DCIS on Breast MRI

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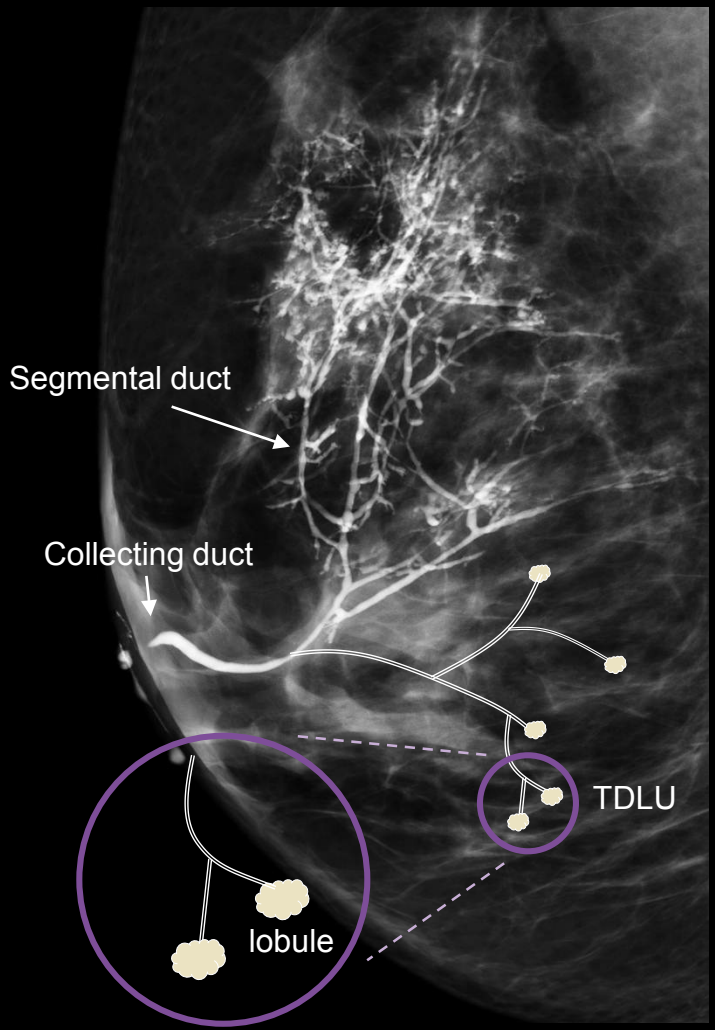
Disclosures

I have no relevant financial disclosures

DCIS Background

- Ductal carcinoma in situ (DCIS); aka – intraductal carcinoma
  - Bloodgood[1], 1908: “comedo-carcinoma”
  - Broders[2], 1932: “ductal carcinoma in situ”
- Intraductal proliferation of abnormal epithelial cells[3]
  - Diagnosis frequency ↑ w/ screening mammography
  - Lacks ability to invade surrounding tissue and metastasize



1. Bloodgood JC. Chapter 31: Kelly and Noble’s Gynecology and Abdominal Surgery (Vol 3)
2. Broders AC. JAMA 1932; 99: 1670-1674
3. Allegra *et al.* J Natl Cancer Inst 2010; 102 (3): 161-169.

Breast Cancer Pathogenesis

- Prevailing theory: DCIS represents the most biologically aggressive lesion in a spectrum of intraductal proliferations
  - Non-obligate precursor to invasive disease

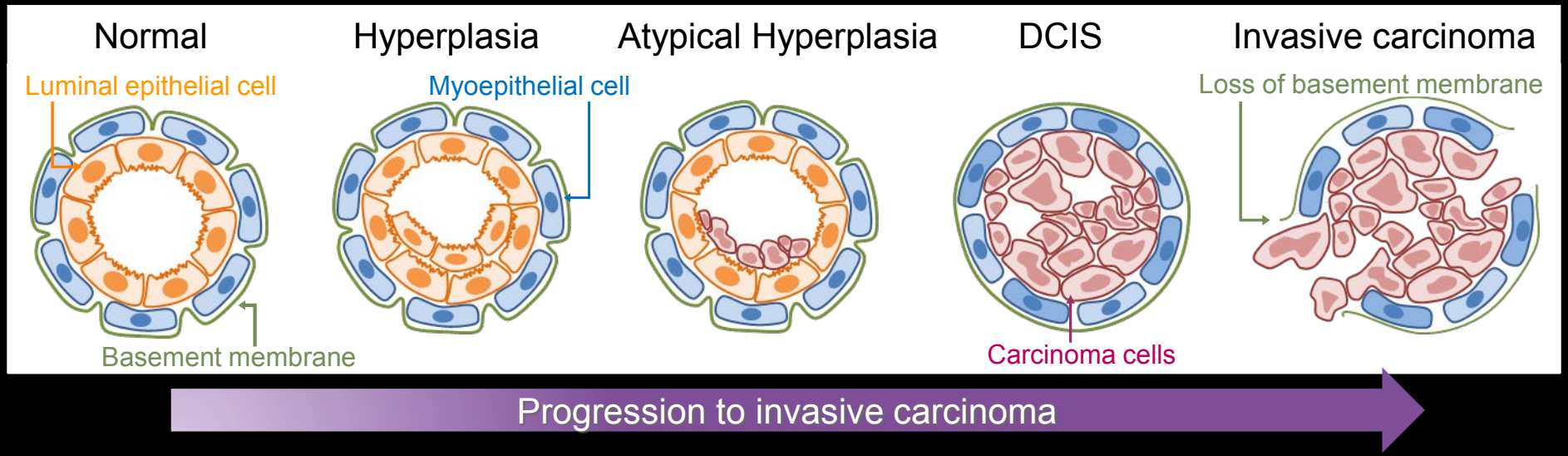
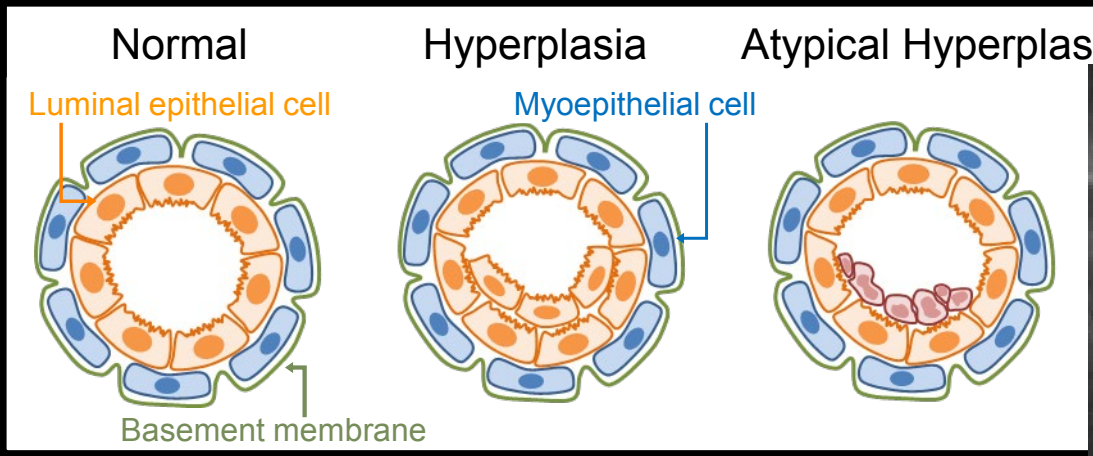


Image adapted from Cichon *et al.* J Mammary Gland Biol Neoplasia, 2010. 15(4): p. 389-97.

Breast Cancer Pathogenesis



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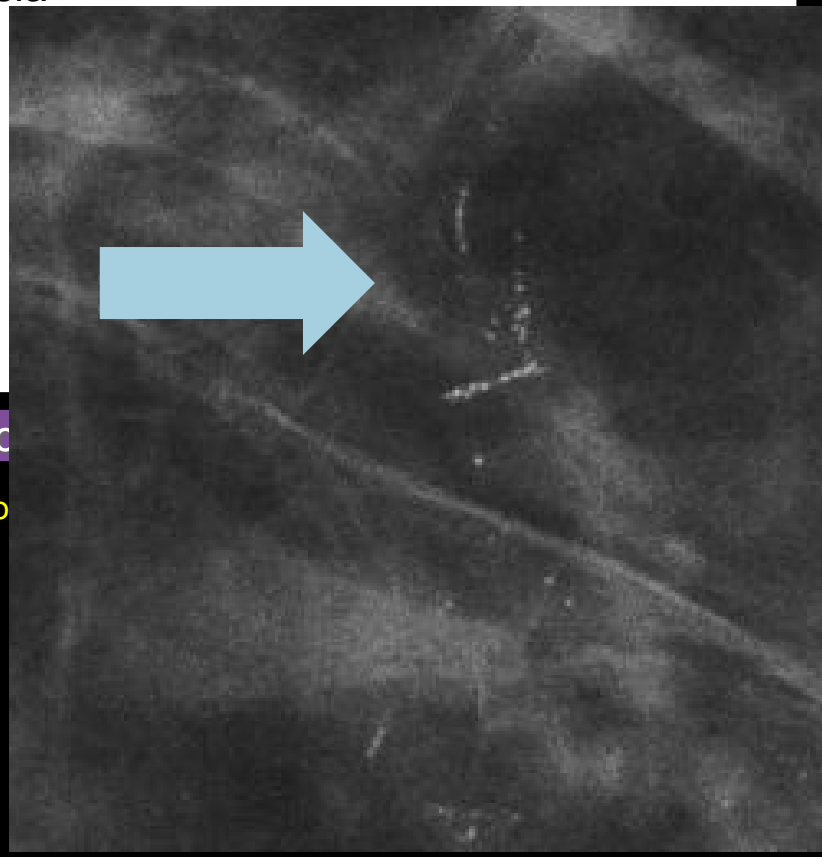
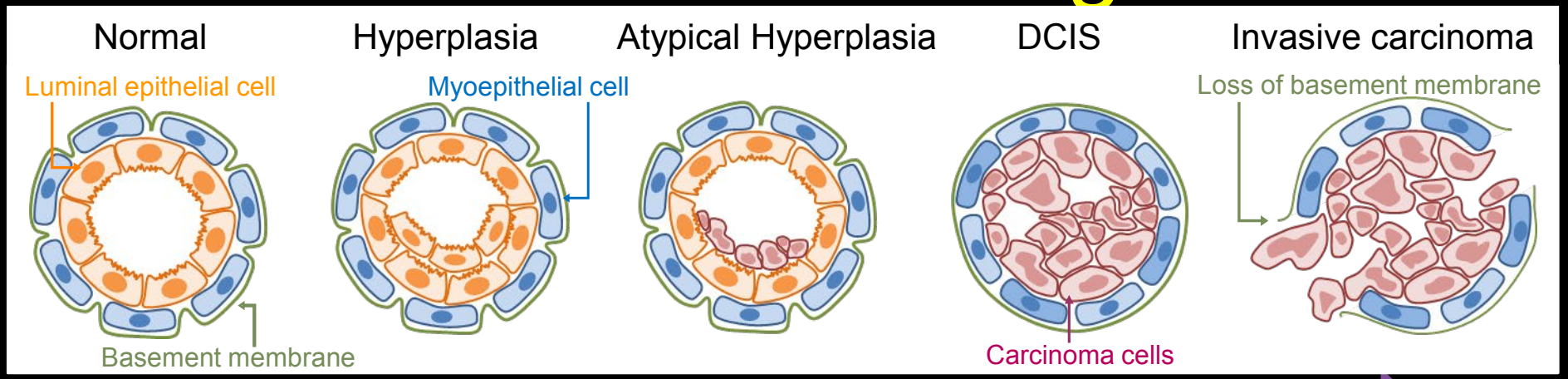


<u>Atypical ductal hyperplasia (ADH)/ Low grade DCIS</u>

Challenging to distinguish on CNB (and imaging)

Monotonous, low-grade, intraductal epithelial proliferations

Breast Cancer Pathogenesis



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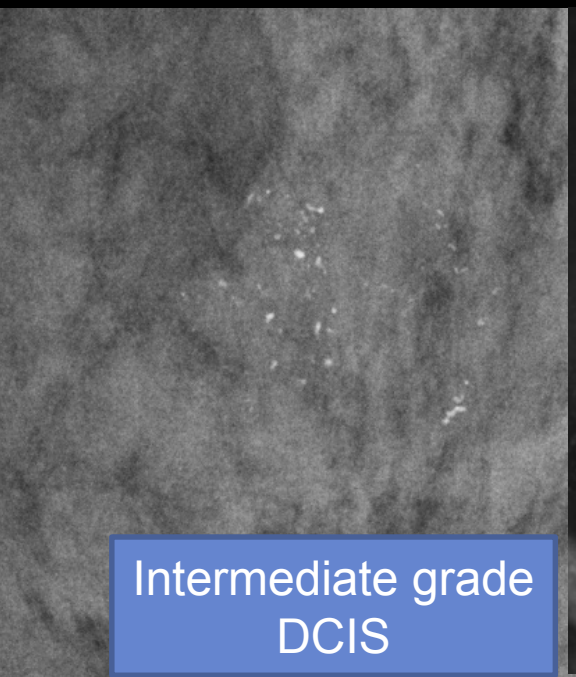
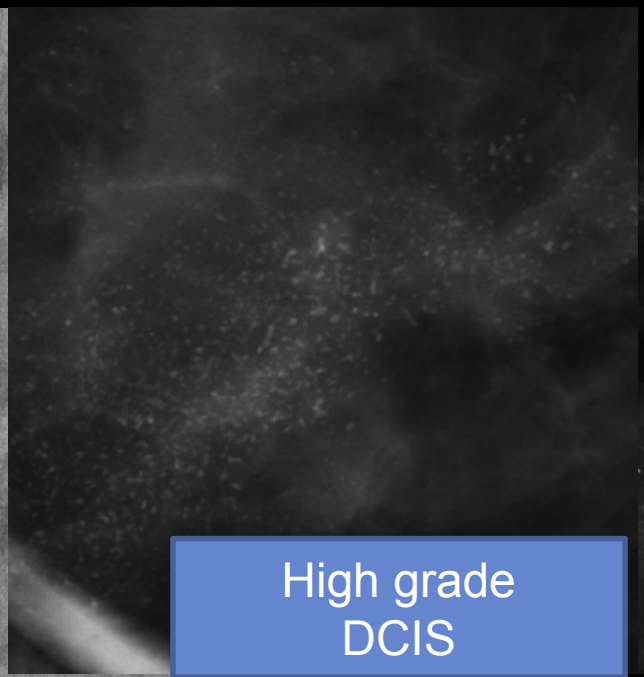
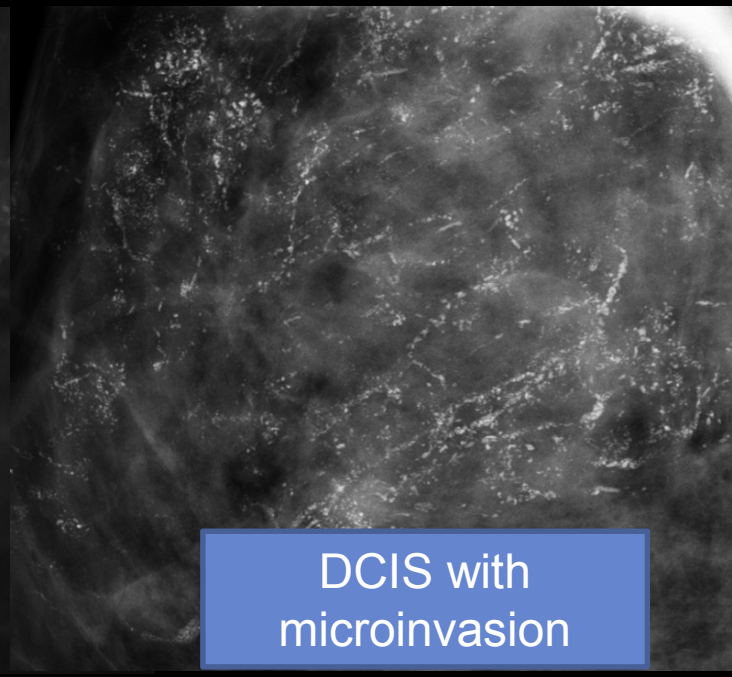
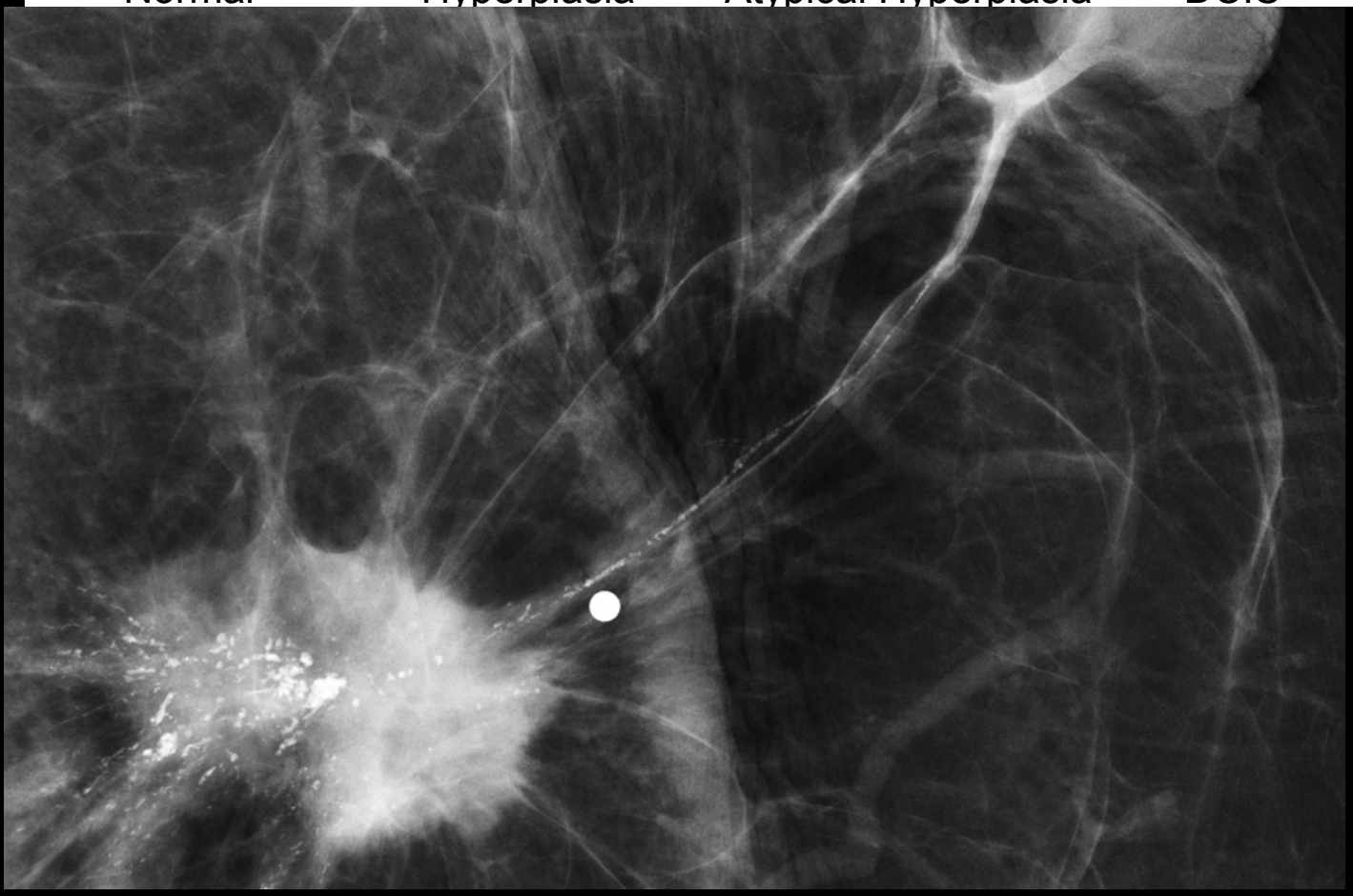


