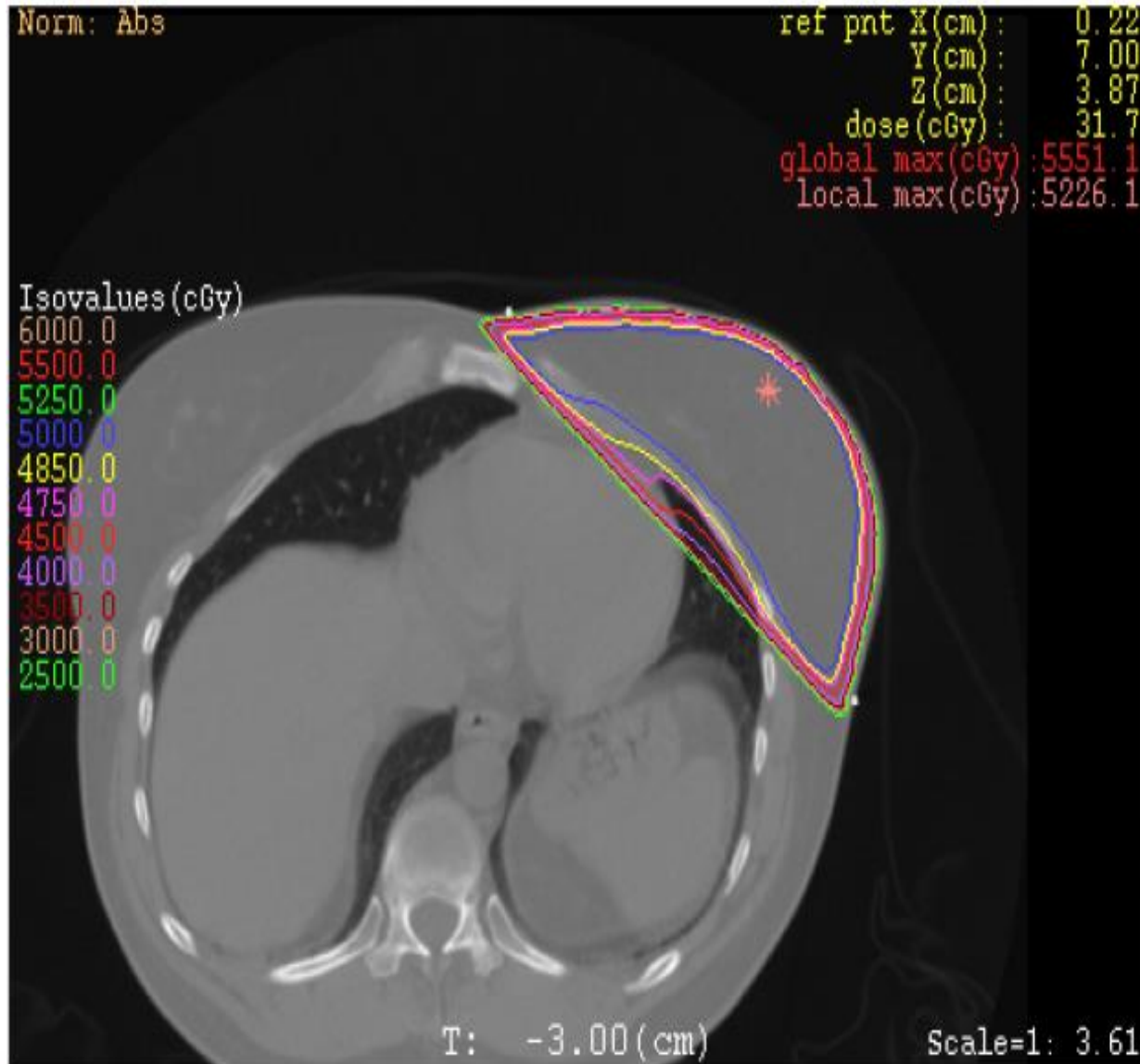
CTV:

