

Breast Cancer Screening in High-Risk Men: A 12-year Longitudinal Observational Study of Male Breast Imaging Utilization and Outcomes

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Learning Objectives

By the end of this journal club, participants will be able to:

- Understand basic anatomy of female and male breast
- Understand male breast cancer epidemiology, risk factors, presentation, pathology, and diagnostic work up
- Understand BIRADS assessment categories
- Understand DDX of a mass in a male breast
- Understand potential need of guidelines for screening mammograms in high-risk males

Module Outline

- I. Case
- II. Background
- III. Article Overview
- IV. Clinical Questions
- V. Key Points

Case Presentation

74-year-old male who presents with left breast mass

PMHx: ESRD s/p kidney transplant (2017), recurrent bacteremia and UTIs, CAD, T2DM, HFpEF, Afib s/p watchman, vascular dementia, prostate cancer s/p prostatectomy (2013) and newly diagnosed RCC in right native kidney

HPI:

- Presented with complicated MDR Klebsiella UTI in the setting of sepsis and acute encephalopathy
- Concern for possible unidentified source of infection due to recurrent bacteremia

Case Presentation

Interval Events:

- Underwent a PET CT for possible unidentified nidus of infection
- Findings: FDG avid microabscess of left obturator muscle AND FDG avid lesion underlying left nipple on PET CT

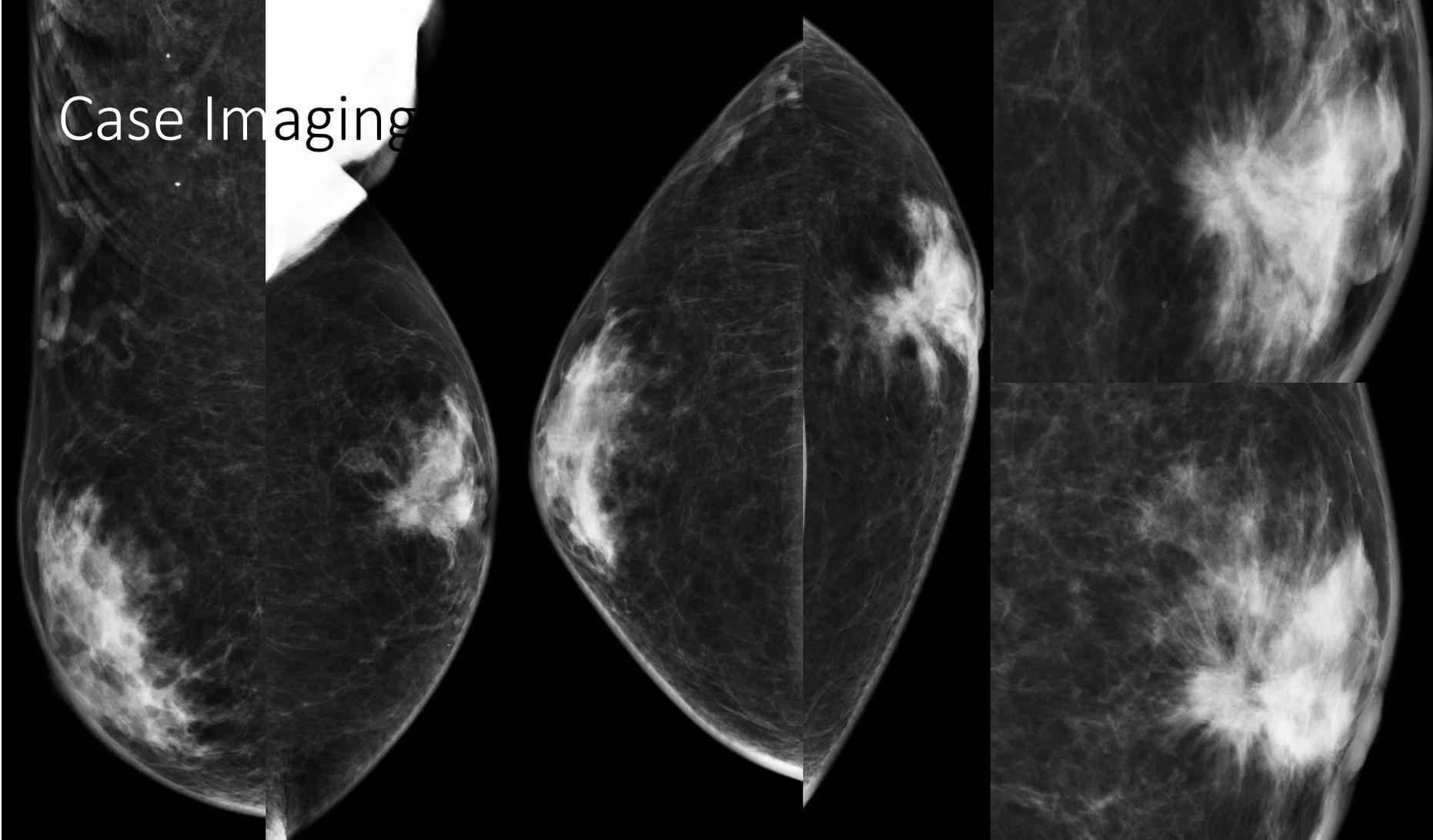
Follow-up:

