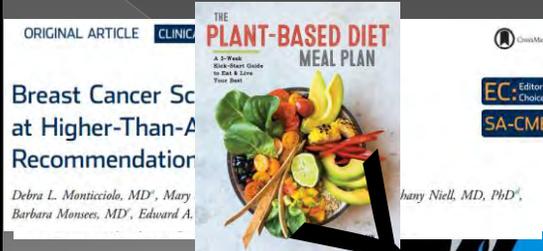


Indications for Breast MRI in 2019



Breast Imaging Fellowship Program
ucp.med.uchicago.edu

What's new in 2019?



ORIGINAL ARTICLE CLINICAL
Breast Cancer Screening at Higher-Than-Average Risk: A Systematic Review and Meta-Analysis
Debra L. Monticciolo, MD¹, Mary Barbara Monsees, MD¹, Edward A. Hwang, MD, PhD¹, and Anthony Niell, MD, PhD¹

THE PLANT-BASED DIET MEAL PLAN
A 3-Week, 100-Calorie, Plant-Based Meal Plan to Eat & Live Your Best

CheckMark
EC Editor's Choice
SA-CME

Objectives

- Understand what is new to the breast MRI indications in the last few years
- How did high risk screening with MRI make it to the ACR/SBI guidelines
- Obtain a better understanding of personalized screening using MRI and Ultrafast MRI

ACR recommendations for breast MRI

- Screening
- Extent of disease
- Additional evaluation of clinical or imaging findings: e.g. problem solving, nipple discharge

1. Breast MRI Screening

What is average, intermediate, and high risk?
When?
Why?
How?



Radiology ORIGINAL RESEARCH • BREAST IMAGING
Performance of Screening Breast MRI across Women with Different Elevated Breast Cancer Risk Indications
Dorothy A. Sippes, MD, MPH¹ • Kishore S. Bork, MD² • Sarah F. Merzelle, PhD³ • Geoffrey M. Badaloff, MD⁴ • Christine Edwards, MD⁵ • Zoe Guim, MA⁶ • Kevin S. Hughes, MD⁷ • Constance D. Lehman, MD, PhD⁸

To evaluate screening breast MRI performance across women with different elevated breast cancer risk indications.

Define High Risk women

- Evidence-based guidelines recommend adjunctive screening with MRI
- Adding MRI demonstrates sensitivities of 71%–100%
- Added by ACS in 2007 and NCCN guidelines since 2017

- (1) Women who are BRCA mutation carriers and their first degree, untested relatives
- (2) Li-Fraumeni and other high-risk predisposition syndromes and polygenic mutations such as Cowden, CHEK-2, PALB2
- (3) Women who received radiation to the chest between the ages of 10–30 years
- (4) **≥0.25% or greater lifetime risk of breast cancer** based on risk models heavily reliant on family history (eg, BRCAPRO, Tyrer Cuzick)

Define Intermediate Risk women

- (1) Women with personal history (PH) of breast cancer
- (2) Personal history of high risk lesion (HRL) such as ADH, ALH, LCIS.
- (3) Women with dense breasts
- (4) Women with approximately **15%–20% lifetime risk of breast cancer** based on risk models heavily reliant on family history (eg, BRCAPRO)

Sippo et al
Radiology 2019

- n= 5170 screening breast MRI exams from 2637 patients
- BRCA/chest XRT
- PH
- HRL
- FH

	BRCA/RT	PH	HRL	FH	Total
CDR	26	12	15	8	13
PPV3	41	36	36	36	29
Sensitivity	84	88	75	77	84
Specificity	92	95	92	91	93

