

ASMER Rad Path Case of the Month

70-year-old male presents with palpable lumps in bilateral axillae radiating into the breasts

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Patient Presentation

Clinical History

- 70 year old male with history of hypertension, obesity, congestive heart failure, poorly controlled diabetes (type 2), arthritis, and depression presents to clinic with complaints of bilateral lumps in the axillae radiating into the breasts.

Family History:

- Leukemia in maternal grandfather
- Breast cancer in second cousin diagnosed at age 57

Social History

- Non-smoker, no drug or alcohol usage, no exercise

Physical Exam

- Bilateral axillary examination revealed multiple mobile lumps felt to be lipomas

Laboratory Data- normal

- CBC
- BMP
- LFTs
- PT-INR

What study should be ordered?

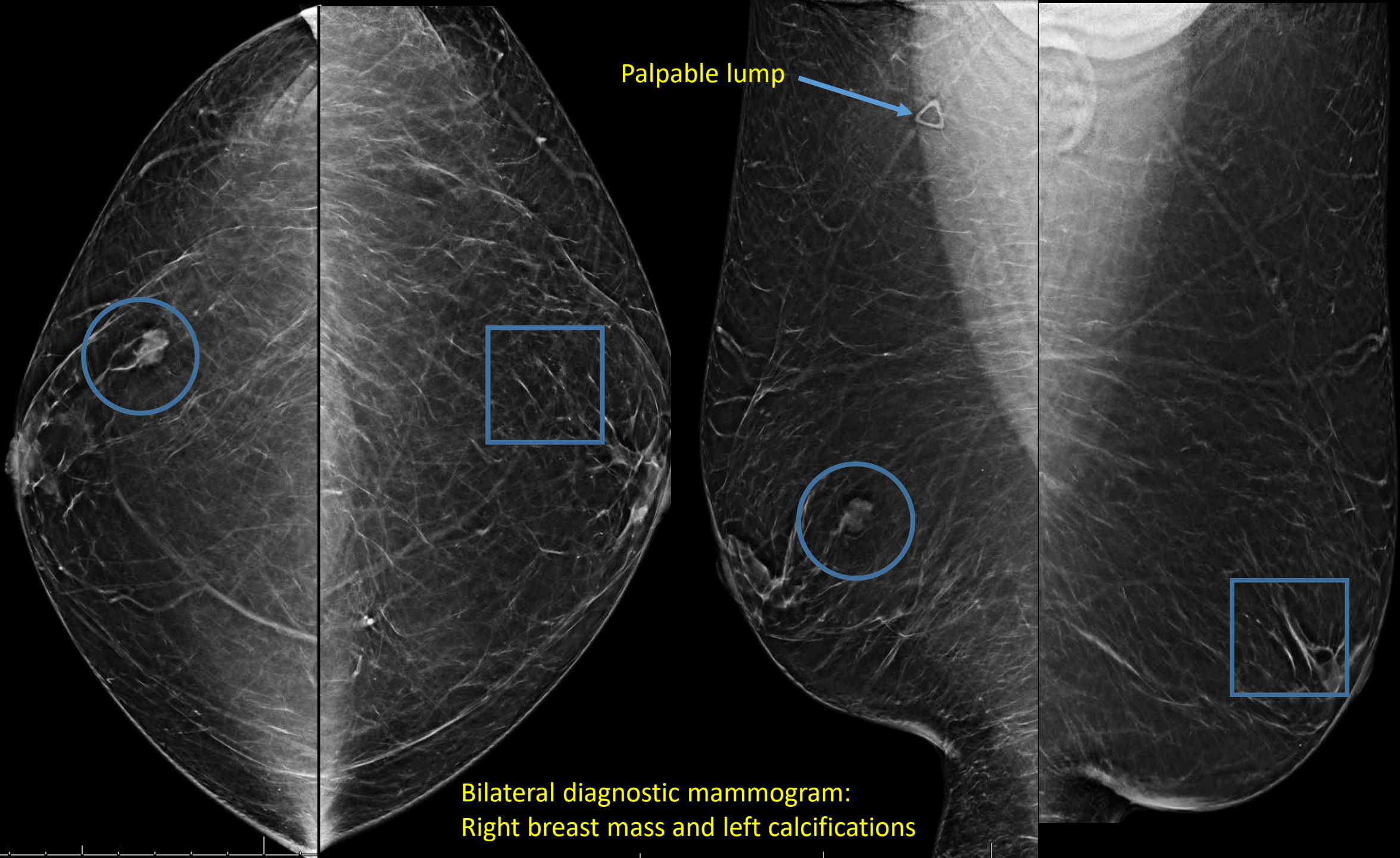
ACR Appropriateness Criteria

Variant 3: Male 25 years of age or older with indeterminate palpable breast mass. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Mammography diagnostic	Usually Appropriate	☼☼
Digital breast tomosynthesis diagnostic	Usually Appropriate	☼☼
US breast	May Be Appropriate	○
MRI breast without and with IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○

Variant 4: Male 25 years of age or older with indeterminate palpable breast mass. Mammography or digital breast tomosynthesis indeterminate or suspicious.