- Patient reports no breast changes (size, pain, redness, breast mass, nipple retraction, swelling, nipple discharge)
- No previous breast biopsies or abnormal mammograms
- Known bilateral gynecomastia noted on previous imaging
- Family history of sister with breast cancer
- Referred to breast radiology for further imaging

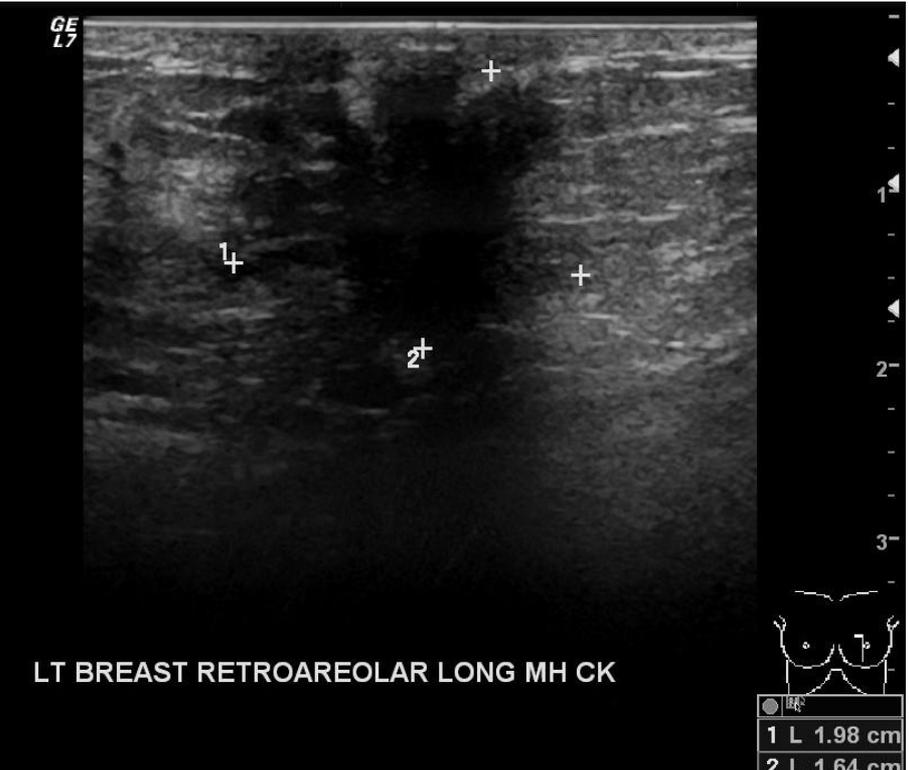
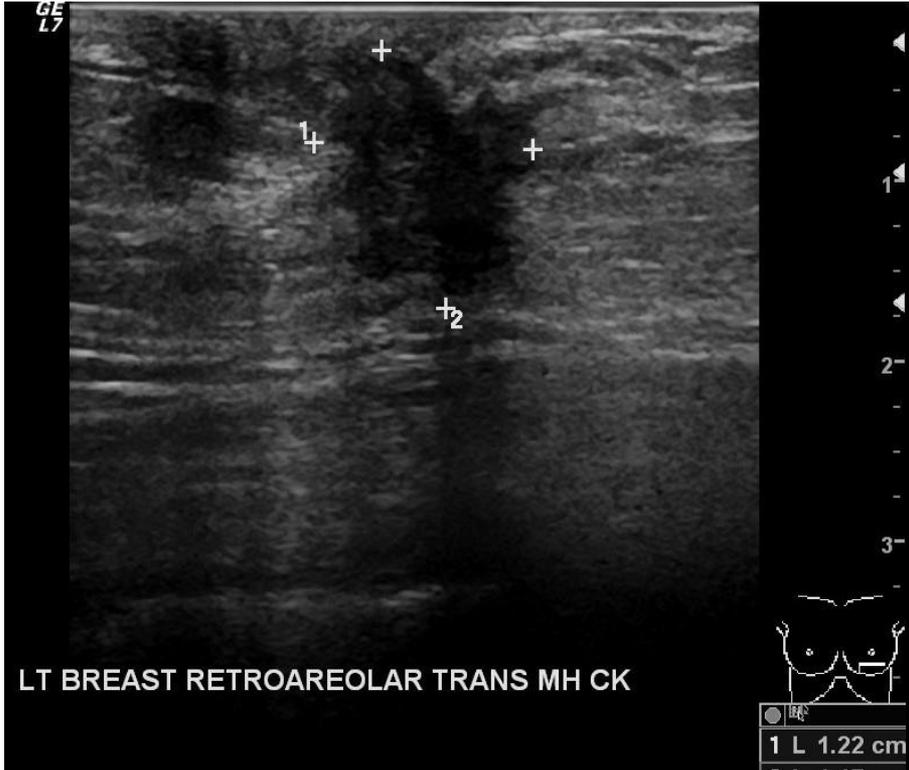
Case Questions

