Imaging Controversy in DCIS Surveillance

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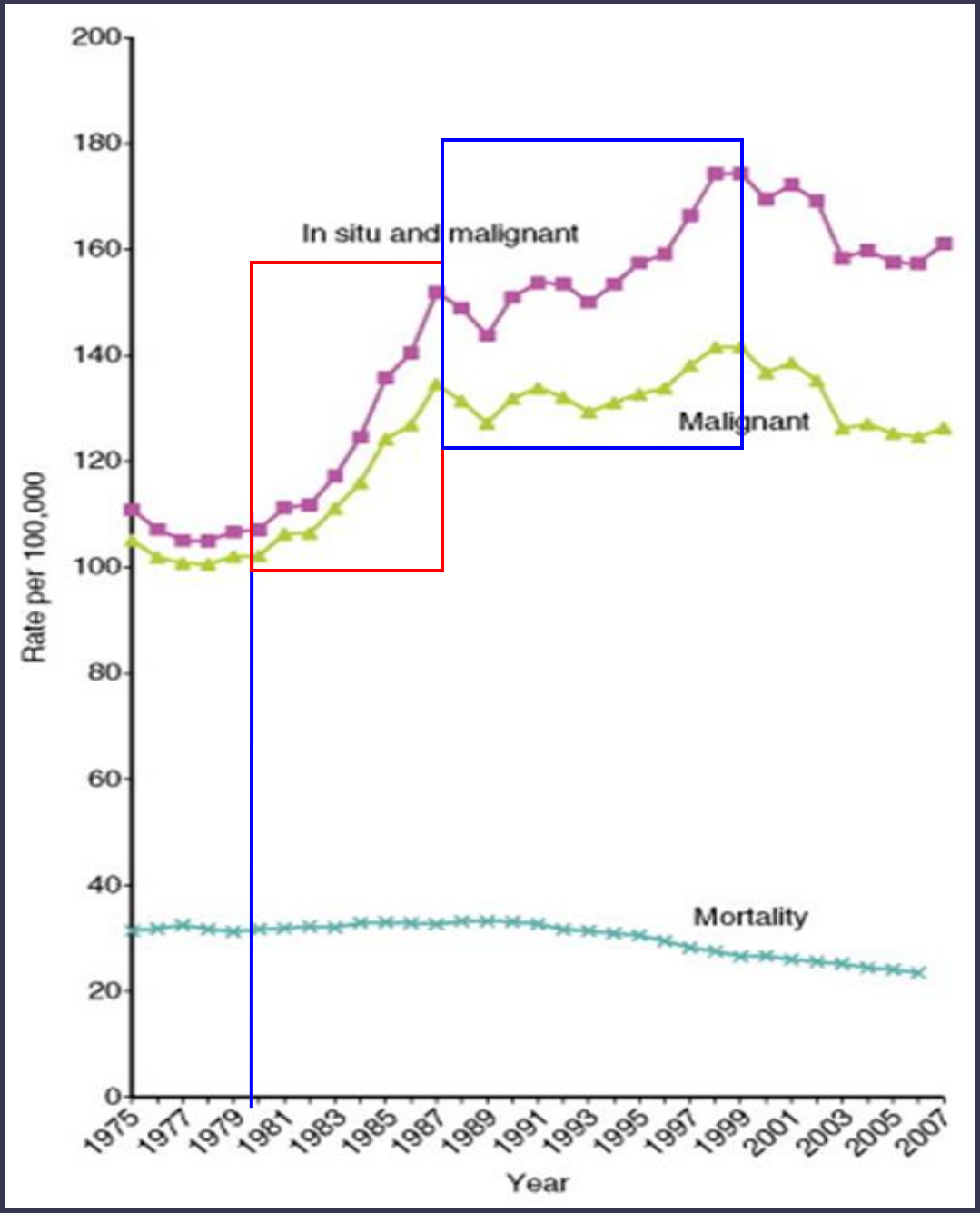
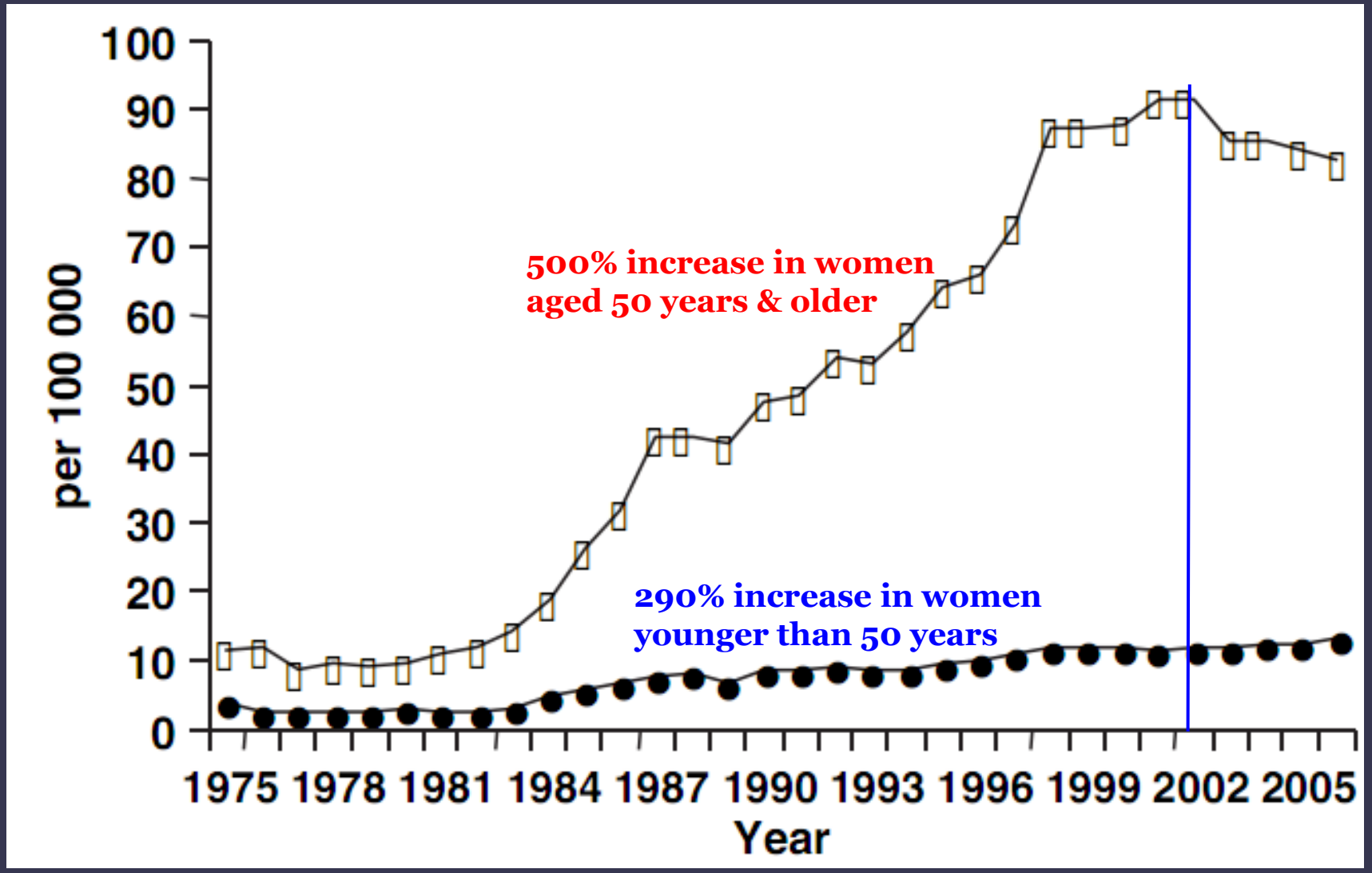
Incidence & Mortality Rate



Bassett et al. Breast Imaging 2011

Age-adjusted Incidence of DCIS



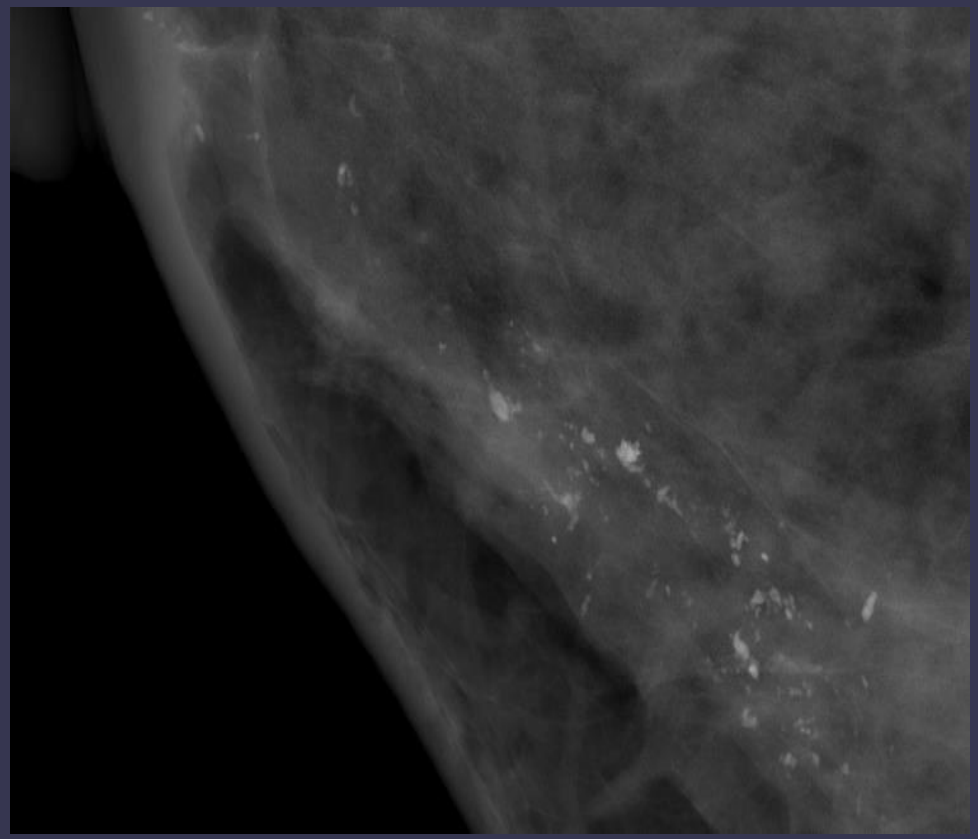
Kerlikowske K. Epidemiology of DCIS. JNCI 2010

DCIS

- Before screening MG – uncommon disease
- ≈ 5% of all breast cancers prior to 1984
  - Present as palpable lump
- Screening MG has changed the demographics of DCIS

DCIS

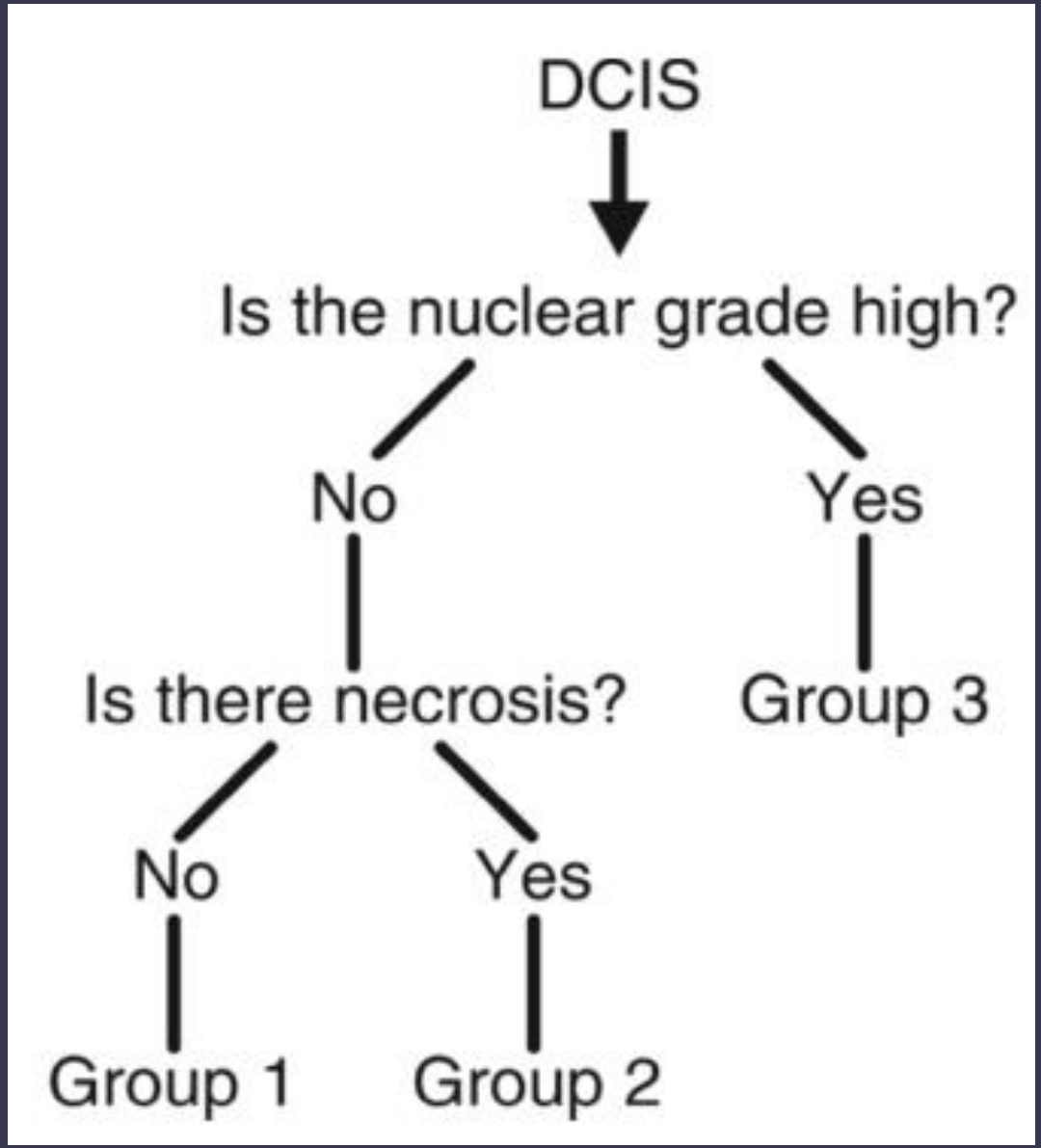
- Recently DCIS represents 20%-30% of breast cancers annually
  - Present as nonpalpable, MG-detected lesions
  - Classic imaging finding - calcifications



Subtypes of DCIS

- Comedo-type DCIS
  - Tends to be more aggressive
  - Dead debris in center of duct ➔ calcifications
- Non-comedo type DCIS
  - Cribriform
  - Papillary
  - Micropapillary
  - Solid

Van Nuys Classification



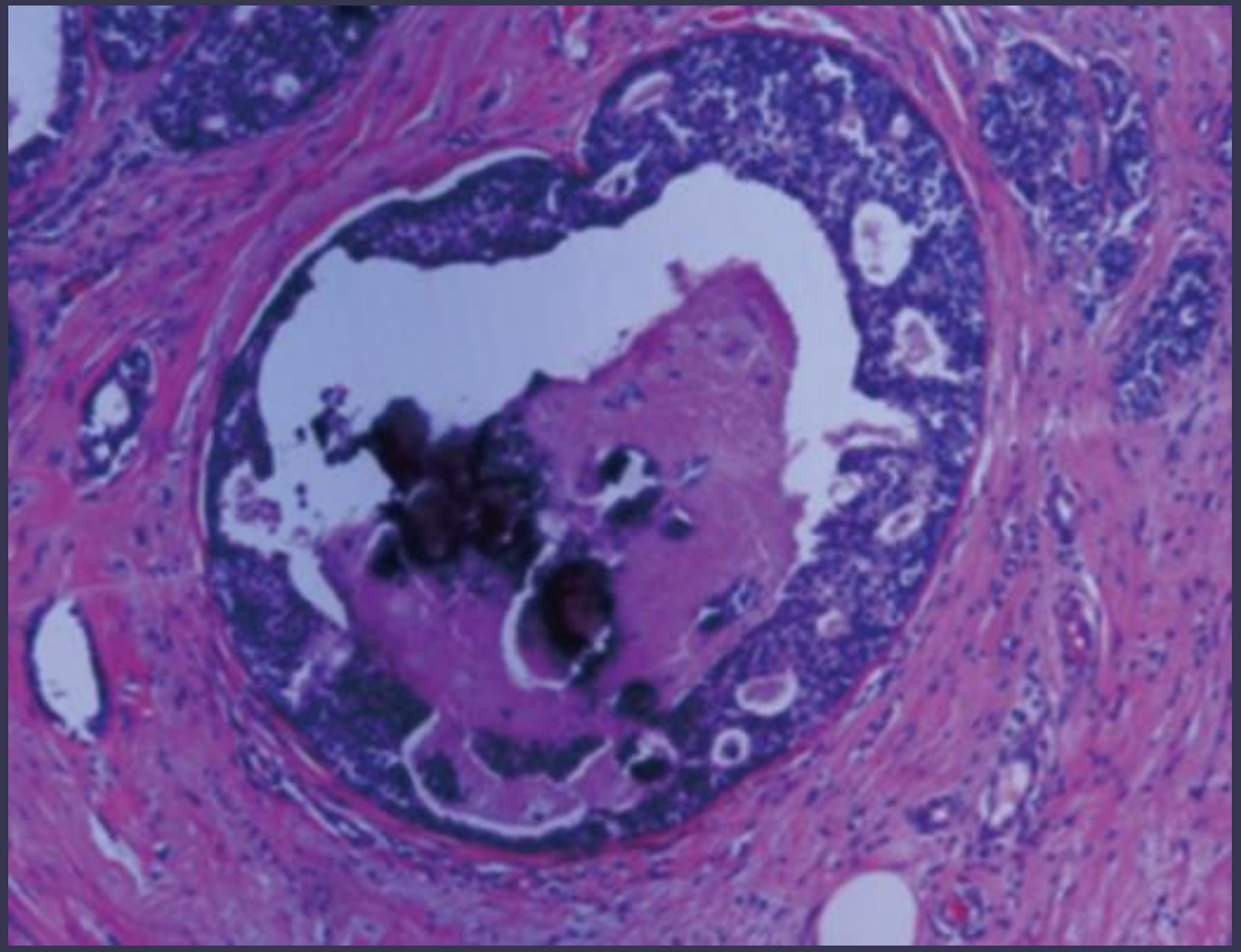
Yamada T. Radiographics 2010;30:1183-1198

