# ARRO*Case*

# Post-Mastectomy Radiation Therapy (PMRT)

**Michael Zhang, MD/PhD**

*Faculty Advisor*: Catherine Park, MD

University of California, San Francisco

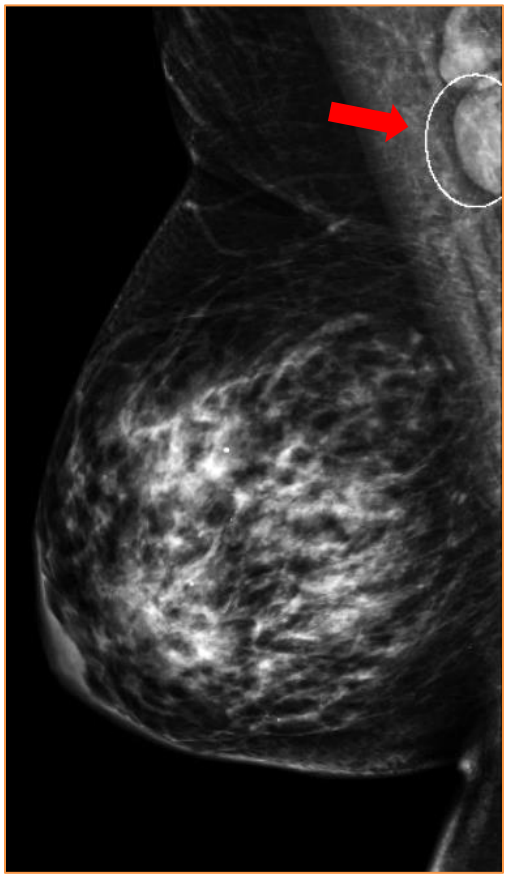
San Francisco, CA

# Learning Objectives

- Discuss a case of locally advanced right sided breast cancer indicated for PMRT
- Estimate the risk of recurrence without adjuvant radiation after neoadjuvant chemotherapy
- Discuss the indications and rationale for PMRT
- Review the rationale for inclusion of axillary, supraclavicular, and internal mammary fields
- Discuss the design and evaluation of 3D radiation fields for PMRT

# Case: Presentation

- 72 year old woman underwent a routine bilateral screening mammogram
  - Findings: Heterogeneously dense breasts. **Prominent lymph node in the right axilla at edge of image.**



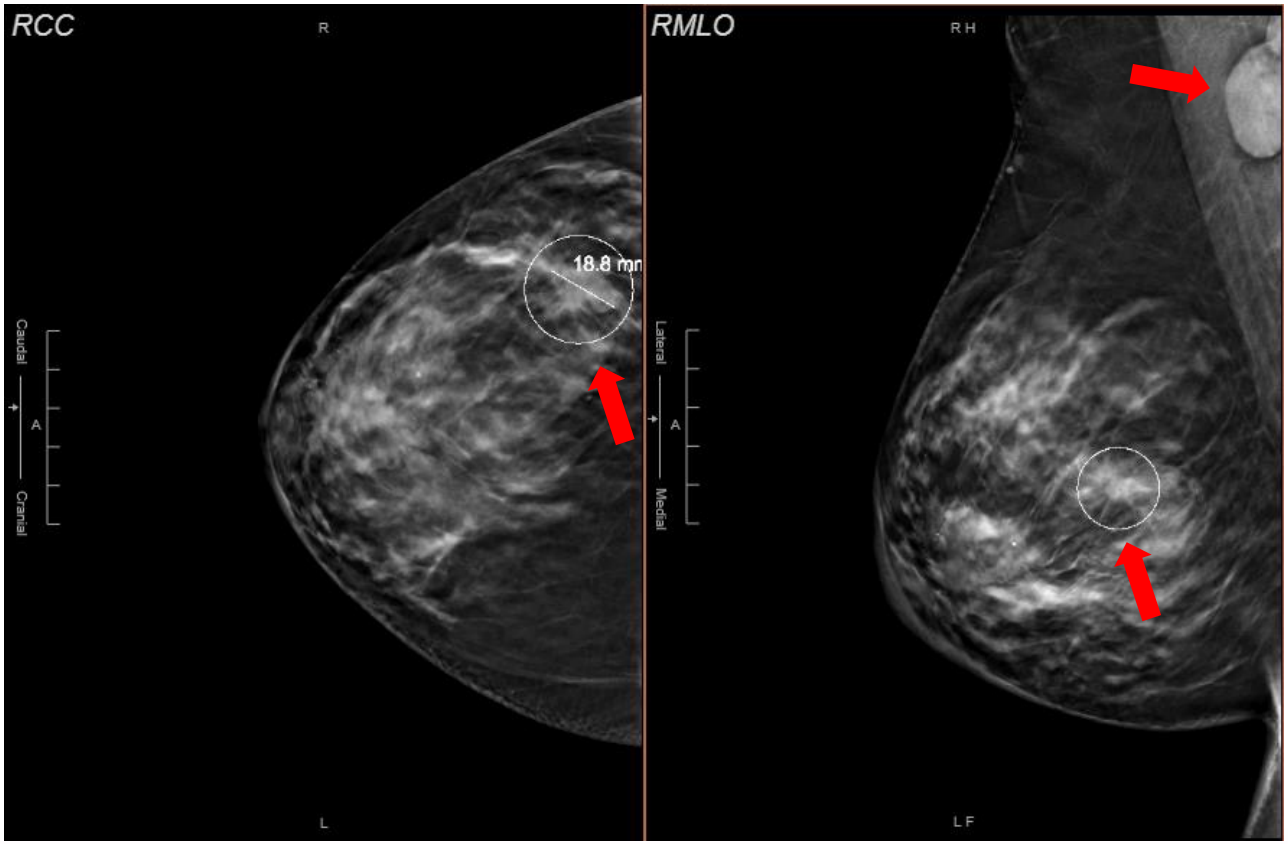
- PMH: diabetes (A1c 6.9, diet-controlled), multiple sclerosis, aortic stenosis, uterine fibroids, HLD
- PSH: L ovary removal for cystadenoma, myomectomy, lap chole, trigger finger release
- FH: Breast cancer (mother at 62y), Prostate cancer (maternal cousin), Diabetes (brother)
- Gyn: G0, menarche 12y, menopause 50s, no OCPs, Provera (2yrs for fibroids)
- Mammograms: Annual since age 54, no prior bx
- Genetics: BRCA 1/2 - negative for germline mutations

# Case: Physical Exam

- General: Alert, well-appearing, NAD
- HEENT: Sclerae anicteric, oropharynx clear
- Lymph nodes: **Mobile R axillary lymph nodes x 2 (2 cm and 1 cm).** No L axillary, cervical, or supraclavicular adenopathy
- Breasts: **R breast with 6 x 6 cm mobile mass in R central outer quadrant; additional 1 cm nodule at mammary edge at 9:00.** L breast without masses or lesions
- Chest: No increased WOB on room air. Lungs clear to auscultation bilaterally.
- Heart: Normal rate and rhythm
- Abdomen: Non-distended, non-tender
- Neurologic: AOx3, grossly non-focal
- Musculoskeletal: No spinal tenderness. No LE edema
- Skin: No rashes

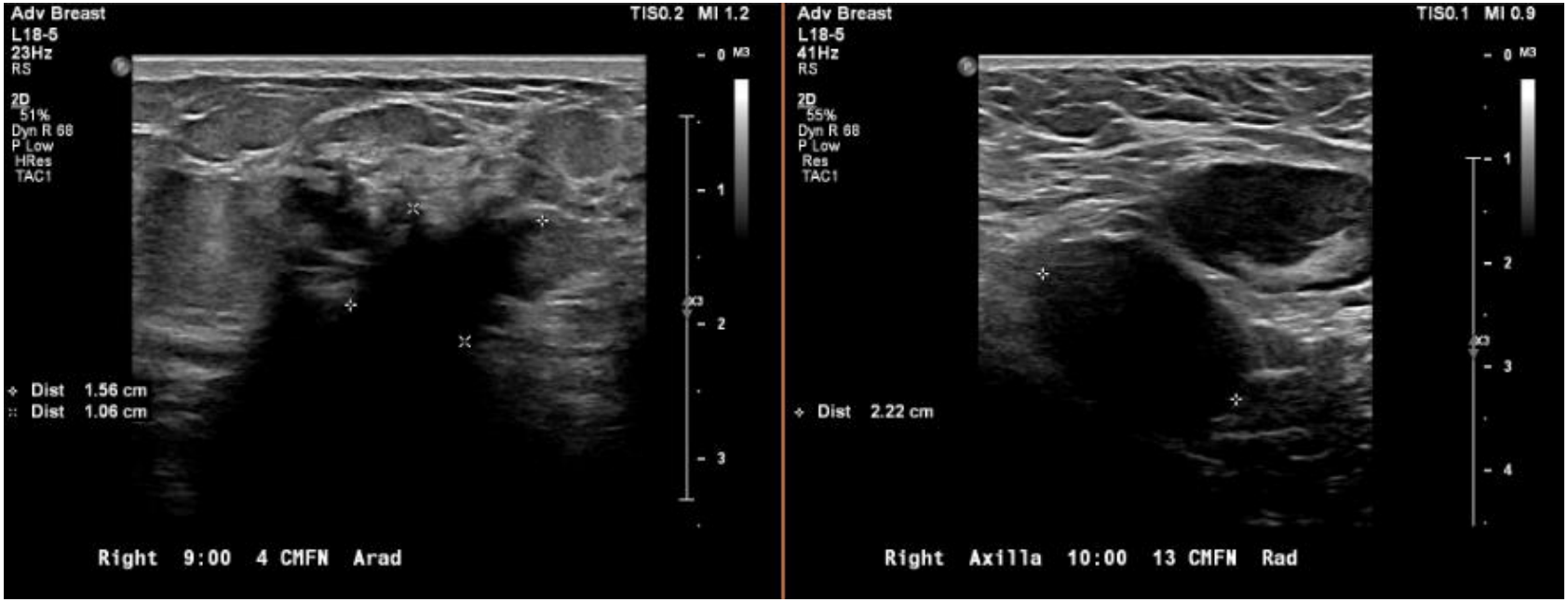
# Case: Work-up

- Diagnostic bilateral mammogram with Tomosynthesis
  - **Architectural distortion with associated 19 mm irregular mass in the outer central right breast, posterior depth. Enlarged lymph nodes in the right axilla.**
  - Left breast benign