- What imaging studies would you perform for this patient?
- What is the most common breast finding in a male?

Case Imaging



Case Imaging



Case Pathology Report

Procedure: Ultrasound-guided Core Needle Biopsy

Diagnosis: Invasive ductal carcinoma, histologic grade 1

ER positive 100%

PR positive 70%

HER 2 negative

Case Questions to Consider

- What histologic subtypes of breast cancer are found in men?
- What are the imaging study recommendations for the diagnostic evaluation of a male breast mass?
- Should high-risk males undergo screening mammography?

Module Outline

I. Case

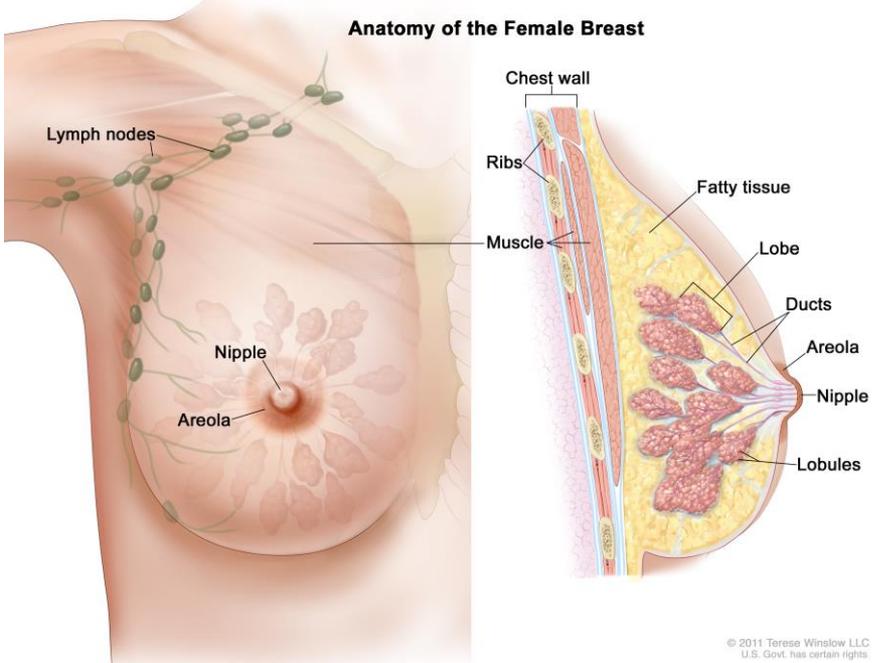
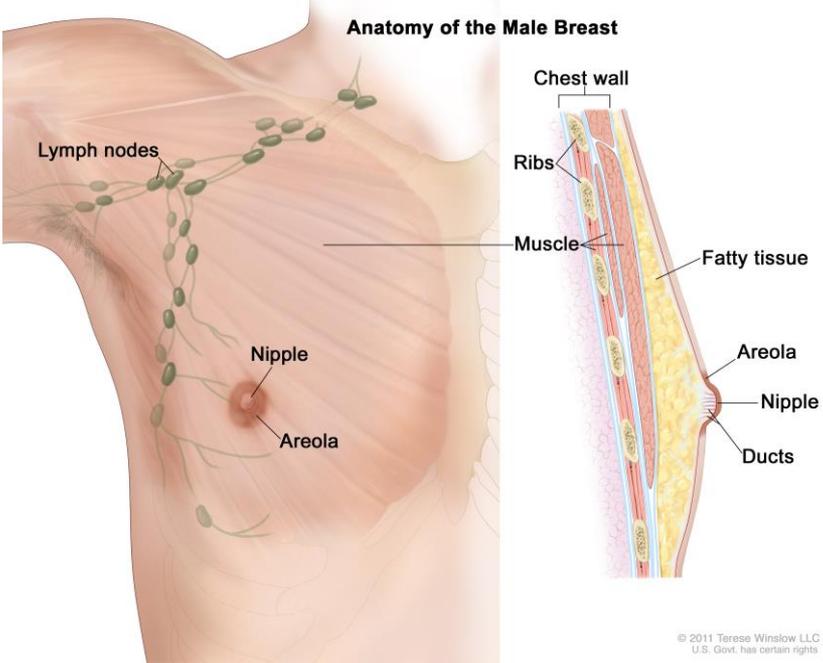
II. Background

