



CUR.A.R.T.E.

ALIMENTAZIONE, RICERCA, TERAPIA, EMOZIONE

Convegno di Fondazione IncontraDonna | PRIMA EDIZIONE

ROMA, 14 | 06 | 2023

BOSCOLO CIRCO MASSIMO

FONDAZIONE
**Incontra
Donna**
OCCUPAZIONE DI SALUTE

SCREENING MAMMOGRAFICO: UN MODELLO DI SANITÀ PUBBLICA IN EVOLUZIONE?

**Screening Mammografico in evoluzione:
nuove tecnologie e AI**
Francesco Sardanelli

Con il contributo non condizionante di:

FUJIFILM



Screening mammografico in evoluzione: nuove tecnologie e AI

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UNIVERSITÀ DEGLI STUDI DI MILANO



Gruppo
San Donato

Disclosures

Advisory board: Bayer

Research/grant support: Bracco

Breast imaging from 1970s to 2020s: a never-ending evolution

Mammography → DM → DBT/synth 2D → **CEM** → CE-DBT

Stereotaxis → *DBT guidance* → *CEM guidance*

US → Real time & Hi-Freq. → Color Doppler → Elastography → ABUS

Fine needle → *Core biopsy* → *VAB*
→ *Image-guided treatment*

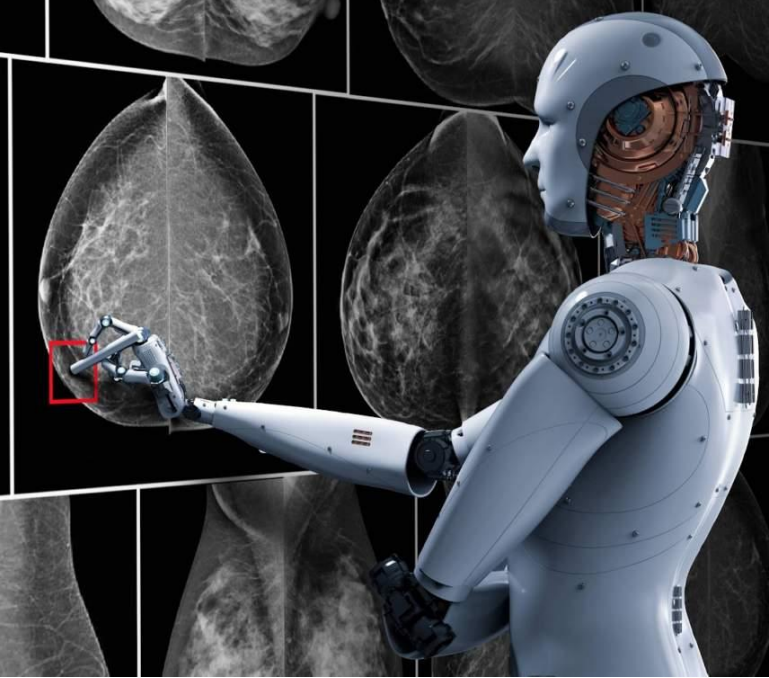
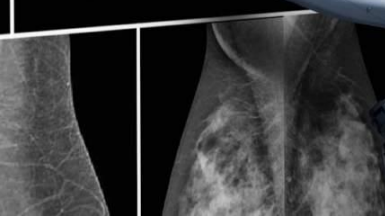
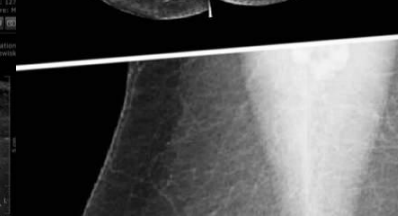
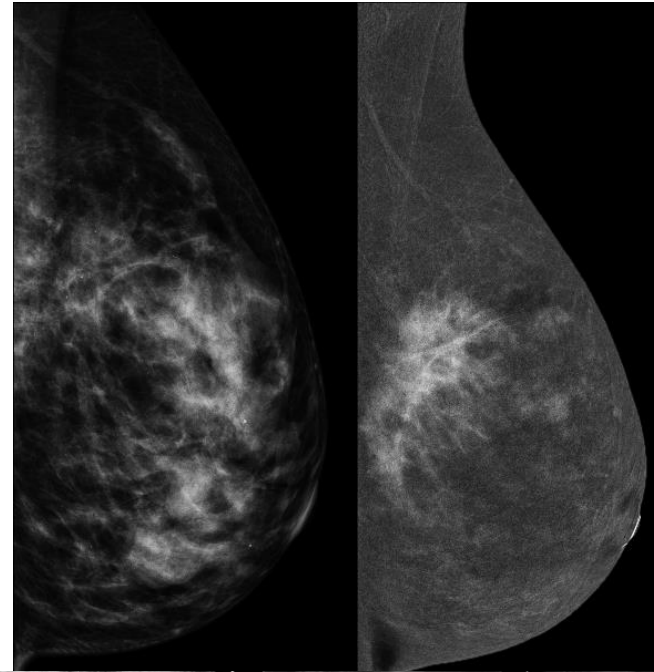
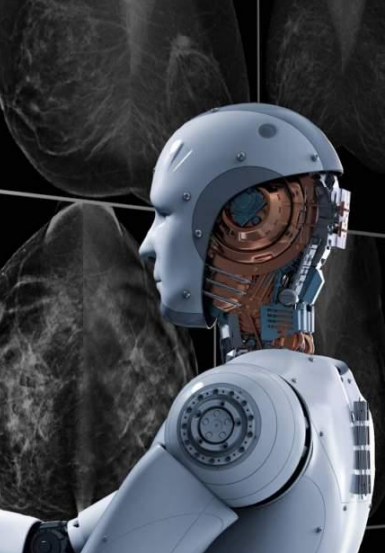
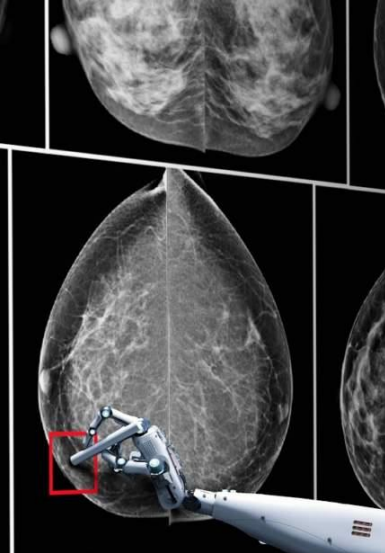
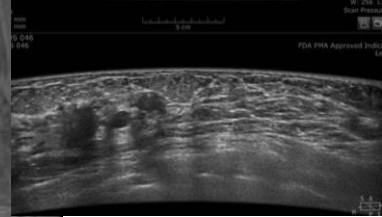
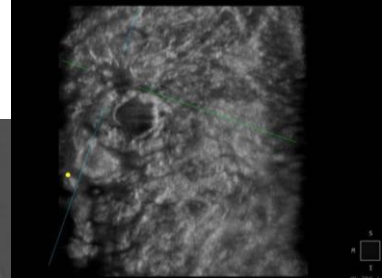
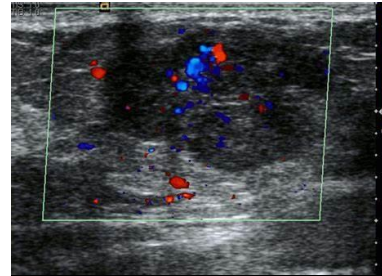
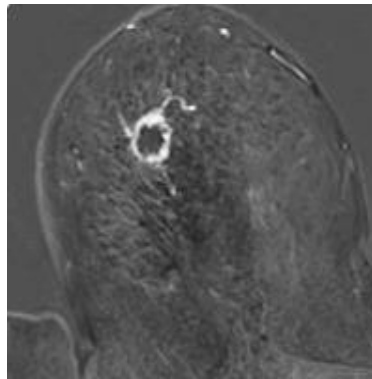
MRI → CE-MRI → DWI

MRI-guidance

(Dedicated breast CT?)

(Optical, photoacoustic BI?)

CAD → **AI (ML/DL)**





European Commission > EU Science Hub > ECIBC

Note: All ECIBC decisions and guidelines are the results of members voting !

European Commission Initiative on Breast Cancer

Improving quality of care and reducing inequality in Europe



European guidelines on screening and diagnosis


Evidence-based guidelines developed by the European Commission.





European quality assurance scheme

Quality assurance for breast cancer services covering the entire breast cancer pathway.

Guidelines Development Group (GDG) (n = 22)

GDG CLINICAL CO-CHAIR	
Axel Gräwingholt	
Curriculum vitae	Declaration of interests
GDG CO-CHAIR OF METHODOLOGY	
Holger J. Schünemann	
Curriculum vitae	Declaration of interests
GDG VICE-CHAIR OF METHODOLOGY	
Markus Follmann	
Curriculum vitae	Declaration of interests
GDG CLINICAL VICE-CHAIR	
Cecily Quinn	
Curriculum vitae	Declaration of interests

Quality Assurance Scheme Development Group (QASDG) (n = 24)

QASDG CHAIR	
Robert Mansel	
Curriculum vitae	Declaration of interests
QASDG VICE-CHAIR	
Francesco Sardanelli	
Curriculum vitae	Declaration of interests

European guidelines on breast cancer screening and diagnosis

Breast cancer screening

Organising breast cancer screening programmes

Screening ages and frequencies **UPDATED**

Use of artificial intelligence **NEW**

Use of tomosynthesis **UPDATED**

Women with high breast density **UPDATED**

Inviting and informing women about screening **UPDATED**

Breast cancer diagnosis

Informing women about their results

Further assessment after the mammogram

Staging of breast cancer

Planning surgical treatment **UPDATED**

Towards the treatment of invasive breast cancer

Inviting and informing women about screening

Women aged 50-69

For inviting asymptomatic women aged 50 to 69 with an average risk of breast cancer (in whom screening is strongly recommended) to attend organised population-based screening programmes, the ECIBC's Guidelines Development Group (GDG):

- **recommends using a letter**
- **suggests using either a letter:**
 - **with the general practitioner's (GP) signature**
 - **with a fixed appointment**
 - **followed by a phone reminder**
 - **followed by a written reminder.**



Moreover, the GDG developed recommendations on the use of electronic means, for which the GDG **suggests using a letter followed by an SMS notification or an automated phone call.**

If these strategies are not available, then, the GDG **suggests either an e-mail or an automated phone call alone.**

Finally, the GDG **suggests not using:**

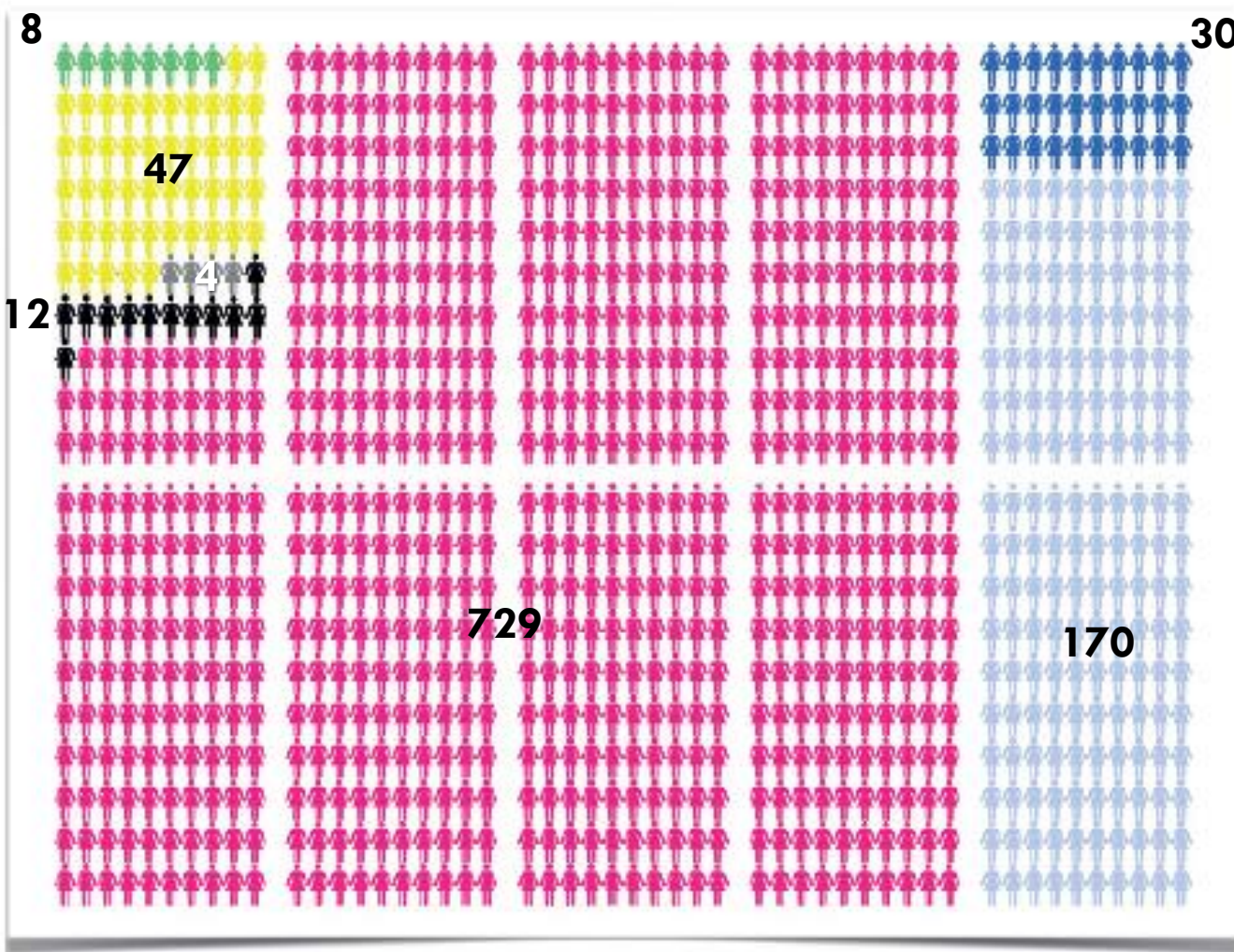
- **a letter accompanied by a face to face intervention**
- **a letter followed by a personalised phone call.**

Informing about benefits and harms of screening








For informing women about the benefits and harms of participating in an organised breast cancer screening programme, the ECIBC's Guidelines Development Group (GDG):

- **suggests using a decision aid**
(conditional recommendation, moderate certainty of the evidence)
- **recommends using numbers in addition to plain language**
(strong recommendation, moderate certainty of the evidence)
- **suggests using infographics in addition to plain language with numbers**
(conditional recommendation, low certainty of the evidence)
- **suggests not using storytelling in addition to plain language with number**
(conditional recommendation, very low certainty of the evidence)

ICONOGRAM SHOWING THE EFFECTS OF SCREENING MAMMOGRAPHY IN EUROPE



Every 1,000 women who attend biennial screening mammography from 50 to 69 years of age, followed up to 79 (30-year observation):

-  8 women survived after a BC diagnosis thanks to the screening
-  Other 47 women survived after a BC diagnosis
-  4 women had a sovradiagnosed BC
-  12 women dead for BC
-  30 women had needle biopsy of benign findings
-  170 women were recalled and had further imaging for benign findings
-  729 women, never recalled, were reassured on the absence of BC

Every 100,000 women who attend biennial screening mammography for 20 years we save 800 lives

Data from Paci et al, Euroscreen WG. Cancer Epidemiol Biomarkers Prev 2014

Screening ages and frequencies

Women aged 40-44: no screening

In the context of an organised screening programme for:

- asymptomatic women
- aged 40 to 44
- with an average risk of breast cancer

the ECIBC's Guidelines Development Group (GDG) **suggests not implementing mammography screening**

(conditional recommendation, moderate certainty of the evidence).