Subtypes of DCIS

- High nuclear grade
  - Large, pleomorphic nucleoli, frequent mitosis
  - Central necrosis
- Intermediate nuclear grade
  - Nuclei that are neither low nor high grade
- Low nuclear grade
  - Uniform cell with small nuclei, minimal nuclear pleomorphism, infrequent mitosis
  - Usually cribriform or micropapillary pattern

Consensus Conference Committee. Cancer 1997;80:1798-1802

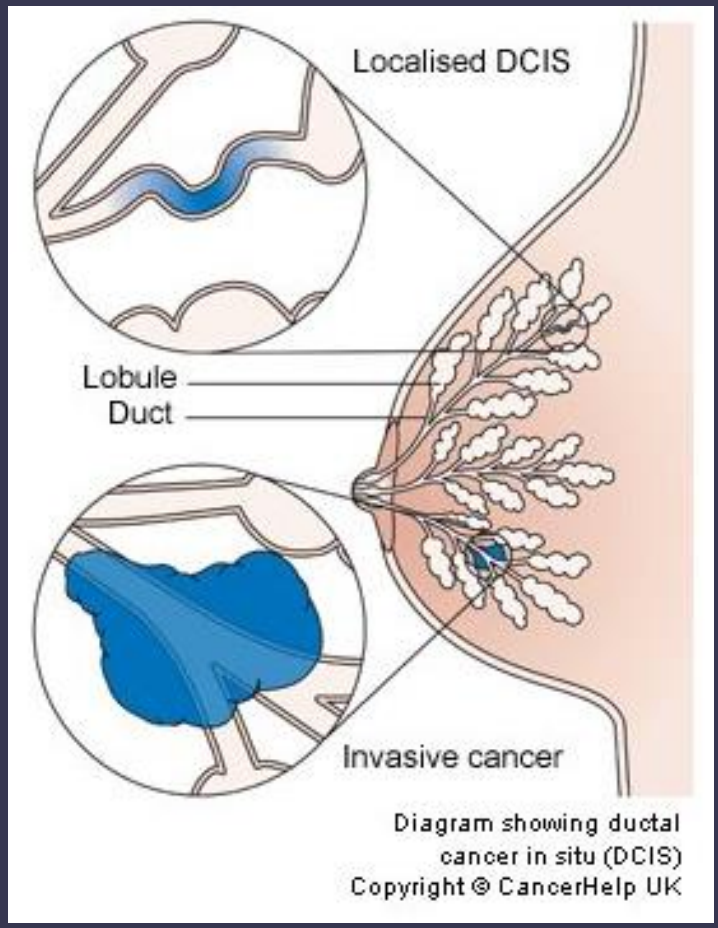
Central Necrosis with Calcification



Yamada T et al. Radiographics 2010;30:1183-1198

Pathology of DCIS

- Starts in TDLU
- Proliferation of malignant ductal epithelial cells without evidence of invasion through the basement membrane



Predictors of Asso. Invasive Cancer

- Meta-analysis: 7350 DCIS at CNB of 52 studies
  - 1736 underestimates – 25.9% (95% CI; 22.5%, 29.5%)
  - 14G automated device (vs. 11G VAB, *P*=.006)
  - High-grade lesion at CNB (vs. non-HG, *P*<.001)
  - Lesion size larger than 20 mm at imaging (*P*<.001)
  - BIRADS score of 4 or 5 (*P*=.005)
  - Mammographic mass (vs. Ca^{++}, *P*<.001)
  - Palpability (*P*<.001)

Brennan ME, et al. Radiology 2011;260:119-128

Predictors of Asso. Invasive Cancer

- HER2 overexpression as a predictor for transition from in situ to invasive cancer
  - 106 patients (mean, 53.4 years)
  - Overexpression of HER2 – the only significant predictor for the presence of invasive disease (OR=6.4; *P*=.01)
  - More powerful predictor on invasion than lesion size or nuclear grade
  - HER2 expression may be up-regulated during in situ stage & down-regulated in more advanced stage

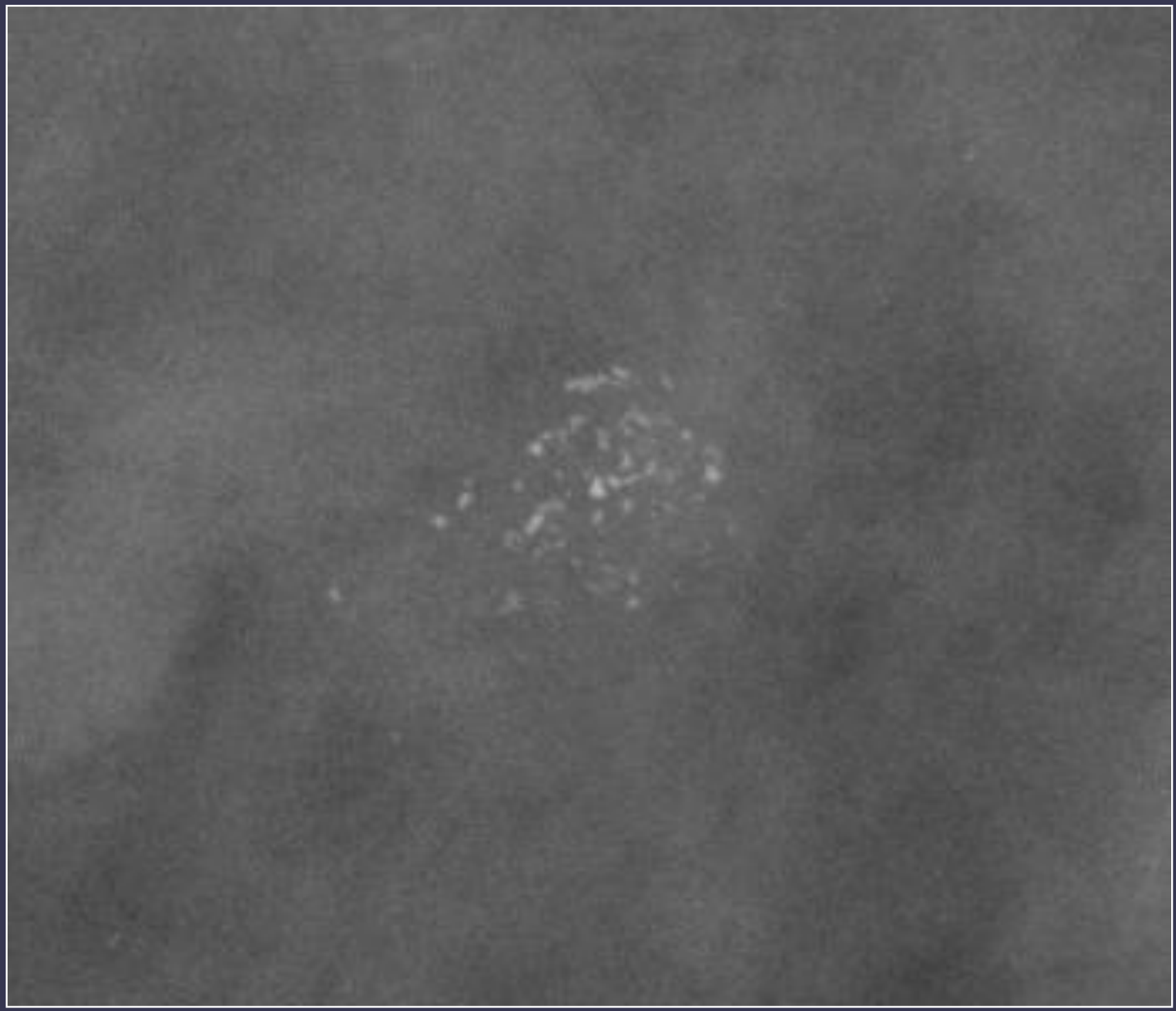
Roses RE, Cancer Epidemiol Biomarkers Prev. 2009;18:1386-1389

MG features of DCIS

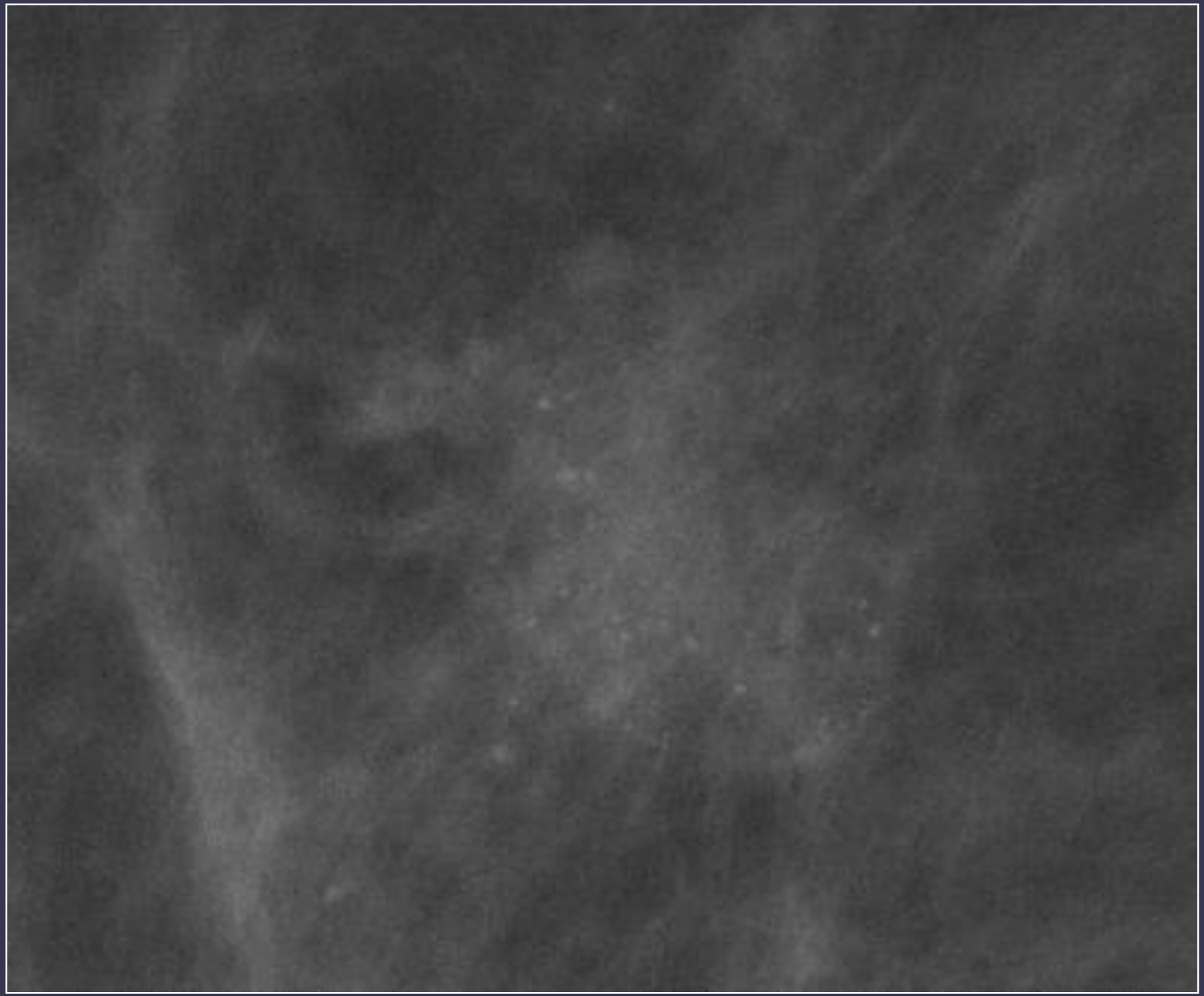
- M/C MG finding in DCIS – microcalcifications (50%~75%)
- Other MG findings – mass (10%), architectural distortion (7%~13%), asymmetry…
- MG sensitivity for detection of DCIS – 87%~95%
  - High-grade DCIS – more likely to be visible on MG
  - Low-grade DCIS – more likely to manifest as noncalcified abnormalities

MG Feature of DCIS

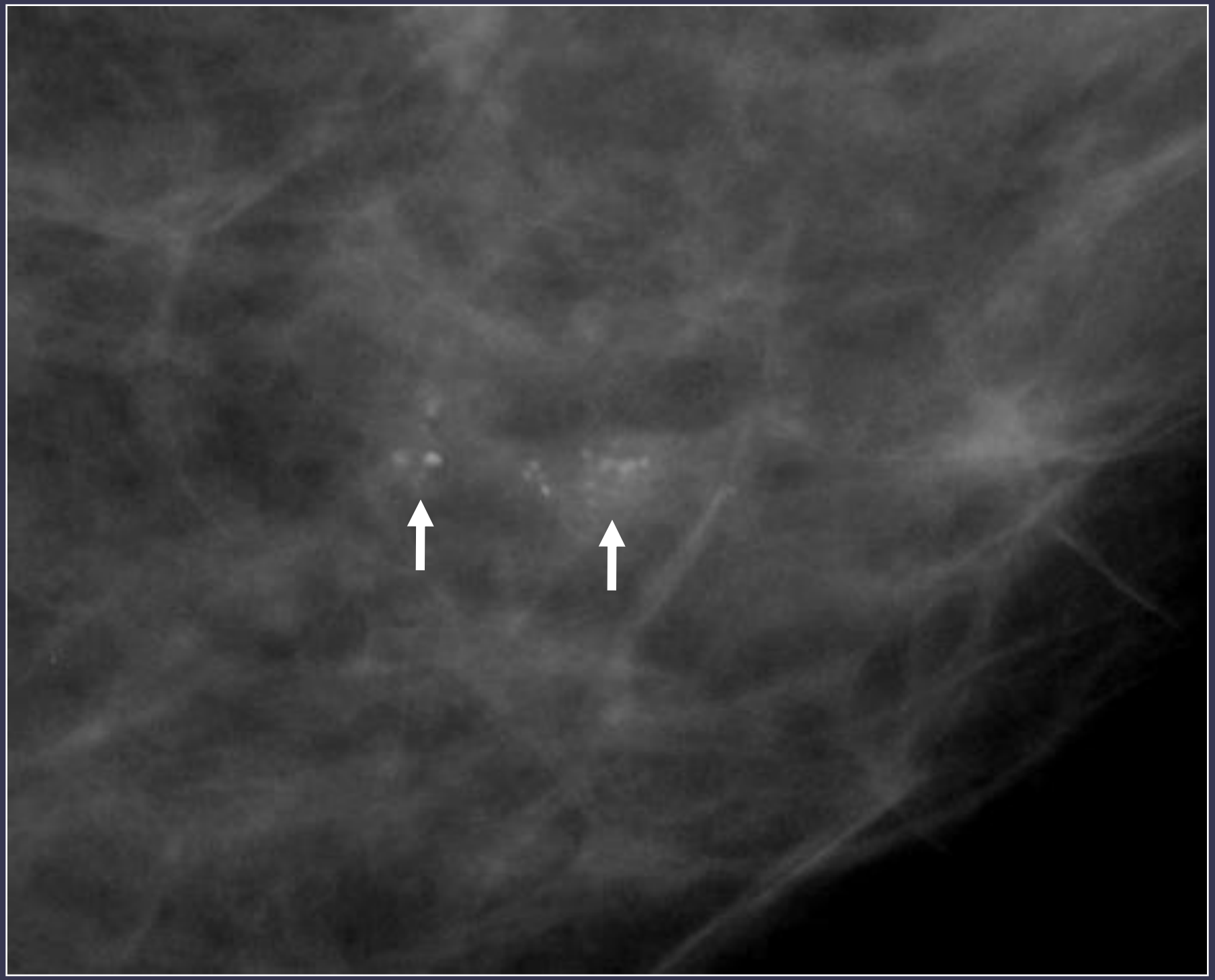
- Calcifications = dead necrotic cells
  - Considerable overlap between the MG appearances of different histologic subtypes
  - Significant association – between fine pleomorphic or fine linear-branching calcifications & necrosis
  - Significant correlation – between round calcifications & presence of low-grade DCIS



Van Nuys group 2 DCIS (0.5 cm)

