



# How to Manage Suspicious Microcalcifications?

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# Disclosures

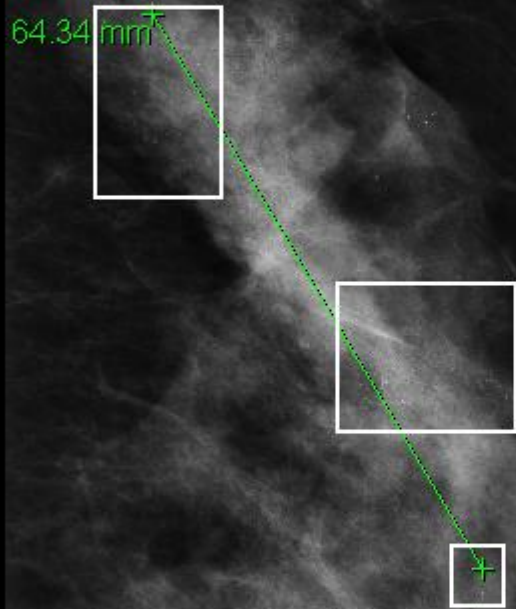
- I have no actual or potential conflict of interest in relation to this program/presentation.
- Research Support : AlvogenKorea
- Others : no disclosure

# Case I

F/43

## Left Magnification

64.34 mm



punctate, amorphous and fine pleomorphic microcalcification segmental or regional distribution in upper outer quadrant of left breast

CATEGORY: **4B**

2D

62%

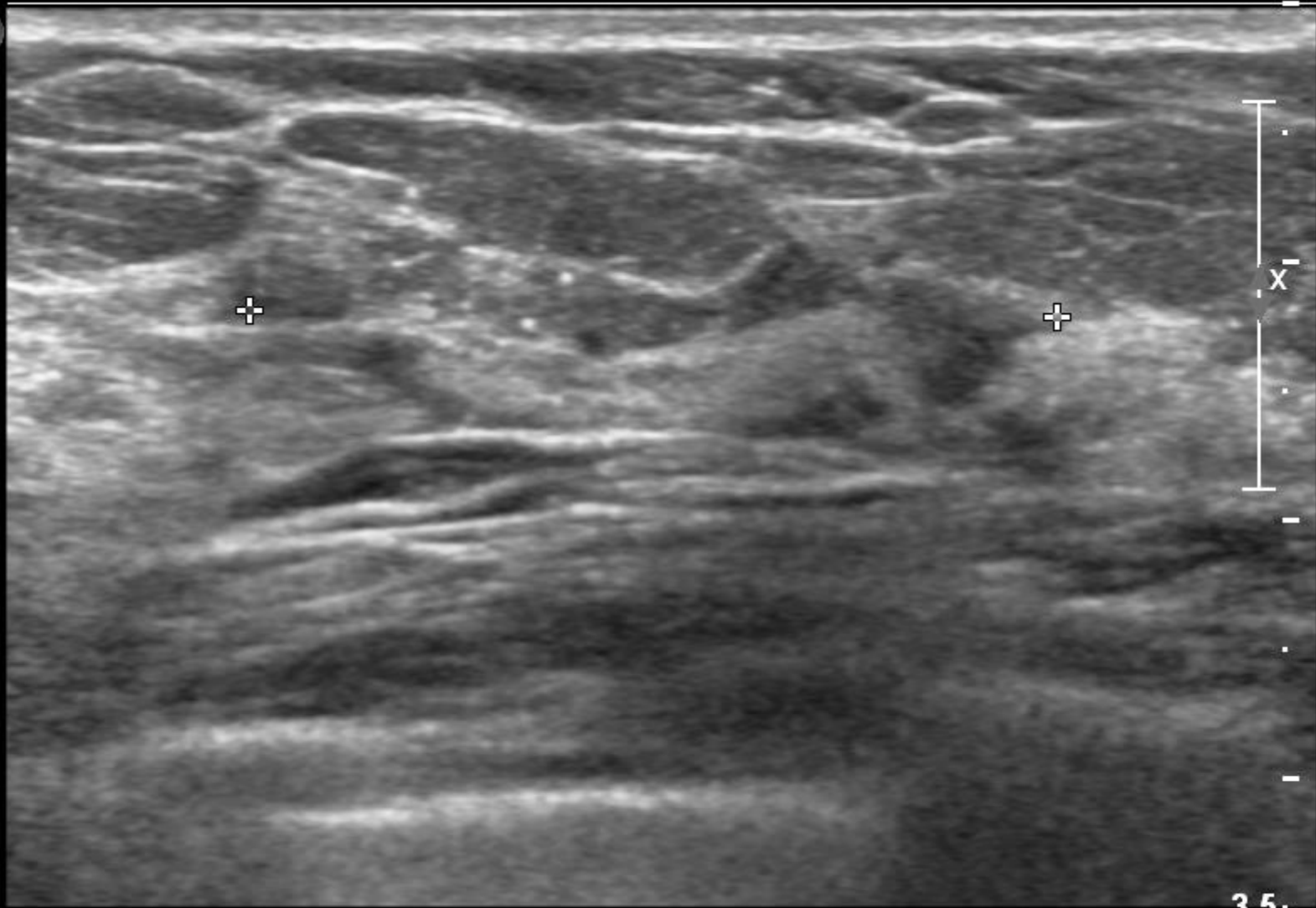
C 63

P Med

Res

TAC1

P



2:00 3CM

3.5

US : About 4 cm non-mass lesion in LEFT 2:00, 3 cm from nipple - CATEGORY: 4C

2D

62%

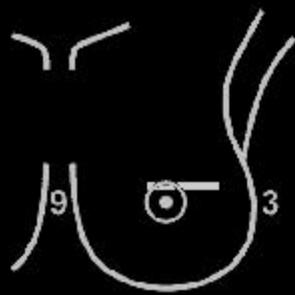
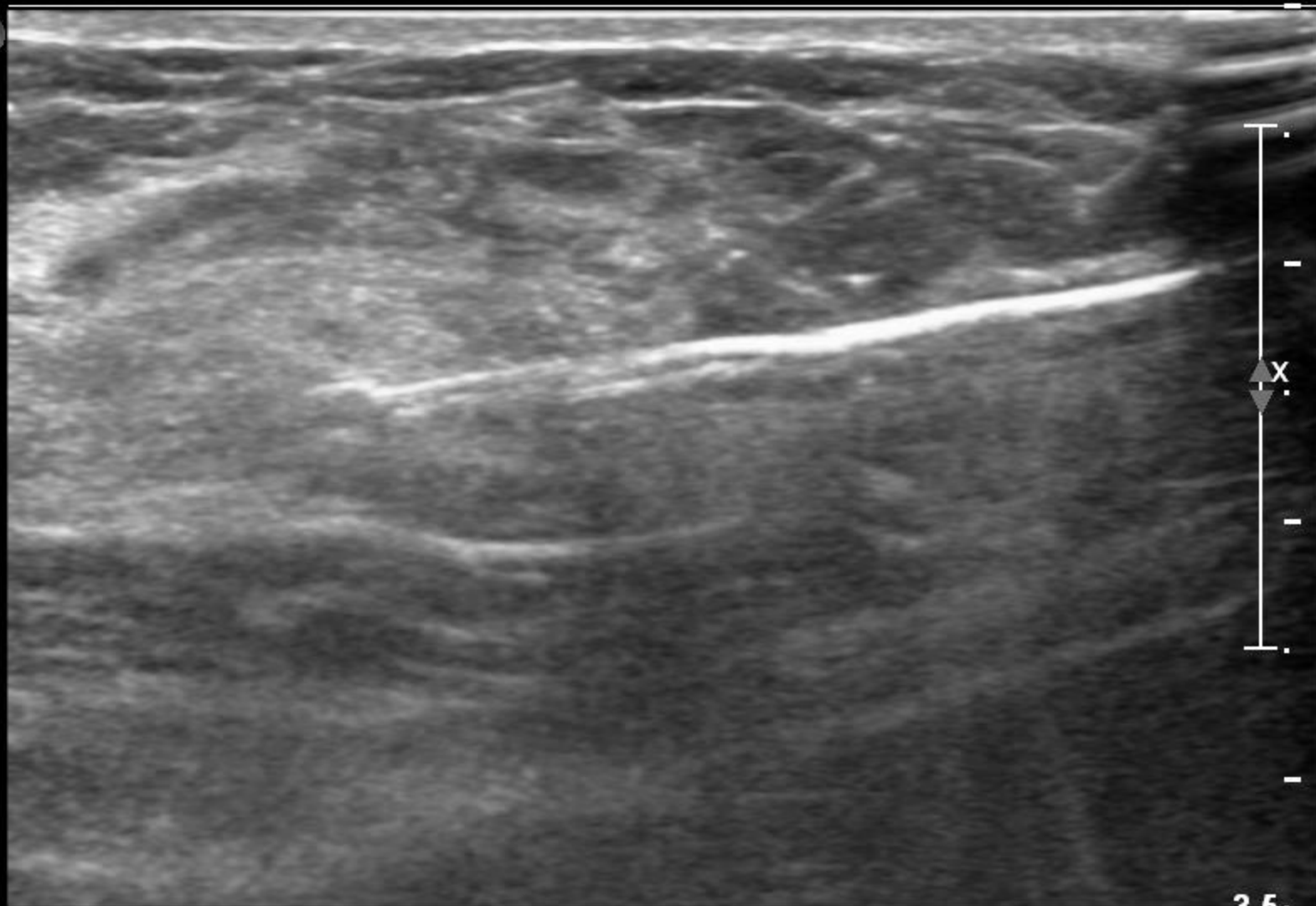
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P Med