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Anatomy of the Breast



Male Breast Cancer

- Accounts for about 0.5-1% of breast cancers annually¹
- **Risk Factors:**
 - Breast cancer in a first degree relative, mutations: BRCA1/2, PTEN tumor suppressor gene (Cowden Syndrome), tumor protein p53 (Li-Fraumeni Syndrome), mismatch repair genes (Lynch Syndrome)
 - Alterations in the estrogen to androgen ratio: hormonal therapies, hepatic dysfunction, obesity, marijuana use, thyroid disease, or an inherited condition (Klinefelter syndrome)
 - Primary testicular conditions: orchitis, cryptorchidism, and testicular injury

Male Breast Cancer

- **Presentation:** painless, firm mass; retroareolar; nipple retraction
- **Pathology:** About 85-90% are invasive ductal carcinomas, rarely lobular carcinomas²
- **Subtype:** hormone-receptor positive, luminal A or luminal B^{2,3}
- **Diagnostic Evaluation⁴:**
 - < 25 years old: US
 - \geq 25 years old: mammography
 - Can use mammography initially for any age if highly suspicious of breast cancer

BI-RADS Assessment Categories

Breast Imaging Reporting and Data Systems

BI-RADS® ASSESSMENT CATEGORIES

includes PPV for
malignancy and
suggested
verbiage for the
accompanying
Recommendation

- Category 0: INCOMPLETE - NEED ADDITIONAL IMAGING EVALUATION AND/OR PRIOR MAMMOGRAMS FOR COMPARISON
Recall for additional imaging and/or comparison with prior examinations
- Category 1: NEGATIVE (0% risk)
Routine mammography screening
- Category 2: BENIGN (0% risk)
Routine mammography screening
- Category 3: PROBABLY BENIGN (<2% risk)
Short interval 6 month follow-up *OR continued surveillance*
- Category 4: SUSPICIOUS (2-95% risk)
Biopsy should be performed in the absence of clinical contraindications
- Category 5: HIGHLY SUGGESTIVE OF MALIGNANCY (>95% risk)
Biopsy should be performed in the absence of clinical contraindications
- Category 6: KNOWN BIOPSY-PROVEN MALIGNANCY (100% risk)
Surgical excision when clinically appropriate