Performance of screening MRI according to breast cancer risk indications

Characteristics of screen detected cancers

Table 4: Characteristics of Screening-detected Breast Cancer

Parameter	BRCA/RT (n = 16)	Personal History (n = 35)	High-Risk Lesion (n = 6)	Family History (n = 10)	Total (n = 67)*
Diagnosis	6	8	1	1	16/67 (24)
DCIS	9	24	3	8	44/67 (66)
ILC	1	2	2	1	6/67 (9)
IMC	0	1	0	0	1/67 (1)
Invasive cancer size	9	20	3	7	39/51 (76)
≤10 mm	1	7	2	2	12/51 (24)
11–20 mm	1	7	2	2	12/51 (24)
Minimal cancer	11	18	2	3	34/49 (70)
Yes	5	17	4	7	33/49 (67)
No	6	1	0	0	7/49 (14)
Axillary lymph node status ^a	13	23	4	9	49/53 (92)
Negative	0	3	1	0	4/53 (8)
Positive	13	20	3	9	45/53 (84)
Hormone receptor status	11	30	6	6	53/67 (79)
ER positive ^b	11	26	6	6	49/53 (92)
PR positive ^b	0	3	0	0	3/43 (7)
HER2 positive ^b	0	3	0	0	3/43 (7)
Cancer stage ^c	6	8	1	1	16/67 (24)
I	10	25	5	0	40/67 (59)
II	0	1	0	0	1/67 (1)
III	0	0	0	0	0/67 (0)
IV	0	1	0	0	1/67 (1)

Sippo et al
Radiology 2019

Discussion

- Evidence of difference in screening breast MRI performance among BRCA/RT or PH or HRL
- No difference in CDR and PPV3 for biopsies performed for women with PH of breast cancer and HRL compared with BRCA mutation and/or RT.
- Worse test performance was found in women with only FH of breast cancer, with lower CDR and PPV compared with those with BRCA mutation/RT.
- Screening breast MRI should be strongly considered for patients with a personal history of breast cancer

Supporting data

multiple publications have shown favorable screening MRI performance in women with a personal history of breast cancer or high-risk lesion.

Author	Comparison	CDR	PPV3
Lehman et al	PH vs. genetic risk	17/100	19-25%
Azari-Kleinman et al	PH vs. genetic risk	18/100	14 – 15%
Schwartz et al	HRL only	12-16/1000	20-24%
Friedlander et al	HRL only	12-15/1000	21-24%

Supporting data

Data from Vreeman et al:

Risk Group	CDR	PPV3
BRCA	21/ 1000	high
PH	12/ 1000	moderate
FH	6/ 1000	low

Lowest PPV was noted in the family history of breast cancer group



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Proven wider acceptance

- Clinical evidence has grown supporting screening breast MRI in women with personal history of breast cancer or a cancer diagnosis before age 50 years.
- 2017 NCCN and 2018 ACR recommendations added their support to consideration of annual screening breast MRI in women with HRL.



1. Breast MRI Screening

- High-risk patients
- Intermediate-risk patients
- Newly diagnosed breast malignancy can detect occult malignancy in the contralateral breast in at least 3% to 5% of patients
- Breast augmentation and Implant evaluation

Case 1:

Clinical Information: 48 year old female with personal history of BRCA 1 mutation carrier. Dense breasts.

CURRENT MRI

PREVIOUS MRI (6 months prior)

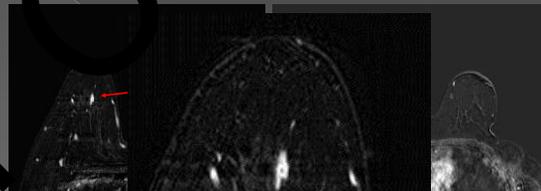


Figure 1. 11 West-
Image: Irregular heterogeneously enhancing mass measuring 10 mm is seen in the right breast 12:00 position (**red arrow**).

in subtraction
Image from 6 months prior: A small focus was seen at right breast 12:00 position (**yellow arrow**), however was not thought to be suspicious given background additional foci in the same breast which have been stable over past 2 years. 6 month follow up MRI was recommended at that time.

WILL YOU BIOPSY THIS LESION?

Pathology showed grade 1 IDC

CONCORDANT?

YES- Lesion demonstrates interval increase in size, suspicious features on MRI (spiculated morphology).

