Updates in Management of Breast Cancer: A Case Review Journey

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Objectives

- Discuss radiographic, pathologic, and clinical evaluation of new breast cancer patients
- Discuss clinical considerations and changing patterns of management in select patient populations including those with:
  - Neoadjuvant systemic therapy
  - Bilateral breast cancer
  - Path CR with positive nodes prior to systemic therapy
  - Breast cancer in the young and elderly age populations
  - Local recurrence/re-irradiation candidates
  - Multifocal disease and breast conservation
  - Pathologic upgrades
  - Locally advanced disease/de novo stage IV
  - Secondary malignancies after BC treatment

Workup/Initial evaluation

- Clinical history + exam
- Diagnostic breast imaging
  - Mammogram with Tomosynthesis ("3-D" mammography)
  - Ultrasound
  - MRI
  - Others- Positron Emission Mammography (PEM), sestamibi scan (MBI), contrast enhanced mammography
    - BIRADS 4: suspicious for malignancy (2-95% chance of cancer(
    - BIRADS 5: highly suggestive of malignancy (>95% chance of cancer)
    - BIRADS 6: Biopsy proven malignancy

Workup/Initial evaluation

- Image guided biopsy with clip placement
  - Core needle biopsy (usually 9-14gauge)
  - Via stereotactic, ultrasound, or MRI guidance

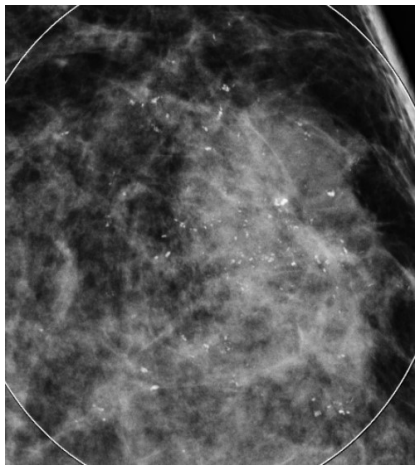
Workup/Initial evaluation

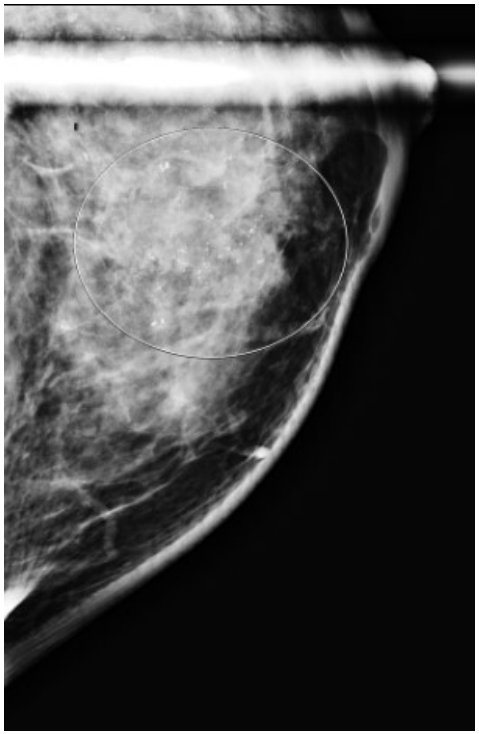
- Histologic evaluation/pathology diagnosis
  - Imaging/pathology concordance
  - Tumor Subtype – lobular vs ductal, invasive vs noninvasive
  - Tumor biomarkers (estrogen receptor, progesterone receptor, Her2-neu receptor)
  - Grade and Stage (TNM)
  - +/- Ki67
- Systemic staging scans
  - PET/CT
  - CT chest/abdomen/pelvis + nuclear medicine bone scan

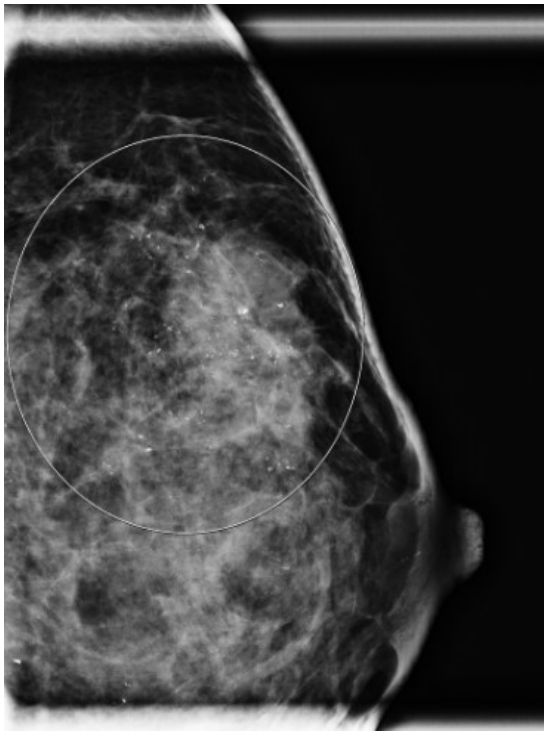
Clinical Case Reviews

Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- HPI: 44F palpable left breast mass.
  - MMG 2022- MRI rec'd for extremely dense breasts, BIRADS 0
- Imaging:
  - MMG– increased left breast calcs (5cm), BIRADS 4





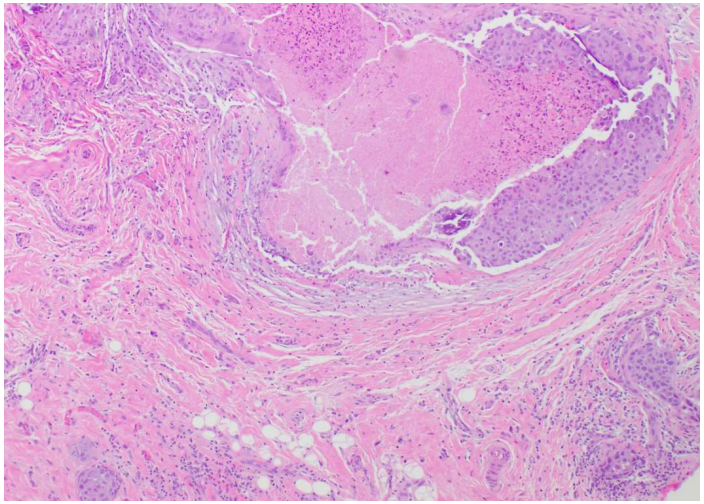


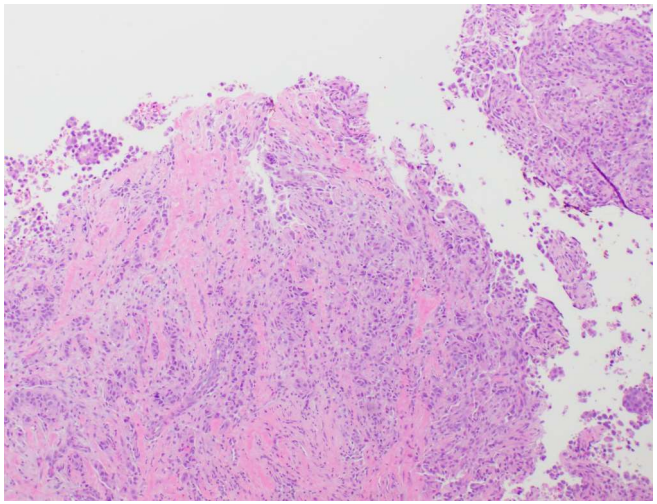
Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- Exam: 3cm palpable superior left breast mass
- Imaging:
  - Left breast U/S– 16x14x15mm mass 1:00 5CFN, BIRADS 4

Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

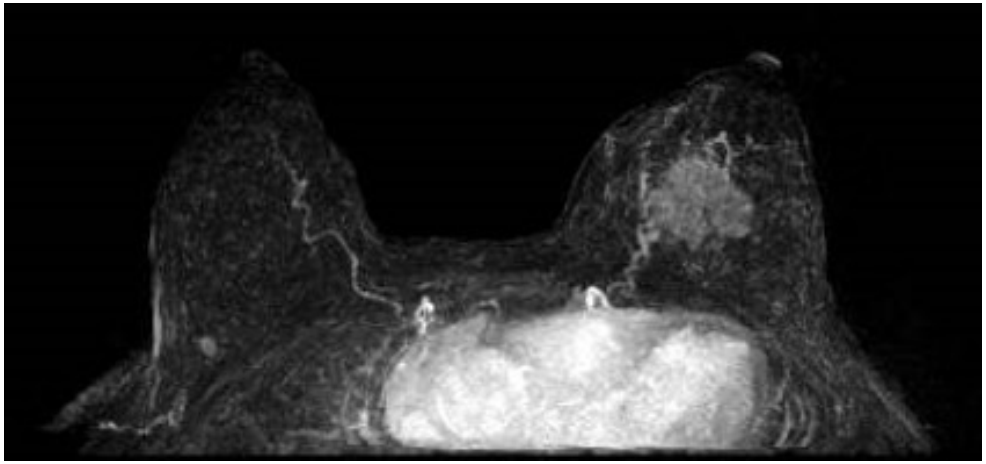
- Biopsy Pathology:
  - LEFT calcs-- IDC, G3, **ER-, PR-, HER2+;** DCIS G3 with calcs; +LVI; clinically T2N0M0 Stage IIA
  - LEFT mass– IDC, G3, **ER+ (20%), PR-, HER2+** (similar morphology)





Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

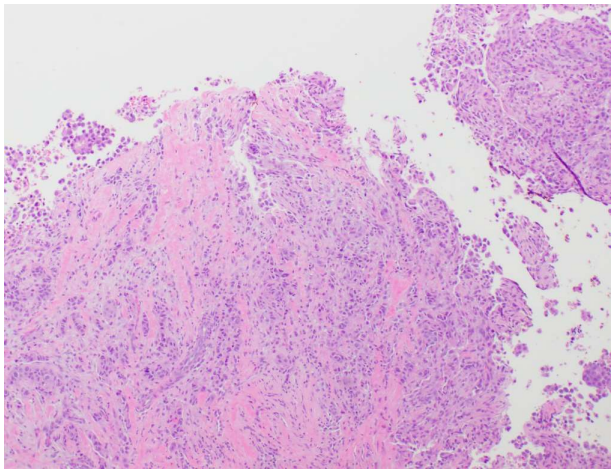
- Imaging:
  - Breast MRI– 33x30x44mm LEFT breast mass and 6x4mm RIGHT breast mass, BIRADS 4
  - Right breast U/S—10mm mass 10:00 6CFN



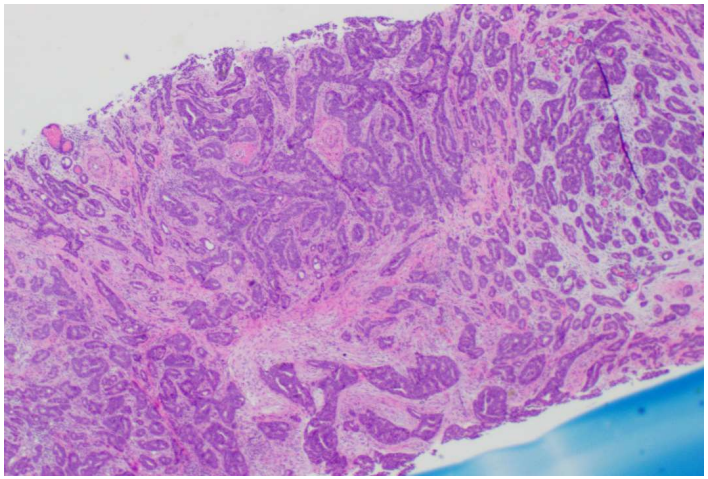
Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- Biopsy Pathology:
  - LEFT calcs-- IDC, G3, **ER-, PR-, HER2+;** DCIS G3 with calcs; +LVI; clinically T2N0M0 Stage IIA
  - LEFT mass– IDC, G3, **ER+ (20%), PR-, HER2+** (similar morphology)
  - RIGHT mass – IDC, G2, **ER+ (95%), PR+ (95%), Her2-** (FISH); DCIS G2; clinically T1bN0M0 Stage IA

LEFT

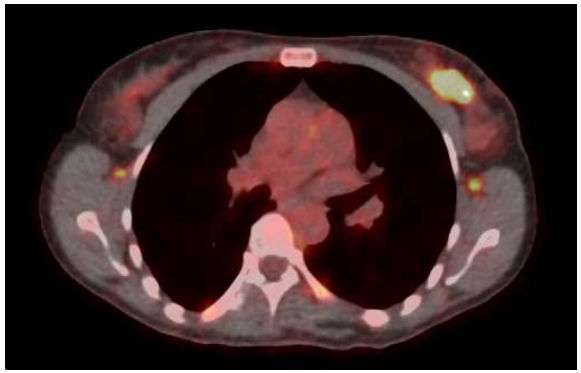


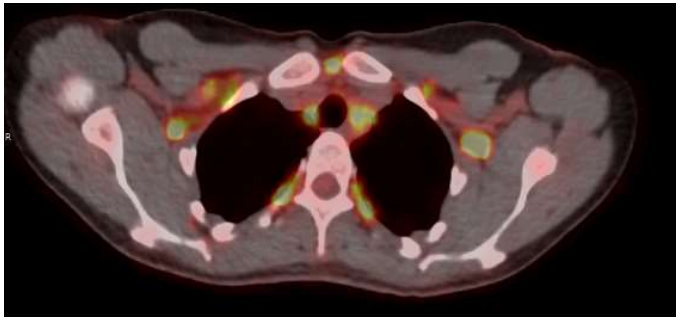
RIGHT

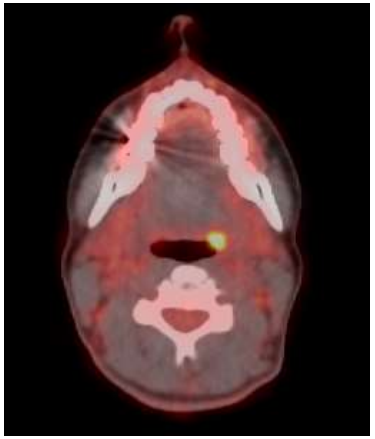


Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- PET/CT– hypermetabolic left breast mass; extensive brown fat neck/thorax
- 7mm uptake base of left tongue → ENT referral → flex laryngoscopy showed asymmetry → direct laryngoscopy with bx (pending)