Differential of Breast Mass in Male

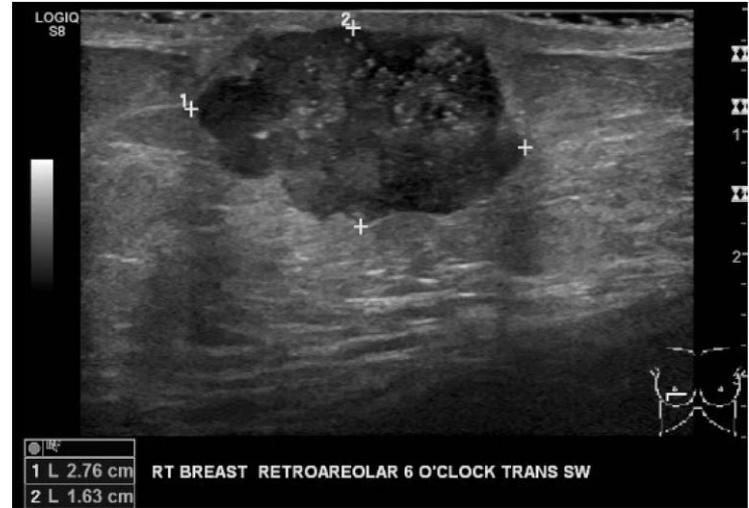
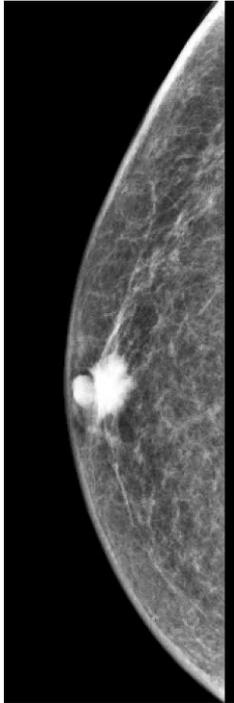
- Gynecomastia
 - Benign proliferation of ductal and stromal tissue elements
 - Most commonly bilateral, but can be unilateral
 - Soft tender mass, mobile, central to nipple
 - Common etiology: medications



Mammogram:
Flame or fan shape

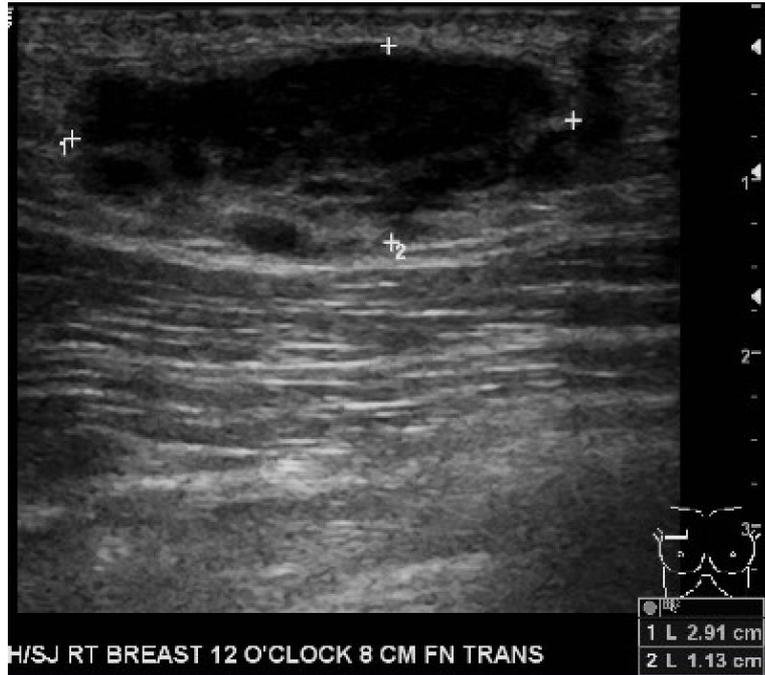
Differential of Breast Mass in Male

- Breast Cancer



Differential of Breast Mass in Male

- Lymph Node



- Others: psuedogynecomastia, infections, lipoma, fibromatosis, granular cell tumor, pseudoangiomatous stromal hyperplasia and more!

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Article Nuts and Bolts

Purpose: To evaluate patterns of male breast imaging utilization, to determine high-risk screening outcomes, and to delineate risk factors associated with cancer diagnosis.

Journal: Radiology, November 2019

Study Type: Retrospective study reviewed consecutive male breast imaging examinations over a 12-year period (2005-2017)

Number of Cases: 1869 men who underwent 2052 examinations

Data: Examination indications, mammogram findings, biopsy/pathology results, patient characteristics, number of person years to achieve a diagnosis

Study Cohort

- Adult men (both symptomatic and asymptomatic) who underwent breast imaging examinations (mammography \pm US) at a tertiary academic medical center between January 2005 and April 2017 for all clinical indications, with at least 1 year of clinical and/or imaging follow up.

