

Current Strategies for Reducing False Positives in US

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Disclosures

- Nothing to disclose

Improving Accuracy

- Improve cancer detection (sensitivity)
 - Optimal technique, correlation with other modalities, careful rad-path concordance
- **Minimize false positives:** biopsy/follow-up of benign lesions (specificity)

Improving Specificity

- Focus on BI-RADS 3 and 4A lesions on HHUS
 - (Final assessments of 3, 4A not given on AUS)
- 12-mo follow-up for BI-RADS 3 on screening US
- Single 6-mo follow-up of probable FA in women < age 35

Dense Breasts: Physician Performed US Multicenter Results

Author	N screens	BI-RADS 3/4 per 1000	Recall Rate (%)	Bx Rate (% women)	PPV3 Bx Performed
Corsetti	9157	4.0	NS	449 (4.9)	50/623 (8.0)
Berg yr1	2659	5.3	401 (15.1)	207 (7.8)	14/264 (5.3)
Berg yr2-3	4841	3.7	356 (7.4)	242 (5.0)	21/276 (7.6)
TOTAL	16,657	4.4	10%	898 (5.4)	85/1163 (7.3)

4.9% of women had biopsies for benign findings vs. 1.2% of women on mammography

Variable Recall Rates by Site

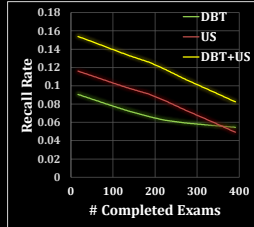
	N Readings	N Recalls US (%)	N Recalls DBT (%)	p-value US vs DBT by site	Overall DBT+US Recalls* (%)
Site A	8288	687 (8.3)	740 (8.9)	0.19	1083 (13.1)
Site B	2502	60 (2.4)	71 (2.8)	0.41	121 (4.8)
Site C	1474	181 (12.3)	67 (4.5)	<0.01	216 (14.7)
Total	12,264	928 (7.6)	878 (7.2)	0.28	1420 (11.6)

Berg RSNA 2017

* After integration across both modalities

Learning Curve

- First 100 exams
 - DBT: 8%
 - US: 11%
 - DBT+US: 15%
- 300-400 exams
 - DBT: 6%
 - US: 5%
 - DBT+US: 9%



Berg RSNA 2017

* $p < 0.01$ for each trend; sustained after exclusion of the year 2 cases

BI-RADS 3 Lesions ACRIN 6666

- 2662 participants, three years of screening
- 519 (19.5%) had 745 B3 lesions on US

Time	New Lesions	BI-RADS 3
0	1920	506 (26.4%)
12	601	12 (23.6%)
24	395	7 (24.6%)
Overall	2916	7 (25.5%)

Barr RG et al Radiology 2013;269:701

BI-RADS 3

- Predominantly a baseline issue for mammography
- There are **new BI-RADS 3 lesions** with each round of screening US
- About 25% of all lesions

ACRIN 6666 BI-RADS 3

- Of 745 BI-RADS 3 lesions on US recommendations
 - 524 (70.3%) 6 mo f/u; 23 (3.1%) 1-yr follow-up
 - 125 (16.8%) Immediate additional imaging
 - 73 (9.8%) Biopsy
- 124 (16.6%) were ultimately biopsied
- 6 (0.8%) malignant (5 patients); only 1 dx at 6-mo f/u
 - 5 (83%) invasive, median 10 mm (2-18), 4/5 (80%) NO
- 12-month follow-up likely sufficient

Barr RG et al Radiology 2013;269:701

12-month follow-up

Nam SY et al J Clin Oncol 2016;34:301-7

- 1666 screening US exams
- 689 (41.4%) BI-RADS 3, 653 had f/u \geq 24 mo or bx (n=31)
- 1/653 (0.2%) malignant, IDC, at 6-mo f/u
- Rec. routine screening at 1 yr for BR3

12-month follow-up?

Moon HJ et al Acta Radiol 2018;59:1045-1050

- 445 women with BI-RADS 3 lesions on US
- 335 had 6-mo f/u and 100 had 12-mo f/u (9-15 mo)
- 3 cancers newly developed, all after 15 mo
- 12-mo f/u may be sufficient

Technologist-Performed Screening US Short-Interval Follow-up

	N screens	N BR3 (%)	N Cancers BR3	Who performed
Kolb 1998	3626	92 (2.5)	0	MD
Kaplan 2001	1862	72 (3.9)	0	tech
Hooley 2012	935	187 (20.0)	0*	tech
Parris 2013	5519	452 (8.2)	Not followed	tech
Destounis 2017	5434	101 (1.9)	0	MD or tech
Overall	17,376	904 (5.2)	None	

Weigert et al CT Experience

	N Screens	N BR3 (%)	N Malignant	Who performed
Prevalence	2706	174 (6.4)	0	tech
Incidence	10,810	694 (6.4)	0	tech

No difference in rates of BI-RADS 3 prevalence vs. incidence screens

Weigert et al. The Breast J 2017;23:34-39

BI-RADS 3 Masses US

- Circumscribed, oval, hypoechoic mass
 - Fibroadenoma (FA) or complicated cyst with debris, some oil cysts
 - Differential: Phyllodes, triple negative grade 3 IDC, less commonly solid-type DCIS
- Probable fat necrosis (3-month follow-up)