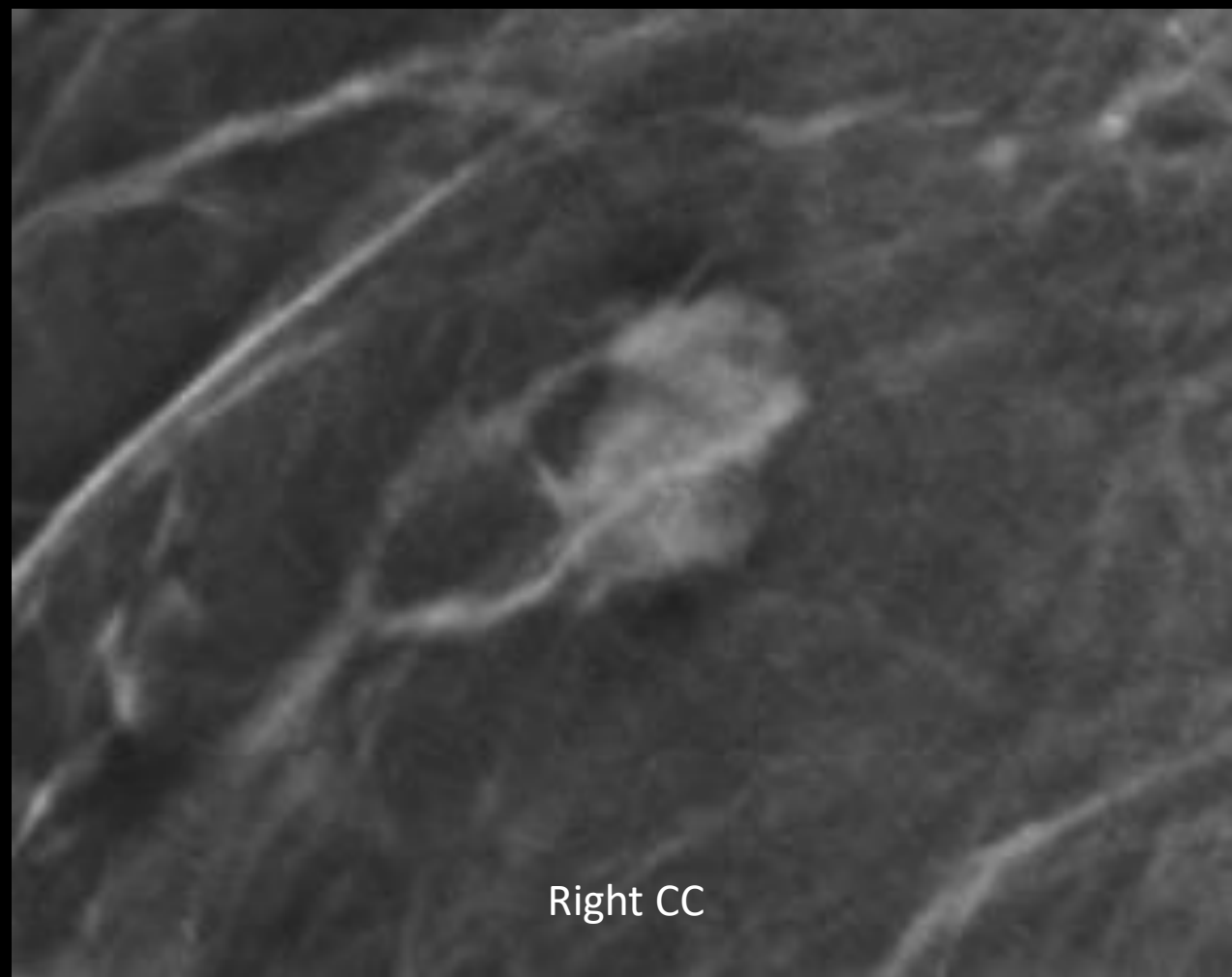
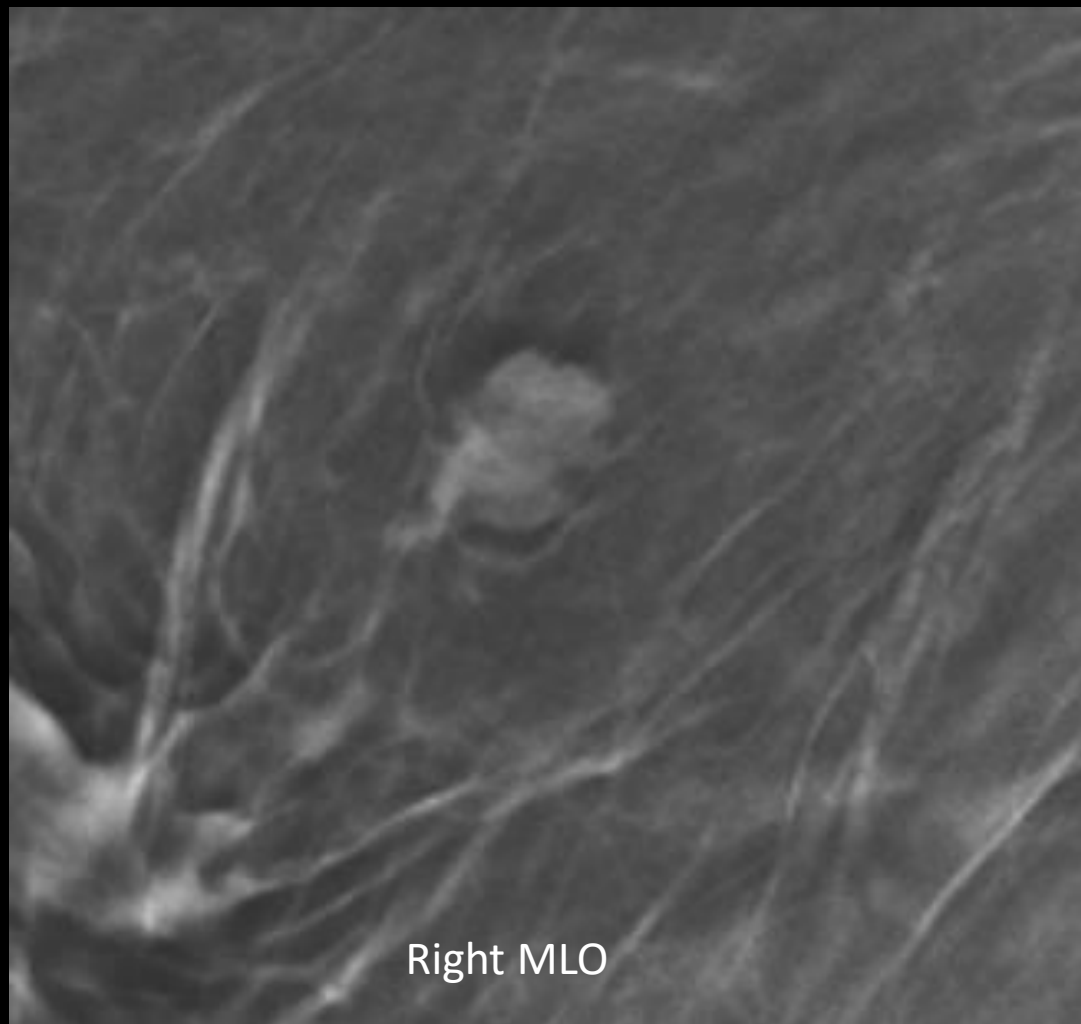
Procedure	Appropriateness Category	Relative Radiation Level
US breast	Usually Appropriate	○
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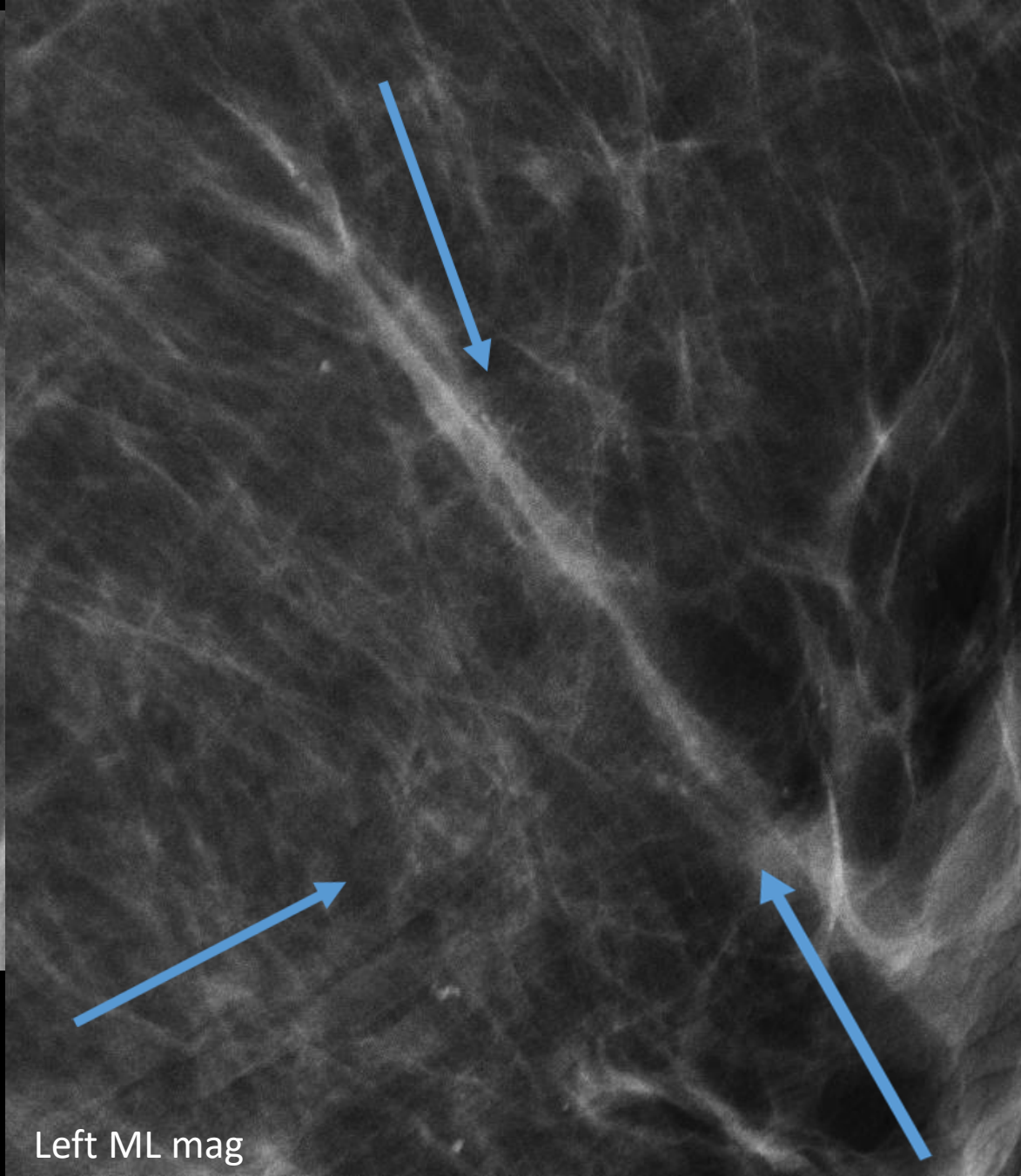