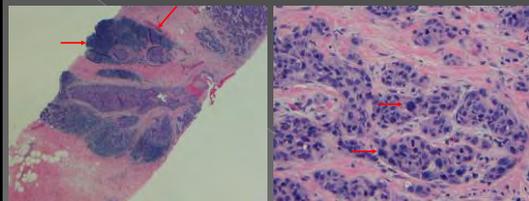


Figure 5, low power H&E: Clusters of ducts and tubules with loss of architecture and malignant cells in loose nests (**red arrows**).

Figure 6, high power H&E: Multiple pleomorphic and mitotic nuclei (**red arrows**) suggesting grade 3 IDC.



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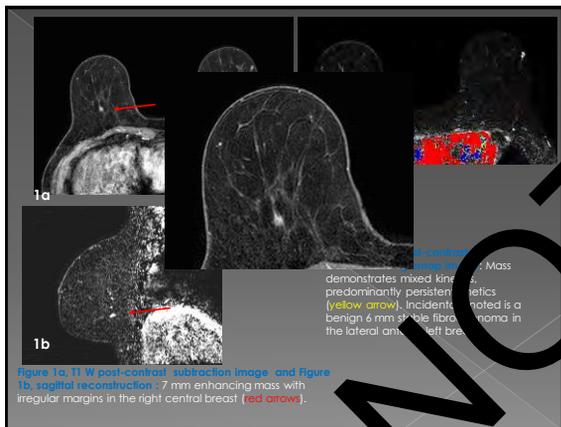
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Discussion

- This case shows the importance of screening high risk patients with MRI to pick up small invasive cancers that are mammographically occult.
- The small focus was seen on the MRI 6 months ago but there were a few other similar foci in the vicinity hence it was not thought to be BIRADS-4.

Case 2:

Clinical Information: 66 year old female with personal history of right breast cancer in 2006 s/p lumpectomy and radiation. Annual surveillance MRI performed.

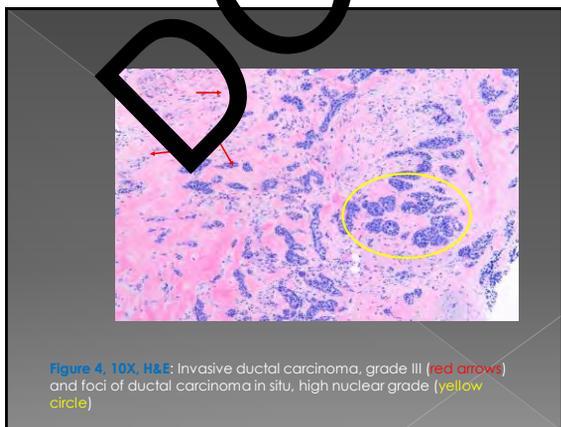


WILL YOU BIOPSY THIS LESION?

YES- After biopsy pathology showed high grade DCIS with IDC-1

CONCORDANT?

YES- Lesion demonstrates suspicious features on MRI (spiculated morphology mass with heterogeneous enhancement) against a quiet background.



Yay!

Chicago Tribune
Do you have dense breast tissue? New Illinois law will require doctors to tell you after mammograms.



Illinois is the 36th state in the nation to pass a law about breast density notification, and the bill sailed through the state legislature with no opposition. Still, the American Medical Association opposes such laws in general, saying that there is no medical consensus on a reliable method for judging breast density and no clinical guidelines that recommend more screening for women just because of dense tissue. The law may also lead to questions about what women should do once they have the information.

What to do next?

A health system may recommend such women receive additional screenings, such as through ultrasounds or MRIs. In Illinois, insurance companies must cover certain supplemental screenings for women with dense breast tissue.

The American College of Radiology supports informing women about their breast density, but warns that supplemental screening "should be a thoughtful choice after a complete risk assessment, not an automatic reaction to breast density itself."

The legislation, signed by Gov. Bruce Rauner on Friday, was spearheaded by Glenview resident and breast cancer survivor Patti Beyer. Beyer doesn't have a family history of breast cancer, but she does have dense breast tissue – a risk factor for the disease. According to the American Cancer Society, women who have dense breast tissue have a "slightly" higher risk of developing breast cancer than those who do not.

Educate and inform women of their breast density in order to achieve their best chances for early detection of breast cancer.