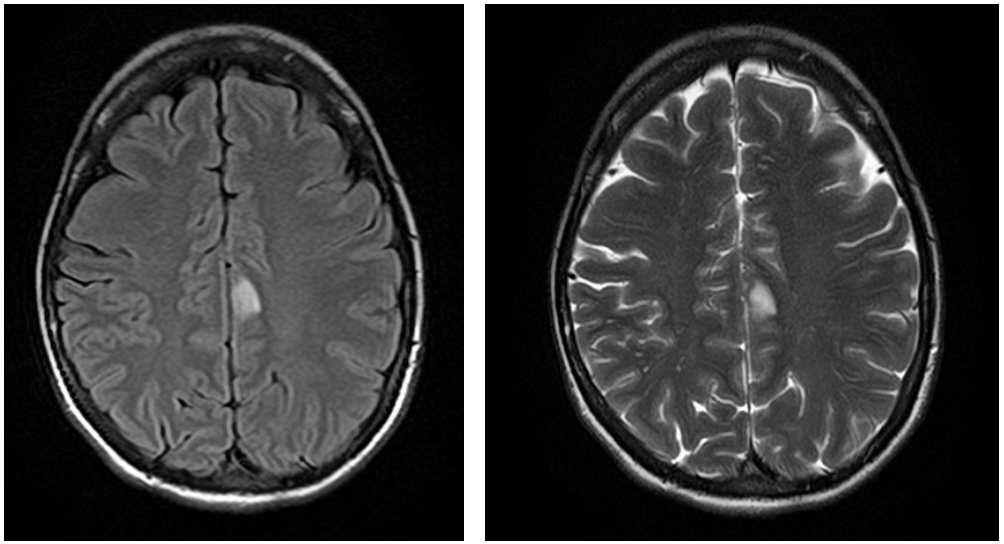






Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- Brain MRI- 14x7mm T2 hyperintensity w/o enhancement– glioma vs met vs inflammation
- → 3m repeat scan, Neuro referral (pending)



Neoadjuvant Systemic Therapy, Bilateral Breast Cancers

- Genetics: negative
- Treatment plan:
  - Neoadjuvant TCHP x6
  - Repeat Breast MRI → Surgery (BCT vs mastectomy)
  - +/- Adjuvant XRT
  - Adjuvant HPx1year, endocrine therapy

Bilateral Breast Cancer

- Incidence synchronous bilateral BC = 1-3%
  - Occur within 6m
- Incidence metachronous bilateral BC 5-6%
  - Occur >6m apart
- Most contralateral BC are considered an independent primary tumor, but a small subset may represent first site mets
- RF bilateral BC– family hx BC, young age, ILC, multicentric BC
- Prognosis typically considered worse OS than unilateral BC

Use of Preop Breast MRI

THE AMERICAN SOCIETY OF Breast Surgeons - Official Statement -

Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast

- Current ASBrS consensus guidelines do not recommend routine use of breast MRI in patients with newly diagnosed Breast Cancer:
- Does not reduce positive margin and re-excision rates with BCT, local recurrence, or overall survival
- MRI use may lead to "false-positive findings... increased ipsilateral and contralateral mastectomy rates and increased time to treatment…increased costs of care and…increased patient anxiety."

Recommendations for Preop MRI:

- Determining extent of cancer, multi-focal or multi-centric tumors, contralateral cancer
- Occult breast cancer in patients with Paget's disease or with axillary nodal metastasis
- Determining extent of disease in patients with BC dx and indeterminate imaging (ILC, extremely dense breasts, discrepancies in tumor size between imaging modalities)
- Assessment for eligibility and response to neoadjuvant therapy
  - After neoadjuvant chemotherapy (NAC), MRI has a sensitivity of 92% to detect residual disease and a specificity of 60% for pathologic complete response (pCR)

Neoadjuvant vs Adjuvant Systemic Therapy

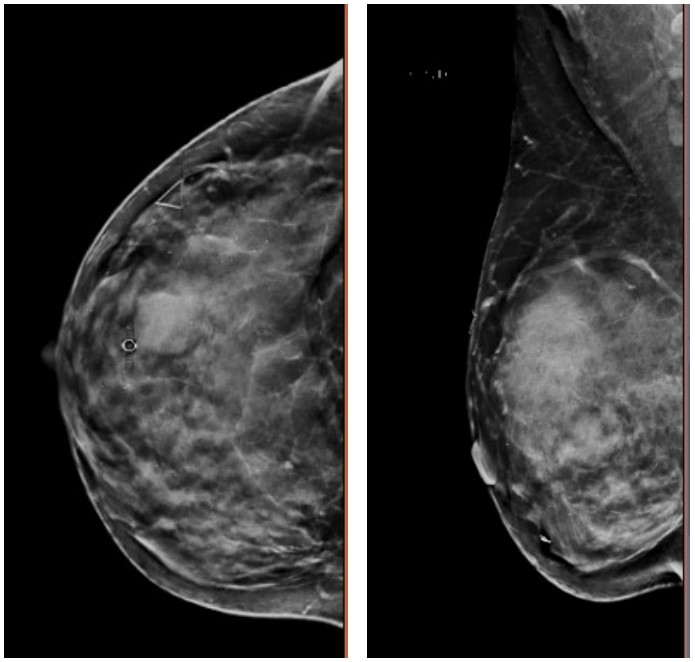
- Multiple trials have shown comparable survival between neoadjuvant and adjuvant systemic therapy
- Benefits of Neoadjuvant systemic therapy (NAC):
  - Downsizing tumor to increase eligibility for breast conservation, reduce extent of surgery
  - Downstaging of the axilla (avoid ALND and associated morbidity)
  - In vivo assessment of tumor response to treatment → can change therapy, opportunity for different adjuvant systemic immunotherapies
  - Halt spread/progression of disease
  - Potentially de-escalate adjuvant therapies (XRT) if PCR achieved

Neoadjuvant vs Adjuvant Systemic Therapy

- Neoadjuvant systemic therapy (NAC) is standard of care for Stage II/III HER2+ BC
- Path CR status used to individualize adjuvant systemic therapy
  - KATHERINE trial: NAC → TDM1 for residual CA on surgical path → 46% risk reduction, 34% improvement OS at 8yrs
  - PCR correlates with favorable outcomes
- No demonstrated survival benefit with NAC compared to adjuvant tx for early Stage I Her2+ BC
- Primary surgery considered for low tumor burden (T1N0) HER2+ BC
  - APT trial: <3cm, N0, Her2+ BC → adjuvant paclitaxel+trastuzamab →10yr DFS 91%, 10yr recurrence free interval 96%
  - APHINITY trial: adjuvant pertuzumab added to trastuzamab +chemo → improved DFS benefit esp for Node+ and hormone negative tumors

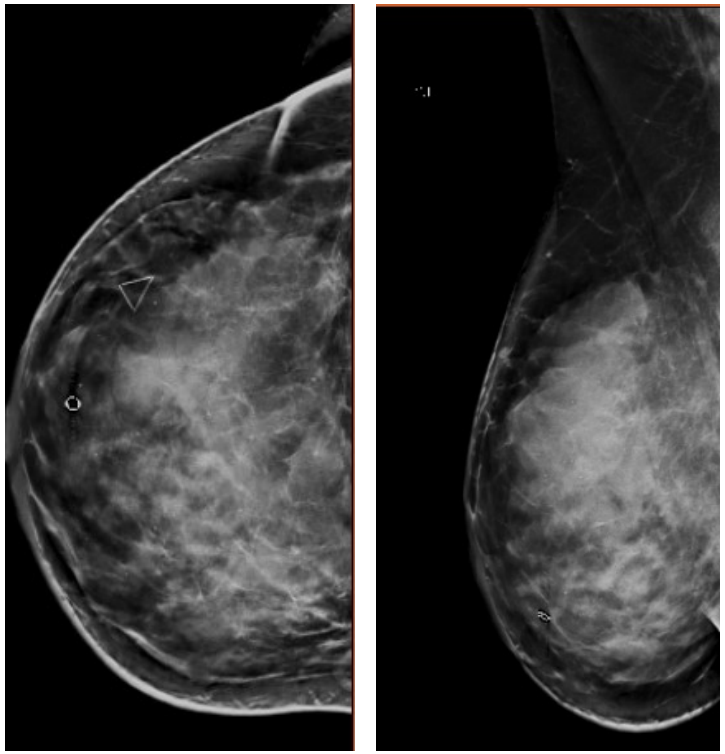
Neoadjuvant Systemic Therapy with Positive Axilla

- HPI: 50F increasing size palpable right breast mass in 8/2023.
  - Hx benign bilateral biopsies 2018 (FCD, cysts)
- Imaging:
  - MMG 3/2023– extremely dense breasts, ovoid right breast mass
  - Right breast U/S 3/2023– 27x12mm benign cyst at 9:00



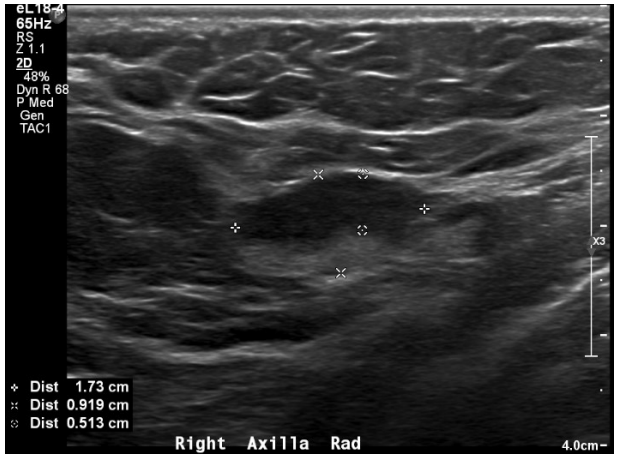
Neoadjuvant Systemic Therapy with Positive Axilla

- HPI: 50F increasing palpable right breast mass
  - 8/2023 Exam: >8cm firm mass superior right breast; skin erythema right LIQ; 2.5cm lipoma right lateral chest wall
- Imaging:
  - MMG 8/2023– increased density



Neoadjuvant Systemic Therapy with Positive Axilla

- Imaging:
  - Right Breast U/S 8/2023– 61x58x35mm suspicious mass, abnormal right axillary nodes

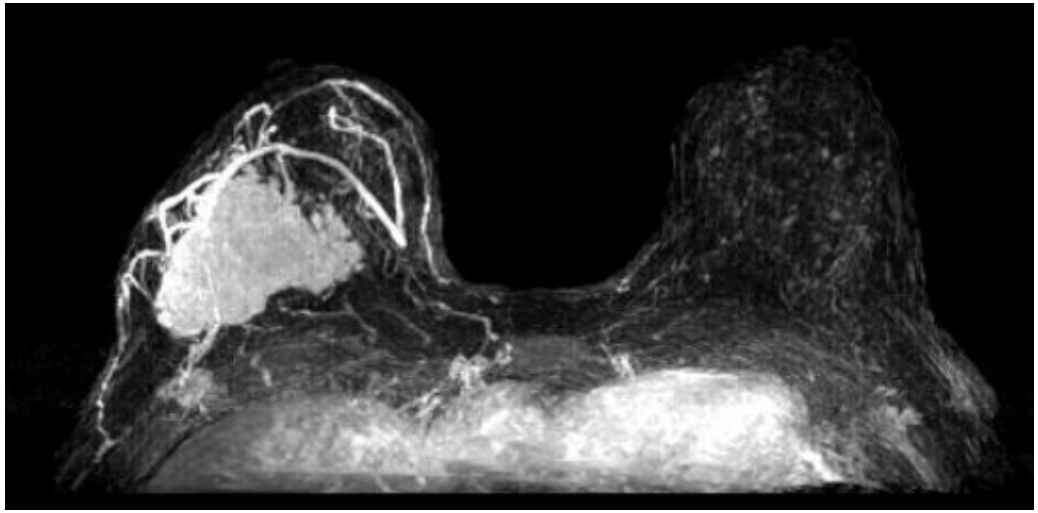


Neoadjuvant Systemic Therapy with Positive Axilla

- Biopsy Pathology:
  - LEFT mass– IDC, G3, **ER+ (90%), PR+ (50%), Her2+;** clinically T3N1M0, Stage IIB
  - LEFT axillary node– metastatic carcinoma, +ENE

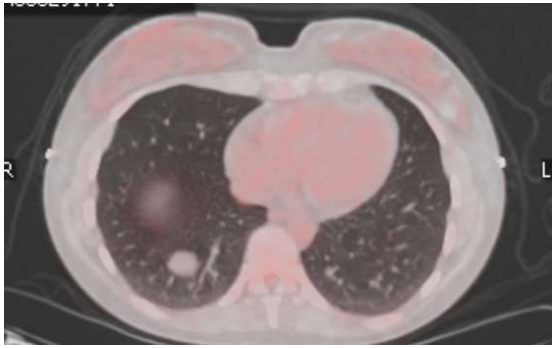
Neoadjuvant Systemic Therapy with Positive Axilla

- Imaging:
  - Breast MRI– 69x51x66mm right breast mass; 6x4mm mass LOQ right breast-intramammary node; abnormal right axillary nodes; skin thickening



Neoadjuvant Systemic Therapy with Positive Axilla

- PET/CT– hypermetabolic right breast mass and axillary nodes; scattered pulmonary nodules, left upper abdomen soft tissue nodule