Women aged 45-49: screening every 2 or 3 years

In the context of an organised screening programme for:

- asymptomatic women
- aged 45 to 49
- with an average risk of breast cancer

the ECIBC's Guidelines Development Group (GDG) **suggests:**

- **mammography screening**
(conditional recommendation, moderate certainty of the evidence)
- **either triennial or biennial mammography over annual screening**
(conditional recommendation, very low certainty of the evidence)

Screening ages and frequencies

Women aged 50-69: screening every 2 years

In the context of an organised screening programme, for:

- asymptomatic women
- aged 50 to 69
- with an average risk of breast cancer

the ECIBC's Guideline Development Group (GDG):

- **recommends mammography screening**
(strong recommendation, moderate certainty of the evidence)
- **recommends against annual mammography screening**
(strong recommendation, very low certainty of the evidence)
- **suggests biennial mammography screening**
(conditional recommendation, very low certainty of the evidence)

Women aged 70-74: screening every 3 years

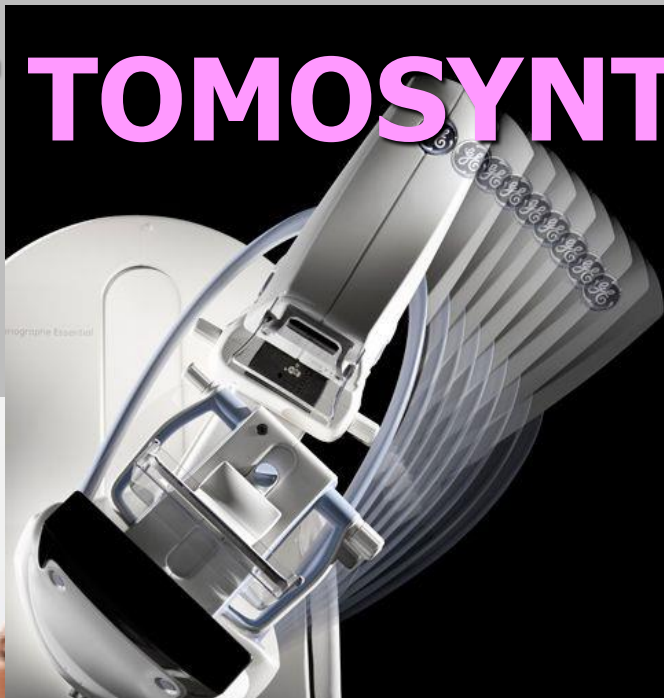
In the context of an organised screening programme, for:

- asymptomatic women
- aged 70 to 74
- with an average risk of breast cancer

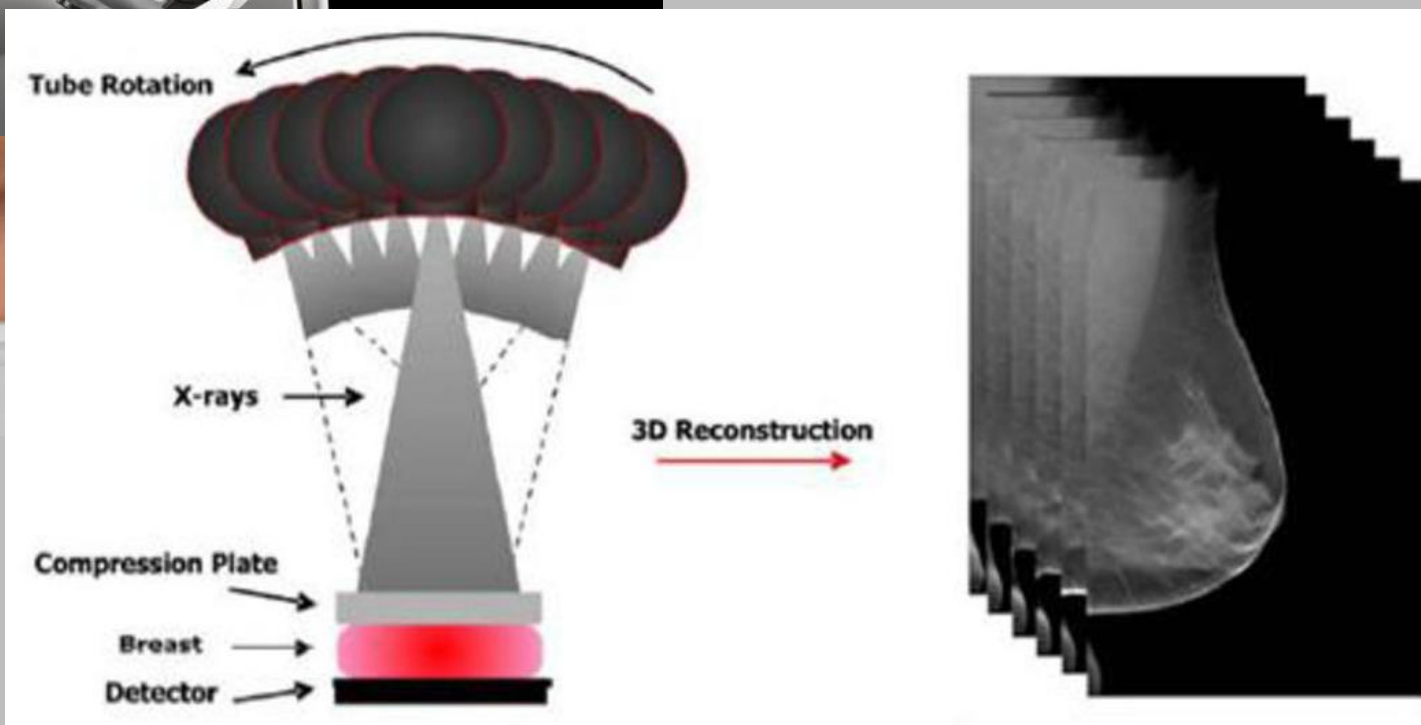
the ECIBC's Guideline Development Group (GDG):

- **suggests mammography screening**
(conditional recommendation, moderate certainty of the evidence)
- **recommends against annual mammography screening**
(strong recommendation, very low certainty of the evidence)
- **suggests triennial mammography screening**
(conditional recommendation, very low certainty of the evidence)

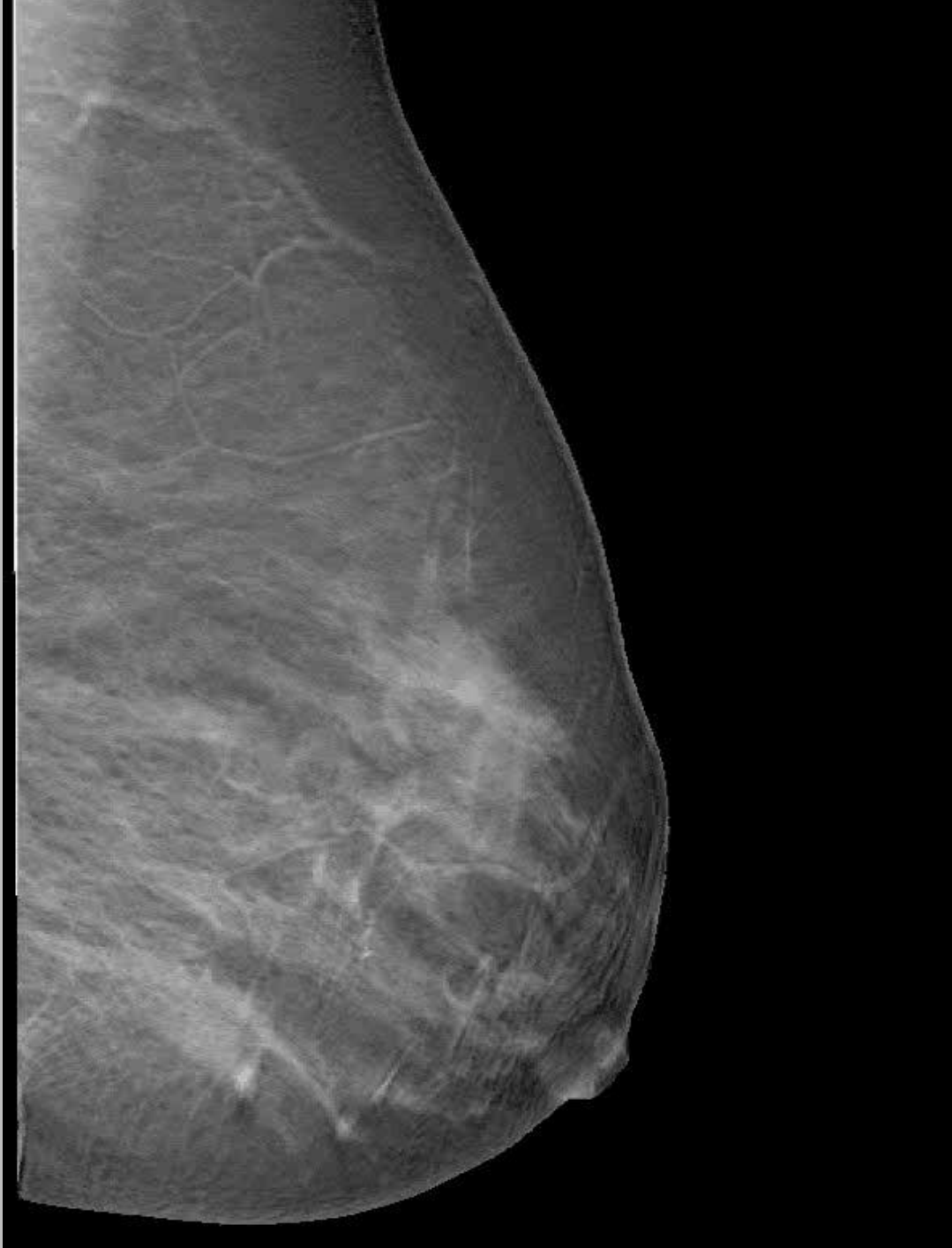
DIGITAL BREAST TOMOSYNTESIS (DBT)



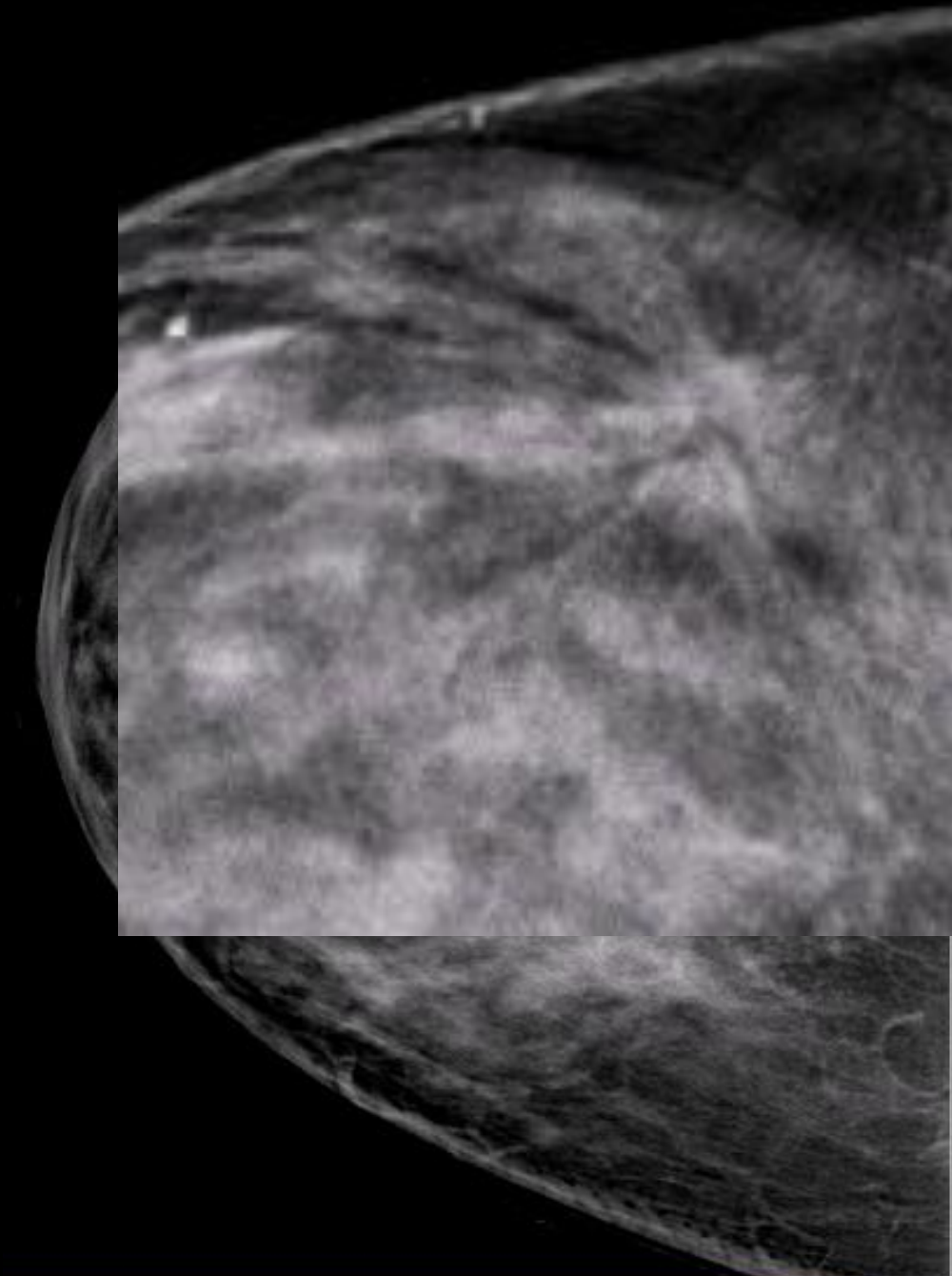
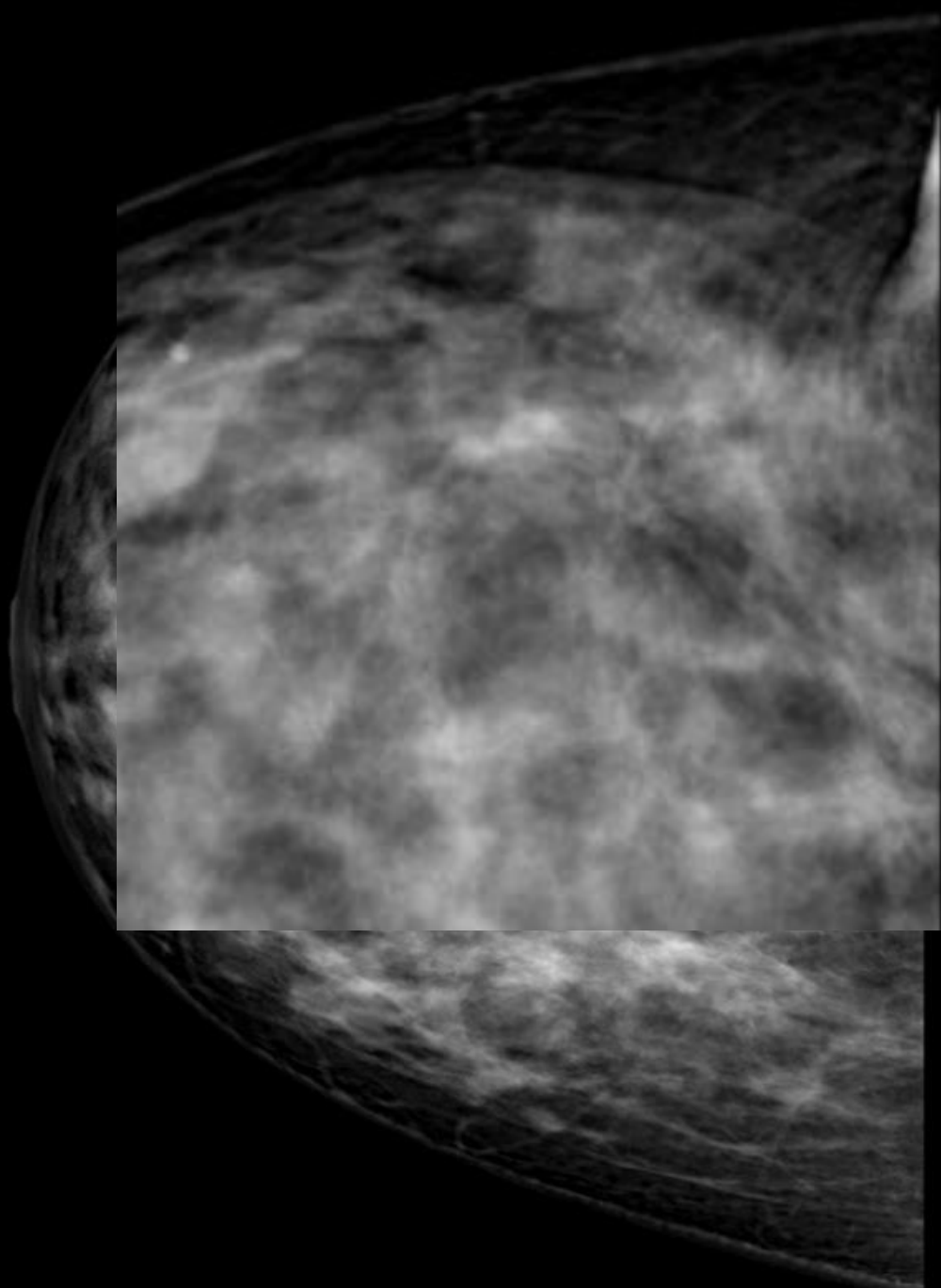
A... partial CT



KJ LMLO



IDC



Tomosynthesis use in screening

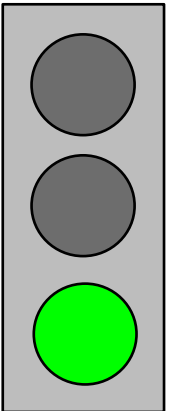
In the context of an organised screening programme, for asymptomatic women with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests:

- **using either DBT or digital mammography**
(conditional recommendation, very low certainty of the evidence)
- **not using both DBT and digital mammography**
(conditional recommendation, very low certainty of the evidence)

Since the GDG made a strong recommendation for screening at ages 50-69, these apply specifically to this age group.

