Breast density, Risk Assessment and Personalized Screening. How to unravel the recommendations.

As we saw in the last post, there are many good reasons to screen average risk women starting at age 40 as there are both mortality and non-mortality benefits from early detection. With very few exceptions, Mammography screening trials and observational studies have determined that early detection improves outcomes.

But what about those 15-20% missed “interval” cancers (false negative screens) that show up despite screening mammography? Why do those happen and how do we minimize them?

There are several reasons for a false negative mammogram with a “missed” or interval cancer. These reasons include:

- screening schedule - longer screening interval is associated with higher rates of interval cancers [1,2]
- aggressive tumours that grow rapidly between screening events [3]
- patient factors, including increased breast density and younger age [4]
- interpretation error (including causes such as poor image quality).
- type of mammogram - digital mammography has been demonstrated to miss fewer cancers in dense tissue than screen-film mammography [5].

We learned in the last post that smaller pre-clinical cancers are associated with better outcomes. Interval cancers present with clinical findings and, as such, are larger with poorer outcomes than screen detected cancers. 34% of breast cancer deaths were found to be caused by interval cancers at failure analysis [6]. Average screen detected breast cancer is 1.3 cm diameter, while average cancer found at clinical palpation is 2.5-2.8cm. Ideally, therefore, interval cancer incidence should be minimized.

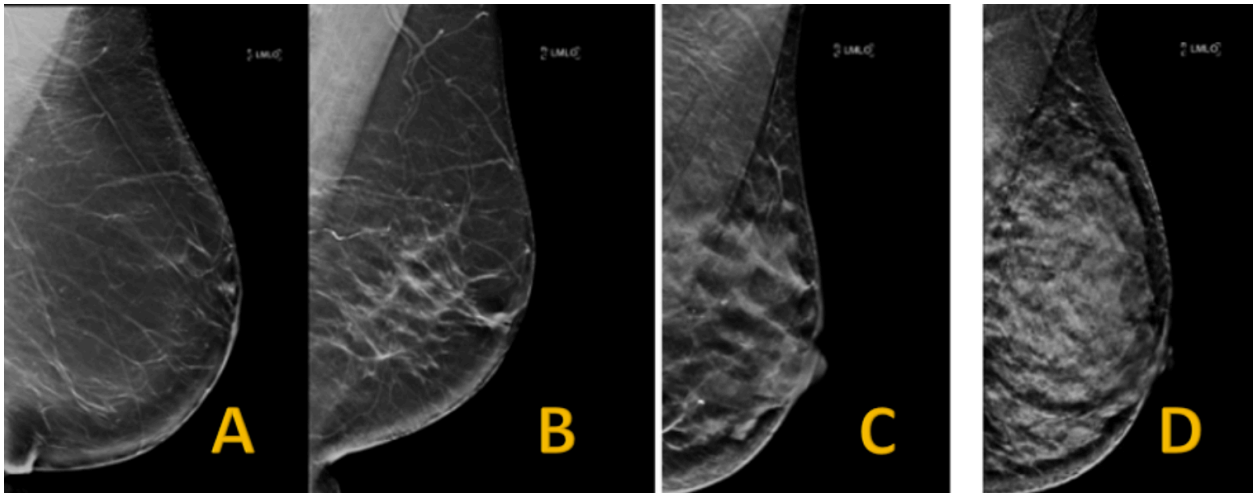
Breast density, risk and supplemental screening

In mammography, the term “breast density” refers to the optical density, or the “whiteness”, of the background breast tissue on a mammogram. This is a mammographic quality and cannot be determined by palpation. About 40% of women have dense tissue, but this varies with age, as the percentage of women with dense tissue drops with increasing age [1]. Mammographic breast density is strongly related to interval cancer for two reasons:

