BI-RADS Category 3: Probably Benign Lesions Detected on Mammography, US and MRI: Characteristics and Follow-up

Susan Orel Roth, MD
Professor of Radiology
University of Pennsylvania
Objectives

For mammography, US and MRI:

- Define BI-RADS category 3
- Review the literature on frequency and outcome of BI-RADS 3 Illustrate cases where finding can be placed in BI-RADS 1 or 2 rather than 3
- Describe types of findings that can be placed in BI-RADS 3
- Discuss possible follow-up algorithms
- Discuss importance of auditing practice
BI-RADS Imaging Lexicon
Breast Imaging Reporting and Data System

- Developed by the ACR (1992) as a tool to reduce variability in terminology used in mammography reporting and to standardize:
  - Terminology in mammography report
  - Assessment of findings
  - Resulting recommendation for action
- 2003 atlas revised and included first edition with US and MRI
- 5th edition recently published
Breast Imaging Reporting and Data System (BI-RADS) 3 Assessment Category

- Originally established for use in mammography
- A finding placed in this category is highly unlikely for malignancy and should have a very high probability of being benign
- Published evidence and current practice support use BI-RADS 3 and short-term follow-up for specific mammographic findings shown to have chance of representing malignancy <2% of cases
Mammography BI-RADS 3
Definition BI-RADS 3

- Defined based on findings at diagnostic mammography
- Very small likelihood of malignancy - 0.3%-1.7%
- Lesions that prove to be malignant
  - Identified by interval change
  - Vast majority in-situ or stage 1
- Offers alternative to biopsy
  - Reduced cost, morbidity, patient anxiety, increased cost effectiveness screening
Periodic Mammographic Follow-up of Probably Benign Lesions
Sickles EA. Radiology 1991; 179:463

- 3,184 (11.2%) interpreted as probably benign
- Localized
  - Cluster of tiny round or oval calcifications
  - Non-calcified, well-defined solid mass
  - Focal asymmetric area of fibroglandular density
- Generalized
  - Discrete clusters of tiny calcifications
  - Scattered tiny calcifications
  - Non-calcified, well-defined solid masses
Periodic Mammographic Follow-up of Probably Benign Lesions
Sickles EA. Radiology 1991; 179:463

• Follow-up consisted of 4 mammograms during 3-3.5 year period
• Compliance declined progressively with each subsequent exam, fell off most strikingly at the final exam (45% completed all 4 mammograms)
• 161 biopsies done (>80% due to change)
• 17 cancers found—overall PPV 0.5%
  – 12 masses—PPV 2%
Periodic Mammographic Follow-up of Probably Benign Lesions
Sickles EA. Radiology 1991; 179:463

- Cases restricted to non-palpable lesions
- Comparison with prior mammograms when available
- **Diagnostic evaluations**
  - Spot magnification views in orthogonal projections
- Use of specific interpretation criteria
Importance of diagnostic work-up
With magnification views: milk of calcium—BI-RADS 2
Non-palpable, non-calcified solid breast masses: likelihood of malignancy based on lesion size and age of patient

Sickles EA. Radiology 1994; 192:439

- 1,403 study cases
- 19 (1.4%) cancers
- Only small differences in PPV for various age and lesion size groups
- Concluded that this type of lesion can be managed with short-interval follow-up regardless of patient age and lesion size
Mammography BI-RADS 3

- Two longitudinal prospective studies 1987-1989 of > 20,000 women each*
- Prospective study > 13,000 women**
- Likelihood of malignancy BI-RADS 3 lesion 0.3%-1.7%
- Follow-up study PPV decreased 1.7% to 0.4%***
  - Lesion growth prompts biopsy
  - Malignancies found had favorable prognosis

* Sickles EA. Radiology 1991
* Varas X. Radiology 1992
** Vizcaino I. Radiology 2001
*** Varas X. AJR 2002
Focal asymmetry
Circumscribed mass on mammography
Category 3 after XRT: Evolving fat necrosis
Mammography BI-RADS

- Percentage of screening mammograms placed into Category 3
  - 1.2%-9.83%; average 5%
  - 1.4%-14%; average 7.7%
  - 1.1%-12.2%; average 6%
- Lower if diagnostic work-up completed
- Recommended that Category 3 used only after completed diagnostic work-up
- 5th edition of BI-RADS-Category 3 on screening will be positive vs. Category 3 on diagnostic will remain negative
Use of BI-RADS 3 in ACRIN DMIST Screening Trial