Apr 15, 2021

UPDATED



Screening in women with high breast density

Digital breast tomosynthesis (DBT)

In the context of an organised screening programme, the ECIBC's Guidelines Development Group (GDG) **suggests:**

- not implementing tailored screening with both DBT and digital mammography for women with high mammographic breast density detected for the first time with digital mammography

(conditional recommendation, very low certainty of the evidence)

- using DBT for women with high mammographic breast density detected in previous screening exams

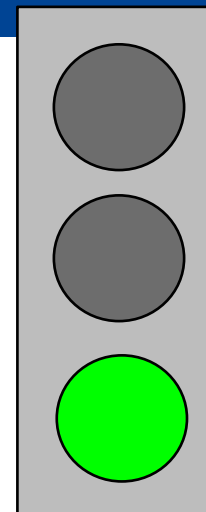
(conditional recommendation, very low certainty of the evidence)

Magnetic resonance imaging and ultrasound

In the context of an organised screening programme, for asymptomatic women with high mammographic breast density, the ECIBC's Guidelines Development Group (GDG) **suggests:**

- not implementing tailored screening with magnetic resonance imaging (MRI)
(conditional recommendation, very low certainty of the evidence)
- not implementing tailored screening with automated breast ultrasound system (ABUS)
(conditional recommendation, very low certainty of the evidence)
- not implementing tailored screening with hand-held ultrasound (HHUS)
(conditional recommendation, low certainty of the evidence)

DBT: YES



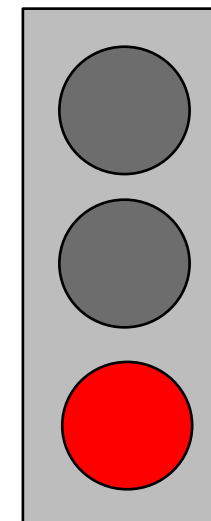
UPDATED

Aug 3, 2021

MRI: NO

ABUS: NO

HHUS: NO



UNCHANGED

Aug 3, 2021

Use of artificial intelligence

Artificial intelligence (AI)

In the context of an organised population-based screening programme, for asymptomatic women with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests:

- **not using single reading supported by AI**
(conditional recommendation, very low certainty of the test accuracy evidence)
- **using double reading supported by AI**
(conditional recommendation, low certainty of the test accuracy evidence)

New

Jan 21, 2022



FUTURE



loading...

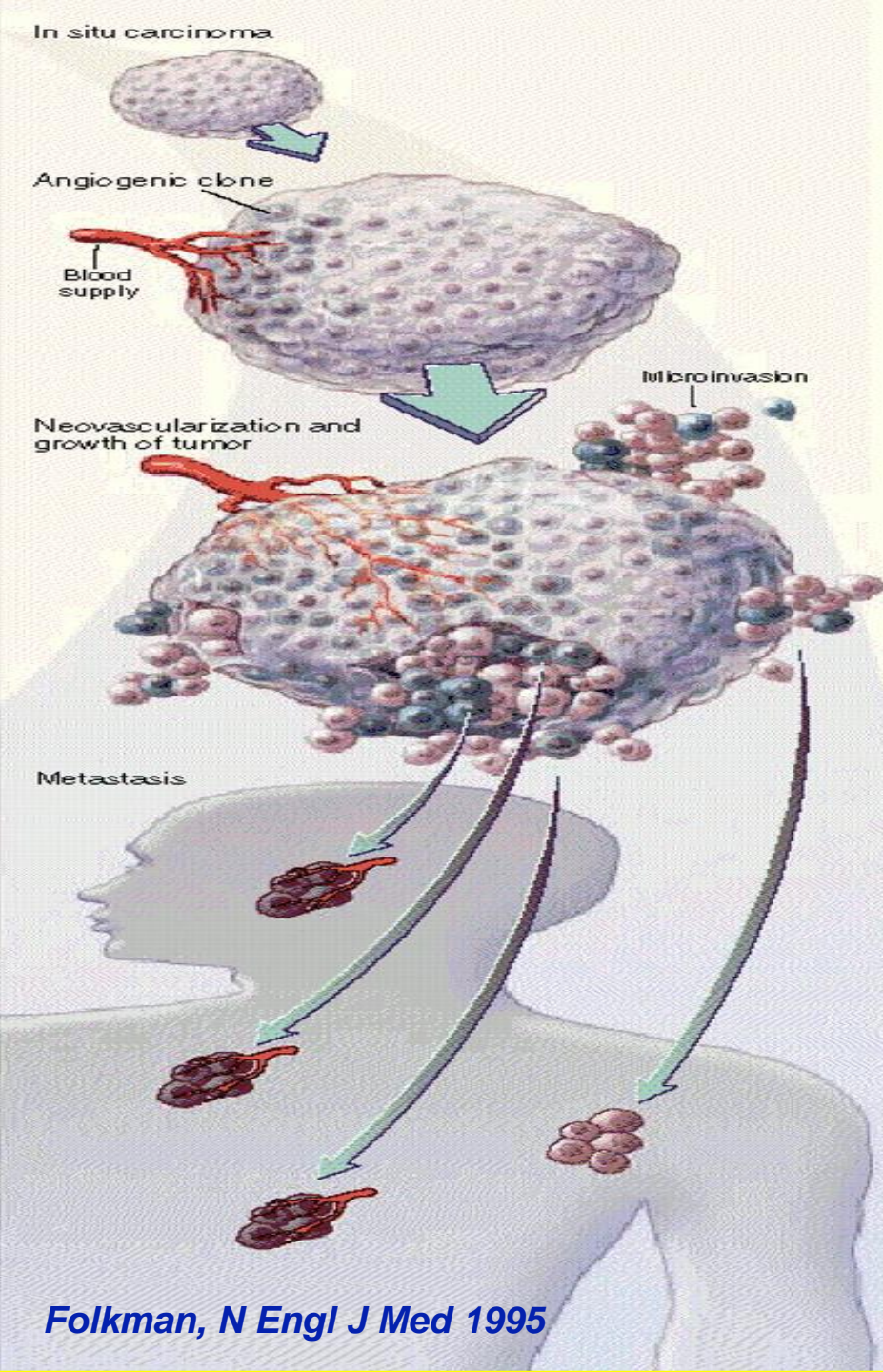
If you want to know the
future, look at the past.

Albert Einstein

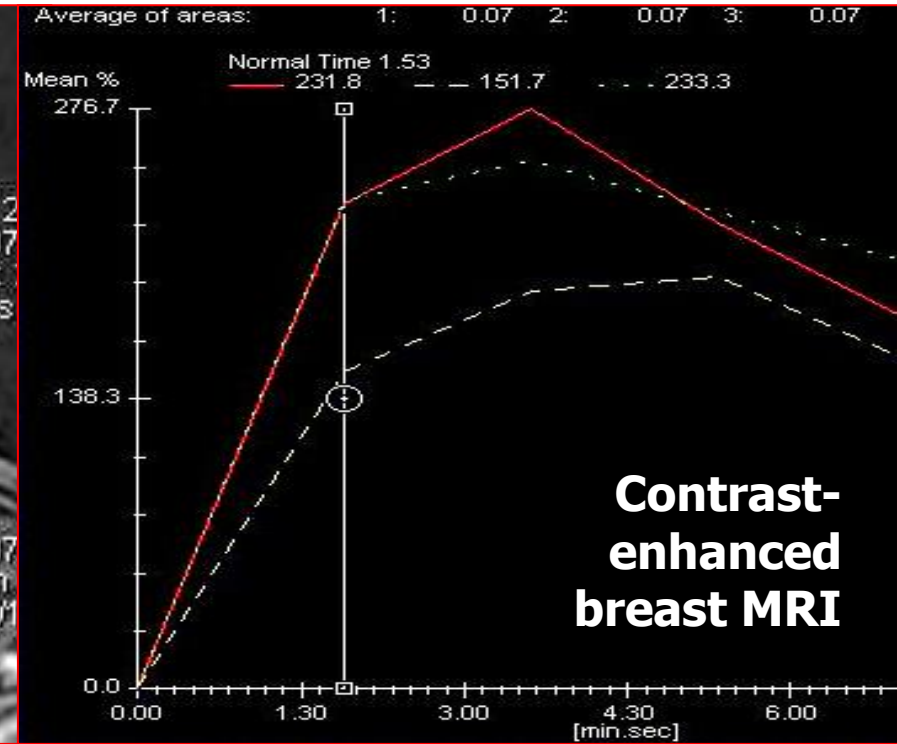
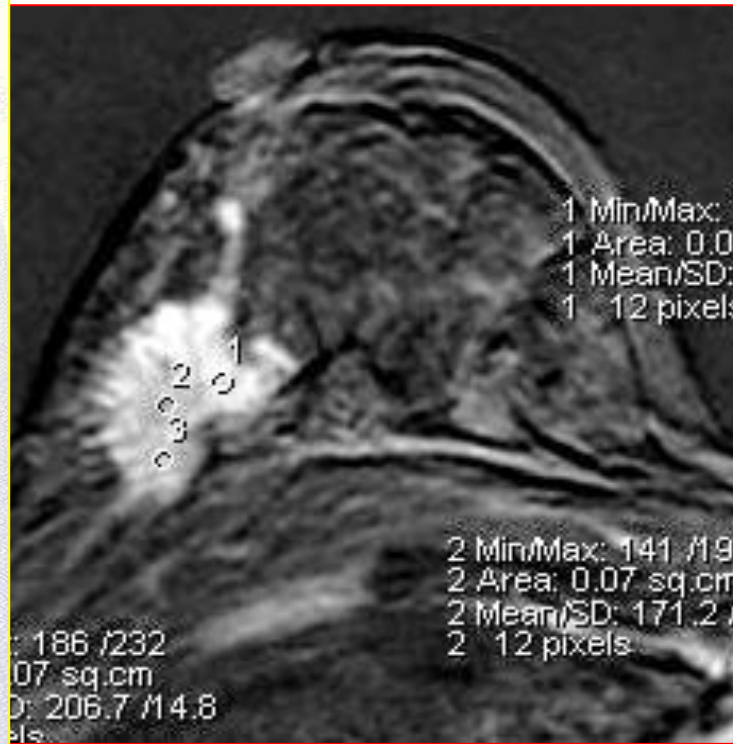
Neoangiogenesis

Increased:

- **Vascularity (new and larger vessels)**
- **Microvascular permeability $\times 8$**
- **Interstitial space $\times 3-5$**



Folkman, N Engl J Med 1995



Gd-enhancement

Sensitivity for invasive cancers $\cong 95\%$



Paget disease, DCIS

2022

> Eur Radiol. 2022 Jun;32(6):4036-4045. doi: 10.1007/s00330-022-08617-6. Epub 2022 Mar 8.

Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI)

Ritse M Mann^{1, 2}, Alexandra Athanasiou³, Pascal A T Baltzer⁴, Julia Camps-Herrero⁵, Paola Clauser⁴, Eva M Fallenberg⁶, Gabor Forrai⁷, Michael H Fuchsjäger⁸, Thomas H Helbich⁴, Fleur Killburn-Toppin⁹, Mihai Lesaru¹⁰, Pietro Panizza¹¹, Federica Pediconi¹², Ruud M Pijnappel^{13, 14}, Katja Pinker^{4, 15}, Francesco Sardanelli^{16, 17}, Tamar Sella¹⁸, Isabelle Thomassin-Naggara¹⁹, Sophia Zackrisson²⁰, Fiona J Gilbert⁹, Christiane K Kuhl²¹, European Society of Breast Imaging (EUSOBI)

2015

Review > Eur Radiol. 2015 Dec;25(12):3669-78. doi: 10.1007/s00330-015-3807-z.

Epub 2015 May 23.

Breast MRI: EUSOBI recommendations for women's information

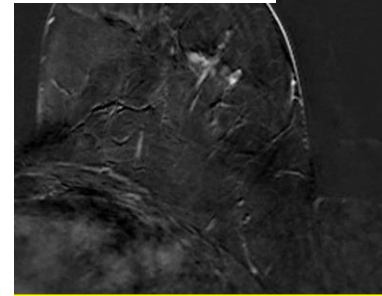
Ritse M Mann¹, Corinne Balleyguier², Pascal A Baltzer³, Ulrich Bick⁴, Catherine Colin⁵, Eleanor Cornford⁶, Andrew Evans⁷, Eva Fallenberg⁴, Gabor Forrai⁸, Michael H Fuchsjäger⁹, Fiona J Gilbert¹⁰, Thomas H Helbich³, Sylvia H Heywang-Köbrunner¹¹, Julia Camps-Herrero¹², Christiane K Kuhl¹³, Laura Martincich¹⁴, Federica Pediconi¹⁵, Pietro Panizza¹⁶, Luis J Pina¹⁷, Ruud M Pijnappel¹⁸, Katja Pinker-Domenig³, Per Skaane¹⁹, Francesco Sardanelli²⁰; European Society of Breast Imaging (EUSOBI), with language review by Europa Donna-The European Breast Cancer Coalition

2010

> Eur J Cancer. 2010 May;46(8):1296-316. doi: 10.1016/j.ejca.2010.02.015. Epub 2010 Mar 19.

Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group

Francesco Sardanelli¹, Carla Boetes, Bettina Borisch, Thomas Decker, Massimo Federico, Fiona J Gilbert, Thomas Helbich, Sylvia H Heywang-Köbrunner, Werner A Kaiser, Michael J Kerin, Robert E Mansel, Lorenza Marotti, Laura Martincich, Louis Mauriac, Hanne Meijers-Heijboer, Roberto Orecchia, Pietro Panizza, Antonio Ponti, Arnie D Purushotham, Peter Regitnig, Marco Rosselli Del Turco, Fabienne Thibault, Robin Wilson



2008

Practice Guideline > Eur Radiol. 2008 Jul;18(7):1307-18. doi: 10.1007/s00330-008-0863-7.

Epub 2008 Apr 4.

Breast MRI: guidelines from the European Society of Breast Imaging

R M Mann, C K Kuhl, K Kinkel, C Boetes

1986

Comparative Study > J Comput Assist Tomogr. Mar-Apr 1986;10(2):199-204.

doi: 10.1097/00004728-198603000-00005.