# Case: Work-up

- Right breast ultrasound
  - Outer central right breast: Vague **16 x 11 x 13 mm hypoechoic, irregularly shaped, not parallel-oriented solid mass with indistinct margins and posterior shadowing** at 9:00, 4 cm from nipple (CFN).
  - Right axilla: multiple enlarged, morphologically abnormal appearing lymph nodes. The largest 22 x 18 x 21 mm at 10:00, 13 CFN



# Case: Work-up

- Ultrasound-guided biopsies
  - Right breast mass (core needle), 9:00, 4 CFN
    - Invasive ductal carcinoma, grade 3, extensive LVI
    - ER+(>99%)PR+(60%)Her2-(IHC 2, FISH neg)
    - Ki-67 30%
  - Right axillary lymph node (FNA)
    - Metastatic adenocarcinoma
  - Biopsy clips placed

# Work-up for locally advanced breast cancer

- H&P
- Imaging:
  - Dx bilateral mammogram, U/S
  - Consider breast MRI
  - If T3N1 or any N2: CT CAP, bone scan or NaF PET, or FDG-PET
    - Plain films for any symptomatic bones or abnormal areas on bone scan
  - If neuro sx: MR Brain
- Biopsy: core needle biopsy of primary and FNA biopsy of any suspicious nodes. ER/PR/Her2 assessment
- Consider genetic counseling if at risk for hereditary breast cancer
- Labs: CBC, CMP, Pregnancy test if childbearing potential

# Considerations for breast MRI

- May be helpful in defining **extent of disease before and after** neoadjuvant systemic therapy
- May be helpful to find **clinically occult primaries** (cT0 cN+)
  - Paget's disease
  - Invasive lobular carcinoma poorly seen on mammogram, U/S, or physical exam
- May help define extent of disease if **multi-focal** or **multi-centric** disease suspected
- Screening for **simultaneous contralateral breast cancer** in patients with inherited susceptibility or strong family history

- MRI should be performed at high volume center with dedicated breast coil and breast imaging radiologists

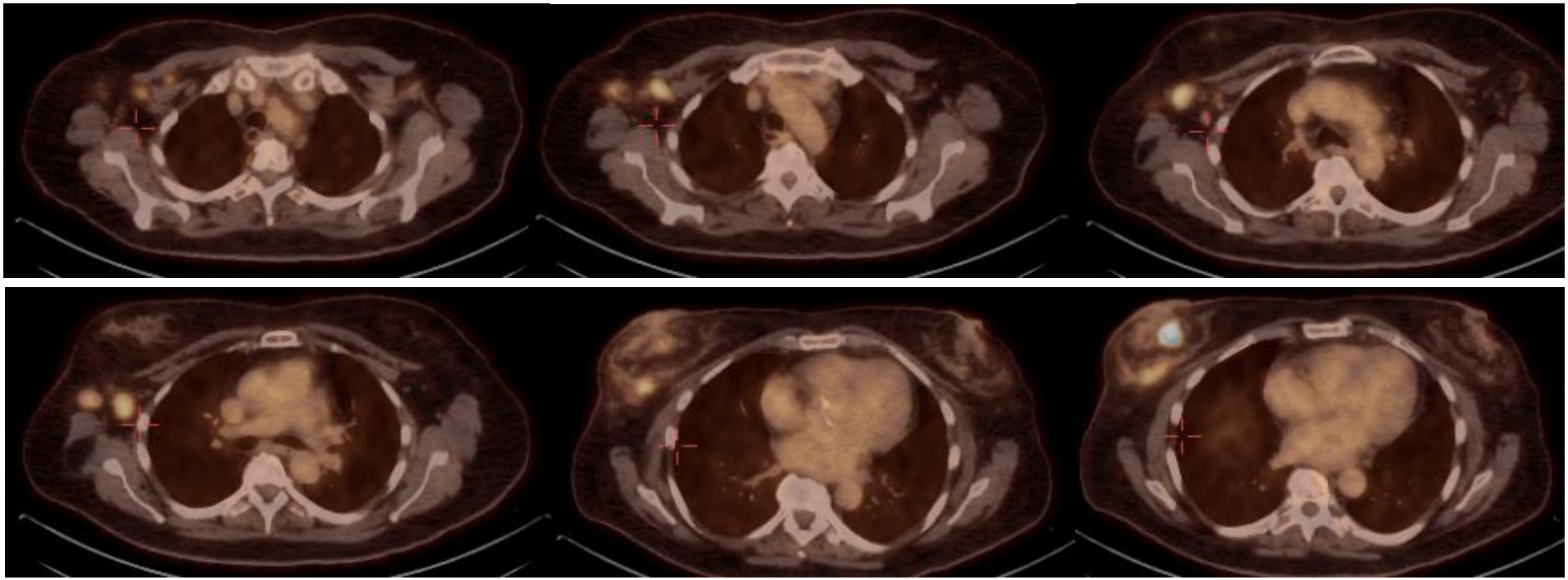
# Indications for genetic/familial assessment

- Young age at dx:
  - **≤45 yo**
  - 46-50 yo but with at last one blood relative with breast/ovarian/pancreatic/prostate cancer, unknown family history, or 2nd personal breast ca.
  - ≤60 yo with **triple negative** histology
- Family hx:
  - 1 close blood relative with breast ca at age ≤50 yo, or
  - 1 close blood relative with ovarian/pancreatic/prostate (metastatic/intraductal/cribiform/high risk)
  - 2 close blood relatives with breast cancer of any age
- Ashkenazi Jewish ancestry
- Male sex

- Consider if personal hx of multiple primary breast cancers (first between 50-65 yo)

# Case: Work-up (cont'd)

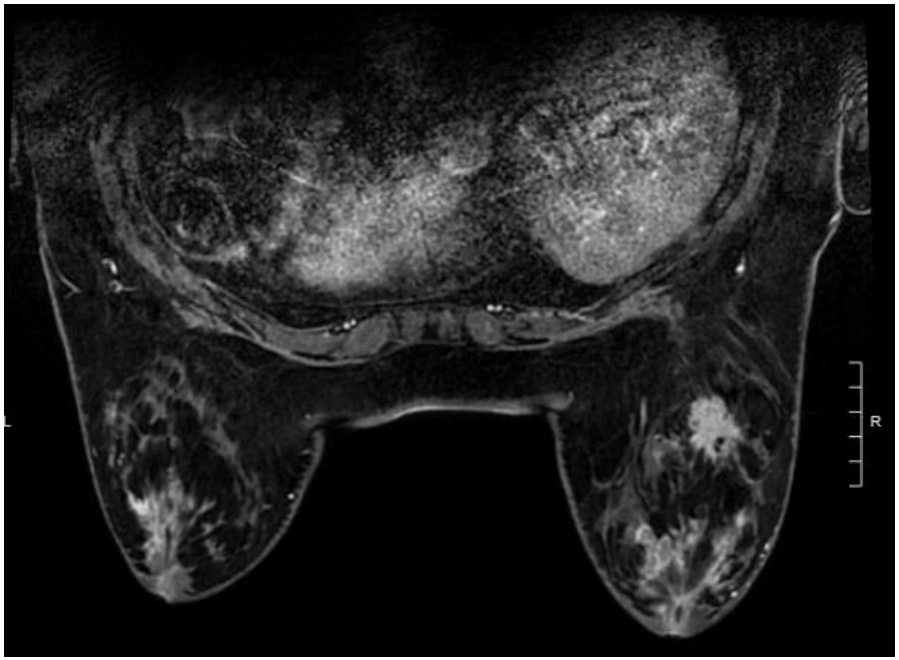
- PET CT
  - Right breast: multifocal uptake in central breast (1.9 x 1.5 cm, SUVmax 16.8) and outer central breast (SUVmax 4.4)
  - Multiple enlarged right axillary and subpectoral lymph nodes, largest 1.9 cm (SUVmax 4.6)
  - No distant metastases