MRI Screening Techniques

VOLUME 32 NUMBER 22 AUGUST 1 2014
 JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Abbreviated Breast Magnetic Resonance Imaging (MRI): First Postcontrast Subtracted Images and Maximum-Intensity Projection—A Novel Approach to Breast Cancer Screening With MRI

Christiane K. Kuhl, Simone Schindler, Kevin Strobel, Hans H. Schild, L. Raff-Diener Hilgers, and Herbert B. Bodeg

- Routine protocol (1 plus 4 plus ultrafast)
- Research purposes, we do Ab-MRI (1 plus 4 plus MRI)

AB-MRI Sensitivity and Specificity

Kuhl et al

Metric	MIP images*		FAST images		FDP†	
	%	95% CI	%	95% CI	%	95% CI
First screening round (n = 643)						
Sensitivity	80.0	58.7 to 99.7	100.0	71.5 to 100.0	100.0	71.5 to 100.0
Specificity	NA	NA	84.4	81.8 to 98.4	84.9	80.4 to 90.6
NPV	NA	NA	75.4	18.0 to 92.2	23.3	0.4 to 59.8
PPV	39.7	18.2 to 100.0	100.0	39.1 to 100.0	100.0	100.0
False screening period (n = 600)						
Sensitivity	90.0	58.7 to 99.7	100.0	71.5 to 100.0	100.0	71.5 to 100.0
Specificity	NA	NA	84.3	80.1 to 96.0	85.0	81.7 to 95.7
NPV	NA	NA	24.6	12.8 to 39.5	22.0	12.3 to 36.0
PPV	89.0	98.1 to 100.0	100.0	99.3 to 100.0	100.0	98.2 to 100.0

Abbreviations: FAST, first postcontrast subtracted; FDP, full diagnostic protocol; MIP, maximum-intensity projection; NA, not applicable; NPV, negative predictive value; PPV, positive predictive value.
 *MIP images were read as positive or negative depending on whether significant enhancement was observed; not applicable for diagnostic accuracy based on MIP images.

Current Imaging Protocol

MRI FULL PROTOCOL WITH ULTRAFAST

ABBREVIATED MRI without ULTRAFAST

Personalized screening (WISDOM TRIAL)

WISDOM Trial Starting Recommendations

Screening Recommendation	Criteria/Threshold
No screening	• Women aged 40-49 with a <1.3% 5-year risk of developing breast cancer
Biennial mammogram	• Women 250 years old • Women with a ≥1.3% 5-year risk (risk of an average 50 year-old woman)
Annual mammogram	• Women aged 40-49 with extremely dense breasts • Women at a ≥1% 5-year risk of developing ER-breast cancer based on susceptibility SNPs
Annual mammogram + annual MRI	• Women who are BRCA1/2, TP53, PTEN, STRK1, CDH1, ATM, PALB2 or CHEK2 positive • Women with a ≥6% 5-year risk (risk of an average BRCA carrier) • Women with a history of mantle radiation



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Springer **EUROPEAN RADIOLOGY**

EUR Rad: 2016; 25(12): 3665-3678
Published online 2016 May 23. doi: 10.1007/s00330-016-3807-z
PMCID: PMC4636525
PMID: 26952130

Breast MRI: EUSOBI recommendations for women's information

Ribeiro M, Milano C, Galloway S, Pasral A, Balizer U, Koch R, Catherine Dolio, Eleanor Cornhill, Andrea Esposito, Eva Faltensberg, Stefan Franz, Michael H. Fruchter, Fenna J. Gilbert, Thomas H. Helberich, Sylvia H. Heywang-Kobrunner, Julia Campos-Hernero, Choklana K. Kuhl, Laura Mantovich, Federica Pediconi, Pietro Panizza, Luis J. Pina, Raed M. Pinnawel, Katja Pinker-Domszay, Pier Stefano, Francesco Santilli, and for the European Society of Breast Imaging (EUSOBI), with language review by Europa Donna-The European Breast Cancer Coalition