Complicated Cysts ACRIN 6666

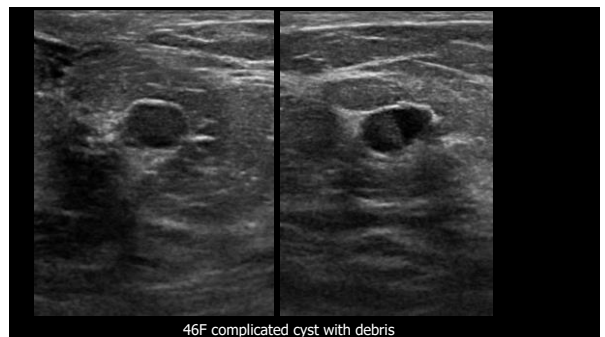
- 376 (14.1%) of 2662 participants
 - 301 (80%) also had at least one simple cyst
 - 84 (22%) multiple, bilateral
- Overall 2/475 (0.42%) such lesions malignant

Berg WA, et al Radiol Clin N Amer 2010;48:931-987

Complicated Cysts

	N	N Malignant (%)
Kolb et al 1998	126	0
Venta et al 1999	308	1
Buchberger et al 1999	133	0
Berg et al 2003	38	0
Chang et al 2007	35	0
Daly et al 2008	228	1
ACRIN 6666	475	2
TOTAL	1343	4 (0.3)

Berg WA et al Radiol Clin N Amer 2010;48:931-987

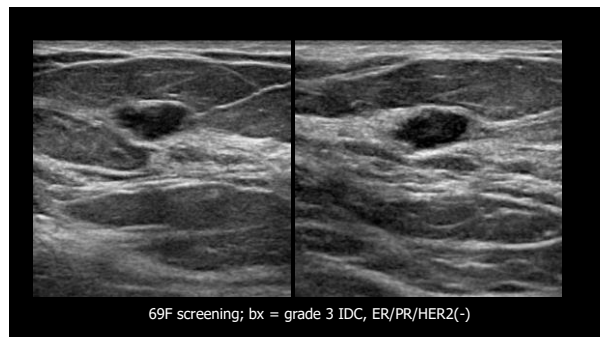
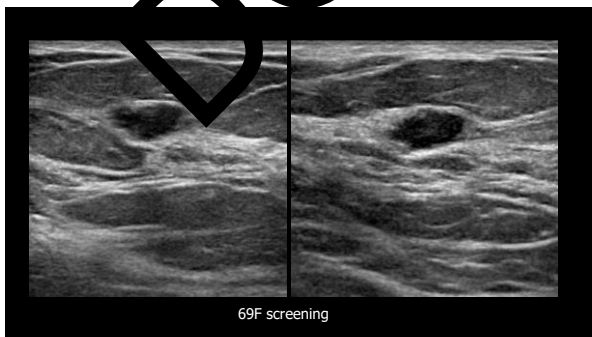
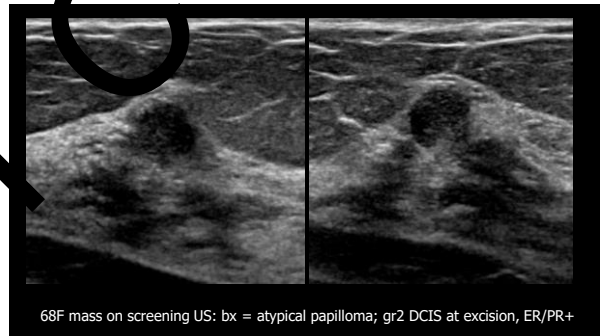
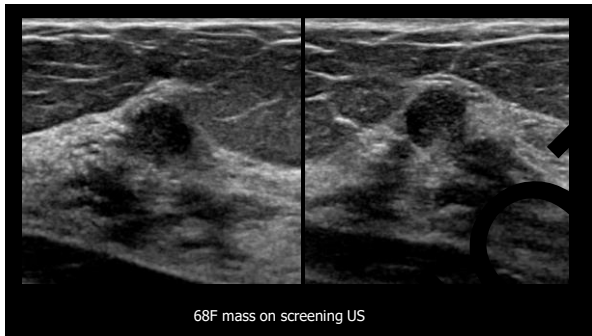
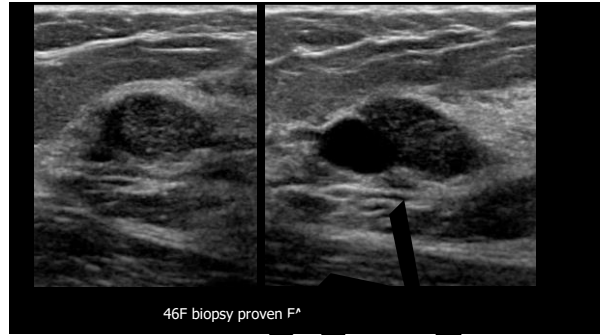
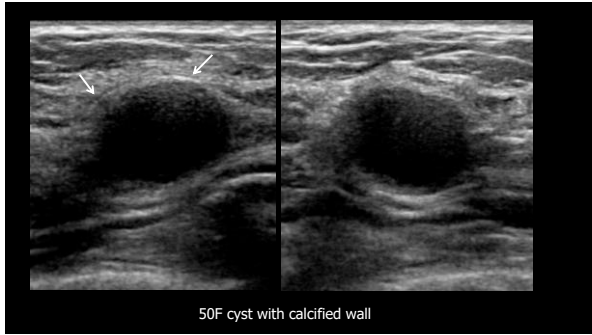


