DIPARTIMENTO DI SCIENZE
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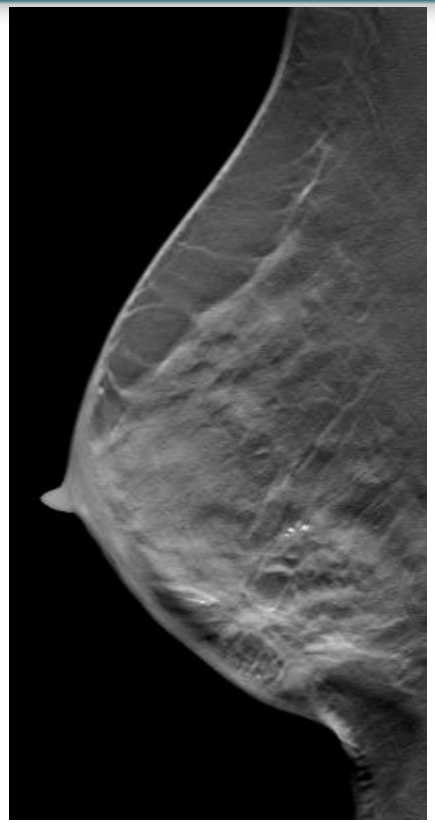


Ductal Carcinoma In Situ

Radiological aspects, including mammography screening, MR-mammography, follow-up after treatment.

Dr. Veronica Rizzo
Sapienza, University of Rome
Department of Radiological, Oncological and Pathological Sciences

Ductal Carcinoma in situ

“Ductal carcinoma in situ (DCIS) is a malignant, clonal proliferation of cells growing within the basement membrane-bound structures of the breast and with no evidence of invasion into surrounding stroma.”

Ductal carcinoma in situ (DCIS): pathological features, differential diagnosis, prognostic factors and specimen evaluation.
Sarah E Pinder
Modern pathology (2010)

Mod Pathol. 2010 May;23 Suppl 2:S1-7. doi: 10.1038/modpathol.2010.56.

Intraductal proliferative lesions of the breast: morphology, associated risk and molecular biology.

Ellis IO[1].

Recommended system for classification of DCIS

High Nuclear Grade DCIS

This is the easiest pattern to recognize.[4] Cells have pleomorphic, irregularly spaced and usually large nuclei exhibiting marked variation in size, irregular nuclear contours, coarse chromatin and prominent nucleoli. Mitoses are frequent and abnormal forms may be seen. High-grade DCIS may exhibit several growth patterns; most commonly as a solid sheet of cell lining the duct and with comedo-type central necrosis that frequently contains deposits of amorphous calcification.

Intermediate Nuclear Grade DCIS

This type cannot be assigned easily to the high or low nuclear grade categories. The nuclei show mild to moderate pleomorphism, which is less than that seen in the large cell variety, but lacks the monotony of the small cell type. The growth pattern may be solid, cribriform or micropapillary.

Low Nuclear Grade DCIS

These types are composed of monomorphic, evenly spaced cells with roughly spherical, centrally placed nuclei and inconspicuous nucleoli. The nuclei are usually, but not invariably, small. Mitoses are few and there is rarely individual cell necrosis. The cells are generally arranged in micropapillary and cribriform patterns.

Mixed Types of DCIS

A proportion of cases of DCIS exhibit features of more than one histological subtype. One of the advantages of classifying DCIS according to nuclear grade is that when there are variations in growth pattern but a dominant cell type, the lesion can be classified on the basis of nuclear grade. Foci of differing nuclear grade may be seen, but such variation in cell type is unusual, although if present, the case should be classified according to the highest nuclear grade.

CHANGING THEORY

From a ***Unique Pathologic Continuum*** theory

→ **IDC**

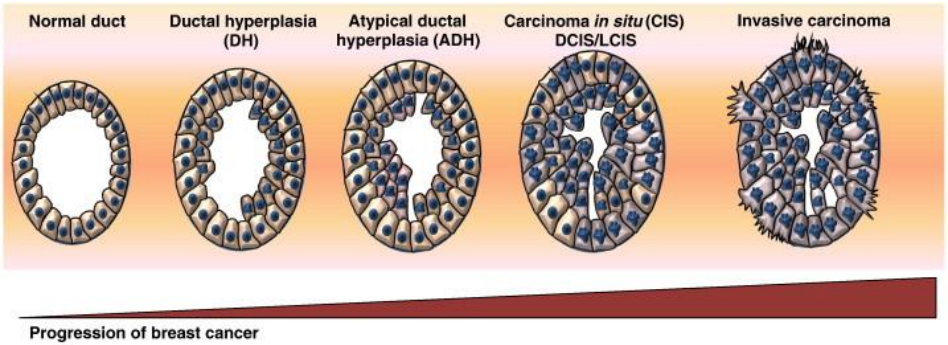
→ **High-grade DCIS**

→ **Non-high-grade DCIS**

→ **ADH**

→ **DH w/o atypia**

Normal tissue



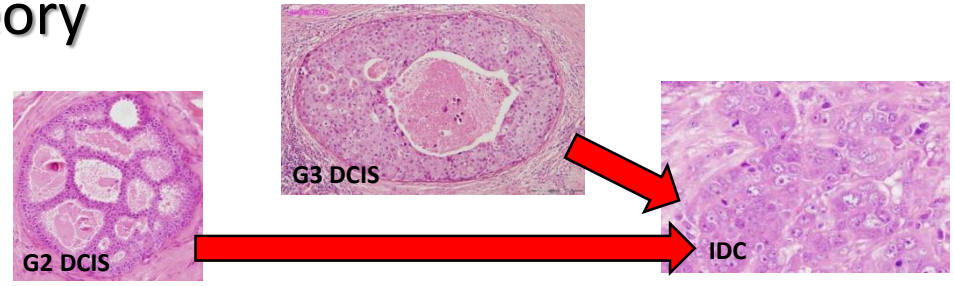
Mukhopadhyay et al, Biochim Biophys Acta 2011

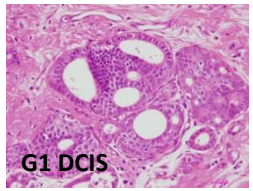
To a potential ***Double Disease*** theory

(High-grade DCIS) → IDC

versus

(Non-high-grade DCIS) → IDC





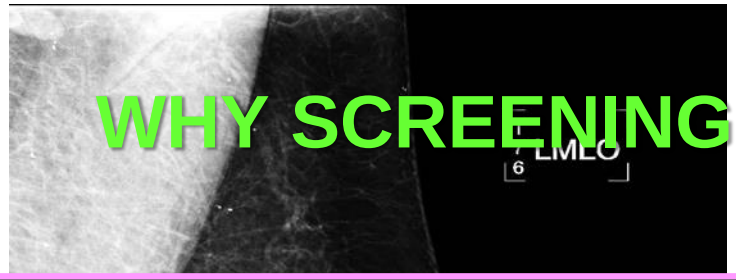
http://www.breastpathology.info/index.html

To detect DCIS

1) *Patient history and risk factors*
2) *Mammography*
3) *Digital breast tomosynthesis*
4) *Ultrasound*
5) *MRI*
6) *Biopsy*

DCIS is primarily diagnosed at imaging because it is most often clinically occult

WHY SCREENING MAMMOGRAPHY?



Earlier diagnosis

↓

Earlier (and more conservative) treatment

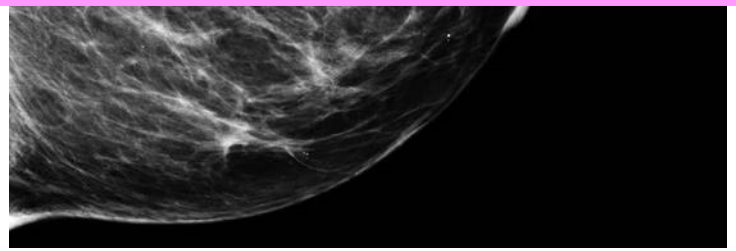
↓

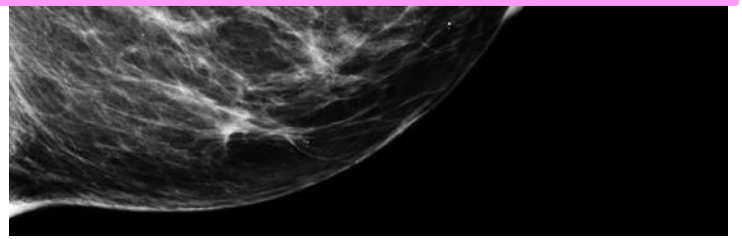
Higher survival

↓

Mortality reduction

THINGS ARE NOT SO SIMPLE…!