# Case: Work-up

- Breast MRI
  - Right breast: multifocal disease spanning spanning approximately 10.9 x 5.9 x 5.3 cm
  - Left breast: large area of regional clumped non-mass enhancement in the central left breast spanning 8.4 x 4.3 x 4.5 cm
  - Right axillary level I, II, and III and subpectoral lymphadenopathy. No left axillary or IMN lymphadenopathy

- Left breast core needle biopsy:
  - Proliferative fibrocystic changes



# Case: Neo-adjuvant Treatment

- Upfront staging: cT3N3a
  - AJCC Stage IIIC (Anatomic)/IIIB (Prognostic)
- Neoadjuvant chemotherapy (NACT)
  - Adriamycin/Cyclophosphamide (AC) x 4 cycles
  - Taxol x 12 weekly cycles
- Pre-surgical Breast MRI
  - Some treatment response but residual disease remained in breast (9.4 cm span) and right axilla (all 3 levels)

# Case: Surgery and Pathology

- Right simple mastectomy and axillary lymph node dissection. No reconstruction

- Pathology:
  - Residual IDC
    - Breast: 5.6 cm, 20% cellularity with treatment effect (RCB-3), Grade 2, LVI+
    - Lymph nodes: 9/15 involved
      - 4 micro-, 5 macrometastases
      - Treatment effect in 3 micro- and 4 macromets
      - ENE-
    - Stage ypT3N2a (Stage IIIB, AJCC 8$^{th}$ Ed. Anatomic)
  - ER+(>95%)PR+(80%)Her2-(IHC 1+), Ki-67 1%
  - Negative surgical margins

- Started adjuvant letrozole

# When to consider PMRT

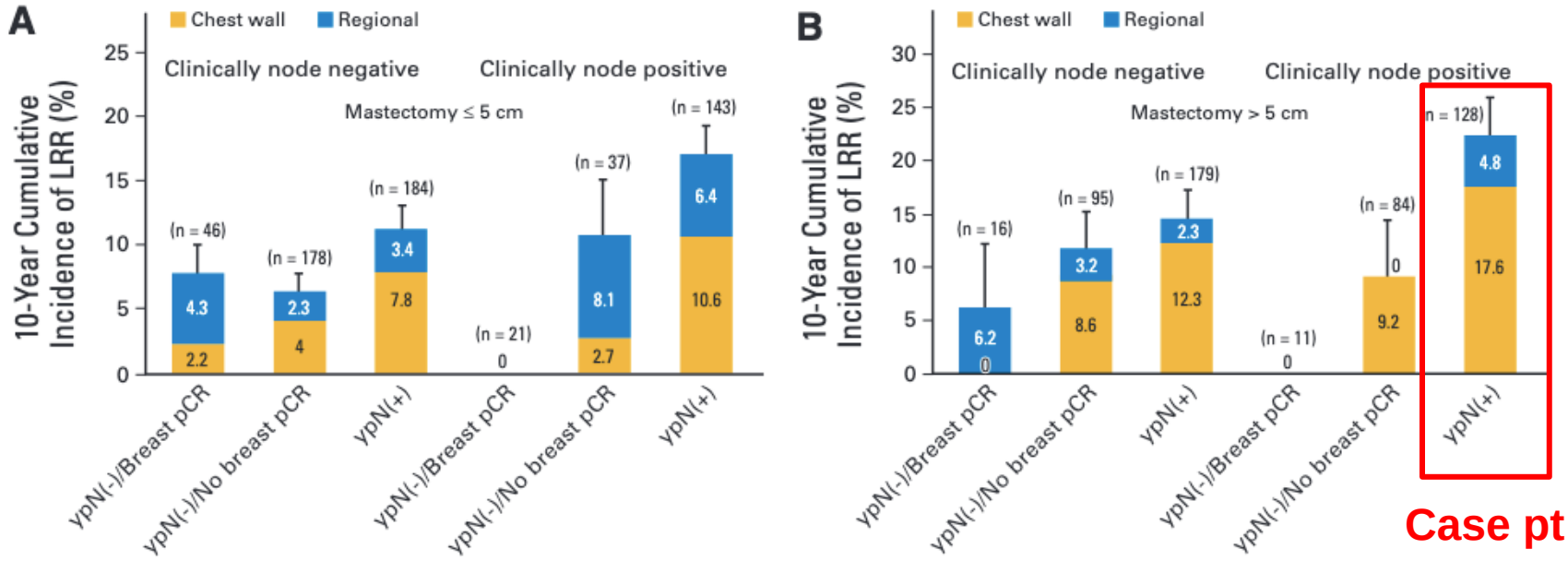
**ASCO/ASTRO/SSO guidelines (Recht *JCO* 2001 and 2016)**

- Node positive (Upfront or after NACT)
  - T1-2N1: consider if age < 40 and no co-morbidities or conditions increasing risk of RT toxicity
    - Small absolute LRR benefit, but low (<10%) even w/o PMRT (Tendulkar *IJROBP* 2012, Zeidan *IJROBP* 2018)
  - PMRT controversial in upfront cN1 with pathologic nodal complete response (ypN0) after NACT
    - Under active investigation in NSABP B-51
- T3/T4 (T3N0 controversial)
- Additional considerations (albeit lacking strong data support):
  - Positive margins
  - Extranodal extension

# What's the estimated recurrence risk without PMRT?

## Combined analysis of NSABP B-18 and B-27 (Mamounas *JCO* 2012)

- Factors associated with increased LRR
  - Upfront clinical node positive
  - Tumor size
  - Poorer response to NACT




Pt recurrence risk predominantly at chest wall (17.6%) vs regional nodes (4.8%) at 10 years

# Rationale for PMRT

- Improves LRF, OS in pN+ pts (3 RCTs)
  - British Columbia (Ragaz *JNCI* 2005)
  - Danish studies
    - 82b - Pre-menopausal (Overgaard *NEJM* 1997)
    - 82c – Post-menopausal (Overgaard *Lancet* 1999)
- Improves 20-yr breast cancer-mortality in pN+ subsets (1-3 and ≥4 LN+), but not pN0
  - EBCTCG Meta-analysis (EBCTCG *Lancet* 2014)

# Rationale for PMRT

## Summary of randomized control PMRT trials:

| | Trial | Years | N | Patient characteristics | | Arms | RT | 10 yr outcomes | | 20 yr outcomes | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | LRF | OS | LRF | BCM/OS |
| Primary Trials | **British Columbia** (Ragaz JNCI 2005) | 1979-86 | 318 | Clinical stage I/II, pN+, pre-menopausal, mastectomy + ALND (med. 11 nodes) -> CMF | | Observation<br>PMRT | CW + Axilla + SCV + IMN<br>37.5 Gy/16 fx<br>5-field (2 tang. AP SCV, PAB, IM) | | | 26%<br>10%<br>***p=0.002*** | 37% (OS)<br>47%<br>***p=0.03*** |
| Primary Trials | **Danish 82b** (Overgaard NEJM 1997) | 1982-89 | 1708 | Path stage II/III, pre-menopausal, mastectomy + ALND (med. 7 nodes) -> CMF | | Observation<br>PMRT | CW + Axilla + SCV + IMN<br>50 Gy in 25 fx (or 48 Gy/22 fx)<br>Electrons to CW/IMN, photon to SCV/axilla, PAB if large separation | 23%<br>9%<br>***p<0.001*** | 45%<br>54%<br>***p<0.001*** | | |
| Primary Trials | **Danish 82c** (Overgaard Lancet 1999) | 1982-90 | 1375 | Path stage II/III, post-menopausal, mastectomy + ALND (med. 7 nodes) -> Tam | | | | 35%<br>8%<br>***p<0.001*** | 36%<br>45%<br>***p=0.03*** | | |
| **EBCTCG Meta-analysis** (Lancet 2014) | | 1964–86 | 700 | Mastectomy + ALND (med. 10 nodes) | pN0 | Observation<br>PMRT | CW + Axilla and/or SCV + IMN<br>Various dose/fractionations | 1.6%<br>3.0%<br>*p>0.1* | | | 28.8% (BCM)<br>26.6%<br>*p>0.1* |
| | | | 1314 | | pN+ (1-3 LN+) | | | 20.3%<br>3.8%<br>***p<0.00001*** | | | 50.2% (BCM)<br>42.3%<br>***p=0.01*** |
| | | | 1772 | | pN+ (≥4 LN+) | | | 32.1%<br>13.0%<br>***p<0.00001*** | | | 80.0% (BCM)<br>70.7%<br>***p=0.04*** |

ALND, axillary lymph node dissection; CMF, cyclophosphamide/methotrexate/5-FU; Tam, tamoxifen; CW, chest wall; SCV, supraclavicular fossa; IMN, internal mammary nodes; EBCTCG, Early Breast Cancer Trialists Cooperative Group; PAB, Posterior-anterior beam; BCM, Breast cancer mortality