Table 1
Indications for breast MRI

Screening of women at high risk of breast cancer
Preoperative staging of newly diagnosed breast cancer (ipsilateral and contralateral)
Evaluation of the effect of neoadjuvant chemotherapy
Evaluation of women with breast implants
Occult primary breast carcinoma (search for breast cancer in patients with metastases and negative mammography and ultrasound)
Suspected local recurrence*
Problem solving (equivocal findings at mammography/ultrasound)**

Staging MRI

- Has made it to the list of breast MRI indications a while back
- Breast cancer subtypes have become essential to estimate prognosis and guide systemic therapy.
- CAD and AI based softwares available e.g. Qlarity

FULL PAPER
Role of MRI in the staging of breast cancer patients: does histological type and molecular subtype matter?

ALMIR G V BITENCOURT, PhD, NARA P PESSIERI, MD, LUCIANA FRANÇA, MD, CAROLINE B SILVA, MD, JOCIANA PALUDO, MD, HUGO L S PAIVA, MD, LUCIANA GRAZIANO, MD, CAMILA S GUATELLI, MD, JULIANA A SOUZA, MD and SILVIA F HENRIQUEZ, MD

CASE 3:

Clinical Information: 71 year old female with known ILC in left breast undergoes staging MRI.

Figure 2. T1 W axial post-contrast subtraction image: Irregularly shaped enhancing mass at the 9:00 position of the left breast with mixed kinetics, corresponding to patient's biopsy proven ILC (blue arrow).

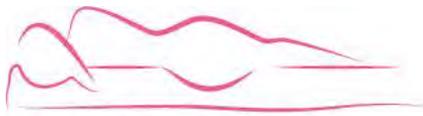
WILL YOU BIOPSY THIS LESION?

YES- Irregular heterogeneous enhancing mass in patient with known ILC in contralateral breast. After biopsy pathology showed LCIS and invasive lobular carcinoma

CONCORDANT?

YES- Synchronous ILC in opposite breast can be seen in approximately 10% of cases

Figure 4. 10X, H&E: Lobular carcinoma in situ, classic type (LCIS) and invasive lobular carcinoma, grade I. Atypical proliferation of monotonous, bland epithelial cells which distend the lobules (red arrow) with Pagetoid extension into adjacent duct (yellow arrow). Intervening stroma also shows invasive lobular carcinoma, grade I (green arrow).



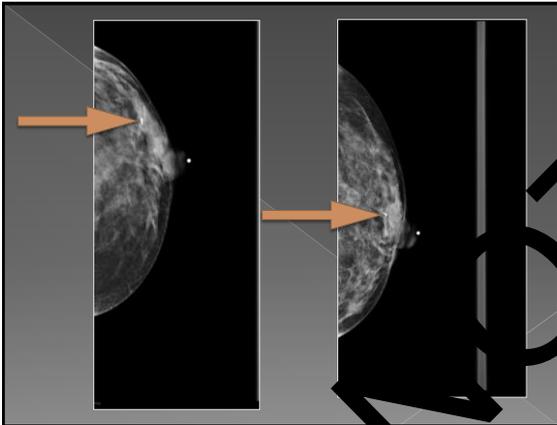
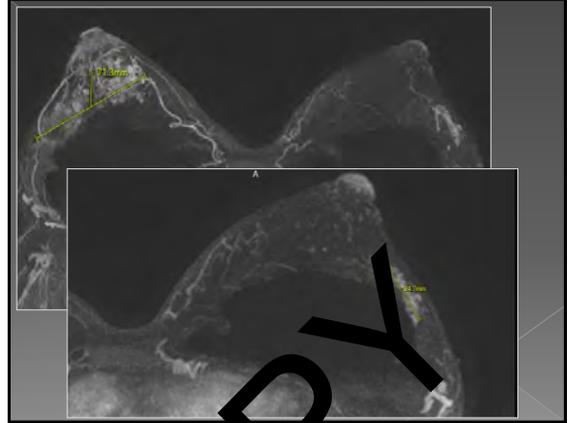
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CASE 4:

Clinical information: 47 year old female presents with known right breast DCIS for staging MRI. No family history of breast cancer.