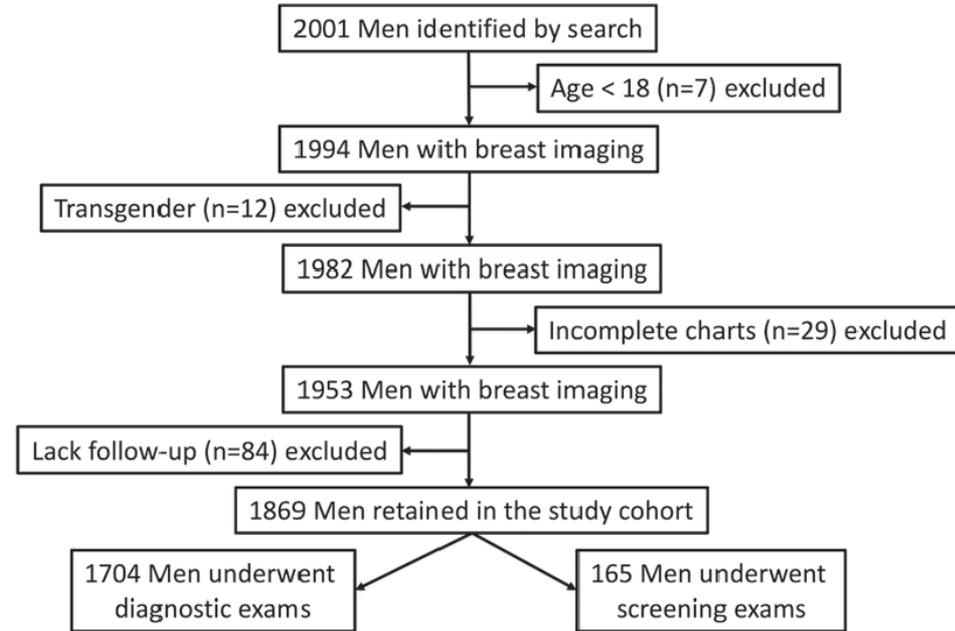


Figure 1: Flowchart demonstrates study cohort inclusion and exclusion criteria.

Material and Methods

- **Screening Examinations:** examinations performed either for surveillance due to a personal history of breast cancer or for screening due to elevated risks predisposing to breast cancer.
 - Mammography used
 - Recorded whether annual or sporadic screening was undertaken
- **Diagnostic Examinations:** examinations performed for evaluation of male breast symptoms, or for follow-up of probably benign findings.
 - Mammography and/or US used
- The number of examinations was defined as the number of single-event breast imaging evaluations.
 - Compared to the total number of exams performed in women each year

Material and Methods Continued

- Examination indications, imaging findings, biopsy recommendations, and pathologic results were correlated with patient characteristics (age, personal and/or family history of breast cancer, any known genetic mutation, and Ashkenazi descent)
- **High-Risk:** men with any known risk factors predisposing to breast cancer such as personal and family history of breast cancer, breast cancer related–genetic mutations, or Ashkenazi descent
- Number of person years screened to achieve a cancer diagnosis was recorded in men with screen detected cancers

Table 1: Characteristics of Men Who Underwent Breast Imaging Examinations between 2005–2017 (n = 1869)

Patient Characteristic	Value (%)
Family history of breast cancer	20.2 (378/1869)
First-degree family history of breast cancer	12.9 (242/1869)
Genetic mutation	2.4 (45/1869)
Ashkenazi descent	1.2 (22/1869)
Personal history of breast cancer	2.5 (47/1869)

Note.—Data in parentheses are numerators and denominators. Median age was 55 years (range, 18–96 years) and mean age \pm standard deviation was 54 years \pm 19.

Results

- **2052 examinations:** 1781 diagnostic (86.8%) and 271 screening (13.2%)
 - All included mammography, 1004 included US
 - All men undergoing screening had personal or family history of breast cancer and/or genetic mutations (BRCA2 being the most common).
 - Screening: 10.9% underwent at least 3 screens, 12.7% underwent 2, and 76.5% underwent 1
- **Yielded:** 2304 breast lesions
- **149 biopsies in 133 men:** 41 (27.5%) were malignant, 108 (72.5%) were benign

Table 3: Histopathologic Analysis of Biopsied Breast Lesions (n = 149)