# PMRT in intermediate risk pts under investigation

- MRC/EORTC SUPREMO trial (awaiting survival data)
  - 1688 patients (2008-2013)
  - Eligibility: pT1-2N1, pT3N0, or pT2N0 with Gr3/LVI
  - Arms: Mastectomy and axillary sampling + neoadjuvant or adjuvant chemotherapy with:
    - No PMRT
    - PMRT (chest wall, SCV/IMN optional, no axilla)
      - 50 Gy in 25 fractions (or 45 Gy/20 fx, 42.56 Gy/16 fx or 40 Gy/15 fx), no boost
  - 2-year QOL outcomes (Velikova *Lancet Oncol* 2018)
    - Mildly increased chest wall symptom score with PMRT at up to 2 years (14.1 vs 11.6) with improvement over years 1 to 2

# PMRT with regional nodal irradiation (RNI)

- Supraclavicular (SCV) and internal mammary nodal (IMN) fields included in British Columbia and Danish RCTs

- **SCV**: Small (1.9%) breast-cancer mortality benefit in EORTC 22922 when combined with IMN RT. No survival benefit
  - Include if ≥4 LN+ or inflammatory breast cancer, recommended for 1-3 LN+

- **IMN**: Small (3.9%) absolute overall survival benefit in DBCG-IMN study, but non-significant in French, though study likely underpowered
  - Greatest benefit if ≥4 LN+ or central/medial tumor

# PMRT with regional nodal irradiation (RNI)

## PMRT patients in 3 prospective randomized or naturally allocated RNI trials:

| | Trial | Years | N | Patient characteristics | Arms | RT | 10 yr outcomes | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | BCM | OS |
| IMN | **French**<br>(Hennequin IJROBP 2013) | 1991-1997 | 1334 | pN+ or central/medial tumor<br>100% mastectomy + ALND | RT CW + SCV + AxI-II (pN+)<br>RT CW + SCV + AxI-II (pN+) + IMN (first 5 intercostals) | 50 Gy equivalent<br>IMN: 45 Gy/18 fx, mixed phot/e- | | 59.3%<br>62.6%<br>*p=0.8* |
| IMN | **DBCG-IMN**<br>(Thorsen JCO 2016) | 2003-2007 | 3089 | pN+<br>T1-2 (93%)<br>mastectomy (66%)/BCS (34%) + ALND | Left: RT Breast/CW + AxII-III + SCV<br>Right: RT Breast/CW + AxII-III + SCV + IMN (first 4 intercostals) | 48 Gy/24 fx<br>IMN: ant. e- or tangent photons | 23.4% (8-yr)<br>20.9%<br>***p=0.03*** | 72.2% (8-yr)<br>75.9%<br>***p=0.005*** |
| SCV + IMN | **EORTC 22922**<br>(Poortmans NEJM 2015) | 1996-2004 | 4004 | Stage I-III<br>pN+ (56%) or central/med. tumor pN0 (44%)<br>BCS (76%)/mastectomy (24%) + ALND | RT Breast/CW (73% of mast. in both arms)<br>RT Breast/CW + SCV + IMN (first 3-5 intercostals) | 50 Gy/25 fx | 14.4%<br>12.5%<br>***p=0.0055*** | 80.7%<br>82.3%<br>*p=0.36* |

ALND, axillary lymph node dissection; BCS, breast conserving surgery; CW, chest wall; NS, not significant (p>0.05); SS, statistically significant (p<0.05)

# Case: RT Simulation

- Supine with arms up on 15 degree breast board
  - Head turned away from treatment side to open up neck
- Wires
  - Surgical: Incision scar and drain sites
  - Boundaries
    - Superior: Clavicular head
    - Inferior: 2cm below inframammary fold (contralateral intact breast may serve as guide)
    - Medial: Midline
    - Lateral: Mid-axillary line
- Bolus
  - Material: Superflab
    - Other: custom Aquaplast cast, or wax
  - 3 mm thickness
    - Up to 1 cm depending if higher energy used

# Mastectomy Scar: To boost or not to boost

- **No prospective data** for mastectomy scar boost – **not standard of care**
  - ASCO guidelines cite insufficient data for recommendation (Recht *JCO* 2001, 2016)

- In practice, usage may be considered in the setting of higher local recurrence risk
  - Close/positive margins
  - Poor in-breast response to neoadjuvant therapy
  - Inflammatory breast cancer

- Use in contemporary clinical trials:
  - Alliance 011202 (Mandated):
    - 10-14 Gy in 2 Gy fractions with electrons (recommended) or photons
  - NSABP B51 (Permissible if positive or close <2mm margins):
    - 12-14 Gy in 2 Gy fractions

# To bolus or not to bolus

- **Usage is variable by geography**
  - Higher in North America (82%) and Australia (65%) than Europe (31%) (Vu *Clin Oncol (R Coll Radiol)* 2007)

- **No randomized prospective data** for its use
  - ASCO guidelines cite insufficient data for recommendation (Recht *JCO* 2001, 2016)

- Large Canadian retrospective study (n=1887) showed no difference local or locoregional control with omission of bolus (Nichol *IJROBP* 2021)
  - Caveat for pt. imbalance/selection bias: omission of bolus in recon. pts (49%) vs non-recon (4%)

# Dose fractionation

- 50-50.4 Gy in 1.8-2 Gy daily fractions is standard of care

- Moderate hypofractionation (HF)
  - If no breast reconstruction, HF may be used off-trial

# Moderate hypofractionation (HF)

- **43.5 Gy in 15 fx** (2.9 Gy/fx) - Chinese randomized control trial (Wang *Lancet Oncol* 2019)
  - 820 pts who underwent mastectomy without reconstruction, pN2 or pT3-4
  - Arms: 50 Gy/25 fx (SF) vs 43.5 Gy in 15 fx (HF)
  - RT: Note that **electron** CW fields were used
  - Outcomes (med f/u 58.5 mo): LRR non-inferior at 5-yr (8.3% HF vs 8.1% SF)
  - Toxicity: Similar acute and late toxicity, Less Gr3 acute skin toxicity with HF (3% vs 8%)

- Extrapolation of efficacy from UK START moderate hypofractionation trials
  - Mostly intact breast but 15% (START A)/8% (START B) of patients underwent mastectomy without immediate reconstruction (Haviland *Lancet Oncol* 2013)

- Safety and efficacy of hypofractionated PMRT (42.56 Gy in 16 fx) with breast reconstruction currently tested in two US randomized clinical trials
  - FABREC (NCT03422003)
  - Alliance A221505 / RT CHARM (NCT03414970)

# Radiation fields

- 3-field technique
  - Tangential fields (x2)
    - Include chest wall, axilla (levels I-III), ±IMN (if clinically indicated and lung/heart dose constraints achievable).
  - SCV field

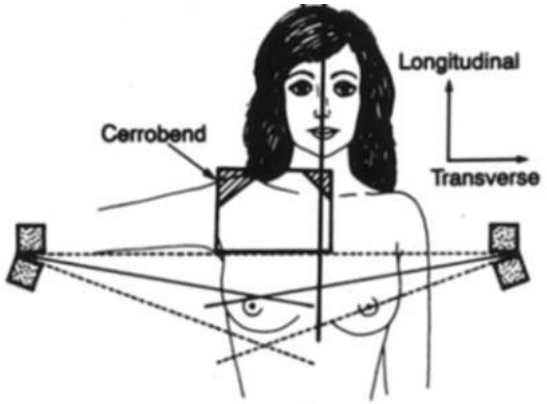
- IMN
  - Partially wide tangents (if lung dose constraints can be met)
  - Matching electron field is an alternative

- Mastectomy scar/drain sites
  - Cover in entirety with tangential fields (preferred) or separate electron field if necessary due to scar extension outside of tangent fields

# 3D planning for PMRT with RNI

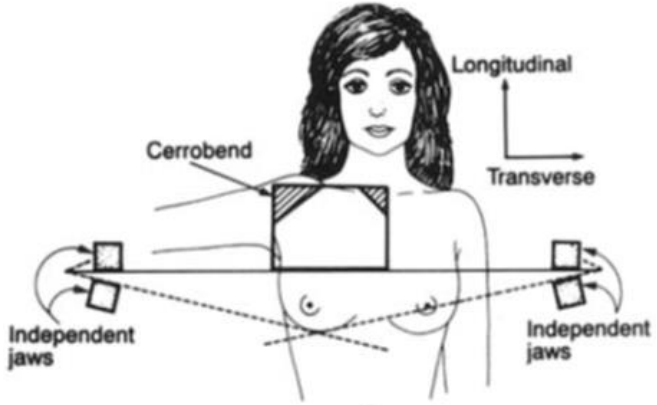
- 3-field most typical (2 tangent fields, 1 SCV field)
- Mono-isocentric technique (Klein *IJROBP* 1994)
  - Half-beam block tangent fields
  - Sup-inf extent of chest wall/breast must fit in half-field
  - To match SCV field, tangent field collimators cannot be rotated