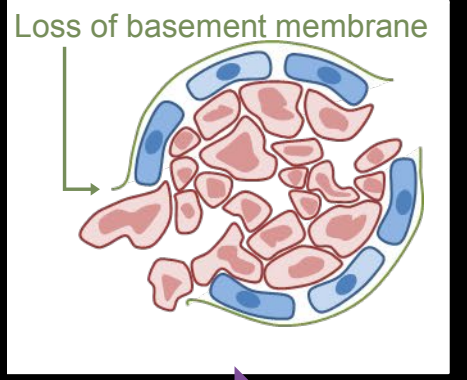




Breast Cancer Pathogenesis

Normal Hyperplasia Atypical Hyperplasia DCIS Invasive carcinoma





Genome Evolution of DCIS

Journal of Pathology
J Pathol 2017; **241**: 208–218
Published online 27 November 2016 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/path.4840

INVITED REVIEW

Genome evolution in ductal carcinoma *in situ*: invasion of the clones

Anna K Casasent,[1,2] Mary Edgerton[3] and Nicholas E Navin[1,2,4]*

Three Models of Invasion

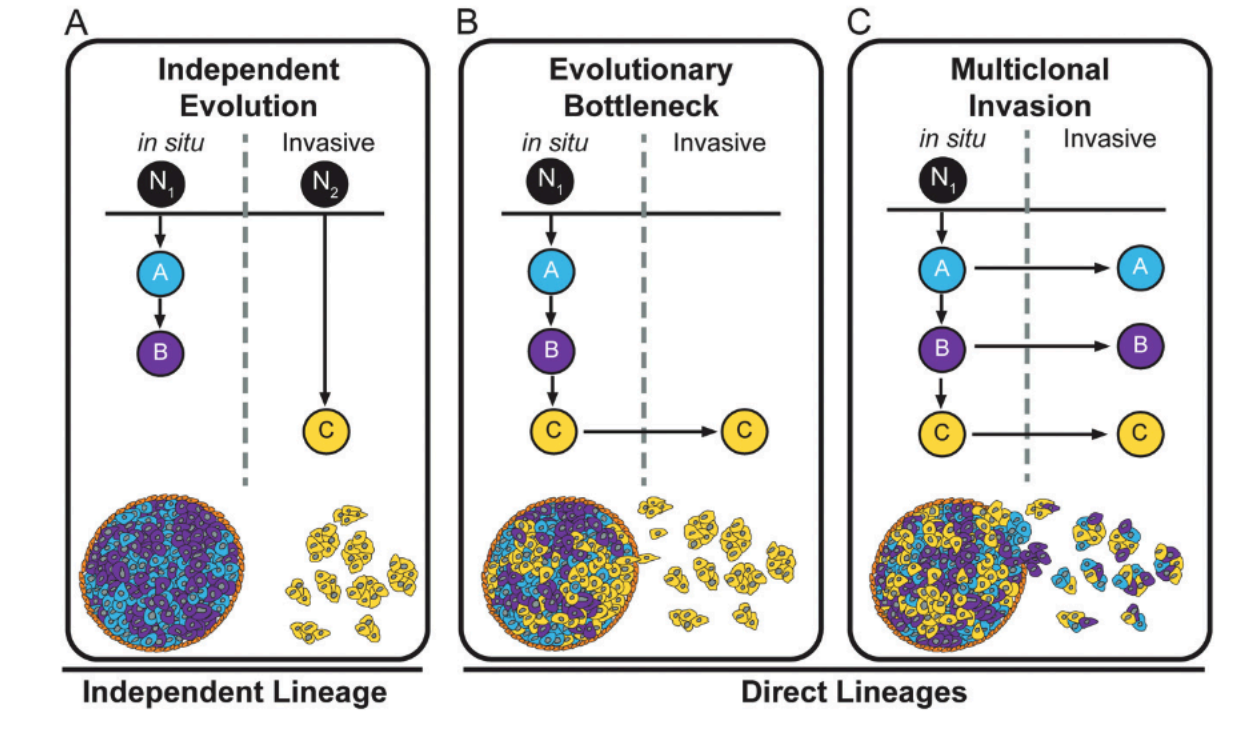


Figure 2

Casasent, Edgerton, and Navin J Path 2017

Genome Evolution of DCIS

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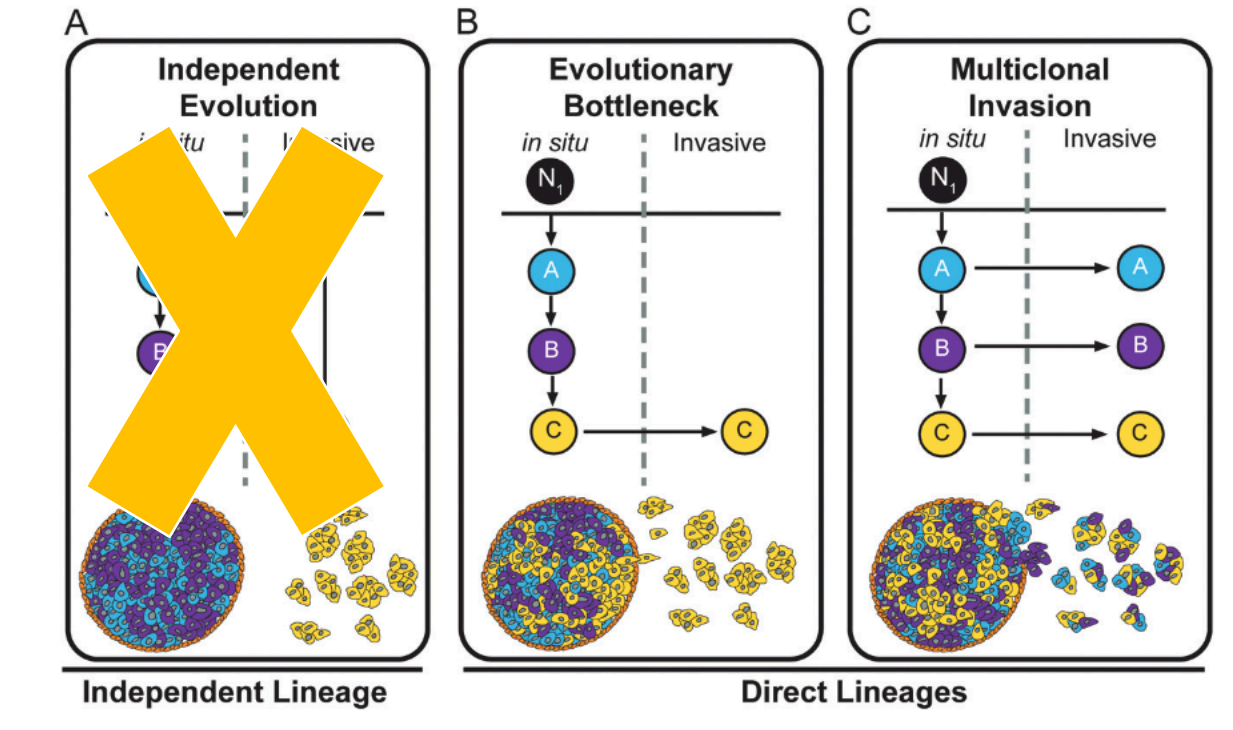


Figure 2

Casasent, Edgerton, and Navin J Path 2017

DCIS Tumor Microenvironment

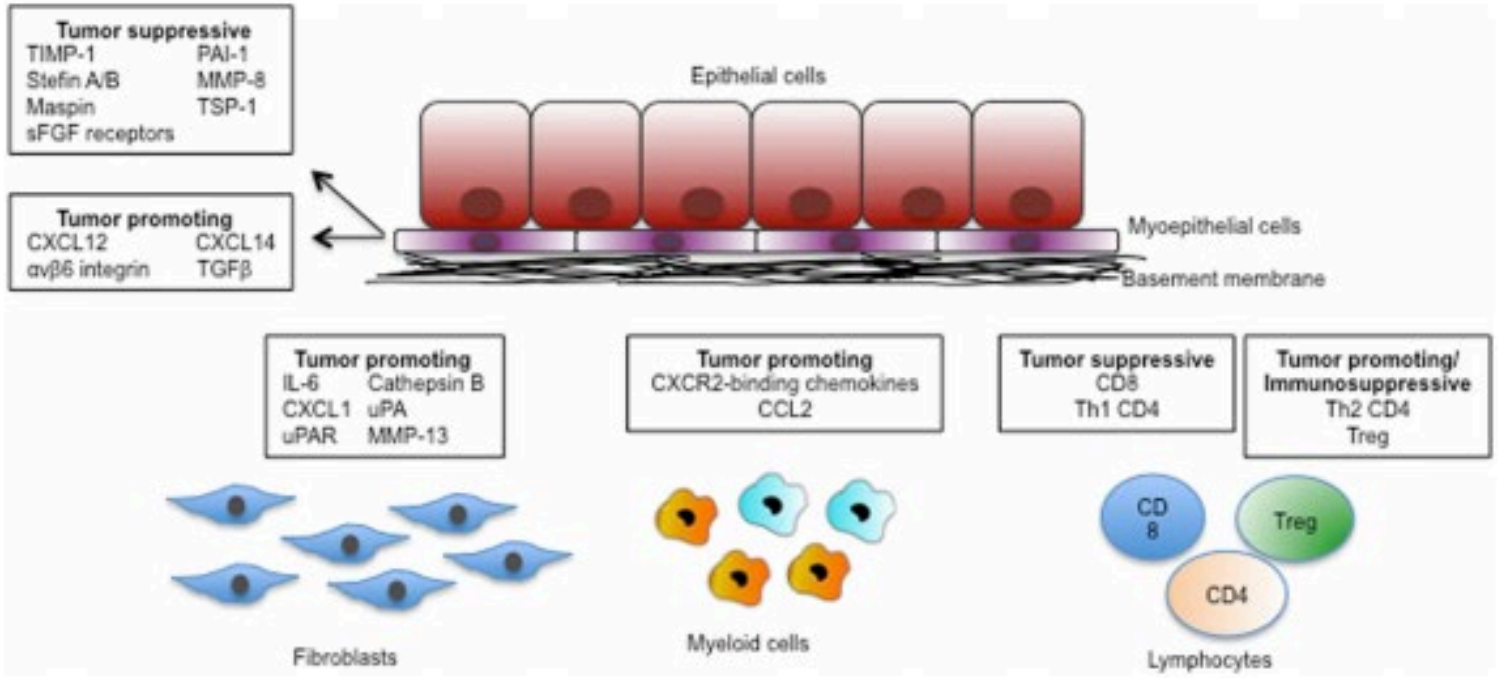


Figure 2

Myoepithelial cells, fibroblasts, and immune cells

Nelson et al. J Mammary Gland Biol Neoplasia. 2018 Dec;23(4):207-221

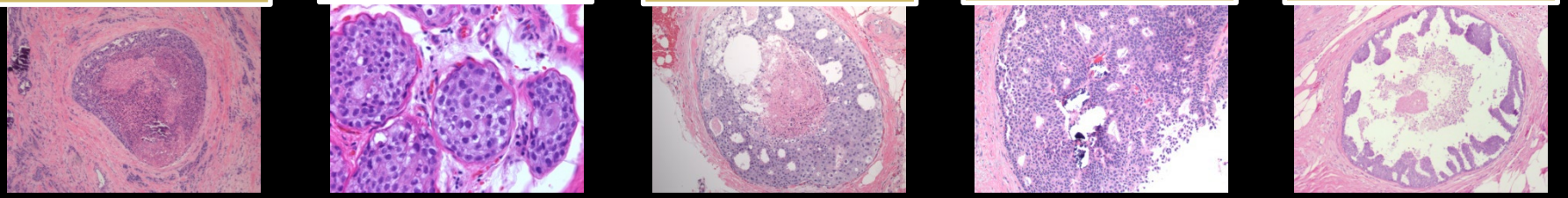
Pathological Classification

Traditional classification

- Independent of presence of necrosis and histologic grade
- Based on architectural pattern
- Not prognostic

Based on architectural pattern:

- Comedo
- Solid
- Cribriform
- Papillary
- Micropapillary



Descriptive but not prognostic

Pathologic Classification

DC

Low/Intermediate Nuclear

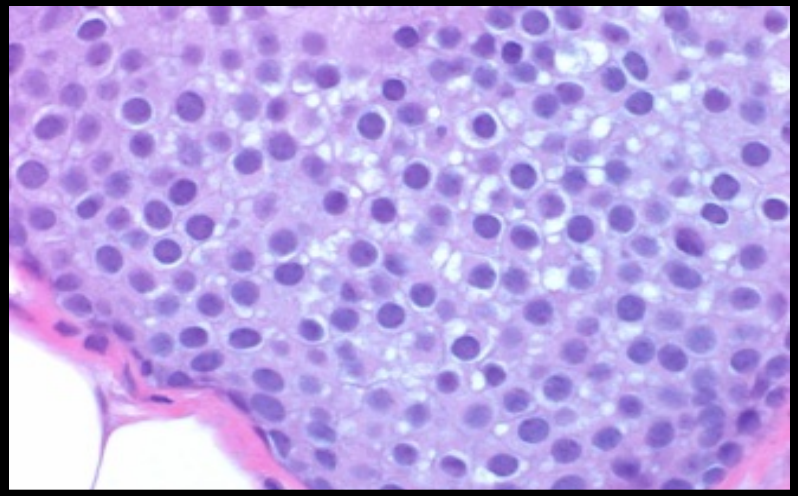
No necrosis

Group 1

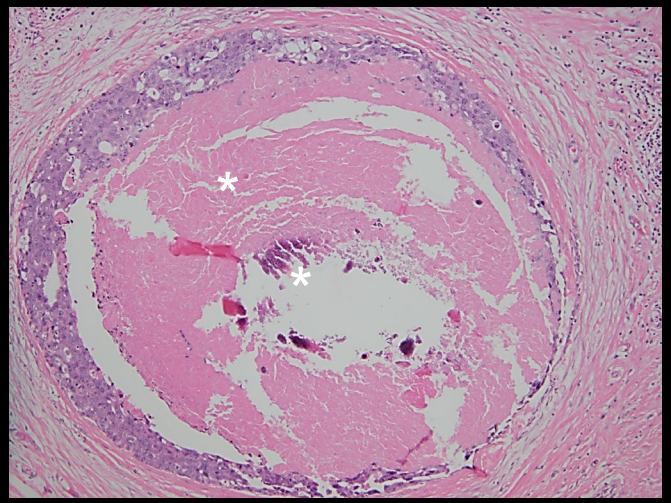
50% of DCIS lesions contain >1 nuclear grade

High Nuclear grade

Group 3



Low grade DCIS with small nuclei, minimal nuclear pleomorphism and infrequent mitoses



High grade DCIS with central “comedo-type” necrosis and microcalcification*

Prognostic Features: Molecular

- Oncotype DX DCIS Score: 12 gene assay with weighting factors

Proliferation Group	Hormone Receptors	Reference Genes
• Ki-67 • STK15 • Survivin • CCNB1 (cyclin B1) • MYBL2	• PR • GSTM1	• ACTB (β-actin) • GAPDH • RPLPO • GUS • TFRC

$$\text{DCIS Score}_{\mu} = 0.31 \times \text{prolif group score} - 0.08 \times \textit{PR} - 0.09 \times \textit{GSTM1}$$

Solin *et al.* J Natl Cancer Inst, 2013. **105**(10): p. 701-10.

Prognostic Features: Clinical

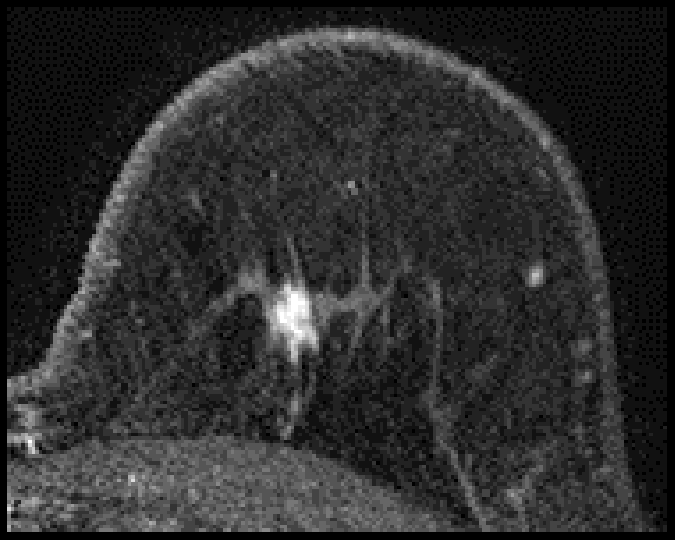
- Younger Age
- Family History of Breast Cancer
- Larger DCIS span
- Positive/Close margins on excision

- Prognostic Models (combine clinical and pathology features)
  - USC/Van Nuys Prognostic Index
  - MSK Nomogram

1. Silverstein MG. Am J Surg. 2003;186(4):337.
2. Rudloff U. et al JCO **2010** 28 (23): **3762-3769.**

DCIS Presentations

- Pre-screening era → mass, nipple discharge, Paget's
- Now > 90% of DCIS lesions are asymptomatic
  - Screening mammography
  - Screening MRI in high-risk patients