- 1114 of 47,599 (2.34%) category 3
  - 791 of 1114 (71%) compliant
  - 70% of noncompliant did get 1 year mammo
- 9 of 1114 (0.81%) had malignancy
  - 6 invasive (all < 2 cm); 3 DCIS
- Majority of radiologists used Category 3 after diagnostic work-up (90% of cases)
Compliance

- Compliance perhaps biggest limitation to using BI-RADS category 3
- DMIST trial 29% non-compliant
- Varas showed improved compliance from 1st study- 76% and 2nd -83%
- Call-back for full work-up important
- Discussion with patient shown to improve compliance
Follow-up Algorithm

- BI-RADS category 3 finding should be followed for 2 years to confirm stability
- Initial recommendation was 6 month, 12 month, 18 month, 24 month exams
- Discussion to eliminate 18 month exam
Ultrasound BI-RADS
Ultrasound BI-RADS

- First edition—2003
- Accumulated clinical experience and by extension from mammography
- Solid mass with circumscribed margins, oval shape and horizontal orientation, most likely a fibroadenoma
  - Should have < 2% risk of malignancy
- Nonpalpable complicated cysts and clustered microcysts might also be placed in this category
Solid breast nodules: use of sonography to distinguish between benign and malignant lesions


- 750 solid breast masses classified prospectively as benign, indeterminate, or malignant
  - Benign had no malignant characteristics and either uniformly hyperechoic or thin echogenic “pseudocapsule” with oval shape or <5 “gentle lobulations”
- Benign features in 625 (83%)
- Malignant features 125 (17%)
Stavros, et al.

- Two masses classified as benign proved to be malignant
  - NPV 99.5%
- Of 125 malignant masses, 123 correctly classified as indeterminate or malignant
  - Sensitivity 98.3%
- Concluded that US can be used to accurately classify some solid masses as benign allowing for follow-up rather than biopsy
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Malignant</th>
<th>Benign</th>
<th>Indeterminate</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Spiculation</td>
<td>Absence of malignant findings</td>
<td>Maximum diameter</td>
</tr>
<tr>
<td></td>
<td>Taller than wide</td>
<td>Intense hyperechogenicity</td>
<td>Isoechogenicity</td>
</tr>
<tr>
<td></td>
<td>Angular margins</td>
<td>Ellipsoid shape</td>
<td>Mild hypoechogenicity</td>
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<td></td>
<td>Marked hypoechogenicity</td>
<td>Gentle bi- or trilobulation</td>
<td>Normal sound transmission</td>
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<td></td>
<td>Shadowing</td>
<td>Thin, echogenic pseudocapusle</td>
<td>Enhanced transmission</td>
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<tr>
<td></td>
<td>Calcification</td>
<td></td>
<td>Heterogeneous echotecture</td>
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<td></td>
<td>Duct extension</td>
<td></td>
<td>Homogeneous echotexture</td>
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<tr>
<td></td>
<td>Branch pattern</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Microlobulation</td>
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</table>
Stavros et al.
US BI-RADS Descriptors

• Shape
• Orientation
• Margins
• Lesion boundary
• Echo pattern
• Posterior acoustic features
US BI-RADS

- US in operator dependent
- Several investigators have reported limited interobserver agreement on US descriptors and categorization
- Reproducibility in use of BI-RADS terminology good except for margin evaluation
  - Lower concordance for smaller masses
All radiologists classified at BI-RADS 3

Abdullah N, et al.
Radiology 2009
Radiologists disagreed on mass margins and BI-RADS category: 3, 4a, 4b.

Pathology: Fibroadenoma

BI-RADS 3 nonpalpable breast masses seen only on US


- Prospective cohort study 2003-2010 of 11,373 consecutive women
- Nonpalpable masses on US only 5.3%
- 562 lesions found in 451 women
- Malignancy rate 0.3% (2/562)
- NPV 99.6%
Probably benign breast masses at US: is follow-up an acceptable alternative to biopsy?