Res

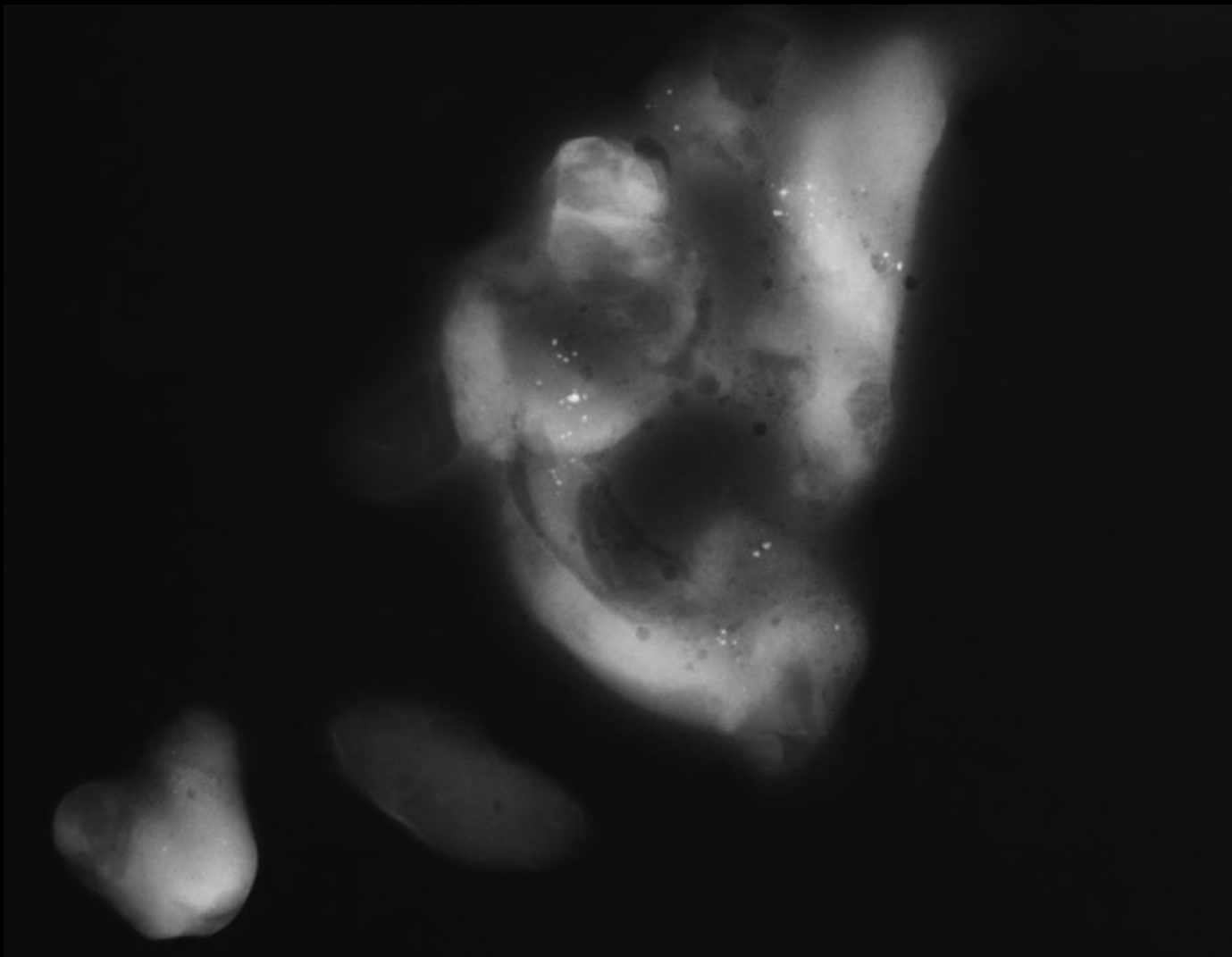
TAC1

P



Left ELITE 10G

3.5



Breast, left upper outer quadrant, vacuum assisted biopsy

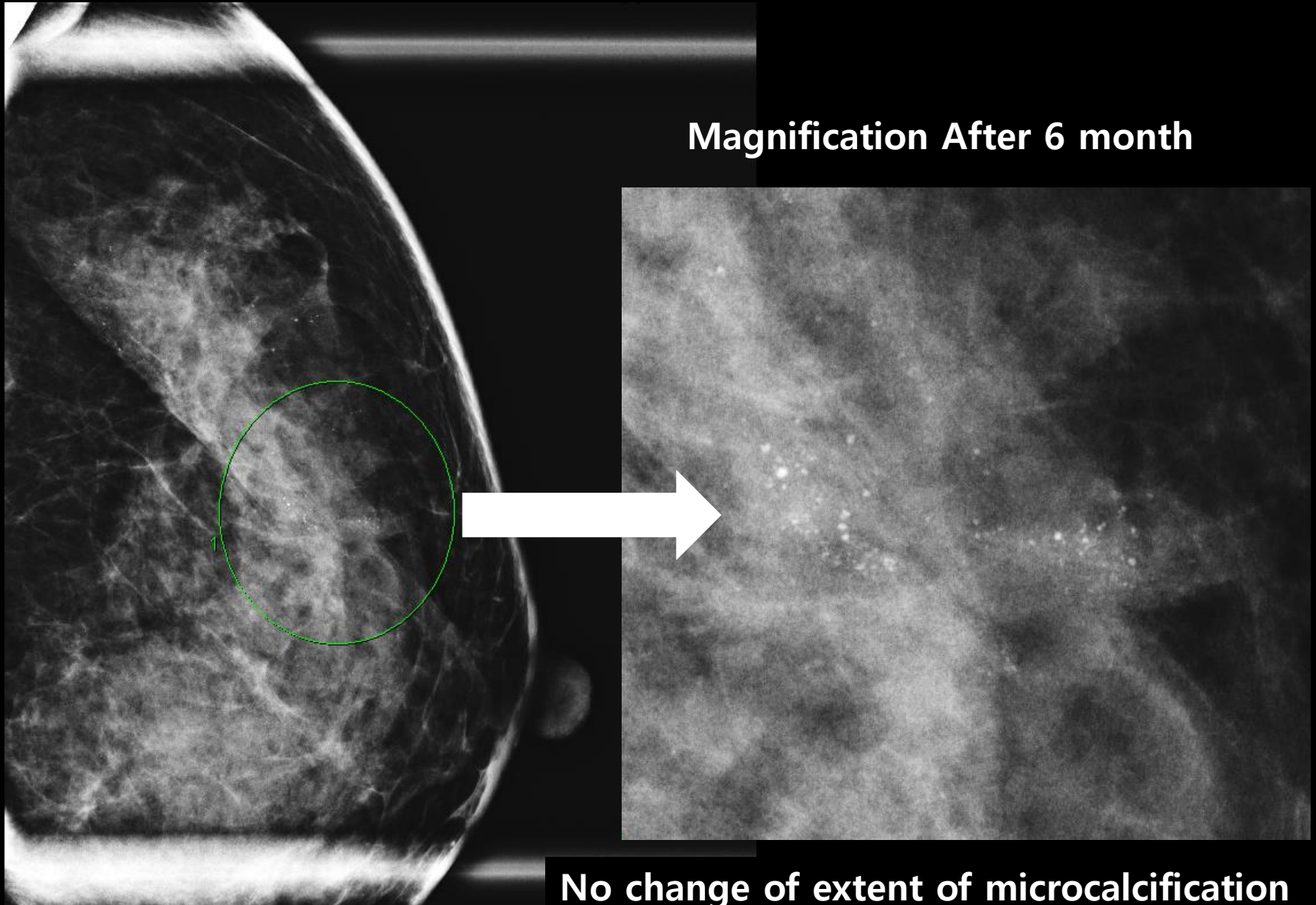
- . **Fibrocystic change**
- . **Sclerosing adenosis**
- . microcalcification in benign duct

[Radiology-Pathology Discordance (BIRADS C4B/C4C – Benign pathology)]

- **How would you do this lesion ?**
  - 1. Surgical excision**
  - 2. Close follow up after 6 month**



Patients did not want surgical excision. She wanted close follow up



**Magnification After 6 month**

**No change of extent of microcalcification**

image-pathology discordant lesion

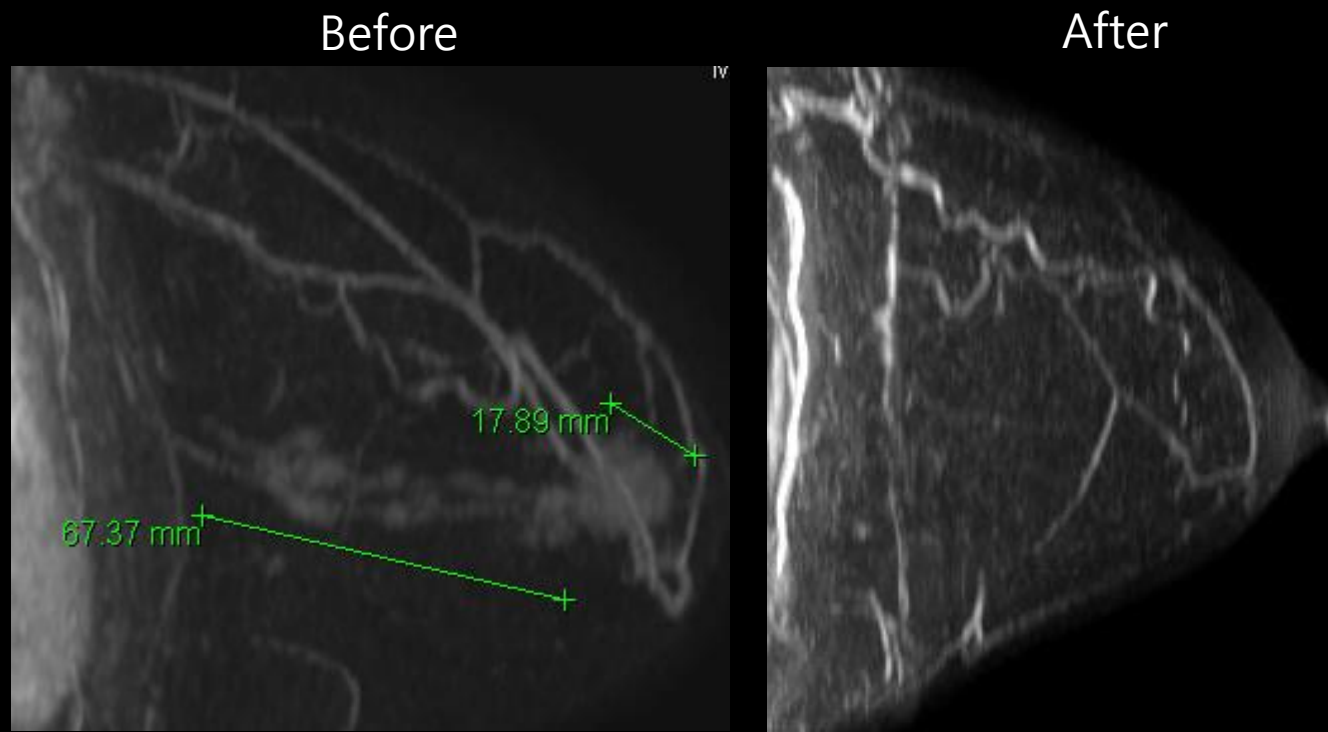
- **How would you do this lesion ?**
  - 1. Surgical excision**
  - 2. Biopsy again**
  - 3. Close follow up after 6month**

# Case II

F/61

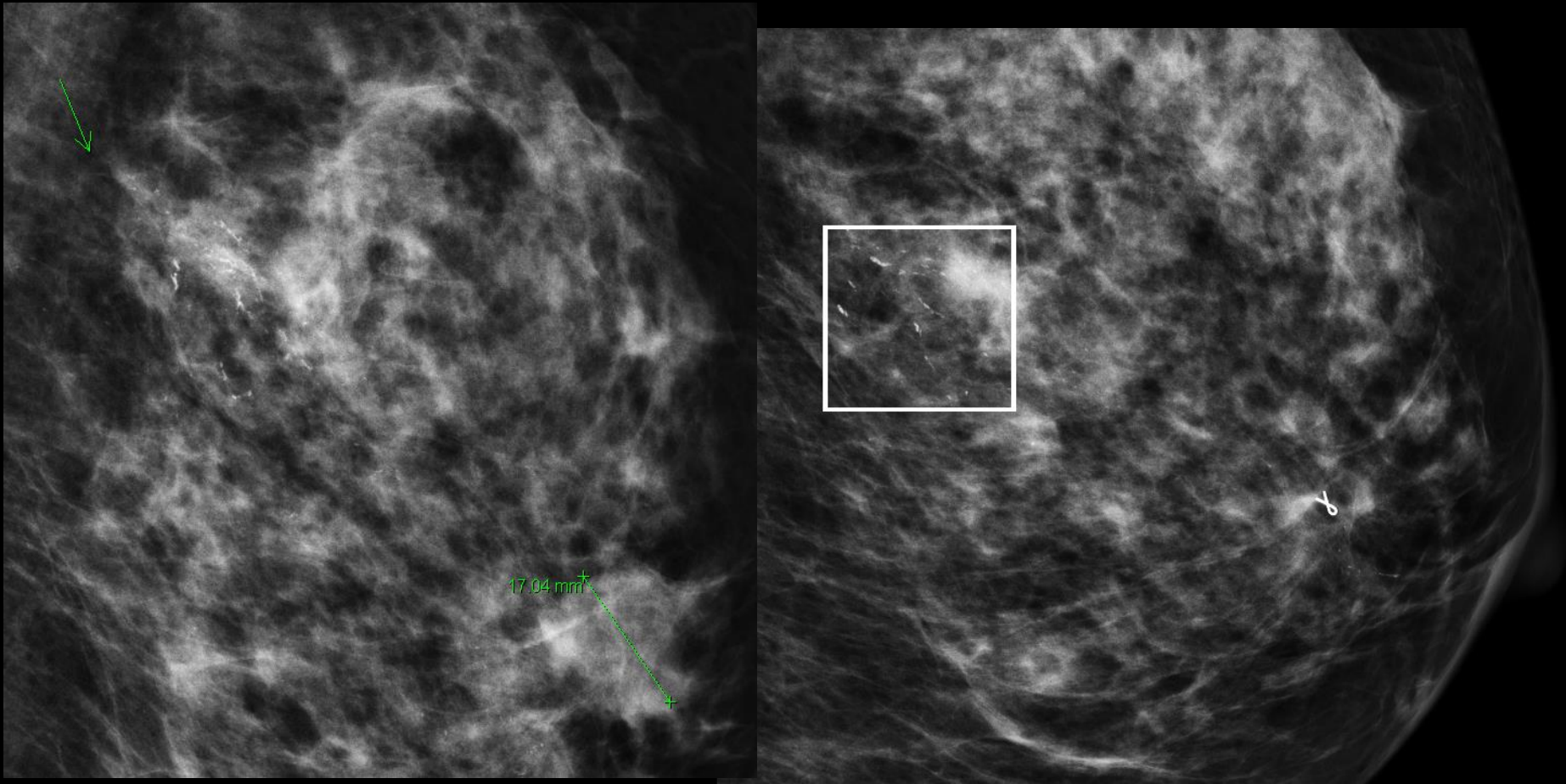
Lt. breast cancer (IDC,ER/PR/Her2 : -/-/+, Ki-67:2+) cT3N0M0