Biopsy Yield and Pathologic Finding	No. of Biopsied Lesions	Percentage
Malignant		
Invasive ductal carcinoma with ductal carcinoma in situ	38	25.5
Ductal carcinoma in situ	3	2.0
Benign		
Apocrine metaplasia	7	4.7
Angiolipoma	6	4.0
Abscess/Phlegmon	5	3.4
Lipoma	10	6.7
Fat necrosis	13	8.7
Fibroadenoma	1	0.7
Hematoma	3	2.0
Gynecomastia	39	26.2
Granulomatous reaction	9	6.0
Lymphoid hyperplasia	7	4.7
Nodular fibrosis	4	2.7
Myofibroblastoma	1	0.7
Cavernous hemangioma	1	0.7
Steatocytoma	1	0.7
Benign, not otherwise specified	1	0.7

Results continued

Table 6: Feature Comparison of Diagnostic- versus Screen-detected Male Breast Cancers

Features	Diagnostic-detected (<i>n</i> = 24)	Screen-detected (<i>n</i> = 5)	<i>P</i> Value
Lesion type (%)			
Mass*	100	40	.003
Calcification only	0	60	.003
Average lesion size†			
Mass (cm)	2.1 (1–3.8)	1.2 (0.8–1.5)	.003
Calcification (mm)	N/A	9 (4–18)	.003
Nodal status			
Axillary node positive (%)	58.3	0	.004

Note.—N/A = does not apply.

* The masses were sometimes associated with calcifications.

† Data in parentheses are ranges.

Results continued

- **Screening:** cancer detection rate (CDR) of 18 per 1000 examinations (95% CI: 7, 41), with cancers diagnosed on average after 4 person-years of screening.
- **Diagnostic:** CDR of 20 per 1000 examinations (95% CI: 14.2, 27.8)

Older age, Ashkenazi descent, genetic mutations, personal history, and first-degree family history were associated with breast cancer.

Table 4: Risk Factors Associated with Malignancy

Feature	Feature Absent	Feature Present	Estimate	Odds Ratio		<i>P</i> Value
				Lower	Upper	
Ashkenazi	22.2 (30/135)	78.6 (11/14)	13	3	49	<.001
Family history*	24.1 (28/116)	39.4 (13/33)	2	1	5	.09
First-degree relative†	24.0 (30/125)	45.8 (11/24)	3	1	7	.03
Mutation	24.5 (34/139)	70.0 (7/10)	7	2	29	.006
Personal history	17.7 (23/130)	94.7 (18/19)	84	11	659	<.001

Note.—Unless otherwise specified, data are percentages, with numerators and denominators in parentheses. The percentage of biopsies with a positive result for malignancy in men with and without each risk factor and the lower and upper limits of a 95% confidence interval for the odds ratio of each risk factor as a predictor of a positive biopsy. Each *P* value is from the generalized estimating equations analysis to test whether the risk factor influences the probability of a positive biopsy.

* Indicates family history of breast cancer not otherwise specified. When specified as in first-degree relative(s), they are categorized separately under “first-degree relative” and not included under the general “family history” designation.

† Indicates family history of breast cancer in first-degree relative(s).

Discussion

- Screening is not common in men, but has the potential to detect clinically occult, early stage breast cancers
- Cancer detection rate are comparable (possibly better) in screening for male breast cancer than female breast cancer^{5,6}
- Screening has a possible mortality benefit in men
- Selective screening for male breast cancer appears to be beneficial, especially in high-risk males
 - No screening guidelines in place for high-risk males

Study Limitations

- Retrospective design
- Single institution with imaging studies interpreted by subspecialized physicians, so may not be generalizable to all practice types
- Selection bias: referral for screening was determined by surgical or medical oncologists and driven by patients due to lack of guidelines
- Family history of breast cancer was patient reported, so may be incomplete
- Lack of baseline patient characteristics, unclear if generalizable

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Clinical Questions

- Should males with a first-degree relative diagnosed with breast cancer undergo screening? Should those with other high-risk features?
- Should we create guidelines for screening in males in order to have a consensus?

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Key Points

- Although less common than gynecomastia, male breast cancer DOES occur – keep it in your differential diagnosis!
- Due to male breast anatomy, most male breast cancers are invasive ductal carcinoma, with hormone positive receptors.
- Mammography screening in high-risk men can detect clinically occult and smaller breast cancers.
- High-risk men (older age, Ashkenazi descent, genetic mutations, personal history, and first-degree family history) are more likely to get breast cancer.
- No current guidelines exist for male breast cancer screening.

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