- Retrospective study 2001-2003
  - 445 non-palpable masses classified BI-RADS 3
- 442 remained stable at f/u 2-5 years
- 2 masses increased; both fibroadenomas
- 1 mass became palpable—cancer
- False negative rate 0.2%
Ultrasound only detected mass. Classified as BI-RADS category 3. Mass became palpable after 4 months. Pathology: IDC
What if mass is palpable?
### Review of Literature Addressing NPV of Breast US in Setting of Palpable Mass

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>BI-RADS US</th>
<th>Cancers/Total</th>
<th>NPV (%)</th>
<th>Palpable or not</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graf</td>
<td>2004</td>
<td>3</td>
<td>0/157</td>
<td>100</td>
<td>Palpable</td>
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<tr>
<td>Maniero</td>
<td>2005</td>
<td>3</td>
<td>1/148</td>
<td>99.3</td>
<td>Palpable</td>
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<tr>
<td>Raza</td>
<td>2008</td>
<td>3</td>
<td>3/356</td>
<td>99.2</td>
<td>Palpable</td>
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<tr>
<td>Park</td>
<td>2008</td>
<td>3</td>
<td>2/312</td>
<td>99.4</td>
<td>Palpable</td>
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<tr>
<td>Harvey</td>
<td>2009</td>
<td>3</td>
<td>2/375</td>
<td>99.5</td>
<td>Palpable</td>
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<tr>
<td>Giess</td>
<td>2012</td>
<td>3 or 4a</td>
<td>3/336</td>
<td>99.1</td>
<td>Palpable</td>
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</tbody>
</table>
Palpable mass in 27 yr. old. BI-RADS 3
Tissue diagnosis desired: FA

Giess et al.
Palpable mass 49-yr-old woman
BI-RADS 4A
Pathology: poorly differentiated IDC
Ultrasound BI-RADS 3

- Solid mass (non-palpable or palpable) with circumscribed margins, oval shape, and parallel orientation can be classified as category 3
  - Should have risk of malignancy < 2%
- Follow-up algorithm based on mammography
  - US at 6, 12, 18 (optional), 24 months
  - Possible hematoma, follow-up 6-8 weeks
Compliance

- Success of probably benign assessment paradigm rests on assumption patient will return for follow-up
- Reported rate of 54% after benign core biopsy (Goodman et al. AJR 1998)
- Reported rate of 82.6% of patients recommended follow-up with US only for 2 years (Raza et al. Radiology 2008)
BI-RADS 3—Ongoing Controversy

• This management strategy is not uniformly accepted
  – Absence of histologic proof
• Should age be taken into account?
  – More cancers in women > 40 years of age
• National screening programs in UK and Sweden not include this category, instead recommending biopsy or routine f/u
Category 3 finding in setting of newly diagnosed cancer?
MRI BI-RADS 3
MRI BI-RADS Lexicon

- 1998-2000 development and refinement of first breast MRI lexicon
- 2003 1st edition of the ACR BI-RADS® MRI lexicon for reporting breast MRI findings; 2nd edition now available
- To standardize the language used in reporting breast MRI finding, to aid clinician understanding; aid scientific research
MRI BI-RADS Lexicon

- Category 0: need additional evaluation
- Category 1: negative
- Category 2: benign finding(s)
- Category 3: probably benign finding—short interval follow-up suggested
- Category 4: suspicious abnormality—biopsy should be considered
- Category 5: Highly suggestive of malignancy—appropriate action should be taken
- Category 6: Known cancer—malignancy—appropriate action should be taken
Published Studies of breast MRI that include data on BI-RADS 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Probably benign exams</th>
<th>Probably benign patients</th>
<th>Compliance with 1st follow-up</th>
<th>Frequency of tissue sampling</th>
<th>Cancer yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuhl 2000</td>
<td>45/363 (12)</td>
<td>42/198 (21)</td>
<td>NR</td>
<td>2/42 (4.8)</td>
<td>1/42 (2.4)</td>
</tr>
<tr>
<td>Liberman 2003</td>
<td>NR</td>
<td>89/367 (24)</td>
<td>70/89 (79)</td>
<td>20/89 (22)</td>
<td>9/89 (10)</td>
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<td>Kriege 2004</td>
<td>275/4169 (6.6)</td>
<td>NR/1909</td>
<td>NR</td>
<td>12/275 (4.4)</td>
<td>3/275 (1.1)</td>
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<td>Eby 2007</td>
<td>NR/809</td>
<td>149/678 (22)</td>
<td>100/149 (63)</td>
<td>8/149 (5.4)</td>
<td>1/149 (0.7)</td>
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<tr>
<td>Eby 2009</td>
<td>260/2569 (10)</td>
<td>236/1735 (14)</td>
<td>146/236 (62)</td>
<td>18/236 (7.6)</td>
<td>2/236 (0.85)</td>
</tr>
</tbody>
</table>