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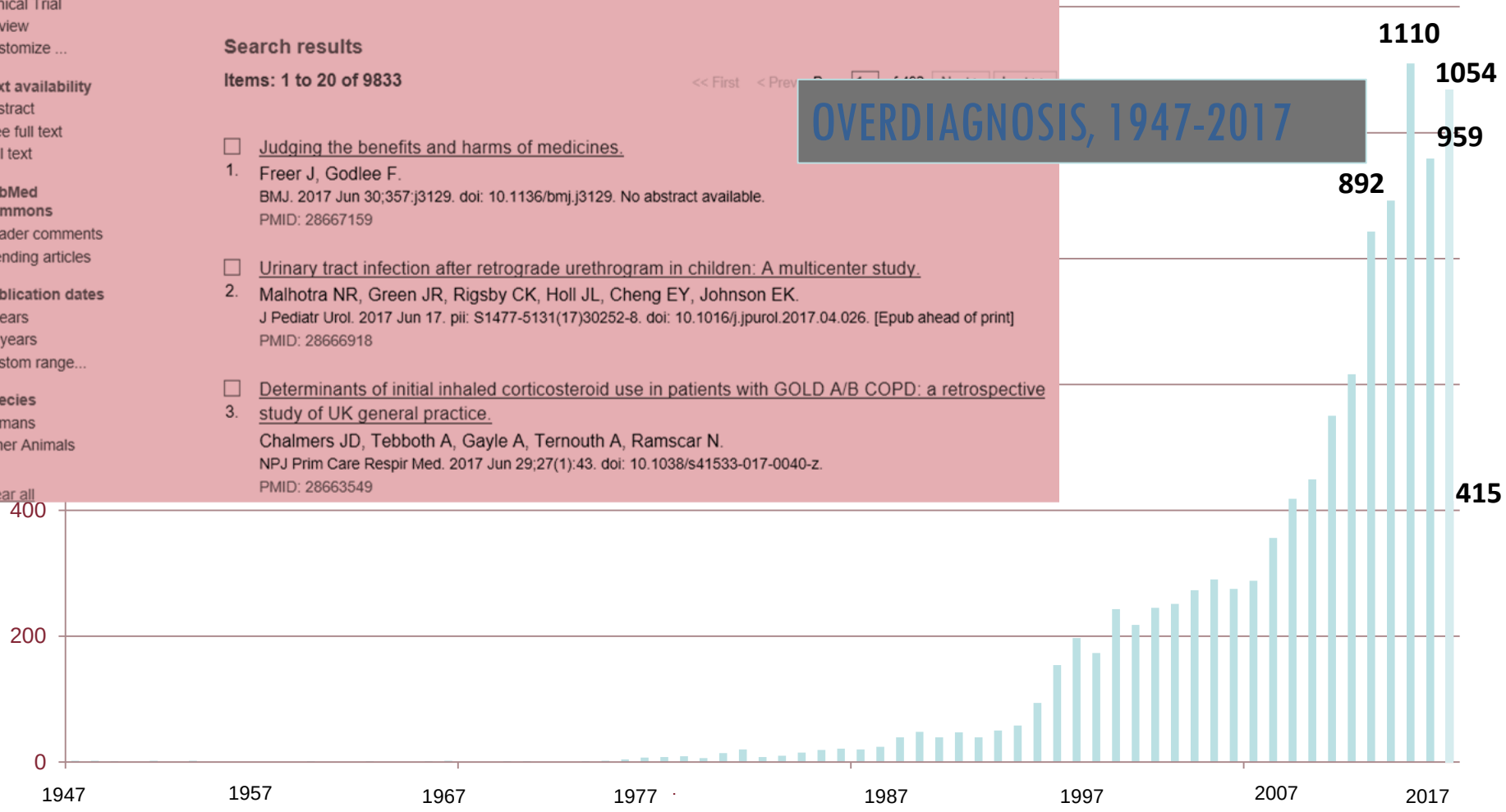
1. Judging the benefits and harms of medicines.
Freer J, Godlee F.
BMJ. 2017 Jun 30;357:j3129. doi: 10.1136/bmj.j3129. No abstract available.
PMID: 28667159

2. Urinary tract infection after retrograde urethrogram in children: A multicenter study.
Malhotra NR, Green JR, Rigsby CK, Holl JL, Cheng EY, Johnson EK.
J Pediatr Urol. 2017 Jun 17. pii: S1477-5131(17)30252-8. doi: 10.1016/j.jpurol.2017.04.026. [Epub ahead of print]
PMID: 28666918

3. Determinants of initial inhaled corticosteroid use in patients with GOLD A/B COPD: a retrospective study of UK general practice.
Chalmers JD, Tebboth A, Gayle A, Ternouth A, Ramscar N.
NPJ Prim Care Respir Med. 2017 Jun 29;27(1):43. doi: 10.1038/s41533-017-0040-z.
PMID: 28663549

OVERDIAGNOSIS, 1947-2017



Eur Radiol 2017;27:2737-2743
Epub 2016 Nov 2.

BREAST

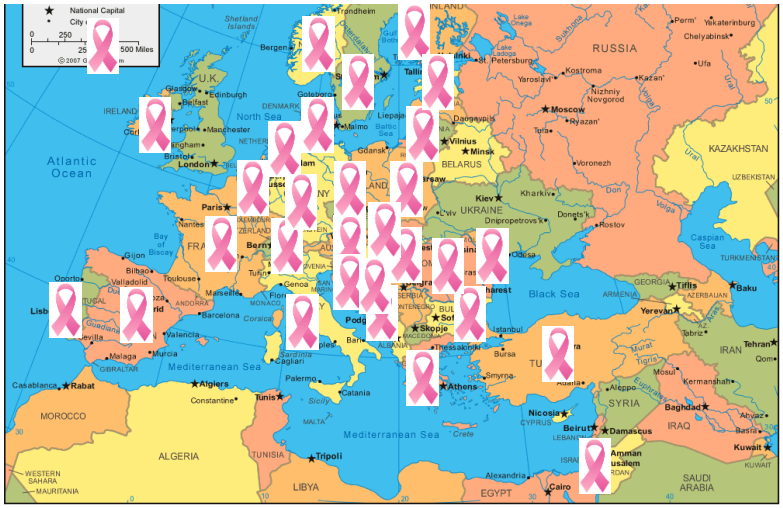
IN SUPPORT OF SCREENING MAMMOGRAPHY

Position paper on screening for breast cancer by the European Society of Breast Imaging (EUSOBI) and 30 national breast radiology bodies from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland and Turkey

Francesco Sardanelli[1,2] · Hildegunn S. Aase[3] · Marina Álvarez[4] · Edward Azavedo[5] · Henk J. Baarslag[6] · Corinne Balleyguier[7] · Pascal A. Baltzer[8] · Vanesa Beslagic[9] · Ulrich Bick[10] · Dragana Bogdanovic-Stojanovic[11] · Ruta Briediene[12] · Boris Brkljacic[13] · Julia Camps Herrero[14] · Catherine Colin[15] · Eleanor Cornford[16] · Jan Danes[17] · Gérard de Geer[18] · Gul Esen[19] · Andrew Evans[20] · Michael H. Fuchsjaeger[21] · Fiona J. Gilbert[22] · Oswald Graf[23] · Gormlaith Hargaden[24] · Thomas H. Helbich[8] · Sylvia H. Heywang-Köbrunner[25] · Valentin Ivanov[26] · Ásbjörn Jónsson[27] · Christiane K. Kuhl[28] · Eugenia C. Lisencu[29] · Elzbieta Luczynska[30] · Ritse M. Mann[31] · Jose C. Marques[32] · Laura Martincich[33] · Margarete Mortier[34] · Markus Müller-Schimpfle[35] · Katalin Ormandi[36] · Pietro Panizza[37] · Federica Pediconi[38] · Ruud M. Pijnappel[39] · Katja Pinker[8] · Tarja Rissanen[40] · Natalia Rotaru[41] · Gianni Saguatti[42] · Tamar Sella[43] · Jana Slobodníková[44] · Maret Talk[45] · Patrice Taourel[46] · Rubina M. Trimboli[2] · Ilse Vejborg[47] · Athina Vourtsis[48] · Gabor Forrai[49]

Key points

- *EUSOBI and 30 national breast radiology bodies support screening mammography.*
- *A first priority is double-reading biennial mammography for women aged 50–69 years.*
- *Extension to 73–75 and from 40–45 to 49 years is also encouraged.*
- *Digital mammography (not film-screen or computer radiography) should be used.*
- *DBT is set to become "routine mammography" in the screening setting in the next future.*



Insights Imaging (2012) 3:7–10
DOI 10.1007/s13244-011-0127-y

STATEMENT

Mammography: EUSOBI recommendations for women's information

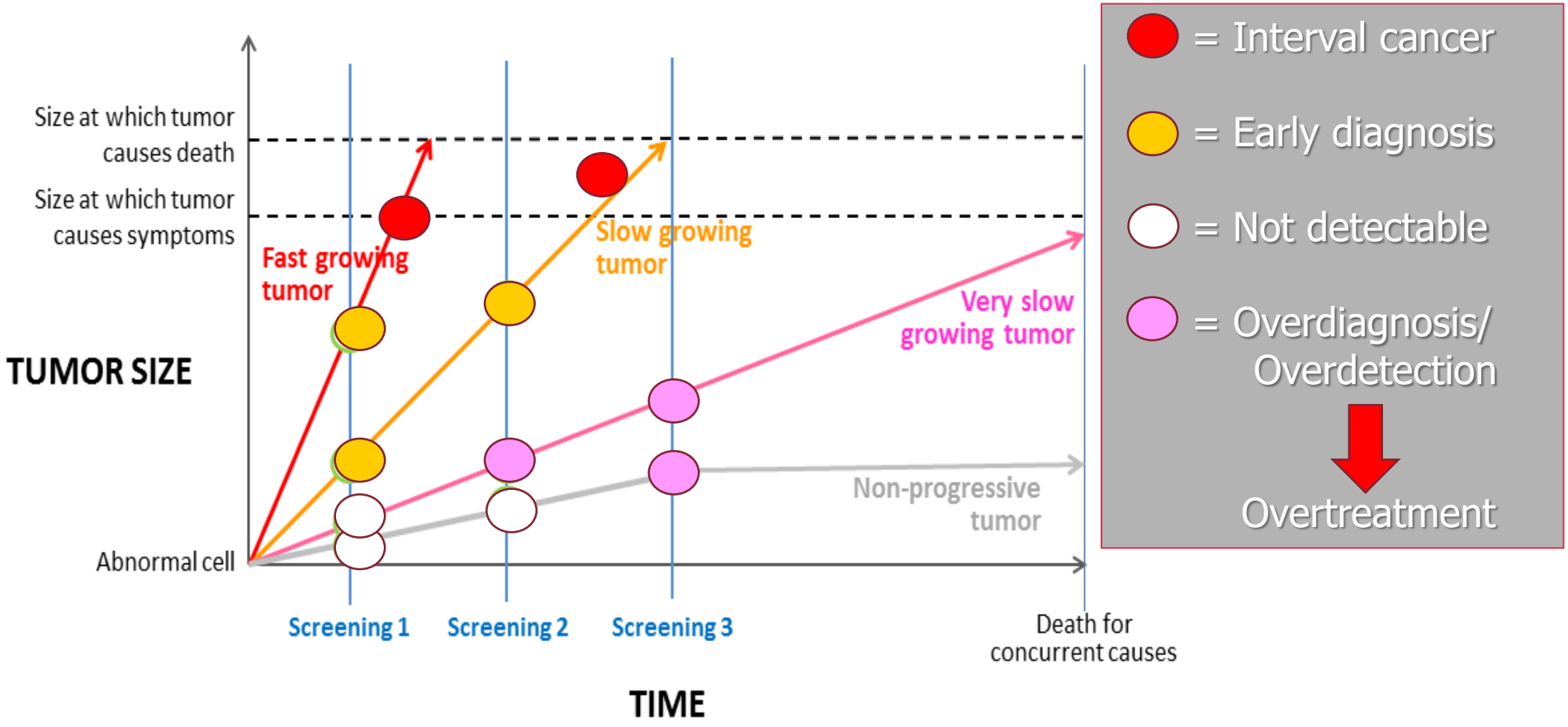
Francesco Sardanelli · Thomas H. Helbich ·
for the European Society of Breast Imaging (EUSOBI)