MR imaging of the breast using gadolinium-DTPA

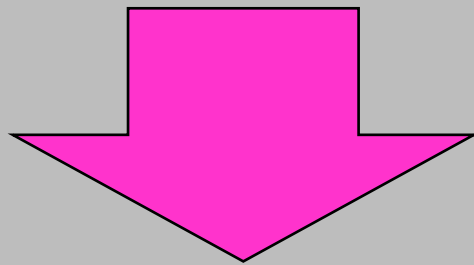
S H Heywang, D Hahn, H Schmidt, I Kruschke, W Eiermann, R Bassermann, J Lissner

PMID: 3950145 DOI: 10.1097/00004728-198603000-00005

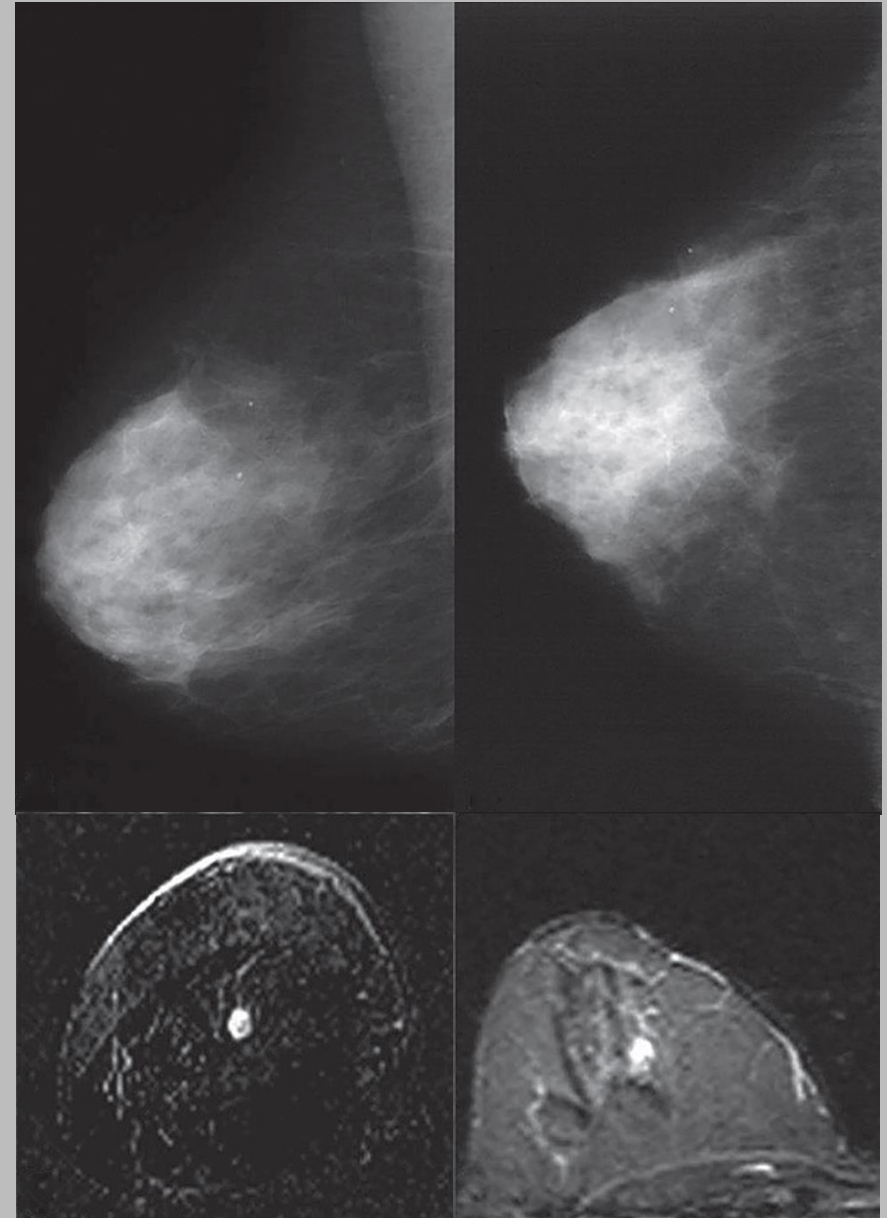
The long way to MRI acceptance

BREAST MRI HIGH-RISK SCREENING

- High breast cancer incidence (>4-5x)
- Data on MRI performance (sens./spec.) with at least 30% increase in sensitivity versus mammography/US
- MRI earlier detection of smaller cancers accepted as a proxy of patient outcome, translated from screening mammography, notwithstanding the concomitant ovarian cancer risk



- Large multidisciplinary acceptance (since 2007, ACS)
- Discussion only on risk thresholds (eg, LTR 20% or 30%)



MRI SCREENING OF HIGH-RISK WOMEN

2007

American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography

CA Cancer J Clin 2007;57:75-89

Debbie Saslow, PhD; Carla Boetes, MD, PhD; Wylie Burke, MD, PhD; Steven Harms, MD; Martin O. Leach, PhD; Constance D. Lehman, MD, PhD; Elizabeth Morris, MD; Etta Pisano, MD; Mitchell Schnall, MD, PhD; Stephen Sener, MD; Robert A. Smith, PhD; Ellen Warner,

American Cancer

ABSTRACT New evidence on breast Magnetic Resonance Imaging (MRI) screening has become available since the American Cancer Society (ACS) last issued guidelines for the early detection of breast cancer in 2003. A guideline panel has reviewed this evidence and developed new recommendations for women at different defined levels of risk. Screening MRI is recommended for women with an approximately 20–25% or greater lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin disease. There are several risk subgroups for which the available data are insufficient to recommend for or against screening, including women with a personal history of breast cancer, carcinoma in situ, atypical hyperplasia, and extremely dense breasts on mammography. Diagnostic uses of MRI were not considered to be within the scope of this review. *(CA Cancer J Clin 2007;57:75–89.) © American Cancer Society, Inc., 2007.*

HIGH-RISK SCREENING: HIBCRIT-1

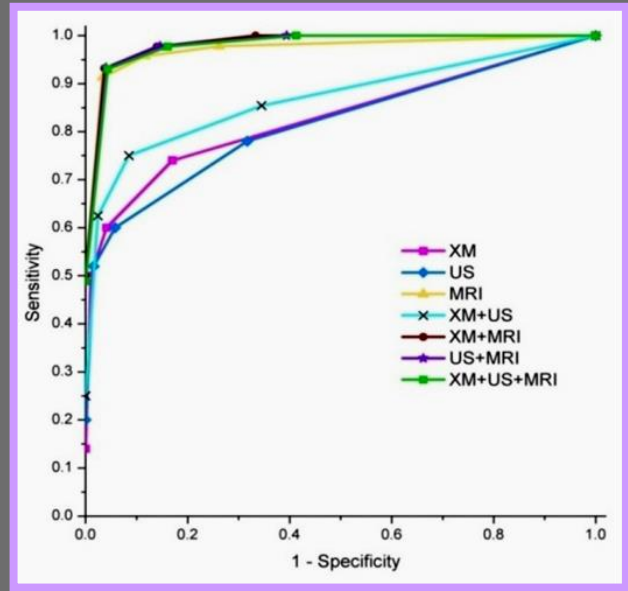
Modality	Sensitivity %	Specificity %	PPV2 %	NPV %	LR+	LR-
CBE	17.6	99.4	60.0	96.1	30.9	0.83
Mammography	50.0	99.1	73.5	97.6	58.1	0.50
US	52.0	99.2	76.5	97.7	66.0	0.48
MRI	91.3*	97.4	61.8	99.6*	35.1	0.09*
Mam + US	62.5	98.4	65.2	98.2	39.0	0.38
MRI + Mammo	93.2	97.0	58.6	99.7	31.5	0.07
MRI + US	93.3	97.1	60.0	99.7	32.0	0.07

* Stat. significance

Overall Sensitivity		
Film-screen	17/31	55%
Digital (CR or FFD)	8/19	42%

Sensitivity for pT1a-b		
Mammo & US	10/20	50%
MRI	18/19	95%

Sardanelli F et al. Invest Radiol 2011



**MRI
alone!**

Supplemental MRI Screening for Women with Extremely Dense Breast Tissue

Dense

M.F. Bakker, S.V. de Lange, R.M. Pijnappel, R.M. Mann, P.H.M. Peeters, E.M. Monninkhof, M.J. Emaus, C.E. Loo, R.H.C. Bisschops, M.B.I. Lobbes, M.D.F. de Jong, K.M. Duvivier, J. Veltman, N. Karssemeijer, H.J. de Koning, P.J. van Diest, W.P.T.M. Mali, M.A.A.J. van den Bosch, W.B. Veldhuis, and C.H. van Gils, for the DENSE Trial Study Group*

Nov 28, 2019



The NEW ENGLAND JOURNAL of MEDICINE

ABSTRACT

BACKGROUND

Extremely dense breast tissue is a risk factor for breast cancer and limits the detection of cancer with mammography. Data are needed on the use of supplemental magnetic resonance imaging (MRI) to improve early detection and reduce interval breast cancers in such patients.

METHODS

In this multicenter, randomized, controlled trial in the Netherlands, we assigned 40,373 women between the ages of 50 and 75 years with extremely dense breast tissue and normal results on screening mammography to a group that was invited to undergo supplemental MRI or to a group that received mammography screening only. The groups were assigned in a 1:4 ratio, with 8061 in the MRI-invitation group and 32,312 in the mammography-only group. The primary outcome was the between-group difference in the incidence of interval cancers during a 2-year screening period.

RESULTS

The interval-cancer rate was 2.5 per 1000 screenings in the MRI-invitation group and 5.0 per 1000 screenings in the mammography-only group, for a difference of 2.5 per 1000 screenings (95% confidence interval [CI], 1.0 to 3.7; $P < 0.001$). Of the women who were invited to undergo MRI, 59% accepted the invitation. Of the 20 interval cancers that were diagnosed in the MRI-invitation group, 4 were diagnosed in the women who actually underwent MRI (0.8 per 1000 screenings) and 16 in those who did not accept the invitation (4.9 per 1000 screenings). The MRI cancer-detection rate among the women who actually underwent MRI screening was 16.5 per 1000 screenings (95% CI, 13.3 to 20.5). The positive predictive value was 17.4% (95% CI, 14.2 to 21.2) for recall for additional testing and 26.3% (95% CI, 21.7 to 31.6) for biopsy. The false positive rate was 79.8 per 1000 screenings. Among the women who underwent MRI, 0.1% had either an adverse event or a serious adverse event during or immediately after the screening.

CONCLUSIONS

The use of supplemental MRI screening in women with extremely dense breast tissue and normal results on mammography resulted in the diagnosis of significantly fewer interval cancers than mammography alone during a 2-year screening period. (Funded by the University Medical Center Utrecht and others; DENSE ClinicalTrials.gov number, NCT01315015.)

Women with extremely dense breasts (ACR category d)

Mammo:MRI randomization = 4:1

Acceptance of MRI = 59%

2-year IC rate

Intention-to-treat

Per-protocol

MRI-group

2.5 per 1,000

0.8 per 1,000

Mammo-group

5.0 per 1,000 (-50%)
($p < 0.001$)

5.0 per 1,000 (-84%)
($p < 0.001$)

MRI detection rate 16.5 per 1,000

MRI PPV1 (recall rate) 17%

MRI PPV3 (biopsy) 26%

MRI FP rate 8%

MRI adverse event rate 0.1%

EUSOBI GUIDELINES

European Radiology

<https://doi.org/10.1007/s00330-022-08617-6>

BREAST



Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI)

Ritse M. Mann^{1,2} • Alexandra Athanasiou³ • Pascal A. T. Baltzer⁴ • Julia Camps-Herrero⁵ • Paola Clauser⁴ • Eva M. Fallenberg⁶ • Gabor Forrai⁷ • Michael H. Fuchsjäger⁸ • Thomas H. Helbich⁴ • Fleur Killburn-Toppin⁹ • Mihai Lesaru¹⁰ • Pietro Panizza¹¹ • Federica Pediconi¹² • Ruud M. Pijnappel^{13,14} • Katja Pinker^{4,15} • Francesco Sardanelli^{16,17} • Tamar Sella¹⁸ • Isabelle Thomassin-Naggara¹⁹ • Sophia Zackrisson²⁰ • Fiona J. Gilbert⁹ • Christiane K. Kuhl²¹ • On behalf of the European Society of Breast Imaging (EUSOBI)

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Abstract

Breast density is an independent risk factor for the development of breast cancer and also decreases the sensitivity of mammography for screening. Consequently, women with extremely dense breasts face an increased risk of late diagnosis of breast cancer. These women are, therefore, underserved with current mammographic screening programs. The results of recent studies reporting on contrast-enhanced breast MRI as a screening method in women with extremely dense breasts provide compelling evidence that this approach can enable an important reduction in breast cancer mortality for these women and is cost-effective. Because there is now a valid option to improve breast cancer screening, the European Society of Breast Imaging (EUSOBI) recommends that women should be informed about their breast density. EUSOBI thus calls on all providers of mammography screening to share density information with the women being screened. In light of the available evidence, in women aged 50 to 70 years with extremely dense breasts, the EUSOBI now recommends offering screening breast MRI every 2 to 4 years. The EUSOBI acknowledges that it may currently not be possible to offer breast MRI immediately and everywhere and underscores that quality assurance procedures need to be established, but urges radiological societies and policymakers to act on this now. Since the wishes and values of individual women differ, in screening the principles of shared decision-making should be embraced. In particular, women should be counselled on the benefits and risks of mammography and MRI-based screening, so that they are capable of making an informed choice about their preferred screening method.

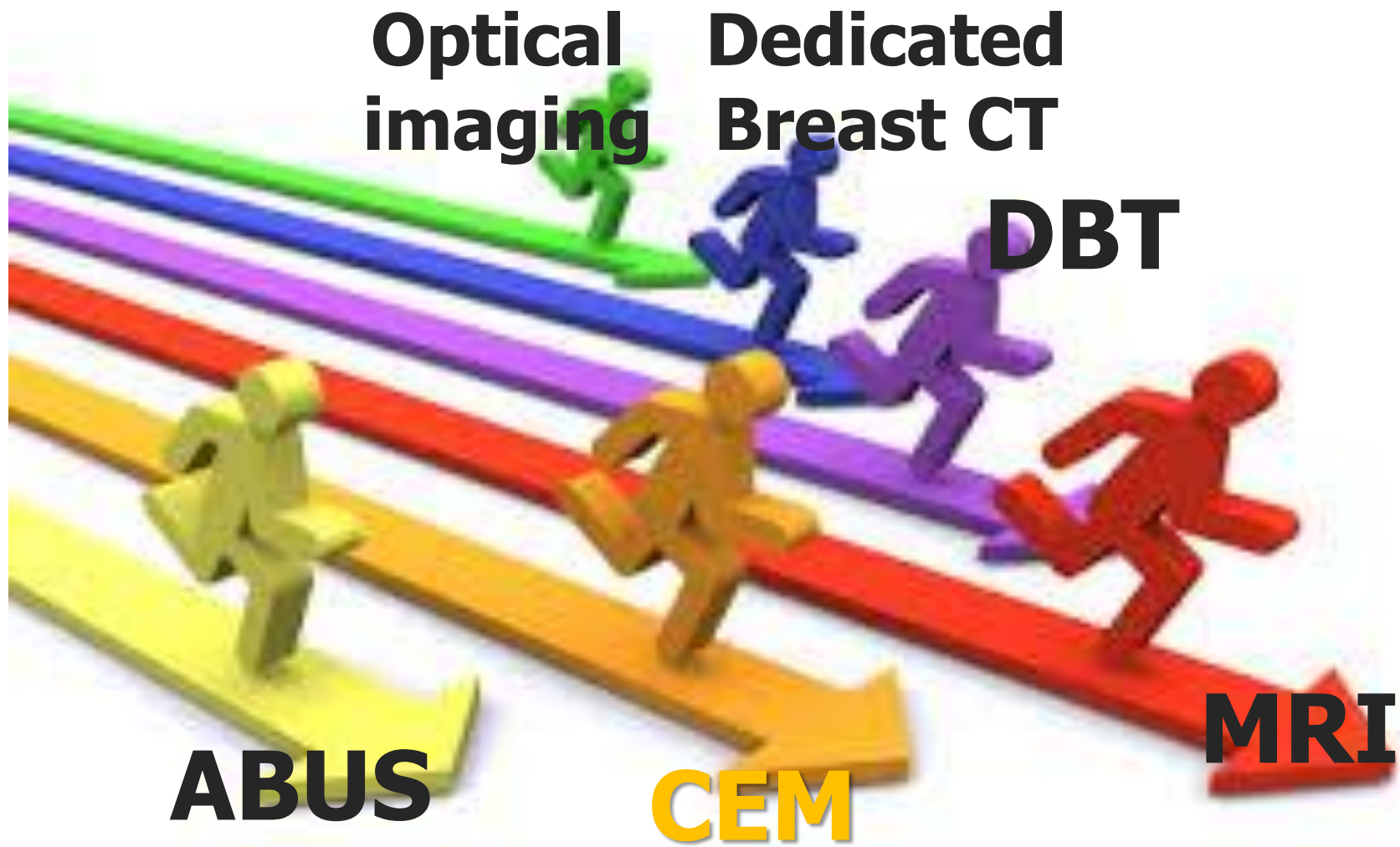
Screening in women with extremely dense breasts Recommendations of the European Society of Breast Imaging