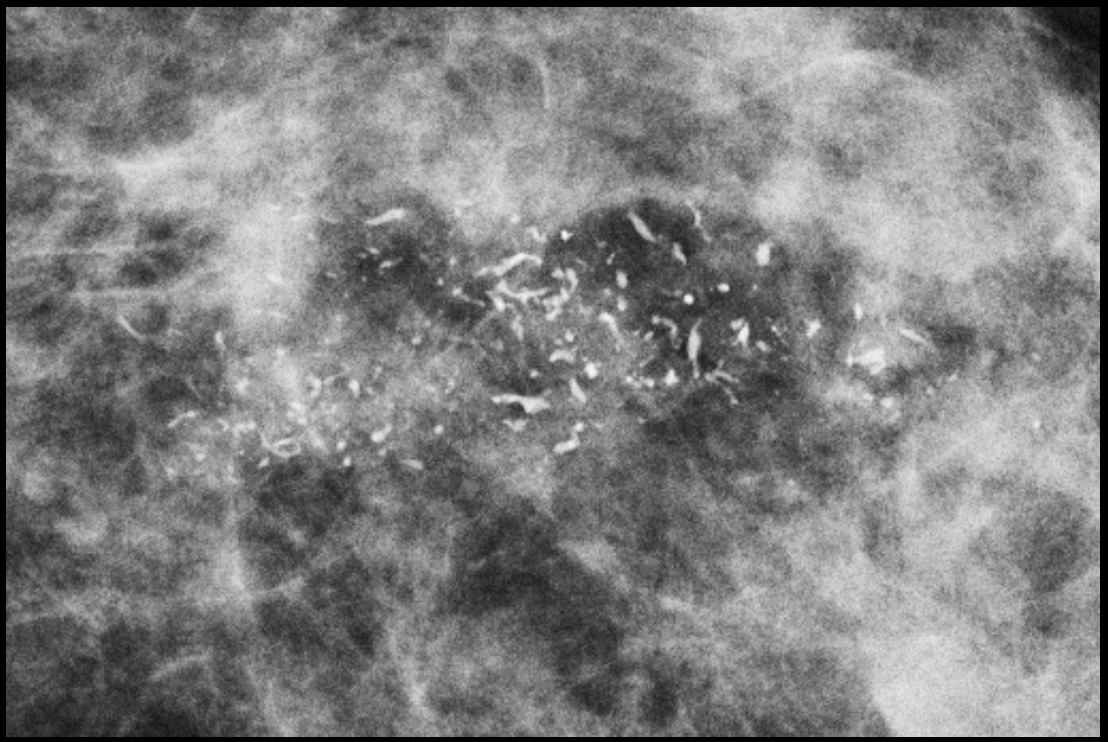
Microcalcifications

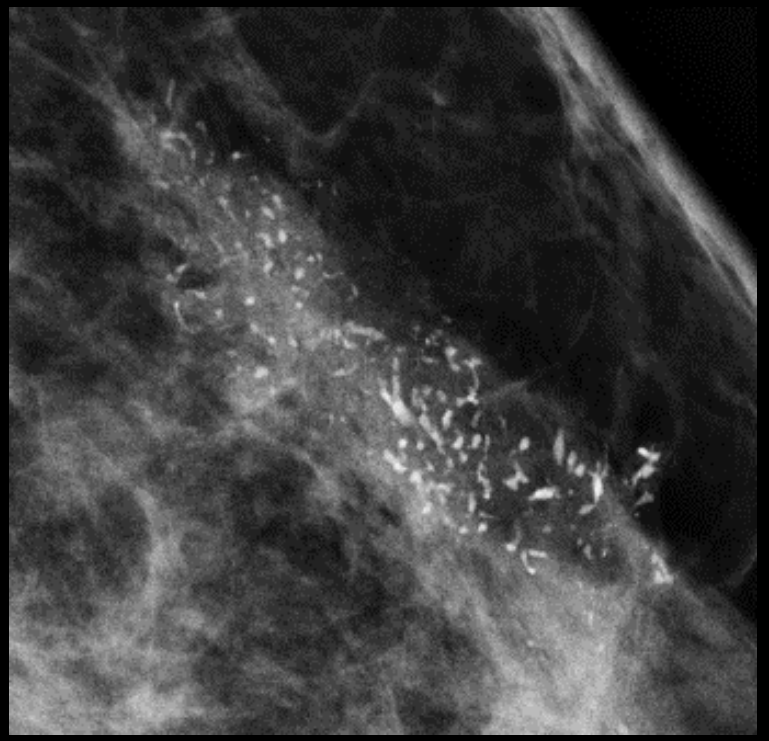
- Two forms of microcalcifications
  - Calcium Oxalate –benign pathology
  - Calcium Phosphate (primarily hydroxyapatite)
    - malignant and benign pathologies

- Unclear why DCIS can exhibit calcifications
  - Degenerative or dystrophic (Passive)
  - Secretory process (Active)
  - Activation of bone matrix proteins (Active)

Mammography

- Hallmark: Segmental or linearly distributed fine pleomorphic/linear-branching microcalcification
- Masses and asymmetries are less common
  - DCIS lesions that present as masses are more commonly low grade





Biology – Mammography Features

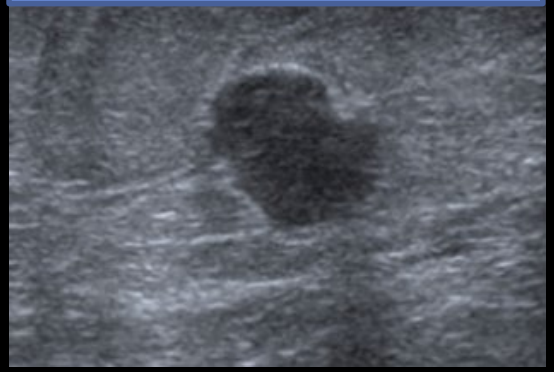
Mammographic Feature	Histology
Mass or asymmetry (no calcifications)[1,2,3]	Low grade
"Rod shaped", ductal distribution, branching calcifications[1]	Necrosis
Round, punctate calcifications[1]	Low grade, Absence of necrosis
Casting-type calcifications[4]	High grade, necrosis
Fine-pleomorphic or fine-linear branching calcifications[2,5]	High grade, necrosis

[1]Evans *et al*. Am J Roentgenol, 1994. 162(6): p. 1307-11.
[2]Barreau *et al*. Eur J Radiol, 2005. 54(1): p. 55-61.
[3]Yang, WT *et al.* Am J Roentgenol, 2004. 182(1): p. 101-10.
[4]Holmberg *et al.* Br J Cancer, 2013. 108(4): p. 812-819.
[5]Holland *et al.* Semin Diagn Pathol 1994;11:181–92.

Ultrasound

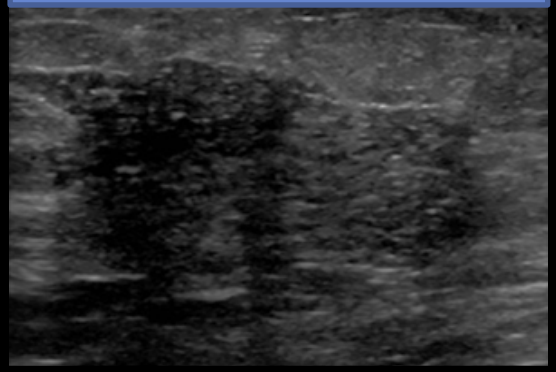
- 8-50% of DCIS lesions are visible on US[1]
- Most commonly presents as a round or oval masses[2,3]
- "Non-mass forms" (e.g. dilated duct with internal echoes) on US are probably under-recognized
  - Account for 60% of DCIS lesions in one study[4]

DCIS



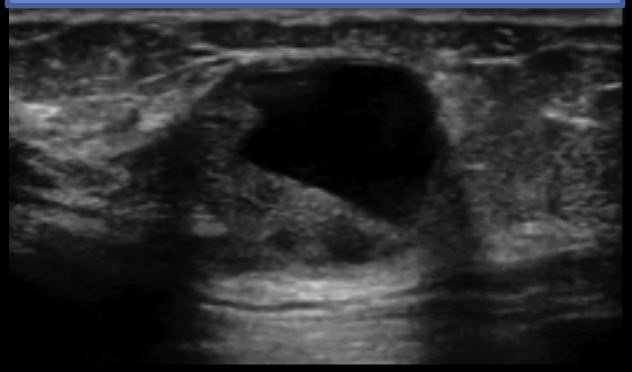
Oval circumscribed solid mass

DCIS with microinvasion



Irregular mass with echogenic foci consistent with calcifications

DCIS (Wantanabe et al[4])



Complex solid and cystic mass

[1] Moon et al. Ultrasound Med Biol 2019 Jan:45(1):68-77
[2] Lee *et al*. J Clin Ultrasound, 2013. 41(8): p. 465-71.
[3] Wang *et al*. Radiographics, 2013. 33(1): p. 213-228.
[4] Watanabe et al. Ultrasound Med Biol 2017 May;43(5):918-925

Biology – Ultrasound Features

- Screen-detected DCIS on US (n=71) vs. Mammography (n=165)[1]
  - High grade: 4.2% vs. 26.1%
  - Comedonecrosis: 33.8% vs. 66.7%
  - Her2 positivity: 8.5% vs. 35.2%

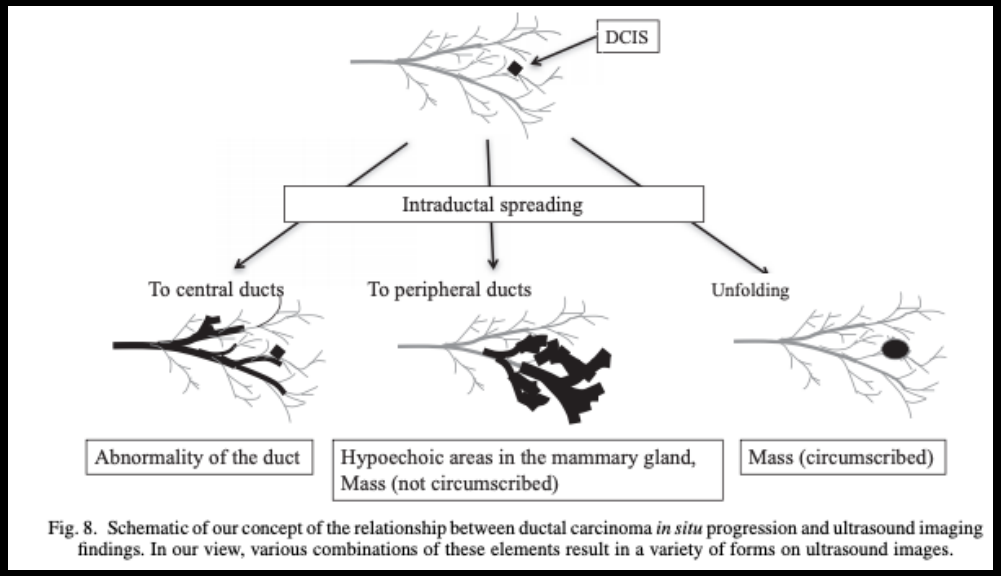


Fig. 8. Schematic of our concept of the relationship between ductal carcinoma *in situ* progression and ultrasound imaging findings. In our view, various combinations of these elements result in a variety of forms on ultrasound images.

Figure from
Watanabe et al. Ultrasound Med Biol 2017 May;43(5):918-925

1. Moon et al. Ultrasound Med Biol 2019 Jan:45(1):68-77

Higher spatial resolution → improved morphologic characterization[2]

MRI superior for DCIS extent evaluation[3]

MRI = most sensitive imaging modality for detection of DCIS and determination of EOD

Breast MRI considered poor for DCIS evaluation[1]

NME identified as an MRI feature[2]

Sensitivity = 92% (vs. 56%); greater proportion of high grade[4]

[1]Boetes *et al.* Eur Radiol, 1997. 7(8): p. 1231-4
[2]Lehman. J Natl Cancer Inst Monogr, 2010. 2010(41): p. 150-1.
[3]Berg *et al.* Radiology, 2004. 233(3): p. 830-49.
[4]Kuhl *et al.* Lancet, 2007. 370(9586): p. 485-92.

Radiology

Science *to* Practice

Christiane K. Kuhl, MD

Science to Practice: Why Do Purely Intraductal Cancers Enhance on Breast MR Images?

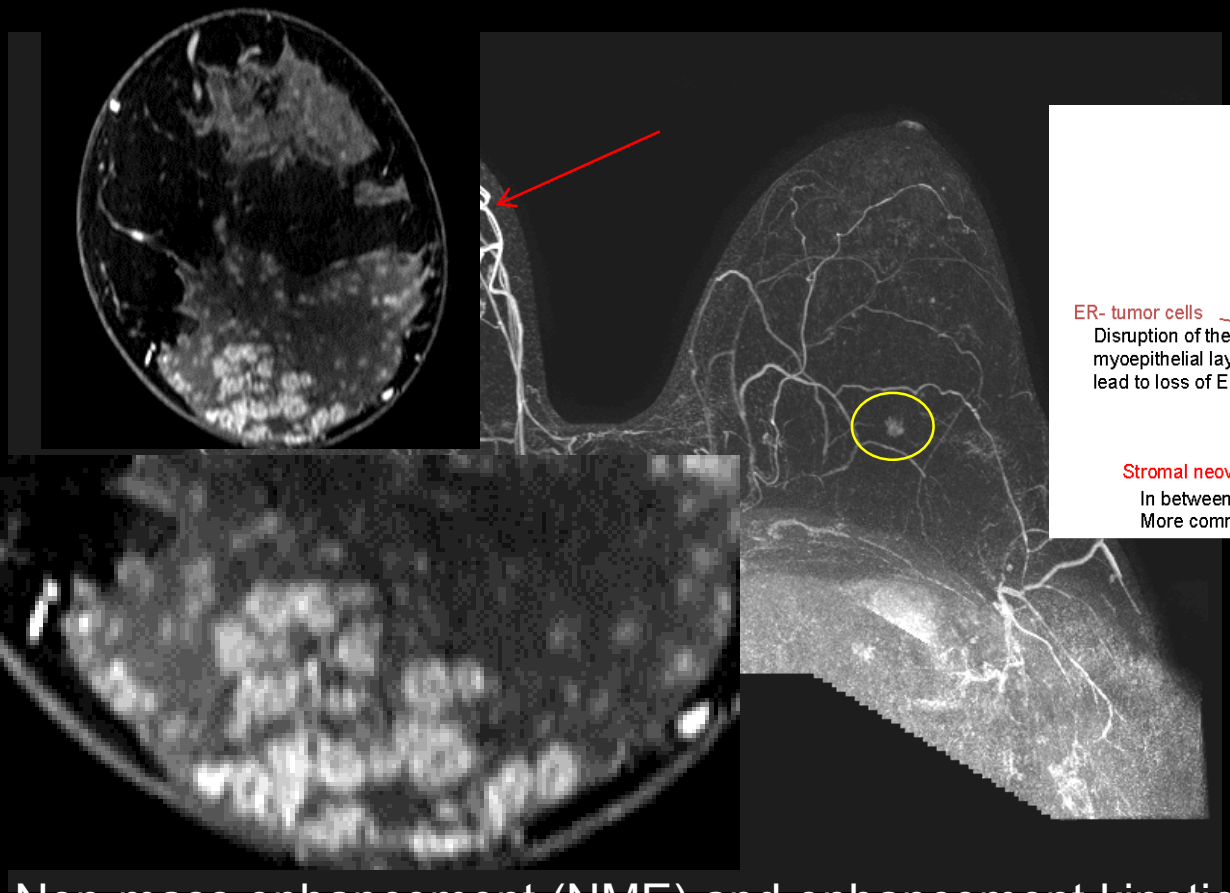
Jansen et al, 2009, Radiology

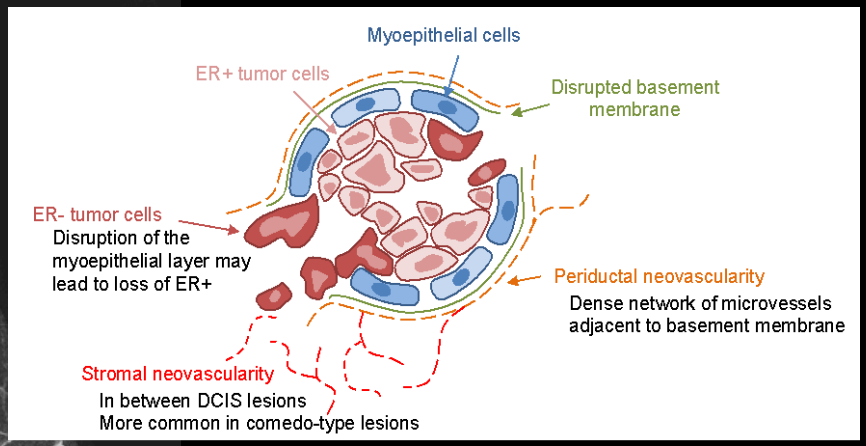
- 23 transgenic mice, all injected with gadolinium
- 12 underwent DCE imaging, 11 were sacrificed 2 min after injection and underwent X-ray fluorescence microscopy

Confirmed gadolinium diffuses into the ducts

MRI Findings

Biology of DCIS on MRI





Non-mass enhancement (NME) and enhancement kinetics are based on abnormal periductal or stromal vascularity, which may be due to disruption in the myoepithelial cells (which secrete angiogenesis inhibitors) that line the duct

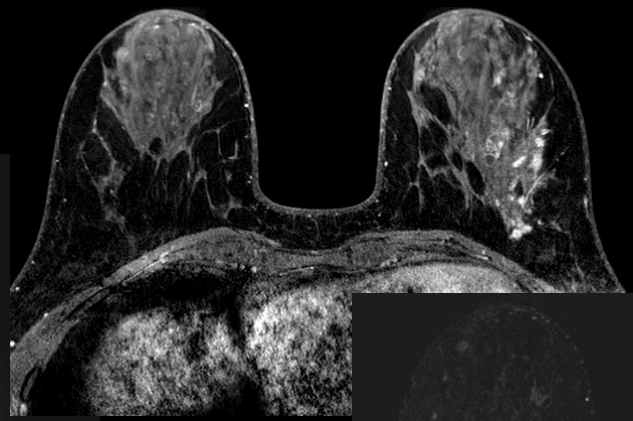
DCIS Appearance on MRI

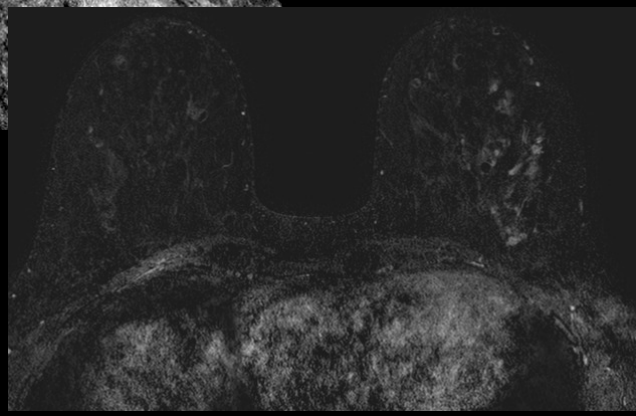
- Non-mass enhancement (NME) 60-80%
- Mass 14-34%
- Focus of enhancement: 1-12%

[1]Yamada *et al.* Radiographics, 2010. 30(5): p. 1183-98.
[2]Buadu *et al*. Radiology 1996; 200(3):639–649.
[3]Jansen *et al*. Radiology 2007;245(3):684–691.
[4]Rosen *et al.* Breast J 2007;13(6):545–550.
[5]Menell *et al.* Breast J 2005;11(6):382–390.
Greenwood et al. Radiographics 2013

Non-Mass Enhancement (NME)

- Discrete from normal BPE
- May extend over small or large regions
- Spots of normal glandular tissue or fat interspersed





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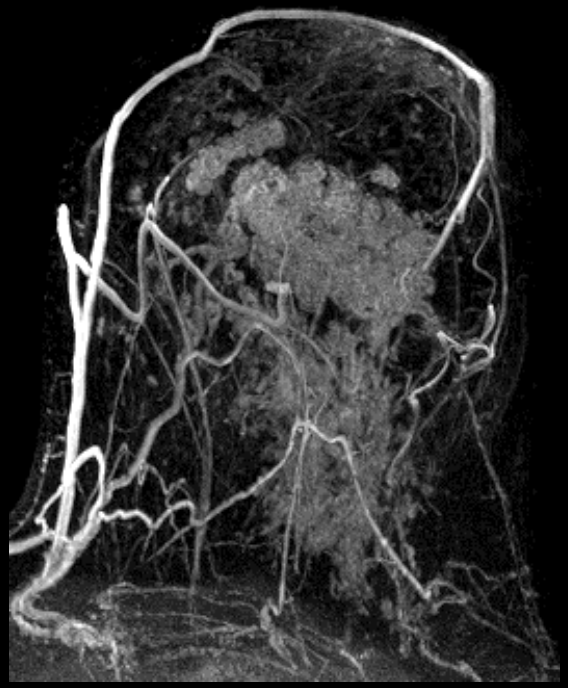