46F complicated cyst with debris



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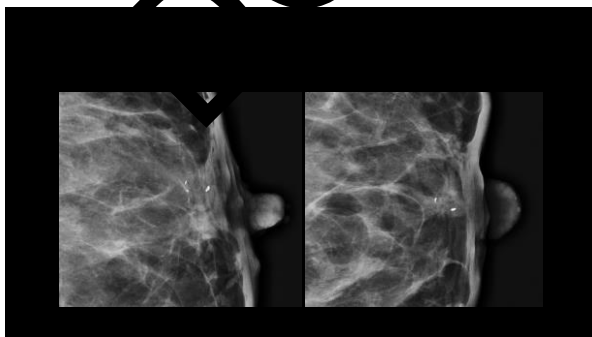
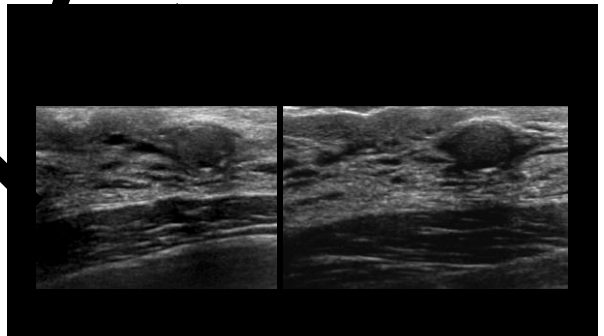
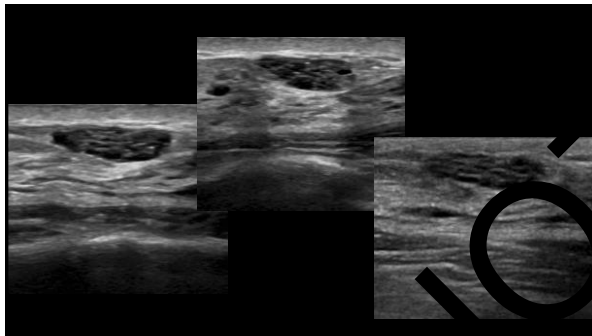
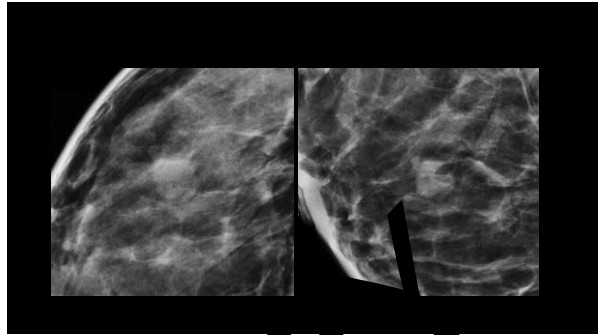


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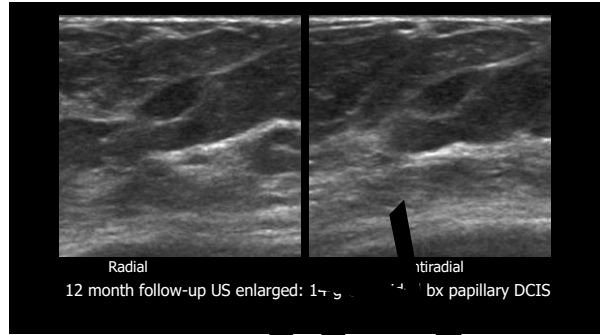
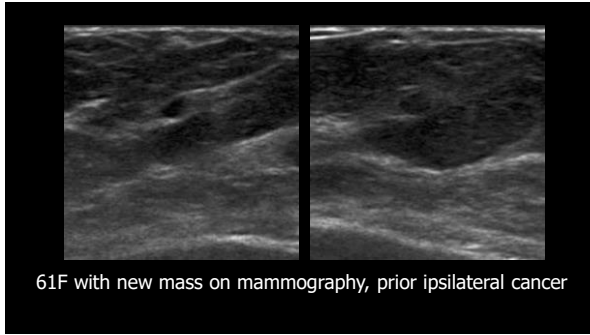
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Many Lesions Should be BI-RADS 2

- Complicated cysts with debris
- Clustered microcysts
- Rim Ca⁺⁺
- Lymph node



- Bilateral avoidable biopsies
 - Fibrocystic changes right
 - Sclerotic cyst wall on left



BI-RADS 3 Screening US

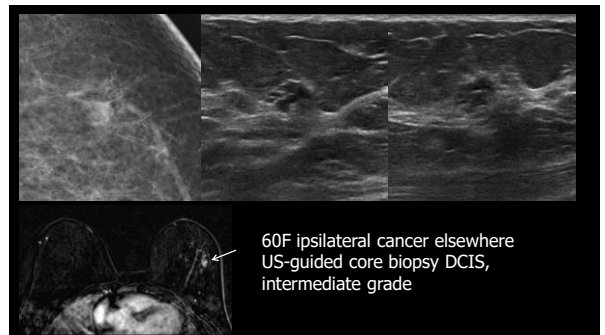
Chae EY et al AJR 2016;206:666-672

- With mammographic abnormality, 4/184 (2.2%) malignant
- Without mammographic abnormality, 4/980 (0.4%) malignant ($p=.025$)

Clustered Microcysts

- 3.9 to 5.8% of US examinations
- 1/235 (0.4%) malignant across 5 series
- Mean age 48 years (32-71)
- Short-interval follow-up if uncertainty
- Caution if new mass on mammogram, post-menopausal woman not on HRT: May merit biopsy

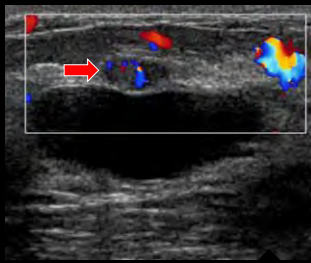
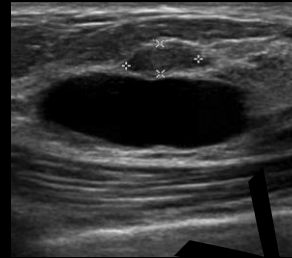
Berg WA AJR 2005;185:952
 Berg WA, et al Radiol Clin N Amer 2010;48:931-987