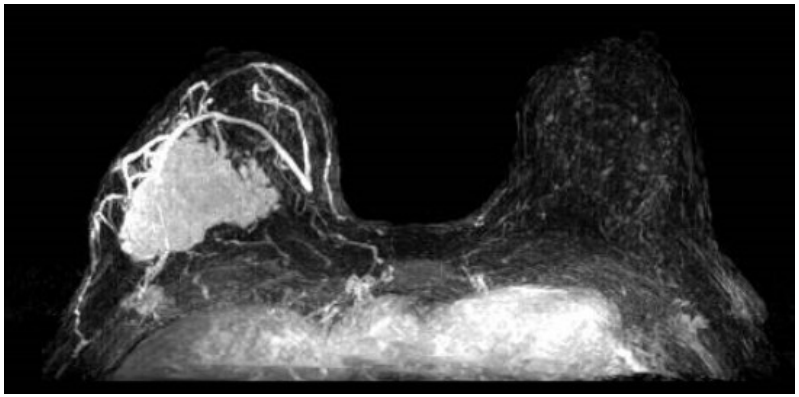
Neoadjuvant Systemic Therapy with Positive Axilla

- Systemic Imaging workup:
  - CT Abdomen/pelvis- ovarian cyst; negative for mets
  - CT Chest– numerous bilateral pulmonary nodules (5-10mm size)
  - MRI Tspine and MRI brain– negative
  - CT guided Right Lung biopsy: negative for malignancy
    - f/up CT Chest 5m– stable nodules, 6m f/up scan rec'd

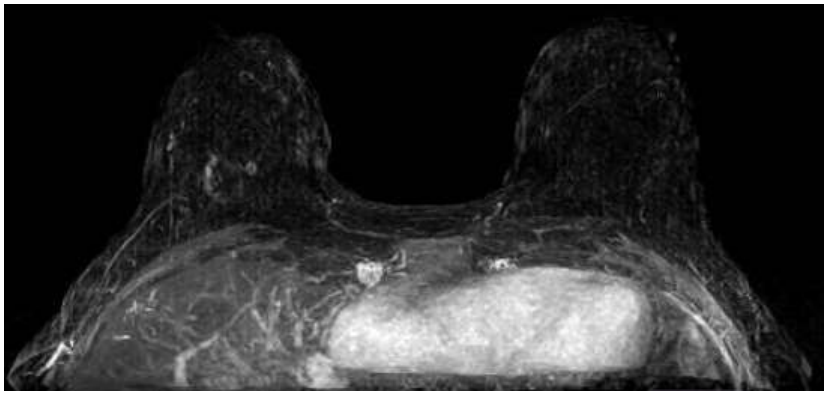
Neoadjuvant Systemic Therapy with Positive Axilla

- Genetics: negative
- Treatment plan:
  - Neoadjuvant TCHP x6
  - Post-treatment Breast MRI– resolution of large right enhancing mass, normal axillary nodes, stable right LOQ mass/node mass

Before



After

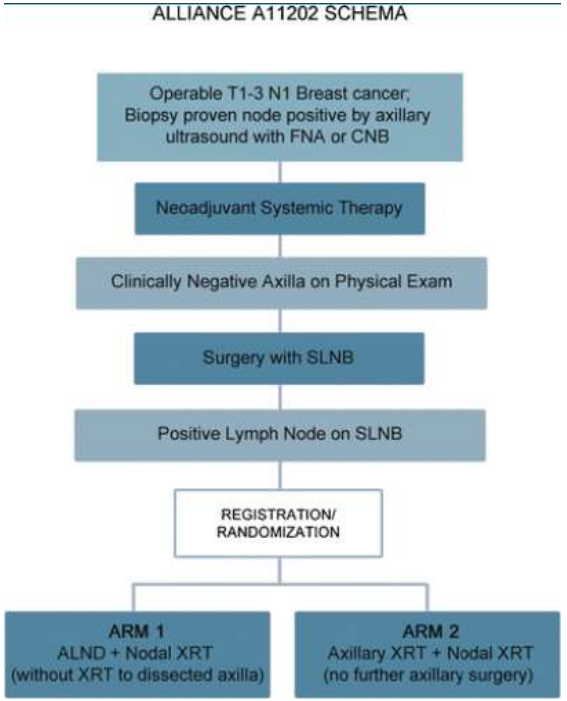


Neoadjuvant Systemic Therapy with Positive Axilla

- Treatment plan:
  - Right skin sparing mastectomy with implant reconstruction, R SLNB/TAD, Axillary reverse mapping (ARM)
    - Path: No residual malignancy in breast; no tumor in 3 SLN; **ypT0N0M0**
  - Adjuvant XRT- 28fx right chest and regional nodal XRT
  - Adjuvant trastuzamab/pertuzamab x1year, tamoxifen

Axillary Management after NAC

- Targeted Axillary Dissection (TAD)
  - After NAC , ~40-70% of patients with cN1 breast cancer will have a pathologic complete response (pCR) in the axilla
  - Targeted axillary dissection (TAD)= SLNB + removal of previously biopsied positive node
  - If nodes are negative post-chemo, no further axillary surgery needed
  - False negative rate of TAD 2.0%; FNR with removal of clipped node alone 4%
- For Positive residual nodal disease after NAC/Positive TAD → Completion ALND (cALND) is standard of care
  - Alliance A11202 trial: evaluating ALND+Regional nodal XRT vs XRT with omission of ALND in cN1 patients with positive residual nodal disease after neoadjuvant chemotherapy



Axillary Management after NAC

Clipping the Positive Lymph Node in Patients with Clinically Node Positive Breast Cancer Treated with Neoadjuvant Chemotherapy: Impact on Axillary Surgery in the ISPY-2 Clinical Trial

Kayla Switalla, B.S., Judy C. Boughey, M.D., Katrina Dimitroff, M.P.H, Christina Yau, PhD, Velle Ladores, B.S, Hongmei Yu, PhD; Mehra Golshan, M.D., M.B.A., Gretchen Ahrendt, M.D., Mara Piltin, D.O., Anne M. Wallace, M.D., M.S., Cindy B. Matsen, MD, MSci, Todd Tuttle, M.D., Cletus A. Arciero, M.D., M.S., Marissa Howard-McNatt, M.D., Jennifer Son, M.D., Chantal R. Reyna, M.D., Marie C. Lee, M.D., Julia Tchou, M.D., PhD., Roshni Rao, M.D., Candice Sauder, M.D., Jennifer Tseng, M.D., Nora Jaskowiak, M.D., Arpana Naik, M.D., Rachael Lancaster, M.D., Lauren M. Postlewait, M.D., Ian Greenwalt, M.D., Kelly Hewitt, M.D., Ayemoethu Ma, M.D., Peter Norwood, PhD, Laura Esserman, M.D., M.B.A, ISPY2 Locoregional Working Group, Rita A. Mukhtar, M.D.

Inclusion criteria:

- Patients enrolled in ISPY-2 who were **cN+ in the axilla**
- Underwent NAC and surgery between 01/2011 and 12/2021

Compared two groups:

Patients with **clip** in lymph node
versus
Patients **without clip** in lymph node

Statistical analyses:

- ISPY-2 Trial Results:

Clipped node cohort, compared to the no clipped node cohort, had…

Higher odds for **SLN +/- TAD only** surgery

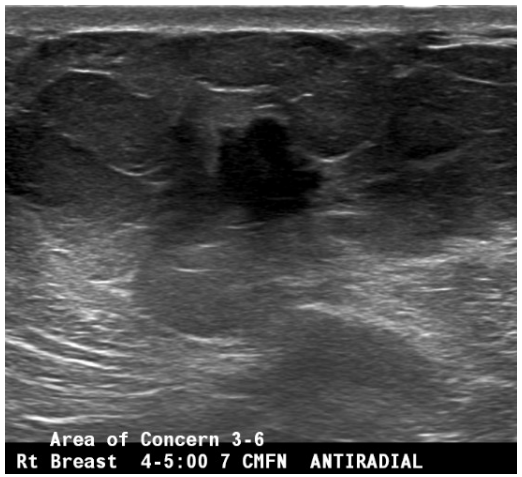
Comparable **FNR** for SLN/TAD surgery

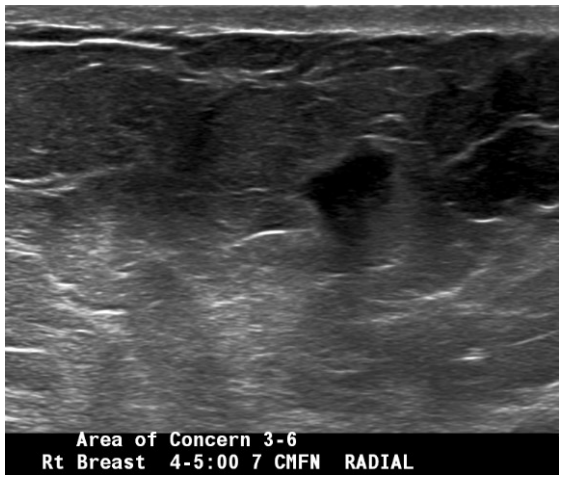
Comparable **EFS**

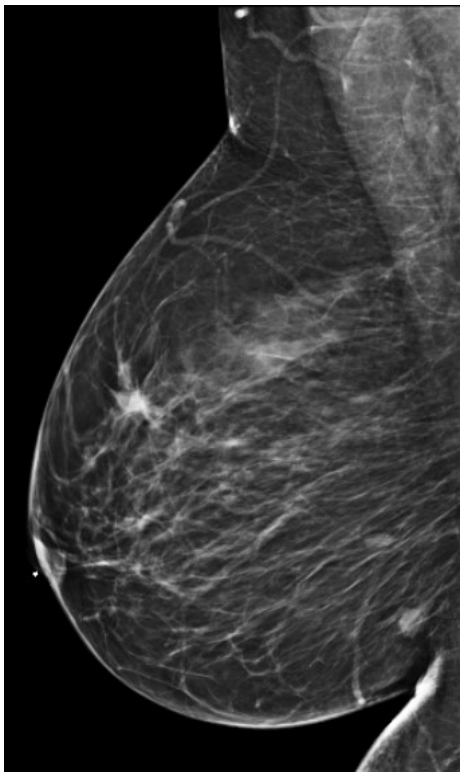
Conclusion:
Clipping the positive lymph node is associated with potential benefit without demonstrated harm and should be recommended

NAC for TNBC and Positive Axilla

- HPI: 49F imaging detected right breast cancer
- Imaging:
  - MMG – new focal asymmetry right breast
  - Right breast U/S—8 x4x10mm mass 5:00 7CFN, BIRADS 4







NAC for TNBC and Positive Axilla

- HPI: 49F imaging detected right breast cancer
  - Exam: no palpable findings right breast; +right axillary mass/adenopathy
- Imaging:
  - U/S right axilla– enlarged axillary node, BIRADS 4

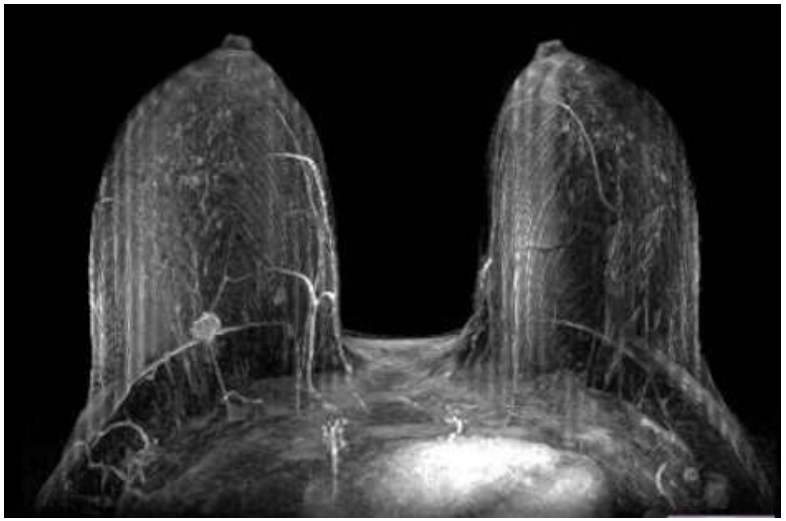
NAC for TNBC and Positive Axilla

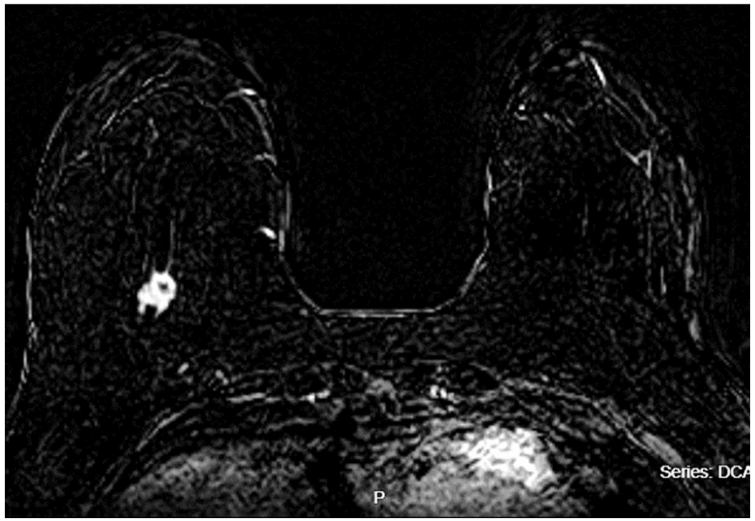
- Biopsy Pathology:
  - RIGHT mass– IDC, G3, **ER-, PR-, Her2-, (TNBC);** clinically T1cN1M0, Stage IIB
  - RIGHT axillary node– metastatic carcinoma