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Concordant!

Biological Pathology Report

FINAL PATHOLOGIC DIAGNOSIS A. Breast, left @ 2:00, ultrasound-guided core biopsy: - High grade Ductal carcinoma in situ

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CASE 5

70 yo male presents with new right breast cancer, for staging MRI

41

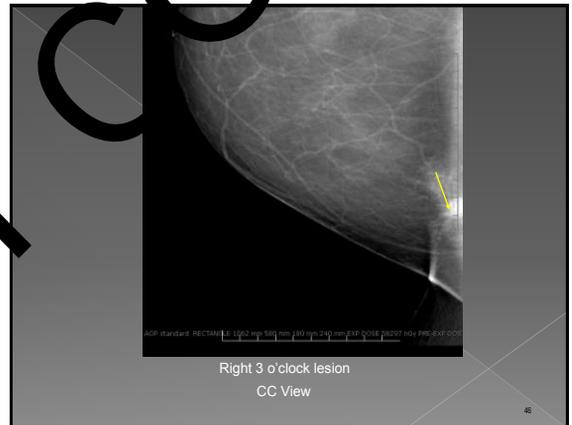
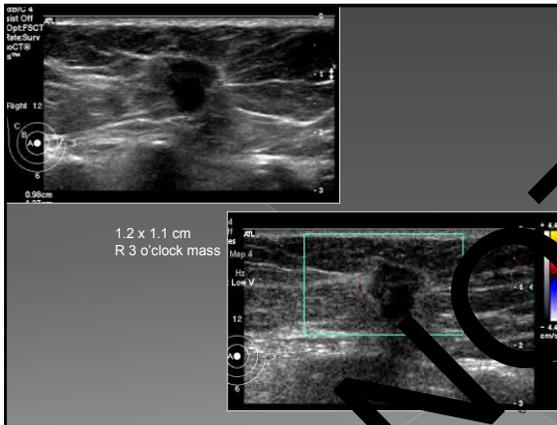
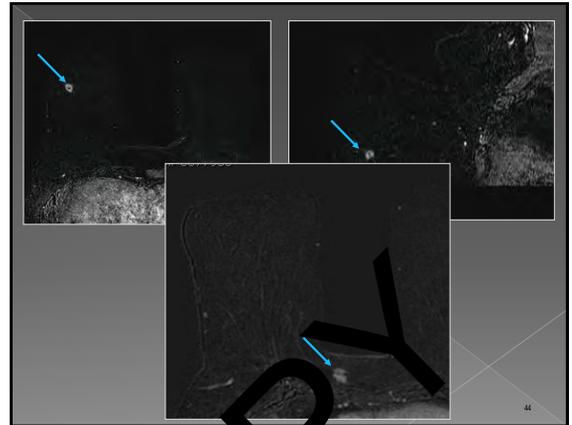
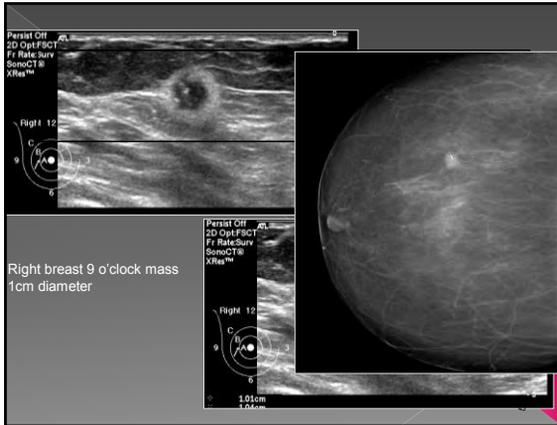


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UChicago Medicine

Imaging neoadjuvant chemotherapy response in breast cancer. Bonnie Joe et al. Radiology: Volume 285: Number 2—November 2017