48F screening US, dense breasts, prior ADH



Berg WA and Mendelson EB. Radiology 2014;272:12-27



Low nuclear grade DCIS

Berg WA and Mendelson EB. Radiology 2014;272:12-27

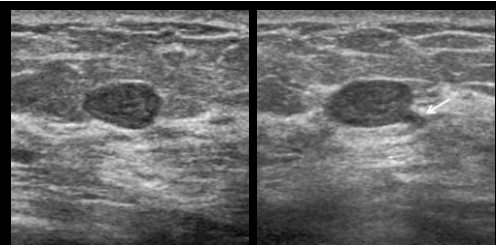
BI-RADS 3 Lesions Synchronous to New Cancer

Kim SJ et al AJR 2008;191:653-8

- 55/482 (11.4%) BI-RADS 3 lesions malignant
 - 36/170 (21.2%) in same quadrant as 1^o
 - 12/122 (9.8%) in different quadrant
 - 8/190 (4.2%) in contralateral breast

Orthogonal Views

- Required for any mass for which future comparison is desirable
 - Not necessary for simple cysts
- Incomplete characterization without this



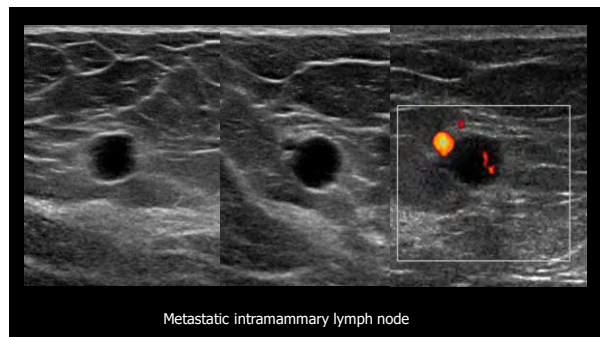
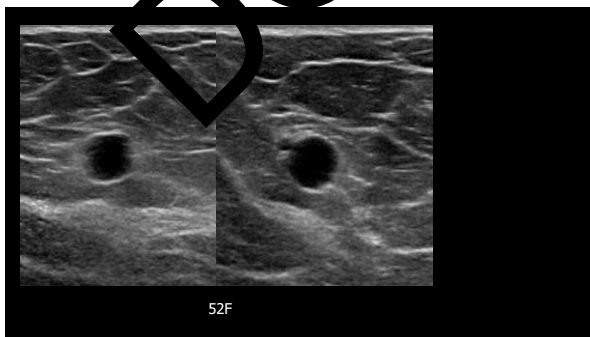
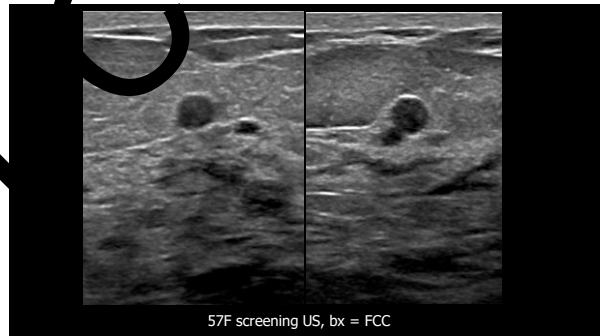
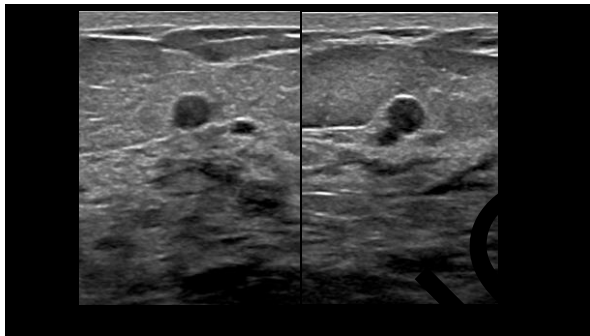
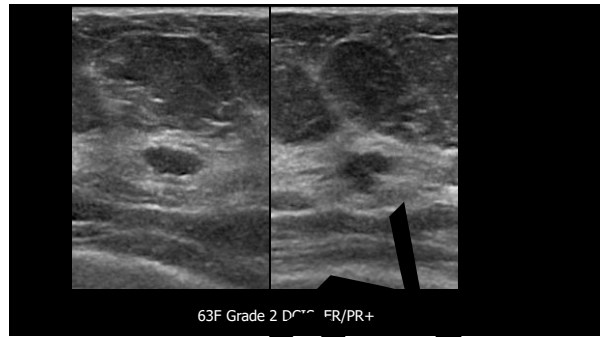
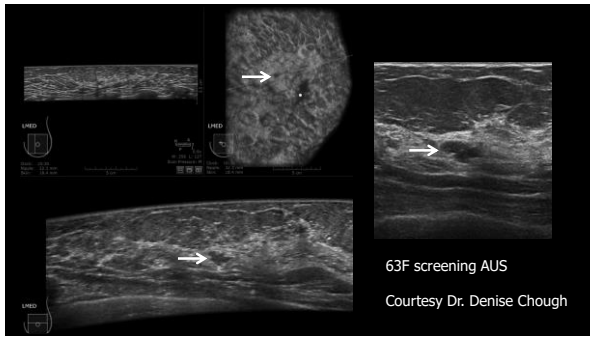
53F Papillary DCIS with microinvasion

Berg WA and Mendelson EB Radiology 2014;262:309-315
Courtesy Dr. Christophe Tourasse