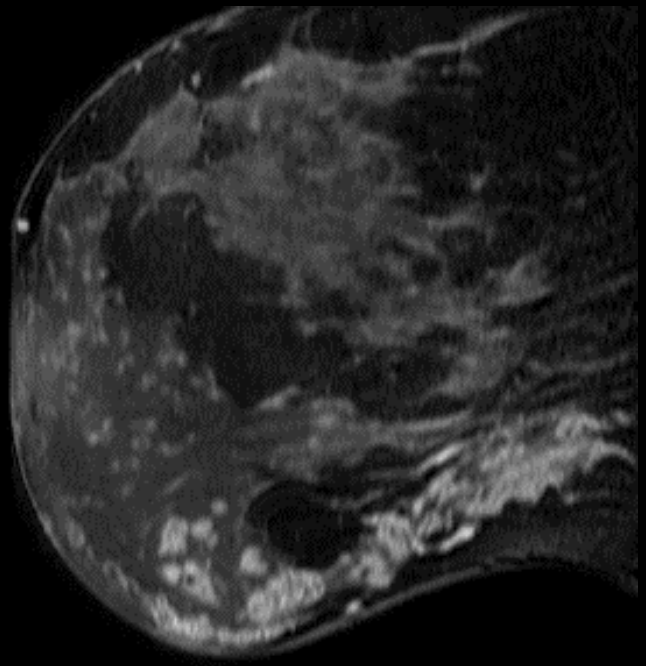

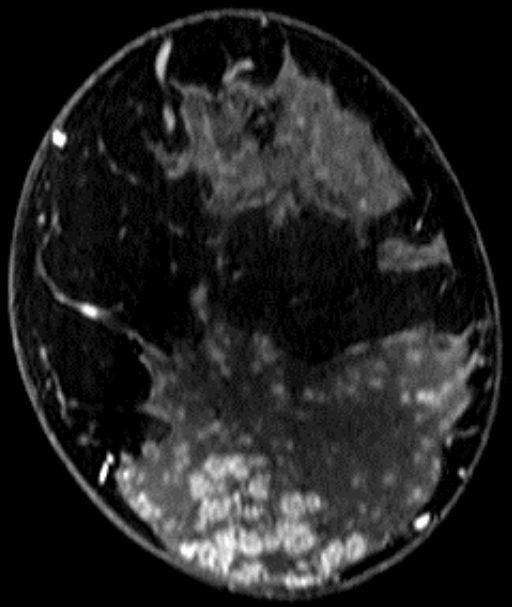

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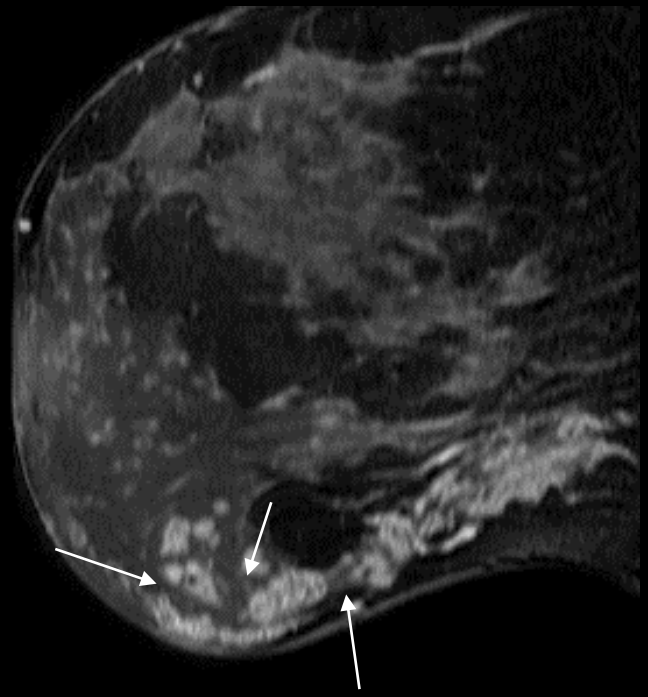
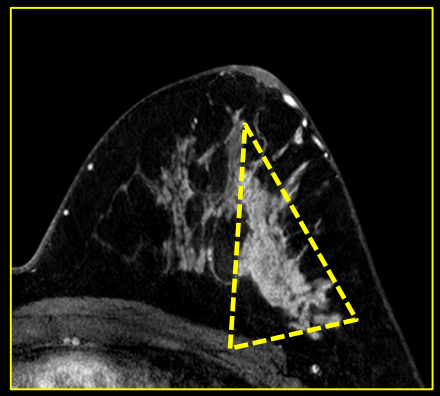
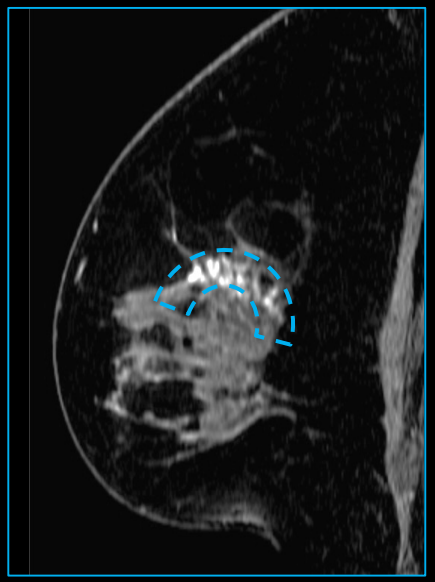


DCIS – NME Distribution

- Segmental: triangle/cone with apex pointing toward nipple
  - Most common distribution (14-77% lesions)
- Linear/ductal: straight or curved, may branch
  - 1-24%
- Focal area: small confined area, generally < 25% of a quadrant
  - 16-33%

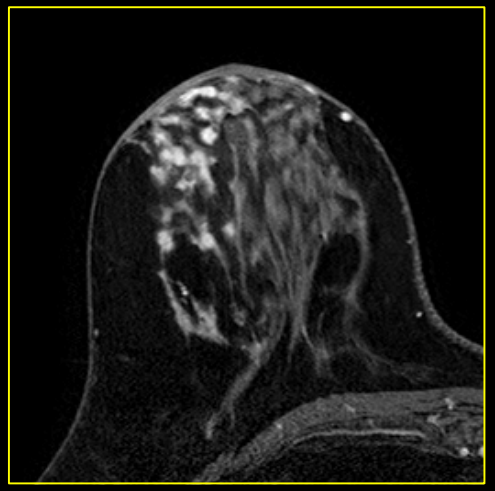


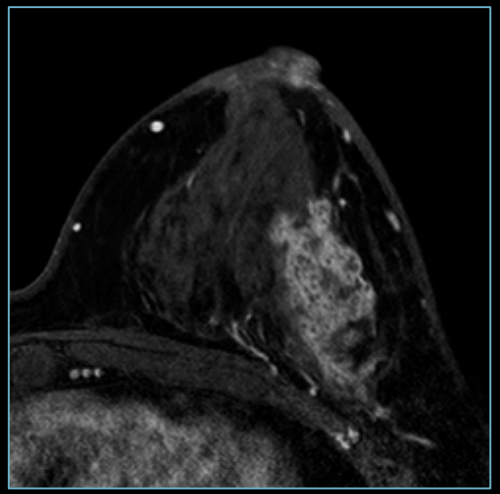


Greenwood et al. Radiographics 2013

DCIS – NME Internal Enhancement

- Clumped: cobblestone- or grape-like
  - 41-64% of DCIS lesions
- Heterogeneous: non-uniform, separated by areas of parenchyma or fat
  - 16-29% of DCIS lesions
- Clustered ring: thin rings around ducts
  - Potentially more specific for malignancy (~63%)



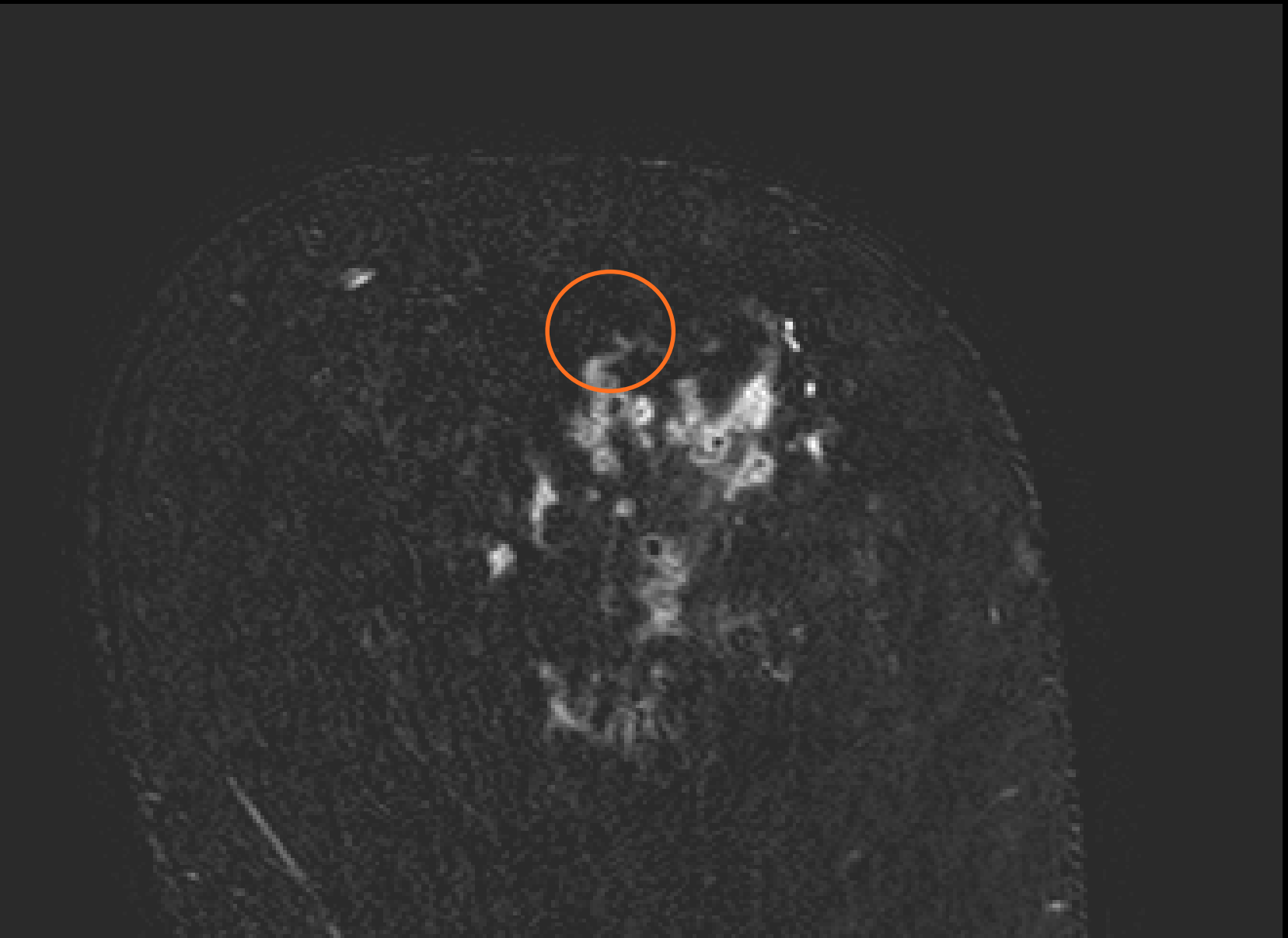


Greenwood et al. Radiographics 2013

DCIS Presenting as a Mass on MRI

- Mass = 3D space-occupying lesion, convexity
- Focus = “dot” of unique enhancement
- Less common DCIS presentation (14-41%)
  - Larger lesions or those that cause focal distention of a duct/TDLU can create a “mass”

NME→ Mass Spectrum



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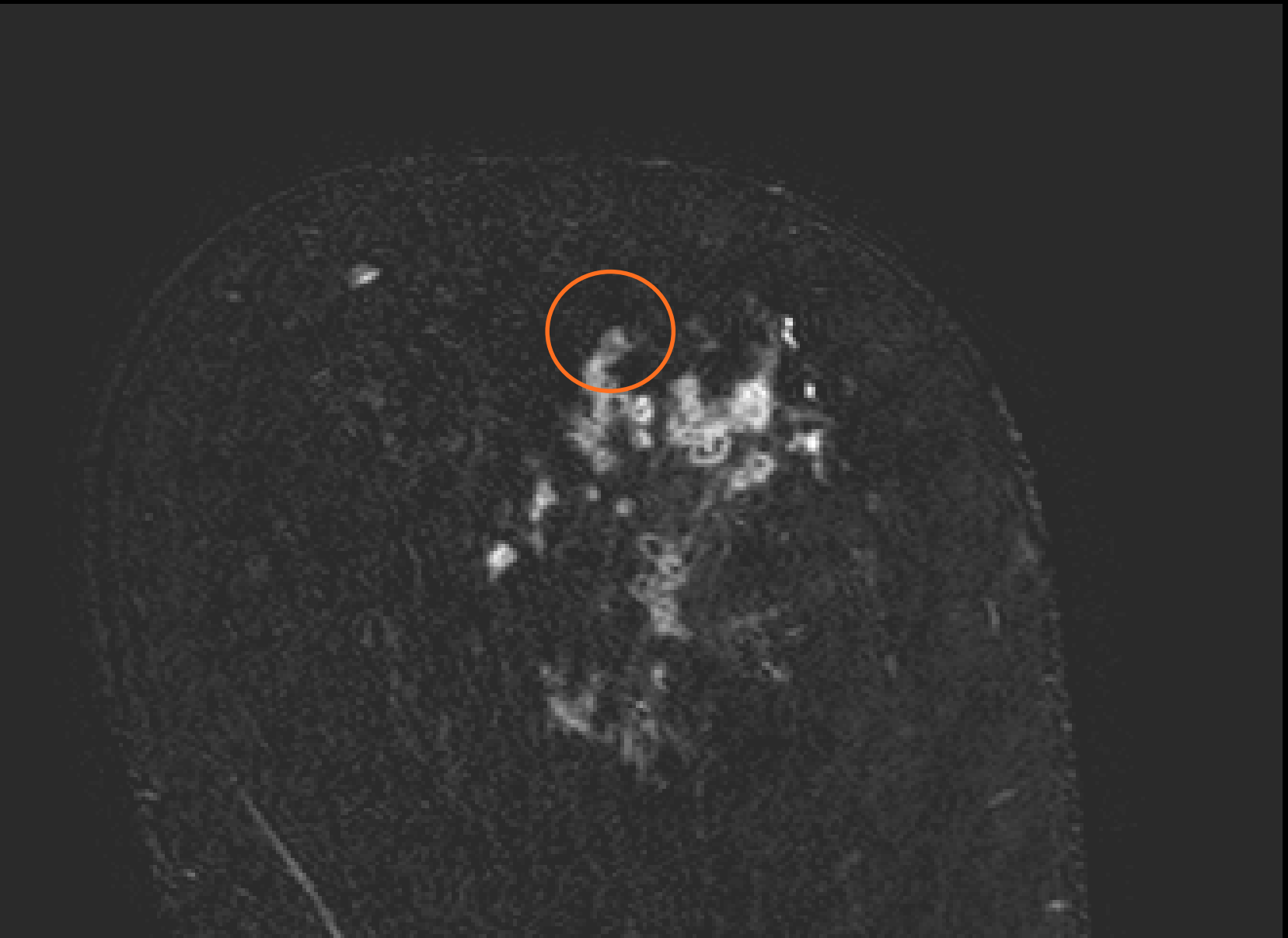

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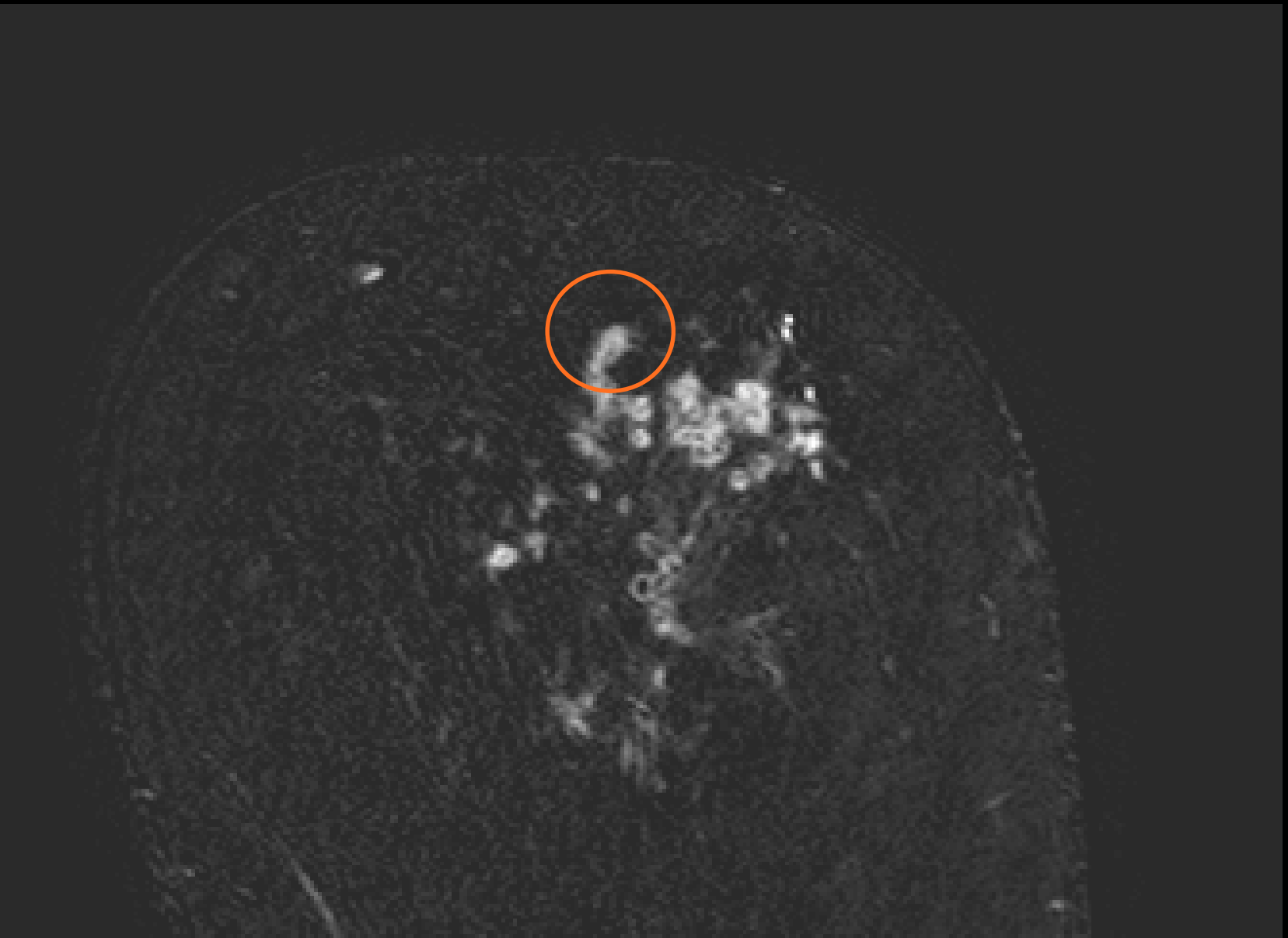