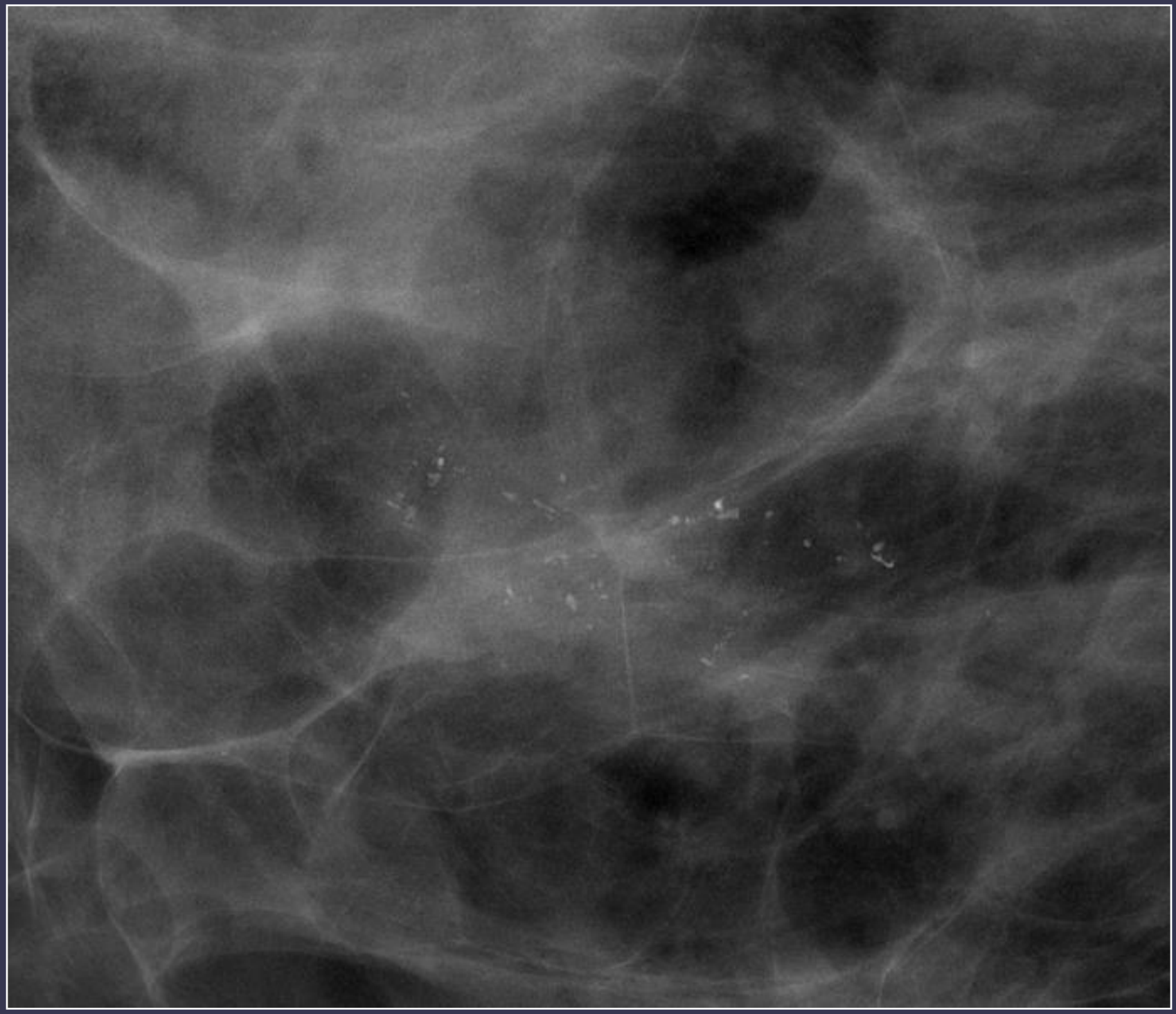


Van Nuys group 2 DCIS (3 cm)

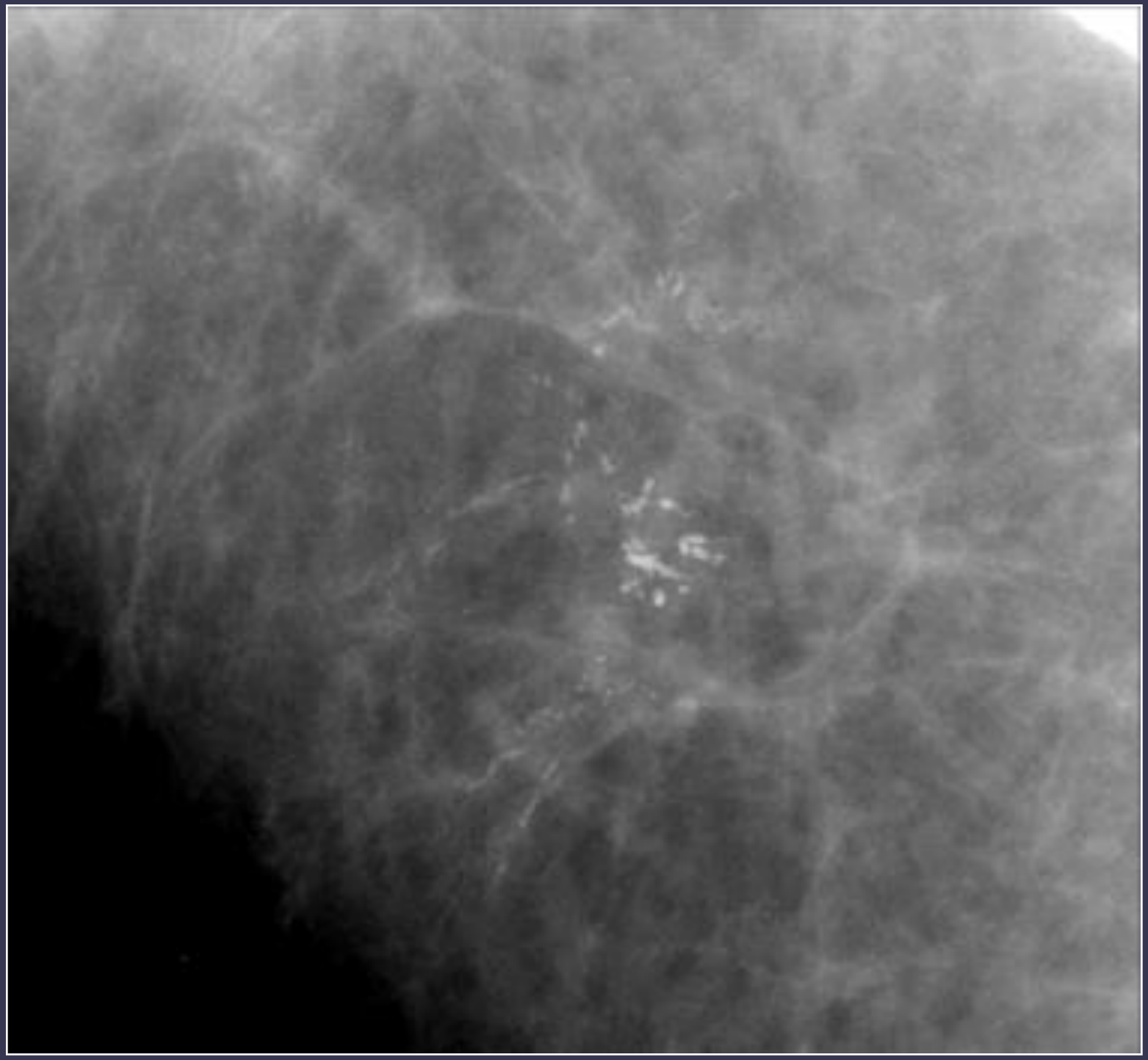


Van Nuys group 3 DCIS

Intermediate-grade DCIS with microinvasion, HER2(+)



High-grade DCIS with necrosis

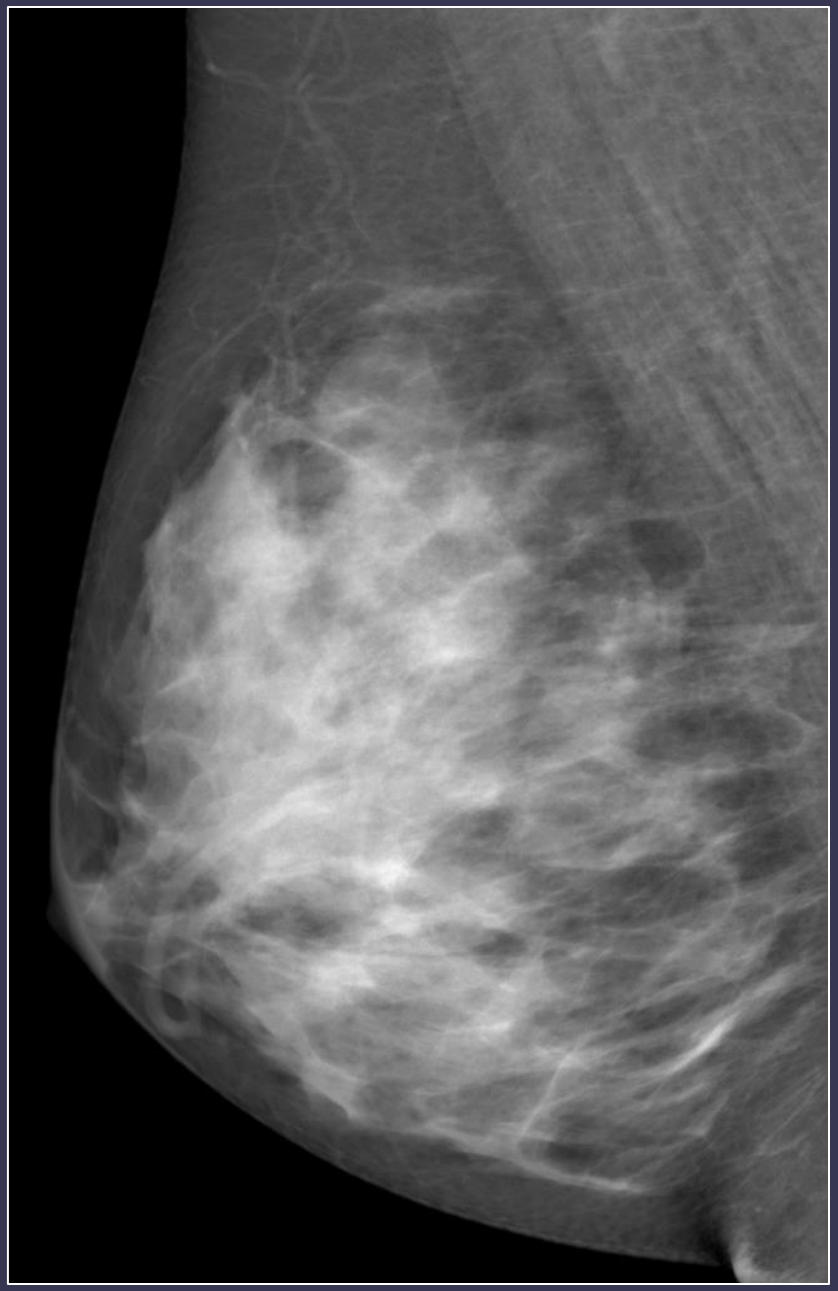


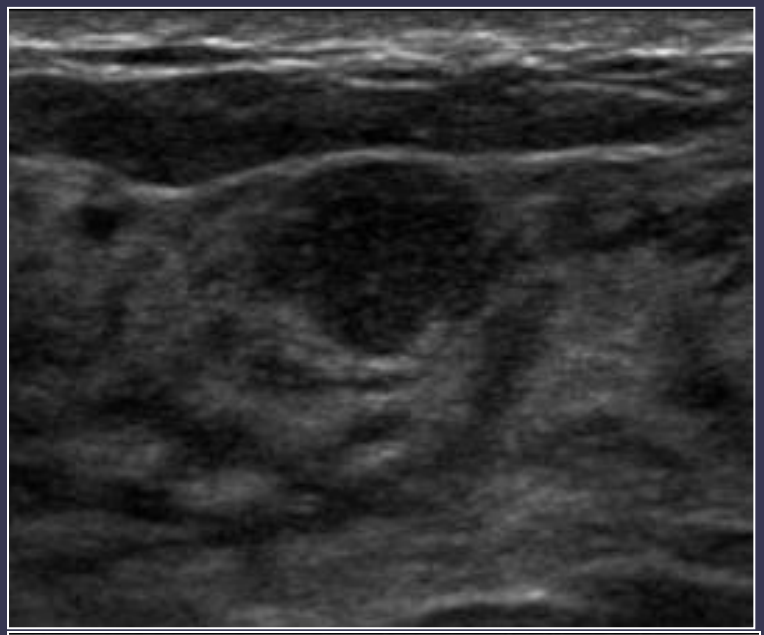
Comedo-type DCIS with necrosis

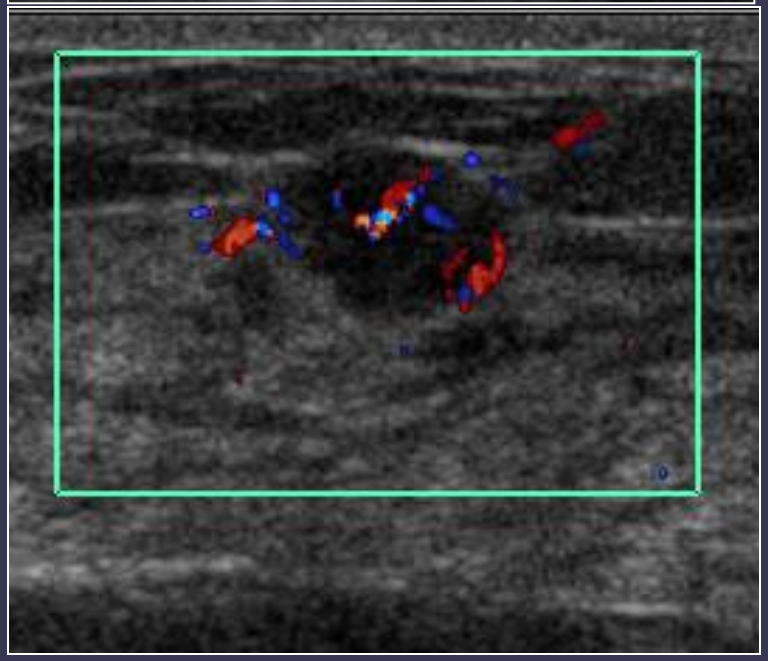
MG Features of DCIS

- Screening-detected calcified vs. noncalcified DCIS *Mun HS, Shin HJ et al. Clin Radiology 2013;68:e27-35*
  - 217 in 212 asymptomatic patients
  - On MG, noncalcified DCIS – FN (49%) or mass (30%) vs. calcified DCIS – calcifications alone (69%)
  - On US, all noncalcified DCIS vs. 62% of calcified DCIS – appeared as a mass
  - On pathology, high NG, necrosis, PR(+), HER2 (+) were more common in the calcified DCIS

Screening US-detected non-calcified DCIS







Low grade DCIS without necrosis

US Features of DCIS

- US features of DCIS
  - Calcified DCIS – echogenic foci located within a mass or duct
  - Noncalcified DCIS – more often in symptomatic patients & mass with microlobulated margin, no posterior acoustic features , pseudomicrocystic app.
  - High-frequency transducer, spectral compounding, speckle reduction algorithm – aid to detect Ca^{++}

US of Calcified DCIS

- US can be performed
  - To evaluate for a possible invasive component
  - To assess the axillary LNs for evidence of invasion
  - To allow the possible US-guided biopsy
  - US can identify 23%~45% of Ca^{++} seen at MG