- Staging Workup:
  - CT Chest/Abdomen/Pelvis – bilateral noncalcified pulmonary nodules (largest 6mm); no definite metastatic disease
  - Nuclear medicine bone scan– negative

NAC for TNBC and Positive Axilla

- Imaging:
  - Breast MRI– 19x16mm mass right breast, biopsy changes right axilla





NAC for TNBC and Positive Axilla

- Genetics: negative
- Treatment plan:
  - Neoadjuvant carbo/taxol/pembrolizumab x4, AC/pembrolizumab x4 (Keynote regimen)
  - Post-treatment Breast U/S– decreased residual mass (3x2x5mm), normal appearing axillary node

NAC for TNBC and Positive Axilla

- Treatment plan:
  - Right partial mastectomy, R SLNB/TAD, ARM
    - Path: No residual malignancy in breast; no tumor in 3 SLN and 1 intramammary node; **ypT0N0M0**
  - Adjuvant XRT- 28fx right chest and regional nodal XRT
  - Adjuvant pembro (patient no show/cx medical oncology appts)

Immunotherapy for TNBC

- KEYNOTE 522 trial– Stage II/III TNBC
  - NAC with 4 cycles paclitaxel/carboplatin +/- pembrolizumab, then 4 cycles doxorubicin/cyclophosphamide +/- pembro
  - Surgery then adjuvant pembro vs placebo up to 9 cycles
  - 64.8% PCR in pembro/chemo group vs 51.2% placebo
  - After median 15m f/up, 7.4% vs 11.8% (placebo) with local or distant recurrence or mortality

- CREATE-X trial—residual Her2- BC after NAC
  - Standard postsurgical tx +/- capecitabine
  - Most benefit in TNBC group --DFS was 69% (cap) vs 56% (placebo) and OS 78% vs 70%

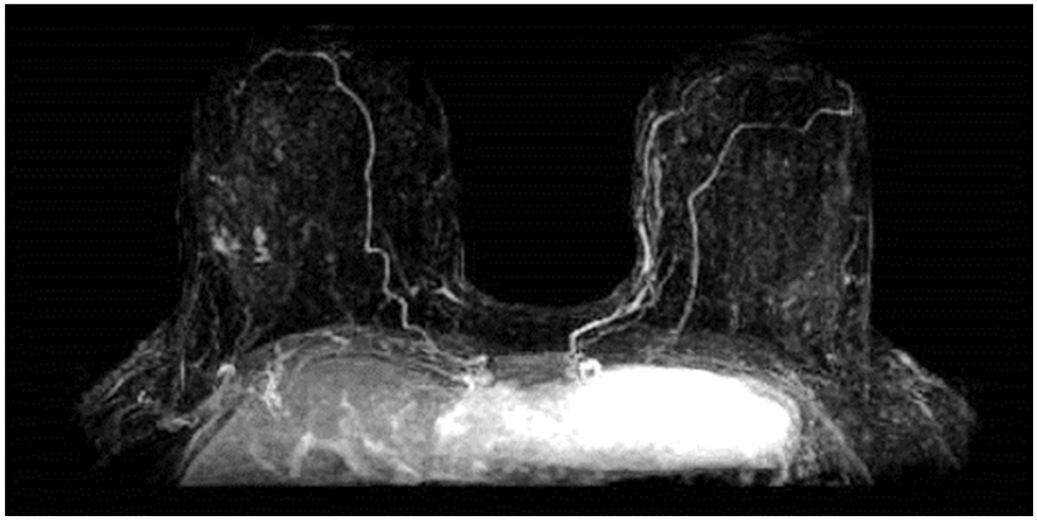
XRT in the cN1 axilla converted to ypN0

- NSABP B-51trial– does regional nodal XRT reduce recurrence?
  - Phase III study, cT1-T3 tumors, N1 pts → NAC → breast and axillary surgery
  - No residual nodal disease → BCT + WBXRT +/- RNI; Mastectomy +/- chest wall and RNI
  - At median 6yr f/up, addition of RNI did not improve 5yr LRR, DFS, OS

- ALLIANCE 11202 trial– ALND vs nodal XRT for residual nodal disease
  - cT1-T3 tumors, N1 → NAC → BCT or Mastectomy
  - Positive residual nodal disease (+SLNB) → ALND + RNI vs RNI only
  - Study ongoing, results pending

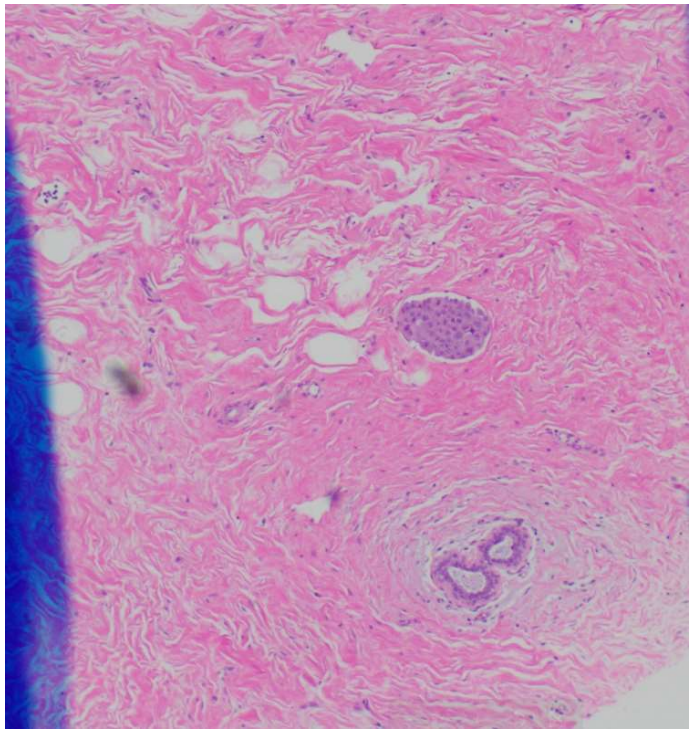
Breast Cancer in Young Patients

- HPI: 27F abnormal screening imaging
  - BRCA2 mutation dx 2021
  - Baseline breast MRI at 25; had right breast bx 2021- FCD, PASH
  - Pregnancy at 26, no imaging in 2022, brief breastfeeding
  - Breast MRI 1/2023- BIRADS 2
- Imaging:
  - Breast MRI 2/24- Right breast clumped non-mass enhancement 1.4 x 0.6cm, BIRADS 4



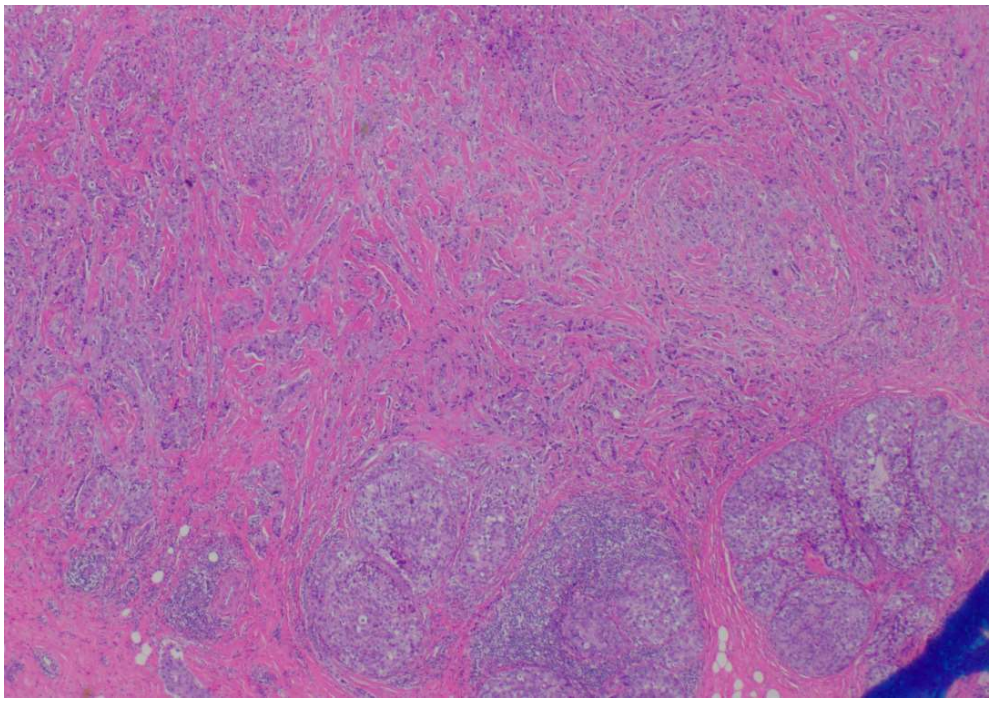
Breast Cancer in Young Patients

- Biopsy Pathology:
  - Right breast– Rare cluster atypical epithelial cells within lymphovascular spaces, consistent with LVI of tumor
- Treatment plan:
  - Right partial mastectomy + right SLNB, bilateral oncoplastic reductions 4/2024



Breast Cancer in Young Patients

- Surgical Pathology:
  - Right breast– IDC G3, 12mm, +LVI (extensive), DCIS G3, 2cm, + EIC; **ER+ PR+ Her2-**; pT1cN0M0
  - Positive margins for invasive tumor
  - 0/1 LN negative



Breast Cancer in Young Patients

- Treatment plan:
  - High Oncotype score (33)
  - Declined fertility consultation/egg retrieval
  - Adjuvant chemotherapy-- ddACT
  - 2nd stage surgery with bilateral completion mastectomy, reconstruction (pending)
  - Adjuvant endocrine therapy/OS (pending)

Considerations for Breast Cancer in Young Patients

- Of >310,000 estimated new breast cancers diagnosed in 2024…
  - Median age of Dx is 63
  - 4% new cancers are < 40yrs old
  - Breast cancer is most common cancer b/w ages 15-39
  - >12,000 women <40yrs were Dx with BC in 2020
  - Younger patients are more likely to be Dx at later stage and with more aggressive tumor subtypes (TNBC, HER2+)

- Long term effects of BC Treatment:
  - Cognitive dysfunction ("chemo brain")
  - Cardiotoxicity from high dose anthracyclines and XRT
  - Financial toxicity
    - Younger age and lower income significant predictors of financial distress

Considerations for Breast Cancer in Young Patients

- Fertility preservation/pregnancy after treatment
  - Pregnancy rate after breast cancer treatment is 40% lower than general population
  - Chemotherapy and antihormonal therapy can contribute to infertility and increased risk premature ovarian failure
  - Advised to wait at least 2 yrs after treatment before trying to get pregnant
  - Interruption of endocrine therapy up to 2 years appears to be safe

Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer

Authors: Ann H. Partridge, M.D., M.P.H., Samuel M. Niman, M.S., Monica Ruggeri, Fedro A. Peccatori, M.D., Ph.D., Hatem A. Azim, Jr., M.D., Ph.D., Marco Colleoni, M.D., Cristina Saura, M.D., Ph.D., +33, for the POSITIVE Trial Collaborators† Author Info & Affiliations

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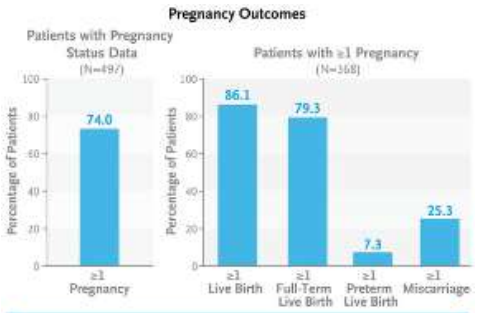


CONCLUSIONS

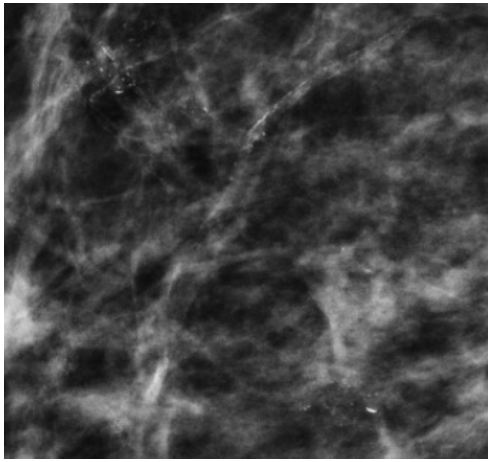
Among women with hormone receptor–positive early breast cancer who wished to attempt pregnancy, interruption of adjuvant endocrine therapy for up to 2 years appeared to be safe with respect to breast cancer recurrence during a median of 3.4 years of follow-up.