**Multi-isocentric**




- Couch kicks: **Required**
  - Kick feet **away** from gantry

**Mono-isocentric**

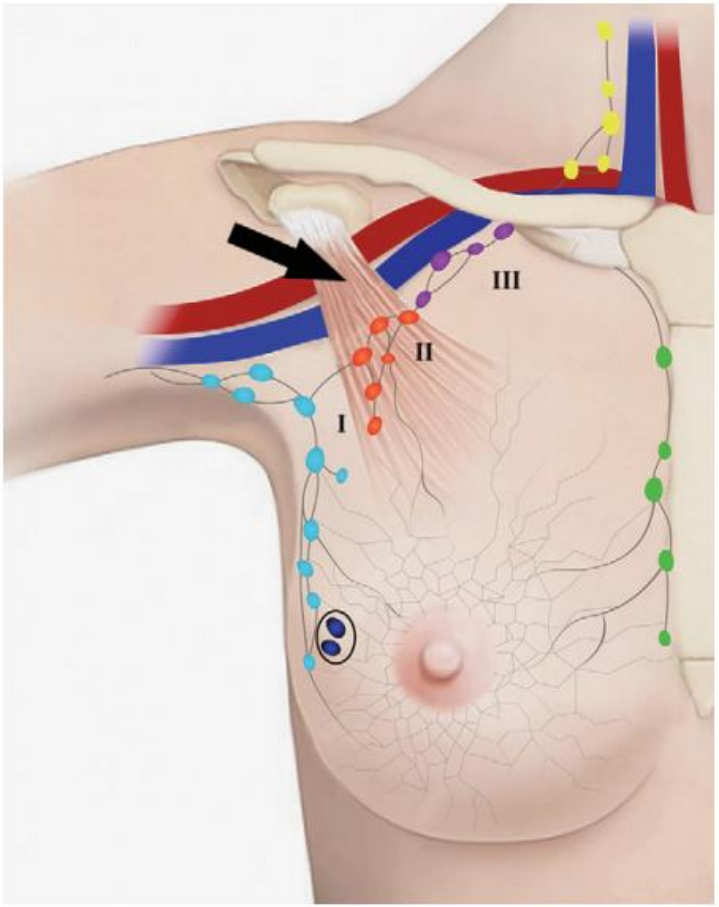



- Couch kicks: **None**

# Target delineation

- Targets
  - Chest wall
  - Axilla (Levels I-III)
  - Supraclavicular fossa
  - Internal mammary nodes
  - Wired scars
- Organs at risk
  - Thyroid
  - Ipsilateral brachial plexus
  - Contralateral breast
  - Esophagus
  - Heart
  - Lungs
  - Spinal canal
  - If L-sided
    - Left ventricle and left anterior descending artery
    - Stomach
  - If R-sided
    - Liver

# Lymph node stations made simple




Axillary levels – Relative to **pec. minor**:

- Level I: lateral
- Level II: post./ant. (contour first!)
- Level III: medial
- Start just below subclavian vessels and go down to 4/5$^{th}$ ribs (Lv I) or obliteration of fat space (Lv II/III)

Supraclav – Bottom of cricoid to bottom of clavicular head

IMN – Along internal mammary vessels from top of 1$^{st}$ rib to top of 4$^{th}$ rib (~3 intercostal spaces)

For detailed boundaries, see contouring atlases (next slide)

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# Contouring consensus guidelines/atlases

- **RTOG** (www.nrgoncology.org/ciro-breast)
- **ESTRO** (Offersen *Radiother Oncol* 2015)
- **RadComp** (www.nrgoncology.org/About-Us/Center-for-Innovation-in-Radiation-Oncology/Breast/RADCOMP-Breast-Atlas)

# Dose goals

Listed are ideal dose guidelines, in parentheses are acceptable limits

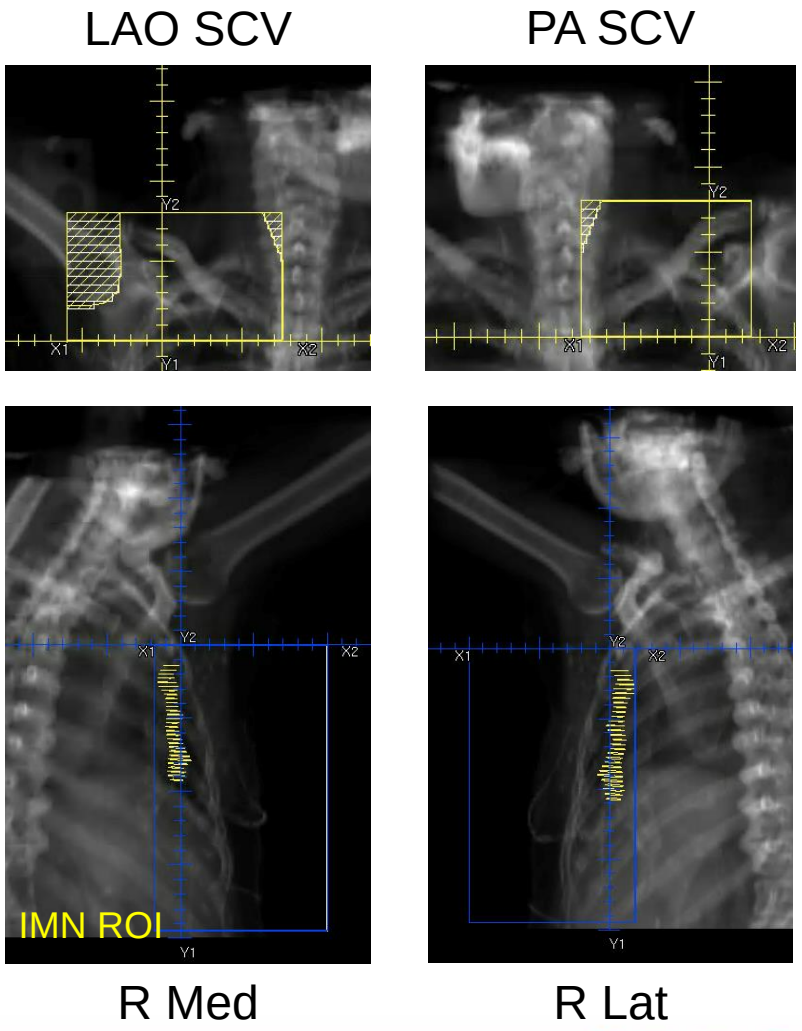
- Dose homogeneity:
  - Chestwall
    - Dmax < 115% (120%) Rx dose
    - V105% Rx dose < 25% (50%)
  - Overall plan
    - Dmax < 130% (140%) Rx dose
    - V10cc < 125% (130%) Rx dose

- Target coverage:
  - Chestwall: D95% Rx dose > 95% (90%)
  - Axilla and SCV: D95% Rx dose > 95% (D90% Rx dose > 90%)
  - IMN: D95% Rx dose > 90% (D90% Rx dose > 80%)

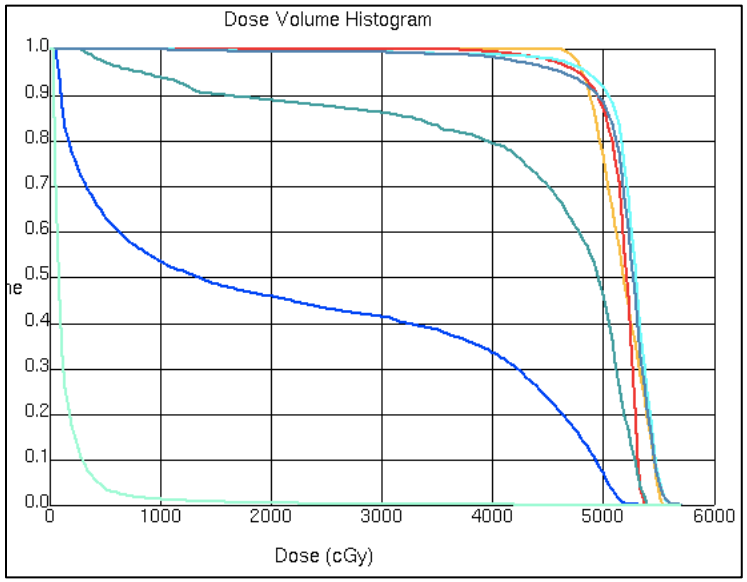
- OARs:
  - Lung (ipsilateral): V20Gy < 30% (38%), V10Gy < 50% (60%)
  - Heart: Dmean < 4Gy (5Gy)

# Case: RT planning – Trial #1

- 50 Gy in 25 fractions
- Mono-isocentric technique used
  - 2x half-beam blocked tangents (6/10 MV photons)
  - LAO SCV field (10 MV)
  - PA SCV field (15 MV) – 15% of SCV MUs to reduce SCV hotspot
- Given high residual nodal positivity, prioritized nodal coverage including (SCV and IMN) while allowing for higher lung dose
  - IMN V95% > 90%
  - Lung V20Gy < 38% (acceptable limit)