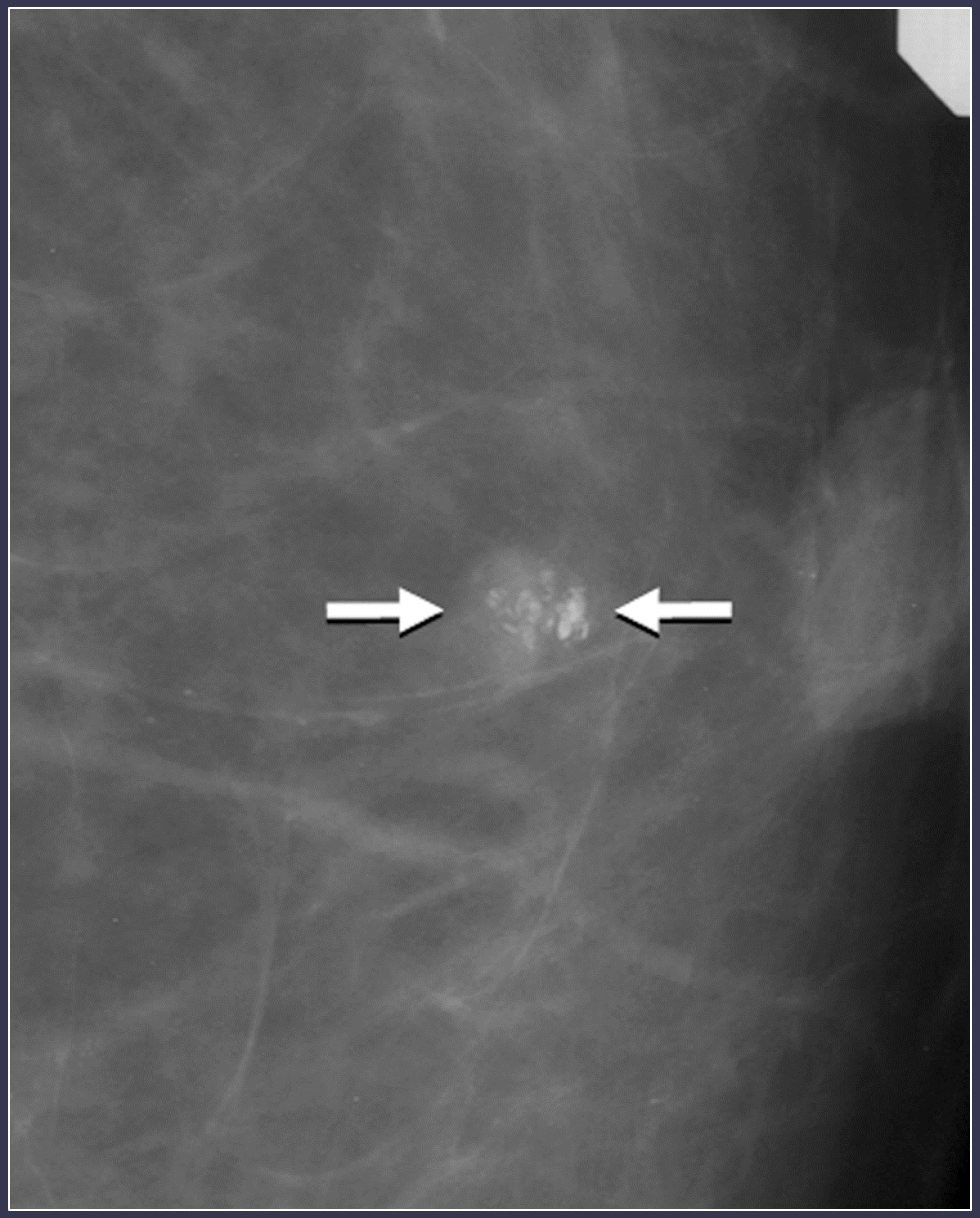
Soo MS et al. AJR 2002;178:941-948

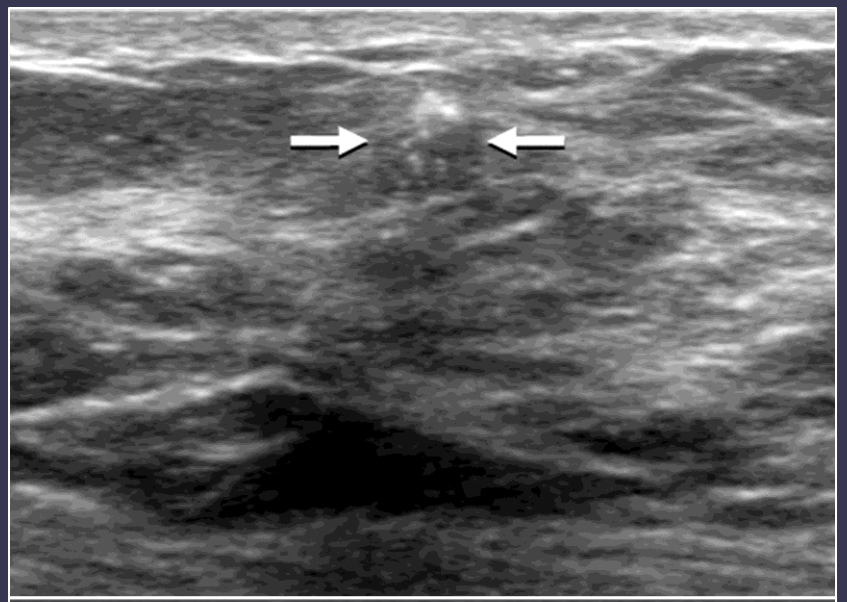
Yu PC et al. Breast 2011;20:495-500

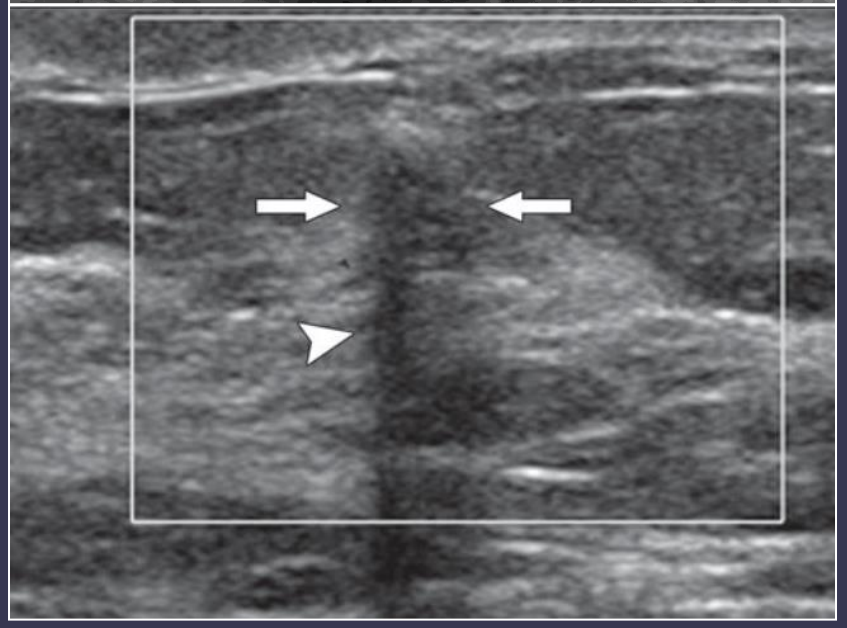
  - Malignant Ca^{++} are more frequently visualized at US than are those associated with benign disease

Moon WK et al. Radiogy 2000;217:849-854

58Y/ Screening MG-detected calcified DCIS





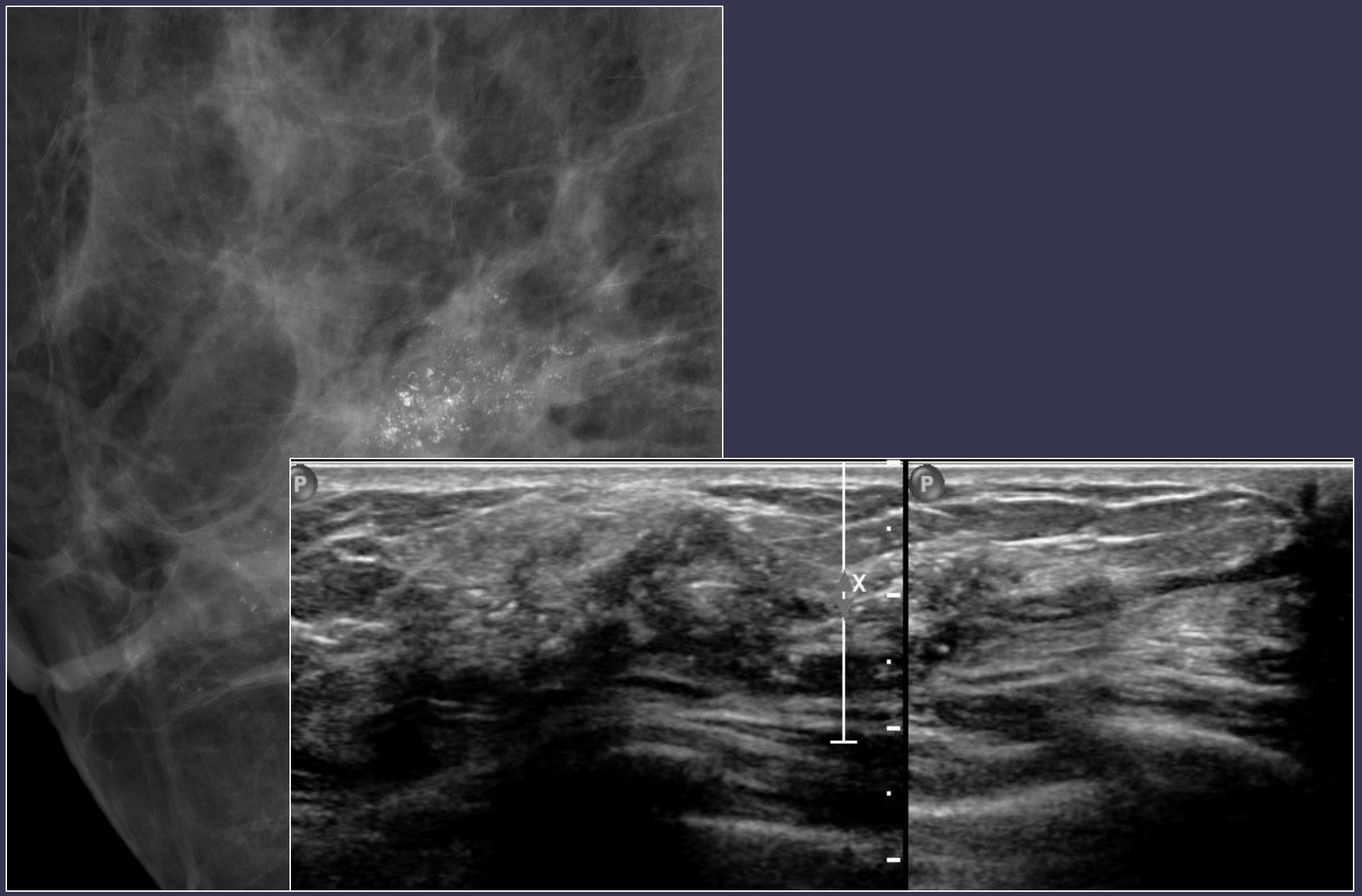


Intermediate grade DCIS with necrosis

A 35-year-old woman with palpable lump

High grade DCIS with necrosis

A 55-year-old woman with palpable lump



Intermediate grade DCIS with necrosis

US of Noncalcified DCIS

- 2%~23% of DCIS – mass or asymmetry on MG
  - Noncalcified DCIS – MG occult palpable lesion, cause for nipple discharge, abnormality on screening US or finding in the evaluation of disease extent
  - Up to 82% of noncalcified DCIS – symptomatic

Ikeda DM et al. Radiology 1989;172:661-666

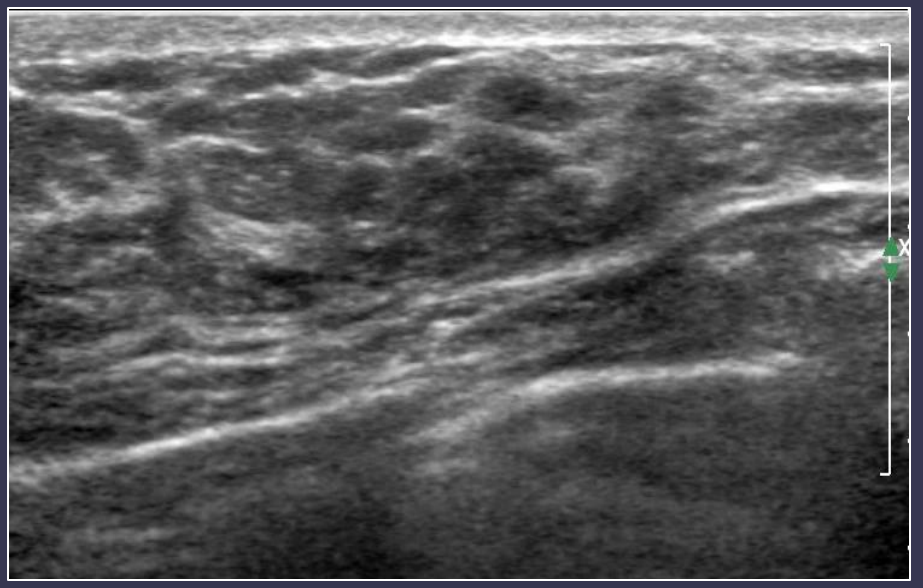
  - Mass – more frequent in non-HG than HG DCIS

Park JS et al. J Ultrasound Med 2010;29:1687-1697

  - Mass – more common in symptomatic than screening-detected DCIS (calcifications & posterior shadowing)

