# Breast Surveillance: High Risk Women, Dense Breasts and HRT

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Consultant Radiologist
St James's Hospital and Beacon Hospital



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# Aims of the talk

- Outline imaging tools and their uses
- Define “high risk” women
- Define NICE Surveillance Categories
- Outline the impact of Dense Breasts
- Outline the impact of HRT on Breast Cancer

# Imaging Tools and their relative advantages

- Mammography
- Digital Breast Tomosynthesis (DBT)

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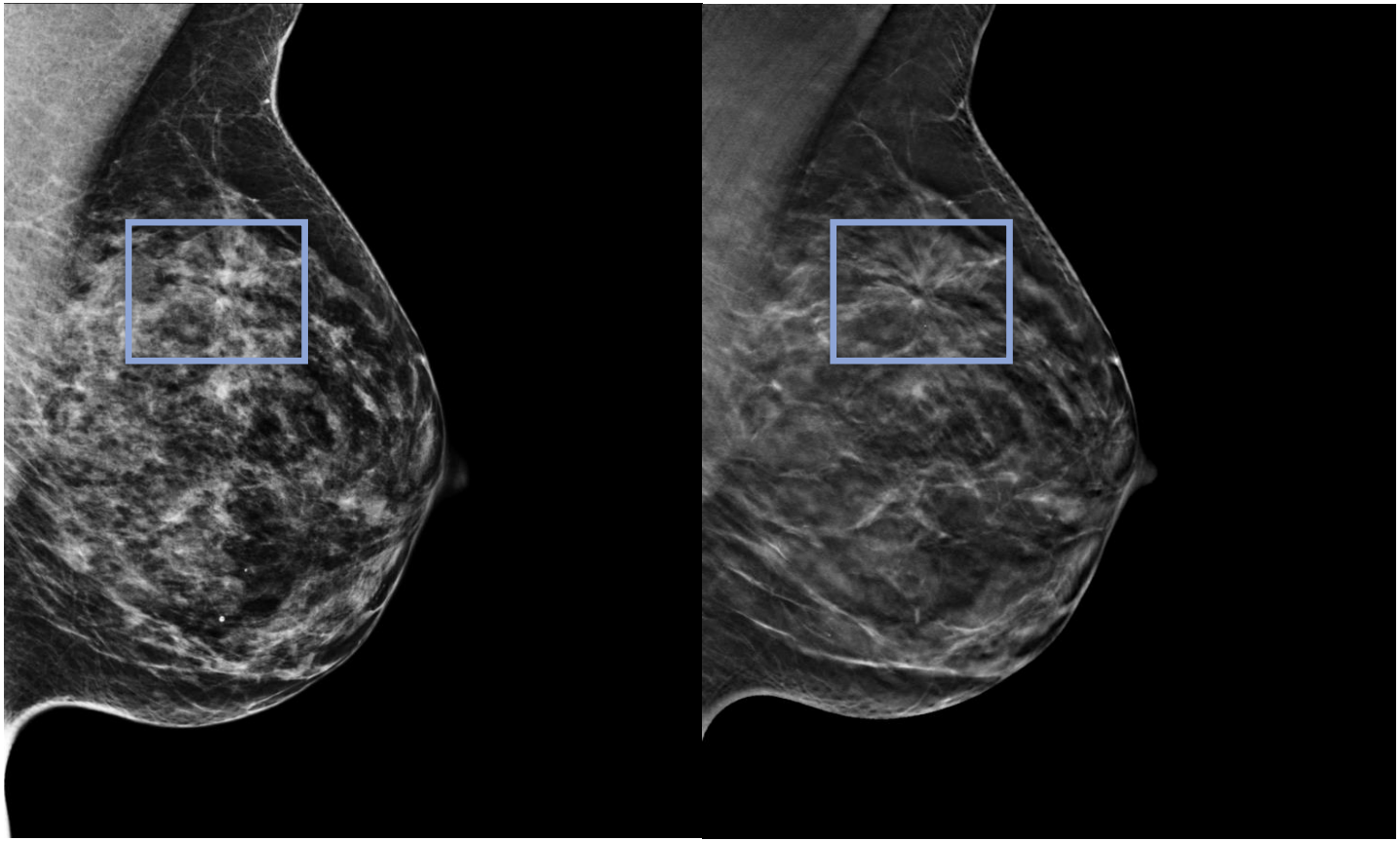
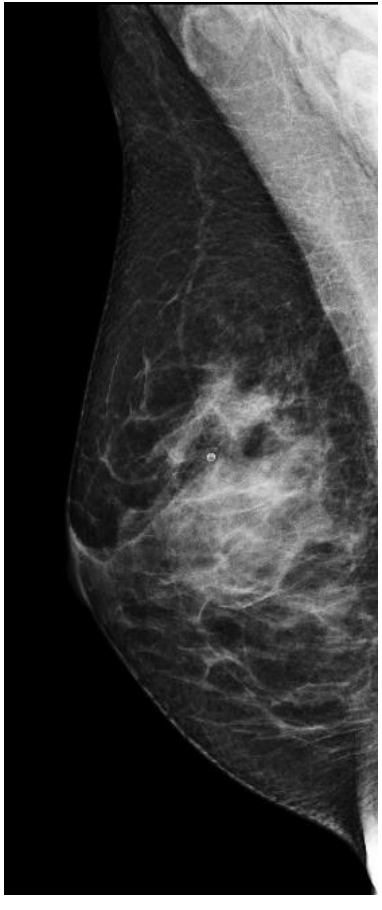
# Conventional Mammogram versus DBT