Overdiagnosis

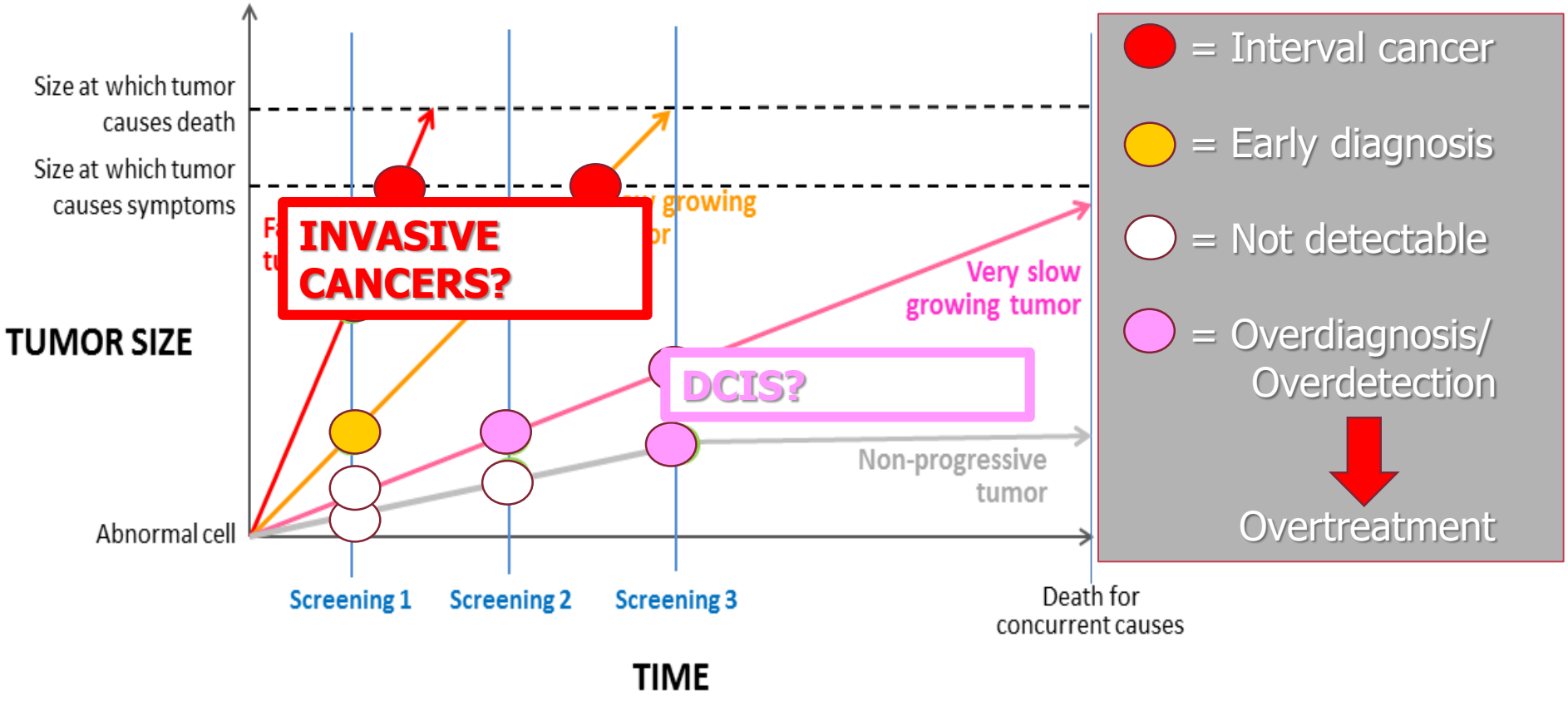
Not all the breast cancers diagnosed with screening are aggressive and fatal cancers. In the absence of screening mammography, some of them (probably 5–20%) would have remained totally free of symptoms [10]. However, these cancers cannot be distinguished from those that, if left undiagnosed and untreated, would be fatal. Thus, if we want to reduce breast cancer mortality, we must accept a rate of overdiagnosed cancers with the consequence of a rate of unnecessary treatments.

OVERDIAGNOSIS

Detection of a disease (lesion) that will never cause symptoms or death during patient lifetime



Detection of a disease (lesion) that will never cause symptoms or death during patient lifetime



THE CONCEPT OF OVERDIAGNOSIS

To diagnose a disease (a lesion)

that would had not been diagnosed within the patient lifetime

TOO MANY TRUE POSITIVES

The test is too much sensitive

A SOCIAL AND ETHICAL ISSUE…

BMJ

GOOD NEWS

BMJ 2014;348:g3701 doi: 10.1136/bmj.g3701 (Published 17 June 2014)

Modern mammography screening and breast cancer mortality: population study

Harald Weedon-Fekjær *researcher*[1 2 3], Pål R Romundstad *professor of epidemiology*[1], Lars J Vatten *professor of epidemiology*[1 4]

Results During 15 193 034 person years of observation (1986-2009), deaths from breast cancer occurred in 1175 women with a diagnosis after being invited to screening and 8996 women who had not been invited before diagnosis. After adjustment for age, birth cohort, county of residence, and national trends in deaths from breast cancer, the mortality rate ratio associated with being invited to mammography screening was 0.72 (95% confidence interval 0.64 to 0.79). To prevent one death from breast cancer, 368 (95% confidence interval 266 to 508) women would need to be invited to screening.

Conclusion Invitation to modern mammography screening may reduce deaths from breast cancer by about 28%.

Reduction in mortality for 50-69 women WHO HAVE screening mammography:

- 44-48% (Puliti, Br J Cancer 2008; Allgood, Br J Cancer 2008)
- Over 50% (Regione Emilia Romagna, Italy)

N Engl J Med 2005;353:1784-92.

Effect of Screening and Adjuvant Therapy on Mortality from Breast Cancer

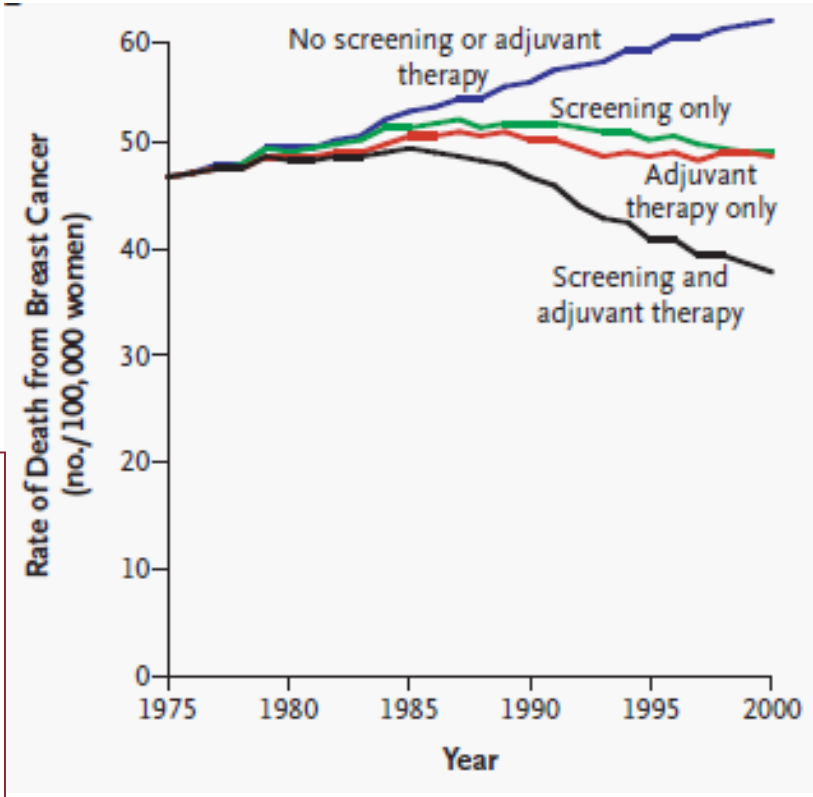
Donald A. Berry, Ph.D., Kathleen A. Cronin, Ph.D., Sylvia K. Plevritis, Ph.D., Dennis G. Fryback, Ph.D., Lauren Clarke, M.S., Marvin Zelen, Ph.D., Jeanne S. Mandelblatt, Ph.D., Andrei Y. Yakovlev, Ph.D., J. Dik F. Habbema, Ph.D., and Eric J. Feuer, Ph.D., for the Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators*

RESULTS

The proportion of the total reduction in the rate of death from breast cancer attributed to screening varied in the seven models from 28 to 65 percent (median, 46 percent), with adjuvant treatment contributing the rest. The variability across models in the absolute contribution of screening was larger than it was for treatment, reflecting the greater uncertainty associated with estimating the benefit of screening.