Adapted from Eby PR, et al AJR 2009; 193:861
BI-RADS Category 3: Mammography vs. MRI

- **Mammography Category 3**
  - Type of findings well described
  - Likelihood of malignancy <2%
  - Low cost relative to biopsy
  - Reported rates 1.2%-15%

- **MRI Category 3**
  - Type of findings not well described
  - Likelihood of malignancy up to 10%
  - Very costly; ? Cost effective relative to core biopsy
  - Reported rates 7%-25%
Category 1 vs. Category 3: What is normal background parenchymal enhancement (BPE)?
Background Parenchymal Enhancement

- Will be addition to 2\textsuperscript{nd} edition of breast MRI BI-RADS lexicon
- Enhancement of presumably normal breast tissue
- BI-RADS background enhancement
  - Minimal (<25%)
  - Mild (25-50%)
  - Moderate (50-75%)
  - Marked (>75%)
- Potential impact on MRI sensitivity and specificity
Background parenchymal enhancement on baseline screening breast MRI: impact on biopsy rate and short-interval follow-up

Hambly et al. AJR 2011; 196:218

- 250 baseline high-risk screening MRI
- 25% minimal; 34% mild; 24% moderate; 17% marked
- Minimal enhancement significantly higher number category 1 and 2
- Category 3 – 43.6%
  – Significantly lower when minimal
- No significant difference in biopsy rate or cancer detection rate among categories
Background Parenchymal Enhancement on Breast MRI: Impact on Diagnostic Performance
Demartini WB et al. AJR 2012; 198:373

- 736 women underwent breast MRI 3/06-6/07
- Moderate or marked background parenchymal enhancement:
  - Significantly more frequent women < 50 years old (p<0.0001)
  - Associated with higher abnormal interpretation rate (30.5% vs. 23.2%; p=0.046)
- But positive biopsy rate, cancer yield, sensitivity and specificity not significantly different
Category 1 vs. Category 3: What is normal background parenchymal enhancement (BPE)?

- Bilateral symmetric enhancement
  - Non-mass like enhancement (NMLE)
    - Non-segmental; no architectural distortion
  - Multiple bilateral diffusely distributed foci
- When cannot assess symmetry
  - Multiple foci are similar in size, morphology, kinetics
  - Multifocal NMLE without suspicious morphology
Foci

< 5 mm “dots”; only on one slice; usually multiple and bilateral
Bilateral Symmetrical Enhancement

Left breast

Right breast

Courtesy Elizabeth Morris, MD; MSKCC
When can’t use symmetry

Moderate background

Minimal background after radiation therapy
Utilization Patterns of BI-RADS 3

• There is a learning curve to placing patients into Category 1 or 2 rather than 3
• It has been shown that utilization of Category 3 in setting of high-risk screening will decrease with subsequent rounds of screening (7.6%; 2.9%; 2.4%)*

*Warner et al. JAMA 2004; 292:1317
Normal background enhancement

High-risk screening
Baseline
BI-RADS 3

5 month follow-up
BI-RADS 1

Category 2 rather than 3

- Fat containing mass
  - Lymph node
- Mass with all benign features of a fibroadenoma
  - Circumscribed, lobulated borders
  - Non-enhancing septations
  - Benign kinetic curve
Post contrast T2

Lymph node
BI-RADS 2
Fibroadenomas

T2 FSE

Post contrast
Recommendations for use of probably benign (Category 3) assessment

- Identify one or more focal areas of enhancement distinct from background enhancement (foci, mass, non-mass)
- Assess morphology, size, stability, distribution
- One or more round or oval masses with smooth margins
- Focal or regional NMLE
- Non-wash out kinetics
- Targeted ultrasound may be considered
  - Suggest US for mass > 5-10 mm in size
Morphology and Kinetics:

Benign morphology

Suspicious kinetics

Use most suspicious feature

Courtesy D. David Dershaw, MSKCC
31 year old BRCA 1 carrier
Characteristics of probably benign breast MRI lesions
Eby PR, et al. AJR 2009; 193:861

- 2,569 consecutive breast MRIs 2003-2006
  - Majority for high-risk screen or staging
- 362 BI-RADS category 3 in 10.1% exams and 13.6% of patients
  - 168 (46%) foci
  - 132 (35%) non-masslike enhancement
  - 62 (17%) masses
- Cancer yield 2 (0.85%) of 236
  - Both DCIS
- No malignancies in 69 foci with 100% persistent enhancement
Category 3 in setting of newly diagnosed cancer?