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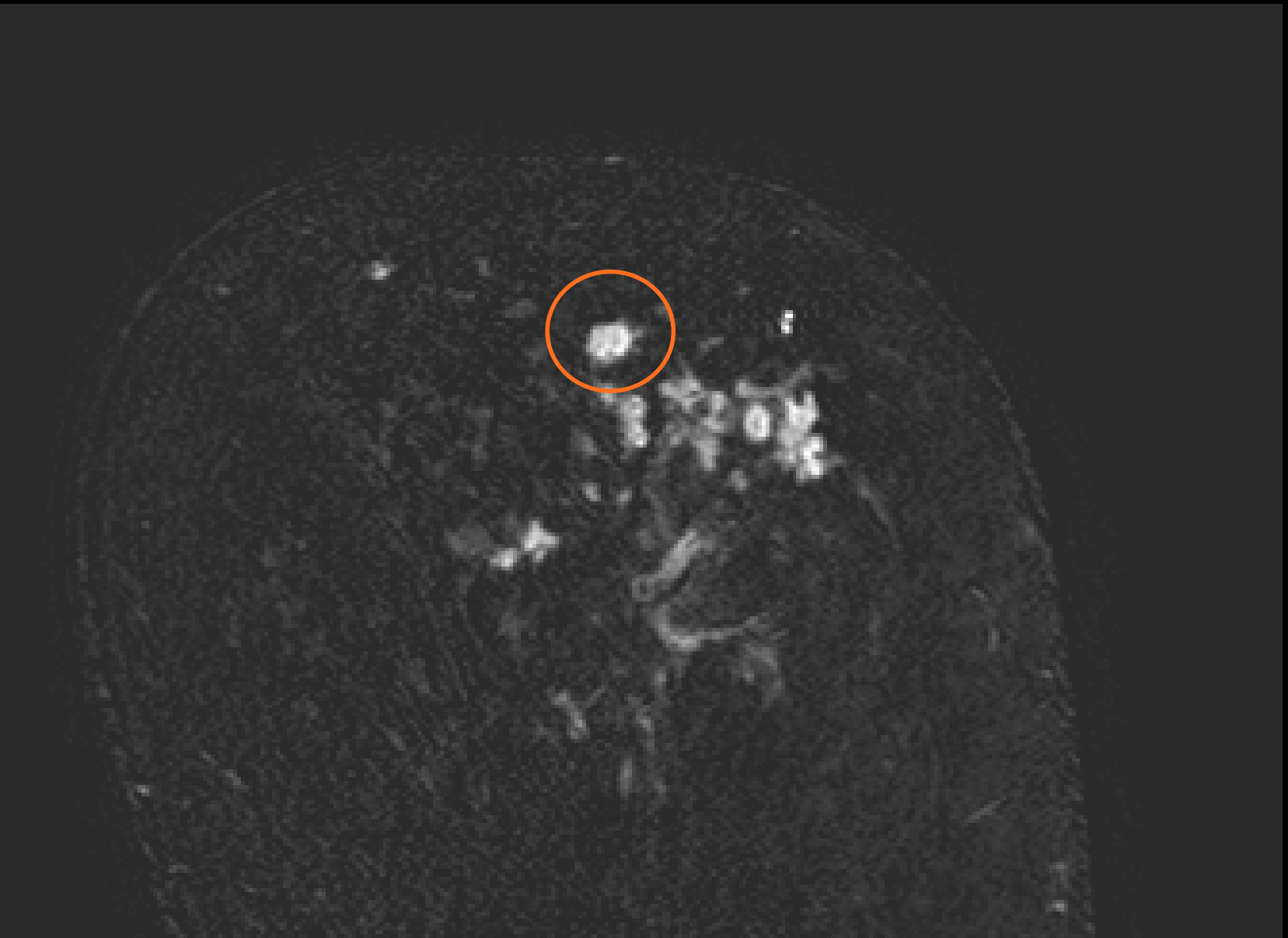
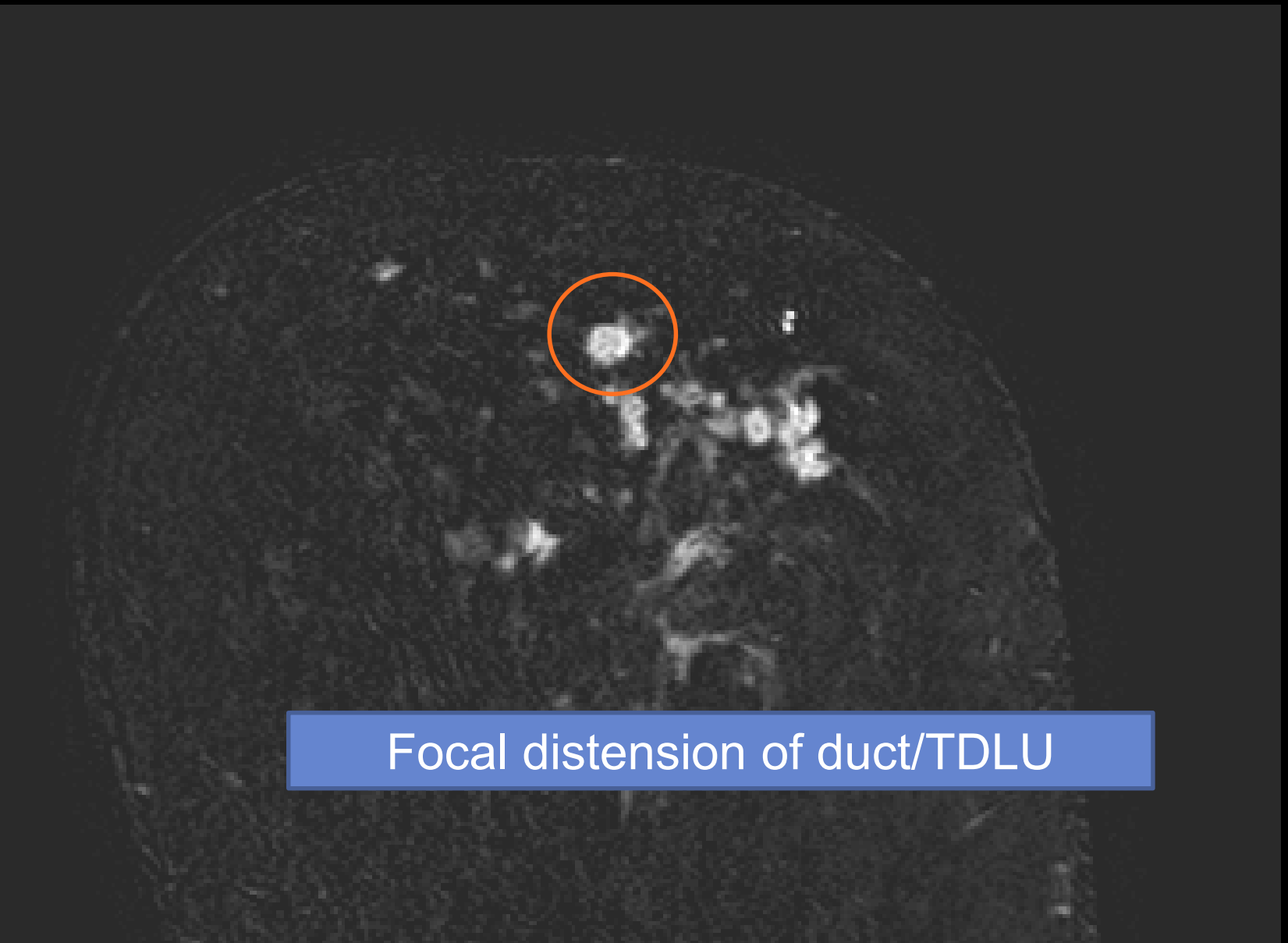
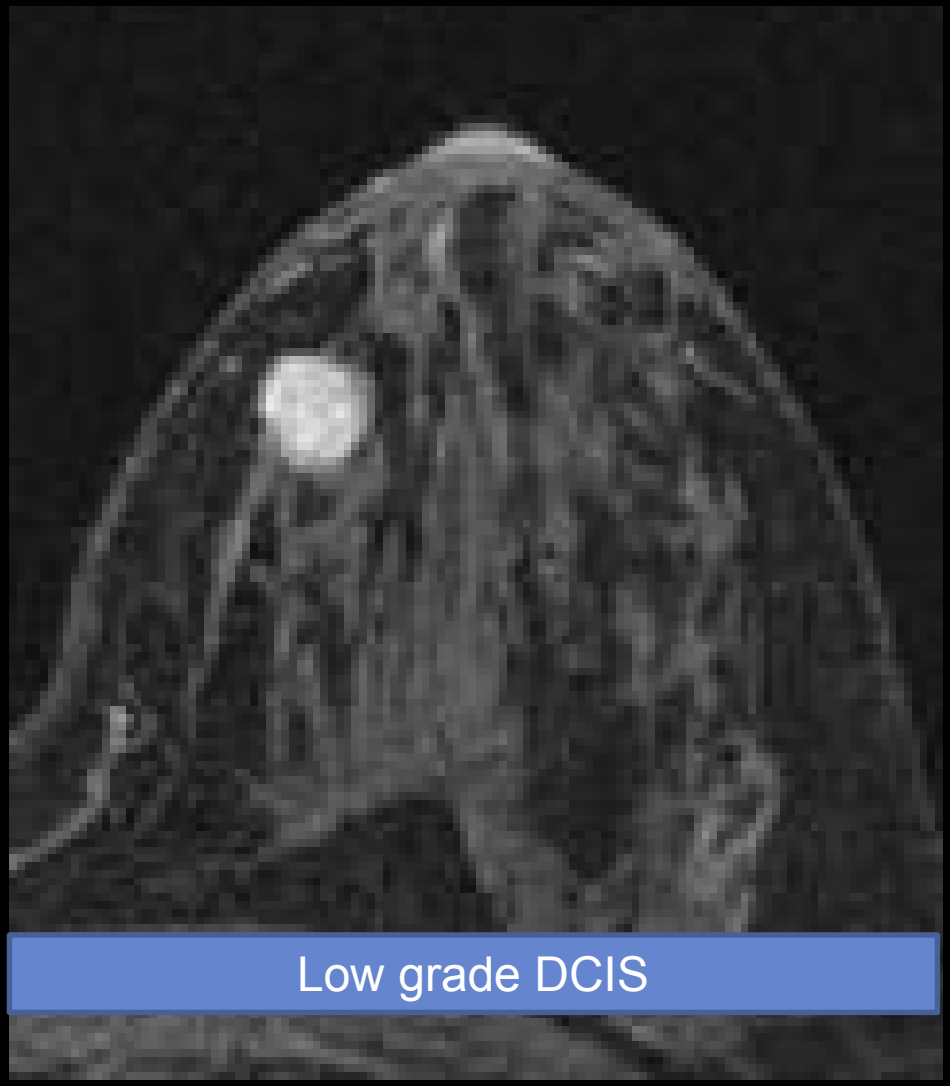