→ neoadjuvant AC #4 → DH #4



1.8 cm-sized malignant mass → Nearly disappeared

7 cm extent malignant non-mass enhancement → Nearly disappeared



Nearly disappeared proven malignant mass in LEFT 3:00 (clip insertion state). Stationary state of malignant calcifications involving left 12:00-4:00 and subareolar area (about 8cm)

- **How would you do ? (Op. type)**

1. **Mastectomy**

2. **Lumpectomy (clip area)**

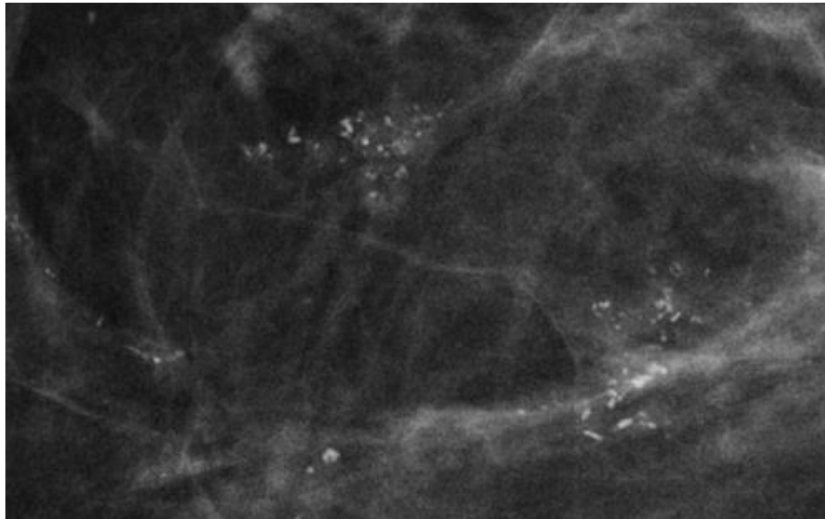
# Contents

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- Diagnosis of Microcalcification  
Image - Report - Biopsy
- Suspicious microcalcification in clinics

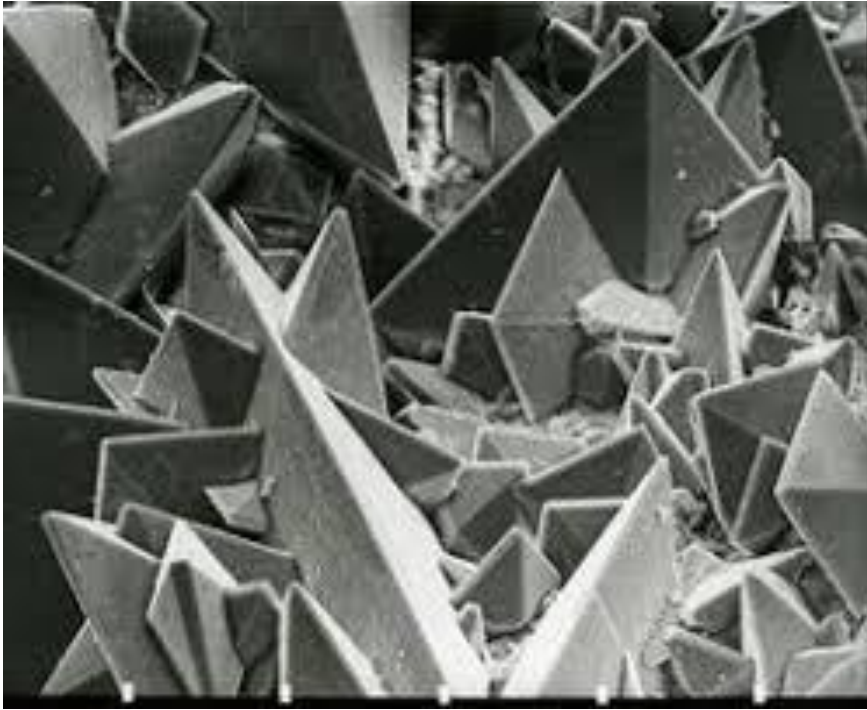
# Microcalcification

“Microcalcification result from the deposition of Calcium oxalate and Calcium phosphate within the breast tissue”





## Calcium Oxalate crystals

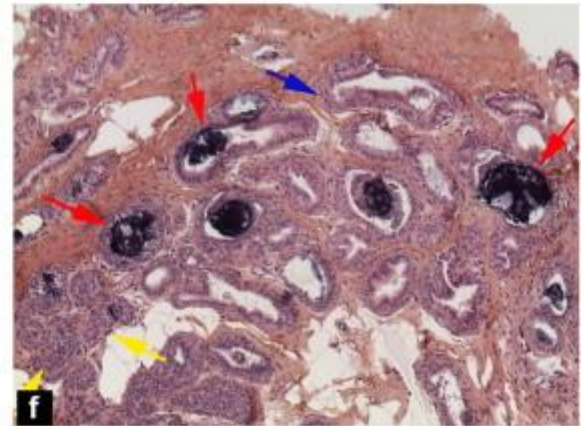
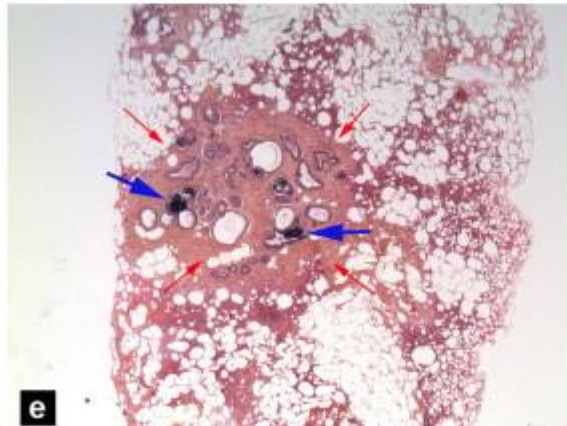
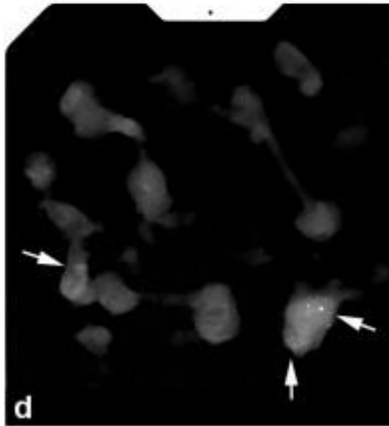
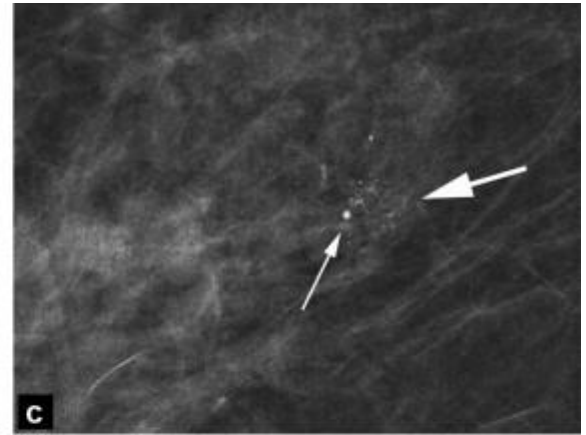
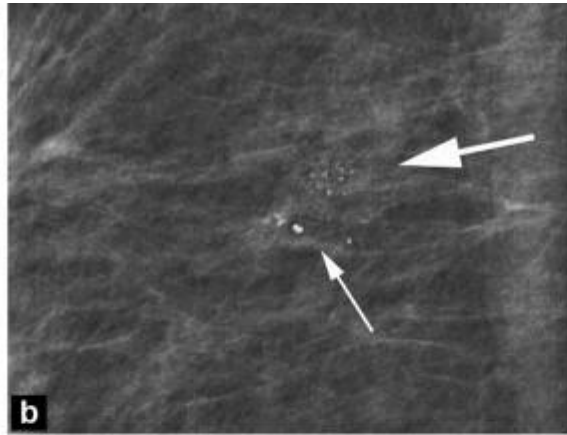
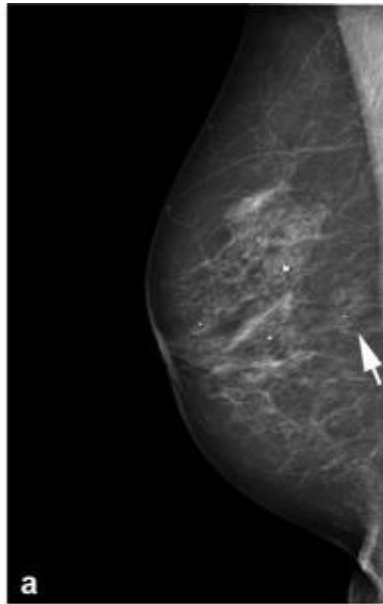


<https://upload.wikimedia.org/wikipedia>

## Calcium Phosphate crystals



<https://www.sciencephoto.com>



# Diagnosis of microcalcification

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- Imaging (Screening)



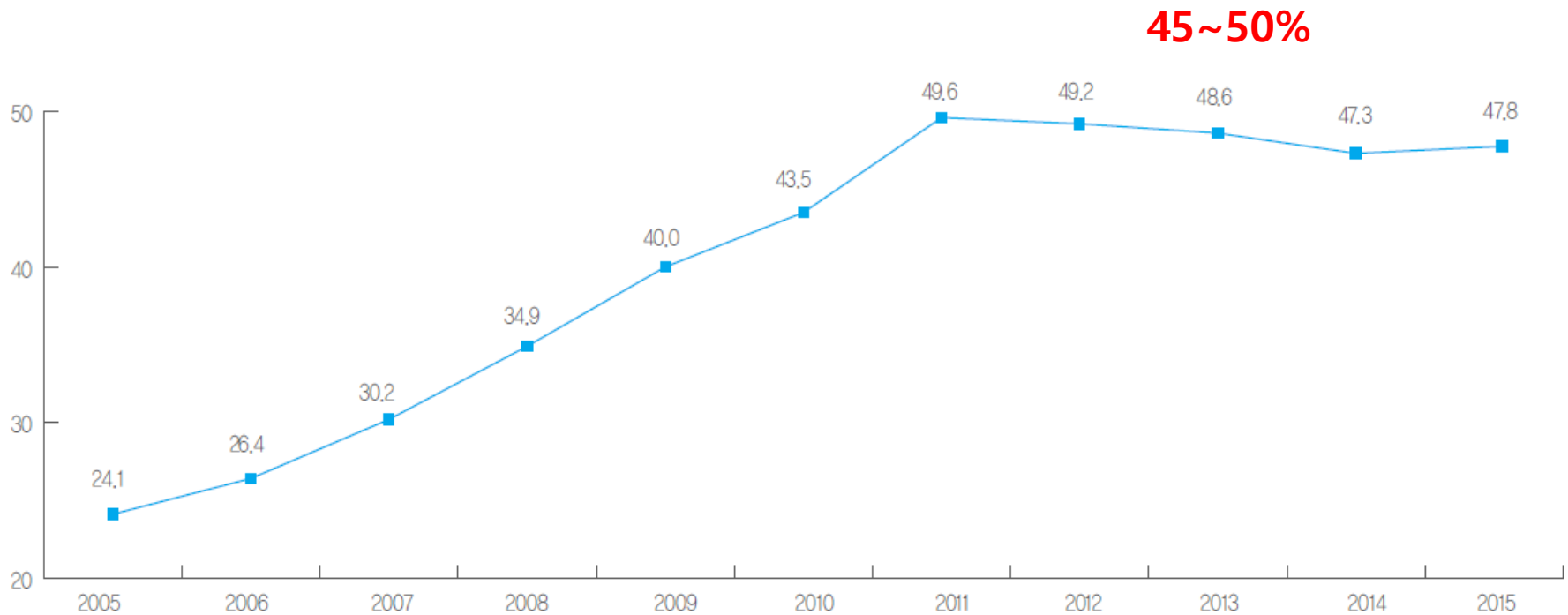
- Reporting (Interpretation)