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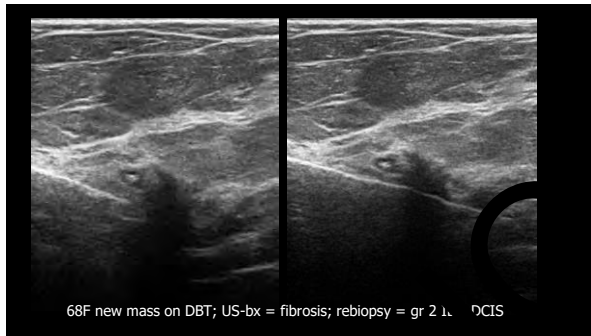
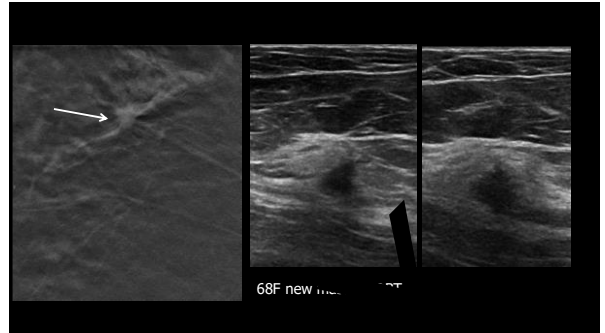


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BI-RADS 2 after B9 bx

- 6-month follow-up is not needed after benign concordant biopsy
- Exception: Fibrosis usually BI-RADS 3
 - 7% of biopsies showing fibrosis ultimately prove malignant

Monticciolo et al AJR 2016, Moon et al AJS 2016
 Johnson et al Radiology 2015, others
 Malik N et al Br J Radiol. 87(1039):20140182, 2014



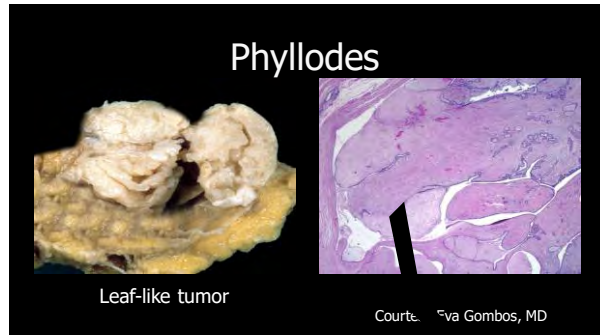
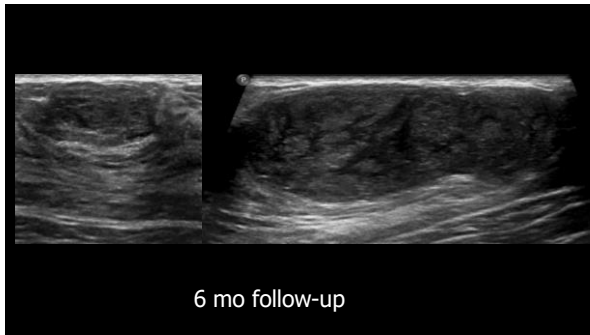
Palpable BI-RADS 3

- In young women, \leq age 34, vast majority are fibroadenomas (FA)
- DDX: Triple negative IDC, phyllodes tumor
- Single 6-mo follow-up sufficient?
- Perform bilateral whole breast US at initial presentation: 15% FAs are multiple, bilateral

Single 6-mo f/u if \leq Age 34

- Marcon M et al EurJRadiol 2017;89:226-233
- 151 BI-RADS 3 masses in 97 women
 - Bx/surgery at presentation in 25 (16%)
 - At 6 mo, 23 downgraded to BR 1 or 2 and 9 upgraded to biopsy BR 4A: 5 FA and 4 phyllodes
 - F/U \geq 18 mo only 1 upgraded to bx = FA

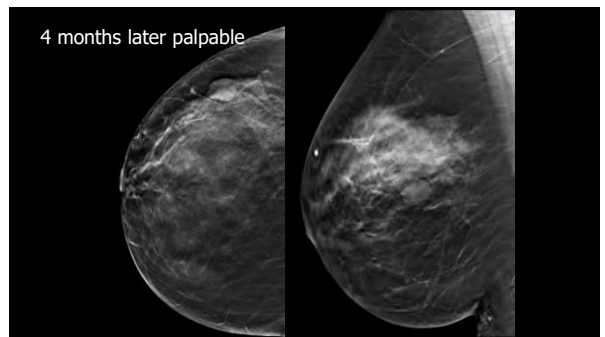
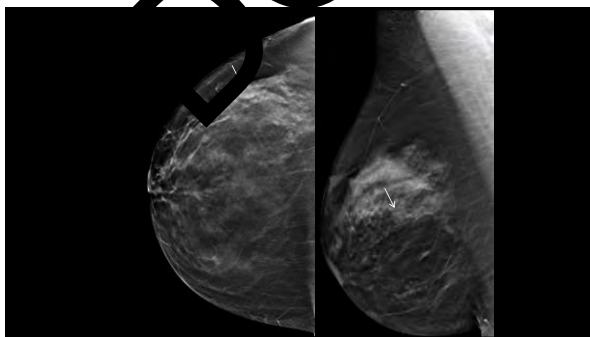
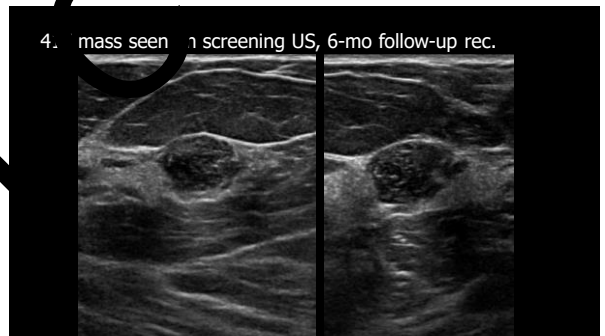