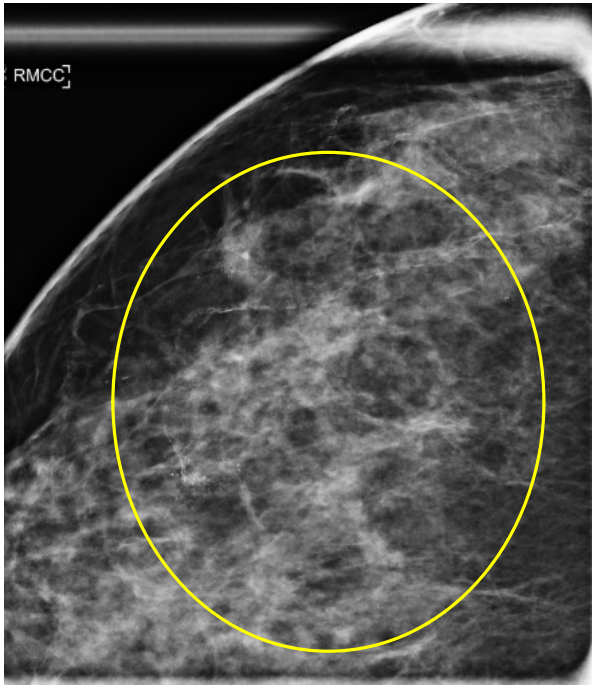
Considerations for Breast Cancer in Young Patients

- Breastfeeding after BC
  - 2 international studies from ESMO 2024
  - Breastfeeding after Breast Cancer in BRCA mutation carriers—4732 pts, 659 pregnancies, 474 deliveries; 23% breastfed
    - No difference in local recurrence, DFS, or OS in Pts who breastfed after cancer tx
  - POSITIVE study—518 women with HR+ BC who temporarily interrupted their breast cancer treatment to have a baby; 317 had at least one live birth and 62% breastfed.
    - No increased BC related events after 3 yrs; longer f/up needed

Multifocal disease with BCT

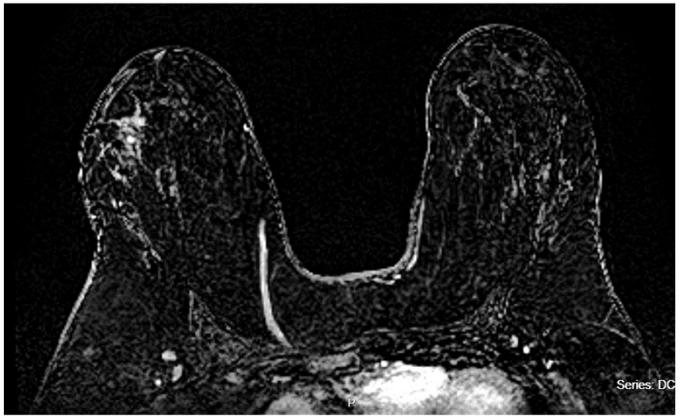
- HPI: 46F imaging detected right BC
- Imaging:
  - MMG 7/2023– at least 3 groups calcifications UOQ Right breast, >7cm

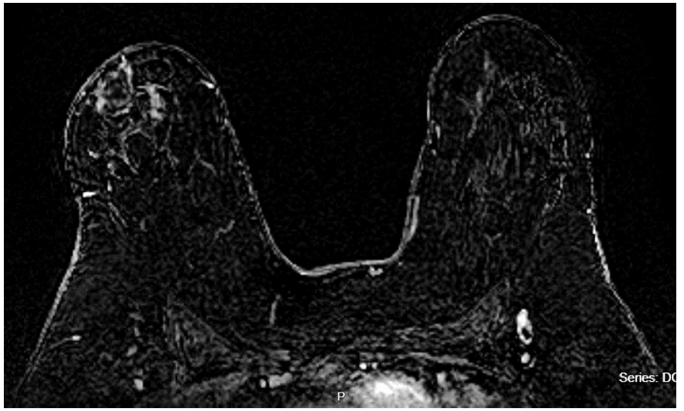




Multifocal disease with BCT

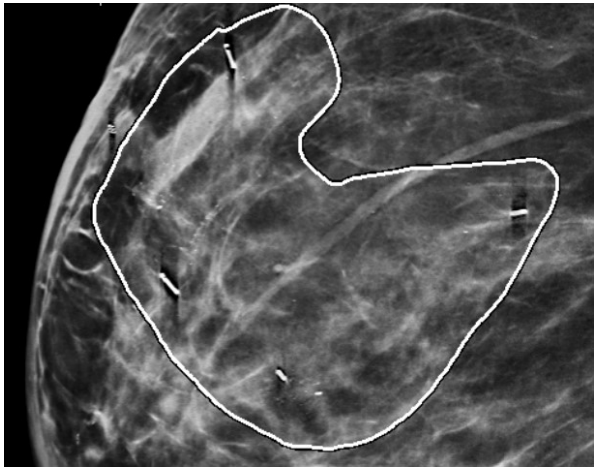
- Biopsy Pathology:
  - RIGHT calcifications—DCIS G2/3, ER+, suspicious for LVI; clinically TisN0M0, Stage 0
- Imaging:
  - Breast MRI 8/23- nonmass enhancement 2.9cm at bx site right UOQ; 2.2cm enhancement 10:00; 2.0cm enhancement 9:00; these correlate with areas of calcifications on MMG

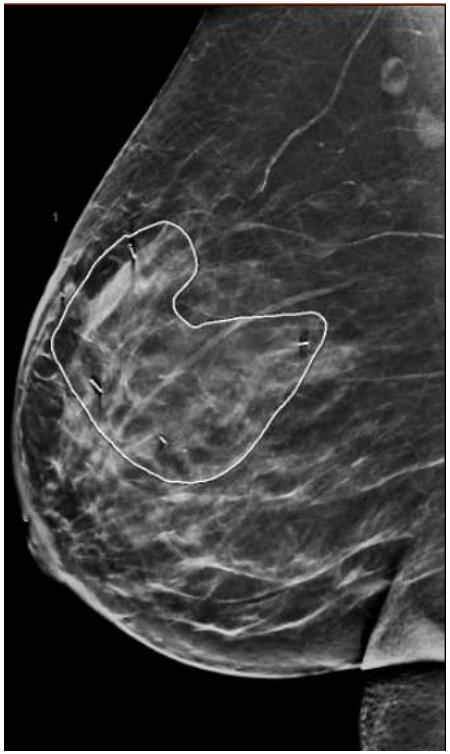




Multifocal disease with BCT

- Genetics: negative
- Treatment plan:
  - 9/2023 Right partial mastectomy with seed localization x4, Right SLNB, bilateral oncoplastic reductions





Multifocal disease with BCT

- Surgical Pathology:
  - **DCIS G2/3, >7cm**, ER+, **focally positive lateral margin**, close (<2mm) additional margins, 0/3LN, pTisN0M0
- Treatment plan:
  - 11/23 Bilateral nipple skin sparing mastectomy with implant reconstruction
- Surgical Pathology:
  - RIGHT breast—residual DCIS G2, 1.5cm, ER+, negative margins; pTisN0M0, Stage 0
- No other adjuvant treatments recommended

Multifocal Disease and BCT

- Multifocal (same quadrant)/multicentric (different quadrants) BC has previously been considered a contraindication to BCT
  - Incidence of multifocal/multicentric (M/M) disease is 6→60%
- BRENDA study– 17centers, 8935pts → No diff in OS or DFS b/w M/M vs unifocal disease in BCT vs mastectomy when correcting for stage and nodal status
- MINDACT study– 3090pts clinically low risk; multifocal tumors more like to have higher genomic risk profile vs unifocal tumor, but no diff in DFS
- ACOSOG Z11102 trial with BCT in M/M breast cancer → prelim data showed 2/3 of pts with BCT achieved negative margins at the first operation. Although the remaining third required further surgery, the conversion rate to mastectomy was only 7.1%.

Multifocal Disease and BCT

- Changes in clinical practice:
  - Increased oncoplastic surgery/better surgical technique
  - Neoadjuvant treatments for tumor downstaging
  - Enhanced breast imaging (MRI)
  - Non-wire localizing devices
  - Need prospective data on XRT for boost and tumor bed marking with oncoplastics

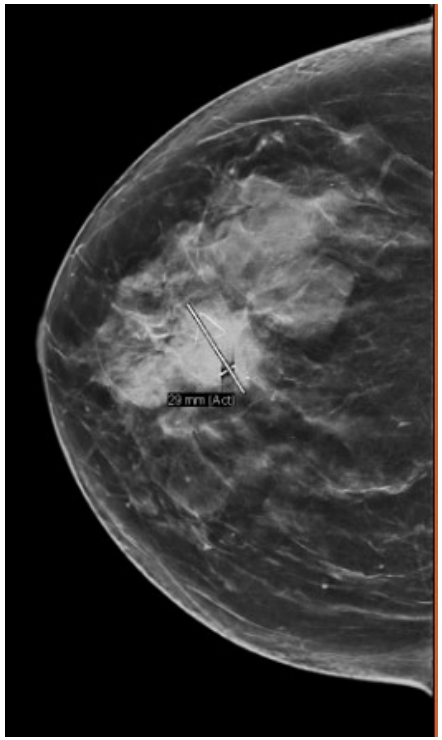
- Current evidence suggests BCT is safe for multifocal multicentric breast cancer (when technically feasible and provided that acceptable cosmetic results can be achieved).

Cancer Pathologic Upgrade

- HPI: 64F with palpable right breast mass
  - Noted mass 1 yr ago, occasional pain, stable size per Pt
  - Hx bilateral benign breast bx 2015
  - Hx multiple bilateral cysts
  - Last MMG 2016
  - Clinical exam: Right breast 4cm mass at 6:00, contour deformity

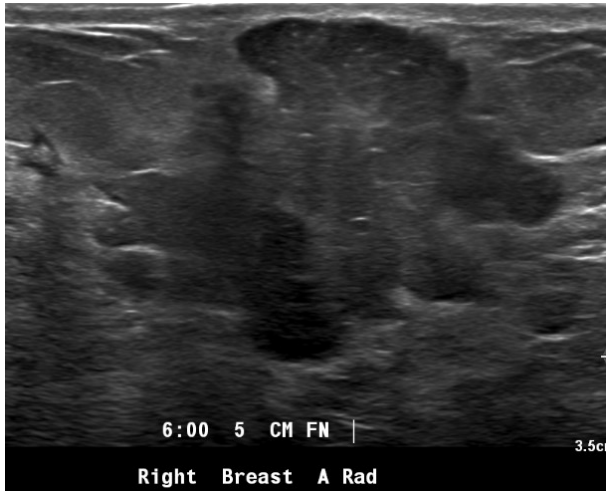
Cancer Pathologic Upgrade

- Imaging:
  - MMG 8/2024– spiculated mass at 6:00, BIRADS 5



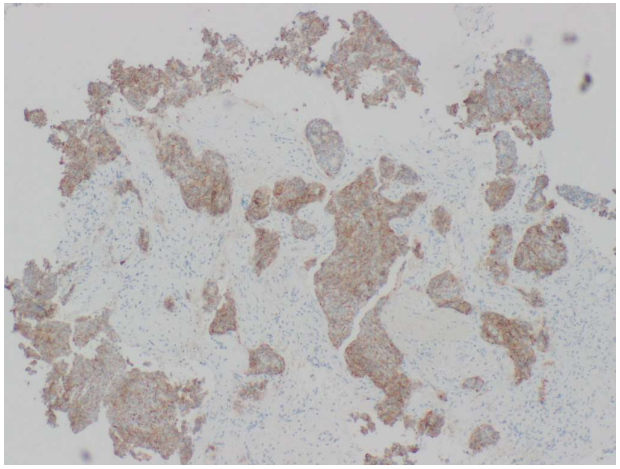
Cancer Pathologic Upgrade

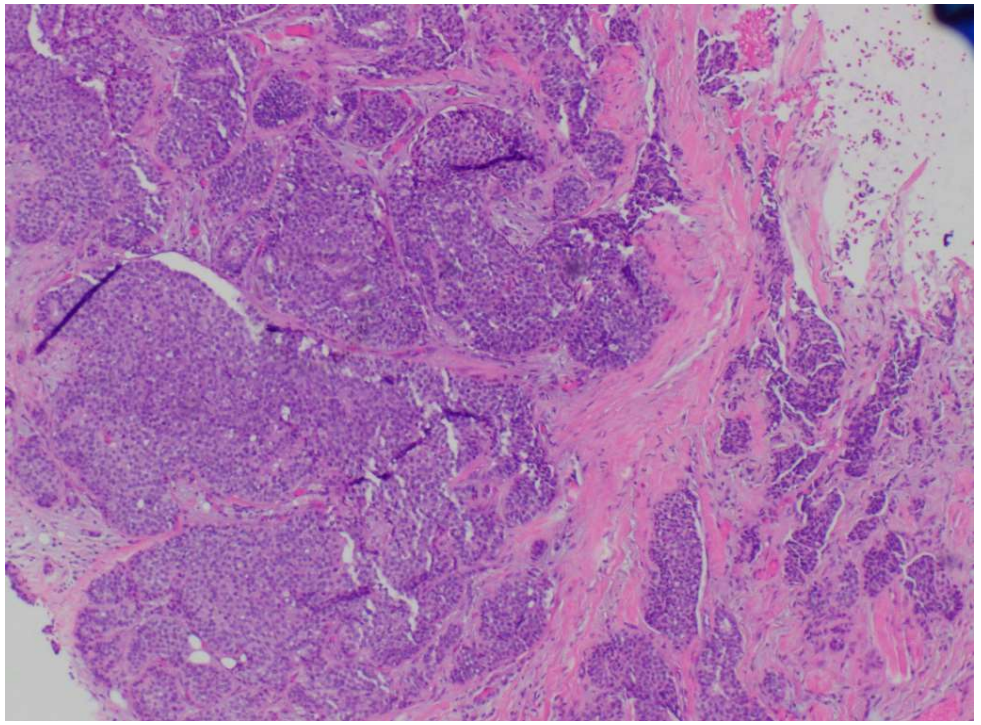
- Imaging:
  - Right breast U/S– 3.5x2.7x3.9cm lobulated heterogenous mass, extends to skin; right axilla negative, BIRADS 5