NME→ Mass Spectrum

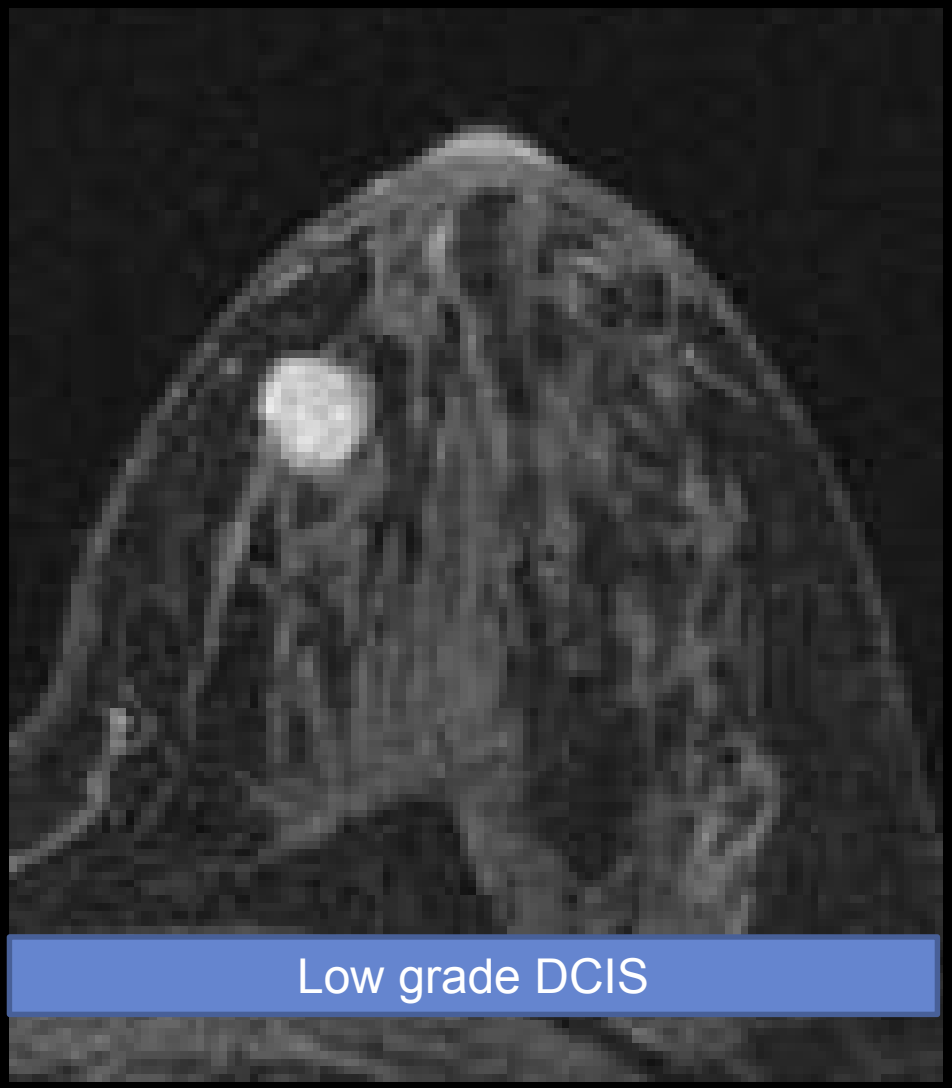


DCIS – MRI Masses

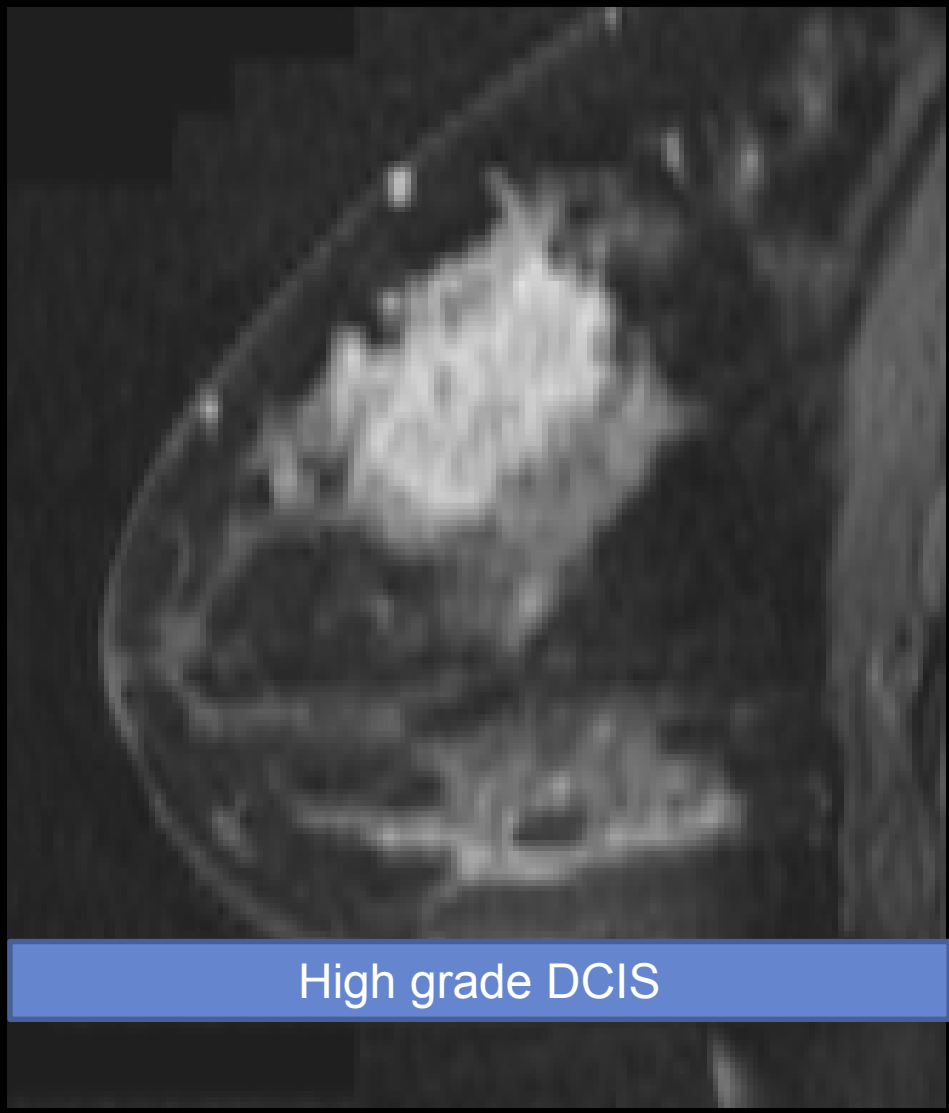


Low grade DCIS

DCIS – MRI Masses

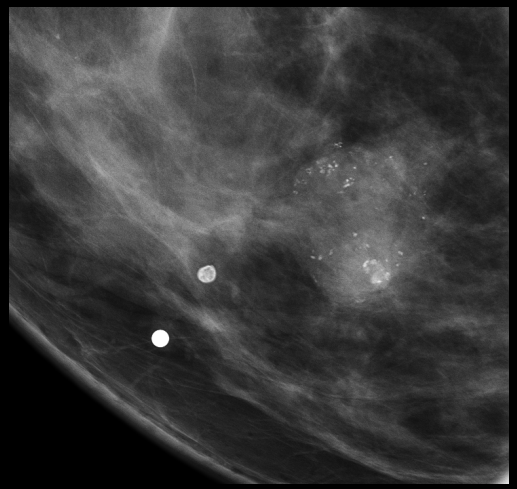


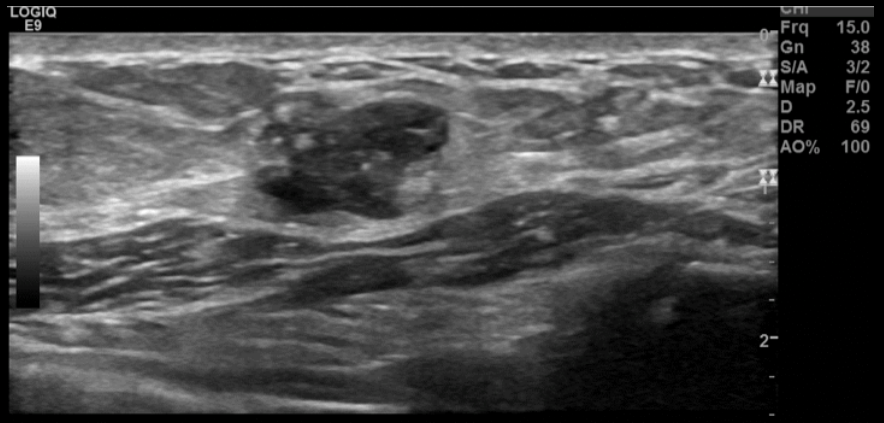
Low grade DCIS



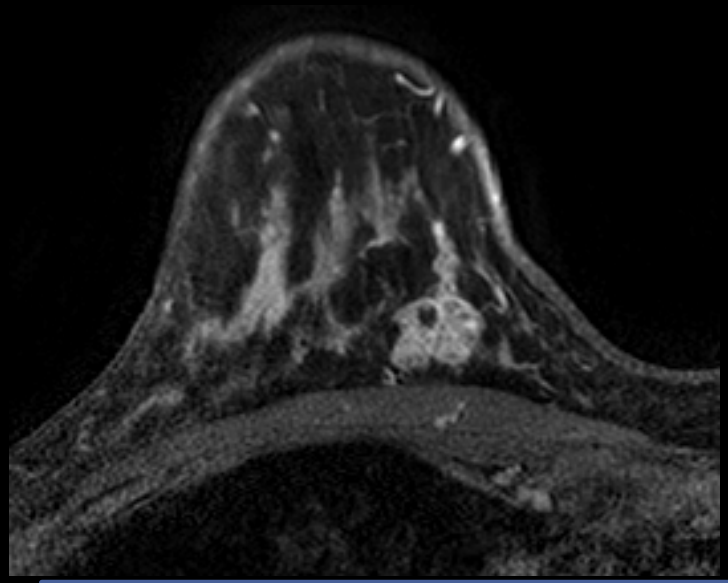
High grade DCIS

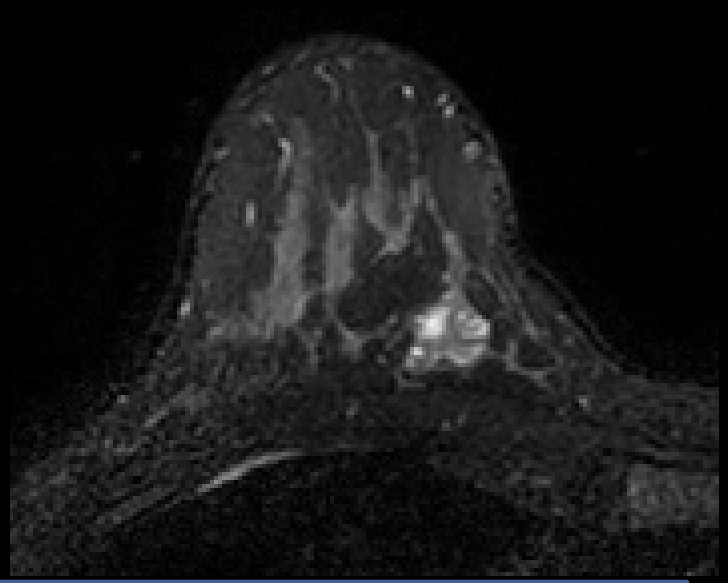
DCIS – MRI Masses





RT BREAST 5 O'CLOCK 7 CM TO N TRANS

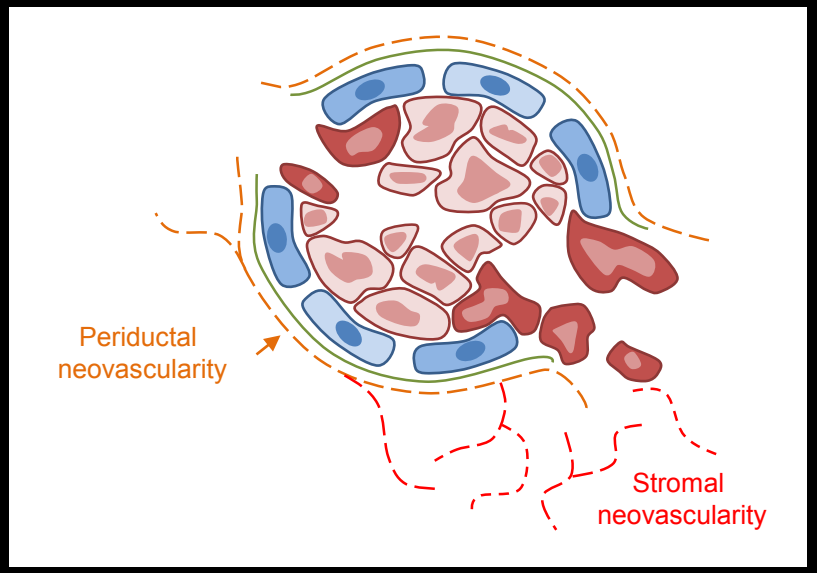




39 yo with palpable left breast mass
High Grade DCIS

DCIS Kinetic Features

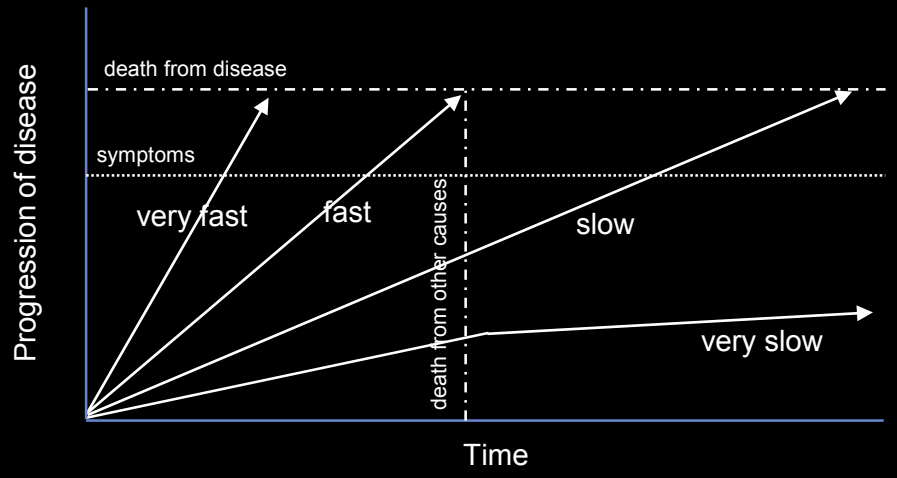
- Indirect measure of perfusion and diffusion of blood/nutrients
  - Periductal space
  - Basement membrane
- DCIS delayed phase is more variable than invasive cancers
  - Washout (28-44%)
  - Plateau (20-52%)
  - Persistent (20-30%)

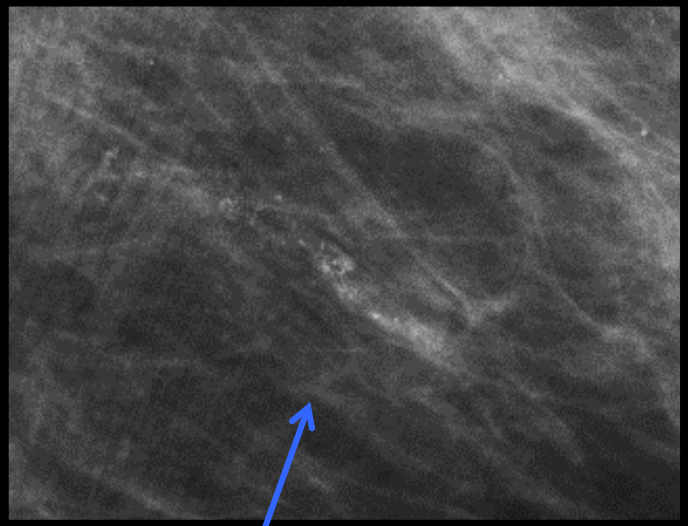


DCIS Clinical Controversies

Overdiagnosis

- Long-term follow-up of untreated DCIS
  - 35% of low-grade DCIS lesions → IDC in 50 years
  - 50% of high-grade DCIS lesions → IDC in 3 years





- Screen detected amorphous calcifications
- Biopsy confirmed low grade DCIS

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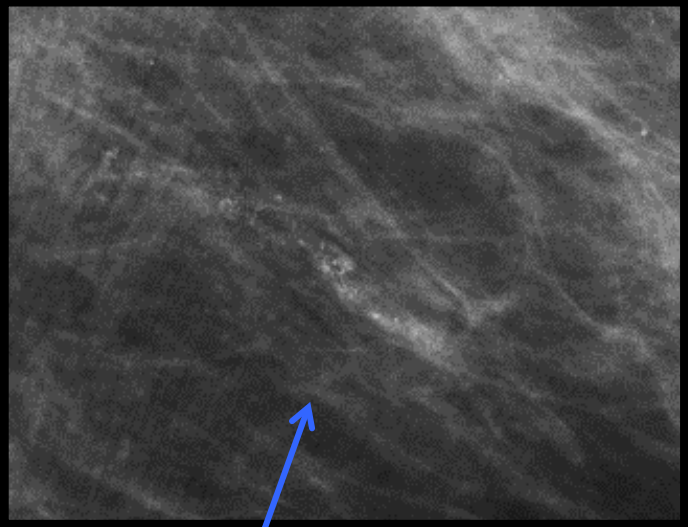

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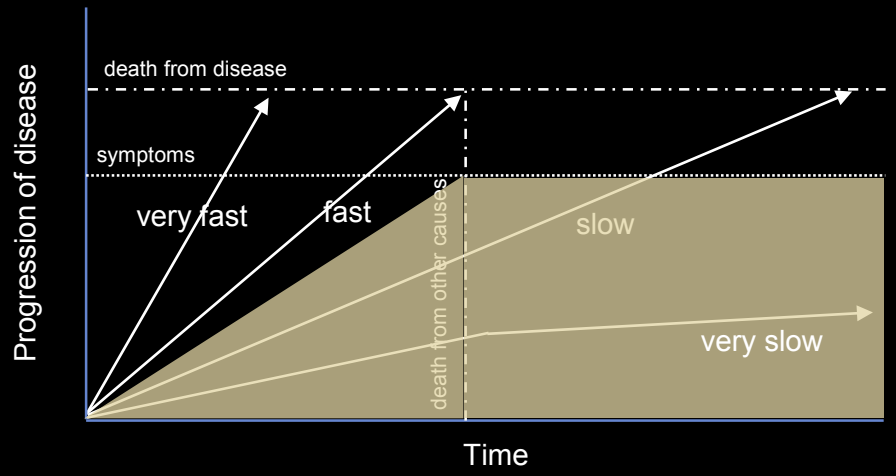

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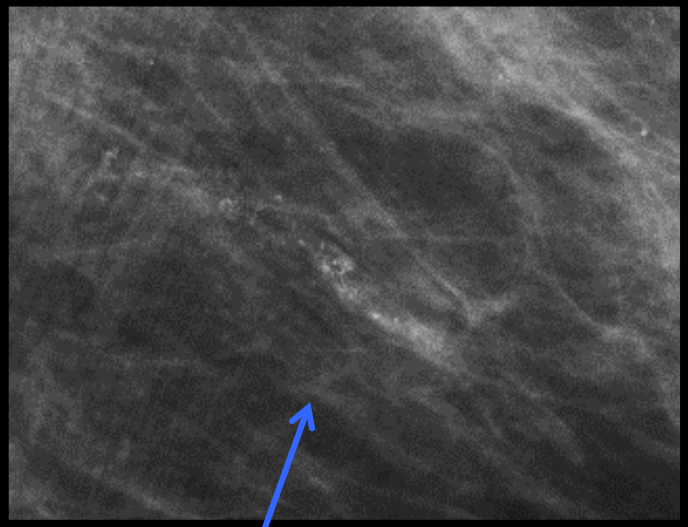

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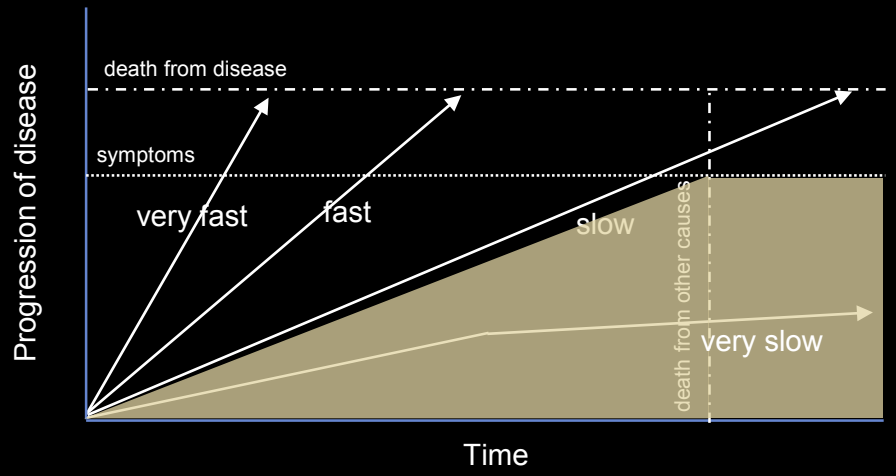
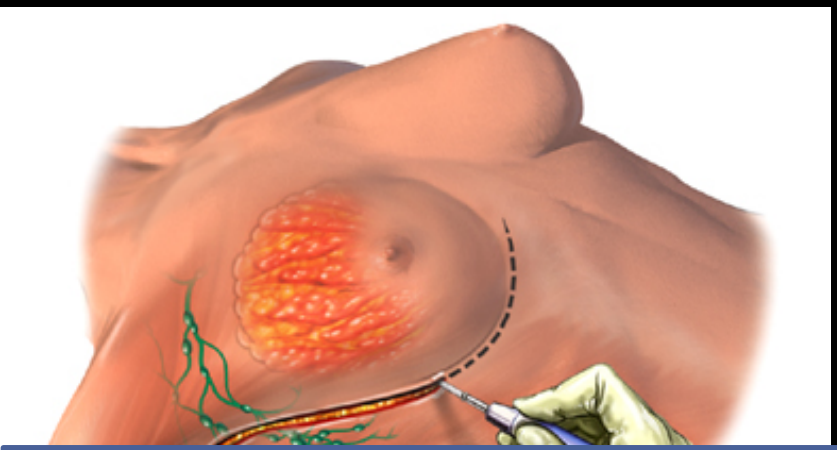


DCIS Clinical Controversies



- 3% of DCIS is treated non-surgically
- 75% of DCIS undergoing BCT include radiation therapy
- 25% of women with DCIS choose an unnecessary mastectomy

Overtreatment

DCIS Clinical Controversies

Overdiagnosis

The New York Times

HEALTH

Prone to Error: Earliest Steps to Find Cancer

By STEPHANIE SAUL JULY 19, 2010

Monica Long had expected a routine appointment. But here she v
her new oncologist's office, and he was delivering deeply disturbi

Nearly a year earlier, in 2007, a pathologist at a small hospit
Cheboygan, Mich., had found the earliest stage of breast cancer fi
Extensive surgery followed, leaving Ms. Long's right breast missi
size chunk.

Overtreatment

HEALTH

Doubt Is Raised Over Value of Surgery for Breast Lesion at Earliest Stage

By GINA KOLATA AUG. 20, 2015

As many as 60,000 American women each year are told they have a very early stage of breast cancer — Stage 0, as it is commonly known — a possible precursor to what could be a deadly tumor. And almost every one of the women has either a lumpectomy or a mastectomy, and often a double mastectomy, removing a healthy breast as well.

DCIS Detection: Evolving Opinions

Journal of Surgical Oncology 1998;69:60–62

GUEST EDITORIAL

How To Prevent Invasive Breast Cancer: Detect and Excise Duct Carcinoma In Situ

BLAKE CADY, MD[1,2]*
[1]The Breast Health Center, Women & Infants Hospital, Providence, Rhode Island
[2]Department of Surgery, Brown University, Providence, Rhode Island

"…currently there is one presumed method to prevent invasive breast cancer, detect and excise ductal carcinoma in situ."

DCIS Detection: Evolving Opinions

Selecting Individualized Treatment for Patients With Ductal Carcinoma in Situ of the Breast: The Search Continues

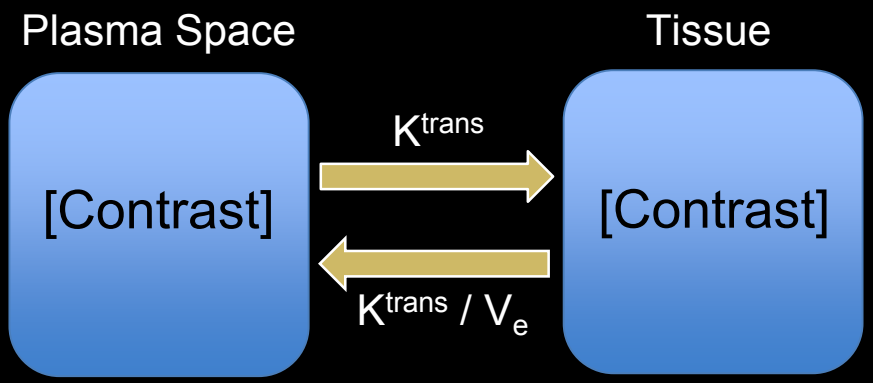
Lawrence J. Solin, *Albert Einstein Medical Center, Philadelphia, PA*

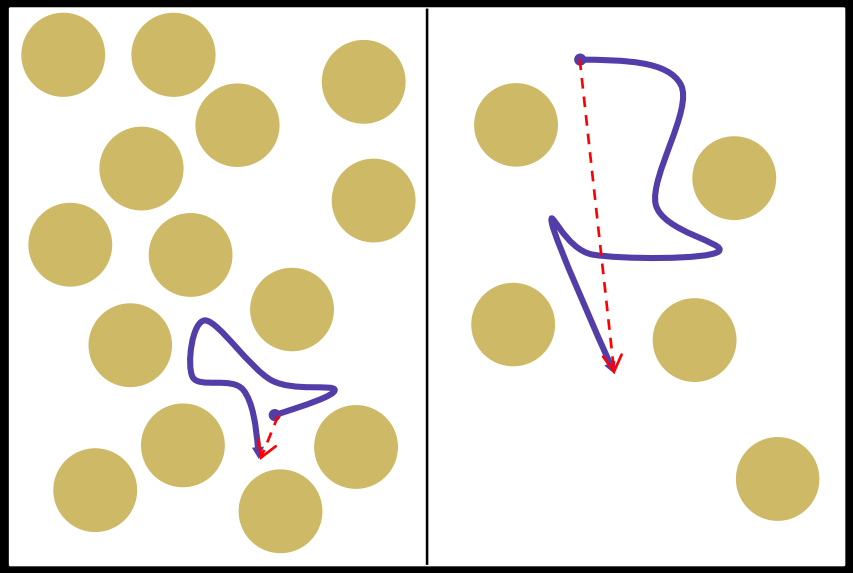
JCO February 20, 2012 vol. 30 no. 6 577-579

- "Although some patients with DCIS will develop a subsequent invasive malignancy over time, most will not."

Opportunities for MRI

- Whole lesion (and normal tissue) assessments
  - High spatial resolution imaging at higher field strengths
  - Dynamic contrast-enhanced (DCE) Pharmacokinetic (PK) modeling
  - Diffusion weighted imaging (DWI)





High cell density Low cell density

DCE PK models assess vascular permeability

DWI probes cellular density

MRI to Improve DCIS management

- Can MRI guide biopsies?
  - Identify “important” calcifications on mammography
- Can MRI improve surgical management?
  - Identify CNB-occult invasive disease
  - Improve accuracy of DCIS extent over conventional imaging
  - Translate to fewer operations without causing “unnecessary” mastectomies
- Can MRI inform biology and risk?
  - Correlate to meaningful surrogate markers of risk of recurrence
  - Independently predict risk of recurrence

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Can MRI Guide Biopsies?