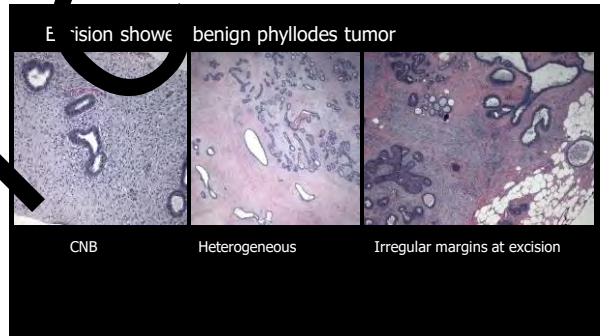
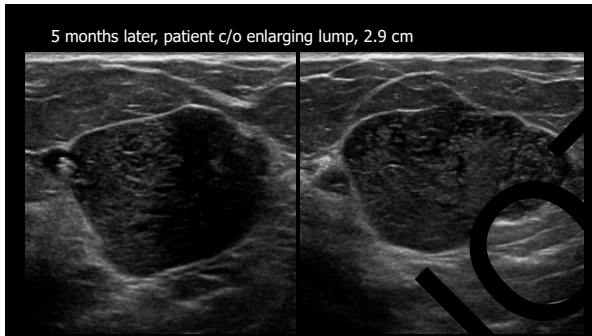
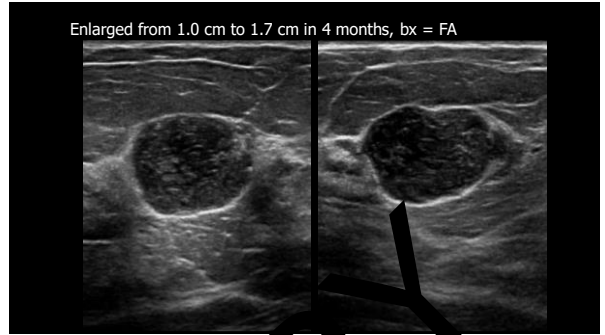
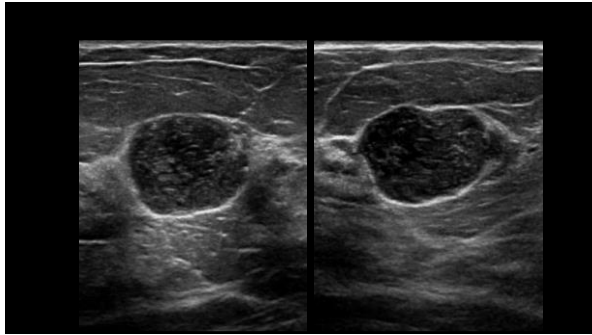


Growth of FA (post FNAB)

Gordon et al Radiology 2003;229:233-238

- Volume growth
 - < 16% per month if < 50
 - < 13% per month if ≥ 50
- Diameter growth
 - < 20% in 6 months any age
- Excision recommended if exceeds limits (2 phyllodes/67 confirmed cases)





BR₃ Masses > 2 cm, B9 Bx

Jung HK et al Ultrasonography 2014;33:200

- 126 BR₃ masses > 2 cm, b9 US CNB (incl. 64 FA) then excised or VAB
- 14 (11%) were borderline phyllodes; 2 (1.6%) were malignant phyllodes

Malignancy Rate ↑ with Age

- < age 30 malignancy rare, FA most common
- 30-39, 1% of lumps malignant
- 40-55, 9% of lumps malignant
- > 55, 37% of lumps malignant

Growing BR-3 Lesions

Ha SM et al BJR 2018;91

- 12,514 BR3 lesions on US 2010-2011
- 738 (5.9%) grew > 20%; 527 had 2-yr f/u or biopsy
- 26/527 (4.9%) malignant (overall 0.2% rate)
- 8/420 (1.9%) malignant with growth only
- 18/107 (17%) malignant w/other suspicious change: margins, shape, echo pattern, orientation

M-B Circumscribed Masses: US

Berg WA et al Radiology 2013;268:673-683

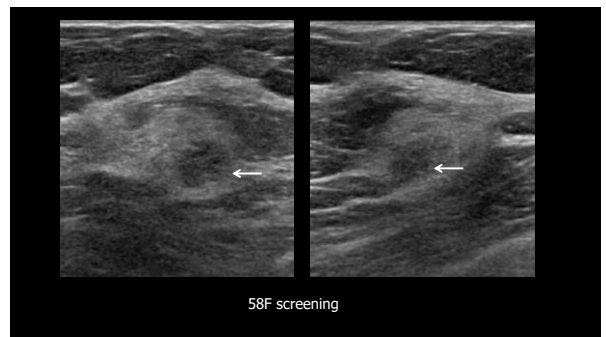
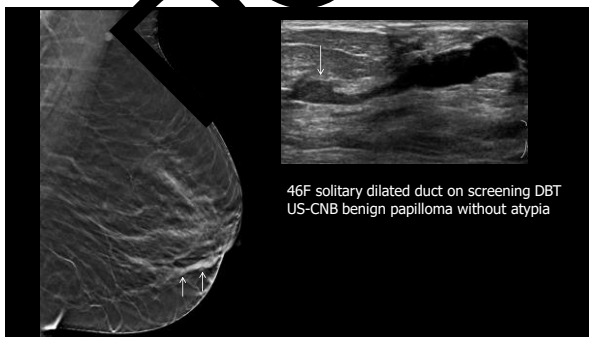
- 2172 women in ACRIN 6666
- 135 (6.2%) participants had 153 unique findings described as M-B masses on screening US over 3 annual screens
 - 98 complicated cysts with debris
 - 43 solid, circumscribed, oval masses
 - 7 solid masses with 2-3 lobulations
 - 5 clustered microcysts
- No malignancies (95% CI up to 2.4%)