CONCLUSIONS

Seven statistical models showed that both screening mammography and treatment have helped reduce the rate of death from breast cancer in the United States.



Mortality reduction:
Screening 46%
Adjuvant therapy 54%

DCIS mammography features

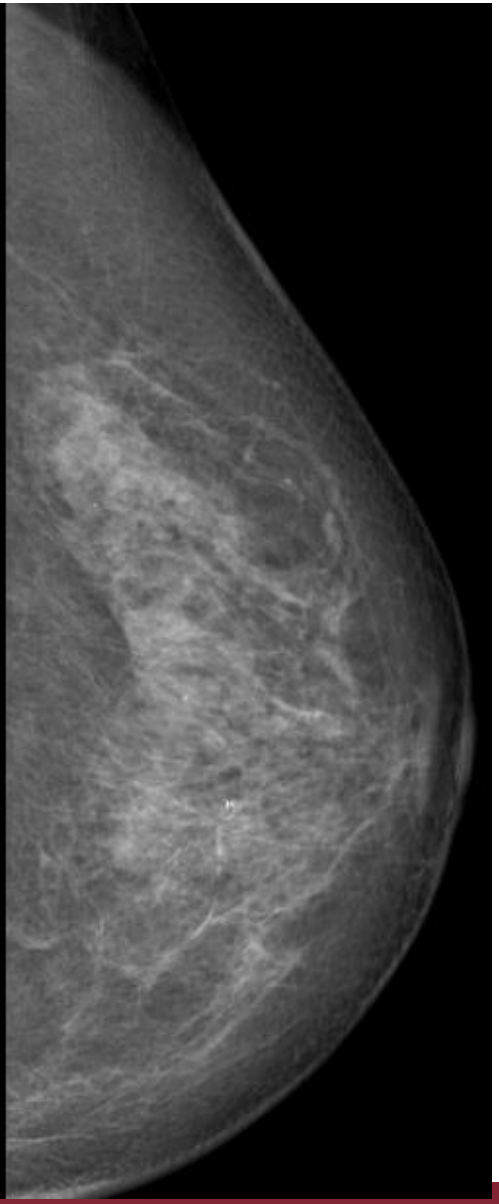
Most DCIS lesions found at mammography present as microcalcifications, with approximately 75% of lesions presenting only as calcifications.

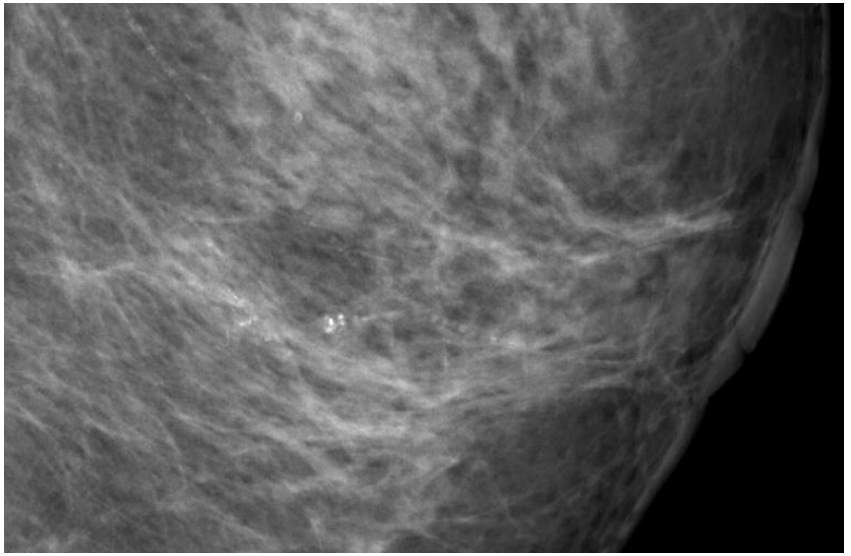
Up to 23% of DCIS may present as a mass or asymmetry.

Roughly 12% are associated with a palpable abnormality.

Mammography of ductal carcinoma in situ of the breast: review of 909 cases with radiographic-pathologic correlations.
Barreau B, de Mascarel I, Feuga C, et al.
Eur J Radiol 2005; 54:55–61