- Biopsy

# Screening MMG in Korea

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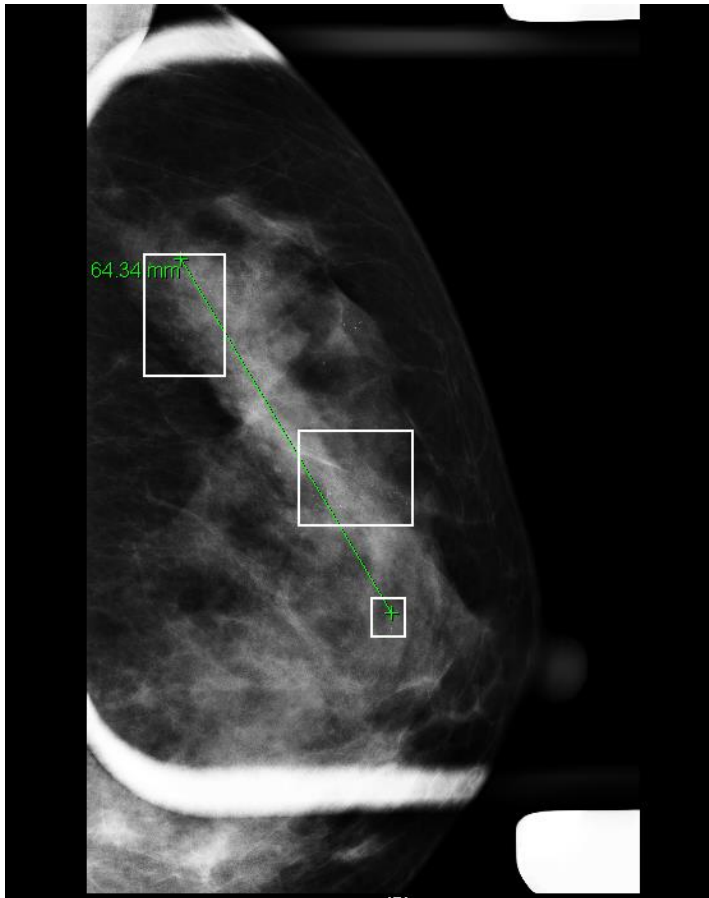
In 2015 (N=1,356,606)

Normal (71.56%), Benign calcification(10.74%), Asymmetry (5.23%),  
Mass(2.08%), **microcalcification(1.0%)**, distortion(1.0%) etc

# Diagnosis – Imaging

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- Magnification views enhancing the morphology of calcifications



# Diagnosis – Reporting

## BI-RADS®

Breast Imaging Reporting and Data System



BREAST IMAGING ATLAS

Mammography

Breast Ultrasound

Breast MR Imaging

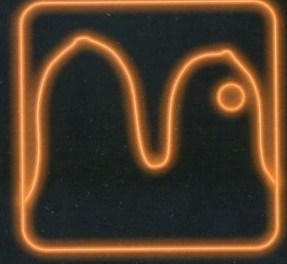
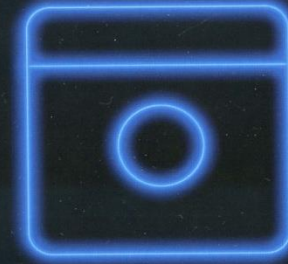
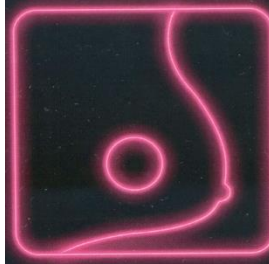


American College of Radiology

## ACR BI-RADS® ATLAS

Breast Imaging Reporting and Data System

2013



**Mammography**

**Ultrasound**

**Magnetic Resonance Imaging**

**Follow-up and Outcome Monitoring**

**Data Dictionary**

**ACR®**  
AMERICAN COLLEGE OF  
RADIOLOGY  
QUALITY IS OUR IMAGE

[BI-RADS Atlas 5th Edition](#) (2013)

# Reporting (interpretation)

**MAMMOGRAPHY**

Breast composition	a. The breasts are almost entirely fatty b. There are scattered areas of fibroglandular density c. The breasts are heterogeneously dense, which may obscure small masses d. The breasts are extremely dense, which lowers the sensitivity of mammography	
Masses	Shape	Oval Round Irregular
	Margin	Circumscribed Obscured Microlobulated Indistinct Spiculated
	Density	High density Equal density Low density Fat-containing
Calcifications	Typically benign	Skin Vascular Coarse or "popcorn-like" Large rod-like Round Rim Dystrophic Milk of calcium Suture
	Suspicious morphology	Amorphous Coarse heterogeneous Fine pleomorphic Fine linear or fine-linear branching
	Distribution	Diffuse Regional Grouped Linear Segmental
	Architectural distortion	
Asymmetries	Asymmetry	
	Global asymmetry	
	Focal asymmetry	
	Developing asymmetry	
Intramammary lymph node		
Skin lesion		
Solitary dilated duct		
Associated features	Skin retraction	
	Nipple retraction	
	Skin thickening	
	Trabecular thickening	
	Axillary adenopathy	
	Architectural distortion	
	Calcifications	
Location of lesion	Laterality	
	Quadrant and clock face	
	Depth	
	Distance from the nipple	



Calcifications	Typically benign	Skin Vascular Coarse or "popcorn-like" Large rod-like Round Rim Dystrophic Milk of calcium Suture
	Suspicious morphology	Amorphous Coarse heterogeneous Fine pleomorphic Fine linear or fine-linear branching
	Distribution	Diffuse Regional Grouped Linear Segmental

# Diagnosis – Reporting

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- Other consideration
  - Size
  - Number
  - Site
  - Evolution over time
  - Associated MMG signs



# Diagnosis – Reporting

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## BI-RADS® ASSESSMENT CATEGORIES

**Category 0: Mammography:** Incomplete – Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison  
**Ultrasound & MRI:** Incomplete – Need Additional Imaging Evaluation

**Category 1:** Negative

**Category 2:** Benign

**Category 3:** Probably Benign

**Category 4:** Suspicious

Mammography Category 4A: Low suspicion for malignancy  
& Ultrasound: Category 4B: Moderate suspicion for malignancy  
Category 4C: High suspicion for malignancy

**Category 5:** Highly Suggestive of Malignancy

**Category 6:** Known Biopsy-Proven Malignancy

# Diagnosis - Biopsy

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## Sono-guided Biopsy



<http://www.breastsurgery.gr>

## Stereotatic Biopsy



<https://www.mayoclinic.org/tests-procedures/breast-biopsy>

# Surgical Biopsy for suspicious microcalcification

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Difficult to do biopsy by device

Location

- ex) subareolar (too close to nipple)
- too close to skin
- too deep (close to muscle)

Underlying clinical problems

- bleeding tendency

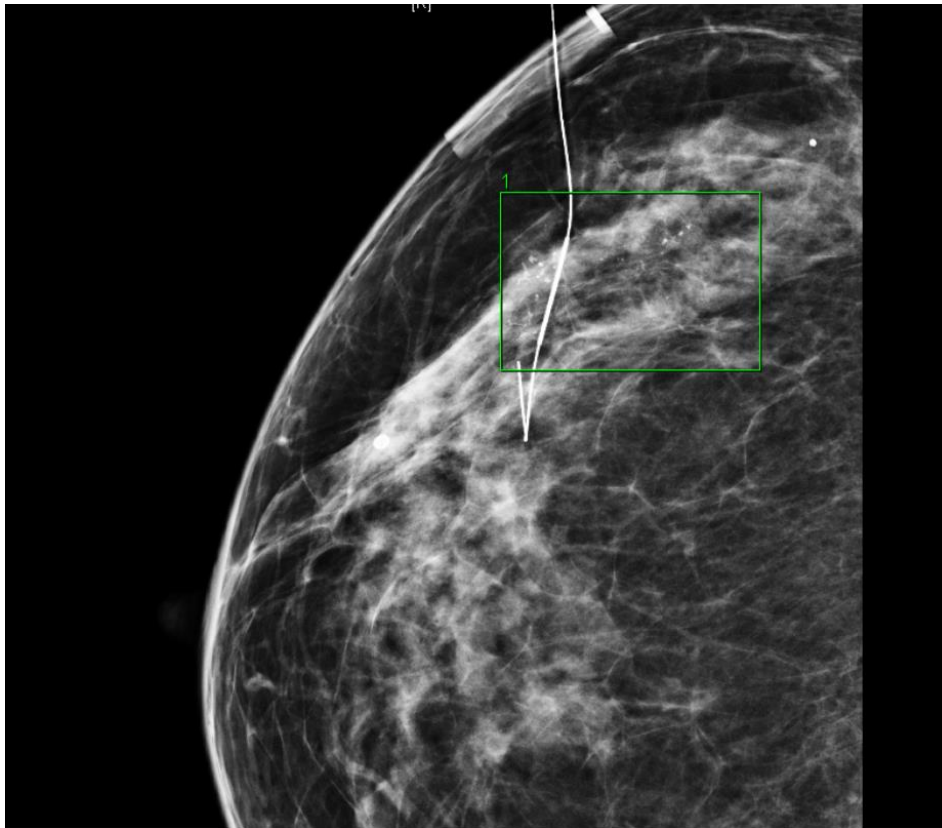
Patient wants surgical biopsy

- .
- .

# Surgical Biopsy for suspicious microcalcification

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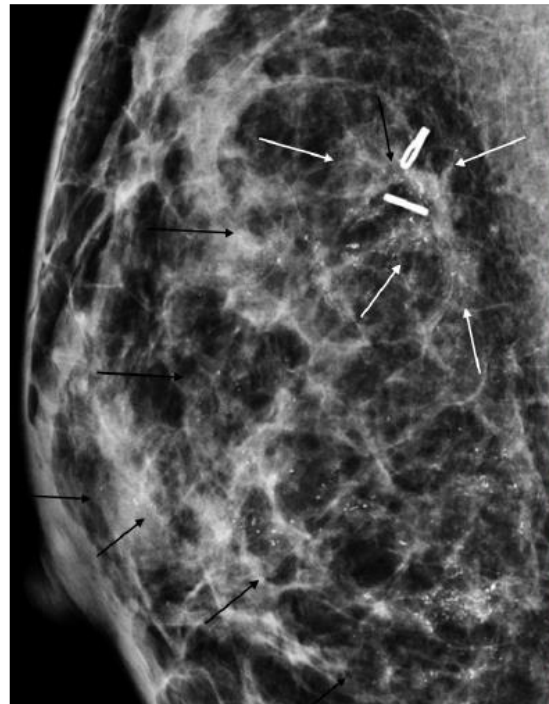
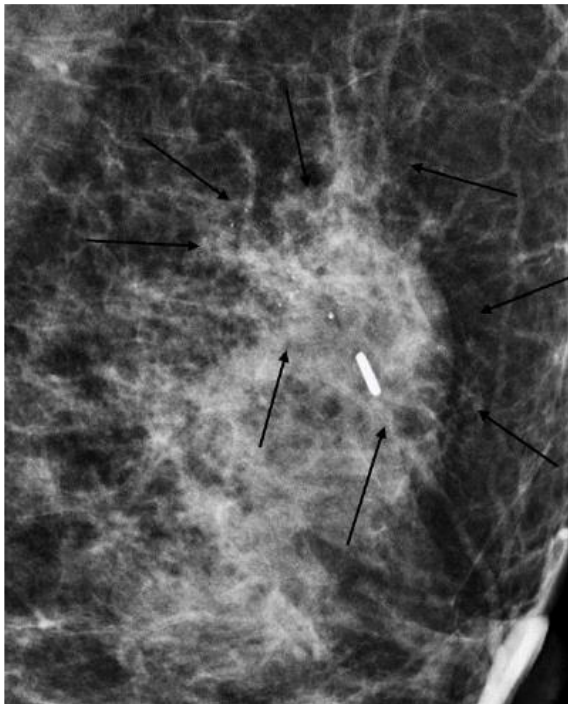
- Localization