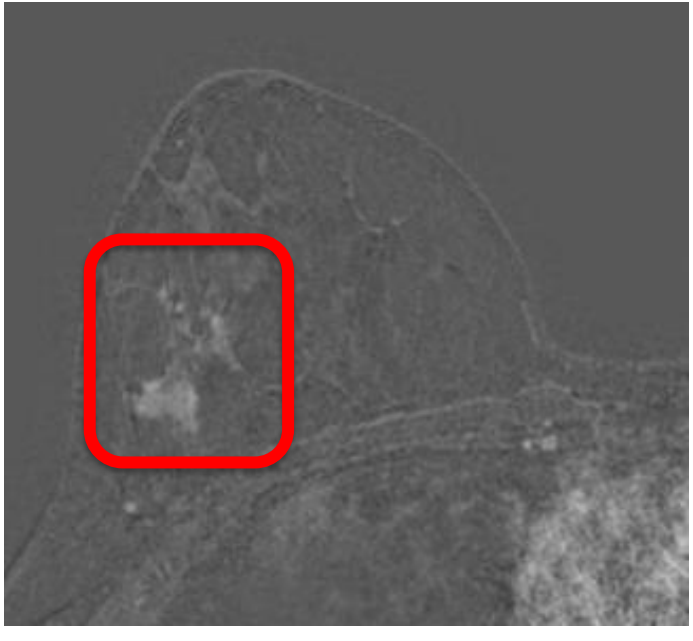


# Imaging Tools and their relative advantages

- Mammography
- Digital Breast Tomosynthesis (DBT)
- Ultrasound
- MRI

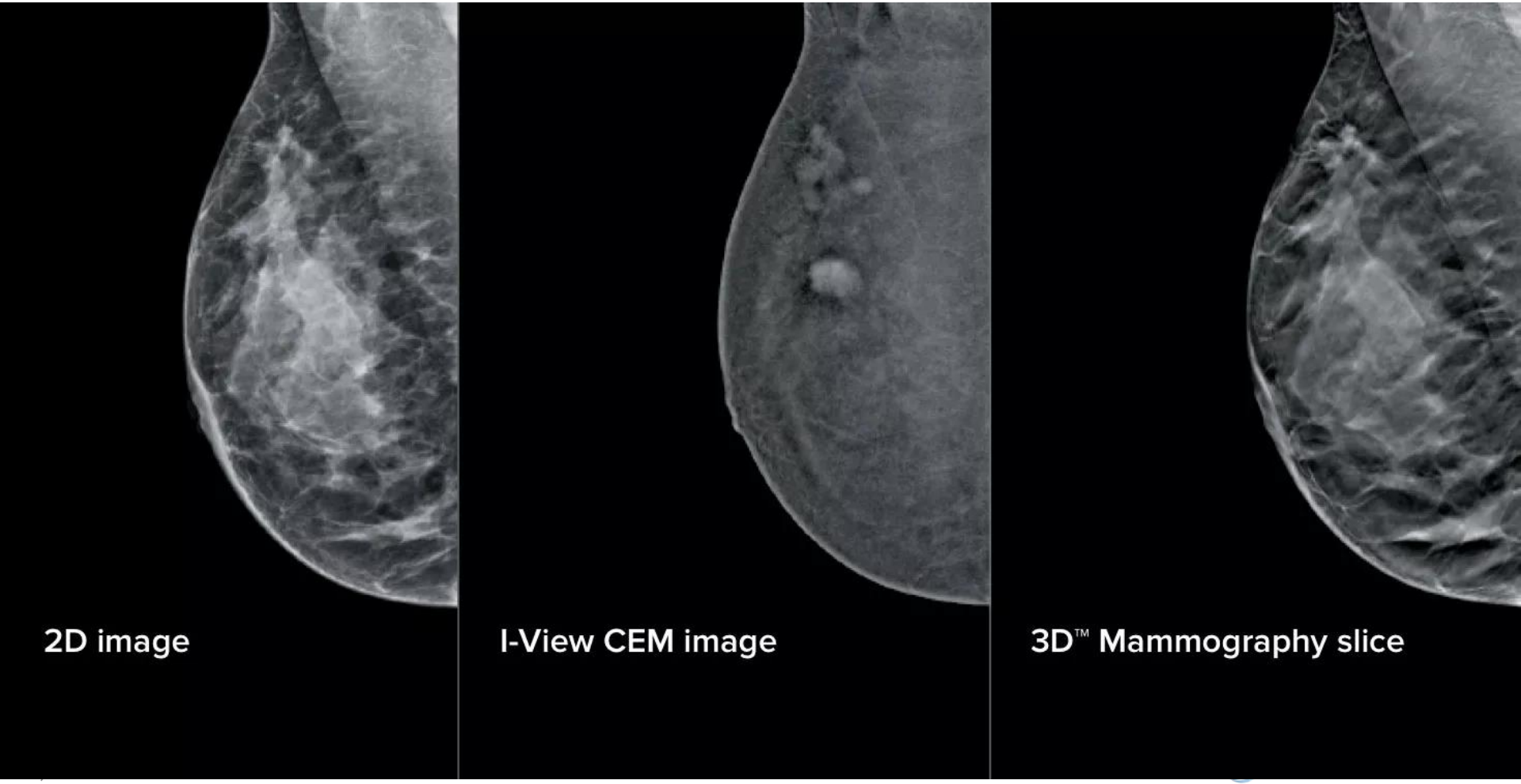
# 29-year-old patient with Breast Cancer



# Imaging Tools and their relative advantages

- Mammography
- Digital Breast Tomosynthesis (DBT)
- Ultrasound
- MRI
- Contrast Enhanced Mammography