Posteriorly - Excludes pec major/minor;
Anterior - Skin;
Cranial/Caudal - Per clinical breast borders;
Medial - Sternal/rib junction;
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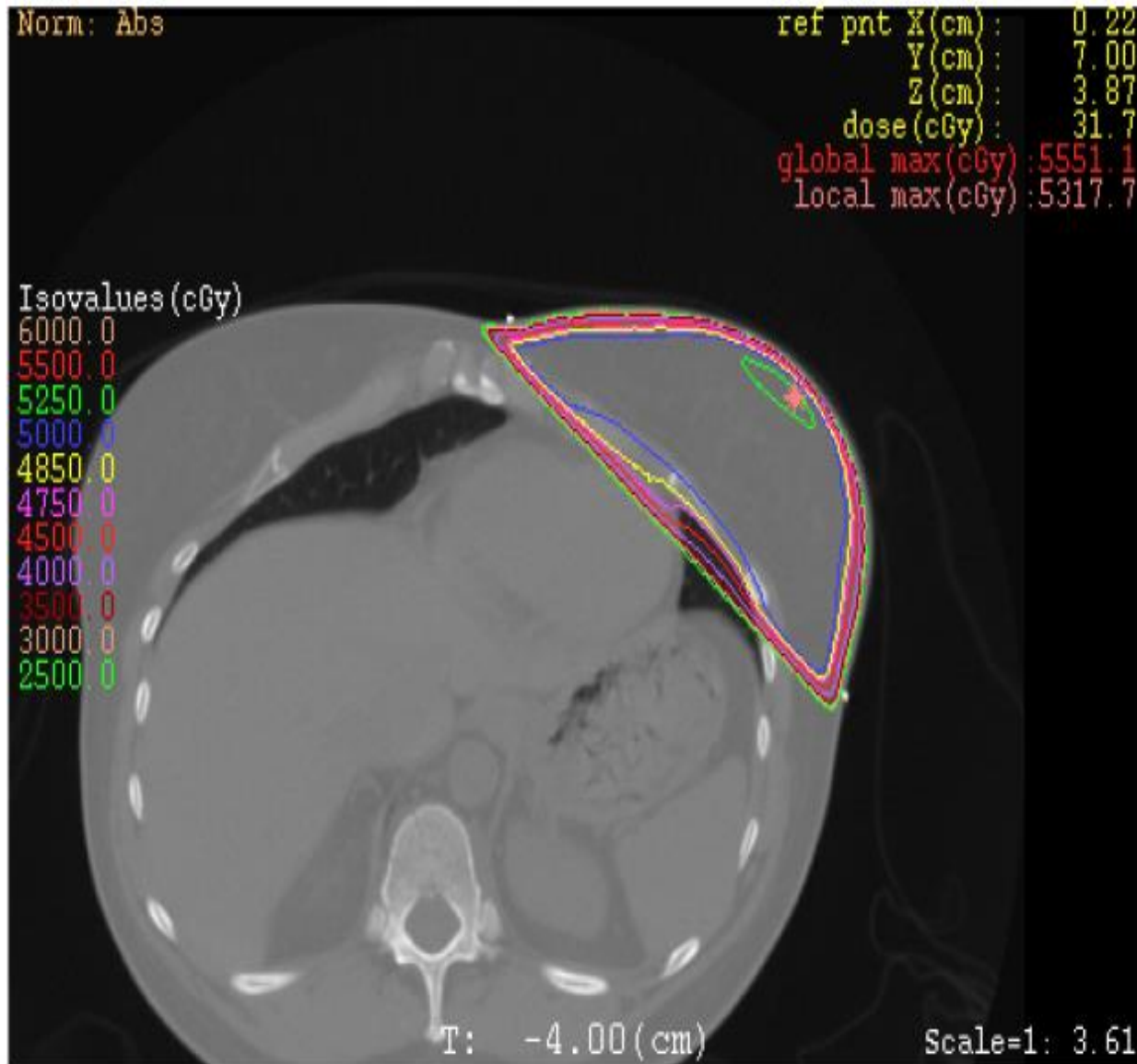
Isodose Distribution