# Biopsy for suspicious microcalcification

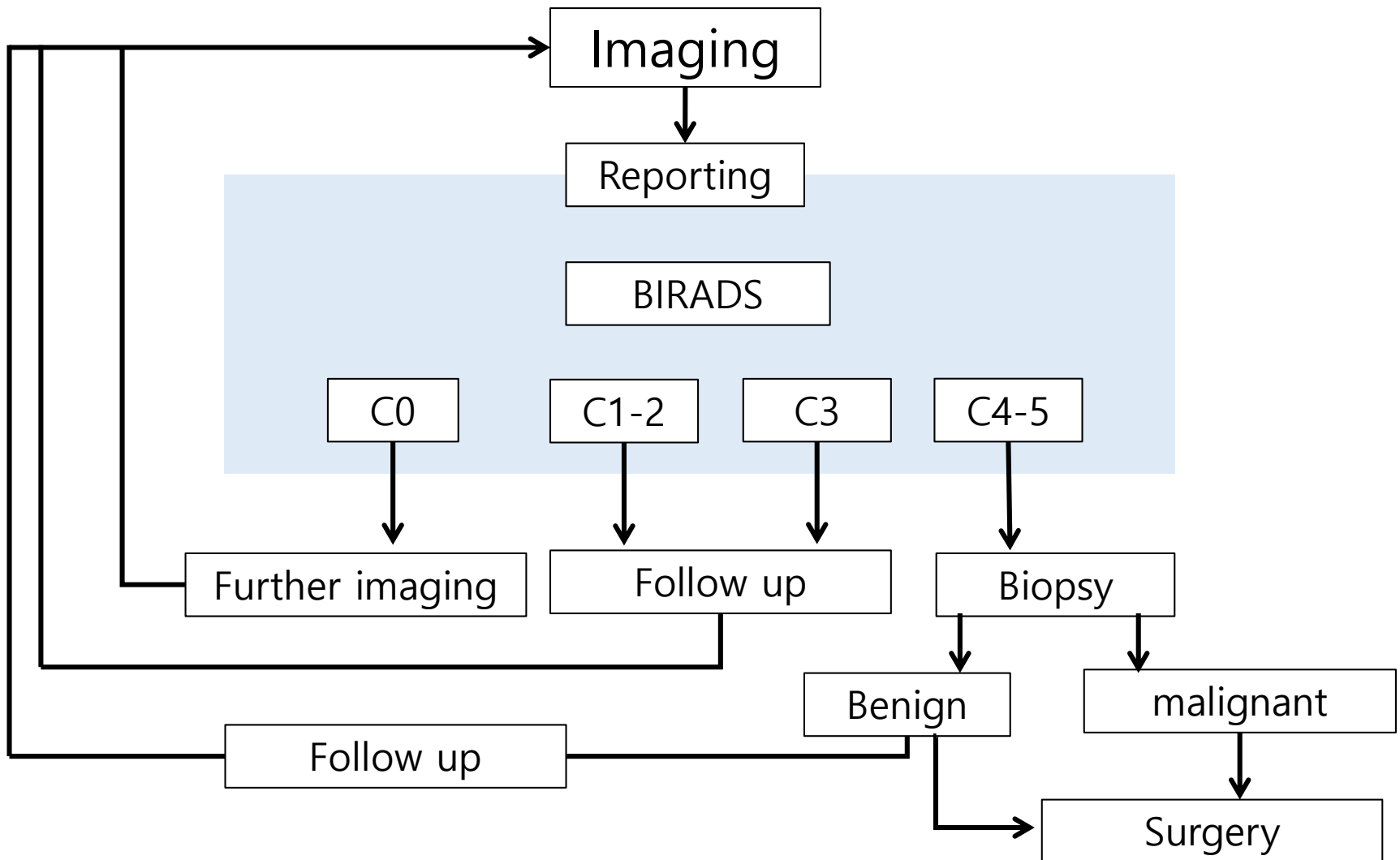
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- Marker clip  
& Post biopsy check of microcalcification



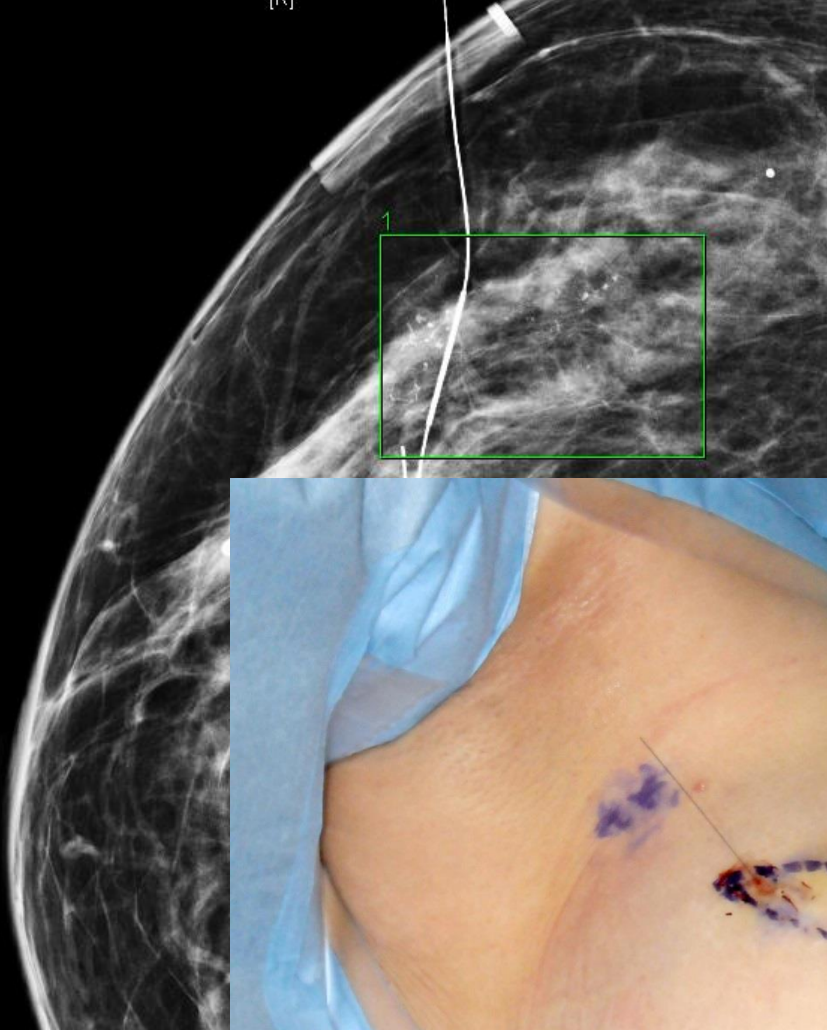
# Suspicious Microcalcification

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Surgery

including microcalcification

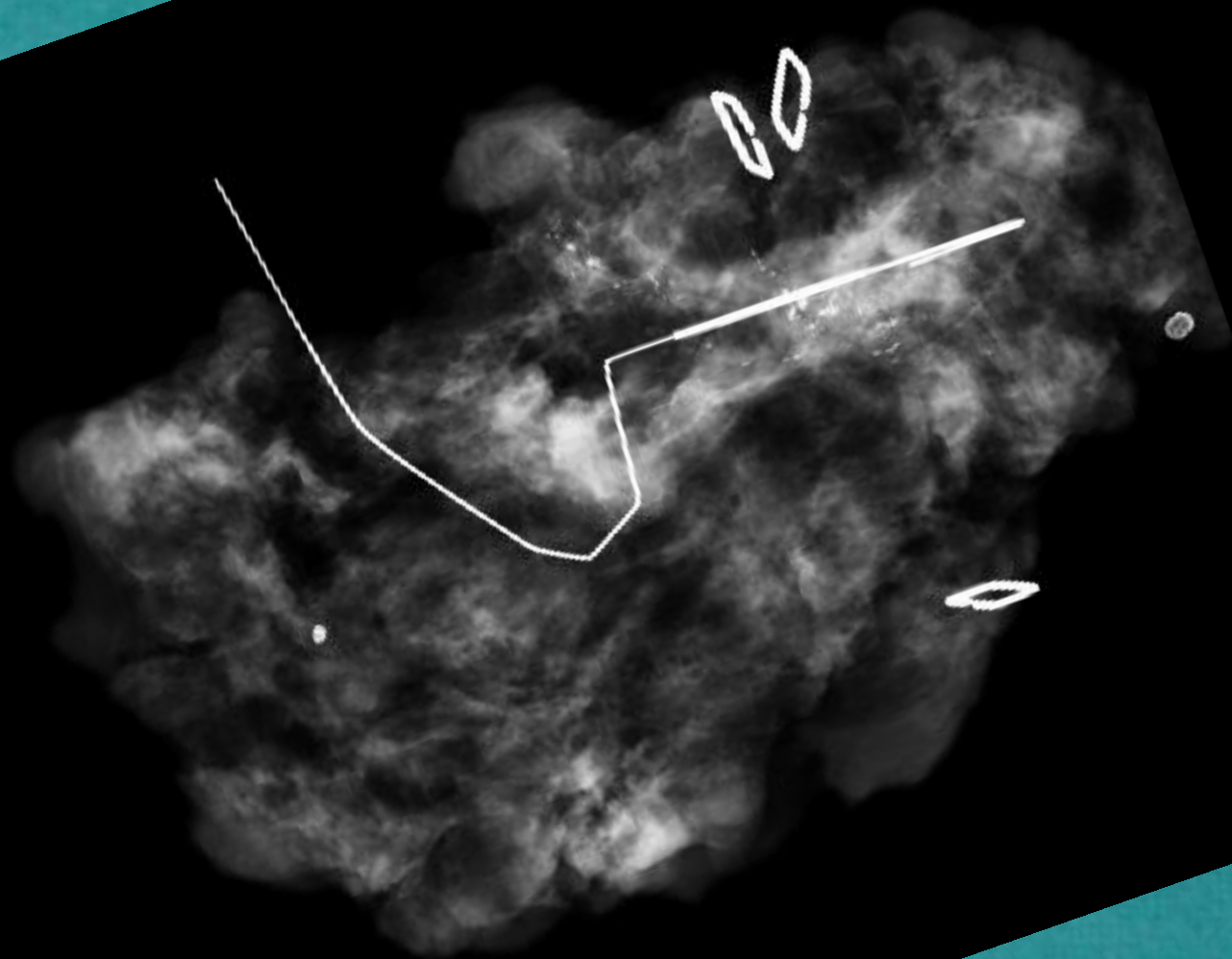


**Breast, right, 10 o'clock, core biopsy :**

**DUCTAL CARCINOMA IN SITU,  
INTERMEDIATE NUCLEAR GRADE  
Microcalcification in tumor**







## **Ductal carcinoma in situ, comedo type;**

- 1) tumor size: 4.0x2.8x0.8 cm (pTis)
- 2) nuclear grade: high with focal necrosis
- 3) Van Nuys classification group: 3 / 3
- 4) lymphovascular invasion: absent
- 5) microcalcification in stroma, and tumor
- 6) **negative resection margins**  
(deep, 0.8 cm; superior, 0.2 cm;  
inferior, 3.0 cm; lateral, 2.2 cm; medial, 0.8 cm)