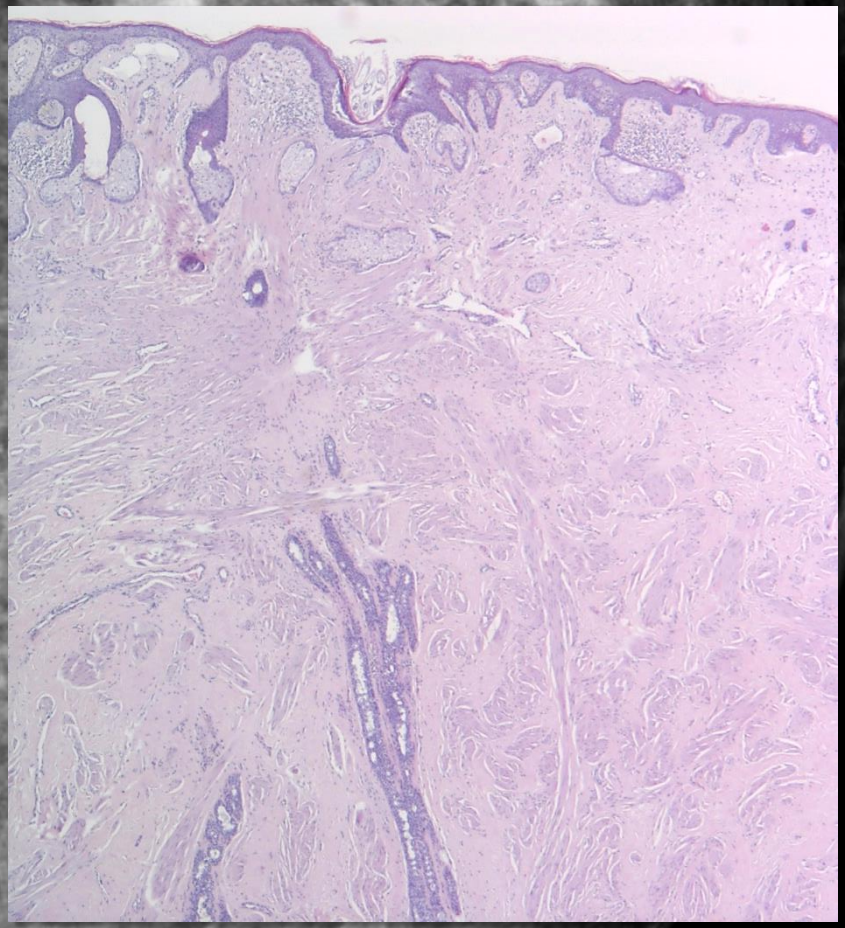
Microcalcifications





Microcalcifications

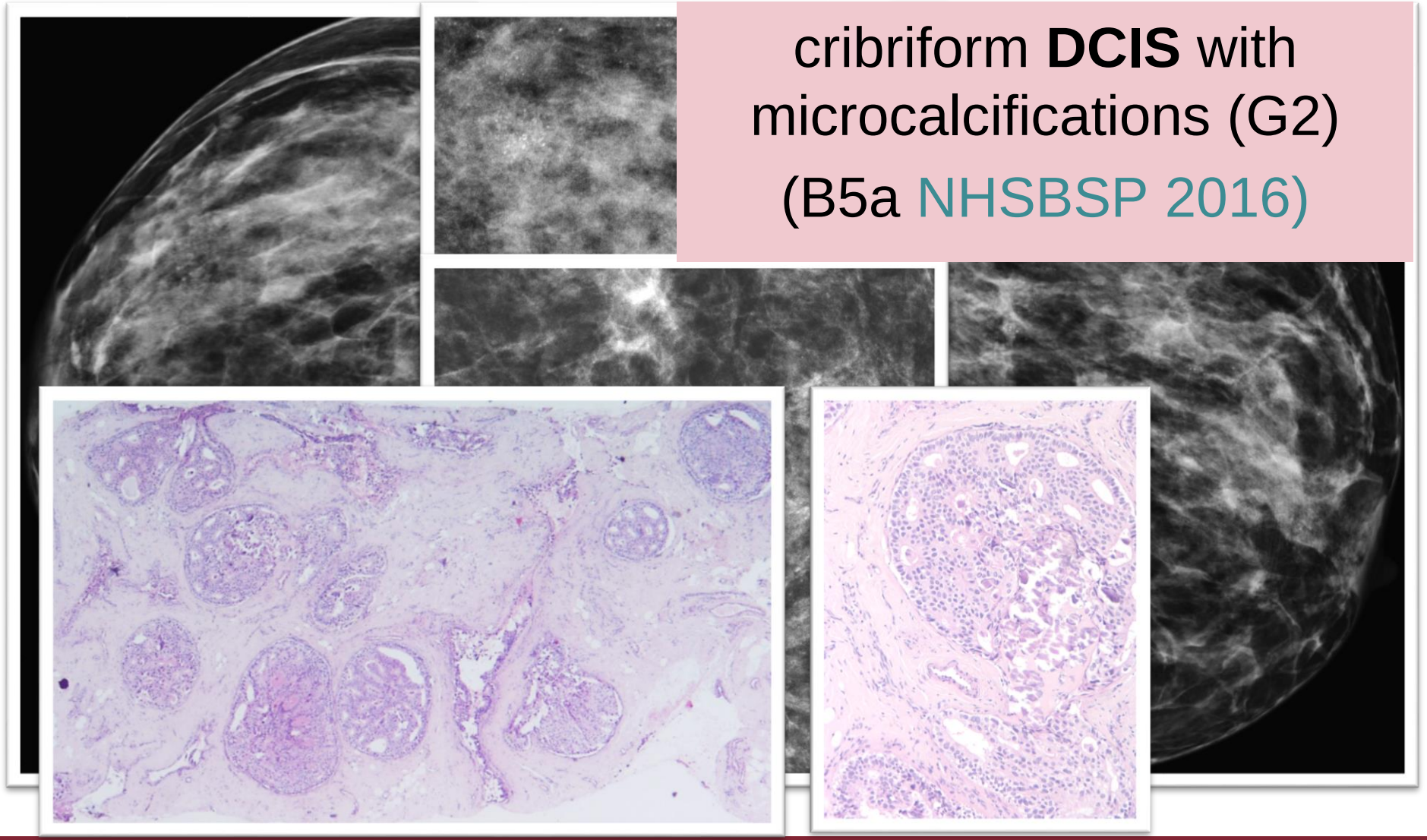
15/02/2017



HG-DCIS, 16 mm, solid and cribriform kind, (G3) with comedonecrosis and coarse calcificazions.
pTis pN0 (sn) (0/2)

6cm

Microcalcifications



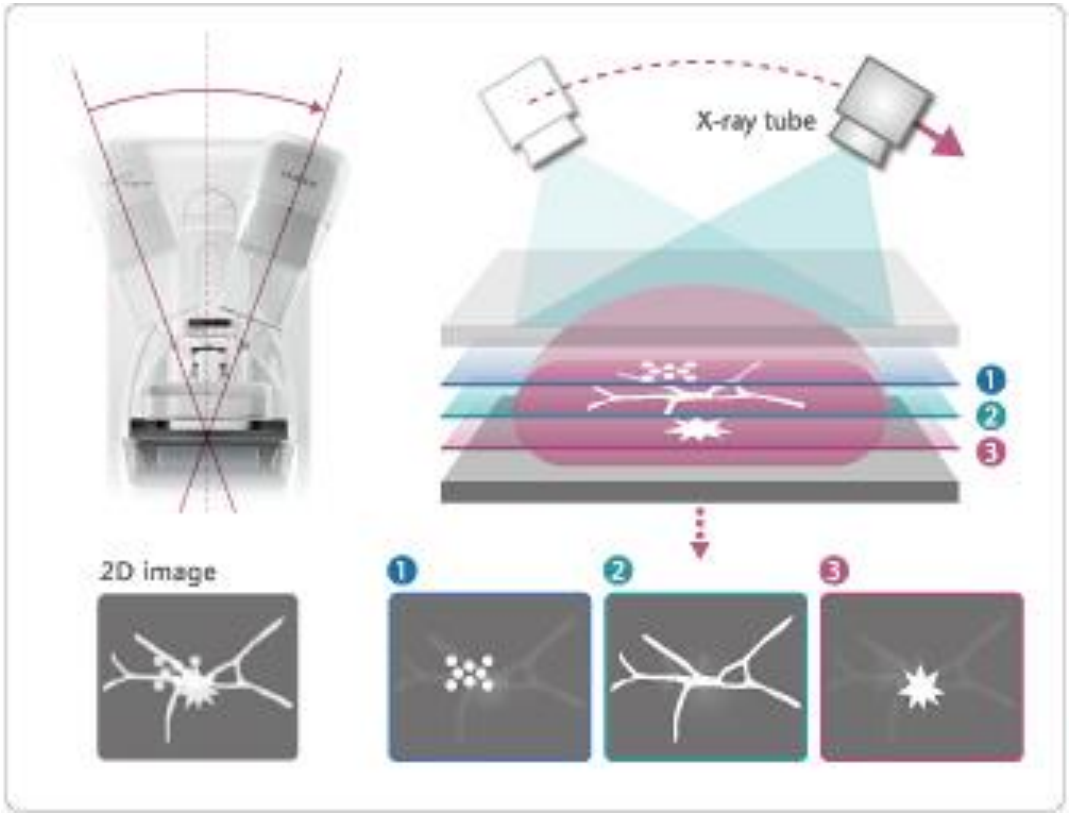
cribriform **DCIS** with microcalcifications (G2)

(B5a NHSBSP 2016)

Digital Breast Tomosynthesis

Digital breast tomosynthesis (DBT) is an imaging technique that allows a volumetric reconstruction of the whole breast from a finite number of low-dose two-dimensional projections obtained by different X-ray tube angles.
It takes to obtain a complete set of projection images reconstructed into thin image slices spaced at 0.5–1.0 mm.

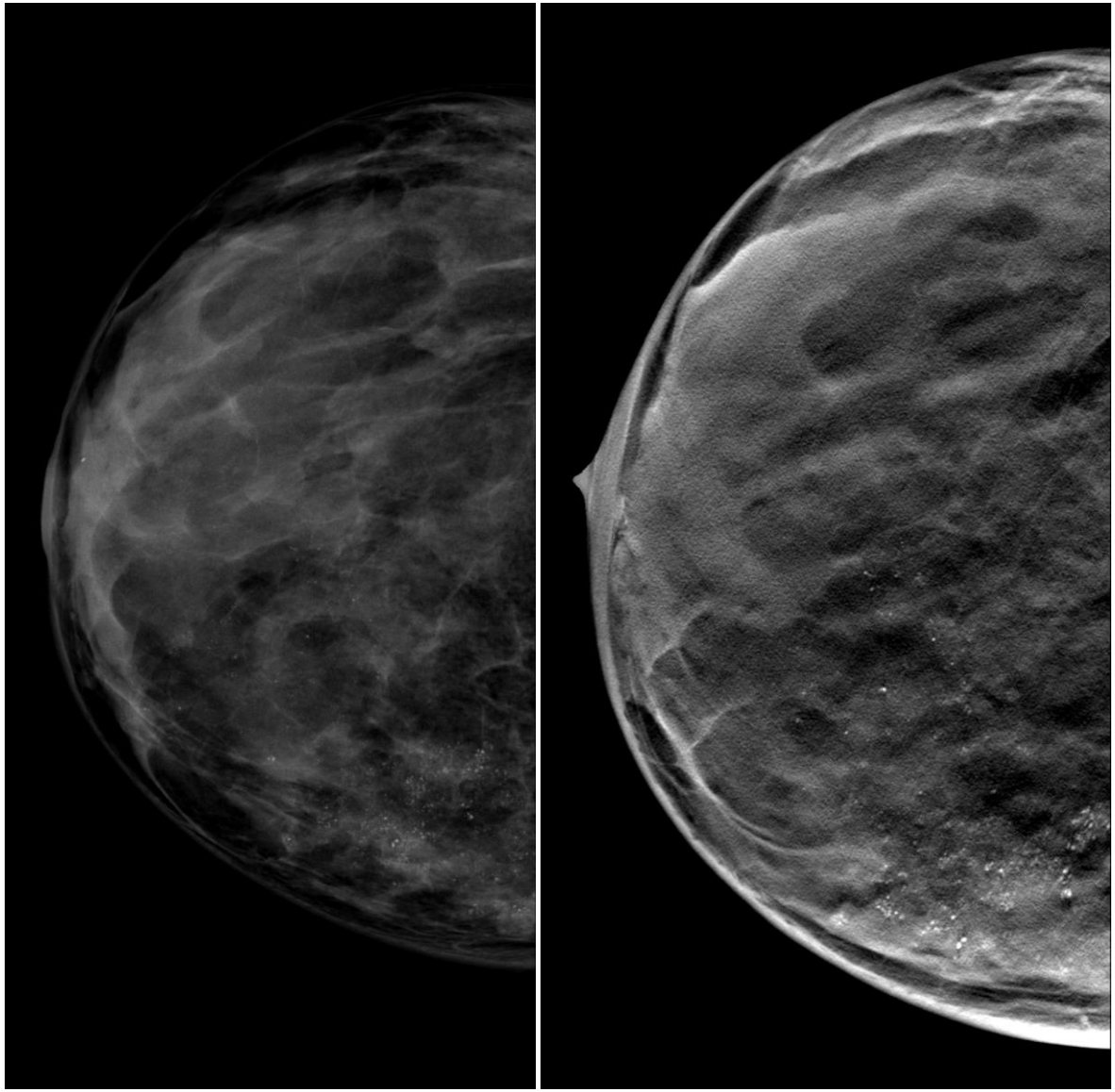
Digital Breast Tomosynthesis



DBT can improve specificity in screening ruling out overlapping structures, facilitating so small lesions identification.