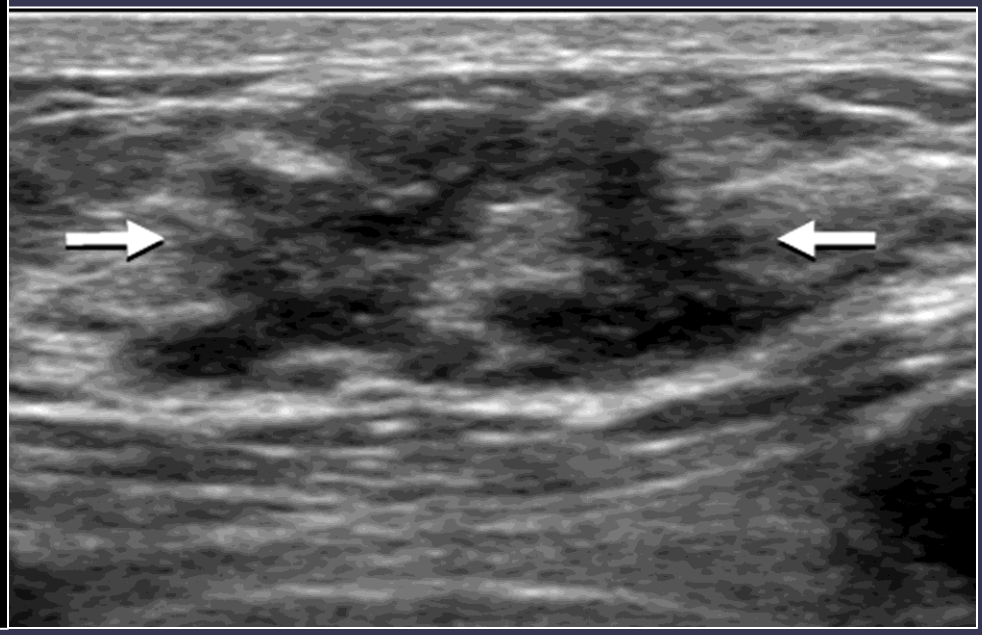
Shin HJ et al. AJR 2008;190:516-525

A 41-year-old woman with palpable lump



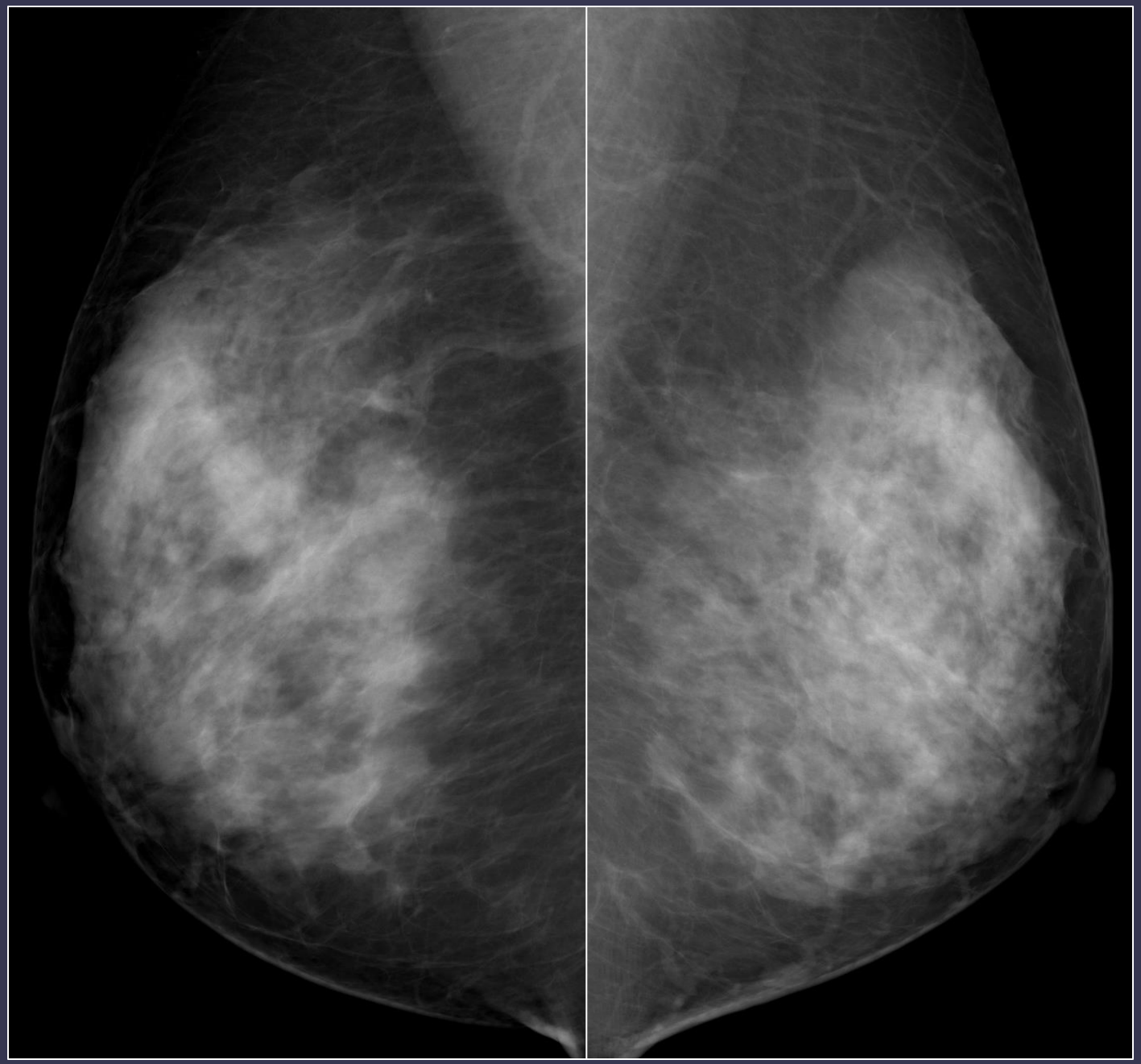
Intermediate grade papillary DCIS

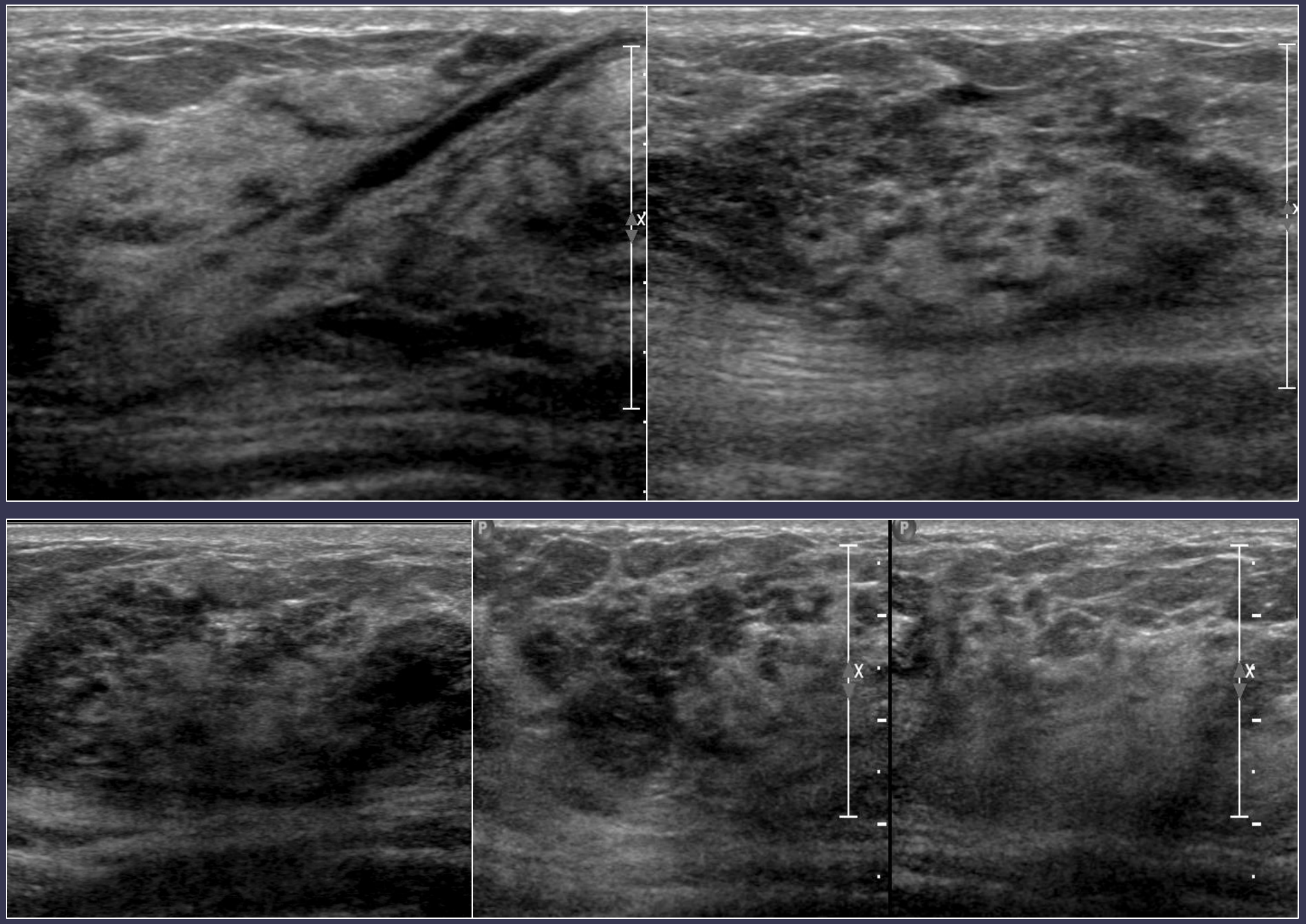
A 41-year-old asymptomatic woman



Intermediate grade DCIS

A 44-year-old woman with palpable lump & bloody discharge in right breast





High-grade DCIS with IDC (9 cm)

DCIS diagnosed at MR-directed US

- 5% of women who underwent preop. MRI – MG occult cancer in contralateral breast → half of which were DCIS

Liberman L et al. AJR 2003;180:333-341

- The rate of correlation between US & MR for nonmass enhancement is low - 12%~40%
  - If no correlate is identified for suspicious nonmass enhancement, MR-guided biopsy should be performed

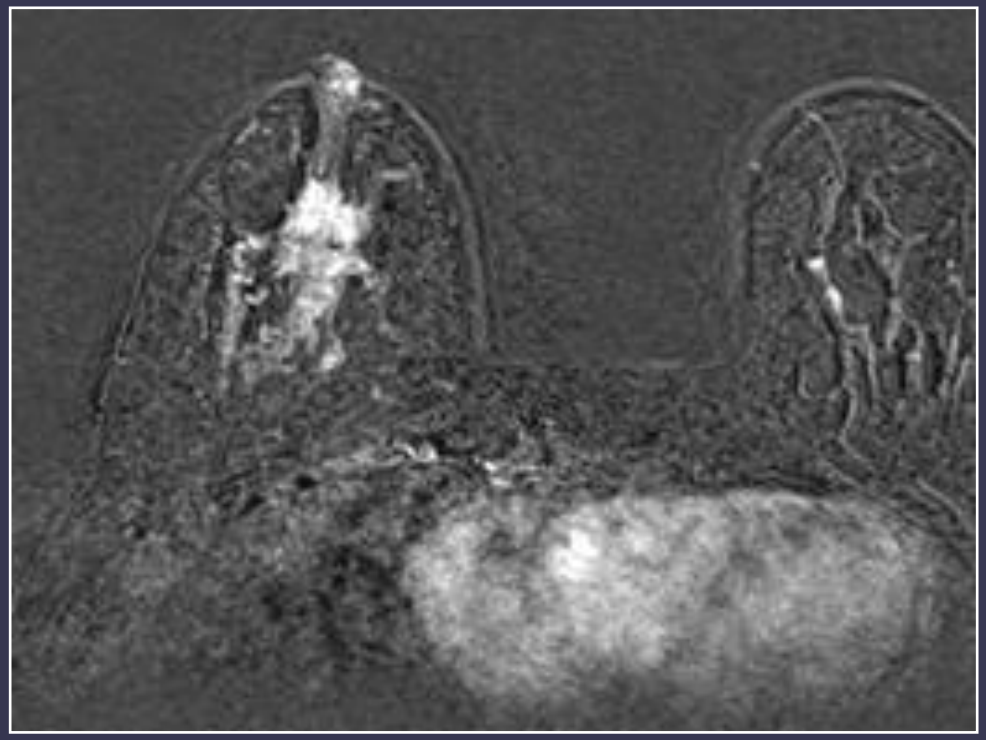
Abe H et al. AJR 2010;194:370-377

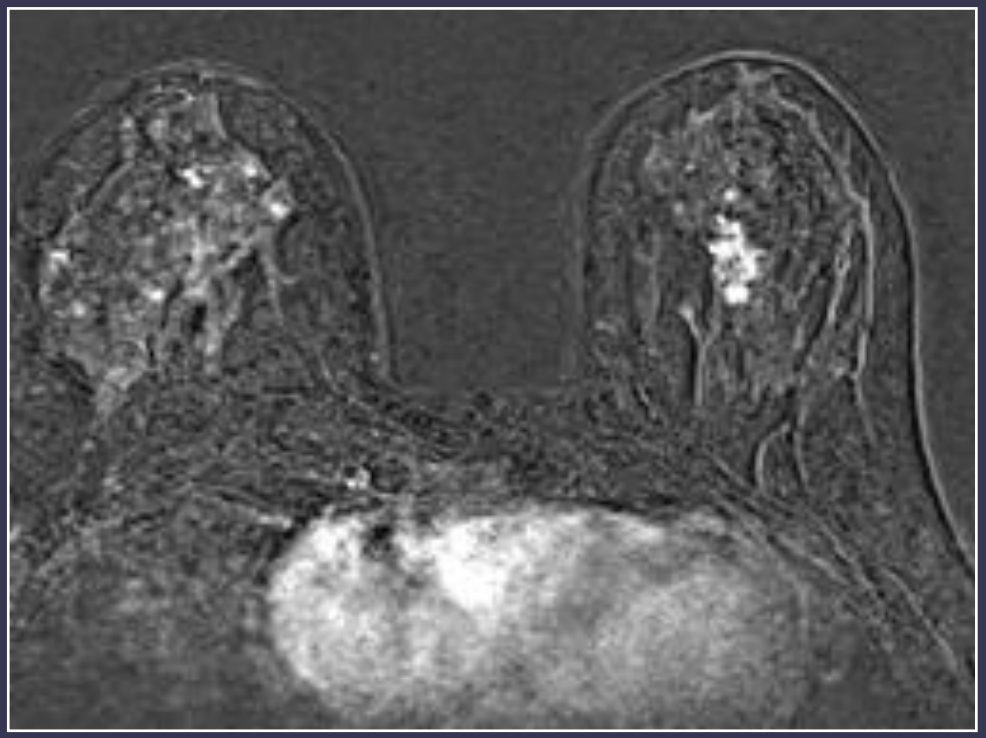
Demartini WB et al. AJR 2009;192:1128-1134

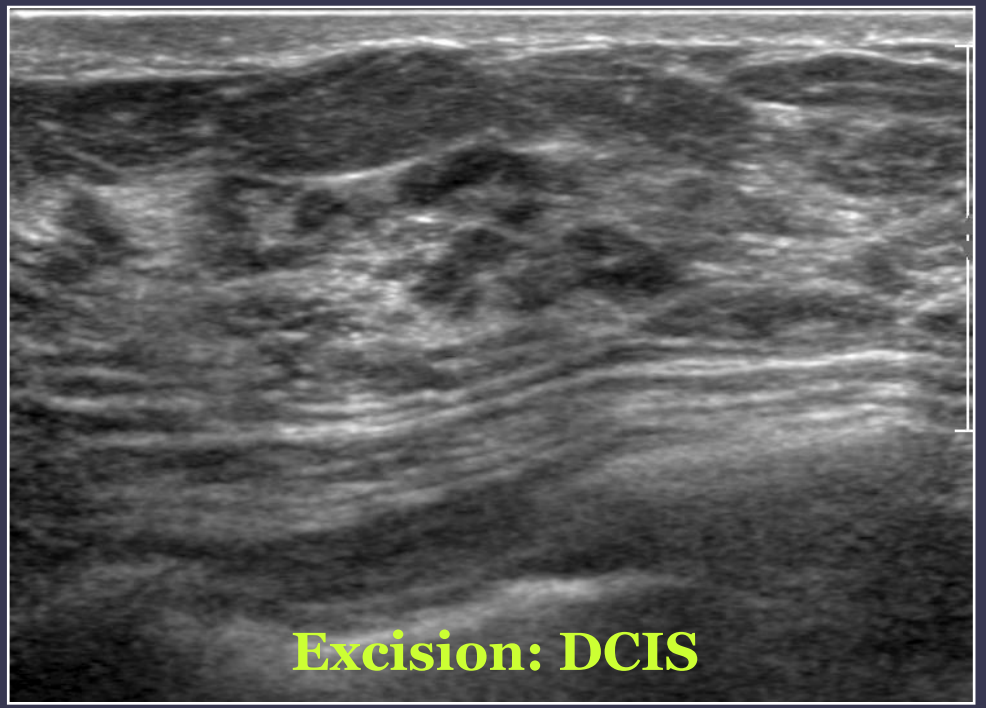
DCIS diagnosed at MR-directed US

- For MR-detected lesion, typical malignant features (spiculation, angular margins, echogenic halo, & posterior shadowing) may be absent
  - A lower threshold should be used at SLUS than at conventional diagnostic or screening US

A 45-year-old woman with known ILC in right breast



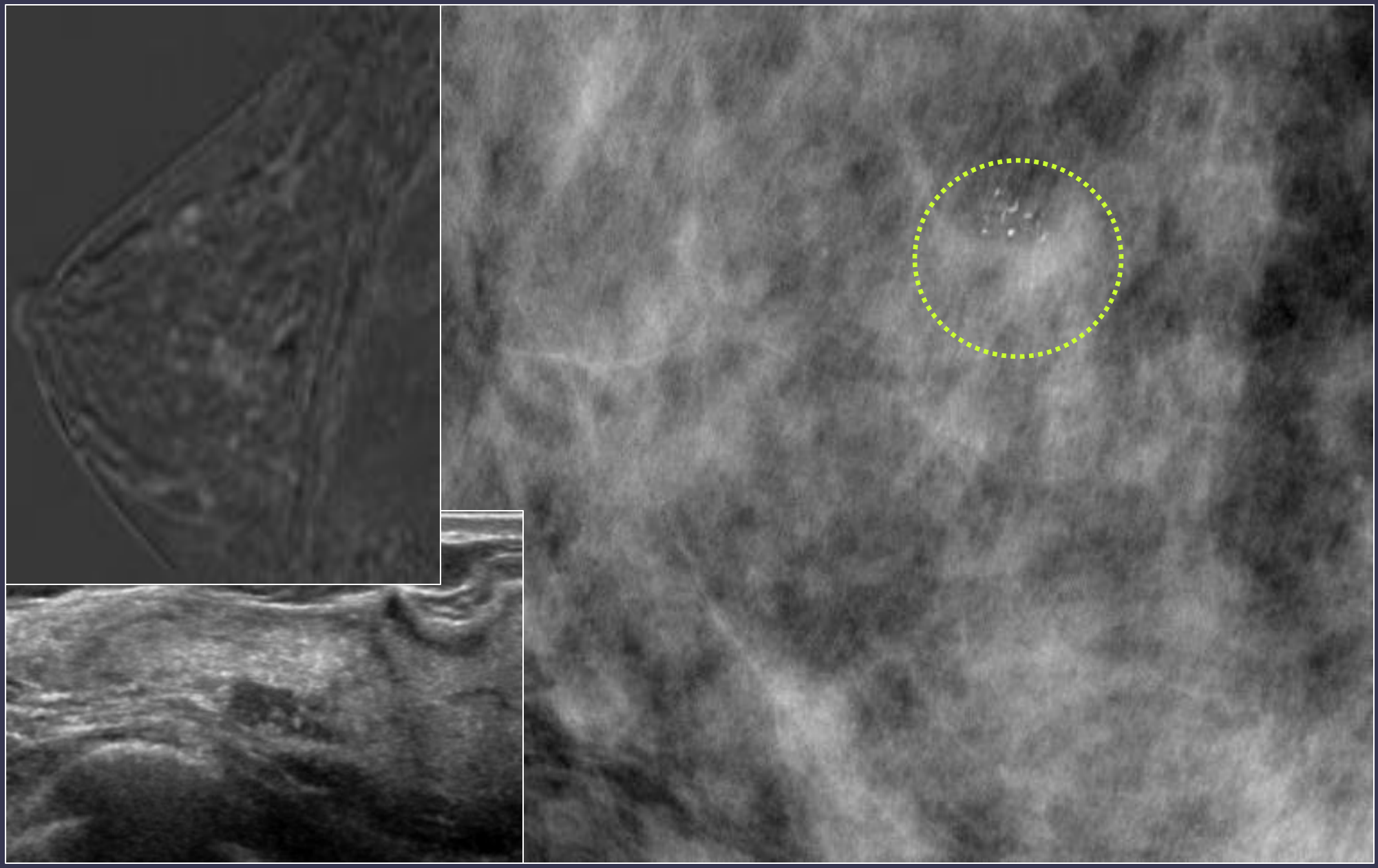




MRI of DCIS

- Initially, multiple studies evaluated detection of DCIS on MRI
  - Based on failure to detect mammographically detected DCIS
  - Based on these data → MRI was limited in detecting DCIS

A 44-year-old asymptomatic woman



Intermediate grade DCIS with necrosis

MRI of DCIS

- Technology evolved – higher spatial resolution & improved spatial resolution
- More recent reports began to emerge showing different data
  - Data supporting that MRI may be superior to MG in detecting DCIS

MRI of DCIS

- MRI surpasses both MG & US in the ability to detect the presence & extent of DCIS including noncalcified DCIS

Kuhl CK et al. Lancet 2007;370:485-492

Berg WA et al. Radiology 2004;233:830-849

- M/C MR finding – nonmass clumped enhancement in a segmental, linear, or regional distribution

MRI of DCIS

- Detection sensitivity of DCIS on preop. MRI
  - 38 DCIS - 89% for MRI vs. 55% for MG

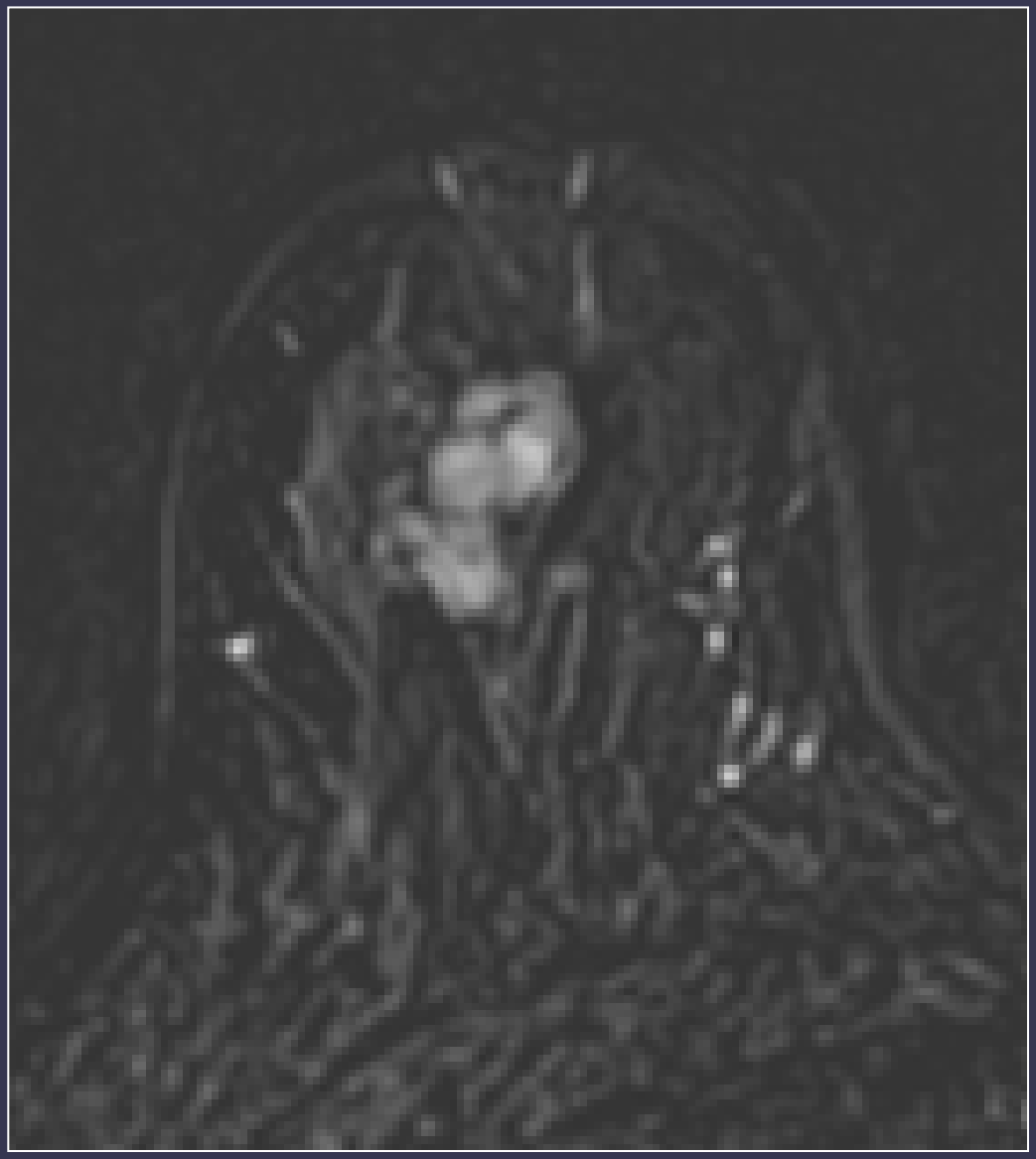
    Berg WA. Radiology 2004;233:830-849
  - 167 DCIS - 92% for MRI vs. 56% for MG
    - High-grade DCIS – 98% for MRI vs. 52% for MG