Palpable lump

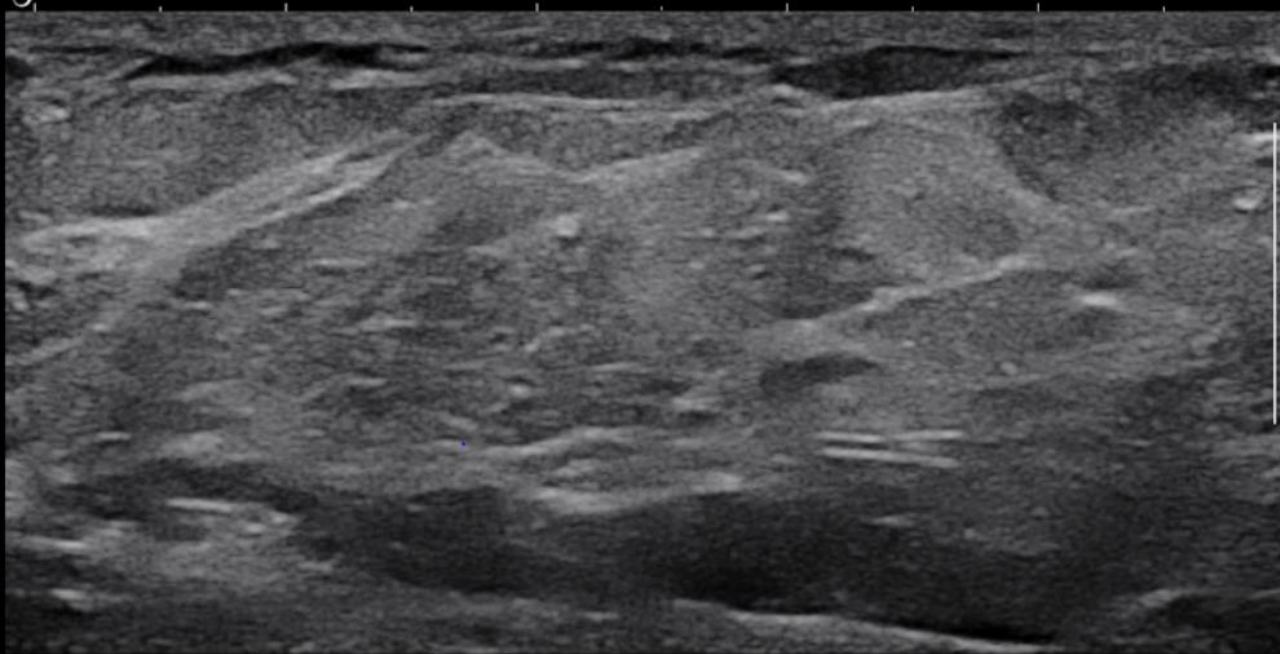
Bilateral diagnostic mammogram:
Right breast mass and left calcifications