- Goal of imaging is to determine the presence and size of residual disease
- for preoperative local therapy planning
- to identify (NON-RESPONDERS) patients who are not benefiting and direct them to alternative systemic therapy or to proceed with surgery
- The importance of quantitative imaging for response assessment has been recognized
- In addition to establishing diagnostic accuracy and precision data, it is important to incorporate patient outcomes as study end points to demonstrate the added value of imaging
- DCE-MR imaging of the breast offers the highest diagnostic accuracy in primary tumor therapy response assessment among the currently established methods (physical examination, mammography, and US).
- Advances in the field of radiogenomics, which links imaging phenotypes to tumor gene expression patterns, will help elucidate the most clinically useful imaging approach to assess neoadjuvant therapy response
- SimBioSys (MRI images, pathology results, receptor status, microenvironment) features to generate TUMORSCOPE

UChicago Medicine

Imaging neoadjuvant chemotherapy response in breast cancer. Bonnie Joe et al. Radiology: Volume 285: Number 2—November 2017

Technique	Biologic Parameter	Feasibility for Clinical Practice	Advantages	Challenges/Drawbacks
US and Phased-array DCE-MR imaging	Tumor vascularity	Moderate for US-based analysis; Pharmacokinetic analysis remains investigational	Decreased diagnostic cost with widely available systems for surface US; Real-time parameters	Response assessed using quality without uniform artifact; Difficult to standardize techniques for pharmacokinetic analysis; Requires additional processing to obtain pharmacokinetic and US parameters
Diffusion-weighted MRI imaging	Tumor cellularity	Strong, in many centers; Difficult practical	No ionizing radiation; Minimal requirement	Response assessed using quality and not measurement; Image artifacts; Inconsistent as standardized for b-values; Requires additional processing to obtain ADC values for quantitative analysis
Proton MR spectroscopy	Choline metabolism	Prostate, routine investigation; Not in breast cancer; Minimal requirement, but alignment of spectrometer volume of interest often based on contrast-enhanced images	Highly sensitive to hyperproliferation	Response assessed using quality and not measurement; Image artifacts; Difficult to standardize technique
FDG-PET	Glucose metabolism	Strong, in many centers; Difficult practical	Highly sensitive to hyperproliferation	No US approval for PET relative values among breast subtypes
PER-PET	Tumor proliferation	Moderate, remains investigational; Not in breast cancer; Minimal requirement	Correlates with Ki67 biomarker for proliferation	No US approval for PET relative values among breast subtypes
FAUCI-PET	Amino acid metabolism	Feasible, FDA-approved tumor and clinically for prostate cancer imaging	Strong uptake in myxoid stromal components	Limited experience for breast cancer response evaluation
¹⁸ F-αGalNAc-PET	Choline metabolism	Feasible, FDA-approved tumor and clinically for prostate cancer imaging	High uptake in response to treatment in HER2+	Short half-life limits diagnostic, limited experience for breast cancer response evaluation



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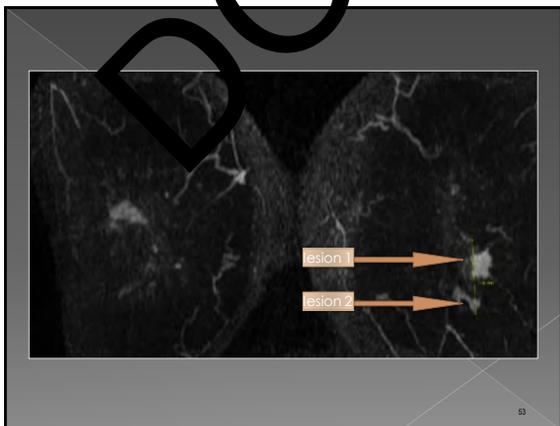
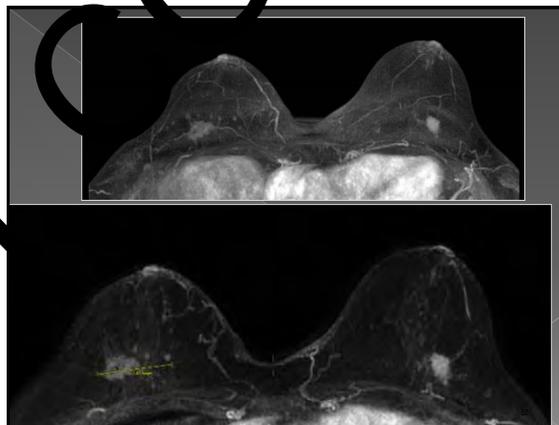
2. Extent of disease