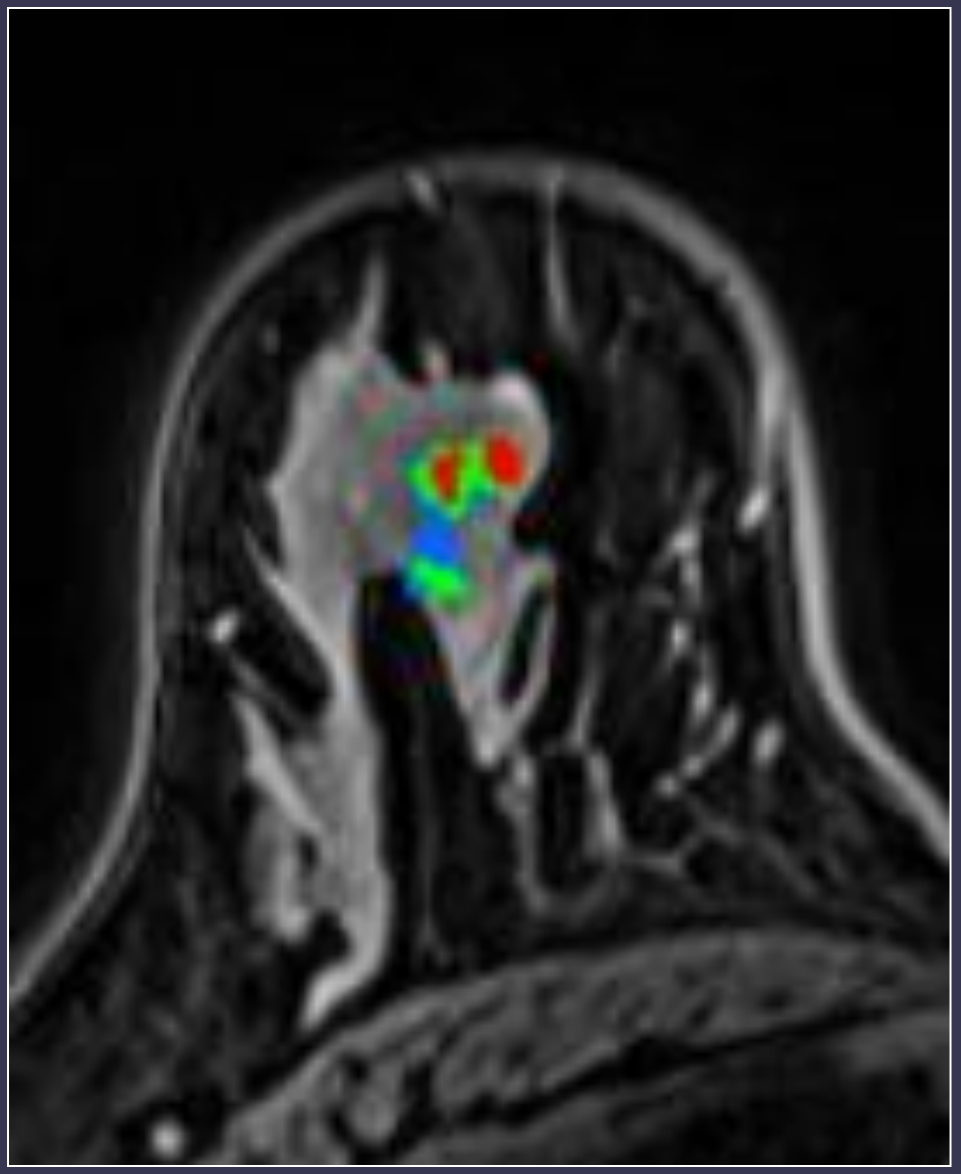
    Kuhl CK et al. Lancet 2007;370:485-492
- MR surveillance trial of high risk women
  - 67% for MRI vs. 50% for MG

    Warner E. JAMA 2004;292:1317-1325
  - 89% for MRI vs. 33% for MG

    Kuhl CK. J Clin Oncol 2005;23:8469-8476

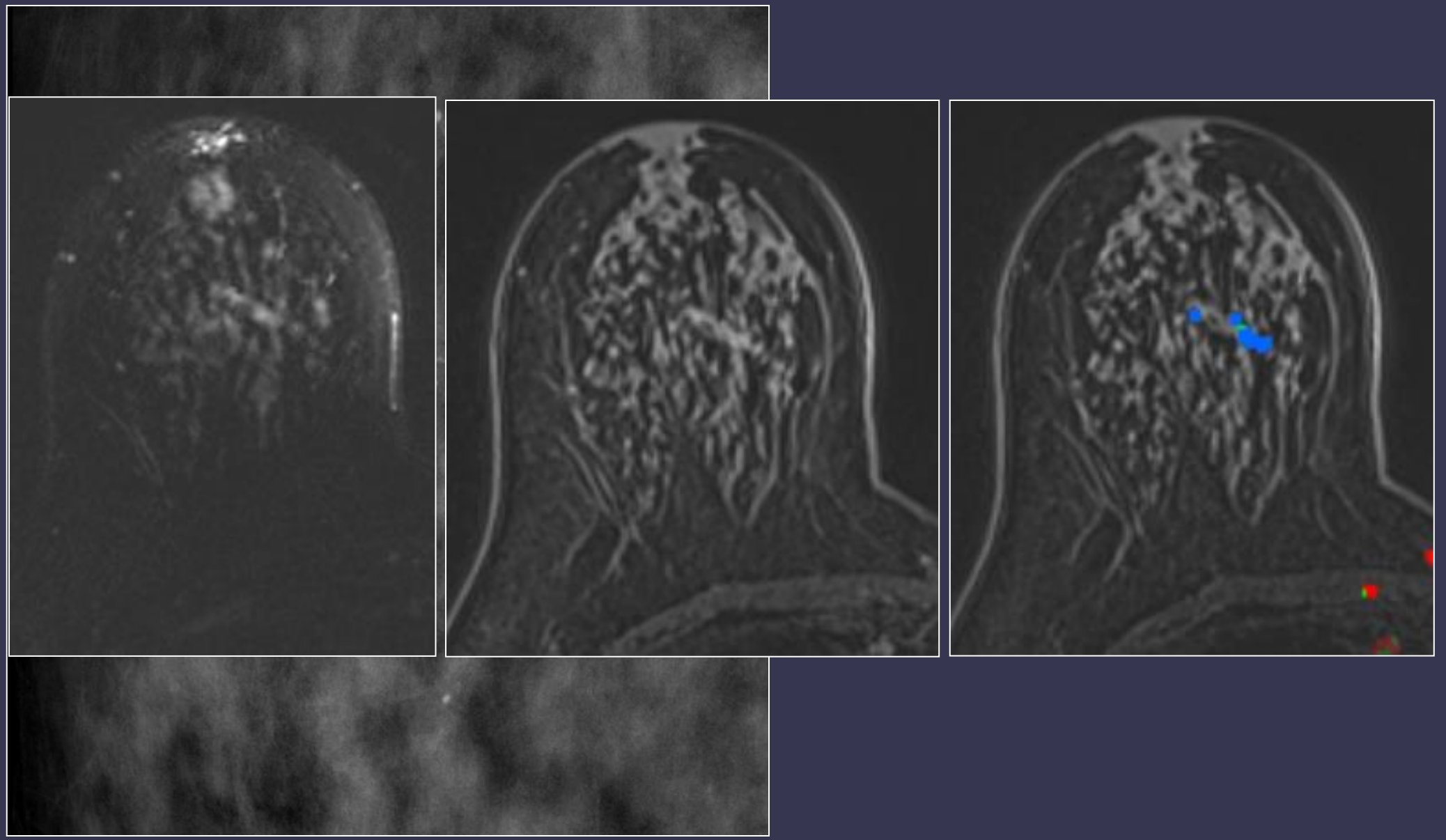
A 59-year-old woman





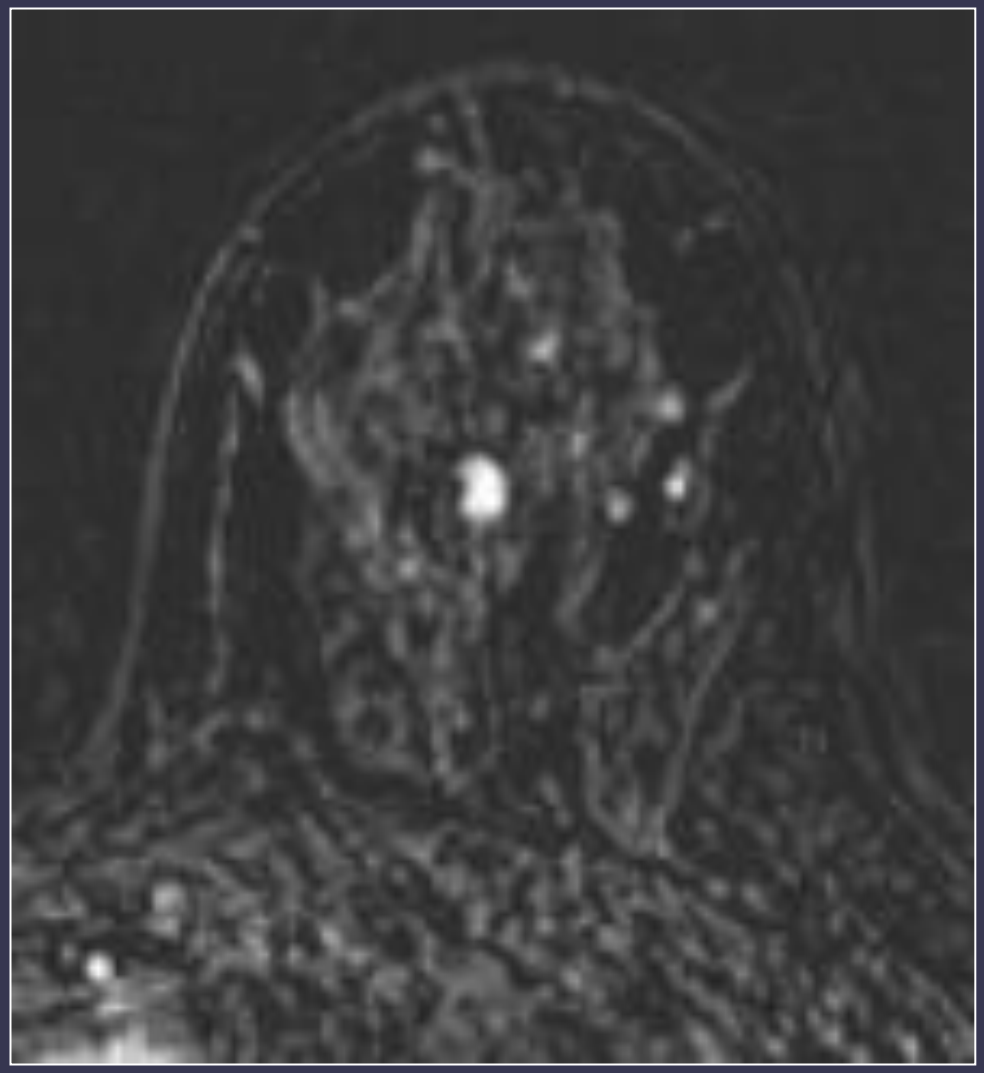
Intermediate grade DCIS (2.4 cm)

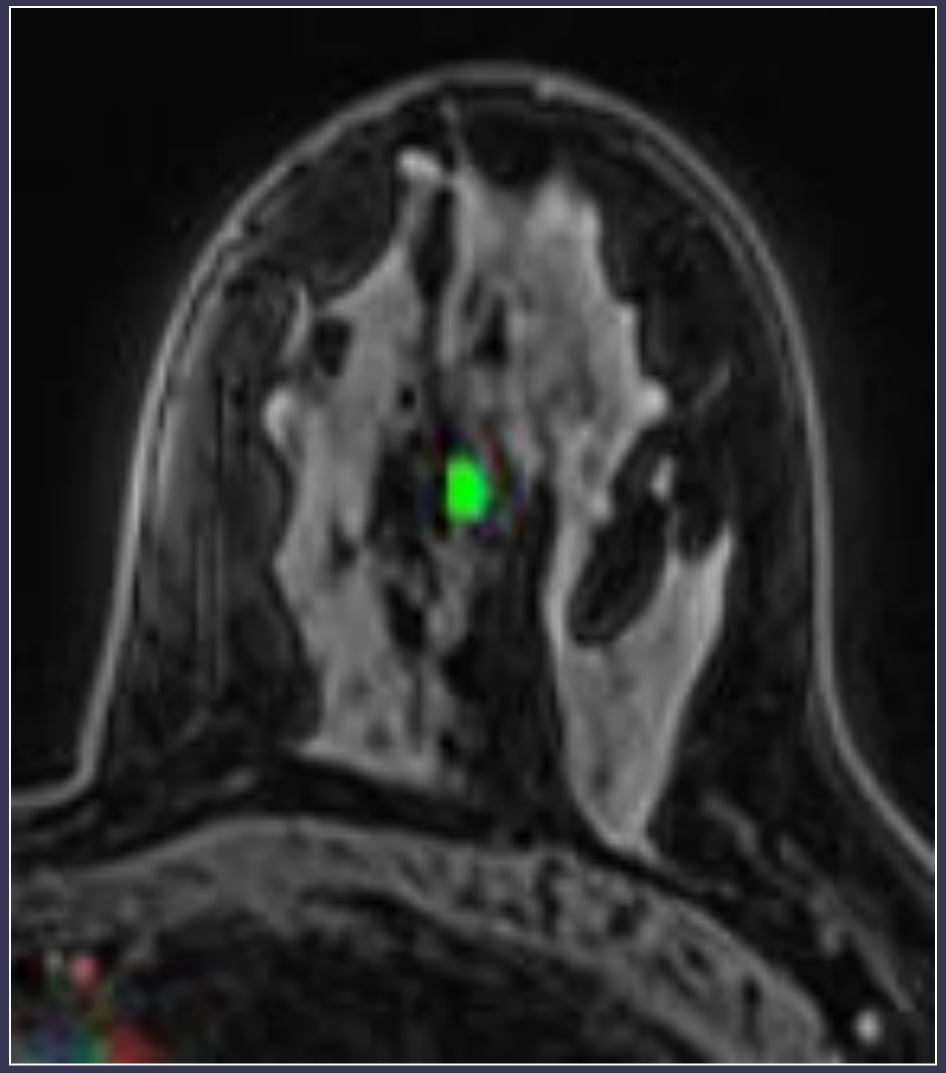
A 58-year-old woman with DCIS on stereotactic Bx



Intermediate grade DCIS (2.0 cm)