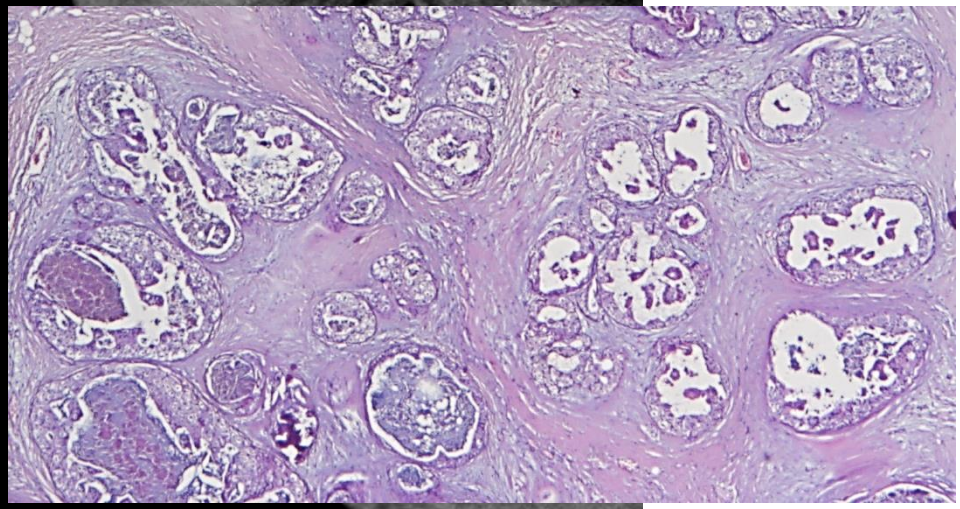
DBT is definitely able to improve dense breasts imaging using a two- projections mammography dose.

Digital Breast Tomosynthesis



DCIS (10 mm) G3

pTis pN0 (sn) (0/2)



SCREENING WITH DBT: READY TO GO?

DIFFICULT ANSWER…

PROS

1. Prospective studies showed that DBT used as an adjunct[1-3] or alternative[4] to 2D-DM allows for a **superior diagnostic performance** when compared to DM alone:
   - **increase in detection rate 0.5-2.7 per 1000** [5]
   - **reduction in recall rate 0.8-3.6 per 100** [5]
1. DBT is now proposed along with synthetic 2D views, practically solving the problem of an increased exposure to ionizing radiation when DBT is performed as an ad adjunct to 2D DM[6-8]

→ **DBT as routine mammography in the next future**

1. Skaane et al. Radiology 2013;267:47-56. 2. Skaane et al. Eur Radiol 2013;23:2061-71. 3. Ciatto et al. Lancet Oncol 2013;583-9. 4. Lång et al. Eur Radiol 2016;26:184-90. 5. Houssami. Expert Rev Med Devices 2015;12:377-9. 6. Svahn et al. Breast 2015;24:93-9. 7. Gur et al. Acad Radiol 2012;19:166-71. 8. Skaane et al. Radiology 2014; 271:655-63.

JAMA, June 25, 2014

454,850 examinations

	DM	DM+DBT
Exams	281,187	173,663
Recalls	29,726	15,541
Biopsies	5,056	3,285
Cancers	1,207	950
Invasive	815	707
DCIS	392	243

Screening with FFDM vs. FFMD + DBT per 1,000 patients

	FFDM	FFDM plus DBT	Percent difference
Recalls	107	91	-15%
Overall cancer detection	4.2	5.4	29%
Invasive cancer detection	2.9	4.1	41%
DCIS cancer detection	1.4	1.4	0%

Friedewald et al, JAMA 2014, 311:24, 2499-2507

But also small indolent invasive cancers may overdiagnosed…!

CONS

1. Lack of evidence for reducing mortality
2. Lack of evidence for reducing interval cancers
3. Lack of evidence for demonstration of cost-effectiveness (e.g., impact on overdiagnosisis, impact of increased reading time[1])

Before introducing DBT in BC screening outside ethical-approved trials (or local approval by health authorities), **we need at least evidence for a** (statistically significant and clinically relevant) **reduction in the interval cancer rate**, to avoid an increase in overdiagnosis.

1. Gilbert et al. Clin Radiol 2016;71:141-50

Ultrasonography

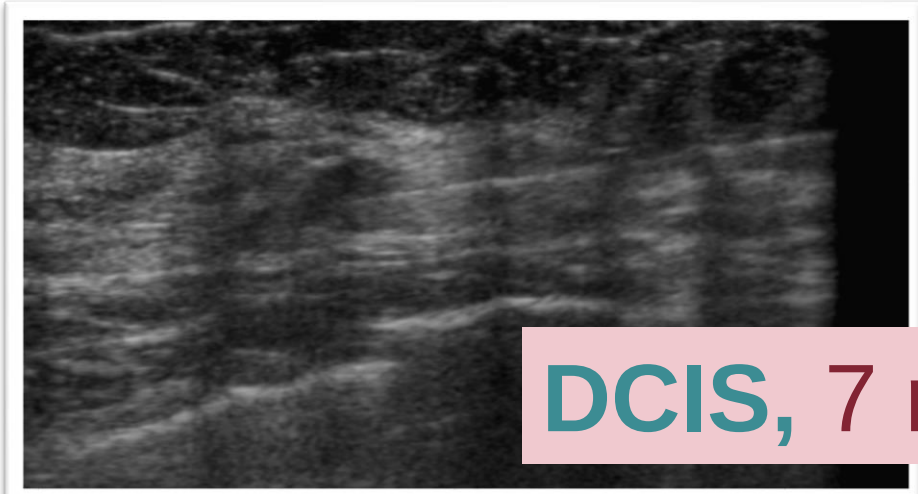
Ultrasound is an important modality that has many benefits in the detection and workup of DCIS.

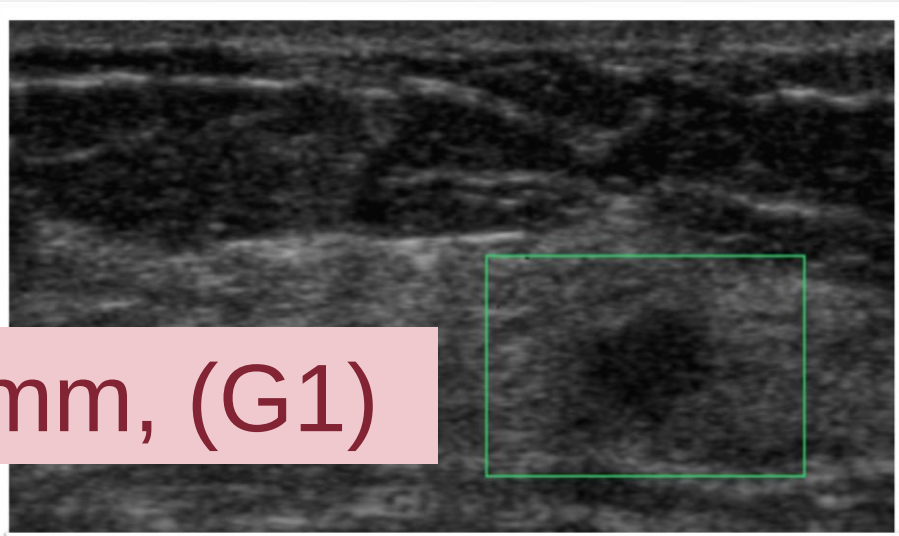
DCIS ultrasound features

A hypoechoic mass with noncircumscribed margins, parallel orientation, and normal acoustic transmission is the most common US finding in DCIS.

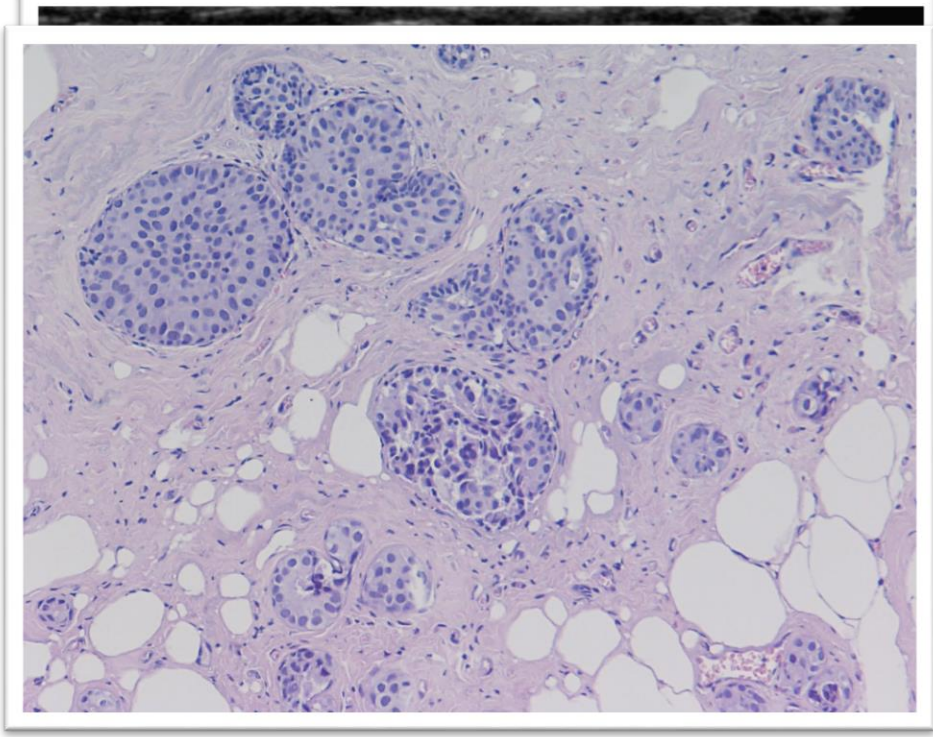
US features are nonspecific and include a mass, intraductal abnormality, or area of altered echotexture.