- a. To determine multifocality and multicentricity in patients with invasive carcinoma and DCIS.
- b. Invasion deep to fascia –to define the relationship of the tumor to the muscular fascia and identify any extension into the pectoralis major, serratus anterior, and/or intercostal muscles.
- c. Postlumpectomy with positive margins –useful for subsequent surgical planning to identify occult multicentric or multifocal malignancy in patients whose pathology specimens demonstrate close or positive margins.
- d. Neoadjuvant chemotherapy – Extremely useful before, during, and/or after chemotherapy to evaluate treatment response and the extent of residual disease prior to surgical treatment.

3. Additional evaluation of clinical or imaging findings

- a. Recurrence of breast cancer
- b. Metastatic cancer when the primary is unknown and suspected to be of breast origin –
- c. Lesion characterization –MRI may be indicated when other diagnostic imaging examinations, such as US and MG (with or without 3D), and physical examination are inconclusive
- d. Pathologic nipple discharge – MRI may also be considered when the clinical suspicion is very high and MG and US are negative

CASE 6
Staging MRI for right breast cancer



Nipple discharge

Ductograms? (DEAD) may detect an underlying abnormality in 14%

APPROPRIATE USE CRITERIA

ACR Appropriateness Criteria® Evaluation of Nipple Discharge

Expert Panel on Breast Imaging: *Su-Ju Lee, MD¹, Sunita Trikha, MD², Linda Moy, MD³, Paul Baron, MD⁴, Roberta M. diFlorio, MD, MS⁵, Edward D. Green, MD⁶, Samantha L. Heller, MD, PhD⁷, Anna I. Holbrook, MD⁸, Alana A. Lewin, MD⁹, Ana P. Lourenco, MD¹⁰, Bethany L. Niell, MD, PhD¹¹, Priscilla J. Slanetz, MD, MPH¹², Ashley R. Stuckey, MD¹³, Nina S. Vincoff, MD¹⁴, Susan P. Weinstein, MD¹⁵, Monica M. Yepes, MD¹⁶, Mary S. Newell, MD¹⁷*



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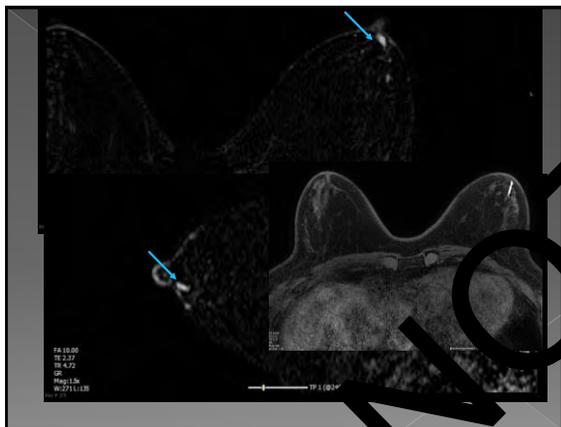
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Nipple discharge

- Nipple discharge has recently emerged as a new indication for breast MRI
- And, an effective alternative to galactography
- Better tolerated by patients?
- overall sensitivity for breast cancer ranging from 90 to 99%

Case 7

47 year old with pathologic left nipple discharge with negative MG and US.



FINAL PATHOLOGIC DIAGNOSIS:
A. Left breast 5:00 location: ultrasound-guided core biopsy:
-Fragments of solid papillary carcinoma, in situ

Summary

- ACR/SBI recommendations are in favor of breast MRI screening for patients with Phyllodes tumor, HRL, genetic mutations.
- Ultrafast and Ab-MRI have strong potential in screening these individuals.
- Risk stratification studies have initiated such as WISDOM and hopefully we can perform the right test for the right reason.
- But...still looking for the perfect test!

Thank you!

kkulkarni@radiology.bsd.uchicago.edu