Right breast mass- tomosynthesis slices

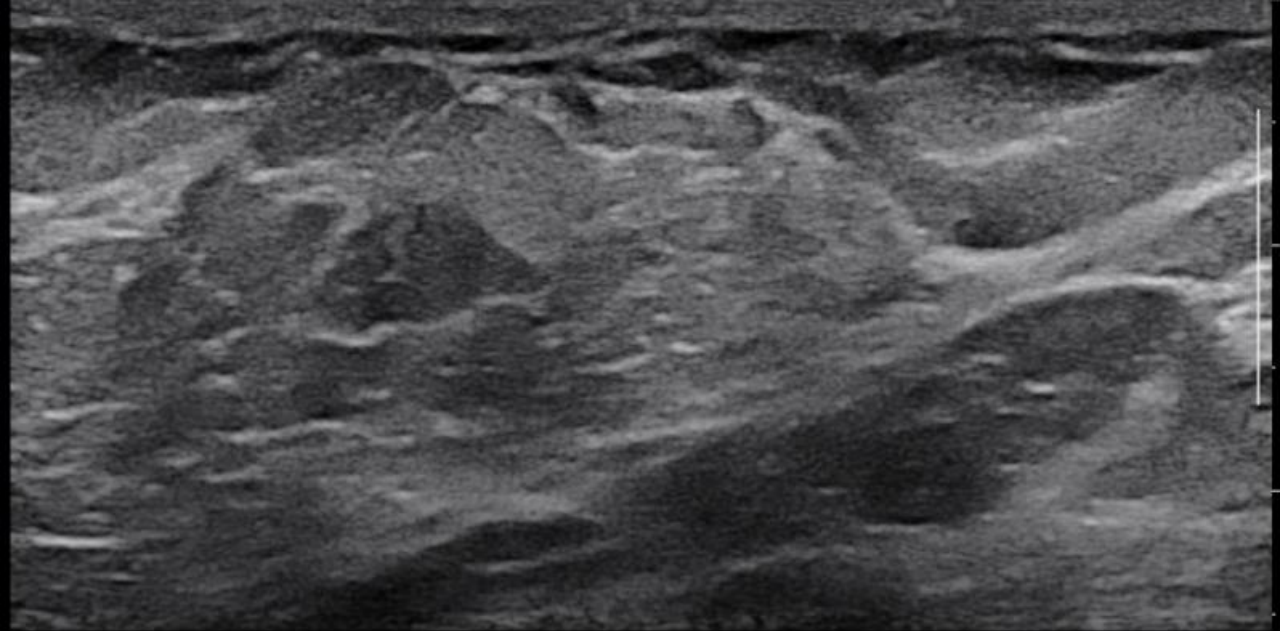




Magnification compression views of the left breast calcifications



RT BREAST RADIAL 9:00 4 cm fn

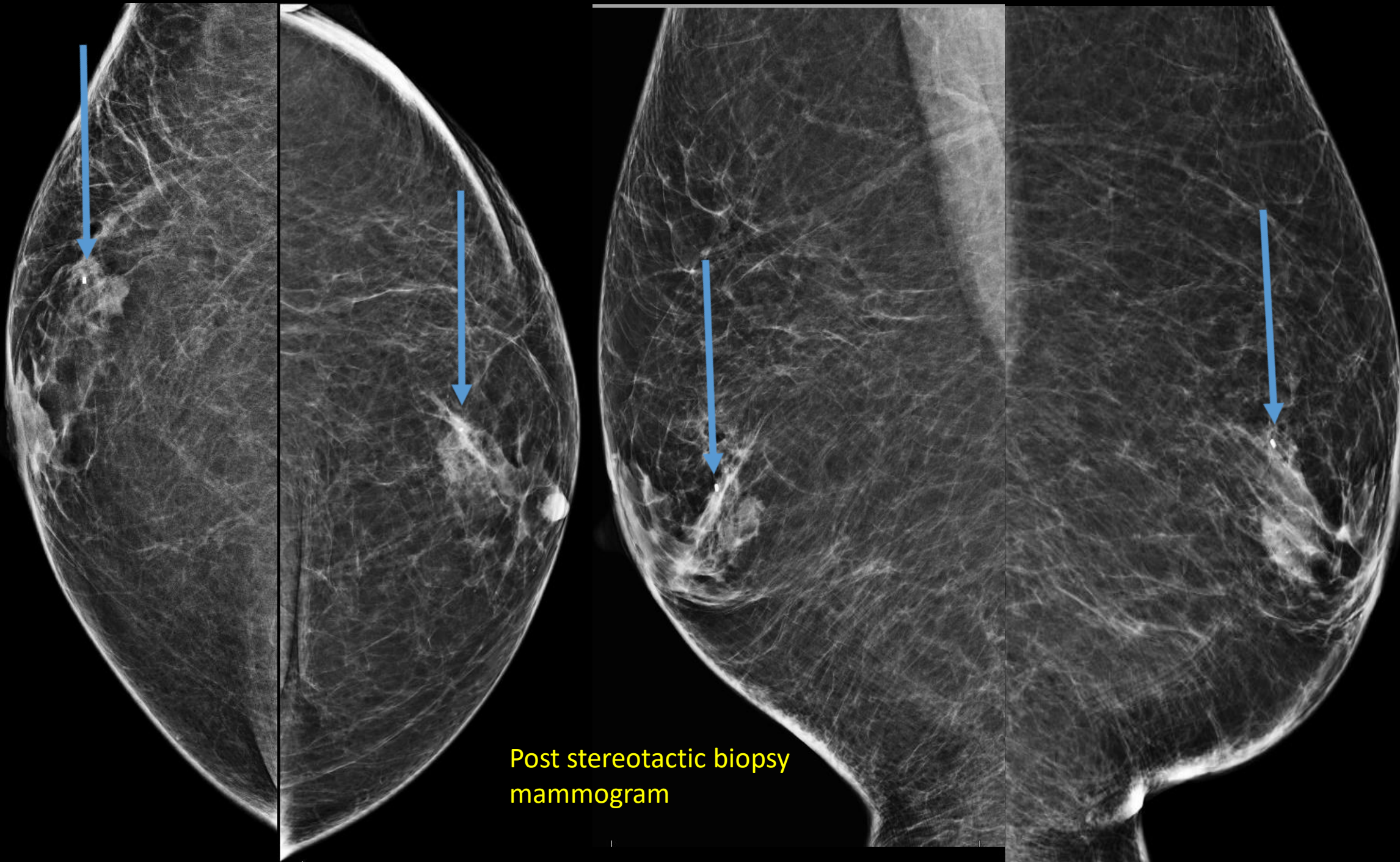


RT BREAST ANTIRADIAL 9:00 4 cm fn

No sonographic correlate to the mammographic mass in the right breast

Bilateral diagnostic work up summary

- Irregular equal density 13 mm mass in the right breast at 8 to 9 o'clock.
- Fine pleomorphic calcifications in a linear distribution in the UOQ of the left breast at 2 to 3 o'clock.
- Palpable masses in both axillae and breasts showed no mammographic or sonographic abnormalities. Lobules of fat were seen.
- Bilateral stereotactic biopsy recommended.
- BI-RADS 4: suspicious