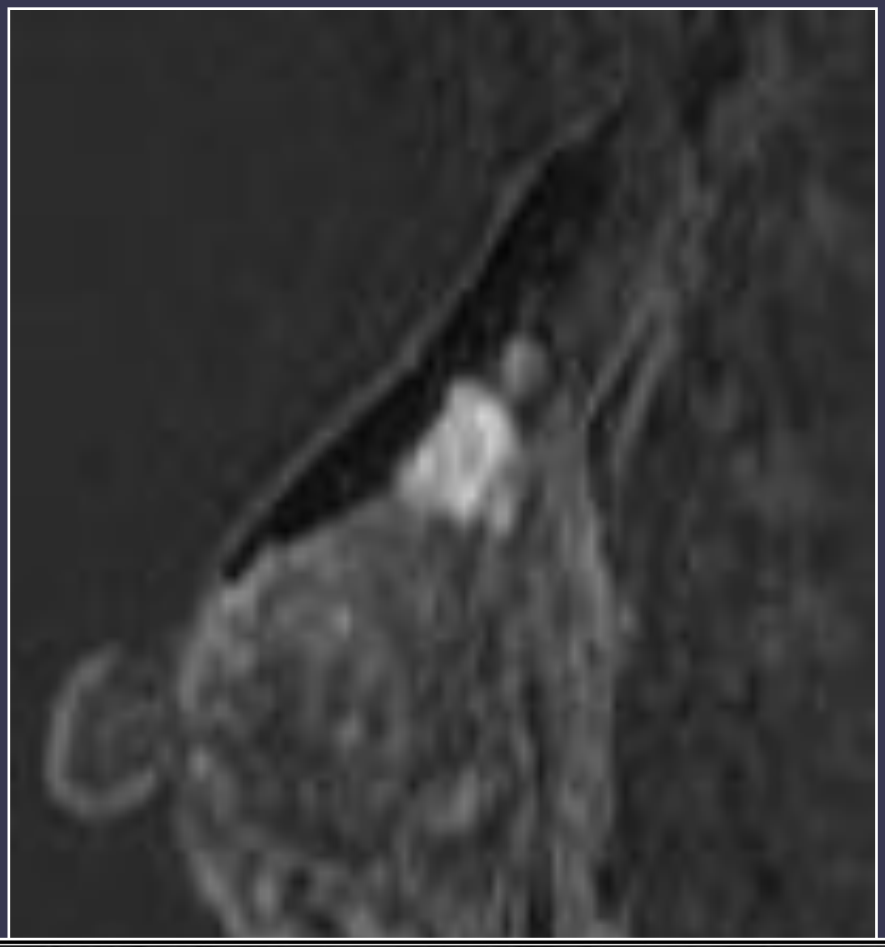
A 45-year-old woman with preop. MRI

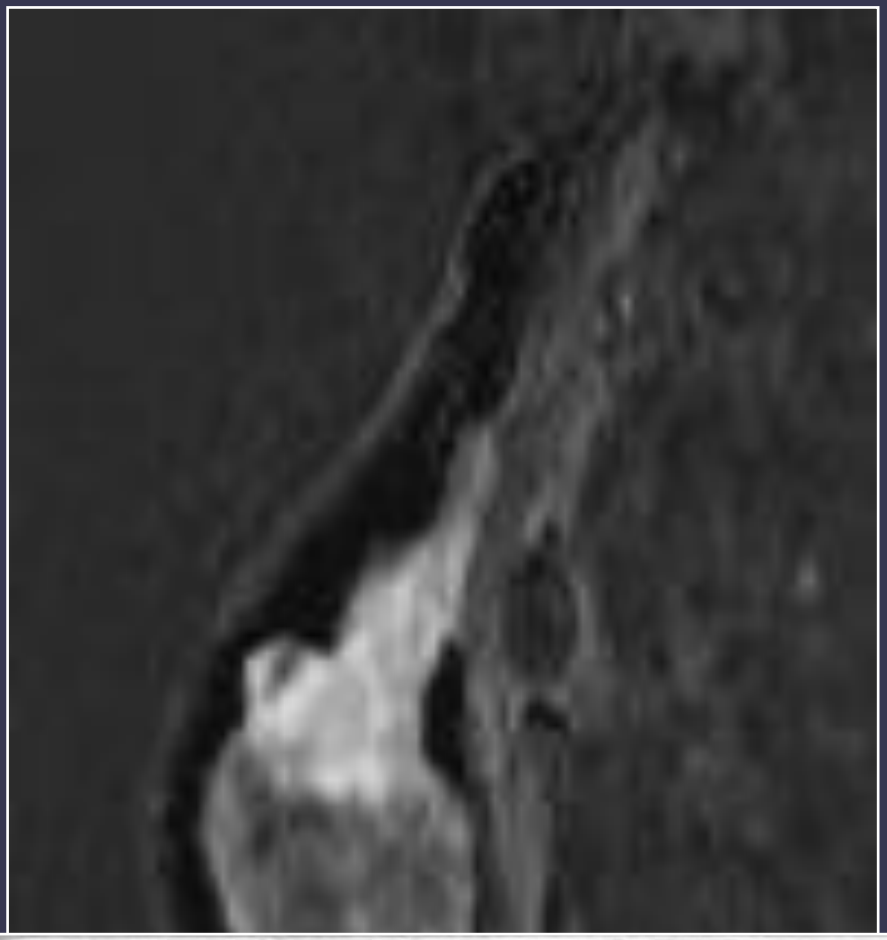




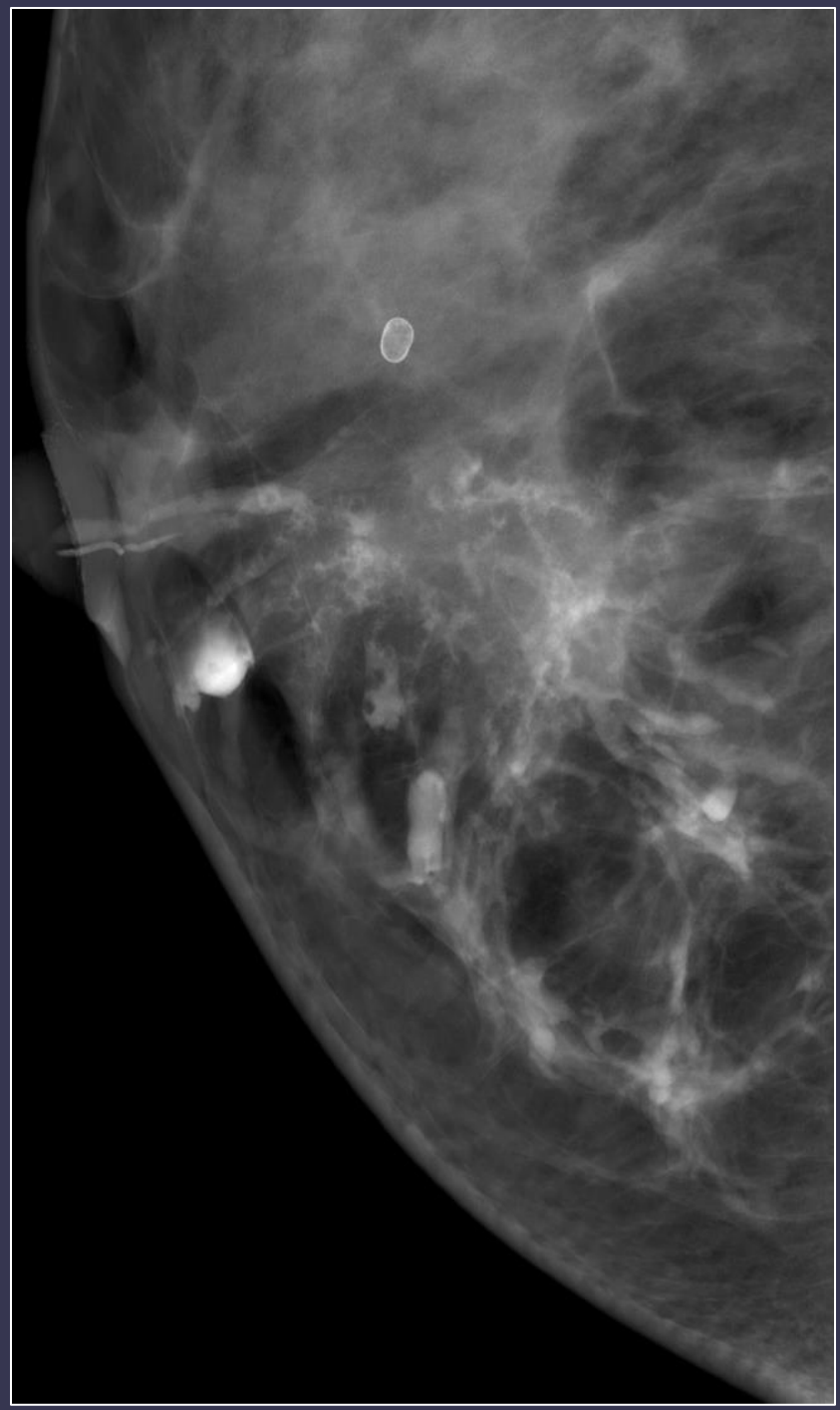
Low grade DCIS without necrosis (0.5 cm)

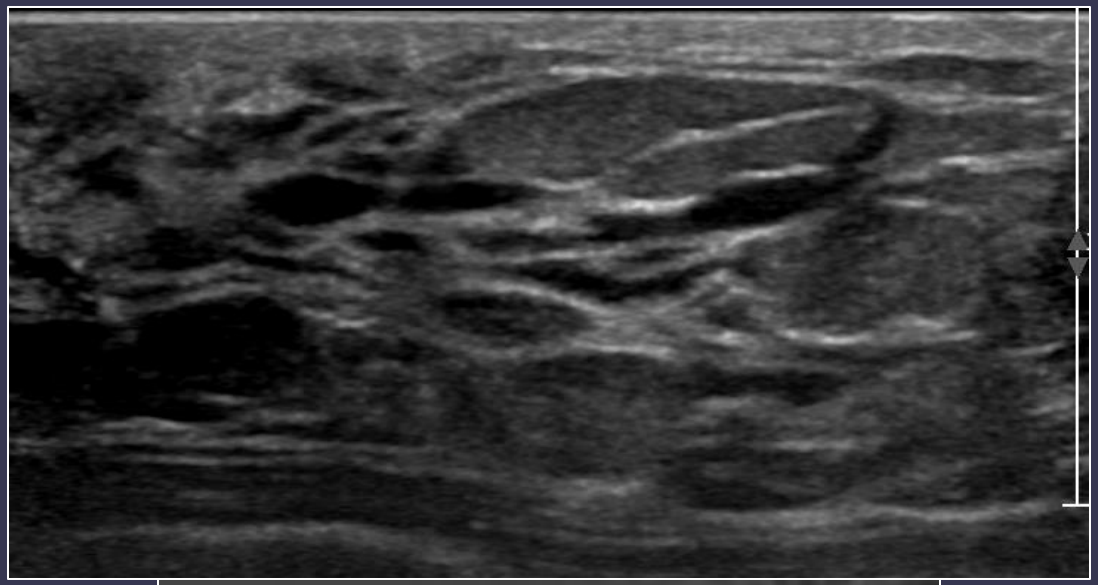
A 50-year-old woman with Known IDC in right breast