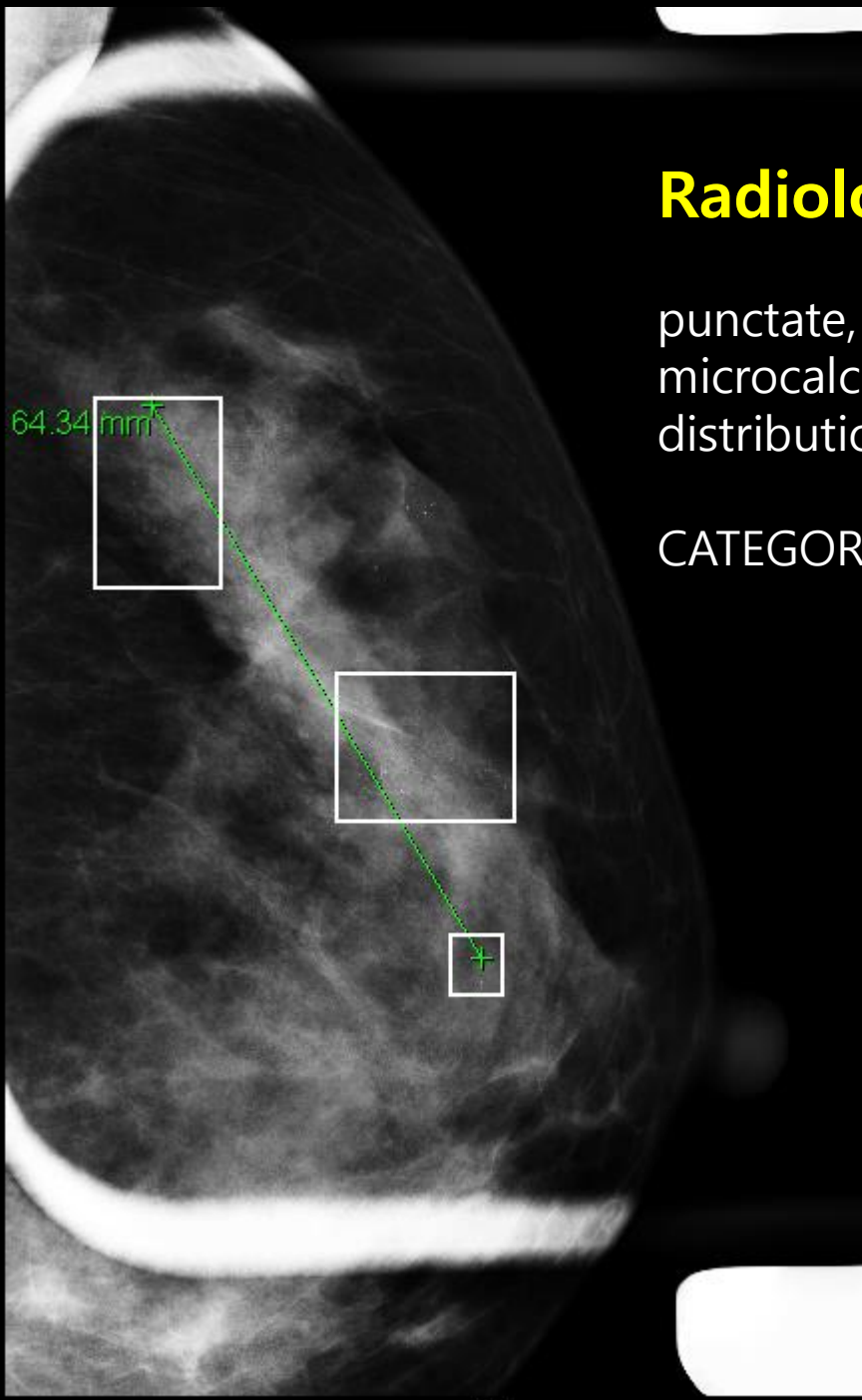
# Suspicious microcalcification in Clinics

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1. Microcalcification  
with Radiology-Pathology discordance
2. Microcalcification  
after Neoadjuvant systemic treatment

**Microcalcification**

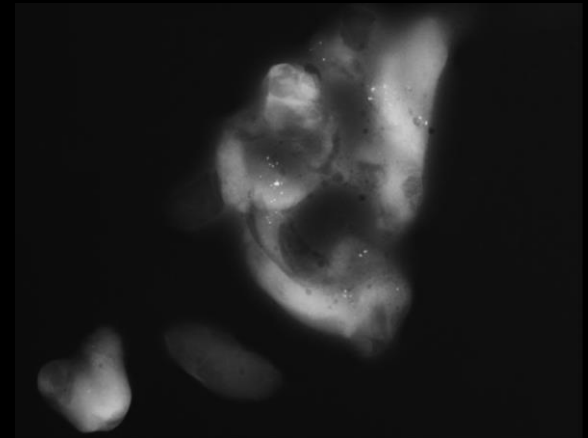
**with Radiology-Pathology discordance**



## Radiology

punctate, amorphous and fine pleomorphic microcalcification segmental or regional distribution in upper outer quadrant of left breast

CATEGORY: **4B**



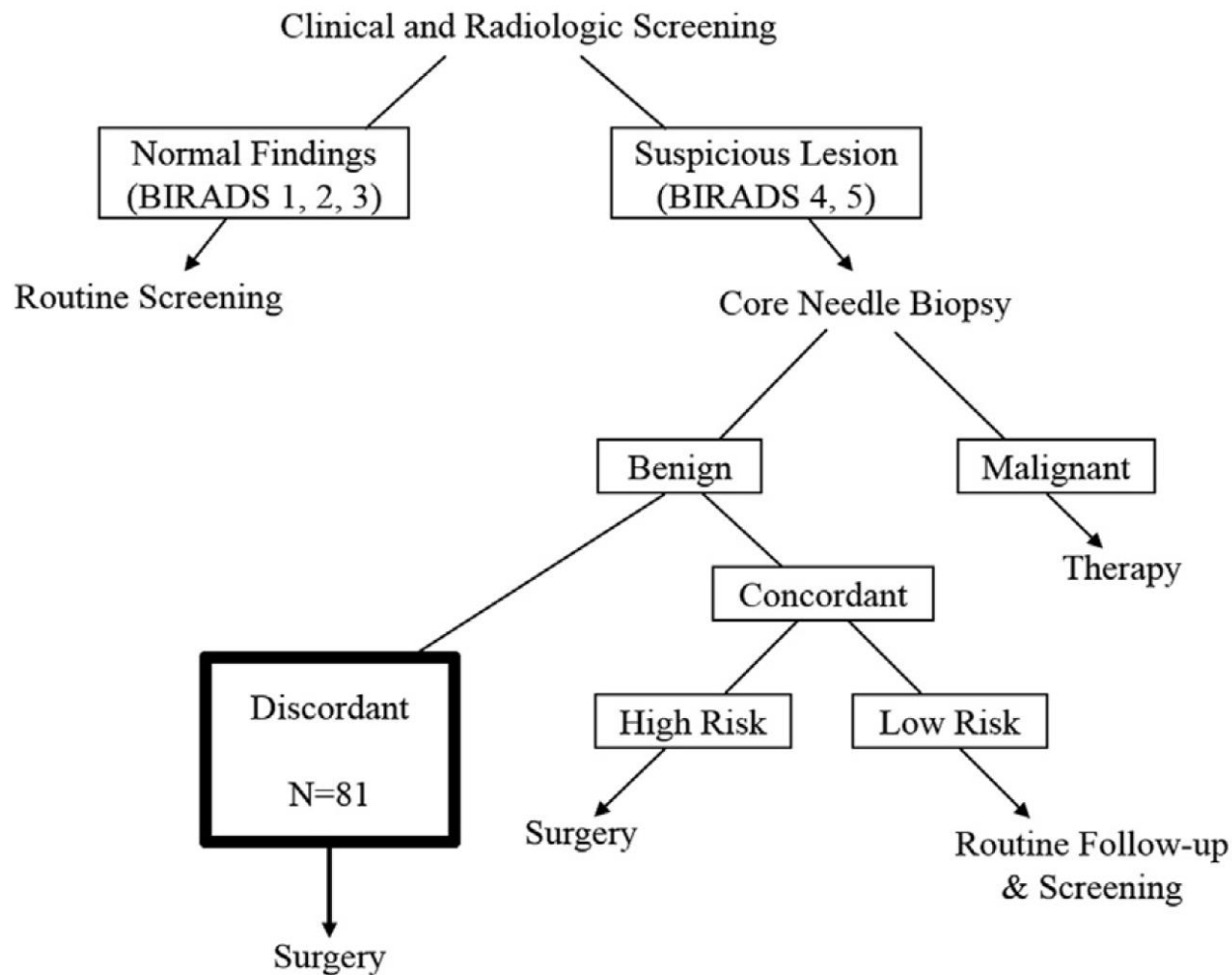
## Pathology

- . Fibrocystic change
- . Sclerosing adenosis
- . microcalcification in benign duct

# Benign pathology

## Surgery for Radiology-Pathology discordance

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# Benign pathology

## Surgery for Radiology-Pathology discordance

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- 6/81 (**7.4%**)
  - invasive carcinoma (2)
  - DCIS (4)

Age, y	Clinical presentation	BI-RADS	Core biopsy method	CNB findings	Final surgical pathology
LAC patients					
52	Palpable mass	4A	14 G ultrasound-guided CNB	Fibroadenoma	DCIS
62	Abnormal screening mammogram	4C	14 G ultrasound-guided CNB	Fibrocystic changes; insufficient glandular tissue for diagnosis	Invasive lobular carcinoma
51	Suspected Paget disease of the nipple	4B	9G MRI-guided VAB	Papilloma; pseudoangiomatous stromal hyperplasia	DCIS
Norris patients					
47	Palpable mass	4C	10 G ultrasound-guided VAB	Fibrocystic changes	DCIS
50	Abnormal screening mammogram	4C	10 G ultrasound-guided VAB	Atypical lobular hyperplasia	DCIS; lobular carcinoma in situ
48	Abnormal screening mammogram	5	12G ultrasound-guided VAB	Pseudoangiomatous stromal hyperplasia	Invasive ductal carcinoma; DCIS

# Benign pathology

## Surgery for Radiology-Pathology discordance

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A total of 1861 SVABs

Discordance rate : 1.2% (23/1861)

**False negative rate : 30% (7/23)**

Lesion Type	Description	BI-RADS	Biopsy Pathology	Needle Gauge	Needle Position	Residual Calcs	Final Pathology
Calcs	Pleomorphic	4c	FCC	9G	Correct	A few	HNG DCIS
Calcs	Pleomorphic	4c	FCC	9G	Correct, scant calcs	Yes	LNG DCIS
Calcs	Pleomorphic	5	FCC	9G	Correct	Yes	IDC/HNG DCIS
Calcs	Amorphous	4b	FCC	11G	Incorrect	Yes	IDC/ING DCIS
Calcs	Pleomorphic	4c	FCC	9G	Incorrect	Yes	HNG DCIS
Calcs	Pleomorphic	5	FCC	9G	Correct	Yes	IDC/HNG DCIS
AD	NA	5	FCC	9G	Correct	NA	ING DCIS



# Benign pathology

## Surgery for Radiology-Pathology discordance

Study	Sample Size (Lesions)	Calcification Cases	Needle Gauge	Discordant Cases	False-negative Discordant Cases (Cancers)
Liberman et al. (10)	741	523/741 (71%)	14G SVAB, 11G SVAB	19/741 (2.5%)	2/17 (11.7%) (only 17/19 lesions had repeat biopsy)
Pfarl et al. (12)	318	166/318 (52%)	11G SVAB	13/318 (4%)	7/13 (53.8%)
Ciatto et al.* (13)	1388	1223/1388 (88%)	11G SVAB	4.4% (N/D not available; false negatives given for all lesions and modalities) 4/1391 (0.29%) (inadequacy rate VAB11G-includes two US cases)	50/151 (33%) (all lesions and modalities combined)
Jackman et al. (14)	1280	766/1280 (60%)	11G SVAB, 14G SVAB	16/1280 (1.3%) (nine with repeat biopsy; six stable imaging follow-up, mean 90 months; one lost to follow-up)	2/9 (22%)
Venkataraman et al. (15)	912	858/912 (94%)	11G SVAB, 8G SVAB	21/471 (4.4%) (471 = total benign lesions after initial biopsy)	3/21 (14%)
Present study	1861	1409/1861 (76%)	11G SVAB, 9G SVAB	23/1861 (1.2%)	7/23 (30%)