- Try to avoid using Category 3 when clinical history is “extent of disease” in newly diagnosed cancer
  - Both ipsilateral and contralateral breast
- Creates uncertainty
- If the finding goes away after treatment, impossible to know if it was background enhancement or treated malignancy
Frequency of malignancy seen in probably benign lesions at contrast-enhanced breast MRI: findings from ACRIN 6667

- MRI screening contralateral breast in patients with newly diagnosed cancer
- 11% 106/969 at least one BI-RADS 3 lesion (145 lesions) in contralateral breast
  - 37 (26%) mass
  - 59 (41%) NMLE
  - 47 (32%) foci
- Malignancy in 1 (0.9%) patient (DCIS)
Contralateral breast screening

Finding: scattered enhancing foci: Normal vs. Lesions

What to do???
Probably Benign Lesions: Follow-up

- Follow-up algorithm not yet defined
- Suggest initial follow-up at 6 months
  - Ideal to image weeks 7-14 of menstrual cycle
- Interval decrease in size or complete resolution
  - Category 1 or 2
- Increase in size or suspicious change in morphology
  - Category 4 or 5
- No significant change
  - Category 3
  - Additional 6 month follow-up; up to 2 years
Probably benign

2 weeks later

Courtesy of Elizabeth Morris, MD; MSKCC
Screening - Progression - DCIS

BI-RADS 3

6 month follow-up

Courtesy of Elizabeth Morris, MD; MSKCC
Downsides of overuse of BI-RADS 3

• Increased cost (at least one, and often multiple 6 month follow-up exams)
  – Insurance carriers may limit or deny coverage for these short-interval exams
• Increased patient anxiety
  – Especially in setting high-risk screening
• Increased frustration of referring clinicians
Follow-up Compliance

• Reported compliance with short-interval follow-up mammography 69%-89%
• More barriers with MRI
  – Higher cost
  – Requires more time from the patient
  – Some insurance companies will deny coverage for breast MRI more than once a year even in highest risk women
  – Reported compliance rates 62%-86%
Auditing your practice

• There will be learning curve to use of BI-RADS category 3
• Critical to audit your practice
• Frequency of use of BI-RADS 3
• Outcome of cases placed in BI-RADS 3
  – Which cases could really be BI-RADS 1 or 2
  – Number of cancers
Conclusions

• Published evidence and current practice support use BI-RADS 3 and short-term follow-up for specific mammographic findings shown to have chance of representing malignancy <2% of cases

• BI-RADS 3 after diagnostic work-up
  – On work-up, may be BI-RADS 1, 2, 3, or 4
  – For findings placed into BI-RADS 3, discussion with patient shown to improve compliance to return for follow-up
Conclusions

BI-RADS 3 for ultrasound:

• Accumulated clinical experience and by extension from mammography
• Solid mass with circumscribed margins, oval shape and horizontal orientation, most likely a fibroadenoma
  – Should have < 2% risk of malignancy
• Demonstrated for both palpable and nonpalpable masses
• Discussion with patient is critical
  – Improves compliance
  – Discuss alternative of biopsy
Conclusions

• Data for use of BI-RADS category 3 for MRI finding much more limited than mammography (and US)
• Bilateral symmetric findings typical of background enhancement; scattered foci; lymph node; cyst; fibroadenomas
  – BI-RADS 1 or 2
• Category 3
  – One or more focal areas of enhancement without suspicious morphology / kinetics
Conclusions

• Follow-up algorithm for MRI not yet defined
  – First follow-up at 6 months—if gone, BI-RADS 1
  – If stable, follow-up every 6 months for 2 years (based on mammography guidelines)

• Critical to audit your practice
  – Frequency and outcome of BI-RADS 3
  – Learning curve—don’t want to overuse
  – Frequency of cancers found