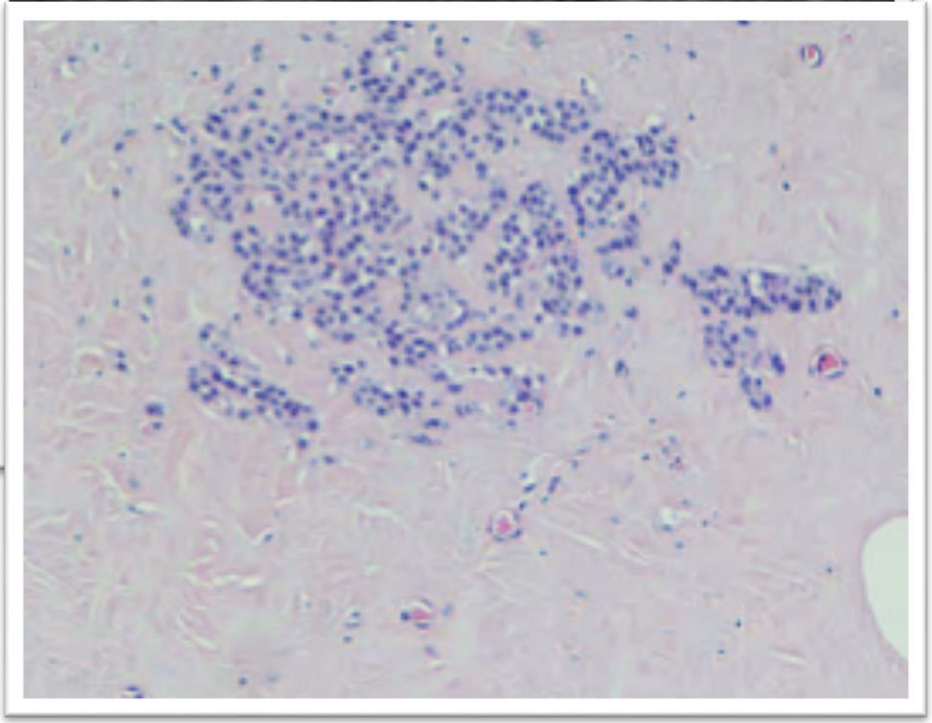
US Appearance of Ductal Carcinoma in Situ
Lilian C. Wang et al.
RadioGraphics 2013





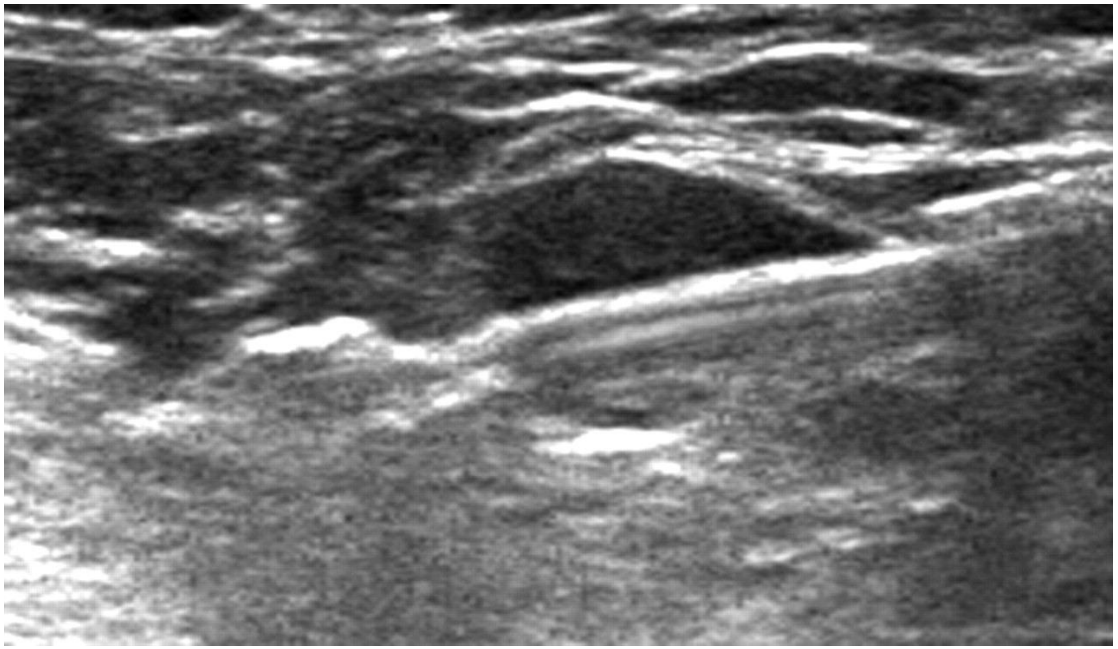
DCIS, 7 mm, (G1)





Ultrasonography

One of the benefits of identifying a corresponding sonographic abnormality in women with mammographically detected DCIS is to use ultrasound to guide interventional (biopsy/hookwire) procedures.



Breast Magnetic Resonance Imaging

Breast MRI is the most sensitive method for detection of breast cancer.

Absence of enhancement excludes breast cancer with a negative predictive value (NPV)> 98%.

Breast Magnetic Resonance Imaging main indications

- Screening of women at high risk for developing breast cancer (e.g. *BRCA1* and *BRCA2* carriers),
- Additional diagnostic test in pretherapeutic breast cancer staging,
- Monitoring of primary systemic therapies,
- Solving problematic diagnostic situations.

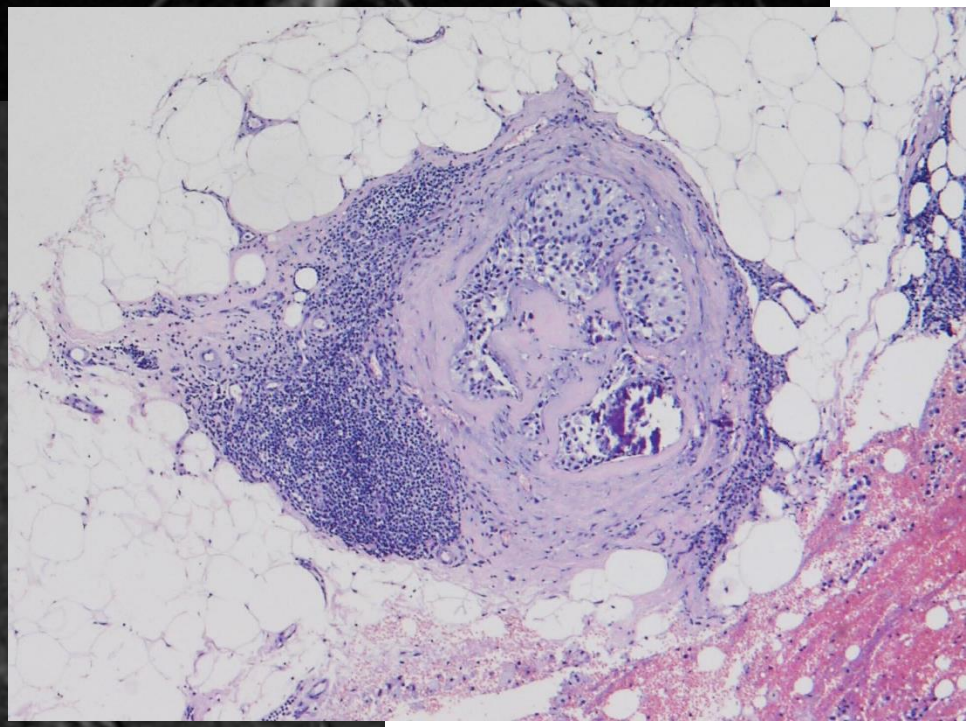
DCIS Features on breast MRI

- DCIS most commonly presents as a non-mass like enhancement.

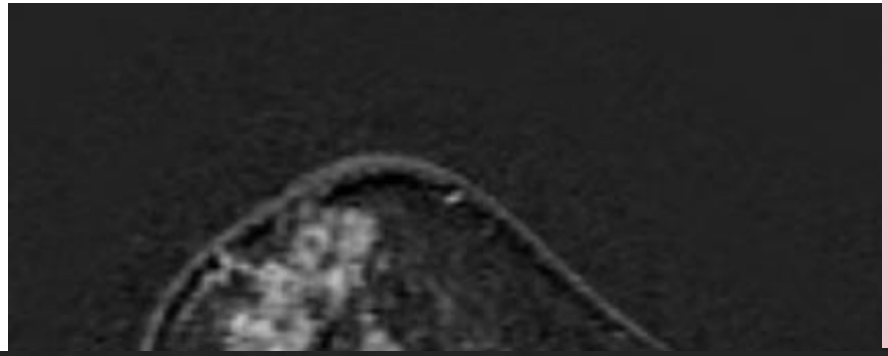
- DCIS does not show a specific distribution pattern: it may be seen as focal, linear (rather suspicious), regional, multiple regional, segmental (rather suspicious).

Linear enahncement

Solid and cribriform **DCIS**,(G3) with comedonecrosis and coarse calcificazions.