Cancer Pathologic Upgrade

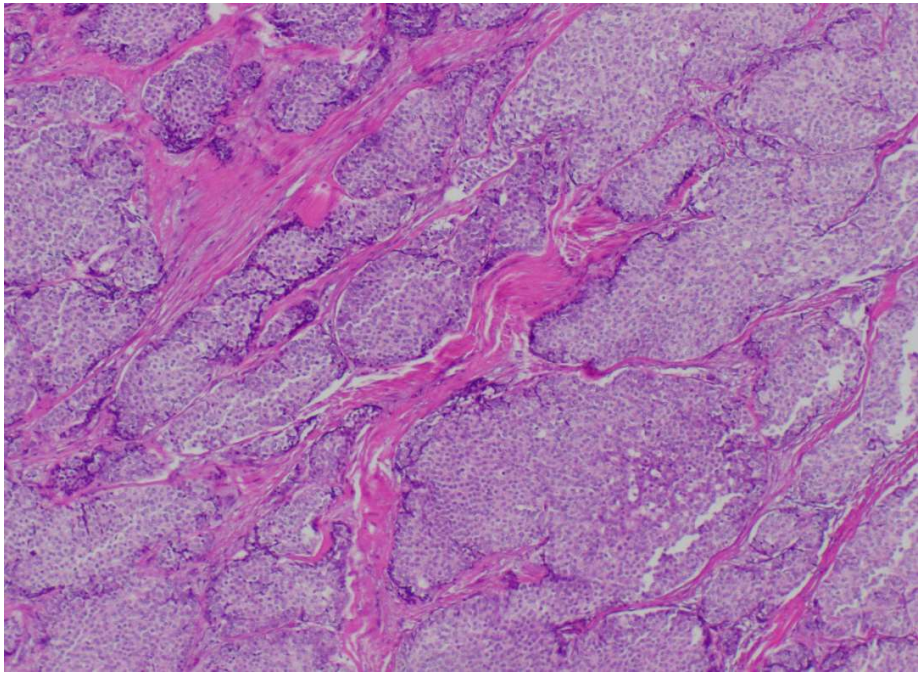
- Biopsy Pathology:
  - RIGHT mass—**solid papillary carcinoma (DCIS equivalent),**suspicious for invasion, **ER+ PR+ HER2+**, at least TisN0M0, Stage 0





Cancer Pathologic Upgrade

- Genetics: declined
- Treatment plan: right simple mastectomy, right SLNB, no recon
- Surgical Pathology:
  - RIGHT breast—**invasive solid papillary carcinoma**, G2, 3.5cm, 0/9LN, **ER+ PR+HER2-**; pT2N0M0, Stage IA
- Treatment plan:
  - Oncotype
  - Adjuvant endocrine therapy



Tumor Heterogeneity/Path Upgrade

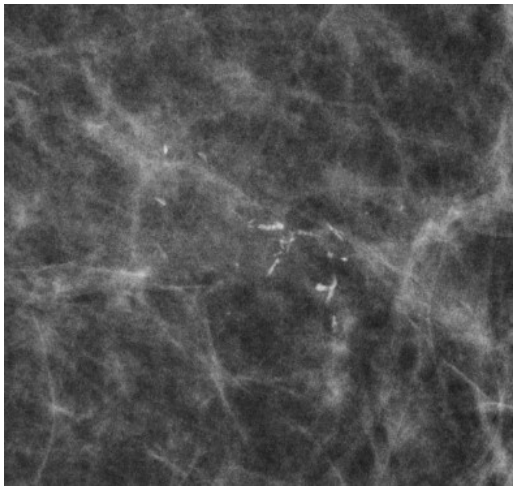
- DCIS → Invasive cancer upgrade rates vary widely in literature
- Estimated 25-60% of untreated DCIS will progress to IDC
- Retrospective study 143 Pts with DCIS and mastectomy; 24.5% upgrade to IDC on surg path
  - Multifocality was predictor for upgrade
  - Positive SLNB 4.8%
- Intertumor heterogeneity includes intratumor cell populations with different characteristic including tumorigenicity, treatment resistance, and metastatic potential
  - Biomarker, grade, and tumor subtype heterogeneity
  - Discrepant HER2 IHC results ranges from 1 to >50%
  - Spatial heterogeneity between breast primary tumor and nodal metastasis

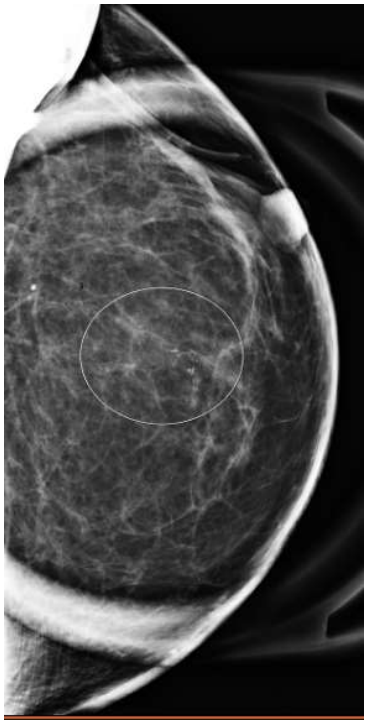
Bilateral Breast Cancer, Re-irradiation

- HPI: 52F with new imaging detected LEFT breast cancer
  - Hx RIGHT BC 2019– IDC, ER+PR+ HER2- pT1cN0M0
    - Partial mastectomy, R SLNB, WBXRT, tamoxifen
  - Hx LEFT BC 2020—DCIS ER+ PR- (LOQ)
    - Partial mastectomy x3 for positive margins, WBXRT +boost
  - Genetics negative
  - Exam: Left breast lateral lumpectomy incision with soft tissue/volume loss and contour deformity in LOQ, skin telangiectasias lateral breast

Bilateral Breast Cancers, Re-irradiation

- Imaging:
  - MMG 5/2024– new LEFT breast pleomorphic linear branching calcifications (UIQ), 15mm, BIRADS 4

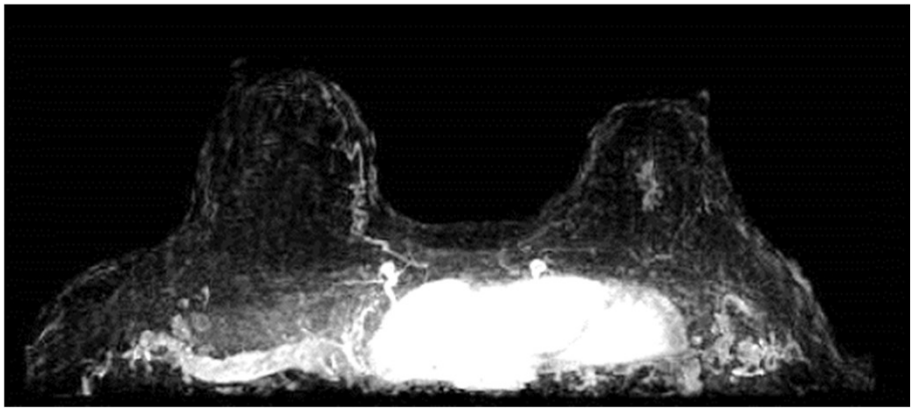




Bilateral Breast Cancers, Re-irradiation

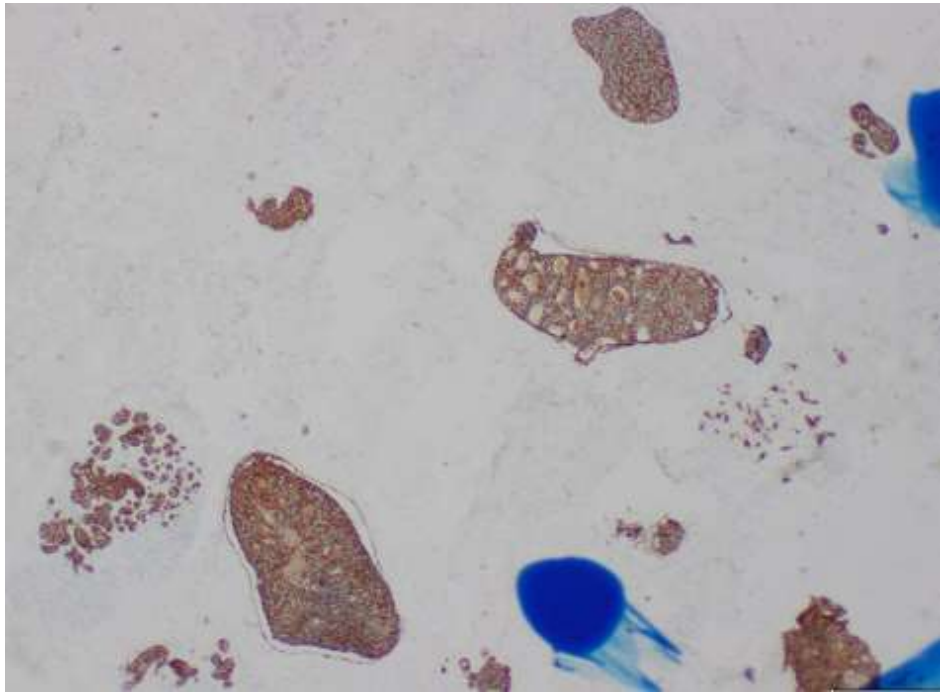
- Biopsy Pathology:
  - LEFT calcifications—**DCIS**, G2, **ER+ PR+,** clinically TisN0M0 Stage 0

- Imaging:
  - Breast MRI 8/24—clumped non-mass enhancement 2.5x1.5cm UIQ



Bilateral Breast Cancers, Re-irradiation

- Treatment plan: LEFT partial mastectomy
- Surgical Pathology:
  - LEFT breast—**invasive ductal carcinoma**, G2, 12mm, in a background of extensive DCIS 2cm, +EIC, margins negative **ER+ PR-HER2+;** pT1cNxM0



Bilateral Breast Cancers, Re-irradiation

- Treatment plan: LEFT SLNB
- Surgical Pathology:
  - LEFT axilla—0/2 LN; pT1cN0M0, Stage IA
- Treatment plan:
  - Adjuvant chemo/HER2 therapy
  - ? Completion mastectomy
  - Adjuvant XRT
  - Adjuvant endocrine therapy

Re-Irradiation Feasabiltiy

NRG Oncology/RTOG 1014: Assess partial beam radiation after a second lumpectomy; Determine whether breast conserving treatment is an acceptable alternative to mastectomy

- In breast recurrence of DCIS or invasive disease > 1 year from prior treatment; <3cm size, unifocal
- ≤ 3 positive nodes, no ECE
- Excision Margins negative
- Defined lumpectomy cavity and lumpectomy cavity/ whole breast reference volume < 30% based on a postoperative pretreatment CT
- Treatment: 15Fxs (45Gy) with 3D conformal; Systemic therapy per medical oncologist
- Results:
  - 5% 5yr re-recurrence; 10% underwent mastectomy
  - 95% OS and distant metastasis-free survival

***Based on best available retrospective and prospective data on ipsilateral recurrence following lumpectomy or lumpectomy with radiation:

- Salvage mastectomy and repeat lumpectomy are both valid options w/ equivalent survival
- Consider adjuvant radiation or re-irradiation
- Surgeons should mark excision cavity

Repeat Lumpectomy/ Re-Irradiation

Selection Criteria for Repeat Lumpectomy

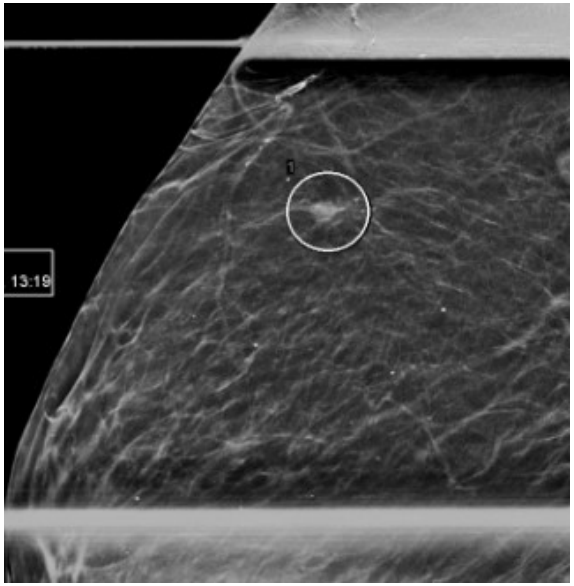
- <2cm, no fixation to skin or chest wall, clinically node negative, no significant RT changes.
  (Kurtz JM Ann Surg 198;207(3):347)
- DFS interval, size and histopathology of the recurrence have been shown to be independent prognostic factors of OS
  (Lee JH J Breast Cancer 2015;18(4):386)
- Small tumors (≤2cm), late (>48 months) *IBTR*
  (Gentilini O Breast J 2019;25(4):619)
- Pts ≥50, unifocal , small (<2-3cm), IBTR ≥48 months
  (Strahlentherapie and Onkologie.2016;192(4):199)
- Low risk recurrent cancers with favorable tumor biology (small, Luminal A) for which rRT may not be required or for IBTR >5 years after primary treatment (*Burstein HJ Ann Oncol 2021;32(10):1216*)
- IBTR <3cm DCIS or invasive, unicentric by MRI, no skin involvement, 0-3 +LN with no ECE (*Arthur DW. JAMA Oncol 2020;6(1):75-82*)
- Older patients (≥35), small tumors (<2cm), Hormone + tumors, longer DFI, absence of LVI (*Baek SY Cancer Control Vol 29:1*)

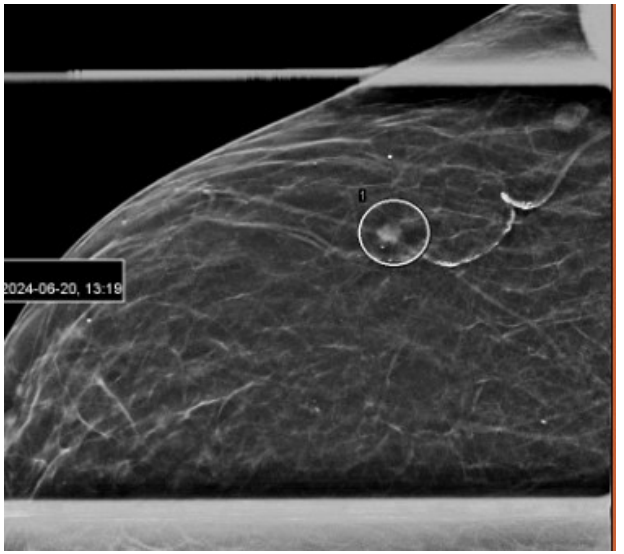
Conclusions:

- Repeat lumpectomy is feasible in selected patients with IBTR
- Negative metastatic workup up for all IBC
- Re-irradiation possible with minimal toxicity and acceptable cosmetic outcome
- Radiation should be offered to patients except for those that would have met criteria for avoidance of RT (low grade DCIS, age > 70 with early stage ER+ , Her2 – tumors)
- Re-irradiation should be offered to patients <70, TNBC, HER2+, poor prognostic criteria, Grade 3, +LVI

Breast Cancer in the Elderly

- HPI: 81yrF with imaging detected RIGHT breast cancer
  - Prior MMG 2021, normal
- Imaging:
  - MMG 6/2024– persistent nodularity UOQ right breast with spiculated margins





Breast Cancer in the Elderly

- Imaging:
  - Right breast U/S 6/2024– hypoechoic lesion 4x5x4mm at 10:00, 13CFN, BIRADS 4

Breast Cancer in the Elderly

- Biopsy Pathology:
  - RIGHT breast mass—IDC G2, **ER+ PR+, HER2-,** clinically **T1aN0M0** Stage IA
- Genetics: negative (VUS in BRIP1, POLE)
- Treatment Plan:
  - Cardiac clearance/heart cath
  - Right partial mastectomy with seed localization

Breast Cancer in the Elderly

- Surgical Pathology:
  - RIGHT breast— residual IDC (2mm), margins negative, **ER+ PR+ HER2-;** pT1aNxM0

- Treatment plan:
  - Adjuvant XRT
  - Endocrine therapy (declined)

Omitting Axillary Surgery in Low Risk Postmenopausal Patients

- SOUND trial
  - IBC, <2cm, clinically N0, negative axillary U/S
  - median age 60; 87% ER+Her2-
  - BCT → SLNB or no SLNB (>90% had XRT and ET); + SLNB 13.7%
  - No difference axillary recurrence, LRR, DFS

Outcome	No Ax Surgery (n=697)	SLNB (n=708)
Distant Disease-free Survival	98%	97.7%
Cumulative Axillary Recurrence	0.4%	0.4%
Disease-free Survival (5 yr.)	93.9%	94.7%
Overall Survival	98.4%	98.2%
Death from Breast Cancer	0.6%	1%

Implementation of *Choosing Wisely* guidelines: Omission of lymph node surgery

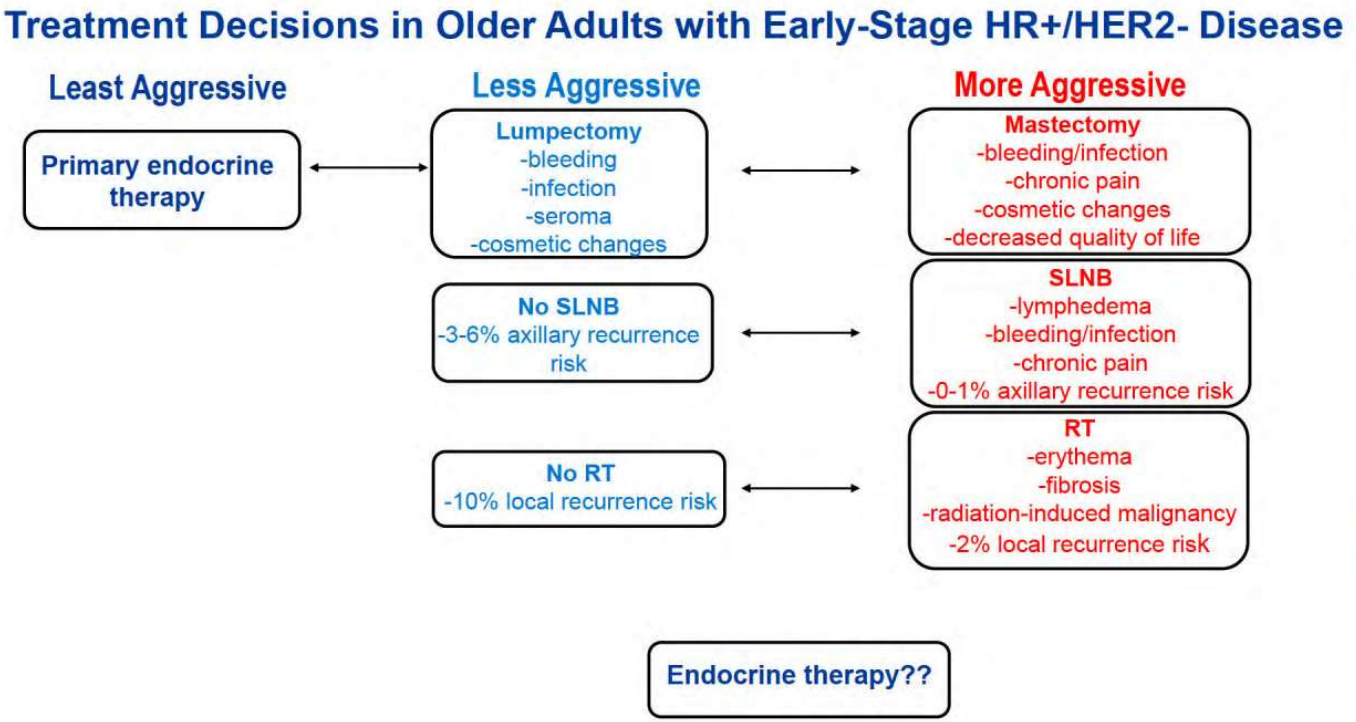
Jenna N. Whitrock MD, MS [a], Catherine G. Pratt MD [a], Szu-Aun Long MD [a], Michela M. Carter MD [a], Jaime D. Lewis MD [a b], Alicia A. Heelan MD, MS [a b]

- Choosing Wisely Guidelines
- Published 2016
- No SLNB in cT1-2, cN0, >70yrs, hormone +, Her2- breast cancers
- From 2017-2020, more than 75% of pts meeting criteria still had SLNB

Omission of XRT in Low Risk Postmenopausal Patients

- CALGB 9343—age 70+, clinical stage 1, ER+
  - BCT →Tamoxifen +/- XRT 10yr LRR 10% vs 2% (favoring tam + XRT)
  - **No difference BC mortality or distant mets**
- PRIME II –age 65+, tumors up to 3cm, ER+, N0, neg margins
  - BCT→ endocrine therapy +/- XRT
  - Similar results to CALGB 9343 (10yr LRR 9.5% vs 0.9% with XRT); higher recurrence with ER-low tumors (19%)
  - **No Difference distant recurrence ,OS, BCSF, regional recurrence**
- LUMINA –age >55yrs, T1N0, G1/2, Luminal A, low Ki67 <13%-
  - BCT + endocrine therapy only
  - At 5yrs, IBLR 2.3%, 1.9% contralateral BC, **all type recurrence 2.7%**
  - 5yr OS 97%

Breast Cancer Treatment in the Elderly



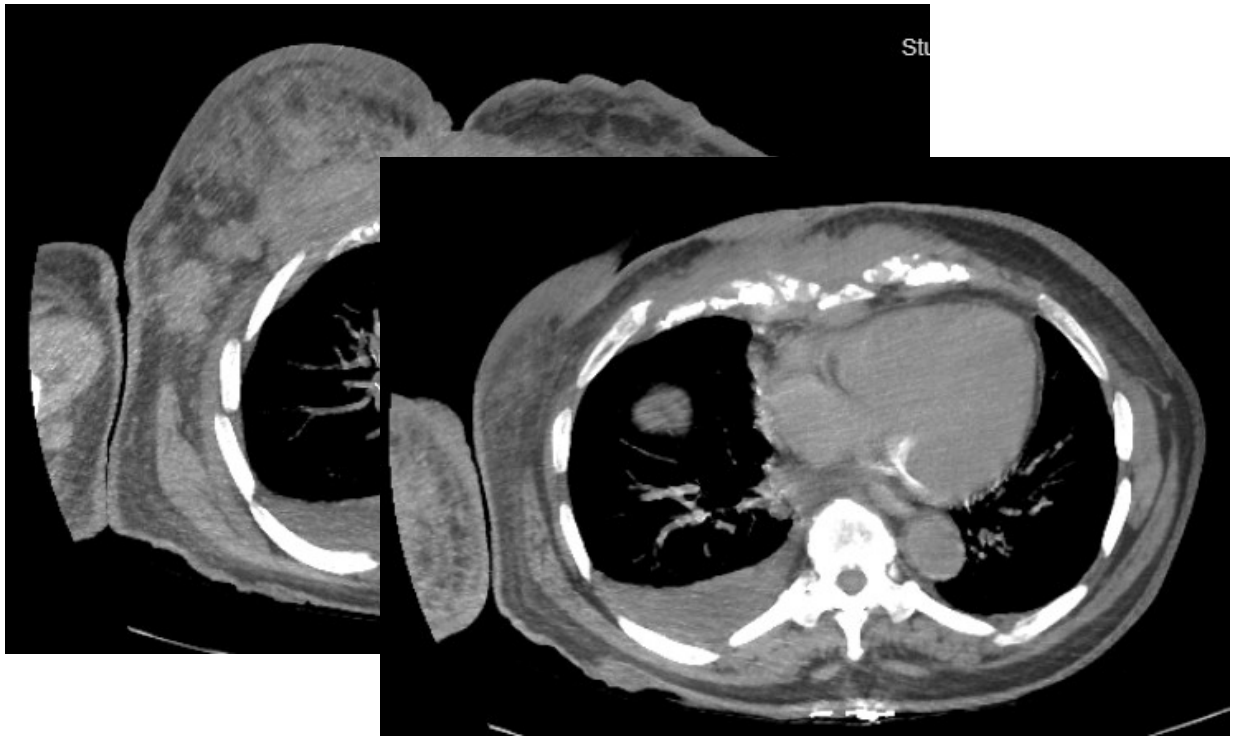
Locally Advanced Disease/De Novo Stage IV

- HPI: 78F presenting with progressive right chest/arm changes
  - Noted firmness in right breast 2019 → mass→ breast contraction→ right arm swelling
  - Saw alternative/holistic provider 2023– "blood poisoning" dx, holistic tx
  - Presented for clinical evaluation 2/2024 to PCP due to failure to improve
  - Exam: right breast contracted and deformed, diffusely edematous, mildly erythematous. Ill-defined palpable mass/firmness across the superior chest extending to the axilla. Very firm mass/matted nodes in the right axilla. Tumor erodes through the skin in the right lower inner quadrant breast and epigastric region. Right neck/supraclavicular area with multiple visible palpable skin nodules consistent with satellite lesions. Matted LAD in right cervical, supraclavicular, and right axillary nodal basins. Left breast also demonstrates lymphedema changes.

Locally Advanced Disease

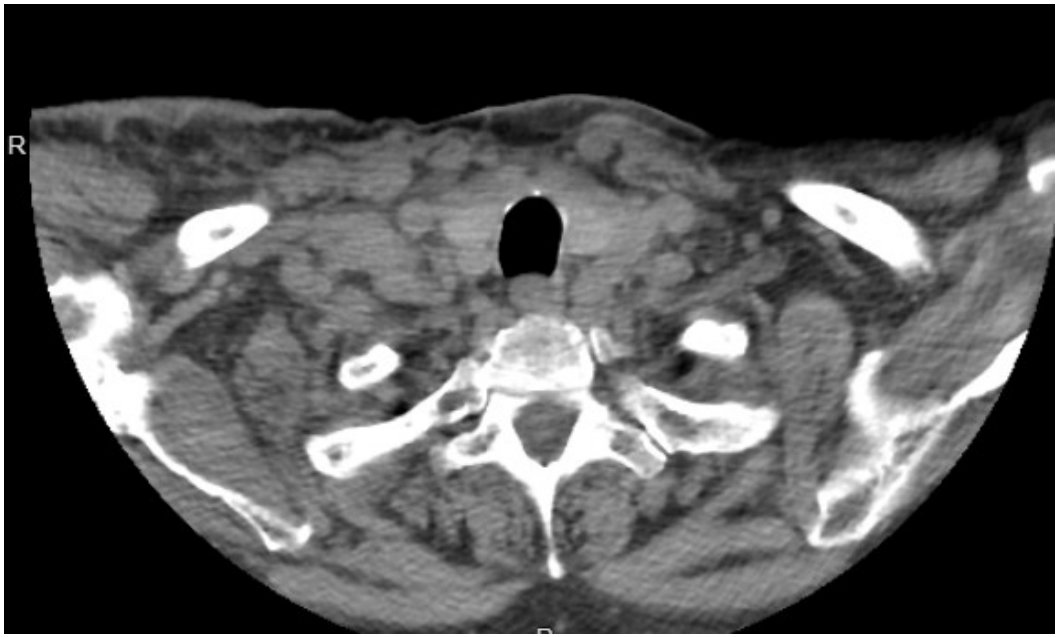
Locally Advanced Disease

- Imaging:
  - CT Chest– large infiltrative mass involving right pectoralis muscle, chest wall, retrosternal extension, upper abdominal wall; size >16cmx7cmx12cm
  - Abnormal right axillary nodes
  - RUE diffuse edema and dermal thickening
  - Right lung effusion
  - Osseous lesions Tspine, pathologic fracture