- EUSOBI now recommends that women should be appropriately informed about their individual breast density – and on the diagnostic and prognostic implications of having dense breasts – by all (European) organizations that offer breast screening, in order to help them make well-balanced choices.
 - EUSOBI now recommends that supplemental screening is recommended in women with extremely dense breasts.
 - EUSOBI now recommends that such supplemental screening should be done preferably with MRI, because for the time being, level I evidence is available only for MRI screening. EUSOBI recommends such supplemental MRI screening to be offered to women with extremely dense breasts, from age 50 to 70, and at least every 4 years, preferably every 2 to 3 years. MRI can be used as a stand-alone screening technique (without mammography).
 - EUSOBI recommends that, where MRI screening is unavailable for reasons explained below, ultrasound in combination with mammography may be used as an alternative. In these cases, however, EUSOBI recommends informing women adequately about the different performance levels of different non-mammographic screening methods.
 - EUSOBI acknowledges the fact that before a population-wide use of non-mammographic screening methods (screening ultrasound and screening breast MRI) is put to practice in women with extremely dense breasts, the necessary quality assurance systems and benchmarks must be established for these non-mammographic screening methods similar to those that are in place for mammographic screening. This will take some time to prepare and to implement; in view of the degree of underdiagnosis associated with pure mammographic screening in women with extremely dense breasts, EUSOBI recommends national societies to act on this now, and with high priority. The EUSOBI guidelines on breast MRI or on screening ultrasound could serve as suitable templates.
 - EUSOBI underscores that, even in the absence of national programs that offer MRI screening as part of national healthcare, women should be informed about this recommendation in an unbiased and objective way according to the principle of “shared decision making”.
- EUSOBI wishes to underscore that “shared decision making” will likely result in more individualized screening approaches. This may interfere with current measures of effectiveness of screening programs that consider overall participation rates as an important indicator of quality. Of course, demonstrating a reduction of mortality on a population wide level requires high participation rates – but this should not lead to discouraging tools that may not yet be broadly available or acceptable, but can effectively avoid premature death from breast cancer in individual women.

In theory, there is no difference between theory and practice.
But in practice, there is.



Manfred Eigen
1967 Nobel Laureate in Chemistry



*A long way for CEM too?
Competition or cooperation?*

Mammography last steps

- **Digital breast tomosynthesis (DBT)**

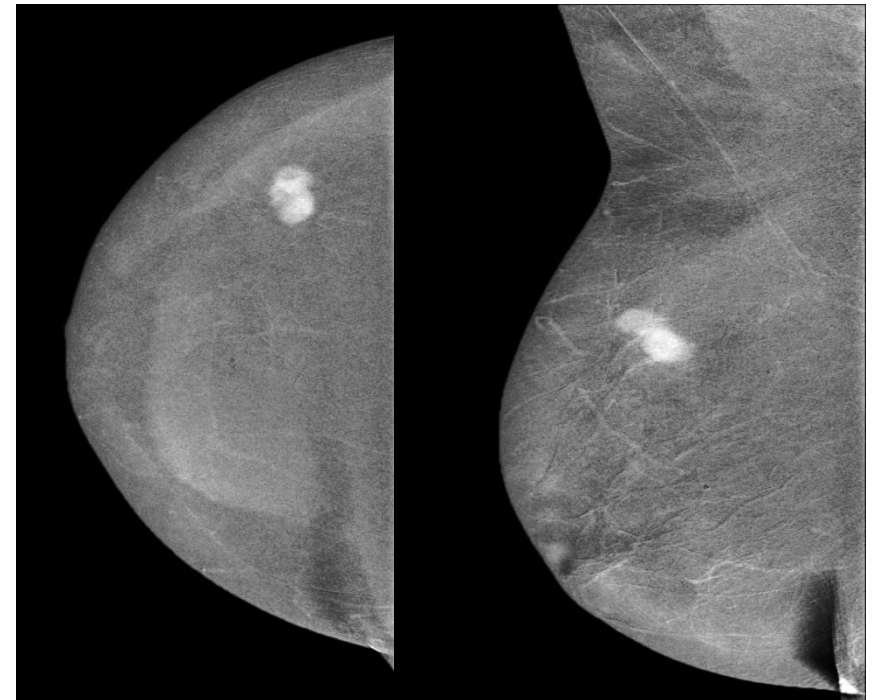
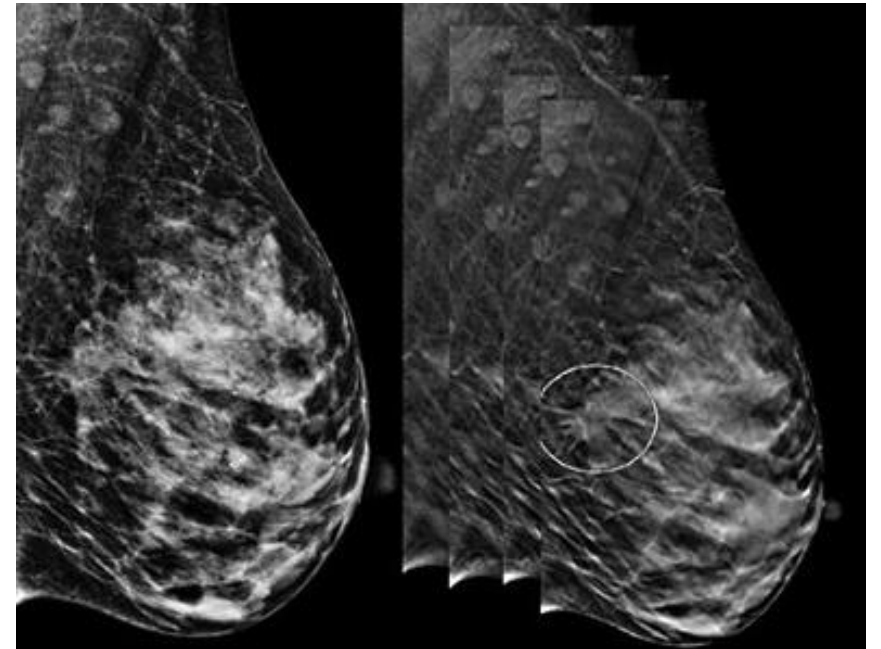
Great promises, lesser achievements

- Increased cancer detection !
- Increased reading time
- Reduction of recall rate ?
- Reduction of interval cancer rate ??
- Possible overdiagnosis

- **Contrast-enhanced mammography (CEM)**

Functional imaging (like MRI, but not dynamic)

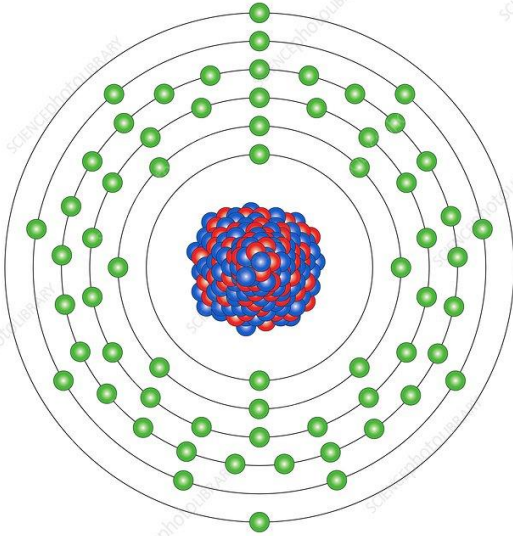
- Diagnostic performance similar to MRI



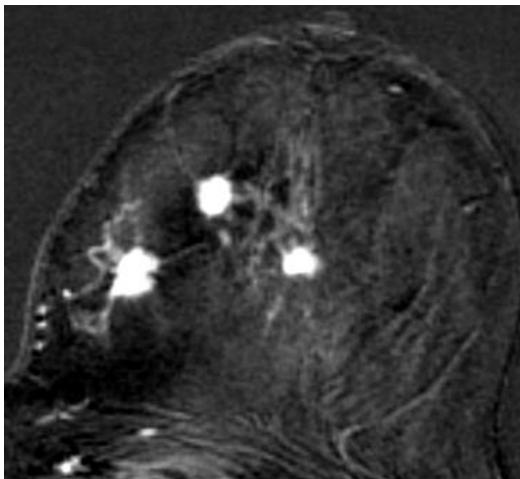
Magnetic field, RF

64: Gadolinium

2,8,18,25,9,2



64 protons 94 neutrons



MRI & CEM

=

**Contrast-enhanced
breast imaging**

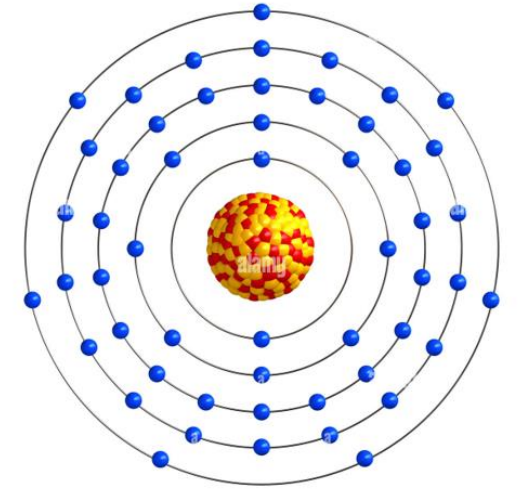
Two-compartment biodistribution
(vascular \leftrightarrow interstitial)

Tumor neoangiogenesis

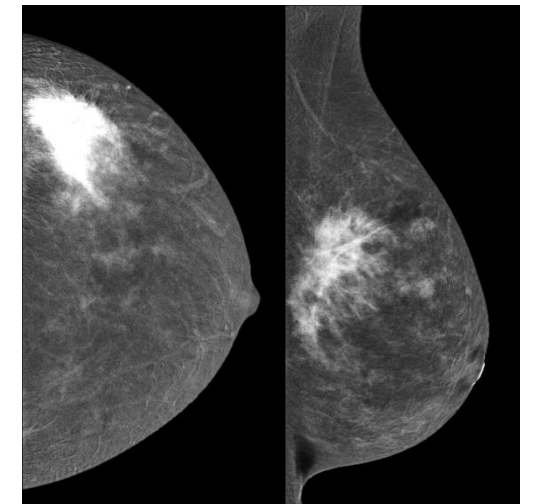
X-ray

53: Iodine

2,8,18,18,7



53 protons 74 neutrons





"Contrast-enhanced mammography" OR "CEDM" OR "CESM"[Title]

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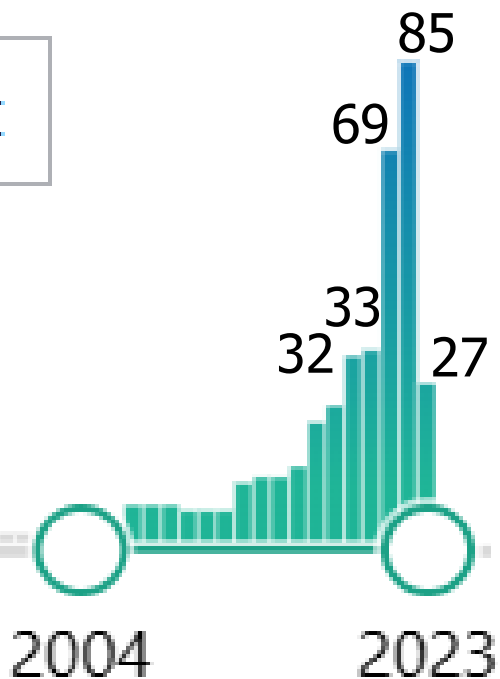
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ults

Page 1 of 31

2023 projection \approx 160

J Magn Reson Imaging. 2023 Mar;57(3):706-726. doi: 10.1002/jmri.26495. Epub 2022 Nov 9.

PMID: 36349728 Review.

Since four decades **mammography** is used for early breast cancer detection in asymptomatic women and still remains the gold standard imaging modality. ...The availability of new and evolving imaging modalities, for example, digital breast tomosynthesis, dynamic-**contrast** ...

Radiomic analysis in **Contrast-Enhanced mammography** using a multi-vendor dataset: Accuracy of models according to segmentation techniques.

CEM versus MRI

	CE-MRI	CEM
Images	Three-dimensional	Two-dimensional
Multiparametric technique	Yes	No
Radiation exposure	No	Yes
Contraindications	Several	Very few
Contrast-related health issues	Yes	Yes
Kinetic contrast analysis	Yes	No
Ease of interpretation	Low	High
Accessibility	Low	Intermediate to High
Cost	High	Low
Diagnostic performance	High	High
Patient preference	Low	High

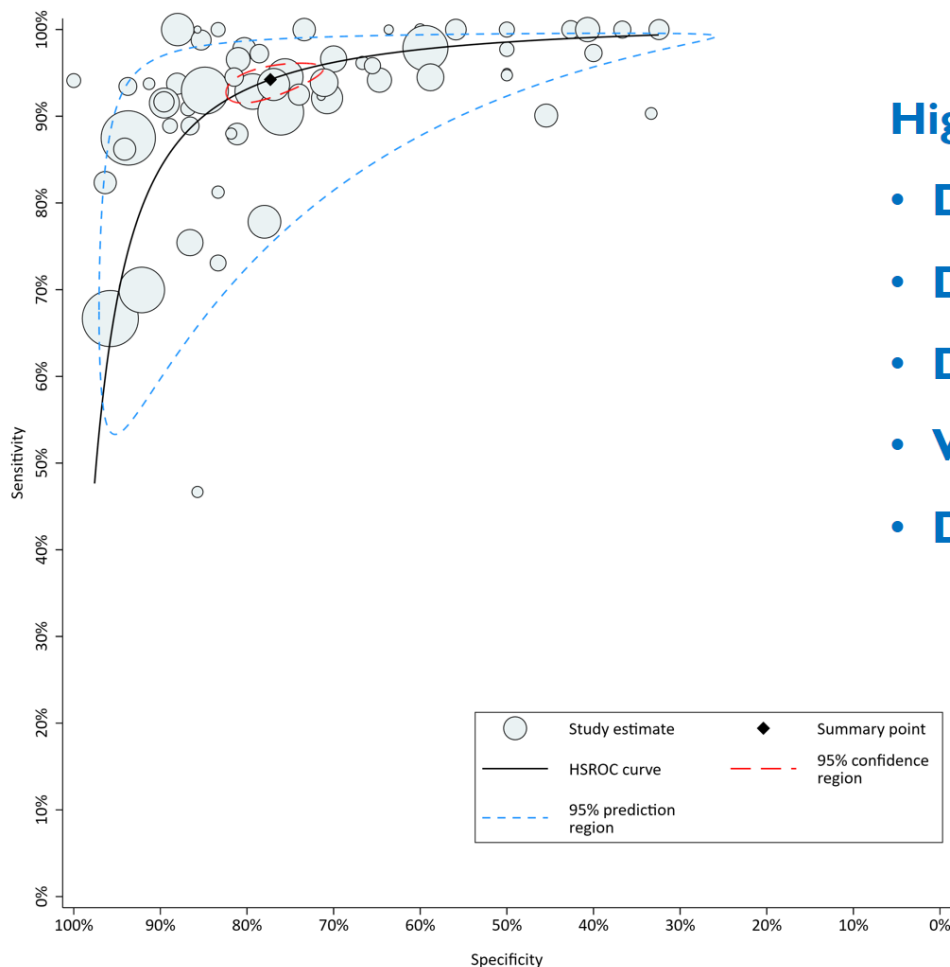
Contrast-enhanced Mammography: A Systematic Review and Meta-Analysis of Diagnostic Performance