2D image
I-View CEM image
3D™ Mammography slice

# High Risk Women

# The true aim of Breast Cancer Screening

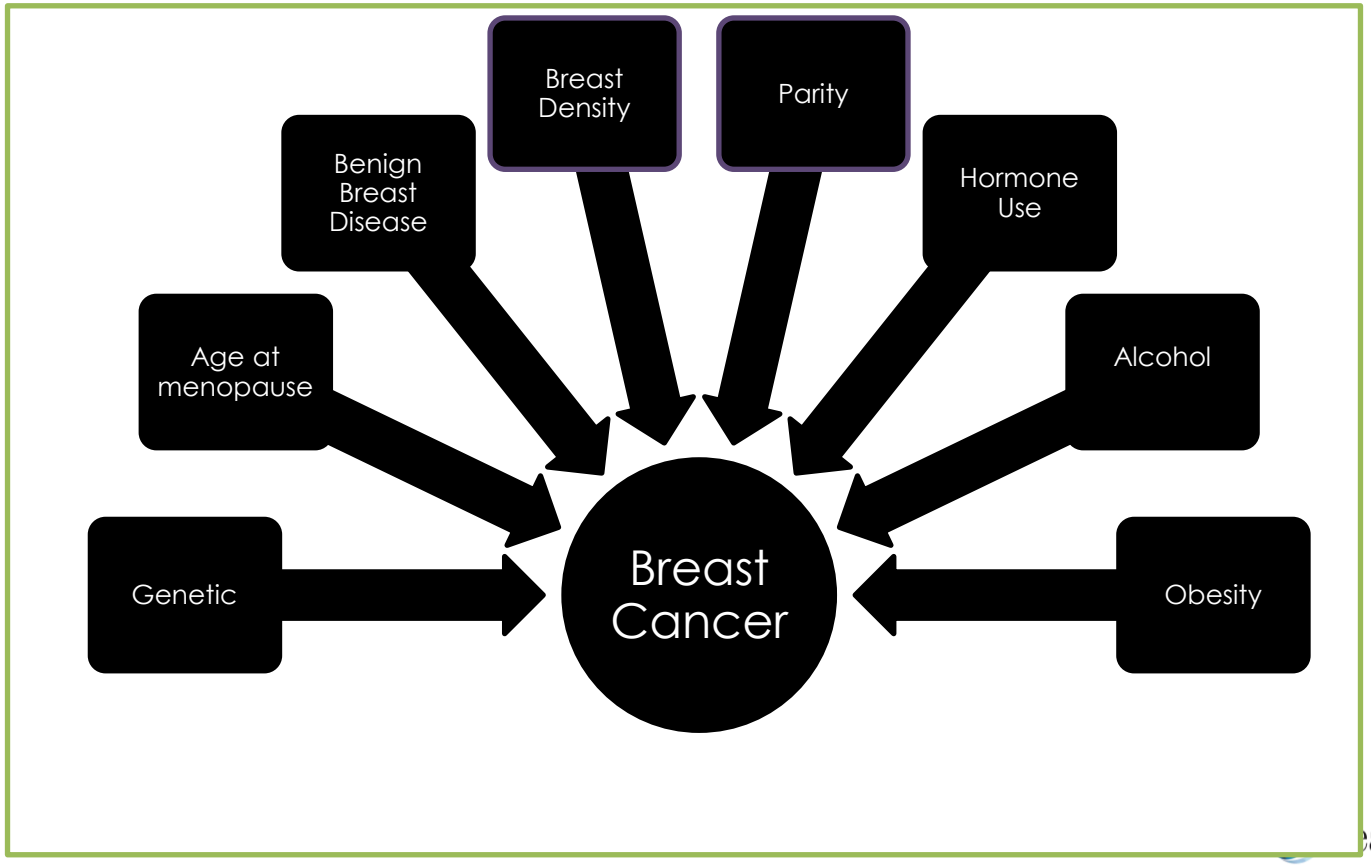
If we could truly identify the ‘at-risk’ population

- We would maximise the cancer detection rates of screening
- Minimise the harms including radiation exposure, false positive recalls and anxiety

# The key is defining who is 'High Risk'?

- This poses a challenge
- BRCA1, BRCA2 and TP53 well known (however incidence is low and account for <5% of cancers)
- There is an estimated 4,500 high risk women in Ireland
- 6% of women under 50 years are moderate risk (25,000 to 40,000)

# Risk factors for breast cancer



# NICE Categories

| | Breast cancer risk category | | |
|---|---|---|---|
| | **Near population risk** | **Moderate risk** | **High risk[1]** |
| **Lifetime risk from age 20** | Less than 17% | Greater than 17% but less than 30% | 30% or greater |
| **Risk between ages 40 and 50** | Less than 3% | 3–8% | Greater than 8% |
| [1]This group includes known *BRCA1*, *BRCA2* and *TP53* mutations and rare conditions that carry an increased risk of breast cancer such as Peutz-Jegher syndrome (*STK11*), Cowden (*PTEN*) and familial diffuse gastric cancer (E-Cadherin). | | | |

# High Risk

Intensive breast surveillance starting as young as 30 years

# Moderate Risk

Annual Mammography from 40 to 50 years

# Irish Breast Cancer Statistics

For the year 2019, women in Ireland aged 15-44 accounted for 13% of breast cancer diagnoses, and 26% were in the 45-54 age group.

In women under 50 years, 80.2% had no significant family history, 9.8% moderate and 10% high

# HTA Assessment 2013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# NICE guidelines: Annual Mammography

Offer annual surveillance to women:

- Aged 40–49 years at moderate risk
- Aged 30–59 years at high risk not gene tested or BRCA negative
- Aged 40–69 years with a known BRCA1 or BRCA2 mutation if having MRI from 30 year

# NICE guidelines: Annual Mammography

Do not offer annual mammographic surveillance to women:

- Aged 29 and under
- Aged 30 to 39 years at moderate risk
- Aged 30 to 49 years who have a greater than 30% probability of being a TP53 carrier
- Of any age with a known TP53 mutation

# NICE Annual Breast MRI

Offer annual MRI to women:

- Aged 30–49 years with a known BRCA1 or BRCA2 mutation and extend to 69 if dense breasts
- Aged 30–49 years without genetic testing but greater than 30% probability of a BRCA1 or BRCA2 mutation
- Aged 20 to 49 (consider to 69) years with a TP53 mutation or greater than 30% of having a TP53 mutation