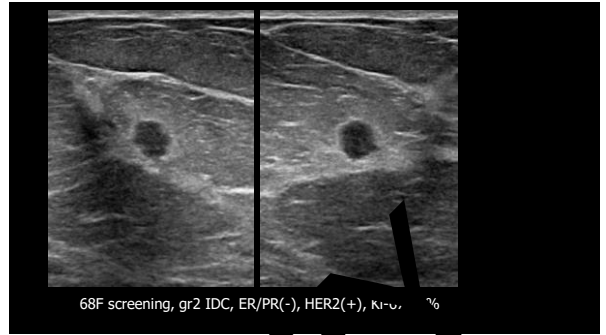
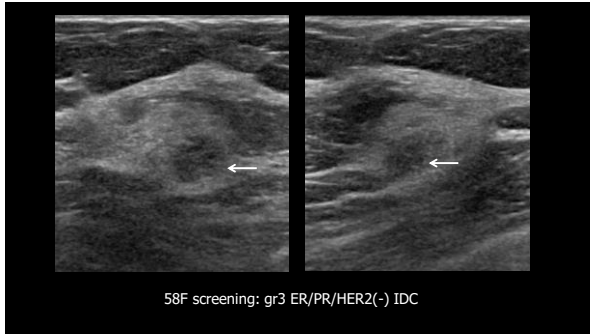
Caution!

- In ACRIN 6666, 2/82 (2.4%) women with multiple bilateral circumscribed masses also had cancer seen only sonographically
- Song SE et al Radiology 2015: A source of false negative screening US was multiple distracting lesions (12/72, 17%, of masses)

BI-RADS 4A

- > 2% to < 10% risk of malignancy, biopsy recommended
- Intraductal mass
- Probable FA but one of the following
 - Focally non-circumscribed margin
 - Heterogeneous echotexture
 - Vertical orientation
 - Posterior shadowing
 - Echogenic rim
 - Associated distortion

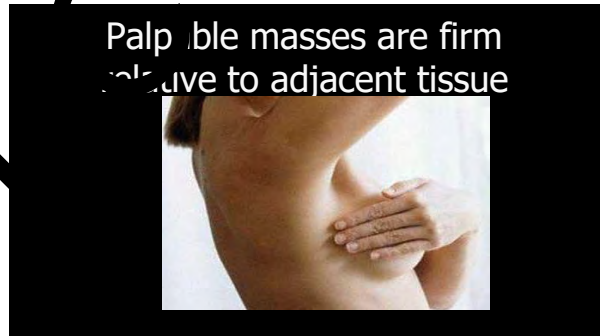




Outcomes of BI-RADS 4A

	N	N Bx (%)	N Malignant (%=PPV3)	Comments
Wiratkapun 2010	281	232	21 (9.1)	Mammo, US
Yoon 2011	1963	1963	149 (7.6)	Age > 40; palpab' single lesions worse
Berg 2012 BE1	193	18	18 (9.3)	Multination' palp/scr -detecte
Jales 2013	389 [^]	389	70 (18.0)	Mix palp not; includes mlob, i gular parallel
Patterson 2014	376	343	9 (2.6%)*	palpable

[^]3 readers, total reads
 * One phyllodes age 25, one BCL age 35; 7 breast cancers < age 30

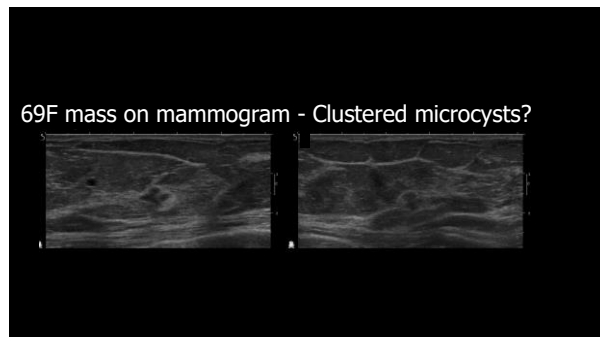
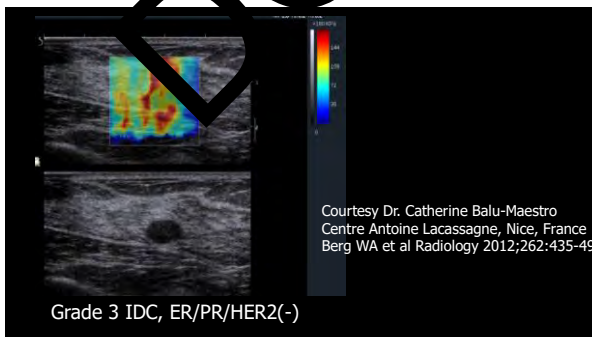
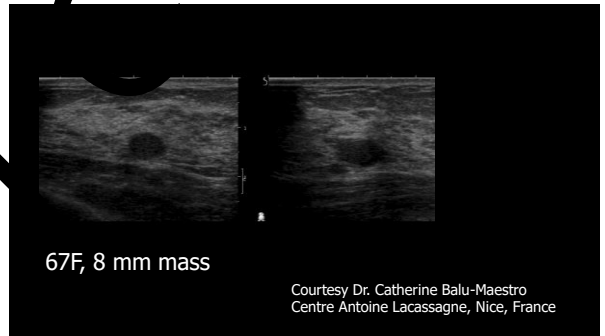
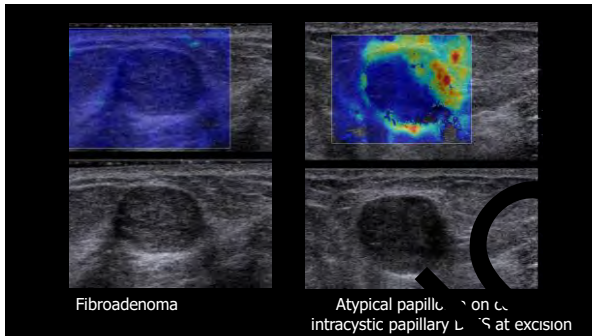
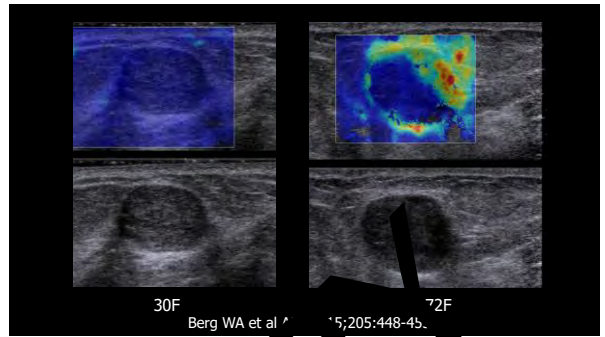
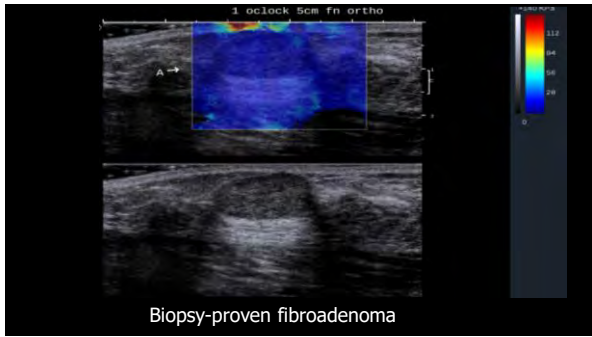