Andrea Cozzi, MD • Veronica Magni, MD • Moreno Zanardo, PhD • Simone Schiaffino, MD • Francesco Sardanelli, MD

2022. doi:10.1148/radiol.211412

**60 studies
(67 study parts)**

**11 049 CEM
examinations in
10 605 patients**



Low-energy and recombined images

Sensitivity: 95%
(95% CI: 92%, 97%)

Specificity: 81%
(95% CI: 76%, 86%)

High heterogeneity

- Different study design
- Different clinical settings (indications)
- Different experience of readers
- Wide timeframe (2011-2021)
- Different reading methods

Summary AUC: 0.94
(95% CI: 0.91, 0.96)

2008

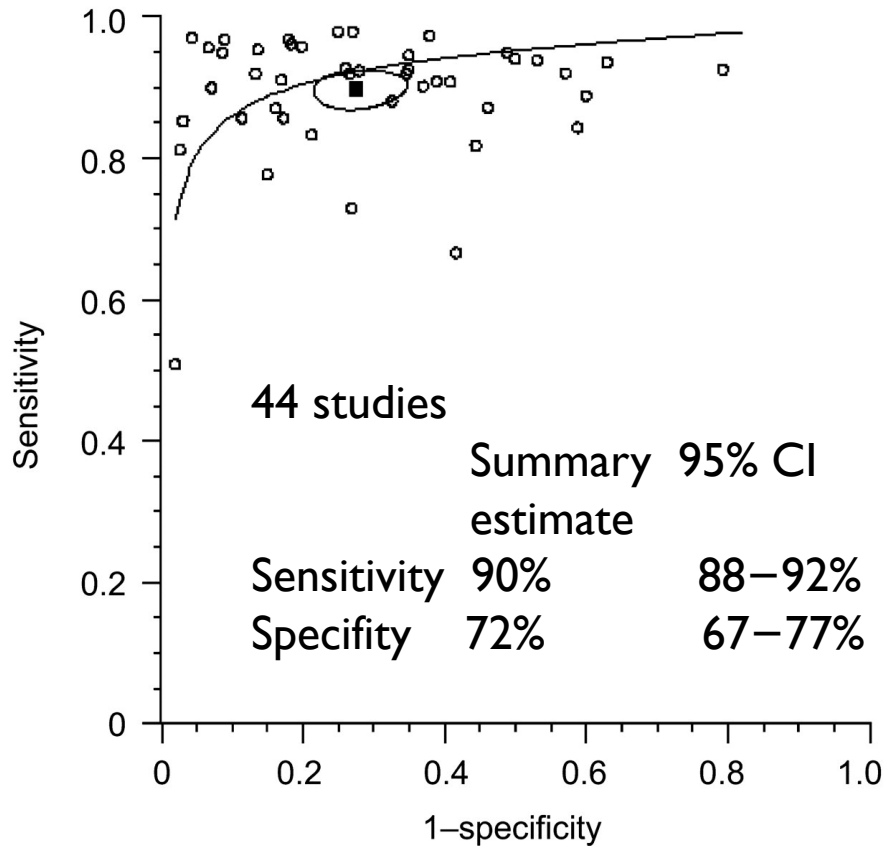
Meta-Analysis of MR Imaging in the Diagnosis of Breast Lesions¹

Radiology

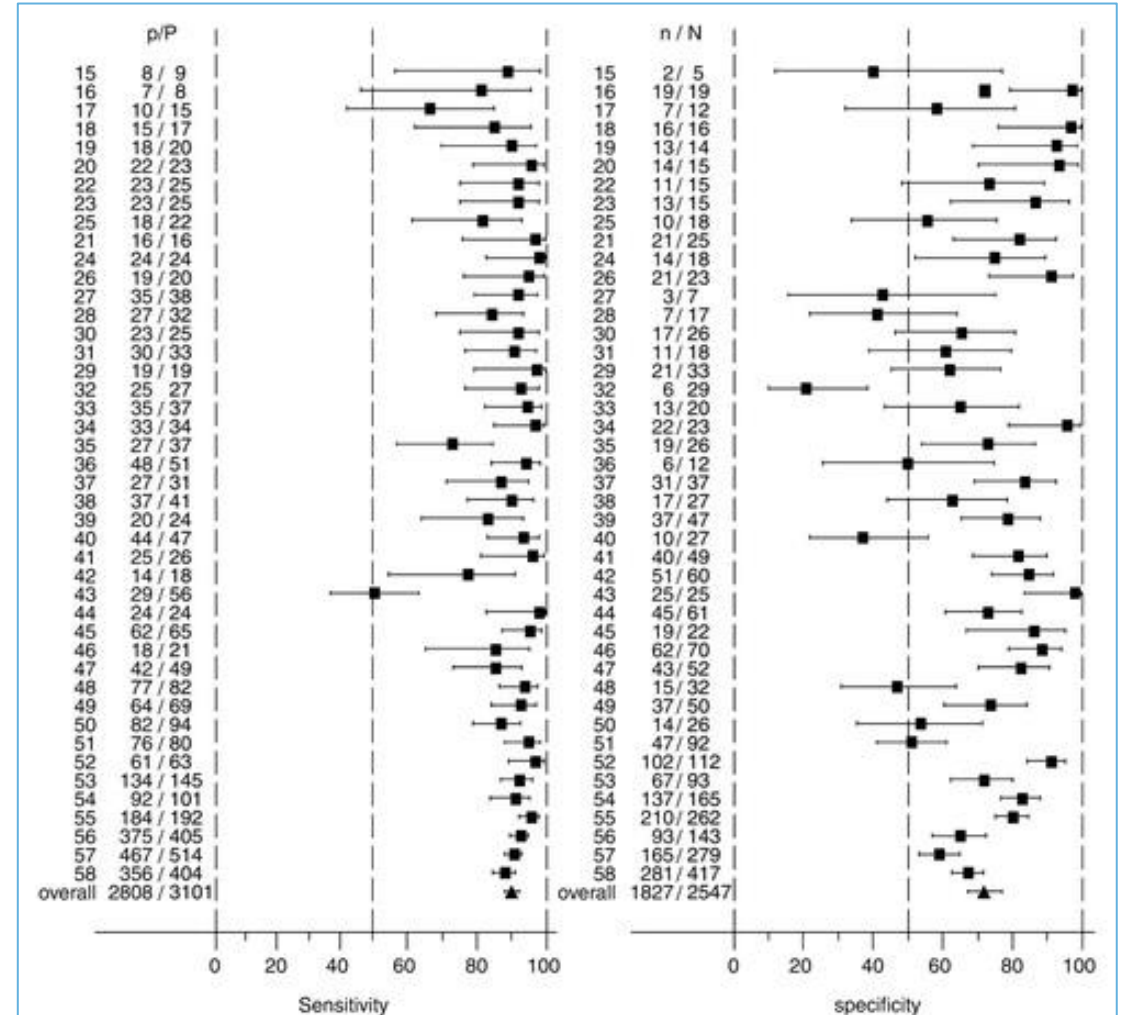
Nicky H. G. M. Peters, MD
Inne H. M. Borel Rinkes, MD, PhD
Nicolaas P. A. Zuihthoff, MSc
Willem P. T. M. Mali, MD, PhD
Karel G. M. Moons, MSc, PhD
Petra H. M. Peeters, MD, PhD

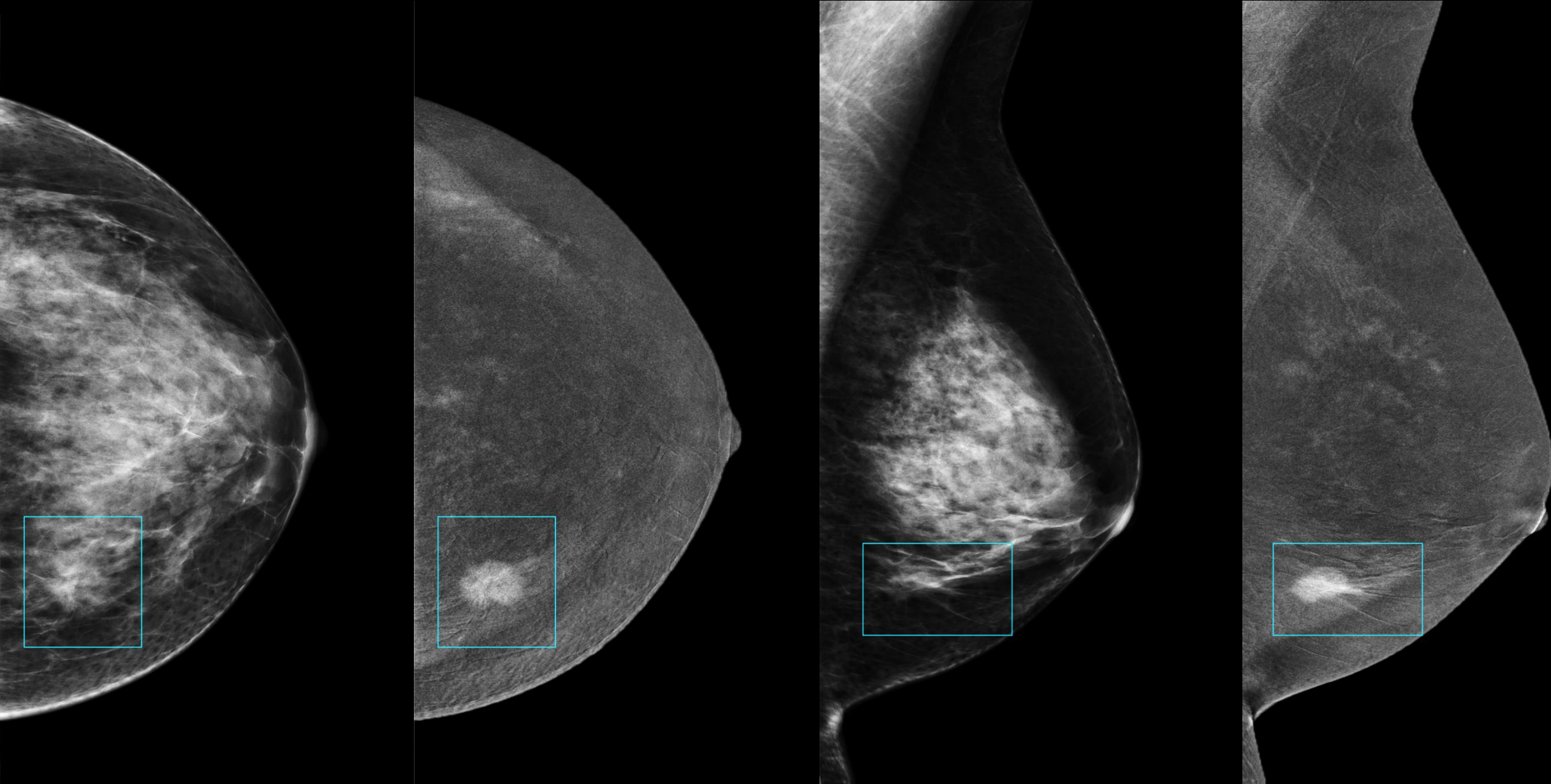
Purpose: To determine, in a meta-analysis, the diagnostic performance of contrast material-enhanced magnetic resonance (MR) imaging in patients with breast lesions.

Materials and Methods: Studies to assess the diagnostic performance of MR imaging in patients suspected of having breast cancer who underwent MR imaging and biopsy from January 1985 through March 2005 were reviewed for inclusion. A sum-



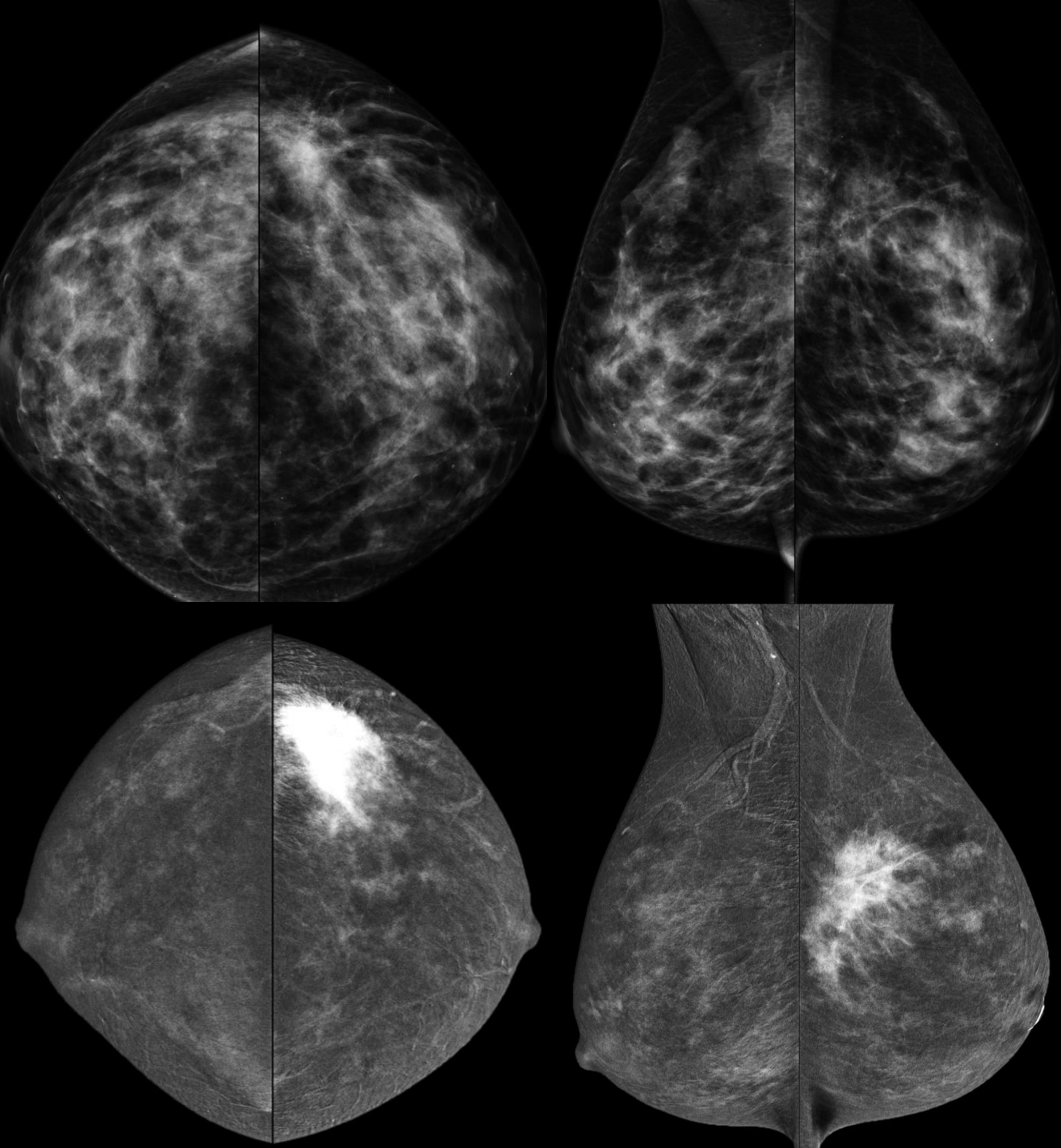
Back to the future!