# Effect on breast cancer deaths per 1000 screened

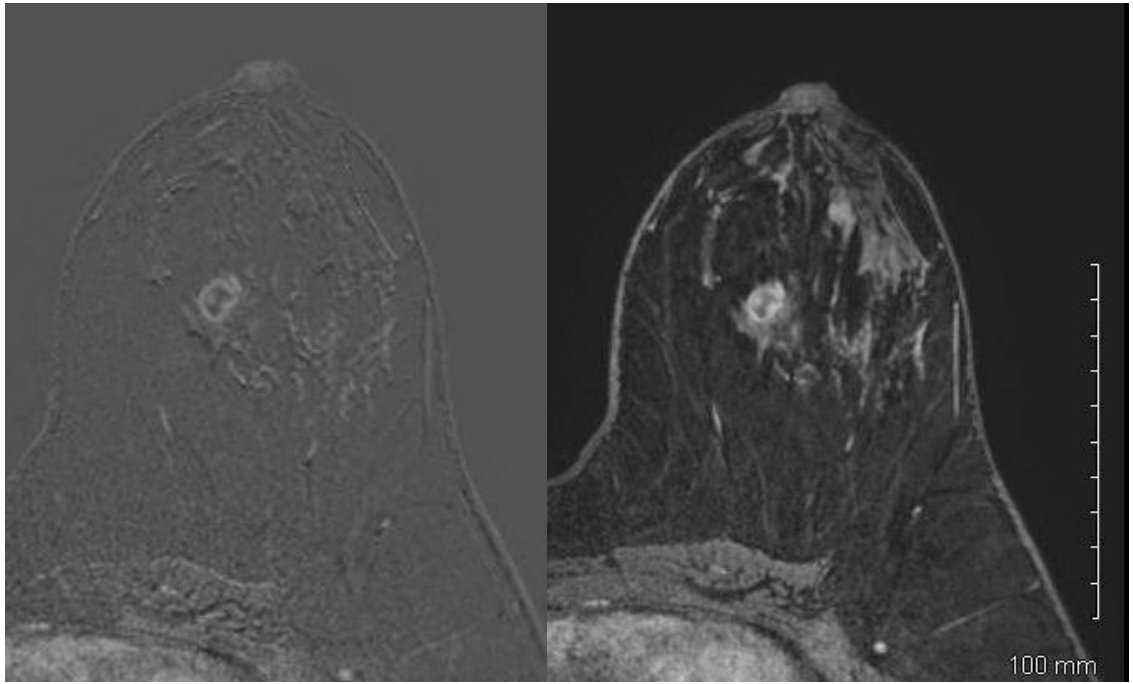
| | |
|---|---|
| **Population Risk. 3 yearly Mammography (Mx) 50-69** | **-3.6** |
| Population Risk. 18-monthly Mx 40-49 + 3 yearly 50-69 | -4.5 |
| Very High Hereditary Risk (RR8). Annual MRI to 40 + Mx/MRI to 73 | -34.6 – 40.6 |

# Ontario Breast Screening Program: High Risk Women

**Results:**

- Recall rate for MRI 15.1% *(7% for Breastcheck)*
- 16.3 cancers per 1,000 screened *(7-9 for Breastcheck)*
- None were detected by mammogram alone
- 65.7% were detected by MRI alone
- 71% were in women who were known gene mutation carriers (30.8 per 1,000)
- The PPV was highest for detection on mammogram and MRI (12.4%)

# 27 year old. BRCA1. Surveillance




9mm IDC Grade 2

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# What should a GP do for a woman with a strong family history?

- Establish that there is a strong family history of breast and/or ovarian cancers
- Refer to a breast family history clinic for assessment
- The assessment should result in a screening recommendation for the woman
- Currently, gene positive patients (BRCA and TP53) can have annual surveillance in the 8 public breast cancer centers.
- Almost other patients have to have screening arranged by their GPs

# High Risk Screening

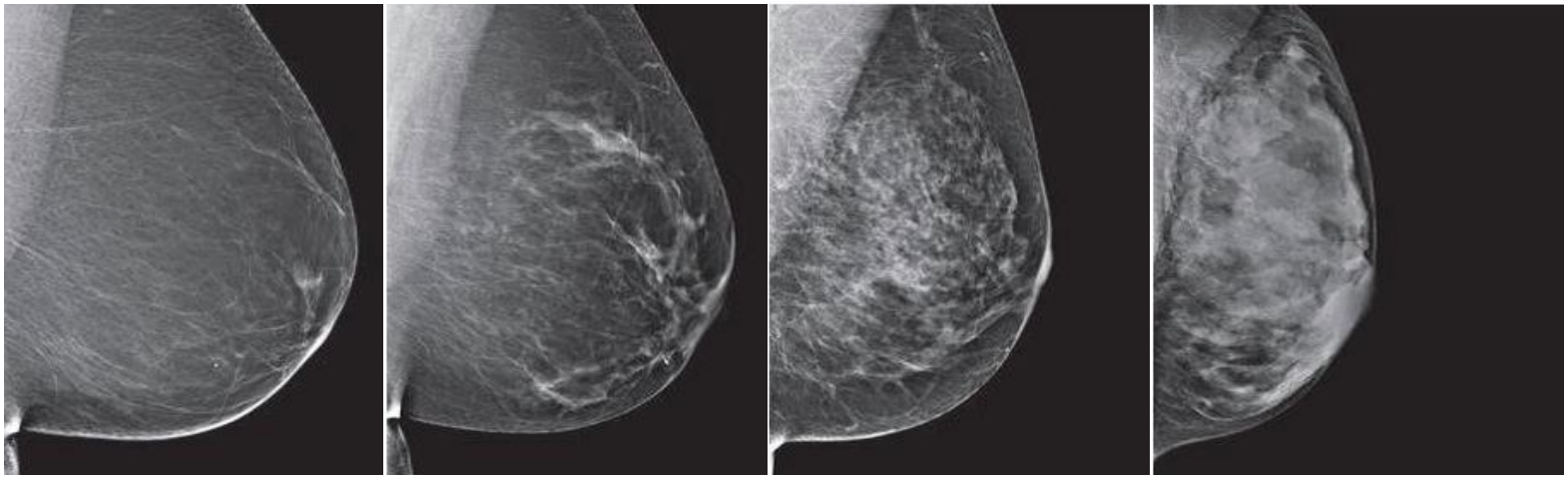
- Woman should be under the care of a breast consultant/ANP led clinic
- Needs to be able to avail of appropriate counselling in case of a recall or need for biopsy
- Needs breast care nursing support
- Should have contact details of service if they notice a new lump
- GP referral direct for MRI screening not advisable as follow-up care is complex