# Case: Dose volume hist. – Trial #1




**ROI Statistics**

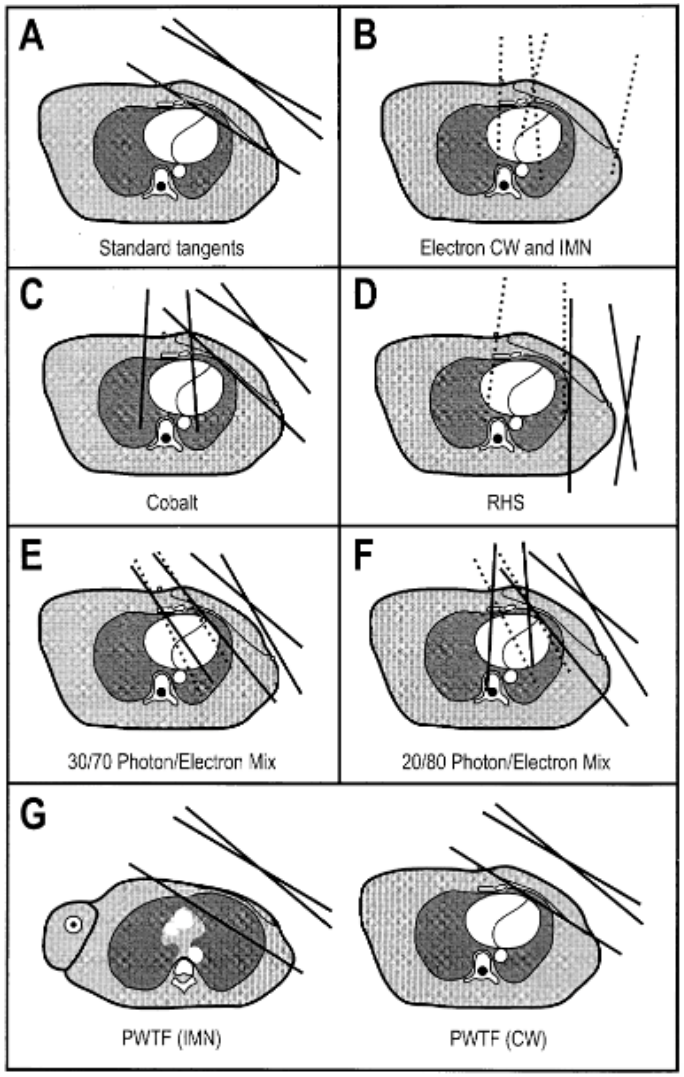
| Line Type | ROI | Trial or Record | Min. | Max. | Mean | Std. Dev. |
|---|---|---|---|---|---|---|
| | CTV_SCV_R | Trial #1 | 4418.17 | 5531.83 | 5171.05 | 215.08 |
| | Lung_R | Trial #1 | 59.37 | 5318.45 | 2206.62 | 2003.92 |
| | IMN_R | Trial #1 | 3189.70 | 5380.96 | 5147.73 | 223.58 |
| | BrachialPlex_R | Trial #1 | 254.32 | 5395.17 | 3438.64 | 2140.66 |
| | Chestwall_R | Trial #1 | 556.13 | 5670.70 | 5227.93 | 418.49 |
| | CTV | Trial #1 | 503.09 | 5697.29 | 5181.70 | 453.45 |
| | Heart | Trial #1 | 29.45 | 4196.98 | 145.76 | 236.04 |

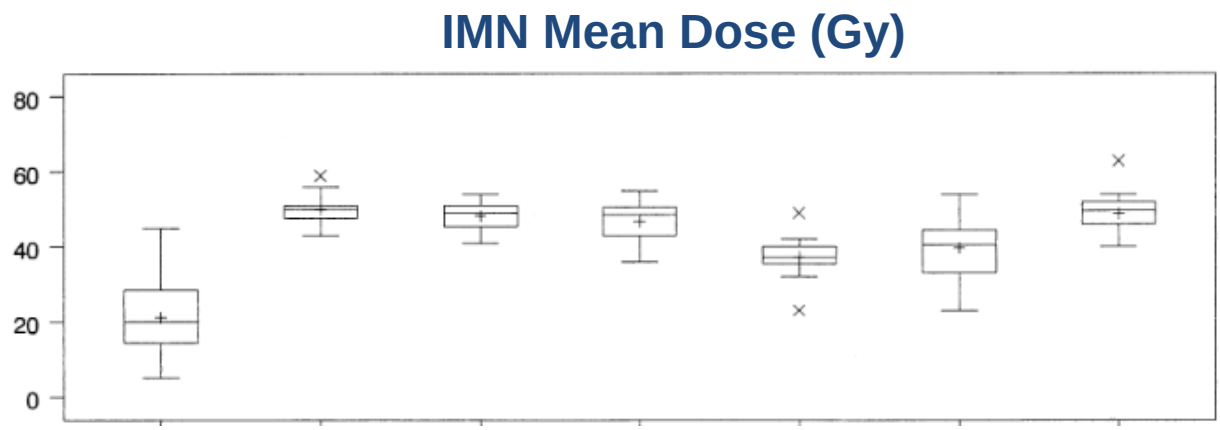
- Target coverage is good, but Lung V20 is too high (46%)

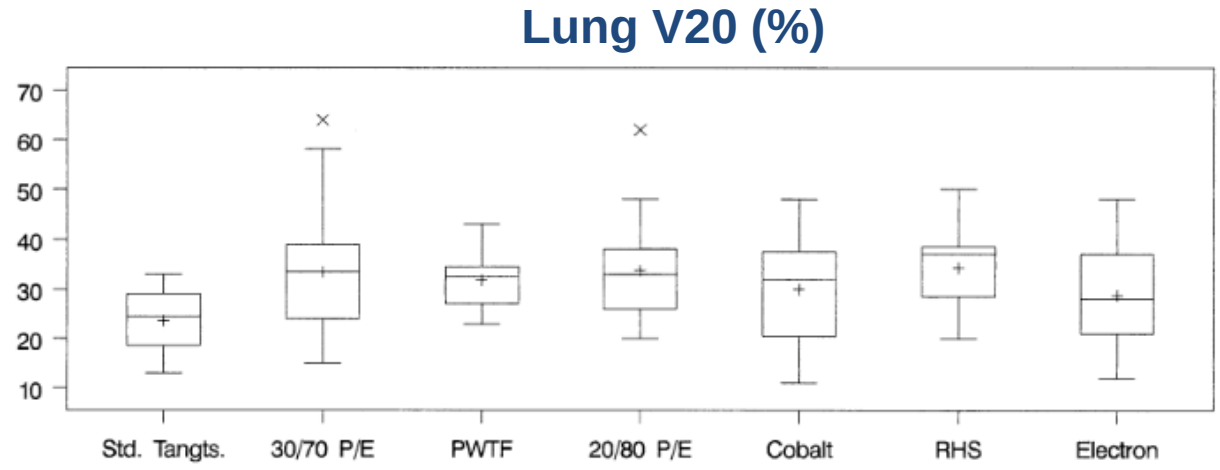
# Ways to decrease lung dose while maintaining adequate target (esp. IMN) coverage

- Move isocenter superiorly
  - Decreases apical lung dose from SCV field
- Block lung in tangent fields inferiorly
  - In order to match SCV field, collimator rotation of tangent fields is not possible. Thus, as the isocenter is moved superiorly, more anterior lung may enter tangent fields.
- May also consider trial of using steeper tangents and covering IMNs with separate electron field
- Protons, IMRT/VMAT
- Deep inspiration breath-hold