**False negative cases : 11.7% ~ 53.8%**

# In my practice

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- In case of discordant microcalcification  
→ Surgery including Bx site
- Check final pathology
- If, DCIS/Invasive ca → MRI check → 2<sup>nd</sup> Surgery
- If, ADH/LCIS or other premalignant lesion  
→ close follow up for high risk

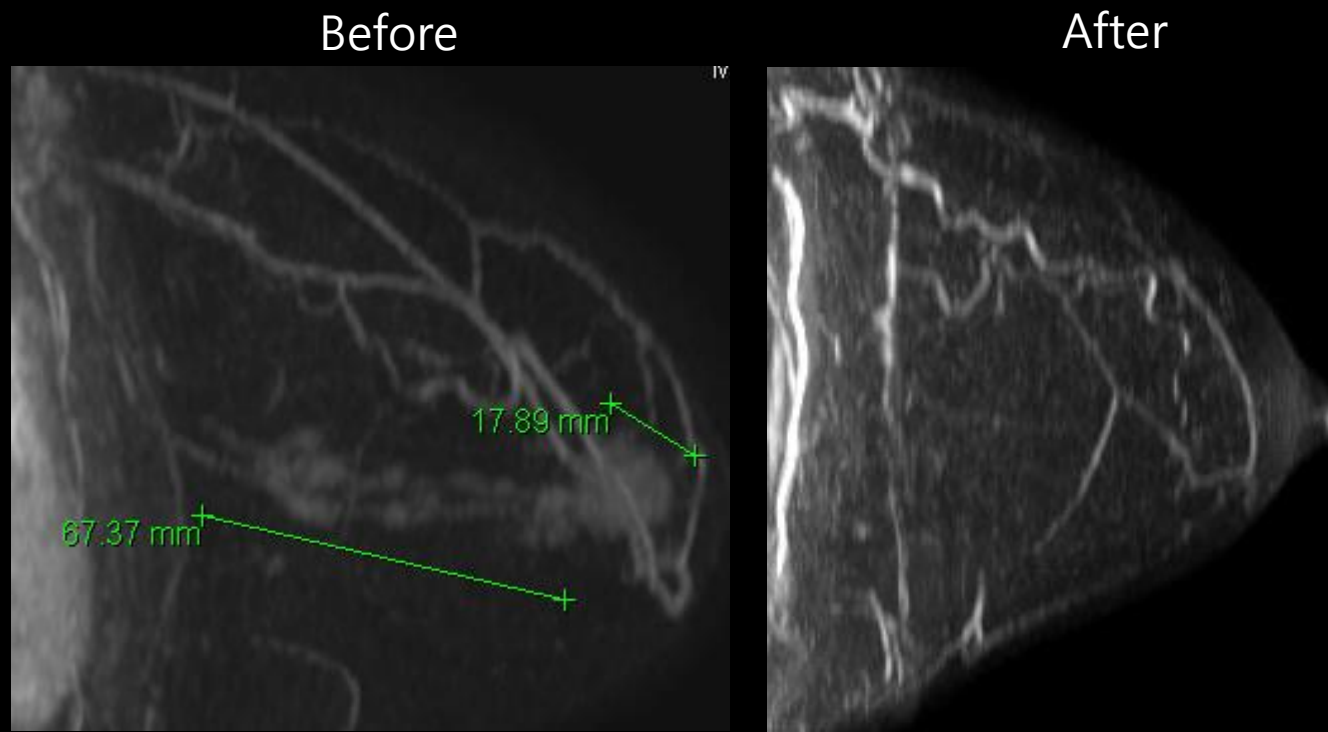
**Microcalcification**

**after Neoadjuvant systemic treatment**

F/61

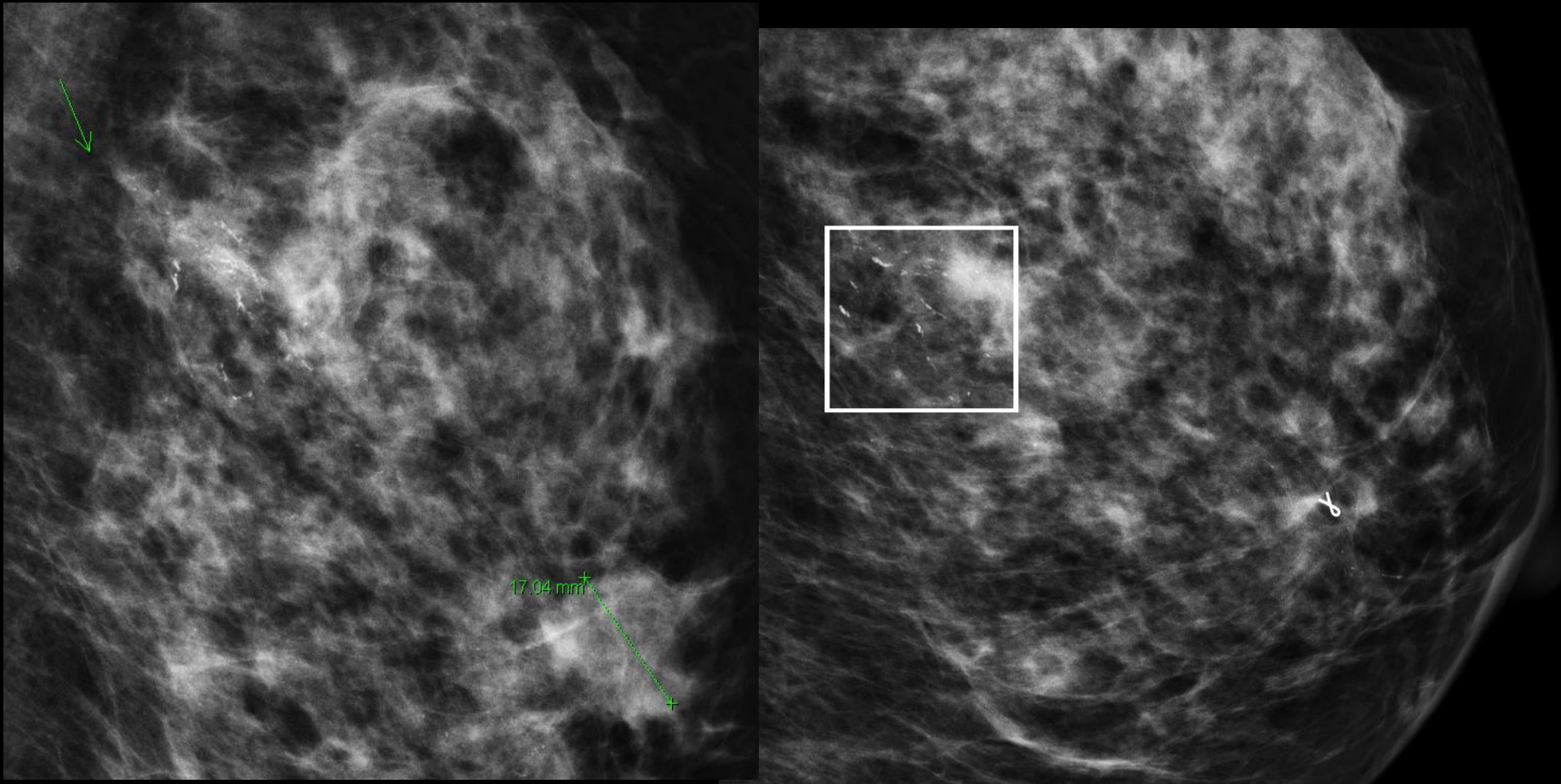
Lt. breast cancer (IDC,ER/PR/Her2 : -/-/+, Ki-67:2+) cT3N0M0

→ neoadjuvant AC #4 → DH #4



1.8 cm-sized malignant mass → Nearly disappeared

7 cm extent malignant non-mass enhancement → Nearly disappeared



Nearly disappeared proven malignant mass in LEFT 3:00 (clip insertion state). Stationary state of malignant calcifications involving left 12:00-4:00 and subareolar area (about 8cm)

# Pathology

. Status post neoadjuvant chemotherapy

## **No residual tumor**

- . Histologic type and grade: cannot be determined (no residual tumor)
- . Tumor size: cannot be determined (no residual tumor)
- . Resection margin: cannot be determined (no residual tumor)
- . Lymphovascular invasion: cannot be determined (no residual tumor)
- . **Microcalcification in benign duct, and stroma**
- . No metastasis in 5 regional lymph nodes (ypN0(sn))  
(0/5: sentinel lymph node #1,2 for frozen biopsy-6, 0/2;  
non-sentinel lymph node #1,2,3,4 for frozen biopsy-7, 0/3)

# Microcalcification after neotx

- The overall agreement of residual microcalcifications on MMG predicting residual tumor extents was lower than MRI in all tumor subtypes

Subtype	Histopathologic residual tumor size (cm)	Microcalcification extent on MG (cm)	ICC <sup>a</sup>	MRI enhancing lesion extent (cm)	ICC <sup>b</sup>
All ( <i>n</i> = 207)	3.78 ± 2.56	3.43 ± 2.71	0.368	3.27 ± 2.22	0.723
HR <sup>+</sup> /HER2 <sup>-</sup> ( <i>n</i> = 88)	4.58 ± 2.54	3.48 ± 2.74	0.390	3.39 ± 2.23	0.677
HR <sup>+</sup> /HER2 <sup>+</sup> ( <i>n</i> = 27)	3.33 ± 2.63	3.44 ± 2.60	0.417	2.96 ± 2.39	0.797
HR <sup>-</sup> /HER2 <sup>+</sup> ( <i>n</i> = 55)	3.29 ± 2.53	4.01 ± 3.16	0.387	3.34 ± 2.09	0.764
TN ( <i>n</i> = 37)	2.91 ± 2.10	2.43 ± 1.57	0.205	3.11 ± 2.32	0.848

# Microcalcification after neotx

Change in calcifications on mammography	Change in MRI enhancement		pCR <i>n</i> (%)
	Resolved <i>n</i> (%)	Decreased <i>n</i> (%)	
Resolved ( <i>n</i> = 3)	3 (100)	0 (0)	3 (100)
Decreased ( <i>n</i> = 15)	5 (33)	10 (67)	4 (27) <sup>a</sup>
No change ( <i>n</i> = 42)	16 (38)	26 (62)	10 (24) <sup>b</sup>
Increased ( <i>n</i> = 24)	14 (58)	10 (42)	9 (38) <sup>c</sup>
New ( <i>n</i> = 6)	2 (33)	4 (67)	3 (50) <sup>d</sup>

Group	No of patients ( <i>n</i> = 90) <i>n</i> (%)	Breast pCR	
		No ( <i>n</i> = 61) <i>n</i> (%)	Yes ( <i>n</i> = 29) <i>n</i> (%)
Decreased/resolved	10 (11.11)	7 (7.78)	3 (3.33)
Decreased			
Decreased/resolved	8 (8.89)	4 (4.44)	4 (4.44)
Resolved			
New/increased/unchanged	40 (44.44)	37 (41.11)	3 (3.33)
Decreased			
New/increased/unchanged	32 (35.56)	13 (14.44)	19 (21.11)
Resolved			
Total	90 (100.00)	61 (67.78)	29 (32.22)



# Microcalcification after neotx

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MMG -calcification	MRI -enhancement	pCR	
		No(n=61)(%)	Yes(n=29)(%)
Decreased/Resolved	Decreased	7	3
<b>Decreased/Resolved</b>	<b>Resolved</b>	<b>4</b>	<b>4</b>
<b>New/Increased/unchanged</b>	<b>Decreased</b>	<b>37</b>	<b>3</b>
New/Increased/unchanged	Resolved	13	19

Modified Table

# Microcalcification after neotx

	Benign calcifications (n = 13)	Malignant calcifications (n = 16)	p value
Lesion type			1.000
Microcalcifications only	3 (42.9)	4 (57.1)	
Mass + calcifications	10 (45.4)	12 (54.6)	
Shape of microcalcifications			0.015
Amorphous	3 (75.0)	1 (25.0)	
Fine linear/linear branching	9 (60.0)	6 (40.0)	
Fine pleomorphic	1 (10.0)	9 (90.0)	
Distribution			1.000
Segmental/regional	9 (42.9)	12 (57.1)	
Grouped	4 (50.0)	4 (50.0)	
Change of calcifications			0.486
Decrease	0 (0.0)	2 (100.0)	
Increase	2 (66.7)	1 (33.3)	
No change	11 (45.8)	13 (54.2)	
Pathologic responses			0.03
pCR	4 (100.0)	0 (0.0)	
Non-pCR	9 (36.0)	16 (64.0)	