# Dense Breasts

# Breast Density Categories

Denser glandular stroma and epithelium and lucent fat
Accounts for the masking effect of dense tissue on visibility of lesions

| Fatty | Scattered Fibroglandular Densities | Heterogenously Dense | Extremely Dense |
|---|---|---|---|



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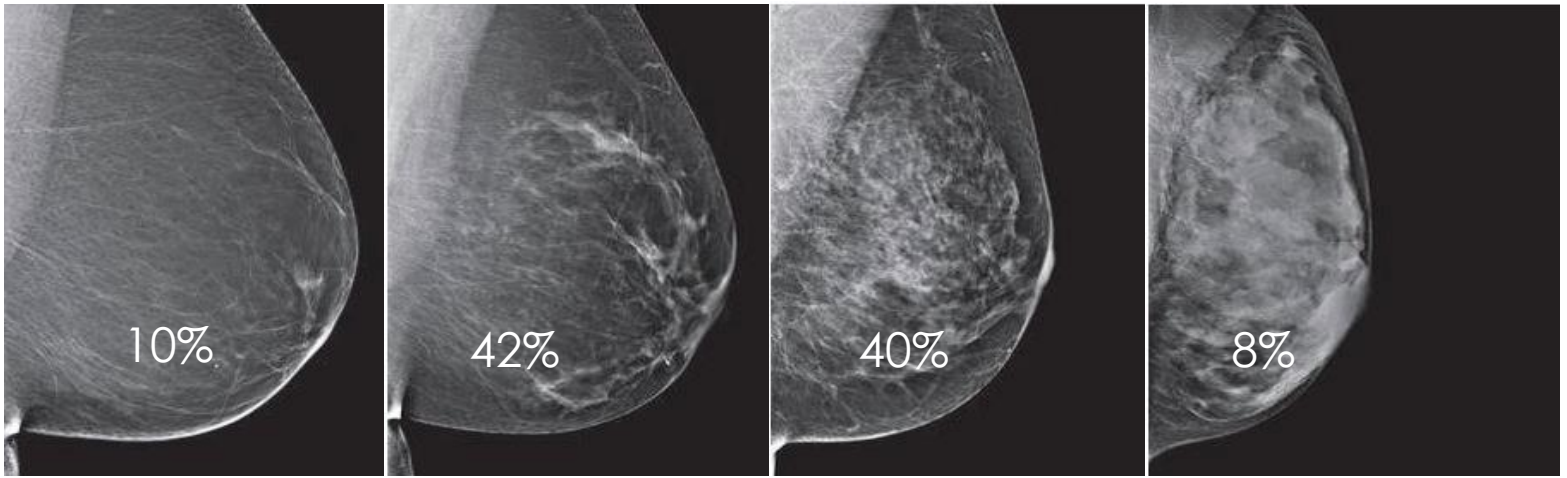


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# Breast Density BI-RADS

**c. The breasts are heterogeneously dense, which may obscure small masses. 40% population**

**d. The breasts are extremely dense, which lowers the sensitivity of mammography. 10% population**

## ‘Dense Breasts’: 50% of the population

# Why is Breast Density Important?

Increased masking of tumours at mammography

Increased risk of breast cancer

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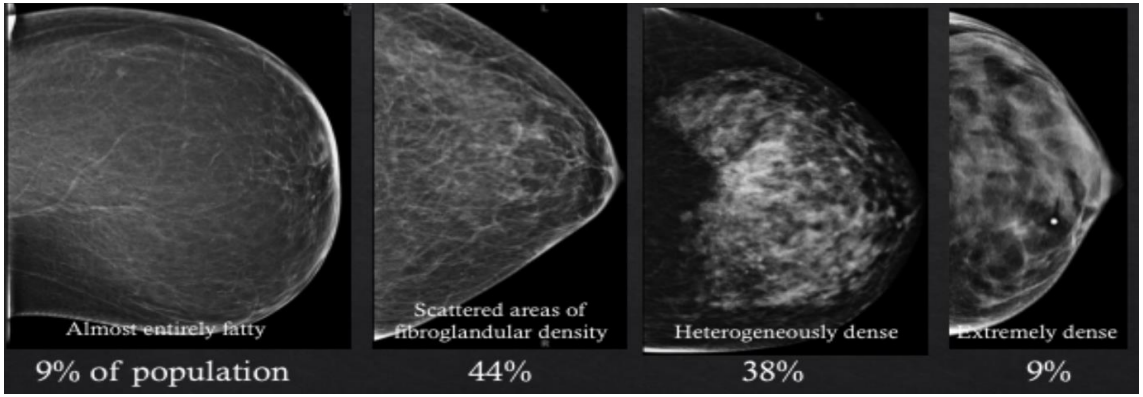
Increased masking of tumours at mammography

**Increased risk of breast cancer**

# Reduced Mammographic Sensitivity

- Independent risk factor for breast cancer
- Sensitivity increases as density decreases