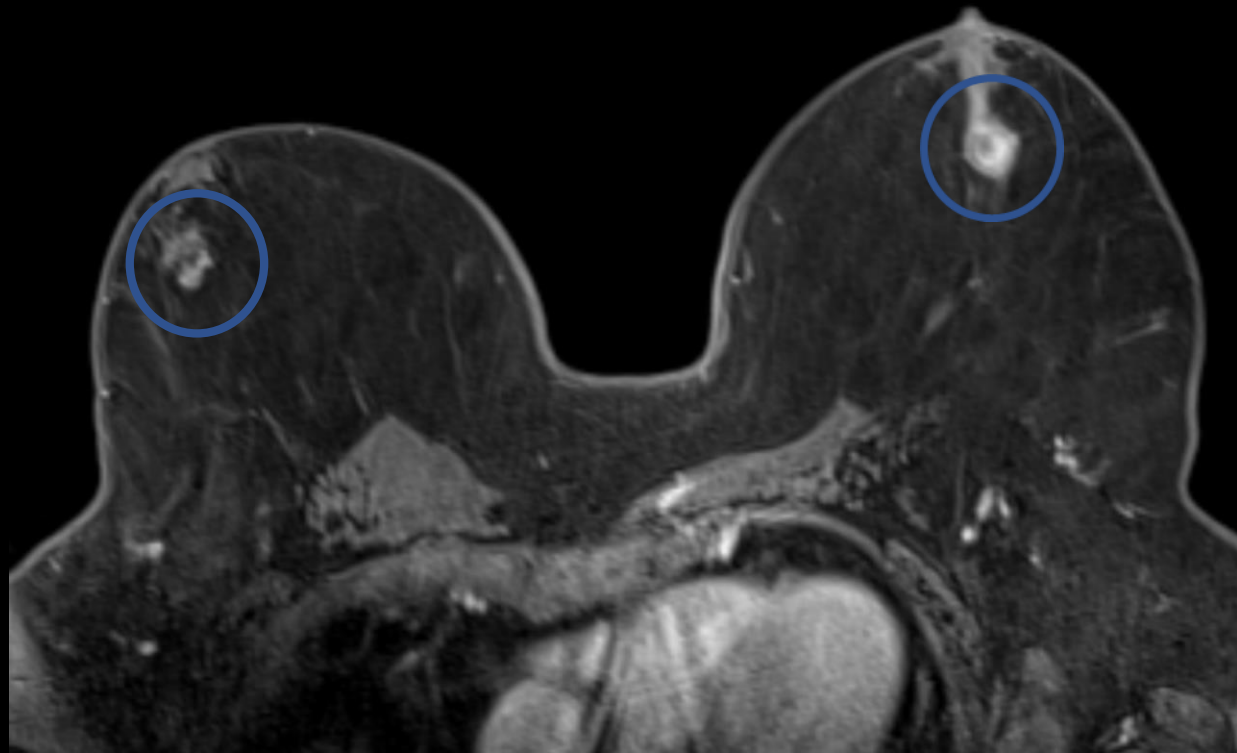


Post stereotactic biopsy
mammogram

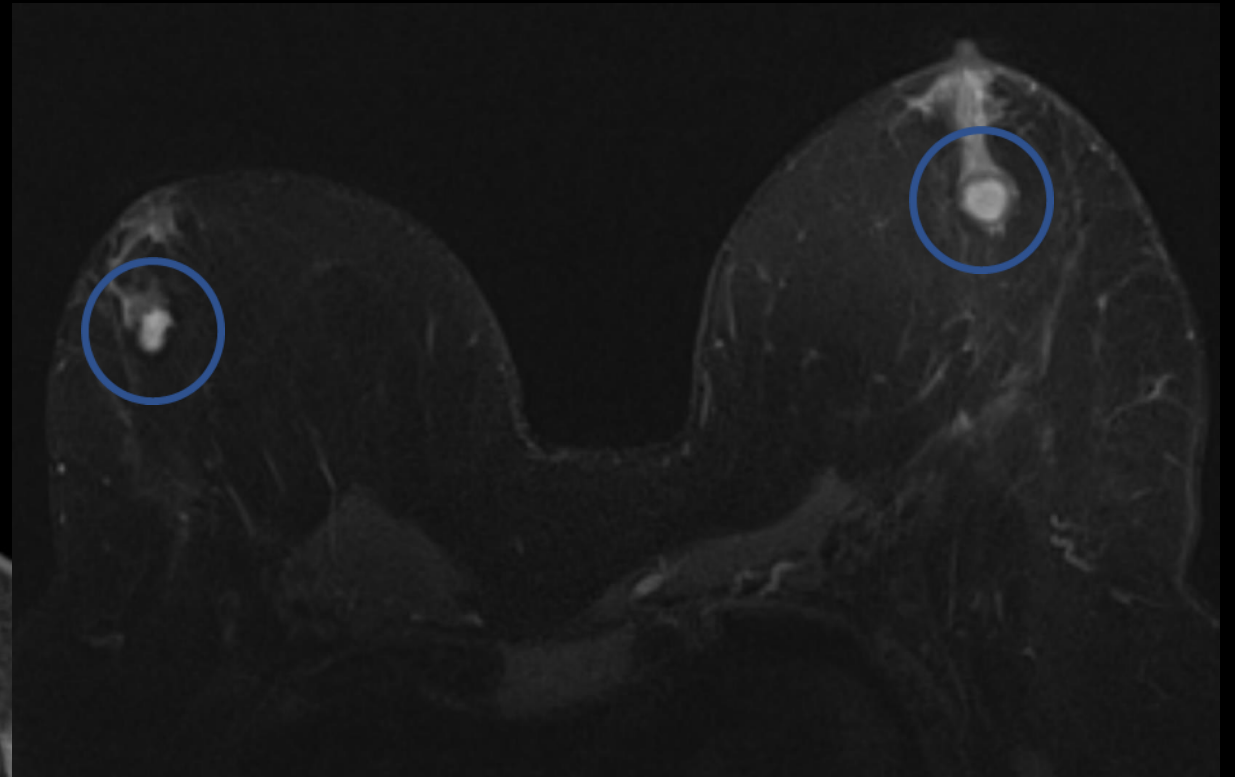
Pathologic Diagnosis

- Left breast: Ductal carcinoma in situ, intermediate grade
 - Microcalcifications associated with DCIS
 - Cribriform, micropapillary, with small focus of necrosis, ER/PR positive (100%)
- Right breast: Mucinous carcinoma, moderately differentiated
 - ER/PR positive (100%), Her2 negative

Bilateral breast MRI: pre-surgical evaluation

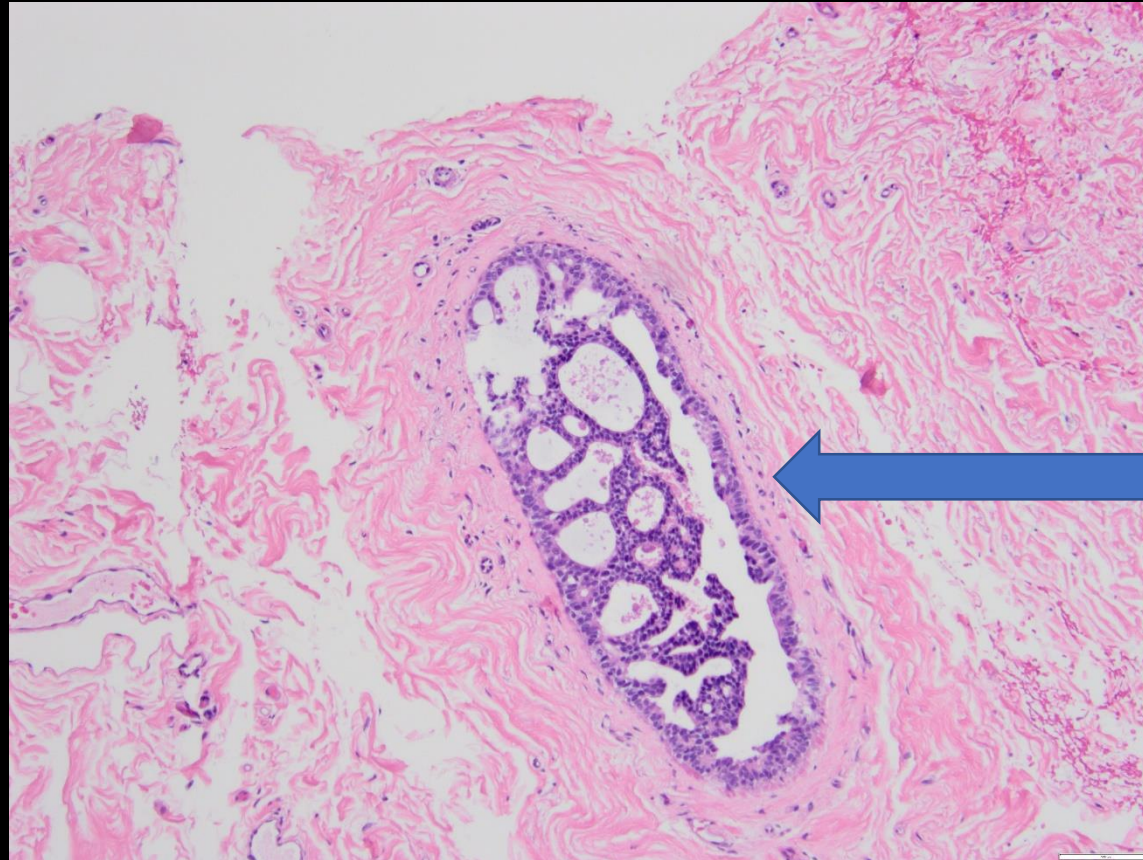


T1 post contrast dynamic image first time point



T2WI shows mucinous cancer is bright (right)
Hematoma is bright (left)