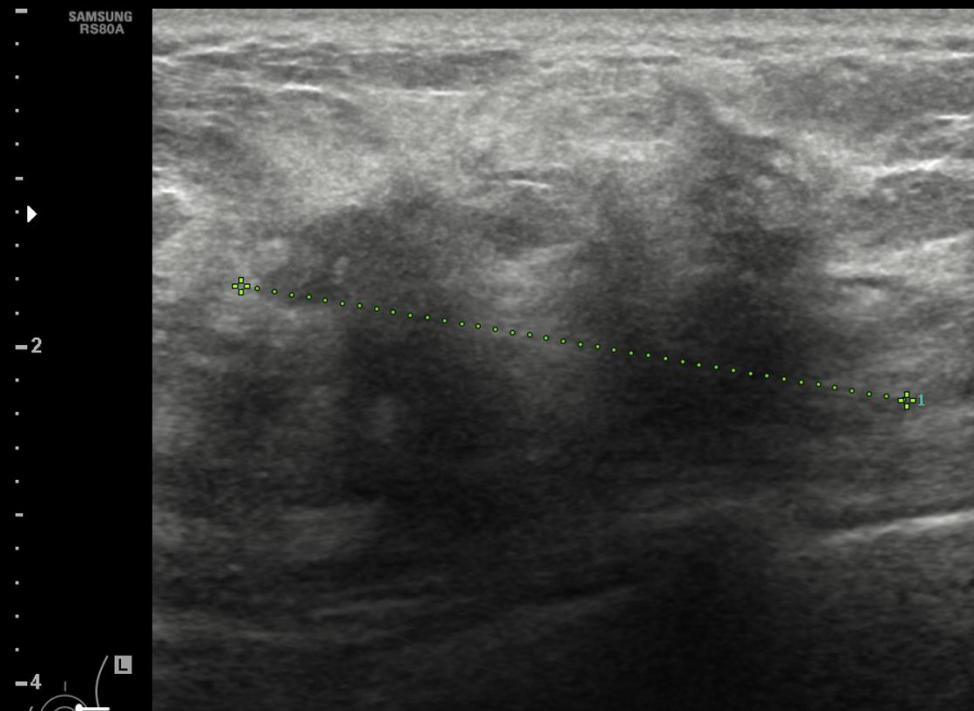
61-yo recalled woman (asymmetric mass at the left breast):
invasive carcinoma NST, grade 1. **CEM TP**

49-yo, no family history; screening, no symptoms



2D G64/DR58/FA8/P90/9.4 Frq Res.4.5cm

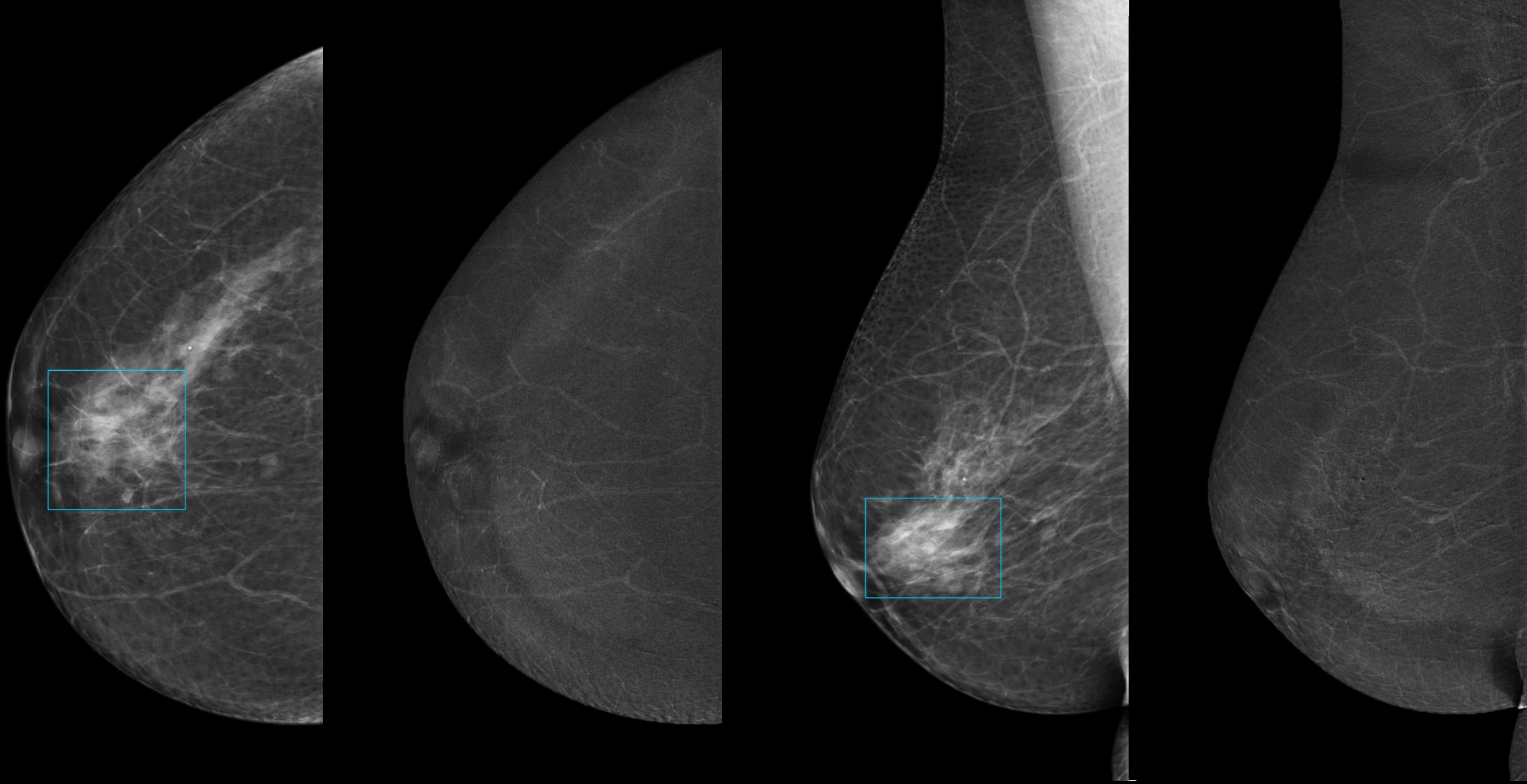
SAMSUNG RS80A



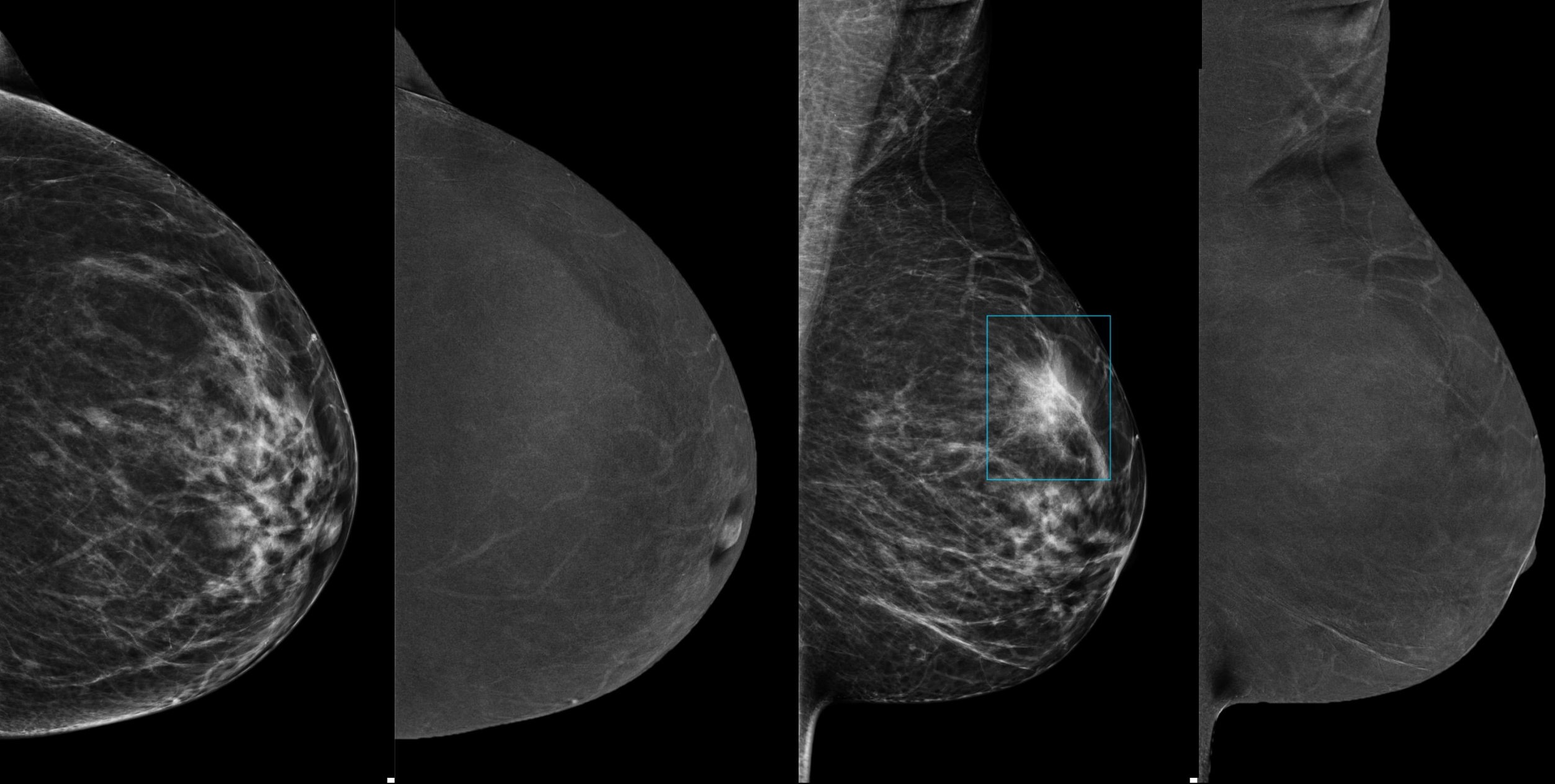
D1 40.08 mm

IDC G2, ER+, PR+, HER2+ Ki-67 20%

CEM TP



A 58-year-old woman was recalled for a suspicious retroareolar irregular mass in the right breast. No enhancement at CEM. US-guided CNB = apocrine metaplasia. CEM TN



A 49-year-old woman was recalled for a suspicious asymmetry in the upper quadrants of the left breast (only on the MLO view). No enhancement at rCEM. US-guided CNB = fibrosis. CEM TN

When MRI is better?

To avoid radiation exposure when screening women at genetic-familial high risk

Radioprotection
© EDP Sciences 2017
DOI: 10.1051/radiopro/2017034



Available online at:
www.radioprotection.org

Radiation induced breast cancer risk in BRCA mutation carriers from low-dose radiological exposures: a systematic review

C. Colin^{1,2,*}, N. Foray², G. Di Leo³ and F. Sardanelli^{3,4}

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² Inserm UMR 1052, Groupe de Radiobiologie, Centre de Recherche en Cancérologie de Lyon, 28 Rue Laennec, 69008 Lyon, France.
³ Unit of Radiology, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy.
⁴ Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy.

Abstract – The aim of this review paper is to clarify the radio-induced breast cancer risk in BRCA mutation carriers with a combined epidemiological and radiological systematic literature search on PubMed (MEDLINE) and EMBA from January 1st, 2000 to June 15th, 2017 using dedicated key words in the domains of research and evaluation: risk modeling, cohort-study, epithelial non-tumoral human breast cells. Only eleven articles were retrieved. These articles are analyzed and discussed. This review shows an association between BC risk and low-dose radiation exposures. There is no consistent data in this literature regarding the risk of BC in BRCA mutation carriers. Biological data point out strong indicators of radiation-induced carcinogenesis pathways. We conclude that the risk of radio-induced BC in BRCA mutation carriers depends on age at exposure and that repeated X-ray breast exposures such as mammography should be used very cautiously in these mutated patients.

Table 2. Number of breast cancer deaths due to mammographic screening per 100,000 BRCA1 mutations carriers with annual 2-view mammography from age 30–60 and biennial mammography from age 60–74 as a function of the mean dose per breast and of the excess risk model (from Obdeijn *et al.*, 2016).

	Mean dose 1.7 mGy	Mean dose 7.1 mGy
EAR model	11	45
ERR model	80	337





**What
about
AI?**

Signs of the times

Corriere della Sera online, Apr 29, 2023



ChatGpt è tornato raggiungibile dall'Italia. Sono state risolte (almeno in via temporanea) le questioni di privacy che il Garante aveva sollevato lo scorso 31 marzo e che avevano portato al blocco di ChatGpt per chi provava a collegarsi dall'Italia (senza usare una Vpn). Uno stop deciso in autonomia dalla stessa OpenAI, che ha aggiunto alcune misure per la tutela dei dati personali degli utenti. Prima di capire che cos'è cambiato rispetto al 31 marzo facciamo un passo indietro, per chi avesse scoperto ora ChatGpt.

Che cos'è ChatGpt? ChatGpt è un chatbot, ovvero un software che sa rispondere alle domande e conversare, in maniera sorprendentemente brillante e (quasi) «umana». Fa parte del recente filone dell'intelligenza

Artificial intelligence



A.I.