Sensitivity 88%

Sensitivity 47%

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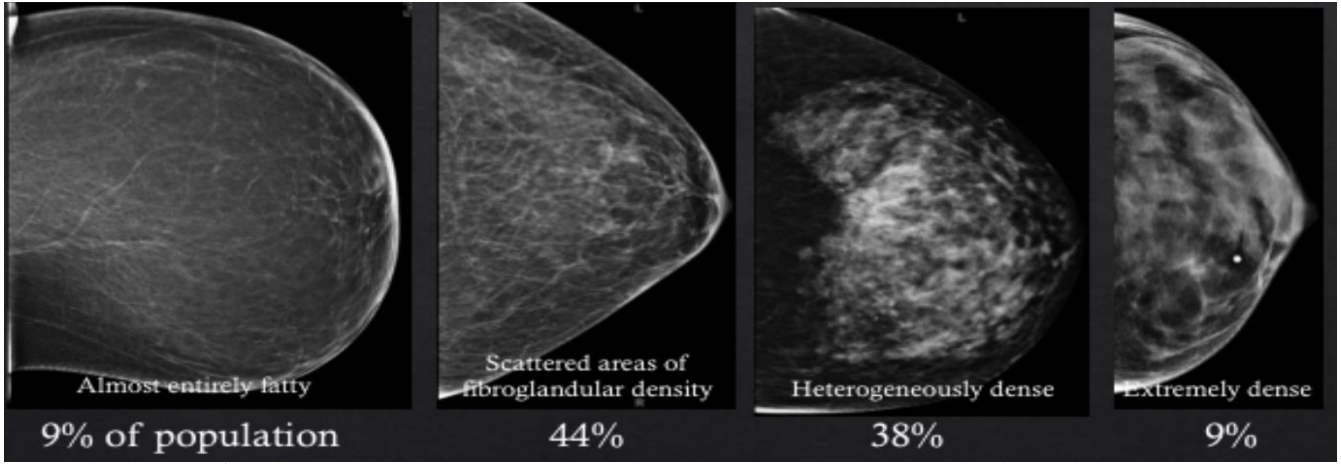
# Increased Risk of Breast Cancer