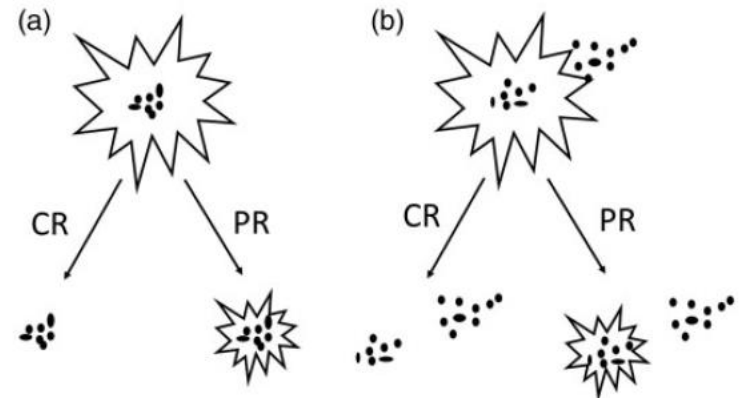
- fine pleomorphic  
~ residual malignancy after NAC
- amorphous  
~ benign after NAC

## Correlation with pathology

- HR+HER2- : MMG > MRI
- HR- HER2- : MMG < MRI

# Microcalcification after neotx

Tumor response after NAC	Change in calcifications after NAC			P value
	Decrease (n = 25)	Increase (n = 11)	No change (n = 44)	
<b>RECIST criteria*</b>				<b>&lt;0.001</b>
Complete response (n = 10)	10 (52.6)	0 (0)	9 (47.4)	
Partial response (n = 41)	10 (24.4)	3 (7.3)	28 (68.3)	
Stable disease (n = 18)	5 (27.8)	6 (33.3)	7 (38.9)	
Progressive disease (n = 2)	0 (0)	2 (100)	0 (0)	
Miller-Payne grade				0.044
1 (n = 10)	2 (20)	3 (30)	5 (50)	
2 (n = 18)	4 (22.2)	3 (16.7)	11 (61.1)	
3 (n = 30)	8 (26.7)	5 (16.7)	17 (56.7)	
<b>4 (n = 10)</b>	<b>2 (20)</b>	<b>0 (0)</b>	<b>8 (80)</b>	
5 (n = 12)	9 (75)	0 (0)	3 (25)	



## Change in microcalcification & tumor response to NAC

- The discrepancy was highest in the group showing CR on MRI with outside calcifications
- In tumors with inside calcifications, the discrepancy was relatively low within an acceptable range

# Microcalcification after neotx

- The extent of microcalcification on mammography after NAC does not correlate with the extent of residual cancer

Pathology	Location of microcalcifications			
	Invasive+in situ	Invasive	In situ only	Benign
Tumor response				
CR	10 (10.4)			10 (10.4)
PR	57 (59.4)	7(7.2)	8(8.3)	23(23.8) 20 (20.7)
SD	29 (30.2)	5(5.2)	3(3.0)	14(14.5) 7 (7.1)
PD	0			
Total	96 (100)			

# Microcalcification after neotx

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- Residual tumor extent  
≠ extent of microcalcification in MMG  
(change of microcalcification)
- Any subtype ?
- Morphology ?
- Distribution ?

# In my practice

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Most cases with residual microcalcification after neo  
→ surgery the area including entire suspicious  
microcalcification

If, Radiologic CR (no enhancement in MR)

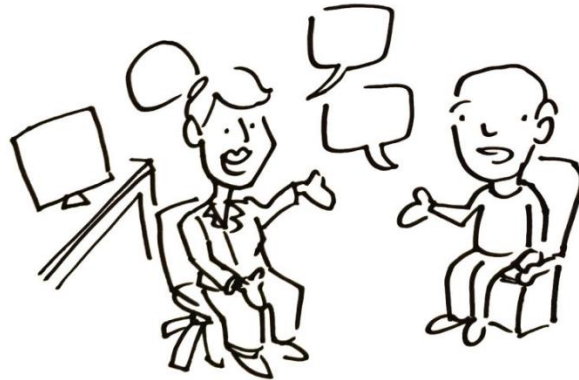
- surgery main lesion just including the clipping site
- check resection margin by frozen Bx

- If margin(+ : invasive cancer /multiple DCIS)
  - surgery including all suspicious  
microcalcification lesion
- If margin(- : others) → check final pathology

# Shared Decision Making

PATIENTS and  
DOCTORS NEED TO

**SIT  
TOGETHER**



TO WORK OUT THEIR  
HEALTHCARE

# In summary

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## 1. Microcalcification

with Radiology-Pathology discordance

→ surgical excision

## 2. Microcalcification

after Neoadjuvant systemic treatment

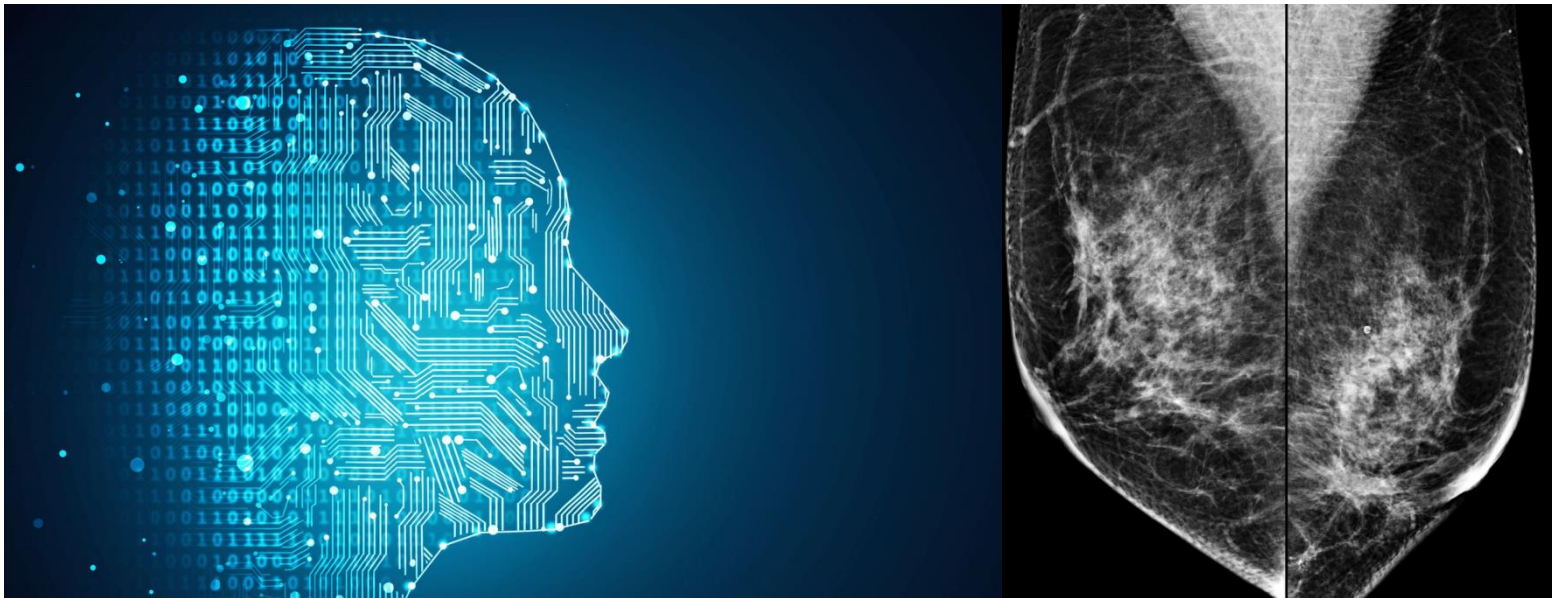
→ surgery including all susp. Microcalcification  
(considering to decrease the extent of surgery  
in specific subtype with radiologic CR)



**Future**

**for Microcalcification**

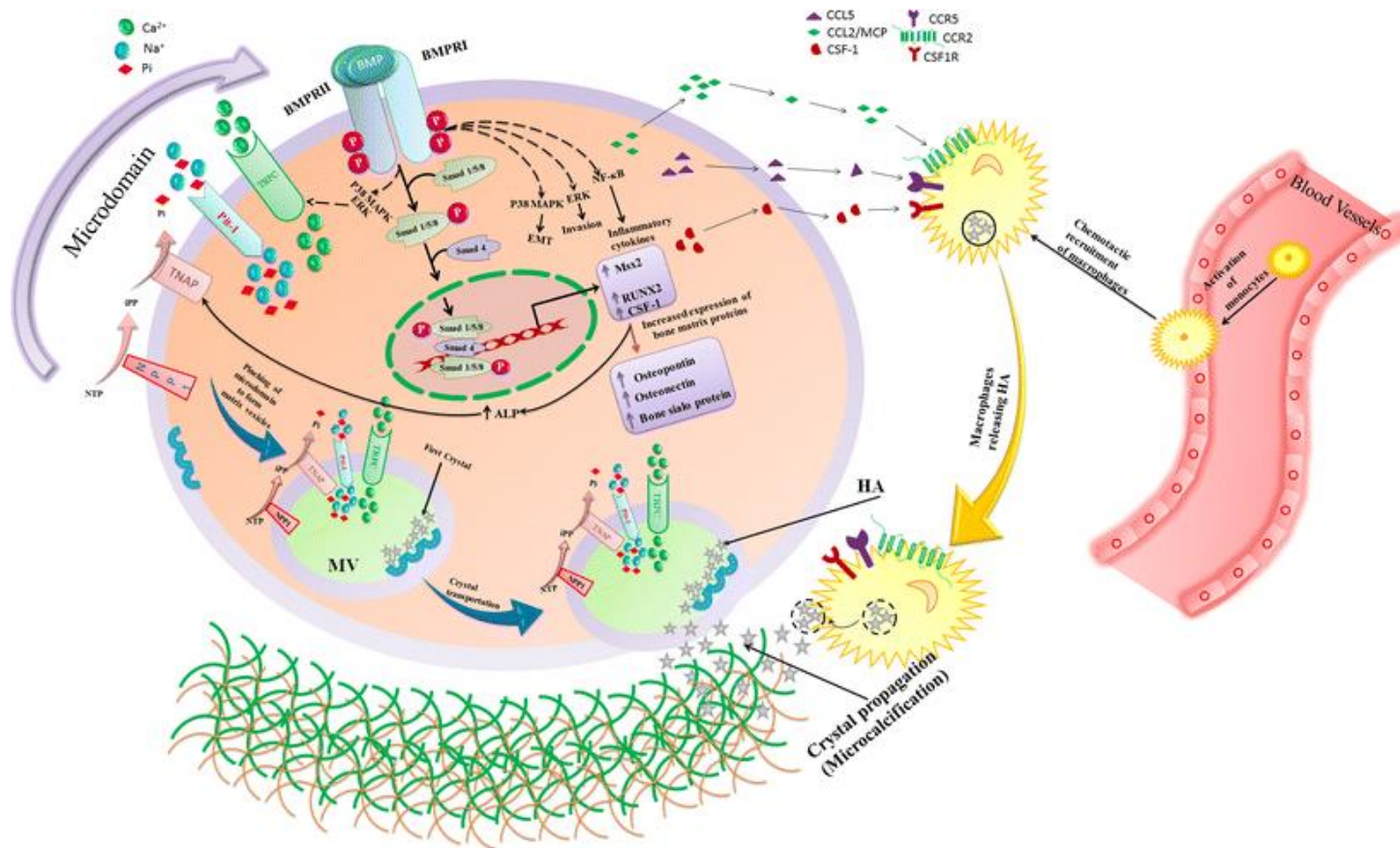
# Radiologic diagnosis : AI(deep learning)



# Biologic characteristics

→ clue to treatment (new drug)

→ clue to diagnosis (new imaging tool)



# Acknowledgment



**Breast Cancer Center**

**Samsung Medical Center**

# Thank you for your attention

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