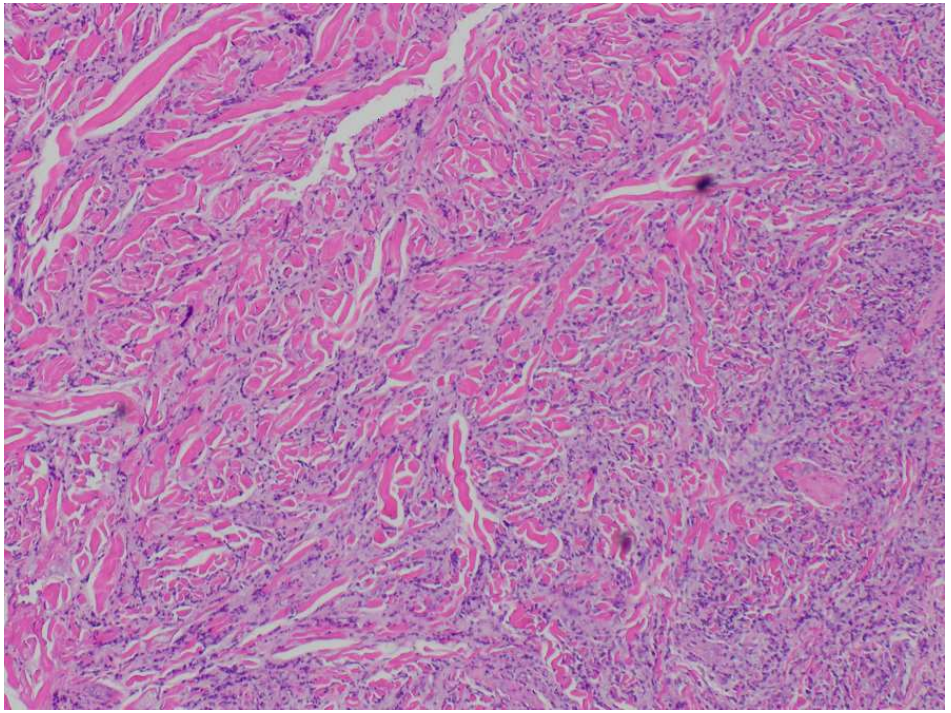
Locally Advanced Disease

- Imaging:
  - CT neck– enlarged level 4/5 cervical nodes, supraclavicular subcutaneous infiltration



Locally Advanced Disease

- Biopsy Pathology:
  - Right chest punch biopsy—invasive lobular carcinoma, G2, **ER+ PR+,HER2-** clinically T4N3M1 Stage IV



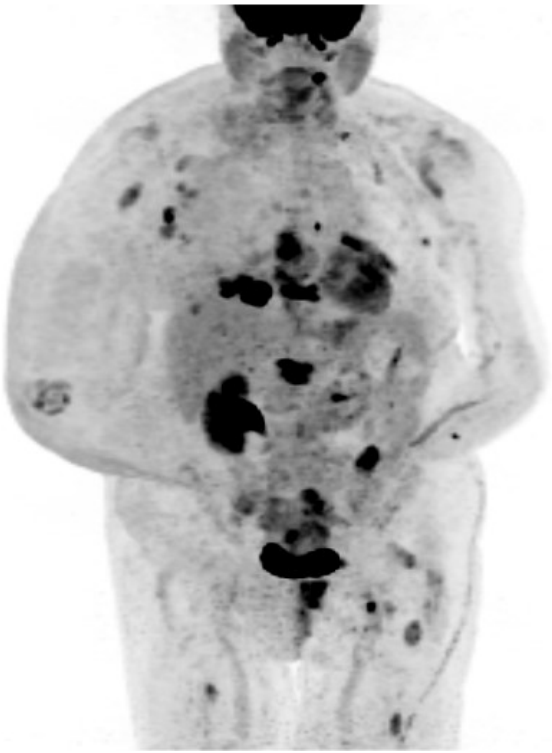
Locally Advanced Disease

- Treatment:
  - Following biopsy, Pt was direct admitted to hospital for uncontrolled HTN (BP 240/112) and AKI (creatinine 11)
  - Bilateral ureteral stents placed for obstructive hydroureter nephrosis; left nephrostomy tube
  - MRI brain – negative
  - CT Abdomen– L2 and pubic bone lytics lesions, renal findings, right chest compressive atelectasis
  - Started on Hemodialysis

- Right Pleural fluid Pathology:
  - Rare malignant cells, consistent with carcinoma/breast primary

Locally Advanced Disease

- Imaging PET/CT:
  - Multifocal hypermetabolic bony metastatic disease
  - Large hypermetabolic right breast mass with direct invasion into the sternum and retrosternal region, with neoplastic skin thickening
  - Moderate hypermetabolic adenopathy in the right axilla
  - Metastatic hypermetabolic adenopathy in the right mid to lower neck, nearly confluent difficult to isolate.
  - Hypermetabolic adenopathy in the left axilla, left internal mammary node, and left external iliac nodal chain.
  - Probable intramuscular hypermetabolic metastatic lesion in the medial right mid to proximal thigh, in the medial quadriceps muscle.



Locally Advanced Disease

- Treatment plan:
  - Letrozole + ribociclib
  - Palliative right breast/chest wall XRT 16fxs
  - OT/Lymphedema therapy

Locally Advanced disease

Locally Advanced disease

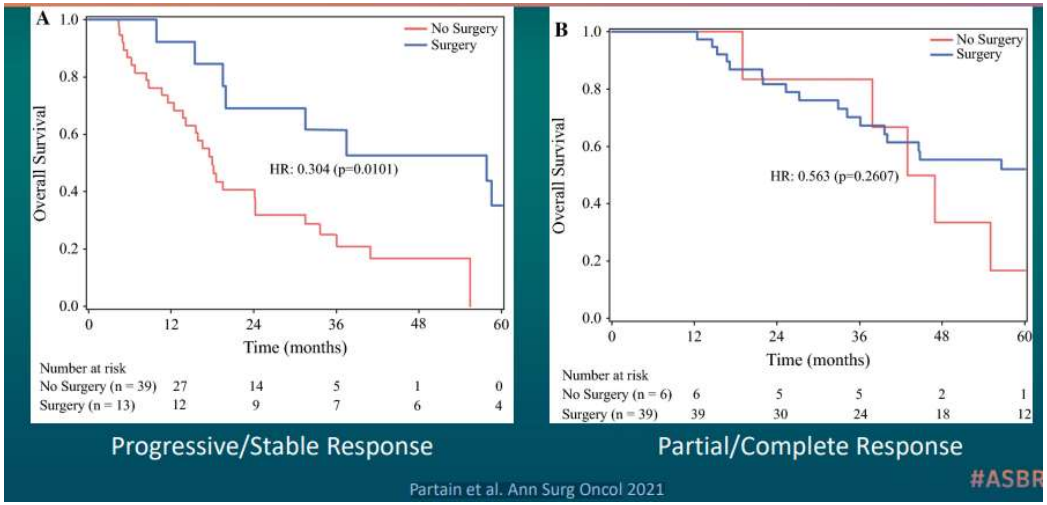
- Treatment plan:
  - Multiple hospital admissions, ureteral stent exchange, AKI
  - Hospice care
  - Deceased 10/2024

Surgery in De Novo Stage IV IBC

› Ann Surg Oncol. 2021 Aug;28(8):4265-4274. doi: 10.1245/s10434-020-09392-8. Epub 2021 Jan 5.

The Role of Mastectomy in De Novo Stage IV Inflammatory Breast Cancer

Natalia Partain [1], Lauren M Postlewait [1], Mediget Teshome [1 2], Kelly Rosso [3], Carolyn Hall [1], Juhee Song [4], Salyna Meas [1], Sarah M DeSnyder [1 2], Bora Lim [2 5], Vicente Valero [2 5], Wendy Woodward [2 6], Naoto T Ueno [2 5], Henry Kuerer [1], Anthony Lucci [7 8]



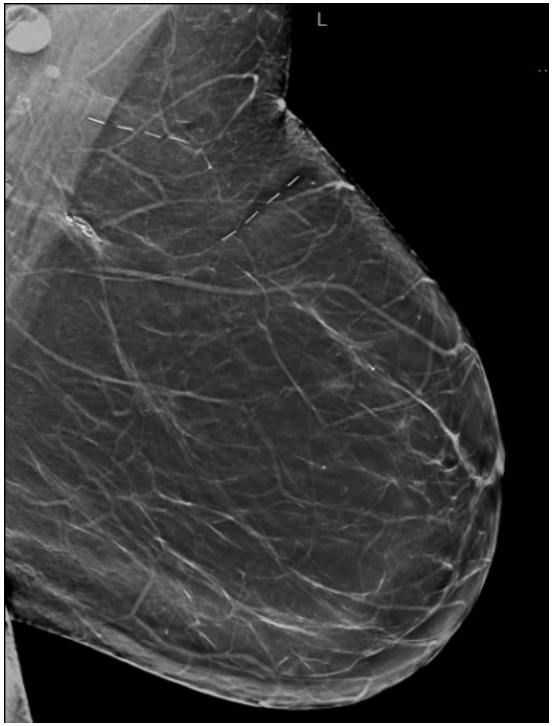
- 97 pts Stage IV IBC in an institutional database (2007-2016)→ MRM or no surgery (non-MRM
- Of the 47 patients who completed trimodality therapy (chemo, MRM, XRT), 6 (12.8%) had a local-regional recurrence.
- Median OS was 19 months in the non-MRM group and 58 months in the MRM group ($p < 0.001$).
- Partial/complete response of distant disease to chemotherapy and receipt of MRM were independently associated with improved OS.
- **Conclusions:** In our retrospective study, MRM in de novo stage IV IBC patients is an independent factor associated with improved OS. Our findings strongly support the need for prospective randomized trials evaluating possible survival benefits of MRM in de novo stage IV IBC patients.

Secondary malignancy after BC

- HPI: 69F presenting with secondary non-breast malignancy
  - Hx LEFT breast cancer DX 2018, IDC G2, 7mm, ER+PR+HER2-, pT1bN0M0
  - s/p left partial mastectomy, left SLNB, IORT
  - Oncotype low risk
  - Anastrozole x5 years

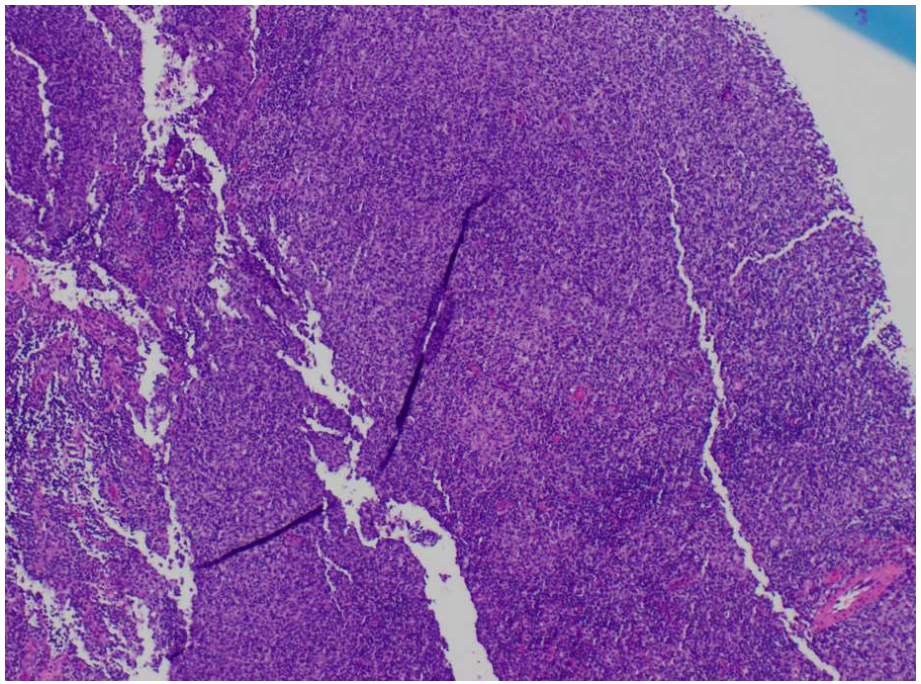
Secondary malignancy after BC

- Imaging:
  - MMG 5/2024– increased size/density left axillary node
  - Left Axilla U/S– single node with cortical thickening 1cm, BIRADS 4



Secondary malignancy after BC

- Biopsy Pathology:
  - LEFT axillary node—**nodal classic follicular lymphoma, CD30+, Stage IIIA**
    - **Positive (FISH) for IGH:BCL2 rearrangement**
    - **FLIPI score 2**
- Genetics: negative (VUS in MSH2)



Secondary malignancy after BC

- Imaging:
  - CT Ab/Pelvis– mildly enlarged mesenteric lymph nodes
  - CT Chest– solitary enlarged left level 1 axillary node
  - CT Neck—no enlarged cervical nodes
  - PET/CT– hypermetabolic LAD in left axilla, mesenteric root, right paramidline lower abdomen; Deauville score 5

Secondary malignancy after BC

- Treatment plan:
  - Asymptomatic, No “B symptoms”
  - Labs WNL
  - Treatment deferred unless symptomatic
  - Not a candidate for curative XRT

Secondary malignancy after BC

- French study of 16705 BC pts treated with chemo, XRT, endocrine therapy
- Median 10.5yr f/up→ 709 pts (4.2%) had 2nd malignancy
  - Chemo →Leukemia
  - Endocrine tx (tamoxifen)→ cervical/endometrial cancer
  - XRT→ leukemia, gyn cancers, sarcomas, lung cancer
  - No relation b/w GI cancers and treatment modalities

Table 2. Ten-year cumulative incidence of second malignancy (Kaplan–Meier estimates).

	n	(%)	95% CI
Gastrointestinal	182	11.5	9.5–13.4
Gynaecologicala	132	8.6	6.9–10.2
Ovary	74	5.0	3.8–6.3
Lung	58	3.7	2.6–4.9
Leukaemia	47	3.3	2.3–4.3
Melanoma	37	2.8	1.8–3.8
Lymphoma	41	2.6	1.7–3.5
Genitourinary	41	2.2	1.4–3.0
Sarcoma	34	2.1	1.3–3.0
Others	25	1.6	0.8–2.3
Thyroid	20	1.4	0.7–2.1
Head and neck	18	1.1	0.5–1.6
Total	709	45.0	41.2–48.7

Questions?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