Relative risk between scattered and heterogeneously dense is 1.5X




Relative Risk 1X

Relative Risk 4.6X

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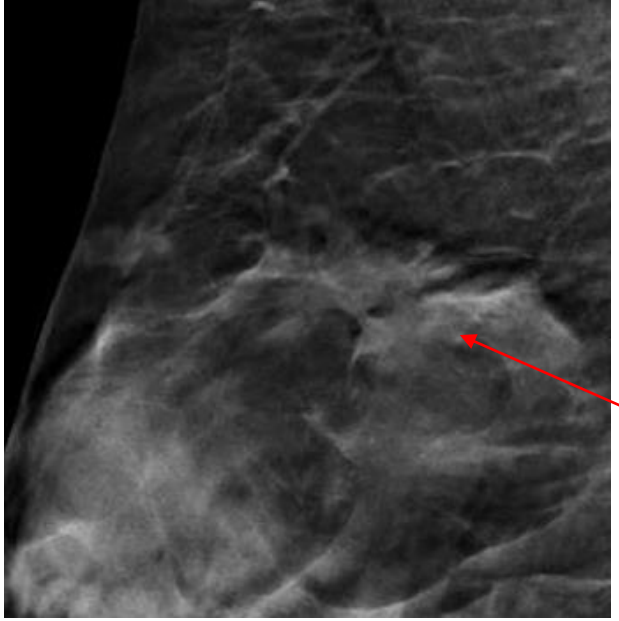
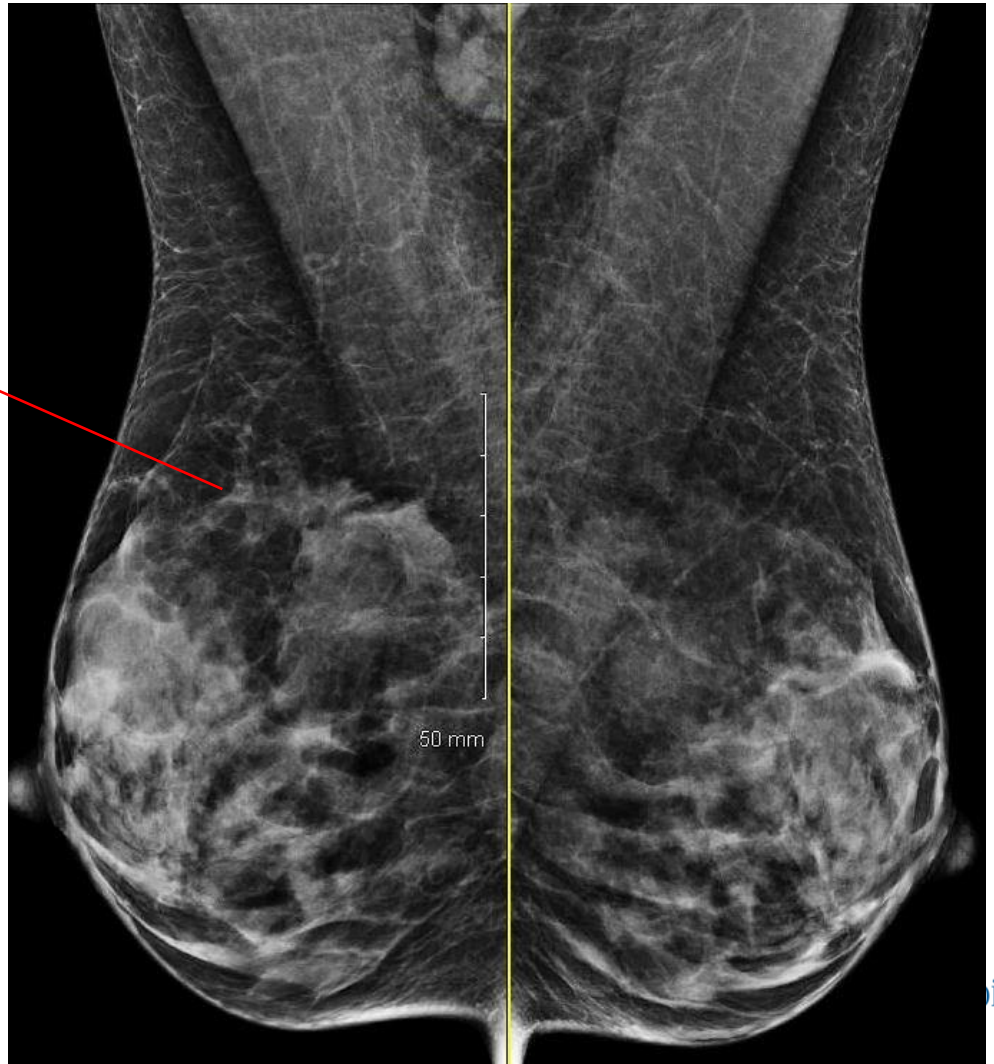
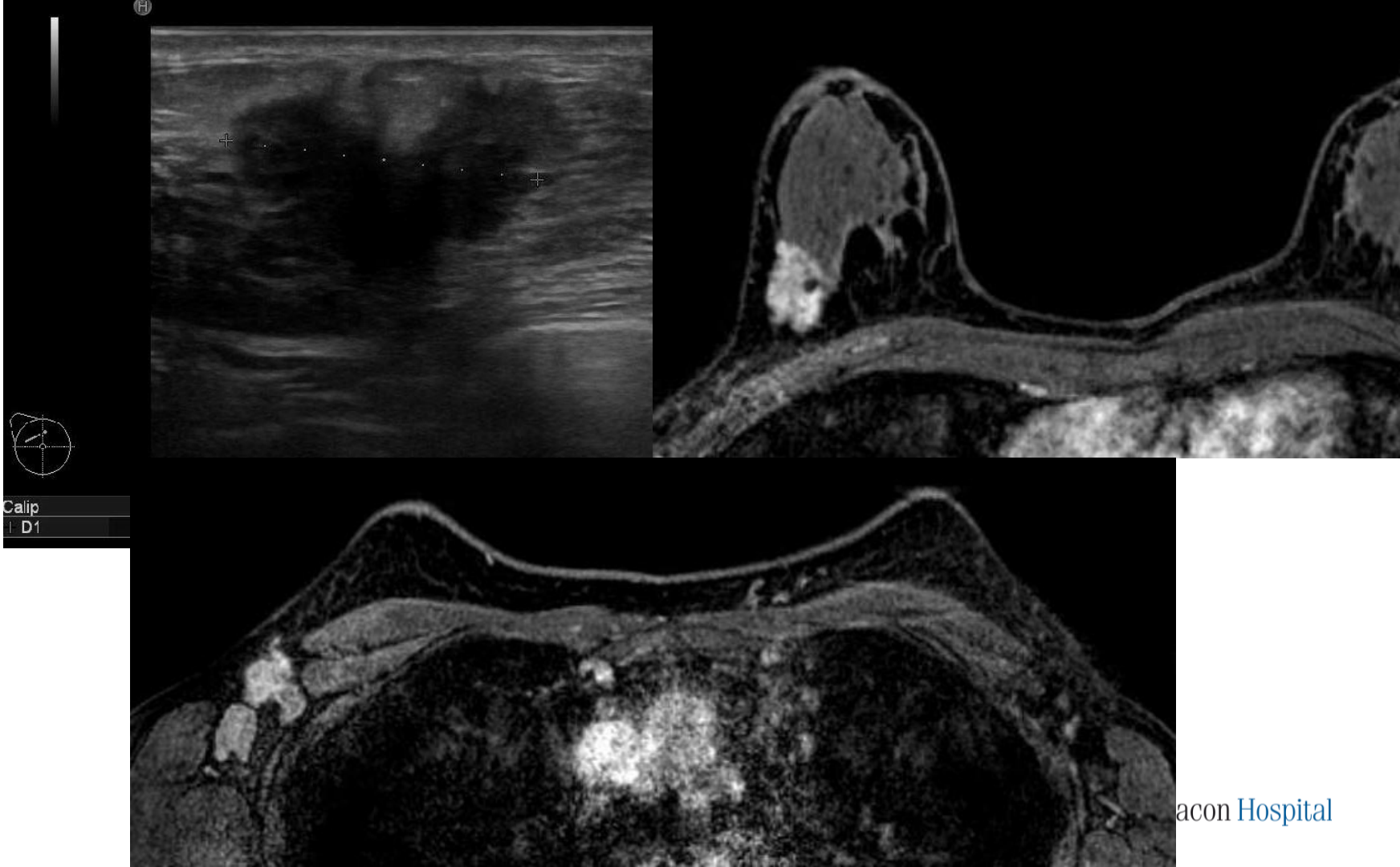





35-year-old.
Right Breast
Lump.

ital

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# Are You DENSE?

exposing the best-kept secret™

# What is Supplemental Screening?

Supplemental screening is adding an additional type of imaging to conventional mammography

- Digital Breast Tomosynthesis (DBT)
- Dual Energy Contrast Enhanced Spectral Mammography (CESM)
- Automated or hand held whole breast ultrasound (ABUS)
- Magnetic Resonance Imaging

# MRI Screening Recommendations in Women of Average Risk with High Breast Density

Prior to 2022:

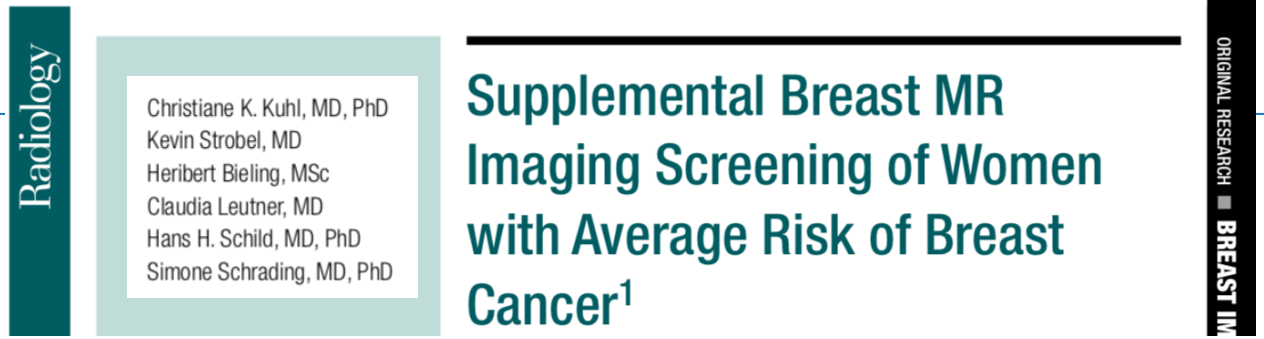
- European Commission Initiative on Breast Cancer (ECIBC) Contributor Group 2019. 'for asymptomatic women with high breast density and negative mammography, the ECIBC suggests not implementing tailored screening with MRI over mammography screening alone

# EUSOBI March 2022

‘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’

What is the evidence?

EA1411 ECOG-ACRIN study and the DENSE trial




Breast MR: overall supplemental cancer detection rate (CDR): 15.5/1000

Supplemental CDR at initial screening: 22.6/1000

Cancers diagnosed with MR were small, node negative (93.4%) and high-grade (41.7%-46%)

No interval cancers were observed

MR imaging screening offered high specificity (97.1%) and high PPV (35.7%)

JAMA | Original Investigation

# Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening

EA1411 ECOG-ACRIN
Feb 2020

Christopher E. Comstock, MD; Constantine Gatsonis, PhD; Gillian M. Newstead, MD; Bradley S. Snyder, MS; Ilana F. Gareen, PhD; Jennifer T. Bergin, MD; Habib Rahbar, MD; Janice S. Sung, MD; Christina Jacobs, MD; Jennifer A. Harvey, MD; Mary H. Nicholson, MD; Robert C. Ward, MD; Jacqueline Holt, MD; Andrew Prather, MD; Kathy D. Miller, MD; Mitchell D. Schnall, MD, PhD; Christiane K. Kuhl, MD, PhD

- 1,444 women lifetime risk <20% with dense breasts
- 77% woman heterogeneously dense and 15% extremely dense
- First round CDR with MRI was 15.2/1,000 compared to 6.2/1,000 for DBT
- Additional contribution of mammography limited

The NEW ENGLAND JOURNAL of MEDICINE

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# Supplemental MRI Screening for Women with Extremely Dense Breast Tissue

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*

Simulation modelling: adding biennial MRI to biennial mammography would save 8.6 additional lives per 1,000 women invited, at a cost of 150,000 Euro per life, or 22,500 Euro per QALY.

MRI alone once every 4 years would save 7.6 additional lives per 1,000 women screened at a cost of 75,000 Euro per life or 11,500 Euro per QALY.

Geuzinge HA, Bakker MF, Heijnsdijk EAM et al (2021) Cost-effectiveness of MRI screening for women with extremely dense breast tissue. J Natl Cancer Inst. 113(11):1476–1483

# In women with extremely dense breasts:

No screen: 5 % die from breast cancer

Biannual screening with mammography reduces the likelihood to die to 4 %, i.e. reduces the risk to die of breast cancer by 20%

DENSE trial: MRI screening every other year reduces the risk to die from breast cancer to 3%, providing a mortality reduction by about 40 %.

# Gadolinium Retention

Mounting evidence has shown there is long-term retention of gadolinium in human tissues.

A small subset of patients have attributed a constellation of symptoms to gadolinium exposure

The association of these symptoms with gadolinium has not been proven

Await results of studies

# Hormone Replacement Therapy

# HRT use

- No evidence to refer for mammography prior to HRT use
- HRT does not significantly increase breast cancer risk or alter screening recommendations.
- Other risk factors should always be taken into consideration

# Understanding the risks of breast cancer

Women's Health Concern

A confidential independent service for women and their partners

**A comparison of lifestyle risk factors versus Hormone Replacement Therapy (HRT) treatment.**

**Difference in breast cancer incidence per 1,000 women aged 50-59.**
Approximate number of women developing breast cancer over the next five years.

NICE Guideline, Menopause: Diagnosis and management November 2015

**23 cases of breast cancer diagnosed in the UK general population**

**An additional four cases in women on combined hormone replacement therapy (HRT)**

**Four fewer cases in women on oestrogen only Hormone Replacement Therapy (HRT)**

**An additional four cases in women on combined hormonal contraceptives (the pill)**

**An additional five cases in women who drink 2 or more units of alcohol per day**

**Three additional cases in women who are current smokers**

**An additional 24 cases in women who are overweight or obese (BMI equal or greater than 30)**

**Seven fewer cases in women who take at least2½ hours moderate exercise per week**

# HRT use

- No evidence to refer for mammography prior to HRT use
- HRT does not significantly increase breast cancer risk or alter screening recommendations.
- Other risk factors should always be taken into consideration
- Increase in breast density from HRT use can increase benign changes such as cysts and increase recall rate for ultrasound
- Increase in breast density reduces the sensitivity of mammography

# Conclusion

- Screening mammography best screening tool
- Addition of DBT modestly improves cancer detection rate
- MRI should be performed for ALL high risk patients under 50 through a breast clinic
- MRI can be performed in population risk women over 50 with extremely dense breasts if available. This is complex for a GP to arrange directly.

EUSOBI european society of breast imaging

ACR® American College of Radiology

NCCN National Comprehensive Cancer Network®

Cochrane

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# Thank you



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