# Alternative beam configurations on IMN coverage and Lung V20



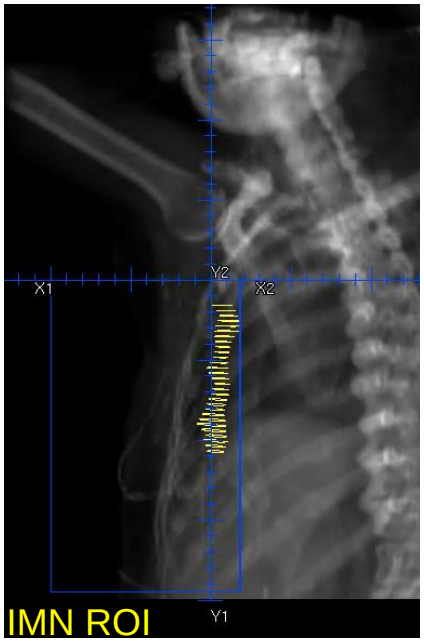




Pierce *IJROBP* 2002

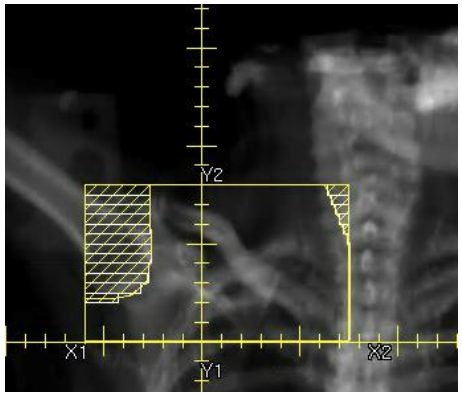
# Case: RT planning – Trial #2

## TRIAL #1

**R medial tang.**

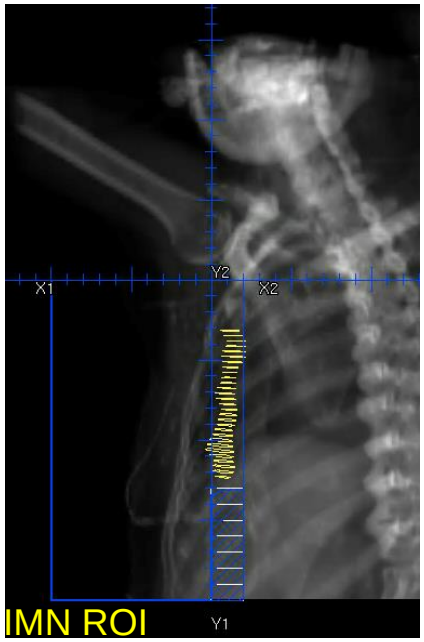



**SCV**

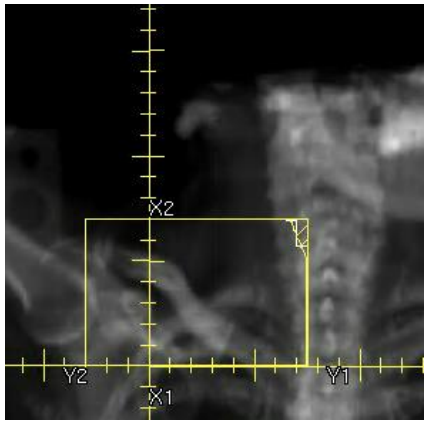



## TRIAL #2

**R medial tang.**



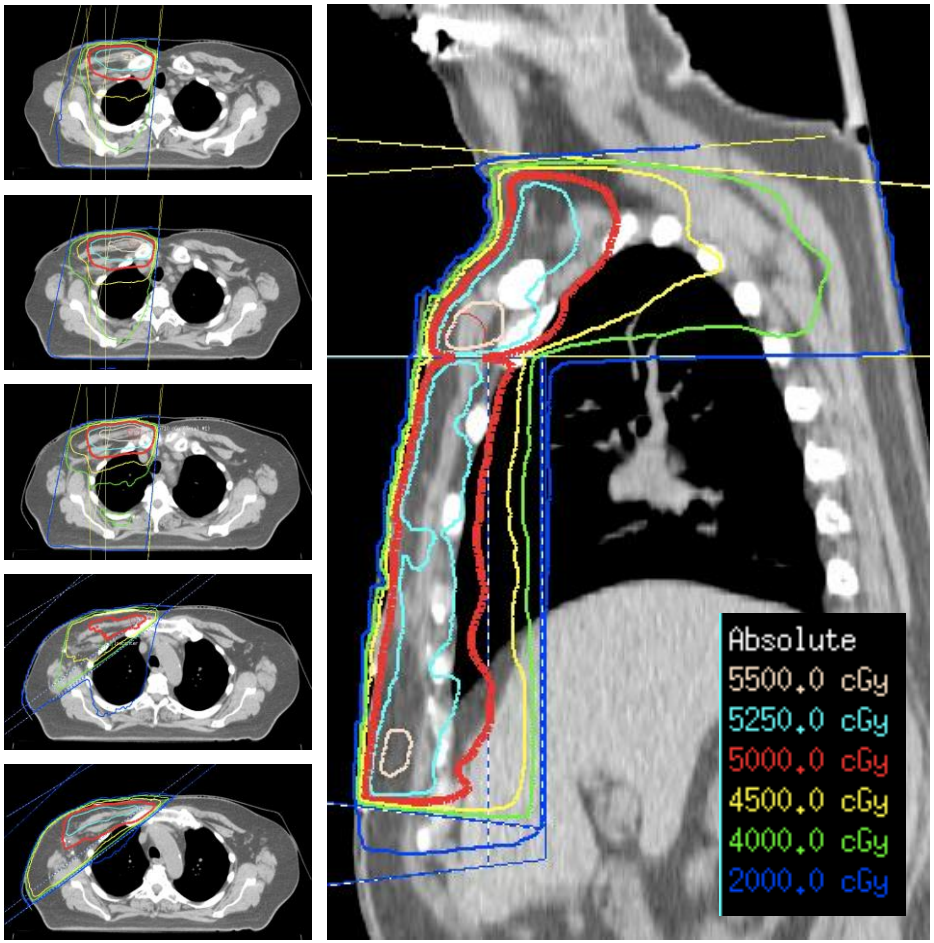

**SCV**



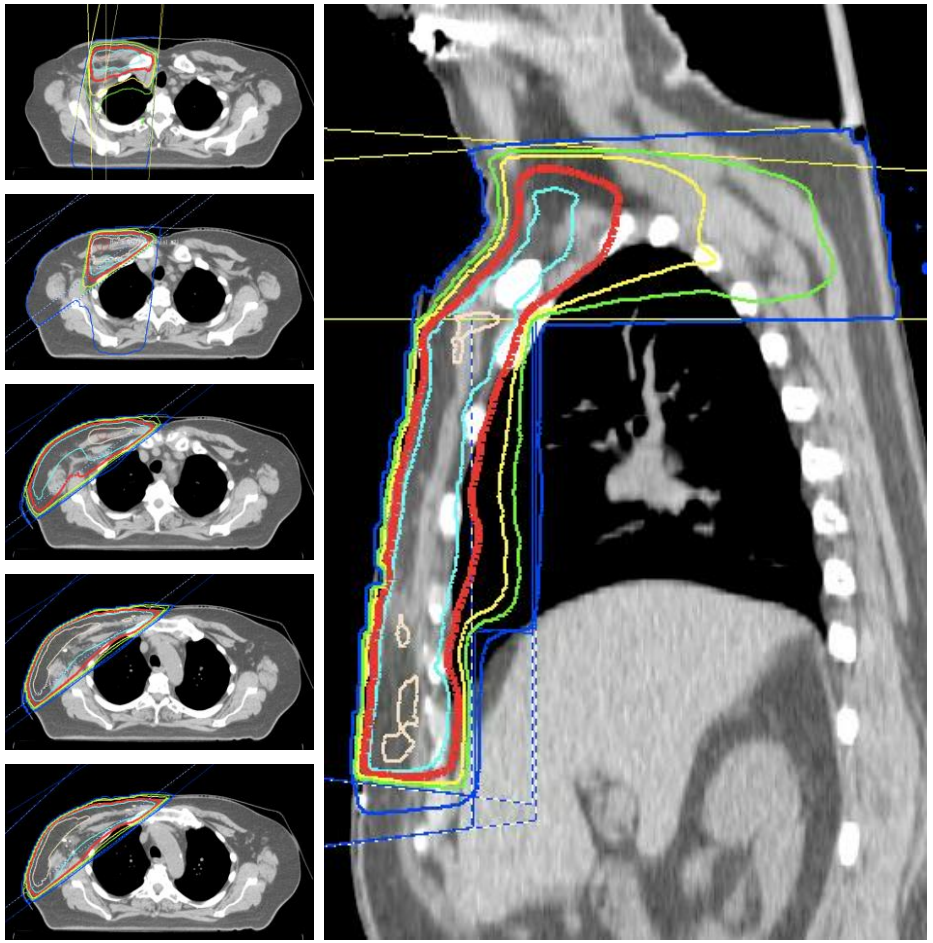

- Changes made in Trial #2
  - Raise isocenter 1.5 cm superiorly
  - Added inferior lung blocks using MLC

# Case: Dose distribution comparison

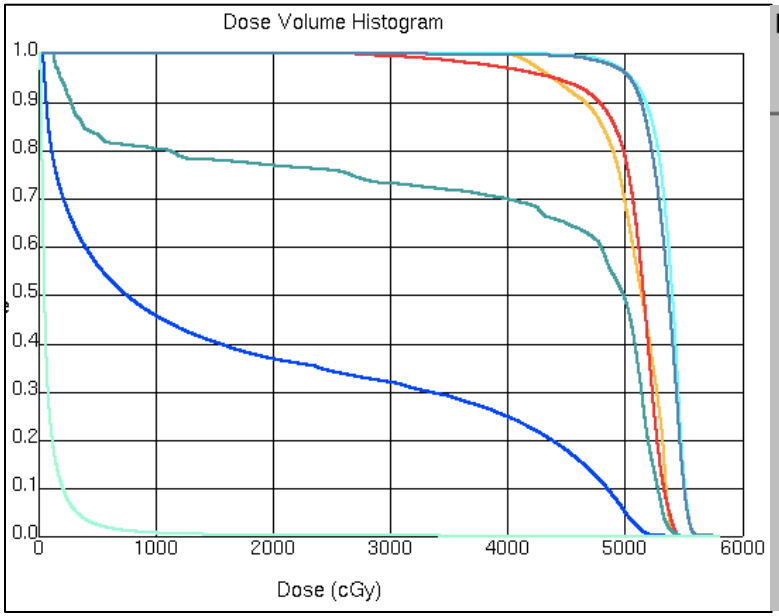
**TRIAL #1**




**TRIAL #2**



# Case: Dose volume hist. – Trial #2




**ROI Statistics**

| Line Type | ROI | Trial or Record | Min. | Max. | Mean | Std. Dev. |
|---|---|---|---|---|---|---|
| | CTV_SCV_R | Trial #2 | 3881.06 | 5444.02 | 5067.54 | 300.02 |
| | Lung_R | Trial #2 | 39.40 | 5334.25 | 1813.80 | 1912.28 |
| | IMN_R | Trial #2 | 2185.68 | 5468.01 | 5064.11 | 385.65 |
| | BrachialPlex_R | Trial #2 | 129.47 | 5466.34 | 3834.21 | 1950.99 |
| | Chestwall_R | Trial #2 | 731.27 | 5625.51 | 5362.26 | 181.32 |
| | CTV | Trial #2 | 731.27 | 5744.80 | 5330.12 | 220.21 |
| | Heart | Trial #2 | 19.76 | 3419.10 | 103.21 | 161.22 |

- Lung V20 down to 36.6% (from 46%), with excellent V95% coverage of IMN (90.5%)

# Case: Radiotherapy course

- Prior to RT start, pt developed 2 open wounds just superior to her mastectomy scar.
  - These were slow to heal, ultimately requiring delay of RT start for 5 weeks to allow for full closure.
- Pt had a significant personal event at the completion of RT. Due to the delay in RT start, her course was moderately hypofractionated to accommodate this.
  - Trial #2 selected, with dose fractionation changed to **43.5 Gy in 15 fx** (from Wang Lancet Oncol 2019)
- Pt had started on letrozole prior to RT and continued it during RT
- Pt completed her RT course without delays or unexpected acute side effects.