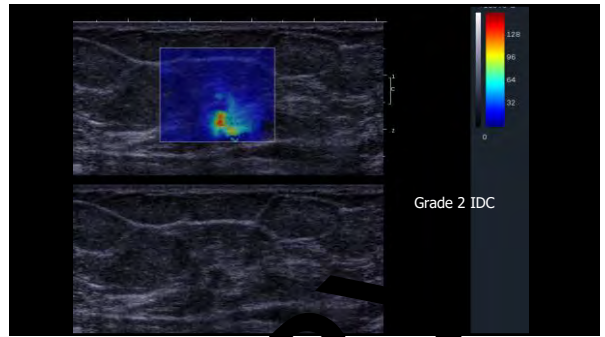
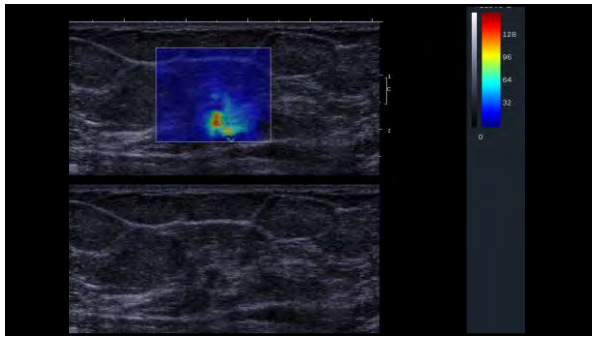
Elastography

- Use to selectively upgrade malignant BI-RADS 3 and downgrade benign BI-RADS 4A
- Addresses BOTH sensitivity and specificity
- Should NOT be used for BI-RADS 4C or 5 masses

Elastography

- Measure of deformation or strain (static elastography) vs. shear modulus via shear-wave velocity (shearwave elastography)
- May reduce false positives
 - Complicated cysts, fibroadenomas "soft"
 - Cancer "stiff"
- Difficult beyond 3 to 3.5 cm depth
- Need for standardized terminology and display





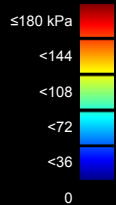
BE1 Multicenter SWE

- 939 lesions from 16 sites in Europe and US
- 181 (19%) masses were oval, circumscribed, no suspicious findings
 - 144 BI-RADS 3, including 4 (2.8%) malignancies
 - 37 BI-RADS 4a with no malignancies

Berg WA et al Radiology 2012;262:435-49

Maximum Elasticity: SWE

- Add associated feature of elasticity
- BI-RADS 3 + E yellow to red
 - All 4 cancers upgraded
 - 8 FP B-R 3 upgraded to biopsy
- BI-RADS 4a + E green to blue/
 - 34 benign lesions downgraded
 - Fewer unnecessary biopsies



Berg WA et al Radiology 2012;262:435-49

Validation in Screening

Lee SH et al Radiology 2014;273:61-69

- SWE prior to bx of masses found on screening US
- 159 masses in development cohort, 21 (13.2%) malignant
- 207 in validation cohort, 12 (5.8%) malignant

Screening: Lee et al

- Downgrade BI-RADS 4a masses dark blue in color or softer than 30 kPa to surveillance (BI-RADS 3)
- Specificity increased dramatically
 - 13/138 (9.4%) to 82/138 (59.4%) or 79/138 (57.2%) development cohort
 - 34/195 (17.4%) to 121/195 (62.1%) or 104/195 (53.3%) in validation cohort
- No loss in sensitivity



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Summary: 12-month f/u BR3

- Seen on screening US, no mammographic correlate
- Multiple bilateral, nonpalpable

Single 6-mo f/u \leq Age 34

- Single 6-mo f/u palpable mass BR3 in women \leq 34 years old, likely FA
- Further study warranted

Biopsy BR3

- Patient with newly-diagnosed cancer
- Patient plans pregnancy
- Follow-up not possible
- Patient preference
- Stiff on elastography
- Suspicious change on follow-up
- Interval growth $>$ 20% in diameter in \leq 6 mo

Summary: Avoid Bx BR4A

- Soft on elastography ($<$ 30 kPa)

Thank you!