Pathology, left breast: Ductal Carcinoma in Situ



Cribriform appearance of DCIS showing cancer cells broken up with irregularly sized spaces

Power: 100x

Stain: H&E

Pathology, left breast: Ductal Carcinoma in Situ

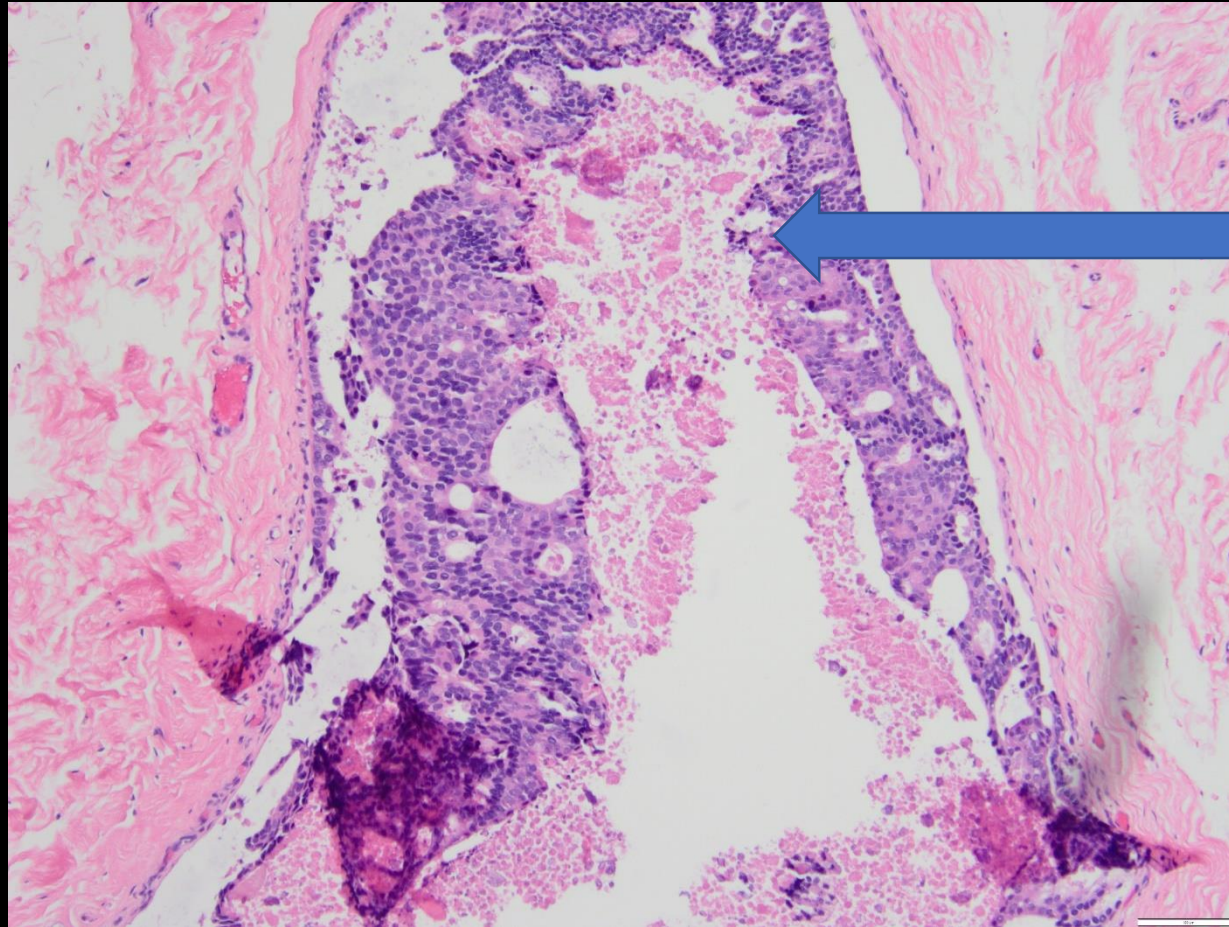


Micropapillary appearance of DCIS showing dilated ducts linked by cancerous cells