# What if this patient had desired breast reconstruction?

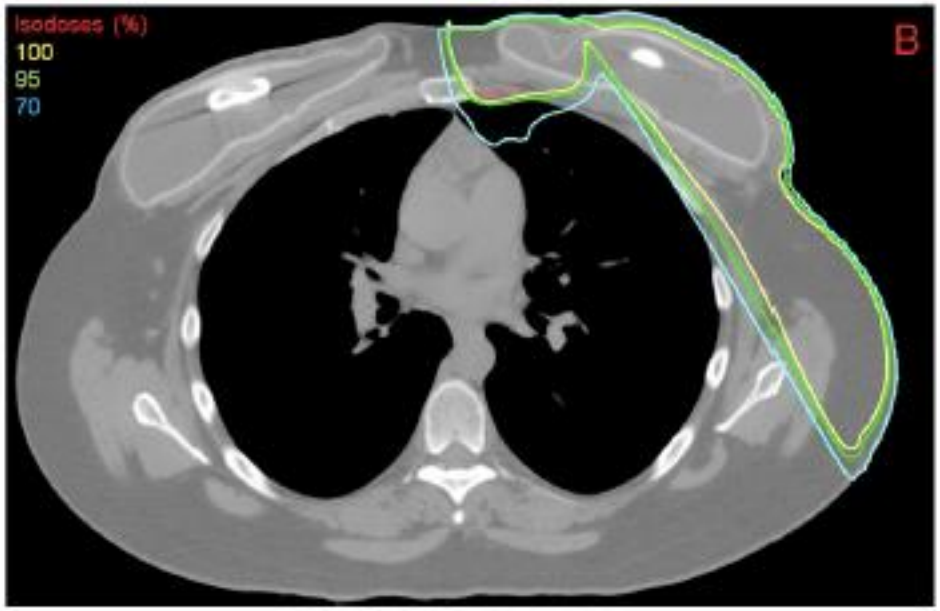
- **Options** for breast reconstruction
  - Autologous (TRAM flap, DIEP flap, etc.) vs implant-based (pre- or sub-pectoral)
  - Immediate (implant at time of mastectomy) vs delayed (tissue expanders at time of mastectomy -> expander-implant exchange at 2nd surgery)
  - Mastectomy may be skin +/- nipple sparing

- **Timing** relative to PMRT for implant based reconstruction:
  - If delayed reconstruction, would typically perform PMRT after tissue expanders (TE) are at maximum desired size
  - No difference in complication rates if PMRT is done after TE or with final implants (Santosa *Plast Reconstr Surg* 2016)
  - Consider delaying expander implant exchange for 6 months to reduce risk of implant failure
    - Small single institution series (n=88). Implant loss if exchanged < 6 mo (22.4%) vs >6 mo (7.7%). (Peled *Plast Reconstr Surg* 2012)

# What if this patient had desired breast reconstruction?

- Complications of reconstruction with PMRT
  - After immediate implant-based recon.: capsular contracture ~30% and implant loss ~10% (Pu *Medicine (Baltimore)* 2018, meta-analysis)
  - Lower relative risk of complications after 2 years with PMRT for autologous (25.6%) vs implant-based reconstructions (38.9%) (Jagsi *JNCI* 2018)
  - Other complications include seroma, hematoma, wound dehiscence, implant extrusion

- Radiation considerations with breast reconstruction
  - **Conventional fractionation** is standard.
    - Moderate hypofractionation is actively studied on clinical trials (FABREC and RT CHARM)
  - Sub-pectoral implants may be better suited for electron/photon matched plans than pre-pectoral implants, which may result in unacceptable cold spots in the chest wall (see image on right, Mitchell *PRO* 2018)



# References


- Recht, A. *et al.* Postmastectomy radiotherapy: an american society of clinical oncology, american society for radiation oncology, and society of surgical oncology focused guideline update. *J. Clin. Oncol.* **34,** 4431–4442 (2016).
- Recht, A. *et al.* Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. *J. Clin. Oncol.* **19,** 1539–1569 (2001).
- Mamounas, E. P. *et al.* Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. *J. Clin. Oncol.* **30,** 3960–3966 (2012).
- Ragaz, J. *et al.* Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. *J. Natl. Cancer Inst.* **97,** 116–126 (2005).
- Overgaard, M. *et al.* Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. *N. Engl. J. Med.* **337,** 949–955 (1997).
- Overgaard, M. *et al.* Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet* **353,** 1641–1648 (1999).
- Thorsen, L. B. J. *et al.* DBCG-IMN: A Population-Based Cohort Study on the Effect of Internal Mammary Node Irradiation in Early Node-Positive Breast Cancer. *J. Clin. Oncol.* **34,** 314–320 (2016).
- EBCTCG (Early Breast Cancer Trialists' Collaborative Group) *et al.* Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* **383,** 2127–2135 (2014).
- Poortmans, P. M. *et al.* Internal mammary and medial supraclavicular irradiation in breast cancer. *N. Engl. J. Med.* **373,** 317–327 (2015).
- Whelan, T. J. *et al.* Regional Nodal Irradiation in Early-Stage Breast Cancer. *N. Engl. J. Med.* **373,** 307–316 (2015).
- Velikova, G. *et al.* Quality of life after postmastectomy radiotherapy in patients with intermediate-risk breast cancer (SUPREMO): 2-year follow-up results of a randomised controlled trial. *Lancet Oncol.* **19,** 1516–1529 (2018).

# References (continued)


- Zeidan, Y. H. *et al.* Postmastectomy Radiation Therapy in Women with T1-T2 Tumors and 1 to 3 Positive Lymph Nodes: Analysis of the Breast International Group 02-98 Trial. *Int. J. Radiat. Oncol. Biol. Phys.* **101,** 316–324 (2018).
- Tendulkar, R. D. *et al.* Impact of postmastectomy radiation on locoregional recurrence in breast cancer patients with 1-3 positive lymph nodes treated with modern systemic therapy. *Int. J. Radiat. Oncol. Biol. Phys.* **83,** e577-81 (2012).
- Wang, S.-L. *et al.* Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. *Lancet Oncol.* **20,** 352–360 (2019).
- Haviland, J. S. *et al.* The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol.* **14,** 1086–1094 (2013).
- Klein, E. E., Taylor, M., Michaletz-Lorenz, M., Zoeller, D. & Umfleet, W. A mono isocentric technique for breast and regional nodal therapy using dual asymmetric jaws. *Int. J. Radiat. Oncol. Biol. Phys.* **28,** 753–760 (1994).
- Offersen, B. V. *et al.* ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1. *Radiother. Oncol.* **118,** 205–208 (2016).
- Pierce, L. J. *et al.* Postmastectomy radiotherapy of the chest wall: dosimetric comparison of common techniques. *Int. J. Radiat. Oncol. Biol. Phys.* **52,** 1220–1230 (2002).
- Chang, J. M., Leung, J. W. T., Moy, L., Ha, S. M. & Moon, W. K. Axillary nodal evaluation in breast cancer: state of the art. *Radiology* **295,** 500–515 (2020).
- Vu, T. T. T., Pignol, J. P., Rakovitch, E., Spayne, J. & Paszat, L. Variability in radiation oncologists' opinion on the indication of a bolus in post-mastectomy radiotherapy: an international survey. *Clin. Oncol. (R. Coll. Radiol)* **19,** 115–119 (2007).
- Nichol, A. *et al.* The Effect of Bolus on Local Control for Patients Treated with Mastectomy and Radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* (2021). doi:10.1016/j.ijrobp.2021.01.019

# References (continued)


- Pu, Y., Mao, T.-C., Zhang, Y.-M., Wang, S.-L. & Fan, D.-L. The role of postmastectomy radiation therapy in patients with immediate prosthetic breast reconstruction: A meta-analysis. *Medicine* **97,** e9548 (2018).
- Jagsi, R. *et al.* Impact of Radiotherapy on Complications and Patient-Reported Outcomes After Breast Reconstruction. *J. Natl. Cancer Inst.* **110,** (2018).
- Mitchell, M. P., Wagner, J. & Butterworth, J. Subcutaneous implant-based breast reconstruction, a modern challenge in postmastectomy radiation planning. *Pract Radiat Oncol* **8,** 153–156 (2018).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