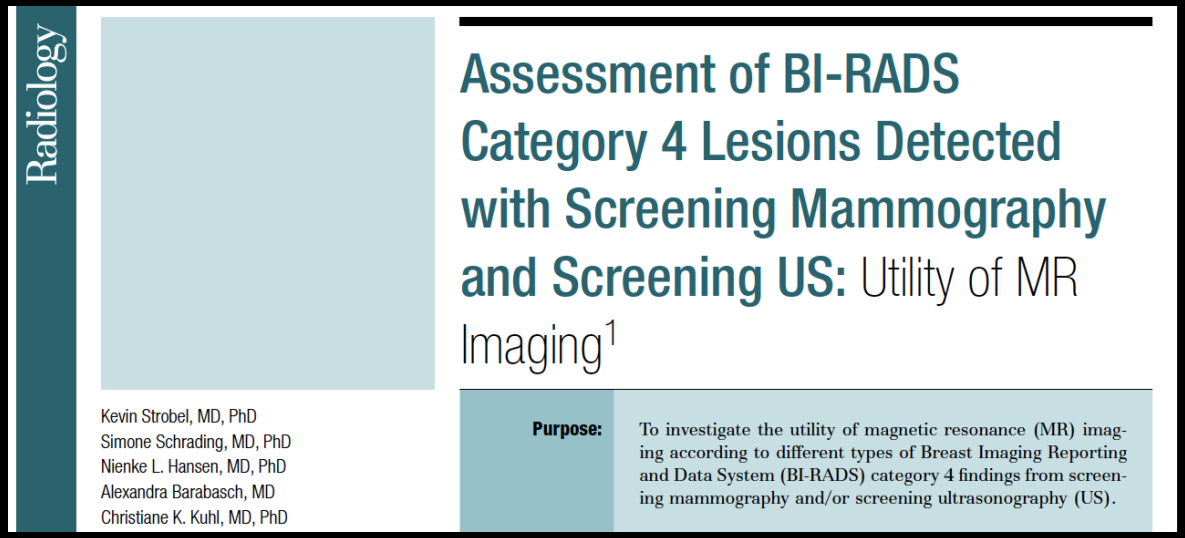
Evolving Paradigm for Imaging, Diagnosis, and Management of DCIS

Colin J. Wells, MD[a], Cristina O'Donoghue, MD[b], Haydee Ojeda-Fournier, MD[c], Hanna E. G. Retallack, MD[d], Laura J. Esserman, MD[d]

J Am Coll Radiol 2013;10:918-923.

- Change risk thresholds for biopsy?
  - Currently 2% risk of malignancy
- Personalized screening approaches
- Utilize advanced imaging to stratify risk and biopsy

Can MRI Guide Biopsies?



Radiology

Assessment of BI-RADS Category 4 Lesions Detected with Screening Mammography and Screening US: Utility of MR Imaging[1]

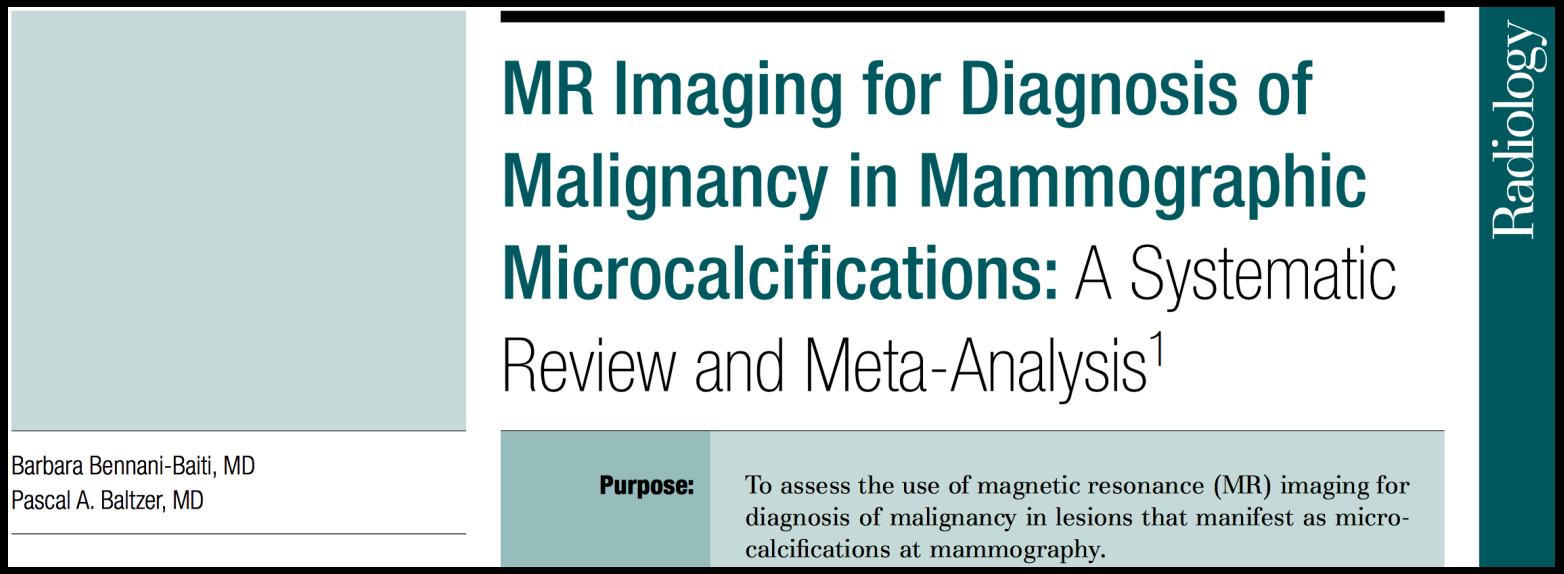
Kevin Strobel, MD, PhD
Simone Schrading, MD, PhD
Nienke L. Hansen, MD, PhD
Alexandra Barabasch, MD
Christiane K. Kuhl, MD, PhD

Purpose: To investigate the utility of magnetic resonance (MR) imaging according to different types of Breast Imaging Reporting and Data System (BI-RADS) category 4 findings from screening mammography and/or screening ultrasonography (US).

- MG finding of "pure clustered Ca^{2+}", n = 78
  - 18/21 MG-detected DCIS lesions were true positives on MRI
  - 3/21 were false negatives (12%) on MRI
    - all were low NG DCIS; 6 to 11 mm in size

Strobel et al. Radiology 2015 Feb;274(2):343-51.

Can MRI Guide Biopsies?



Radiology

MR Imaging for Diagnosis of Malignancy in Mammographic Microcalcifications: A Systematic Review and Meta-Analysis[1]

Barbara Bennani-Baiti, MD
Pascal A. Baltzer, MD

Purpose: To assess the use of magnetic resonance (MR) imaging for diagnosis of malignancy in lesions that manifest as microcalcifications at mammography.

- 60% of biopsies of calcifications → benign pathology
- Pooled NPV to exclude invasive/microinvasive disease was 99%

Bennani-Baiti and Baltzer, Radiology 2017 Jun;283(3):692-701.

Can MRI Guide Biopsies?

Original contribution

Is breast MRI a helpful additional diagnostic test in suspicious mammographic microcalcifications?

Pascal A.T. Baltzer*, Barbara Bennani-Baiti, Alexander Stöttinger, Alexander Bumberger, Panagiotis Kapetas, Paola Clauser

Department of Biomedical Imaging and Image-guided Therapy, Allgemeines Krankenhaus, Medizinische Universität Wien, Austria

- 152 suspicious Ca^{2+}, MRI <8 weeks prior to biopsy
  - 81 benign, 71 malignant (41 DCIS, 30 invasive)
- 32 cases were downgraded to BI-RADS 2/3 on MRI
  - Missed 2 DCIS lesions, both non-high grade, ER+, her2-
- NPV=94%

Baltzer et al. MRI 2018 46:70-74.

MRI to Improve DCIS management

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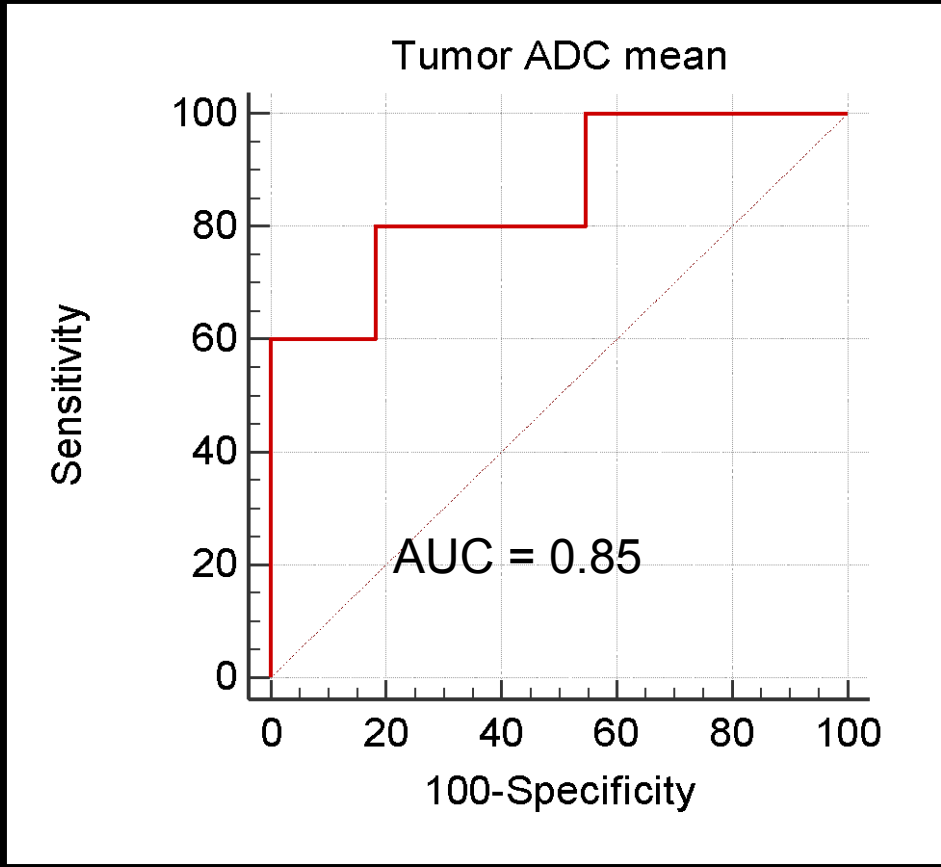
Can MRI Identify CNB-occult Invasive Disease?

- Goto et al., 2012, Eur Radiology
  - NME lesions with increased T2 signal and larger size more likely to upgrade to invasive disease

- Wisner et al., 2013, Breast Journal
  - Reader study: invasion correlated with presence of a mass and “perception of occult invasion”
  - Invasion correlated with washout (SER) when % enhancement was 130%

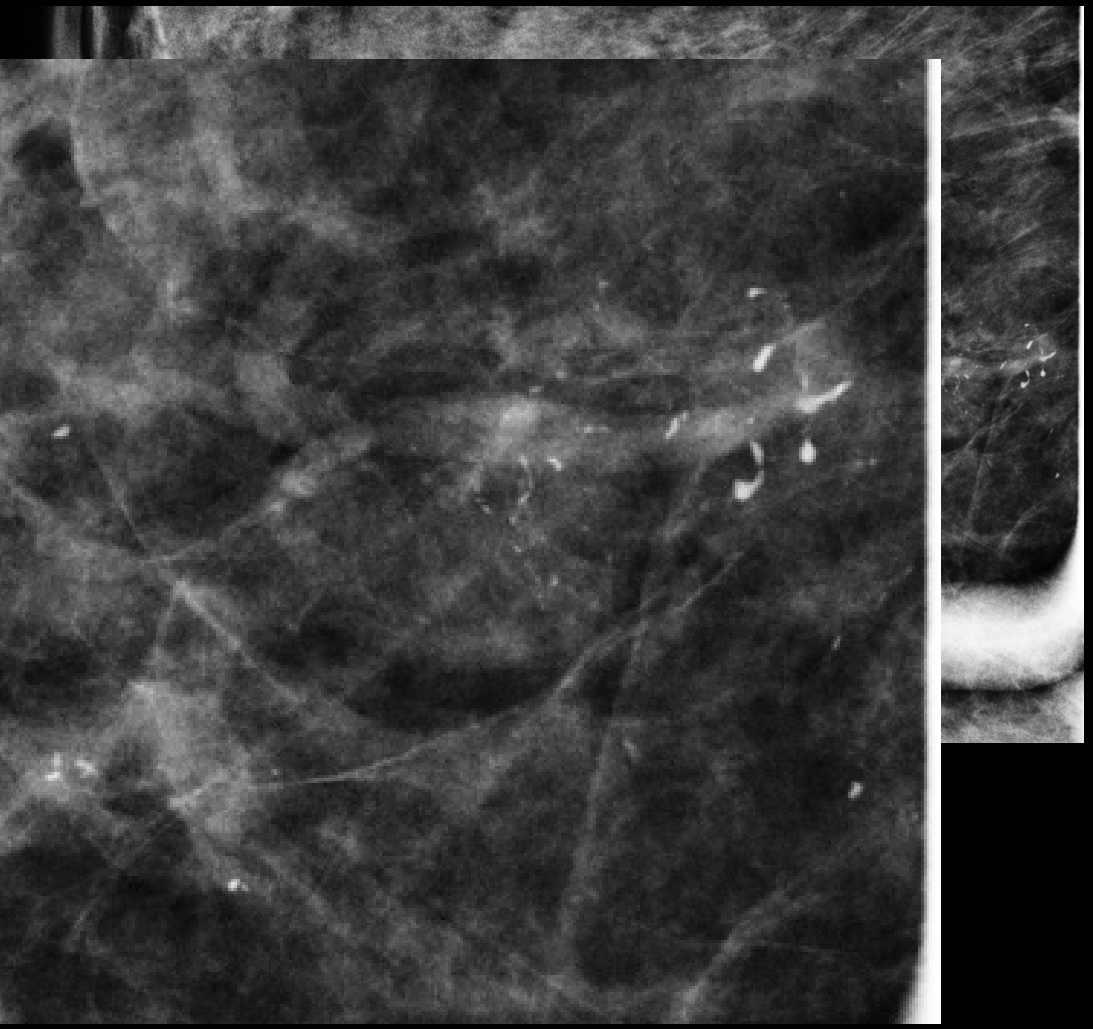
Can MRI Identify CNB-occult Invasive Disease?

- 16 MRI-detected lesions yielding DCIS on CNB
- 5/16 lesions (31%) upgraded to IDC at surgery
- Lower ADC correlated with upgrade to invasion (p=0.03)



Parsian S, Rahbar H, Chai X, Carroll T, Liu CL, Lehman CD, Partridge SC. Presented at ISMRM Workshop on MRI in the Management of Breast Disease: Past, Present, and Future 2015

Can MRI Improve Pre-operative Extent of Disease?

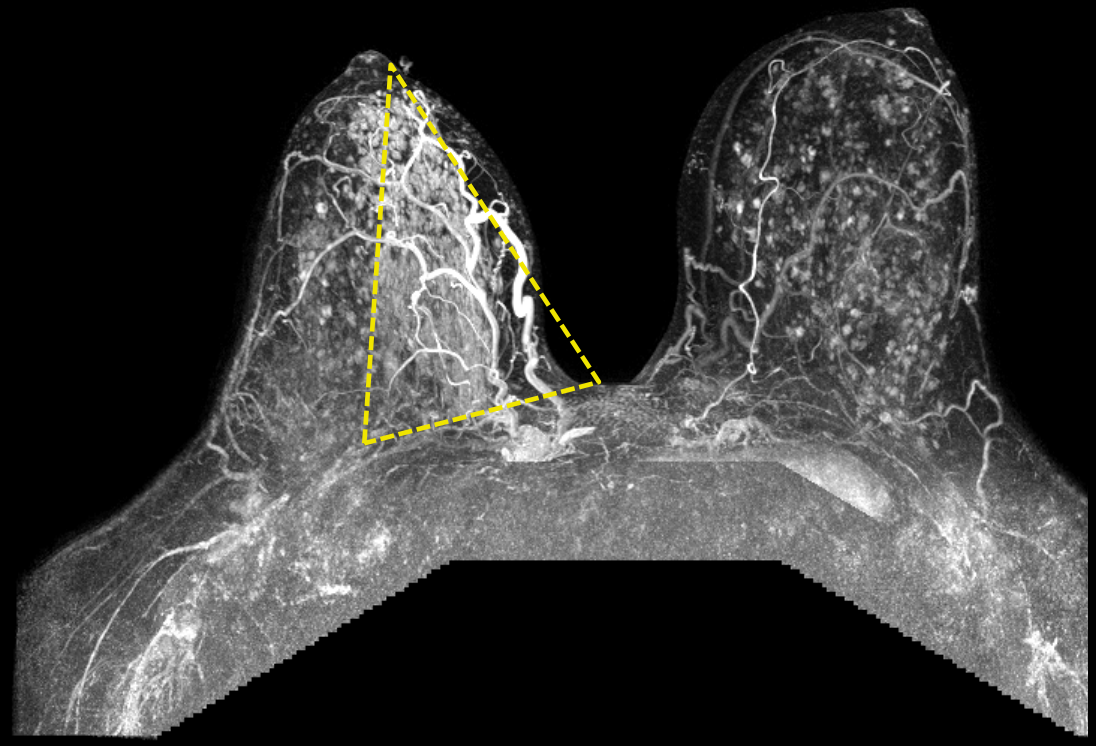


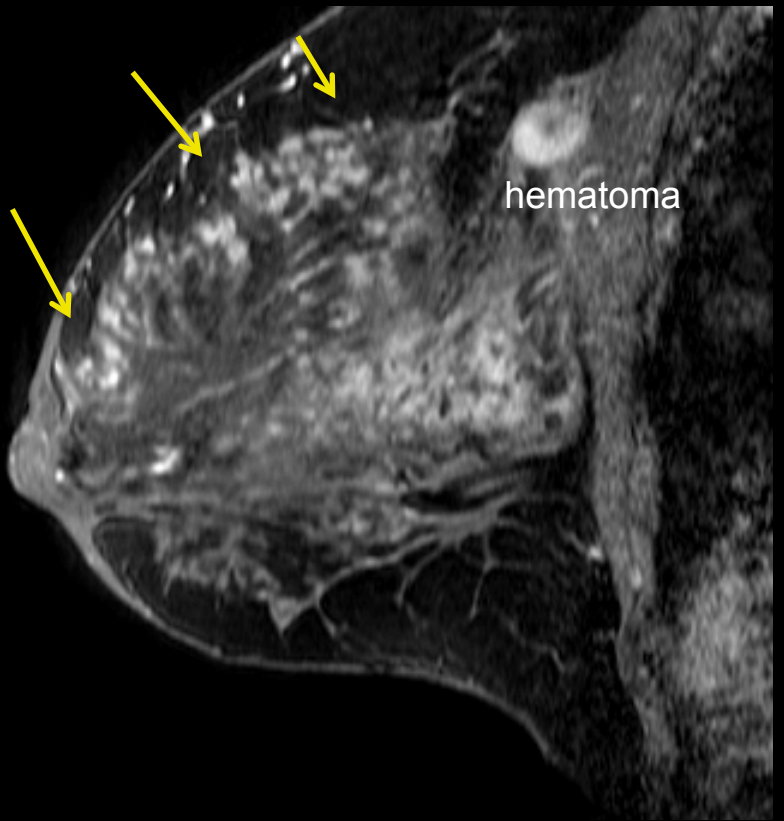
52 year old woman with mammographically detected grouped, fine pleomorphic calcifications spanning 30 mm in UIQ

Pathology→Intermediate to high nuclear grade DCIS

DCIS EOD Example

Marked BPE, left breast is negative



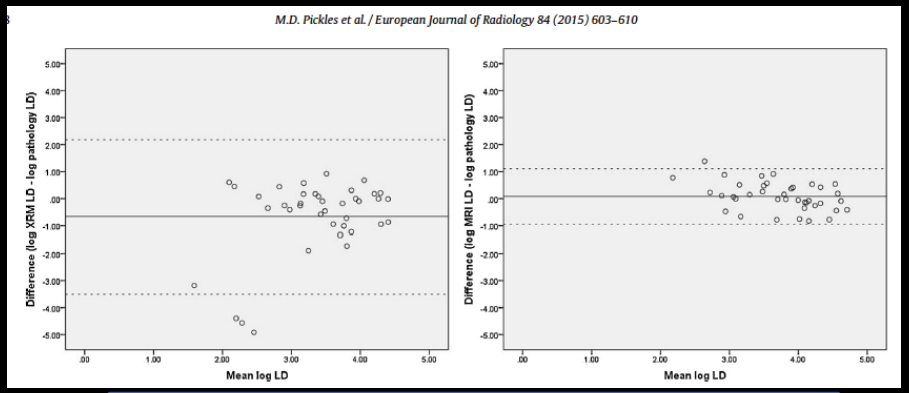


Segmental NME spanning 10 cm

MRI-guided biopsy of the anterior aspect → high grade DCIS

Can MRI Improve Pre-op Evaluation of DCIS Extent?