Power: 100x

Stain: H&E

Pathology, left breast: Ductal Carcinoma in Situ

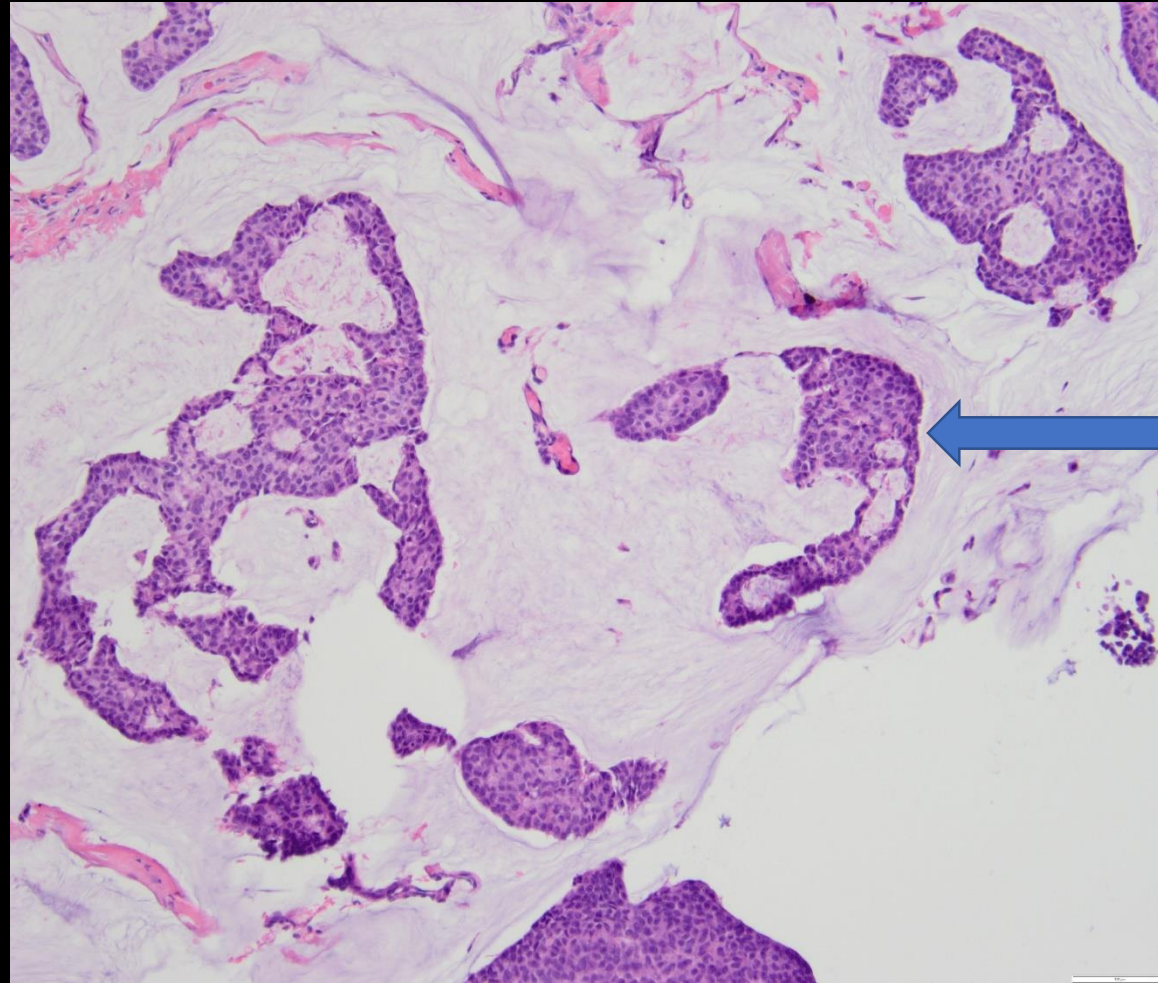


Comedonecrosis
appearance of DCIS
showing cancerous
cells surrounding
central area of
necrosis

Power: 100x

Stain: H&E

Pathology, right breast: Mucinous Carcinoma



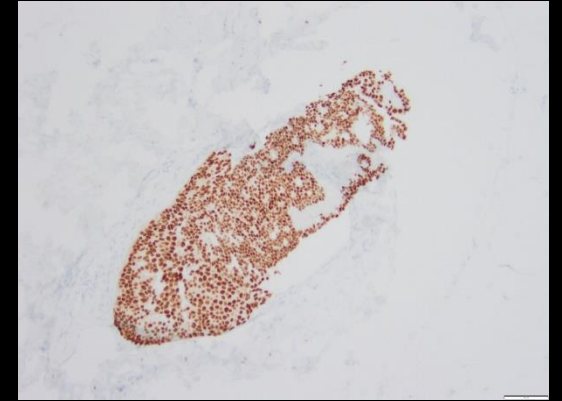
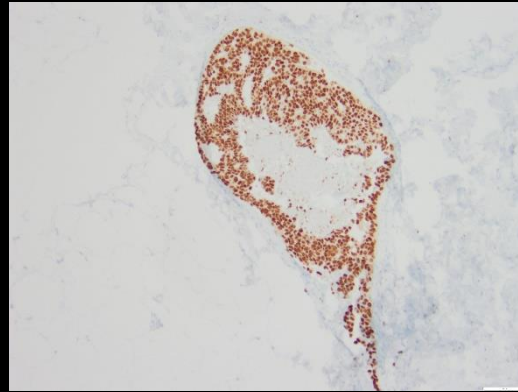
Floating cancer cells suspended in pools of mucinous material

Power: 100x

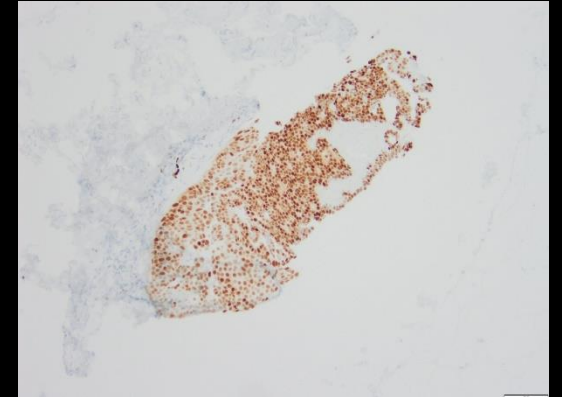
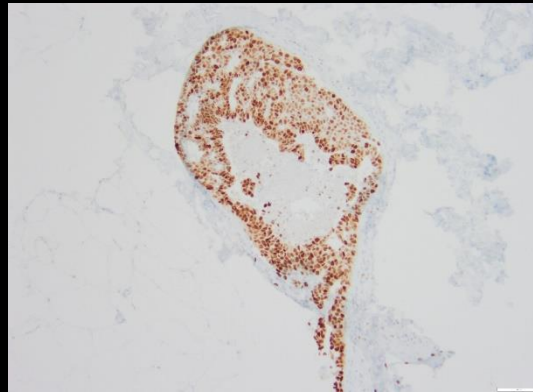
Stain: H&E

ER and PR staining, left breast: DCIS

ER Staining



PR Staining

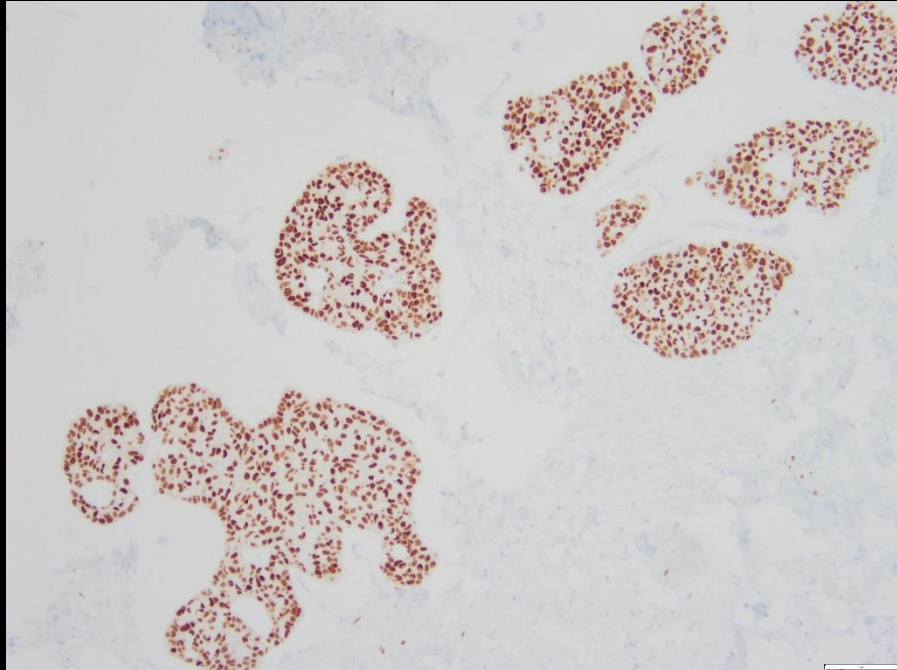


Power: 100X

Stain: DAP

Immunohistochemistry Staining revealed DCIS was 100% Estrogen Receptor and Progesterone Receptor positive