AI



Ai

The Age of AI

And Our Human Future

Henry A.
Kissinger

x

Eric
Schmidt

x

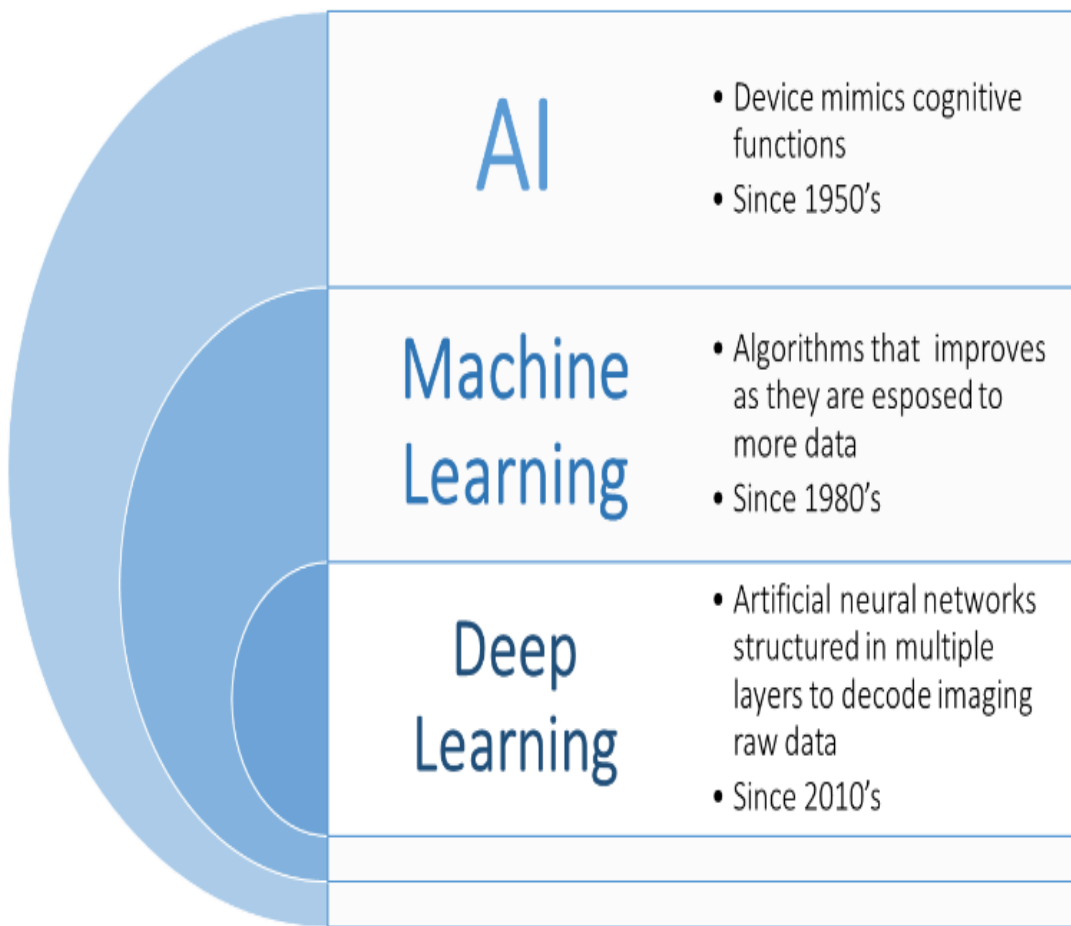
Daniel
Huttenlocher

AI's promise of epoch-making transformations

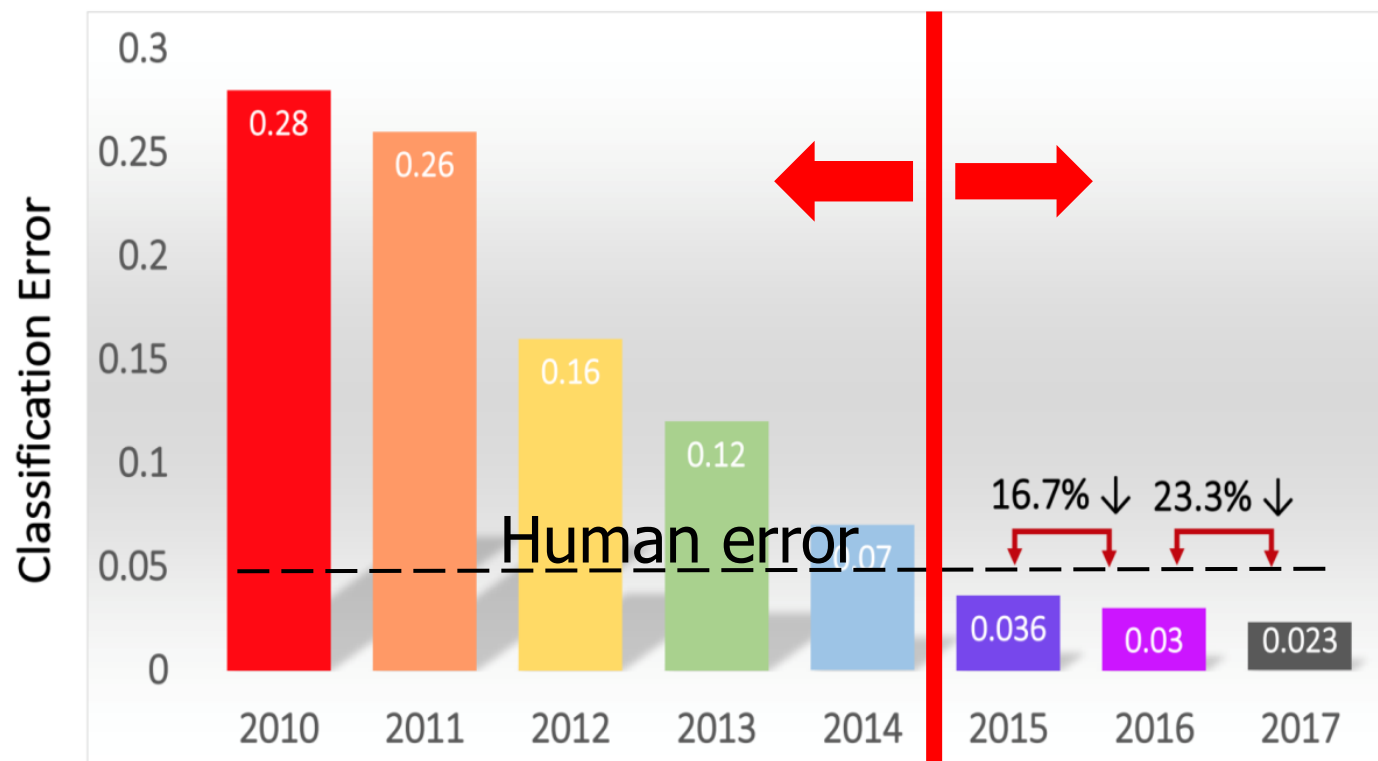
AI is not an industry, let alone a single product. It is an enabler of many industries and facets of human life: scientific research, education, manufacturing, logistics, transportation, defense, law enforcement, politics, advertising, art, culture, and more. The characteristics of AI – including its capacity to learn, evolve and surprise – will disrupt and transform them all.

From the Preface

The age of AI: and our human future. London: J Murray; 2021. p. 4

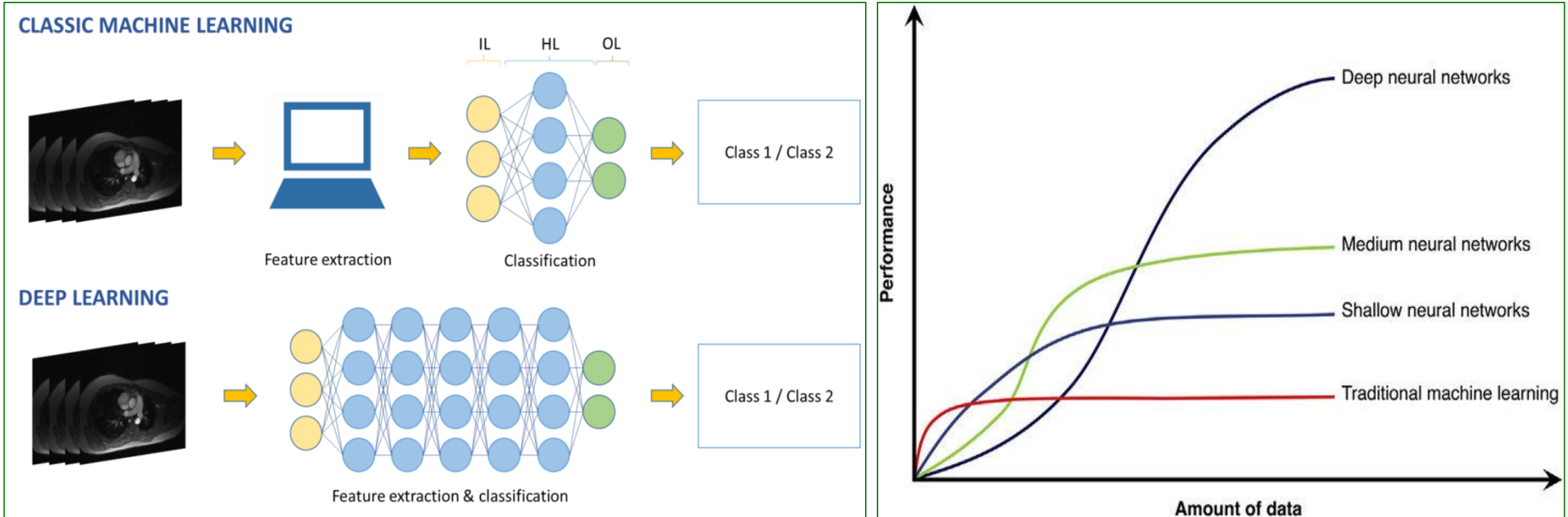


*Pesapane, Codari, Sardanelli
Eur Radiol Exp 2018*



ImageNet website, accessed May 2019

Machine Learning (ML) *versus* Deep Learning (DL)



European Radiology
Experimental 2018

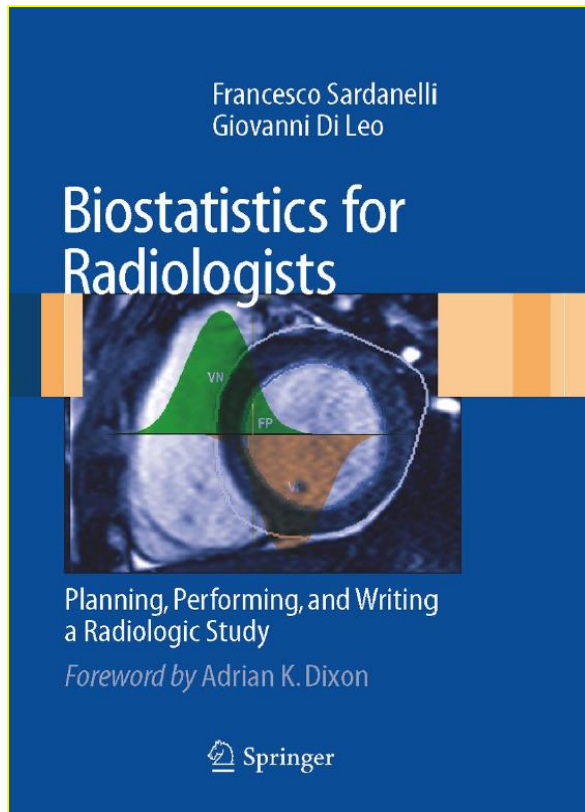
Artificial intelligence in medical imaging:
threat or opportunity? Radiologists again at
the forefront of innovation in medicine

Filippo Pesapane^{1†}, Marina Codari^{2†} and Francesco Sardanelli^{2,3}

Tang, An, et al. "Canadian Association of Radiologists
white paper on artificial intelligence in radiology."
Canadian Association of Radiologists Journal (2018).

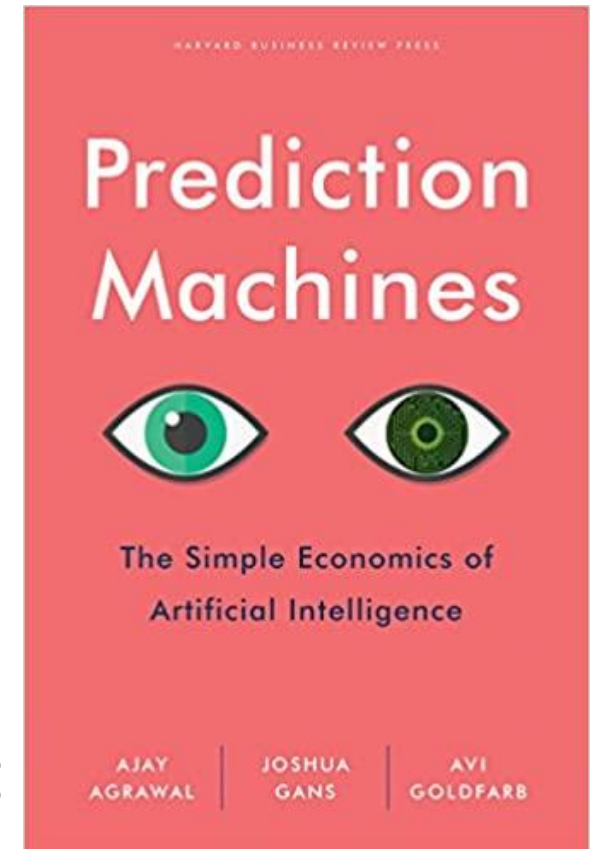
AI versus Statistics

AI is “only” a method for data analysis, but...



**Predictions for groups
of subjects/patients**

**Prediction for each
individual subject/patient**



Standalone AI for Cancer Detection at Screening Digital Mammography and Digital Breast Tomosynthesis: Systematic Review and Meta-Analysis

Table 2: Pooled Estimates of Performance Measures for Radiologists and Standalone AI for All Included Studies and Study Type Subgroups

Variable	Sensitivity		Specificity		AUC*	
	Radiologists	AI	Radiologists	AI	Radiologists	AI
All studies ($n = 16$)	73.6 (68.7, 78.0)	80.6 (74.3, 85.7)	89.6 (82.7, 93.9)	85.7 (74.1, 92.6)
Reader studies ($n = 6$)	72.4 (64.1, 79.4)	80.8 (68.0, 89.3)	81.6 (75.7, 86.4)	76.9 (55.2, 90.0)	0.81 [0.014]	0.87 [0.010]
Studies using historic reads ($n = 7$) [†]	72.6 (63.7, 80.1)	75.8 (70.2, 80.6)	96.4 (94.9, 97.4)	95.6 (93.7, 96.9)	0.96 [0.022]	0.89 [0.037]
Digital breast tomosynthesis studies ($n = 4$) [†]	77.9 (73.1, 82.0)	88.8 (80.2, 94.0)	81.6 (37.8, 97.0)	63.1 (22.1, 91.1)	0.79 [0.020]	0.90 [0.011]

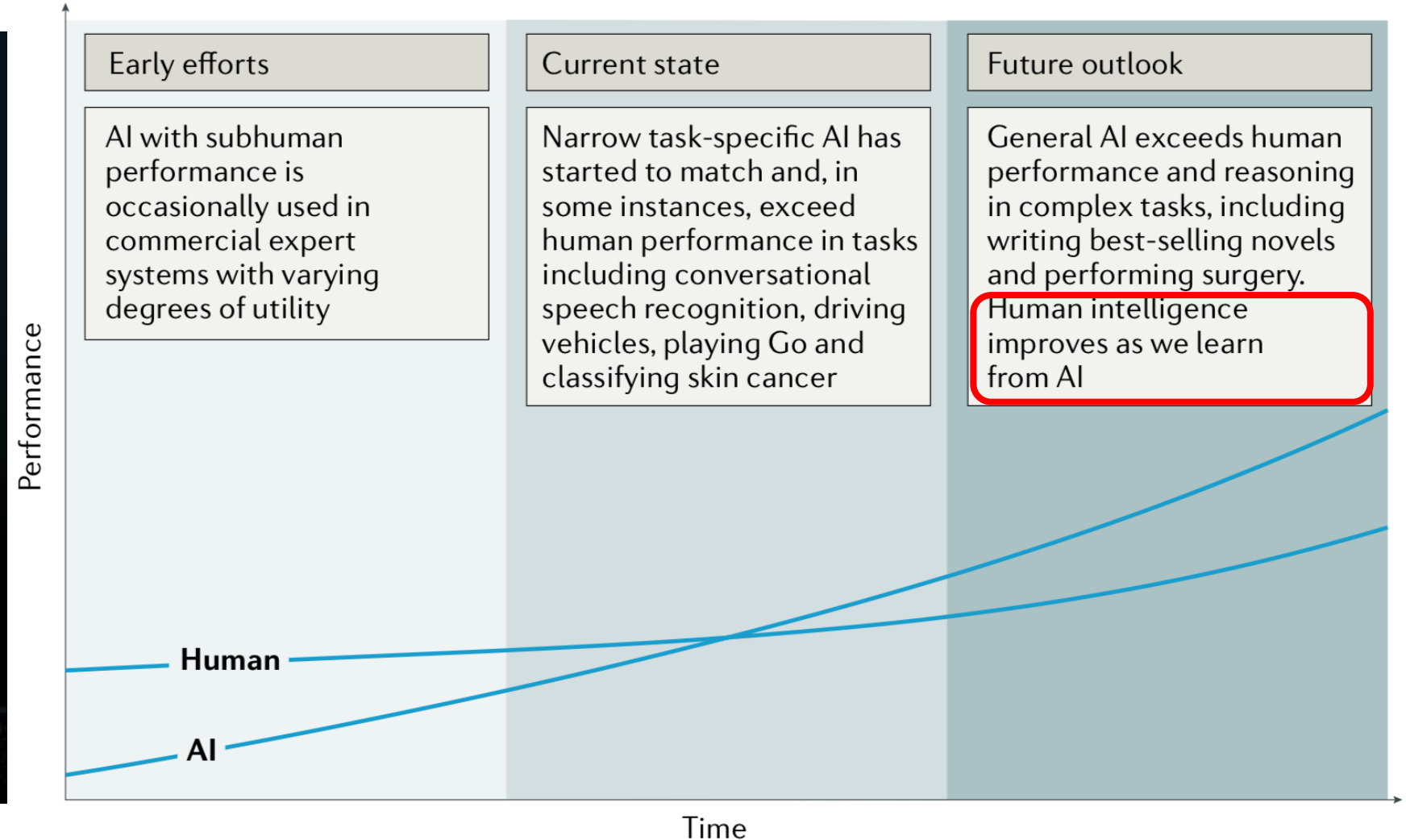
- Pooled AUCs were higher for standalone AI than radiologists in the six reader studies on digital mammography, but not for historic cohort studies.
- Four studies on digital breast tomosynthesis showed higher AUCs for AI versus radiologists.

Key messages

1. Screening mammography reduces BC mortality by 40%
2. To be extended from 45 to 74 years of age
3. MRI screening for women at genetic-familial high-risk (BRCA, etc.)
4. Women with extremely dense breast should undergo MRI or CEM screening every 3-4 years
5. A perspective for AI as one of the two screening readers (*AI-in-the-loop*)



Where are we going?



**Thanks
for your attention**

francesco.sardanelli@unimi.it



CURA.R.T.E.
ALIMENTAZIONE, RICERCA, TERAPIA, EMOZIONE

Convegno di Fondazione IncontraDonna | PRIMA EDIZIONE

ROMA, 14 | 06 | 2023

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