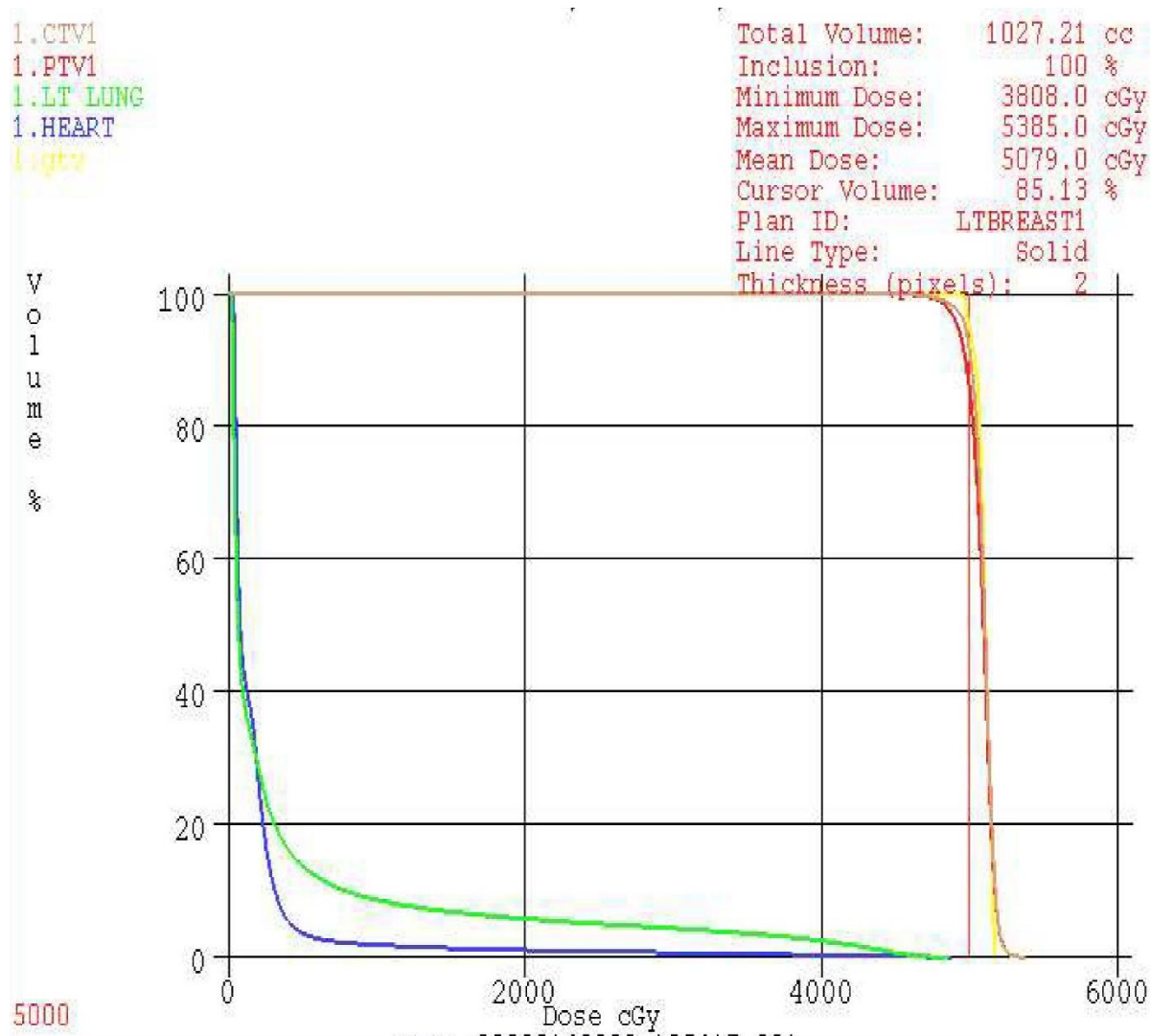
Isodose Distribution



Isodose Distribution



Dose Volume Histogram



Dose-Volume Constraints

(Per RTOG 1005)

Structure	Constraint	Percent
PTV	47.5 Gy	>95%
PTV Max Dose	57.5 Gy	
Heart	20 Gy	<5%
Ipsilateral Lung	20 Gy	<15%
Contralateral Lung	5 Gy	<10%
Contralateral Breast	Dmax 3.10 Gy 1.86 Gy	<5%
Thyroid	Max point dose does not exceed 2% of prescribed dose	

Surveillance and Follow-up

- History and physical exam every 6-12 months for 5 years, then annually
- Mammogram every year
 - 6-12 months post-radiation therapy if breast conserved

Teaching Points

- Multidisciplinary management is critical in the treatment of patients with DCIS
- The use of radiotherapy after lumpectomy in patients with DCIS decreases the risk of ipsilateral breast tumor recurrence in all patients but does not improve overall survival
 - This risk reduction becomes increasingly small in patients with favorable features such as age > 60, small, unifocal low grade tumors excised with widely negative margins (> 1 cm).
 - Thus, lumpectomy alone or lumpectomy followed by Tamoxifen can be considered in these patients
- The use of Tamoxifen in patients with ER+ DCIS reduces ipsilateral and contralateral breast tumor recurrence
- Patients undergoing mastectomy generally do not require adjuvant radiation

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