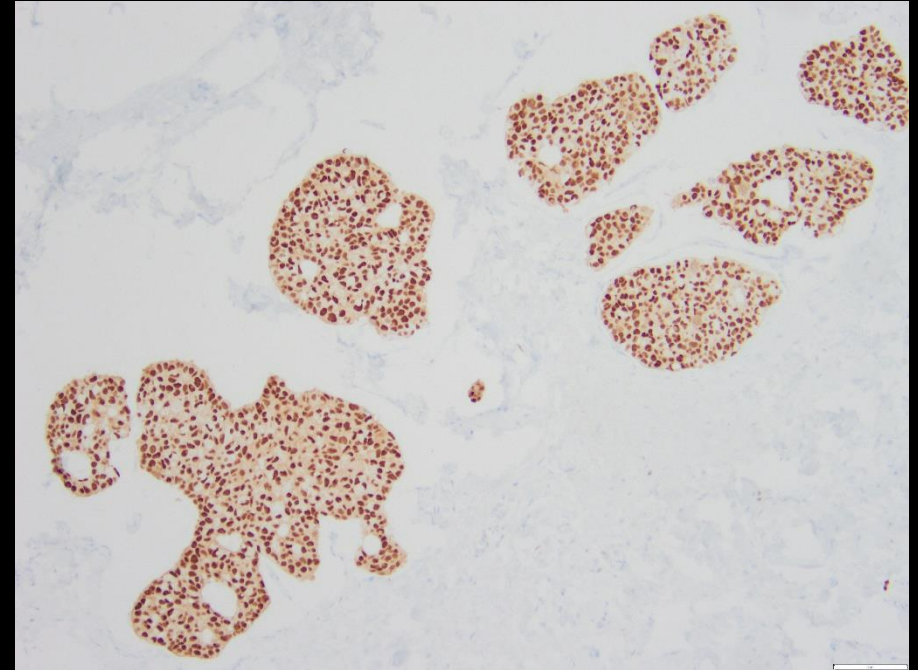
ER and PR staining, right breast: Mucinous Carcinoma



Power: 100x

Stain: DAP

ER Staining



Power: 100x

Stain: DAP

PR Staining

Immunohistochemistry Staining revealed Mucinous Carcinoma was 100% Estrogen Receptor and Progesterone Receptor positive

Male Breast Cancer

- Male breast cancer is rare and accounts for < 1% of all breast cancer diagnoses in the U.S.
- Average age of presentation is greater than that of women which is likely related to lack of awareness and no screening.
- Overall worse prognosis compared to women due to most cancers being found at a later stage.
- Common presentations: palpable painless mass, skin ulceration, nipple retraction or discharge
- Ipsilateral lymphadenopathy is common.

Molecular subtypes of invasive male breast cancer

- Ductal carcinoma (not otherwise specified)- 87%
- Carcinoma with mixed ductal and lobular features – 5.9%
- Papillary carcinoma – 3%
- Invasive lobular carcinoma – 1.4%
- Mucinous carcinoma – 1 %
- Cribriform, tubular, metaplastic, adenoid cystic, and others- <1% each

Risk factors for male breast cancer

- Increasing age
- Testicular malfunction and increased estrogen
- Family History
- Radiation exposure
- Genetic mutations (BRCA2 > BRCA1)
- Cowden and Klinefelter syndromes
- Alcohol consumption
- Liver disease
- Jewish or central African population

Ductal Carcinoma in Situ (DCIS) of the Male Breast

- A rare lesion representing 0.1% of all breast cancers and <0.1% of all cancers in men
 - Malignant proliferation of endothelial cells confined to breast ducts
 - Approximately 90% are Estrogen Receptor + or Progesterone Receptor +
 - Approximately 10% are HER2neu positive
 - Usually low to intermediate grade

Mucinous Carcinoma in men

- Mucinous Carcinoma is extremely rare and accounts for 1% of all breast cancers in men
- Gross pathology reveals a soft, gelatinous appearing mass
- Histopathology demonstrates low grade proliferation of cells dispersed in between pools of mucus
- Radiographic Findings
 - Low density masses with well circumscribed margins on mammography
 - Iso/hypoechoic lesions than can be both homogenous/heterogenous, and can have solid/cystic components on ultrasound
 - Circumscribed mass with high signal intensity on fat saturated T2 weighting on MRI
 - Can often be confused with benign lesions
- It has been suggested that mucinous carcinoma has a better prognosis than most other forms of breast cancer, however given the rarity of cases, hard to make definitive conclusions

Treatment

- Standard treatment for male breast cancer is surgery followed by adjuvant treatment (endocrine, chemotherapy, and radiation)
- Radical mastectomy used to be the standard surgical intervention
- Current guidelines prefer simple mastectomy or local tumor excision and adjuvant therapy
- Radiotherapy is mandatory following breast conserving surgeries
 - Indicated if positive lymph node and tumor larger than 5 cm with margin positivity
- Radiotherapy decreases local recurrence and improves long survival in women
- Data for men suggests local tumor control, but no overall survival benefit

Treatment (continued)

- Chemotherapy used in patients not responsive to hormone therapy (ER, PR, and Her2 negative) which significantly increases survival rates for 5-10 years
- Adjuvant endocrine therapy recommended since majority of male breast cancer are hormone receptor positive
 - Most patients undergo 5 year trial of tamoxifen with same prognostic indications as women
 - Studies evaluating the benefits for aromatase inhibitors such as anastrozole and letrozole have not been fully evaluated in men

Prognosis and Survival

- The mortality rate for male breast cancer remains unchanged since 1975
- Overall 5-year survival rate- 40-65%
 - Stage 1 (5-yr SR)- 75-100%
 - Stage 2 (5-yr SR)- 50-80%
 - Stage 3 (5-yr SR)- 30-65%
- Median survival for patients with metastatic disease (bone, lung, liver or brain) is 26.5 months

Our Patient

- Mastectomies were recommended as the left breast calcifications (DCIS) extended to the subareolar region and required excision of the nipple areolar complex.
- He has pulmonary hypertension and mastectomy provided the best chance of avoiding radiation.
- He was most comfortable electing bilateral mastectomies.

References

1. Yalaza M, Inan A, Bozer M. Male Breast Cancer. *J Breast Health*. 2016;12(1):1-8. Published 2016 Jan 1. doi:10.5152/tjbh.2015.2711
2. Abdelwahab Yousef AJ. Male Breast Cancer: Epidemiology and Risk Factors. *Semin Oncol*. 2017 Aug;44(4):267-272. doi: 10.1053/j.seminoncol.2017.11.002. Epub 2017 Nov 9. PMID: 29526255.
3. Nofal MN, Yousef AJ. The diagnosis of male breast cancer. *Neth J Med*. 2019 Dec;77(10):356-359. PMID: 31880271.
4. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. *Ann Oncol*. 2013 Jun;24(6):1434-43. doi: 10.1093/annonc/mdt025. Epub 2013 Feb 20. PMID: 23425944.
5. Serdy KM, Leone JP, Dabbs DJ, Bhargava R. Male Breast Cancer. *Am J Clin Pathol*. 2017 Jan 1;147(1):110-119. doi: 10.1093/ajcp/aqw207. PMID: 28171879.
6. Gao Y, Heller SL, Moy L. Male Breast Cancer in the Age of Genetic Testing: An Opportunity for Early Detection, Tailored Therapy, and Surveillance. *Radiographics*. 2018;38(5):1289-1311. doi:10.1148/rg.2018180013
7. Almir G, Bitencourt V, Graziano L et al. MRI Features of Mucinous Cancer of the Breast: Correlation With Pathologic Findings and Other Imaging Methods. *AJR* 2016 206:2, 238-246
8. Brents M, Hancock J. Ductal carcinoma in SITU of the Male Breast. *Breast Care*. 2016;11(4):288-290. doi:10.1159/000447768