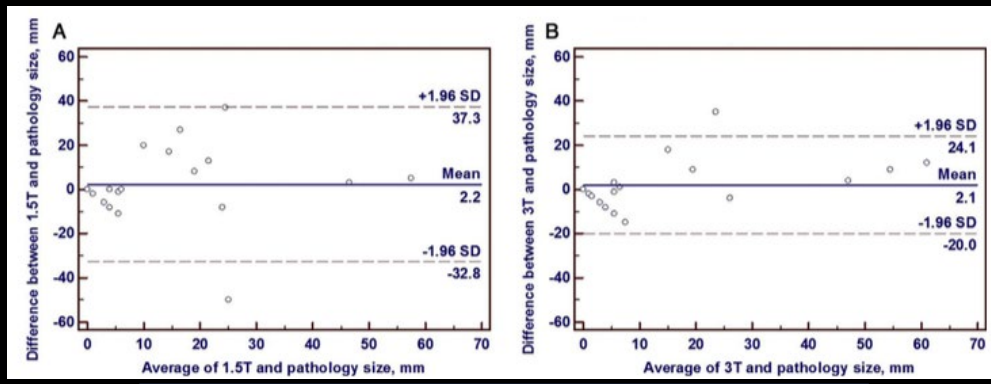
3T MRI vs. MG



Pickles et al, 2015 EJR

- 39 patients with CNB-diagnosed DCIS
- All underwent preoperative MG and 3T MRI
- 3T MRI more closely represented pathologic extent than MG

1.5T vs. 3T MRI



Rahbar et al, 2015 EJR

- 20 patients with CNB-diagnosed DCIS
- All underwent preoperative 3T and 1.5T MRI
- 3T MRI more closely represented pathologic extent than 1.5T

Can MRI Translate To ↓ Surgeries?

Systematic review

Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma *in situ*

A. Fancellu[1], R. M. Turner[2], J. M. Dixon[4], A. Pinna[1], P. Cottu[1] and N. Houssami[3]

[1]Department of Clinical and Experimental Medicine, Unit of General Surgery 2, Clinica Chirurgica, University of Sassari, Sassari, Italy, [2]School of Public Health and Community Medicine, The University of New South Wales, and [3]Screening and Test Evaluation Programme, School of Public Health, Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia and [4]Breakthrough Breast Cancer Research Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, UK

Correspondence to: Dr A. Fancellu, Department of Clinical and Experimental Medicine, Unit of General Surgery 2, Clinica Chirurgica, University of Sassari, Viale San Pietro 43, 07100 Sassari, Italy (e-mail: afancel@uniss.it)

Conclusion: Preoperative MRI in women with DCIS is not associated with improvement in surgical outcomes.

Challenges

- Patient populations of MRI vs. no-MRI
- Surgical practices
- Patient preferences

JAMA Oncology | Original Investigation

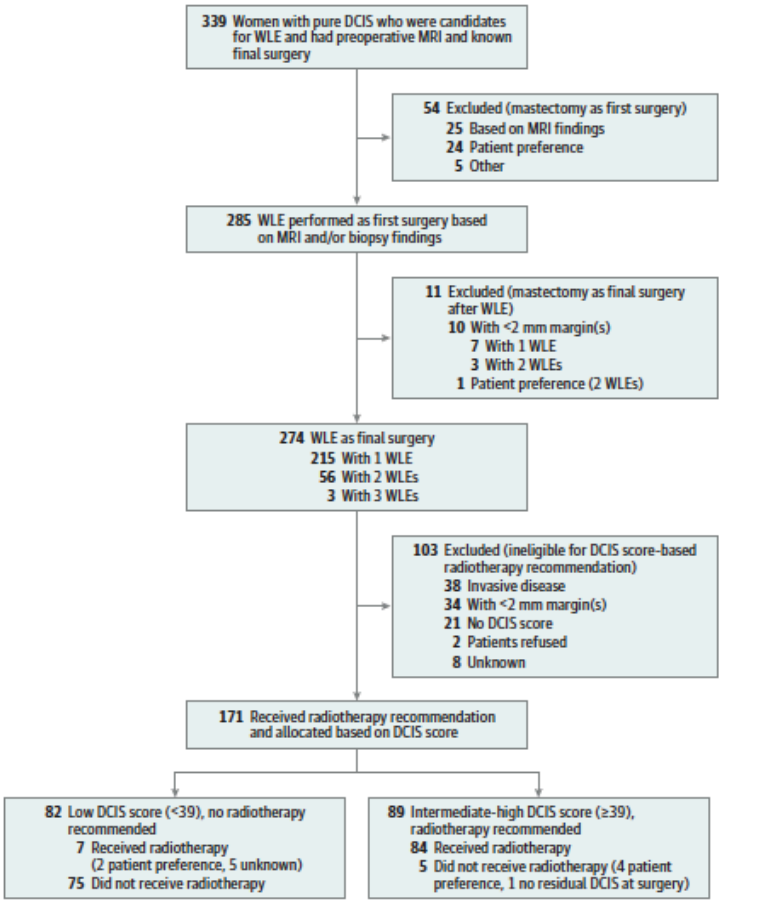
Association of Magnetic Resonance Imaging and a 12-Gene Expression Assay With Breast Ductal Carcinoma In Situ Treatment

Constance D. Lehman, MD, PhD; Constantine Gatsonis, PhD; Justin Romanoff, MA; Seema A. Khan, MD; Ruth Carlos, MD; Lawrence J. Solin, MD; Sunil Badve, MD; Worta McCaskill-Stevens, MD; Ralph L. Corsetti, MD; Habib Rahbar, MD; Derrick W. Spell, MD; Kenneth B. Blankstein, MD; Linda K. Han, MD; Jennifer L. Sabol, MD; John R. Bumberry, MD; Ilana Gareen, PhD; Bradley S. Snyder, MS; Lynne I. Wagner, PhD; Kathy D. Miller, MD; Joseph A. Sparano, MD; Christopher Comstock, MD

ECOG-ACRIN cancer research group

Reshaping the future of patient care

Figure. Flow Diagram of a Nonrandomized Clinical Trial

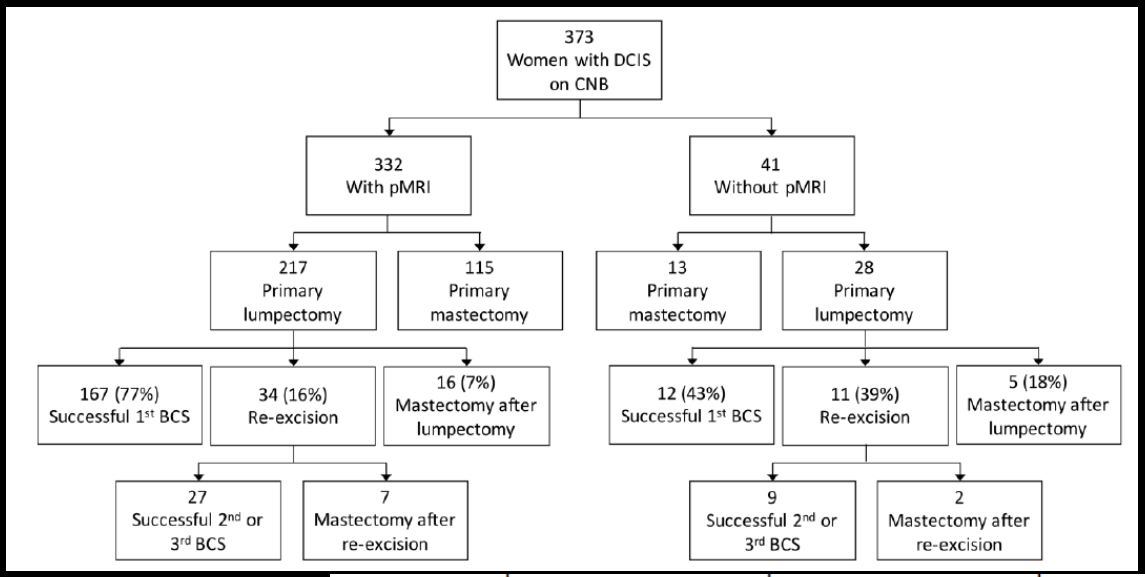


339 women w/ CNB-diagnosed pure DCIS

- MRI findings → <½ of mastectomies
- 285 attempted WLE after MRI
  - 274 successful (96%)
  - 215 single successful WLE (75%)
- 91% compliance with recommendation for no radiation on basis of MRI and Oncotype Score

Lehman et al. JAMA Oncology Jan 17 PMID: 30653209

UW study: Lam et al



- pMRI vs. no-pMRI
  - fewer surgeries (1.2 vs. 1.5, P<0.001)
  - single successful BCS (77% vs. 43%, p<0.001)

Variable	Present Study (N=217)	Prior Studies: Morrow JAMA 2009 (N=359)	Prior Studies: Langhans JAMA 2017 (N=727)	Differences: Present study vs. Morrow JAMA 2009 Value*	(95% CI)	p-value	Differences: Present study vs. Langhans JAMA 2017 Value*	(95% CI)	p-value
Years	2004-2013	2005-2007	2010-2013						
Source	Institutional Database	SEER Registry	Danish National Registry						
Successful BCS	194 (89.4%)	318 (88.0%†)	650 (89.4%)	1%	(-4, 7%)	0.69	0%	(-5, 5%)	>0.99
Single successful BCS	167 (77.0%)	218 (57.3%†)	456 (62.7%)	20%	(11, 27%)	**<0.001**	14%	(7, 21%)	**<0.001**
Number of surgeries	1.3 ± 0.5	1.5 ± 0.6	1.4 ± 0.6	-0.22	(-0.31, -0.12)	**<0.001**	-0.17	(-0.25, 0.08)	**<0.001**

*Values are the calculated as the difference in percentage or mean number of surgeries (present study minus the prior study);

†Percentages are weighted to account for the survey design

Presented at SSO 2016, manuscript in press

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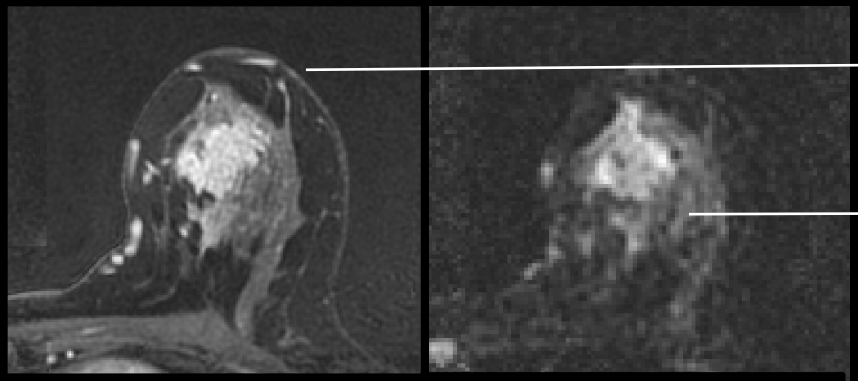
Can MRI inform DCIS Biology & Risk?

MRI Feature	Histology
Focus of enhancement	Small, low grade, ER+
High ADC	Low nuclear grade
Linear ductal lesions	High Ki-67
Heterogeneous enhancement	ER+, low CD68
Clumped regional NME	Large, ER-, high Ki-67

[1]Esserman *et al.* J Clin Oncol, 2006. 24(28): p. 4603-10.
[2]Iima, M., *et al*. Radiology, 2011. 260(2): p. 364-72.
[3]Yamada *et al.* Radiographics, 2010. 30(5): p. 1183-98.
[4]Rahbar *et al*. Radiology, 2012. 263(2): p. 374-82.

Modeling MRI Features to Predict Nuclear Grade

High nuclear grade DCIS lesion

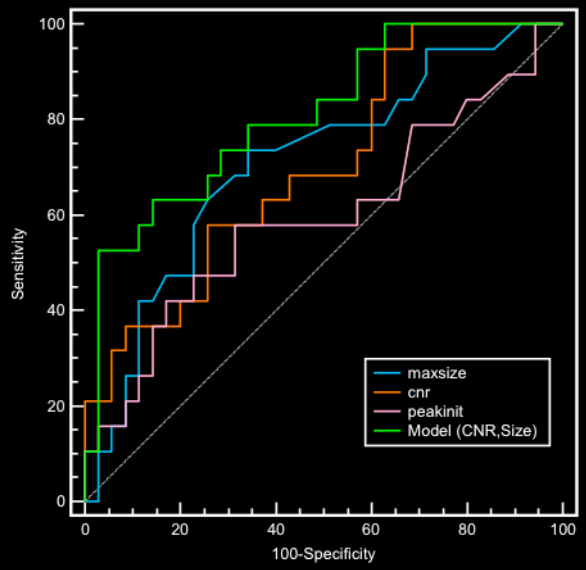


DCE MRI DWI

Maximum lesion size
Peak enhancement

DWI signal (CNR)
Apparent Diffusion Coefficients

Best model combined maximum DCE MRI lesion size and DWI CNR



Rahbar, H., et al. Radiology, 2012. 263(2): p. 374-82.

MRI Radiomics to Predict Biology

Computer-Aided Heterogeneity Analysis in Breast MR Imaging Assessment of Ductal Carcinoma In Situ: Correlating Histologic Grade and Receptor Status

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Purpose: To identify breast MR imaging biomarkers to predict histologic grade and receptor status of ductal carcinoma in situ (DCIS).

- 55 DCIS lesions visible on MRI, 44% HNG, 80% ER+, 18% her2+
  - Smaller surface-to-area ratio predicted HNG
  - 17 radiomics metrics predicted her2 amplification
  - No features predicted ER+

Chou et al. JMRI 2017. 46:1748-1759

High-risk Tissue Microenvironment

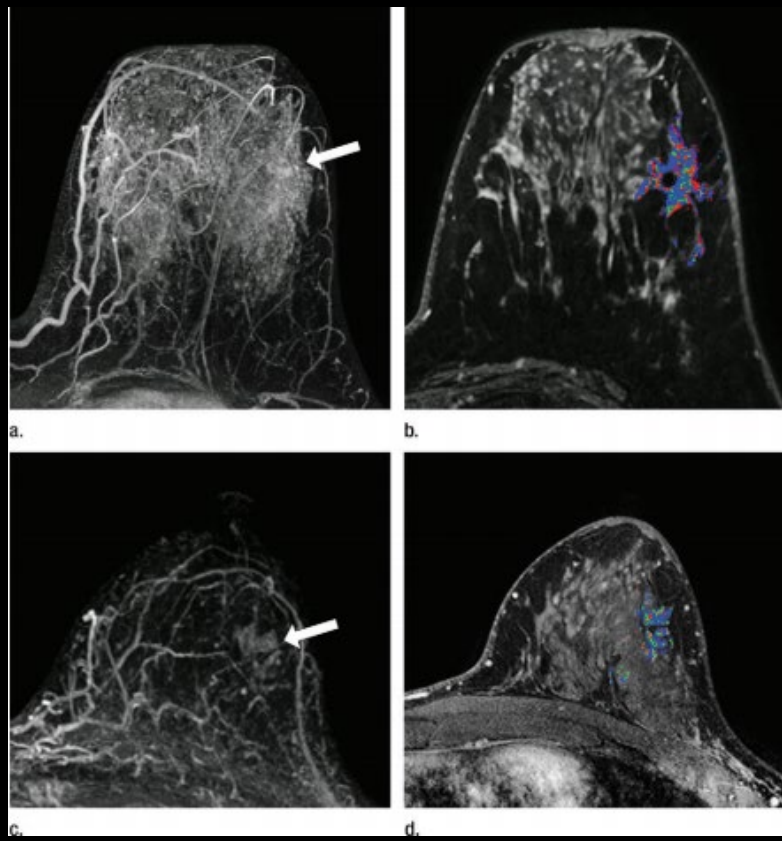
- Microenvironment role is underexplored to date
- Increasing evidence that normal tissue features, including BPE[1,2,3], may be a marker of breast cancer development
- BPE adjacent to DCIS lesions may be a marker of DCIS recurrence[4]
  - 215 cases of pure DCIS →15 ipsilateral recurrences
  - BPE AUC = 0.885

1. Dontchos et al. Radiology 2015 Aug; 276 (2):371-80
2. King et al. Radiology 2011. July: 260 (1): 50-60
3. Grimm et al. Academic Radiology. 2018.
4. Kim et al Radiology. 2014 Mar;270(3):699-707.

Radiology

Ductal Carcinoma in Situ:
Quantitative Preoperative Breast MR Imaging Features Associated with Recurrence after Treatment[1]

MRI Parameter	Recurrence Case Median (Range)	Non-Recurrence Control Median (Range)	Adjusted P-Value	Odds Ratio
FTV (cm^3)	9.3 (0.5-43.7)	1.3 (0.4-5.0)	0.01	∞
Lesion peak SER	1.7 (1.2-1.9)	1.2 (0.9-1.7)	0.03	4.3
BPE Mean (%)	58 (31-86)	41 (27-70.5)	0.02	20.6



- Smaller volume DCIS lesions with lower peak SER and lower ipsilateral BPE were less likely to recur after treatment

Luo et al. Radiology 2017. Dec; 285(3) PMID: 28470744

MRI to Improve DCIS management

- Can MRI guide biopsies?
  - Newer data are promising, not ready for practice
  - Change in BI-RADS thresholds?

MRI to Improve DCIS management

- Can MRI guide surgeries?
  - MRI is more accurate than MG for EOD evaluation
  - Sites that take a multidisciplinary approach are more likely to benefit practically (fewer surgeries)
  - Future research needs to control for important confounding factors (QOL, surgeon preference, etc)

MRI to Improve DCIS management

- Can MRI inform biology and risk?
  - Preliminary studies
    - Can correlate with surrogate markers of risk
    - Independently predict risk of recurrence
  - Future Studies
    - MR Radiomics
    - Standardize and validation of metrics in multi-center trials

Summary

- DCIS is a controversial breast pathology
- Imaging of DCIS reflects its heterogeneous biology
- MRI is the most sensitive tool for DCIS detection, and preferentially identifies higher grade disease
- MRI has the potential to assist in decreasing overdiagnosis and overtreatment of DCIS

Thank you!

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