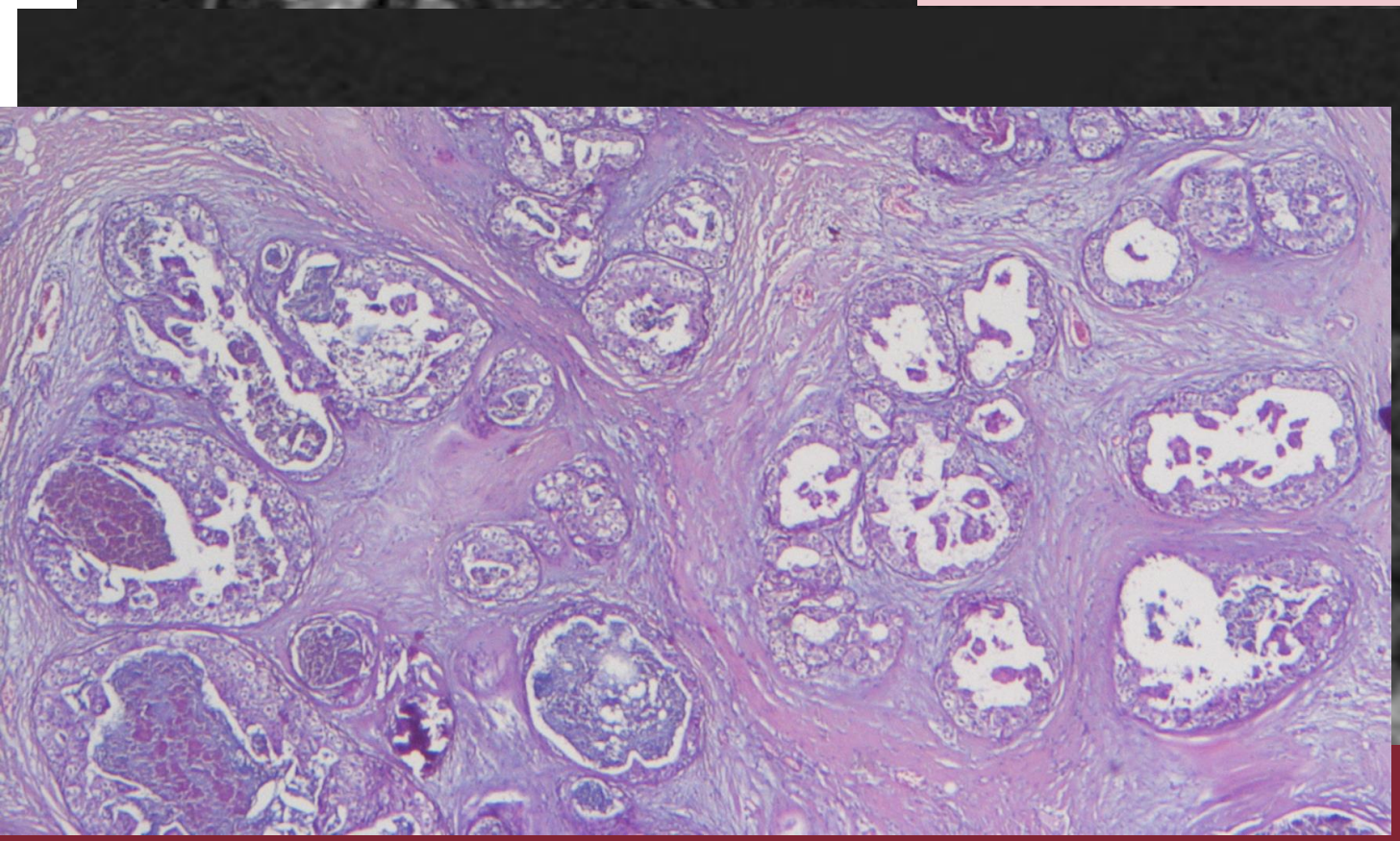


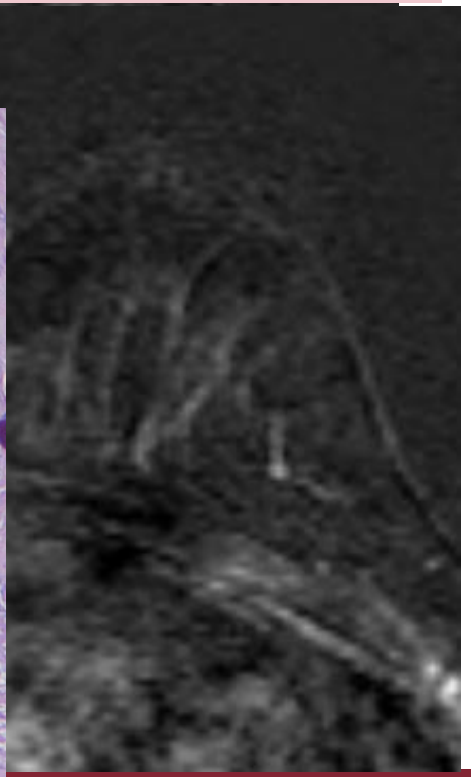
Segmental enahncement



DCIS (10 mm) G3

pTis pN0(sn) (0/2)»





MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study

THE LANCET **Lancet 2007**

Christiane K Kuhl, Simone Schrading, Heribert B Bieling, Eva Wardelmann, Claudia C Leutner, Roy Koenig, Walther Kuhn, Hans H Schild

5-year period, 7319 women: MRI and mammography
193 with pure DCIS. 167/193 had undergone both tests

Diagnosis

Mammo 93 (56%)

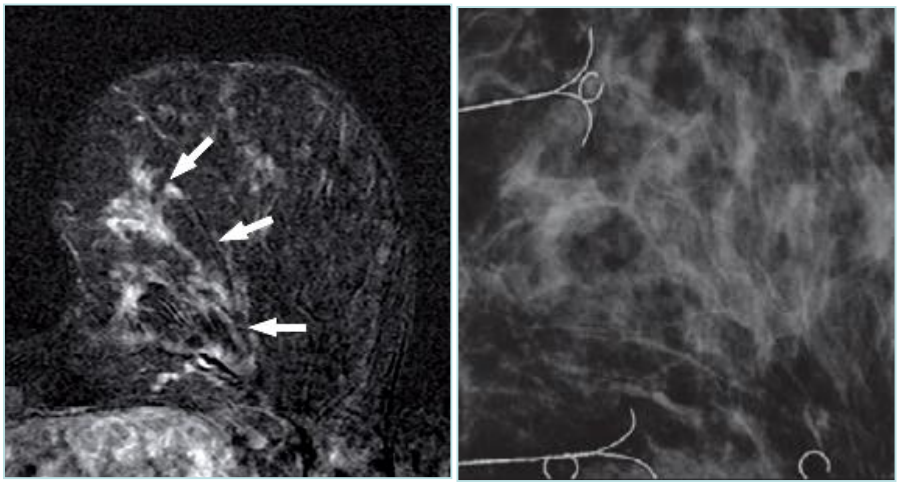
MRI 153 (92%) (p<0.0001)

89 high-grade DCIS

Missed by mammo, MRI-det. 43 (48%)

MRI-detected 87 (98%)

Missed by MRI, mammo-det. 2 (2%)



High-grade DCIS without necroses in a 48-year-old asymptomatic woman

Age, menopausal status, personal or family history of breast cancer or of benign breast disease, and breast density of women with MRI-only diagnosed DCIS did not differ significantly from those of women with mammography-diagnosed DCIS.

When the entry criterion is not only mammographic detection, MRI shows a higher sensitivity than mammography for DCIS, especially high-grade DCIS

Breast cancer must be considered a chronic condition, even in patients who are free of disease.

Follow-up

The aims of follow-up are:

-to detect early local recurrences or contralateral breast cancer,

-to evaluate and treat therapy-related complications,

-to motivate patients continuing hormonal treatments

-to provide psychological support and information in order to enable a return to normal life.

Primary Breast Cancer: ESMO Clinical Practice Guidelines 2015

Follow-up

Mammographic surveillance appears to be associated with a reduction in mortality in women with a history of breast cancer.

The main purpose of mammography is to find early local disease relapses.

Furthermore, mammographic surveillance can observe the presence of new second breast neoplasms quickly.

Follow-up

Routine ultrasound examination at follow-up is not recommended due to the high rate of false positives.

It could be useful if clinically indicated or to investigate suspicious mammography images.

Eur Radiol
DOI 10.1007/s00330-011-2226-z

BREAST

Surveillance mammography for detecting ipsilateral breast tumour recurrence and metachronous contralateral breast cancer: a systematic review

Clare Robertson · Senthil Kumar Arcot Ragupathy · Charles Boachie · Cynthia Fraser · Steve D Heys · Graeme MacLennan · Graham Mowatt · Ruth E Thomas · Fiona J Gilbert · and the Mammographic Surveillance Health Technology Assessment Group

F Gilbert 2011

Diagnostic performance of surveillance tests

	IBTR (routine surveillance)			MCBC (routine surveillance)		
Test	**No of studies**	**Sensitivity (%)**	**Specificity (%)**	**No of studies**	**Sensitivity (%)**	**Specificity (%)**
XRM	2	(67–71)	(63–85)			
Ultrasound	1	43	31			
MRI	2	100	(93-94)	1	91	90
CE	2	(43–89)	(56–76)			
Combined XRM & CE	1	100	67			
Combined XRM & ultrasound				1	95	99
Combined XRM, CE & ultrasound				1	64	84
Combined XRM, CE, ultrasound & MRI				1	100	89

MRI has the best performance
Mammography has the next best performance

Follow-up

Breast MRI is the most sensitive technique but is also the most expensive

So is not recommended as a routine examination in breast cancer follow-up.

Eventually, breast MRI could be considered as a second level exam in clinical suspicion of relapse with inconclusive mammography examination.

- **Physical examination** should be performed every 3-6 months in the first 3 years after primary treatment, every 6-12 months in the following 2 years and then once a year.

- Annual ipsilateral and/or contralateral **mammography**.

- Unless clinical suspicion of disease recurrence, no further examinations are indicated (Chest X-ray, CT, MRI, scintigraphy, PET-CT, U.S. etc.) in routine practice.

EUSOBI
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Annual Scientific Meeting 2019
European Society of Breast Imaging

SAVE THE DATE
October 3-5, 2019
Budapest/Hungary

For questions……Federica.pediconi@uniroma1.it.

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