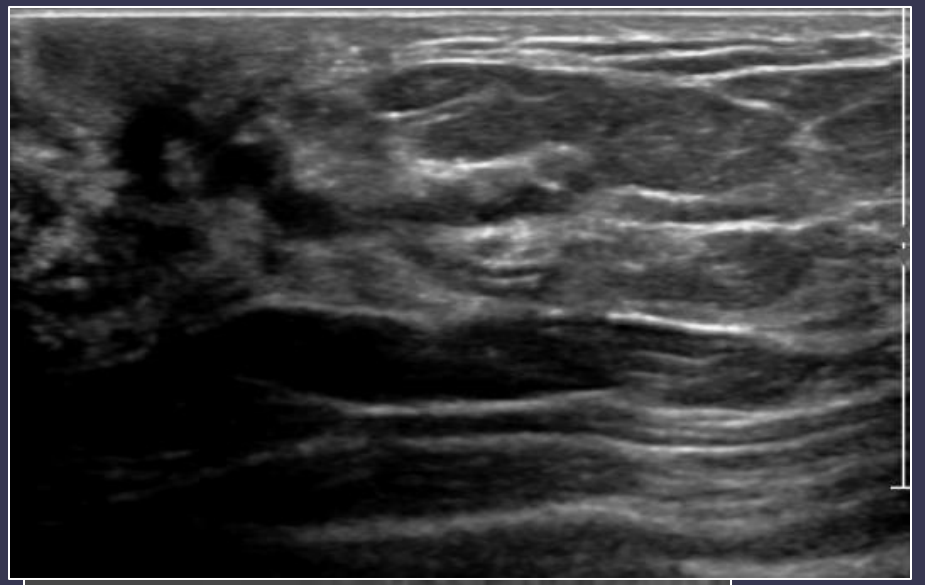


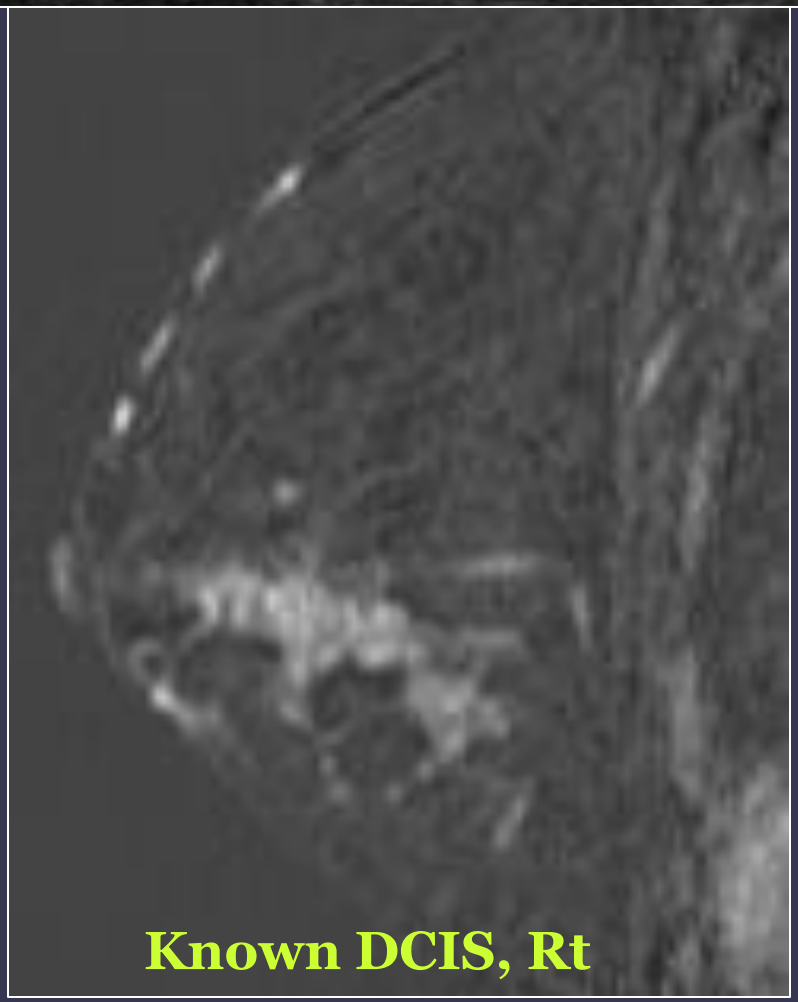


A 50-year-old woman with right nipple discharge

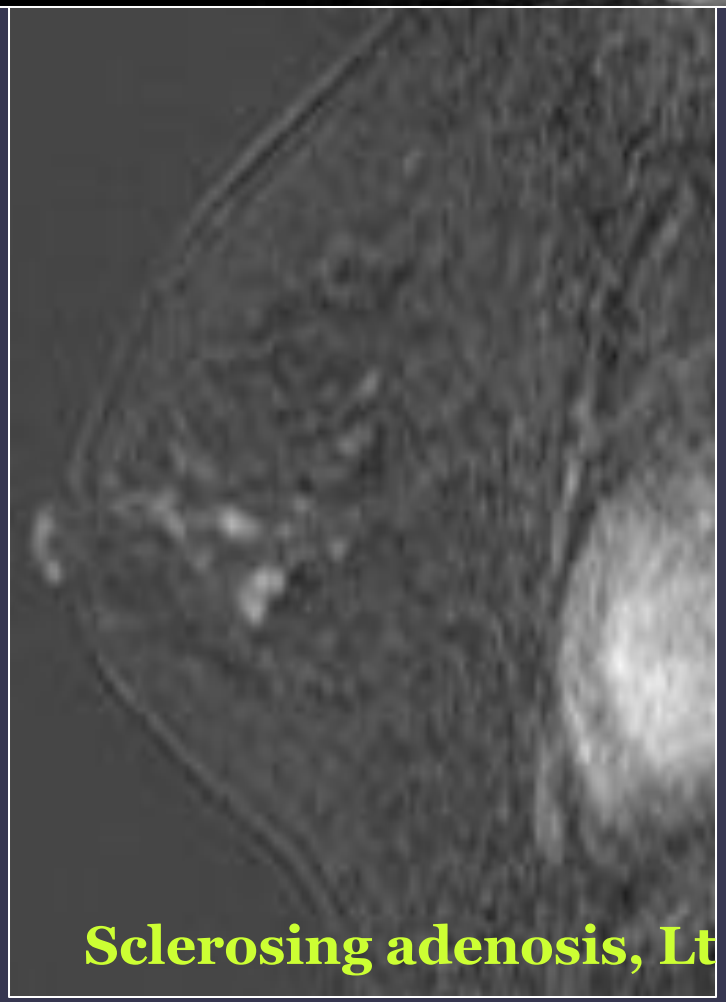






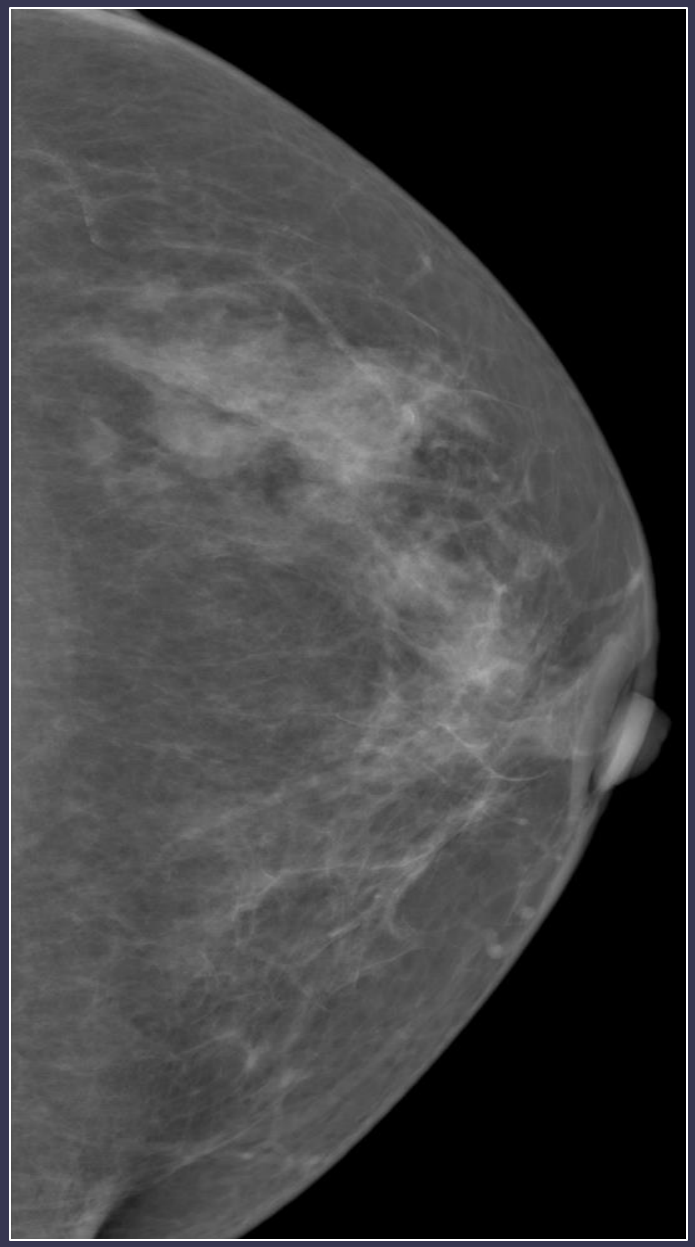


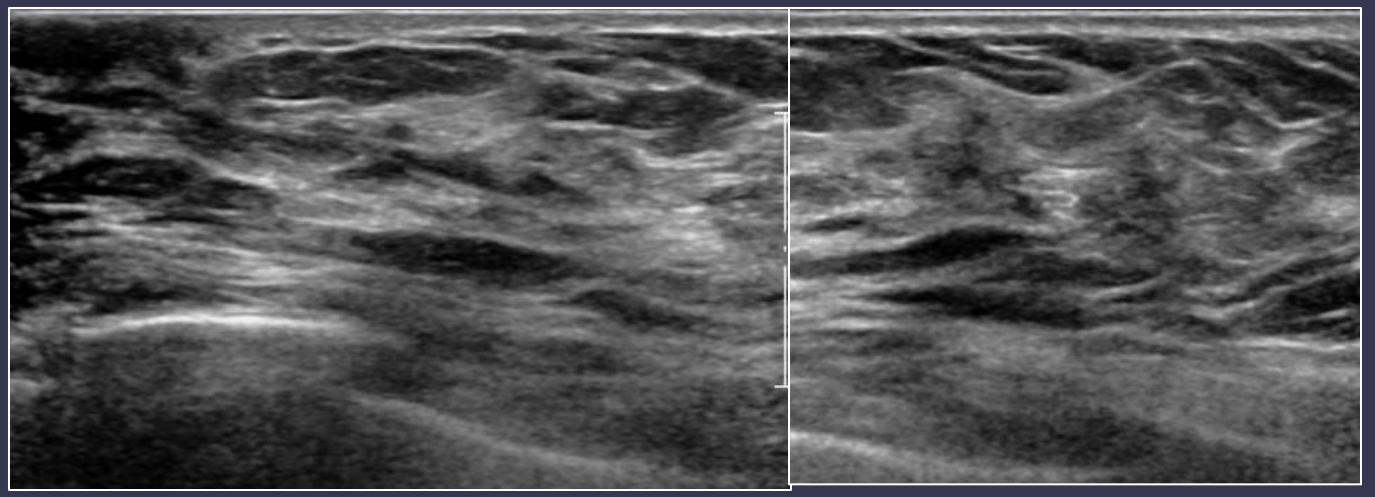
Known DCIS, Rt

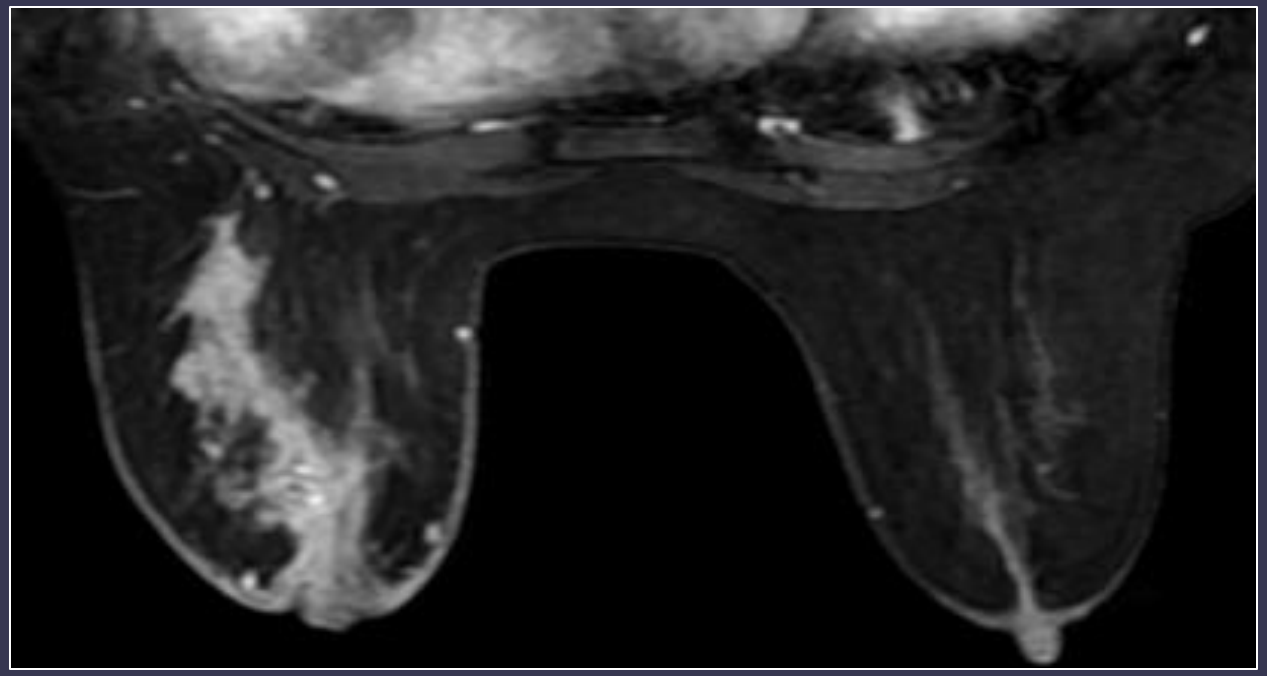


Sclerosing adenosis, Lt

A 66-year-old woman with left nipple discharge







High grade DCIS with necrosis (5 cm)

ADC as an Imaging Biomarker

- ADC as an MR imaging biomarker of low-grade DCIS

Iima M et al. Radiology 2011;260:364-372

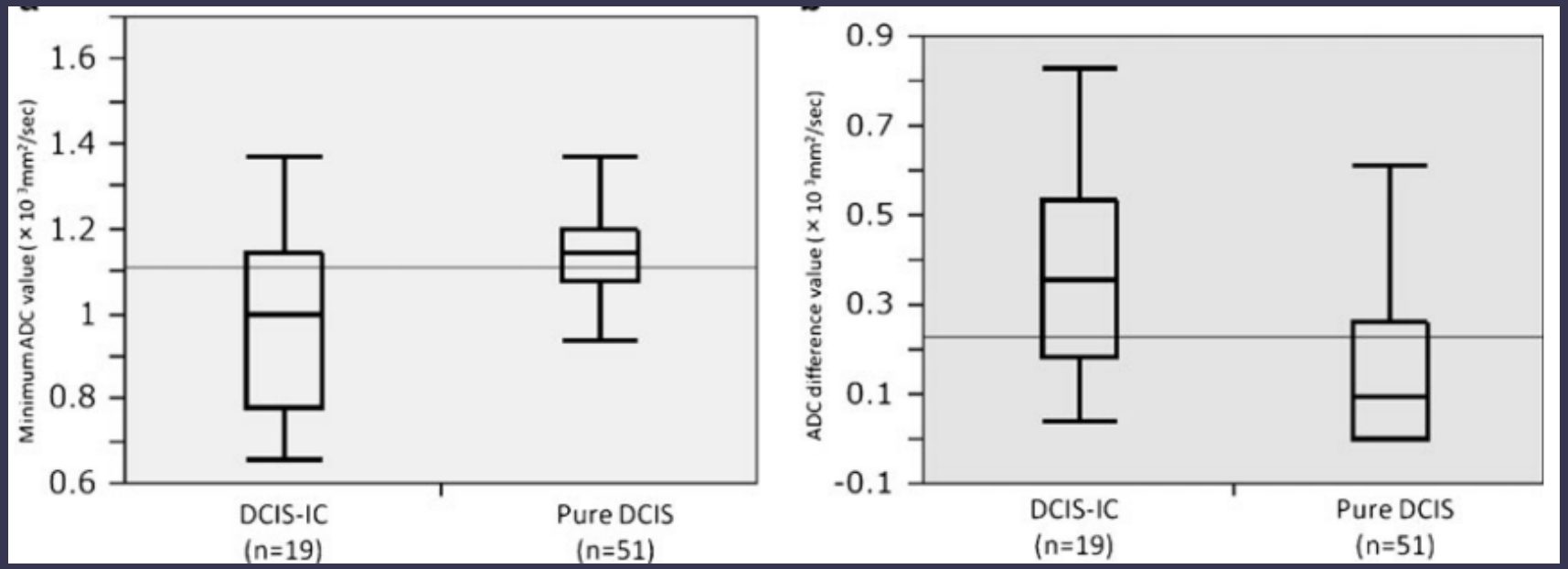
  - 22 DCIS (7 low-G, 5 intermediate-G, 7 high-G, 3 microIDC)
  - A threshold of 1.30 X 10^{-3} mm^2/sec for minimum ADC in the diagnosis of low-grade DCIS → 100% specificity & 100% PPV

	ADC ($\times 10^{-3}$ mm^2/sec)				
Grade	Adjusted Mean	Median	Range	95% CI	*P* Value*
Low	1.42	1.41	1.07–1.76	1.31, 1.54	Ref
Intermediate	1.23	1.12	0.97–1.52	1.10, 1.36	.03
High	1.19	1.23	1.01–1.58	1.08, 1.30	<.01

	ADC ($\times 10^{-3}$ mm^2/sec)			
Grade	Sample Mean	Range	95% CI	*P* Value*
Low	1.35	1.07–1.55	1.24, 1.46	Ref
Intermediate	1.09	0.98–1.26	0.97, 1.22	<.01
High	1.11	1.00–1.26	1.01, 1.22	<.01

ADC as an Imaging Biomarker

- Detection of invasive component using ADC
  - 70 DCIS (51 pure DCIS vs. 19 DCIS-IC)
  - Minimum ADC for DCIS-IC ($0.99 \pm 0.04 \times 10^{-3}$ mm²/sec)– lower than that of pure DCIS ($1.15 \pm 0.03 \times 10^{-3}$ mm²/sec)
  - ADC difference for DCIS-IC ($0.38 \pm 0.05 \times 10^{-3}$ mm²/sec) – higher than that of pure DCIS ($0.17 \pm 0.03 \times 10^{-3}$ mm²/sec)



Role of MRI in DCIS

- Disease extent frequently underestimated at MG due to incomplete lesion calcification

- COMICE (Comparative Effectiveness of MRI in breast cancer) trial *Turnbull L. et al. Lancet 2010;375:563-571*
  - 816 MRI group vs. 806 no MRI group
  - Has not shown any reduction in reoperation rate with use of preop. MRI

Role of MRI in DCIS

- Retrospective study of 218 patients (64/154)

Davis KL et al. Ann Surg Oncol 2012;19:3270-3274

  - No significant difference in reexcision rates (34% vs. 39%)
  - Despite use of preop. MRI, 9% were converted to mastectomy d/t positive margins (8% for no MRI)

	MRI	No MRI	*P* value
Preoperative imaging	154	64	
Weight of excision (g)	48.7	49.1	NS
Patients with reexcisions	42/123 (34 %)	20/51 (39 %)	NS
Initial mastectomy	32/154 (20 %)	12/64 (19 %)	NS
Conversion to mastectomy	11/123 (8.9 %)	3/51 (7.8 %)	1
Overall mastectomy rate	43/154 (27.9 %)	15/64 (23.4 %)	NS

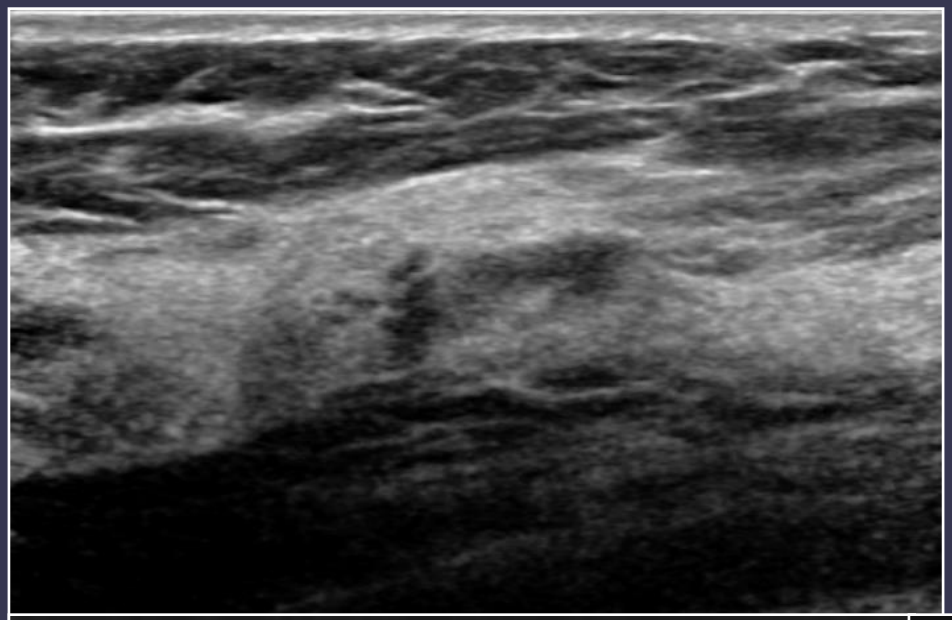
Role of MRI in DCIS

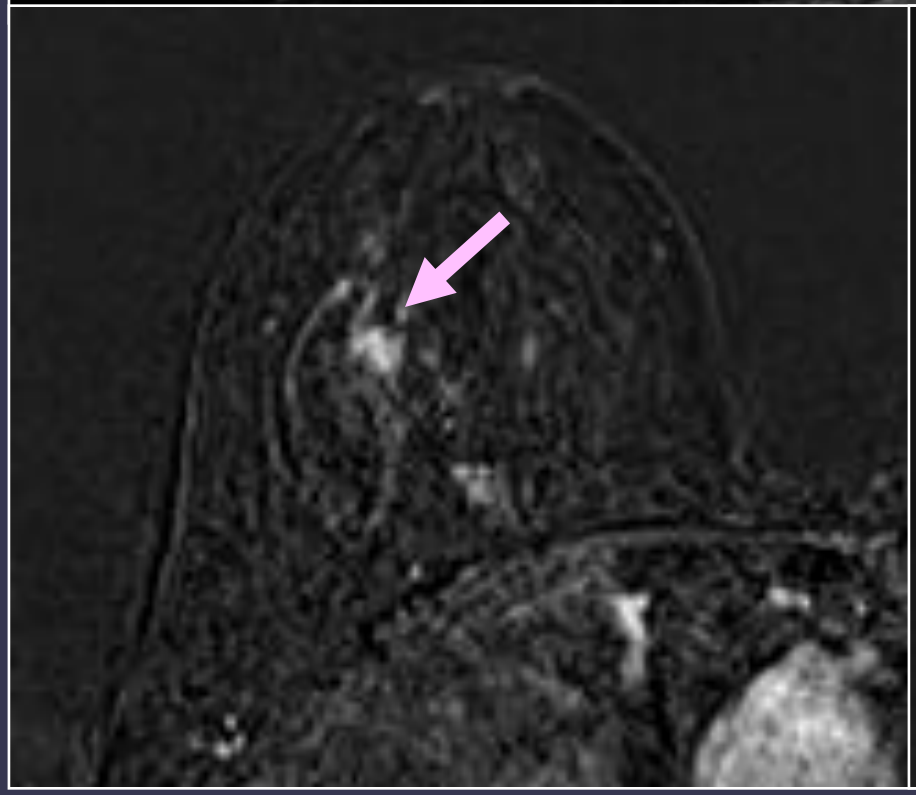
- Prospective, 352 DCIS (217 MR vs. 135 no MR)

Pilewskie M, et al. Ann Surg Oncol 2013;20:1522-1529

  - Initial op. type & number of reoperation – similar
  - Additional biopsy rate – 38% in MRI group vs. 7% in no MRI group
  - ≥2 additional biopsies – 18% of MRI group vs. 2% of no-MRI group (P<.0001)
  - Cancer diagnosis – 26% of MRI & 33% of no-MRI (P=.73)
  - Disease extent of DCIS – 52% of MG were accurate compared with 41% of MRI

A 53-year-old asymptomatic woman





Two foci of intermediate grade DCIS

Take-home message

- DCIS is a preinvasive lesion to invasive breast cancer & makes up approximately 30% of breast malignancies detected by screening MG
- Majority of DCIS are detected on MG as Ca^{++}
- US features of DCIS are nonspecific and may be subtle → recognizing the US features will become important for detection of early-stage breast cancer
- Nonmass clumped enhancement in a linear or segmental distribution is the most common appearance of DCIS on MRI

Thank you for your attention