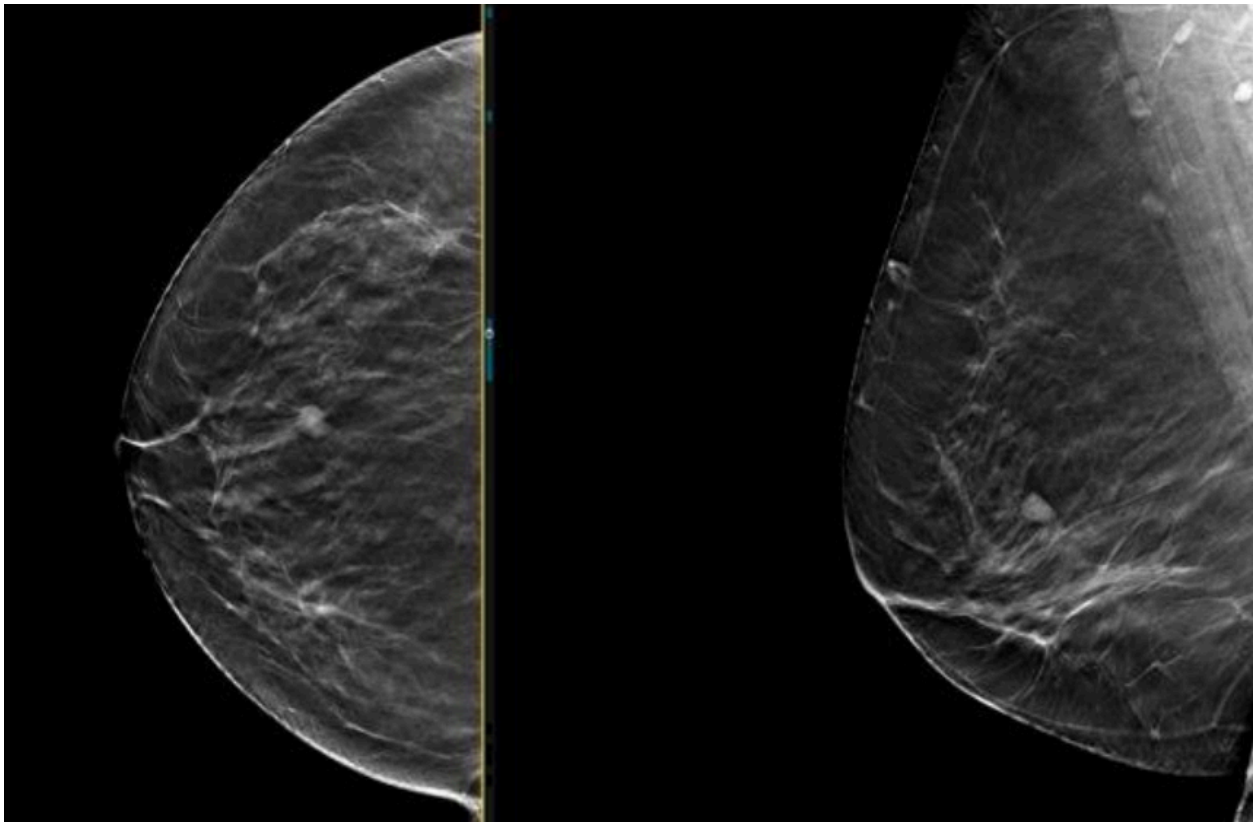
- Dense breast tissue is an independent risk factor for developing breast cancer. There is at least 2X risk for the densest breast category, similar to or even higher than the risk associated with having a first degree relative with breast cancer[1]; in fact, it is considered a biomarker for breast cancer risk.
- Dense breast tissue also creates a masking effect leading to delayed diagnosis. The densest breast tissue has a 17.8 X odds ratio for interval cancer in comparison with the fattiest tissue [1].

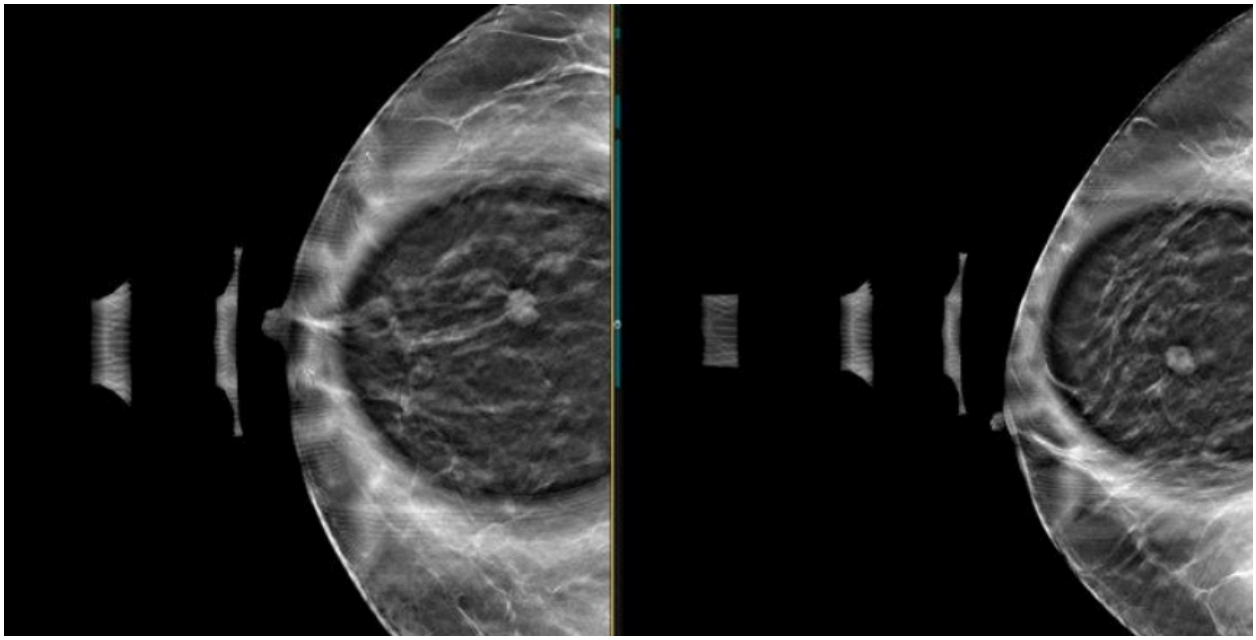
Mortality reduction from mammographic screening has been found to be smaller in women with dense breasts than fatty breasts [7]. For women with dense breast tissue and no other risk factors, screening supplemental breast ultrasound should be offered, understanding that this also roughly increases x 2 the chance of being recalled, followed up or having benign biopsy. Women should understand adding ultrasound also means that breast cancers found are likely to be smaller, earlier stage and more likely to be treated with intent to cure [8] and that supplemental ultrasound has been shown to decrease interval cancer rates to those similar to non-dense mammography interval cancer rates [9,10].

From left to right, these are examples of mammographic densities A to D. The last 2 images on the right, densities C and D, are considered dense.

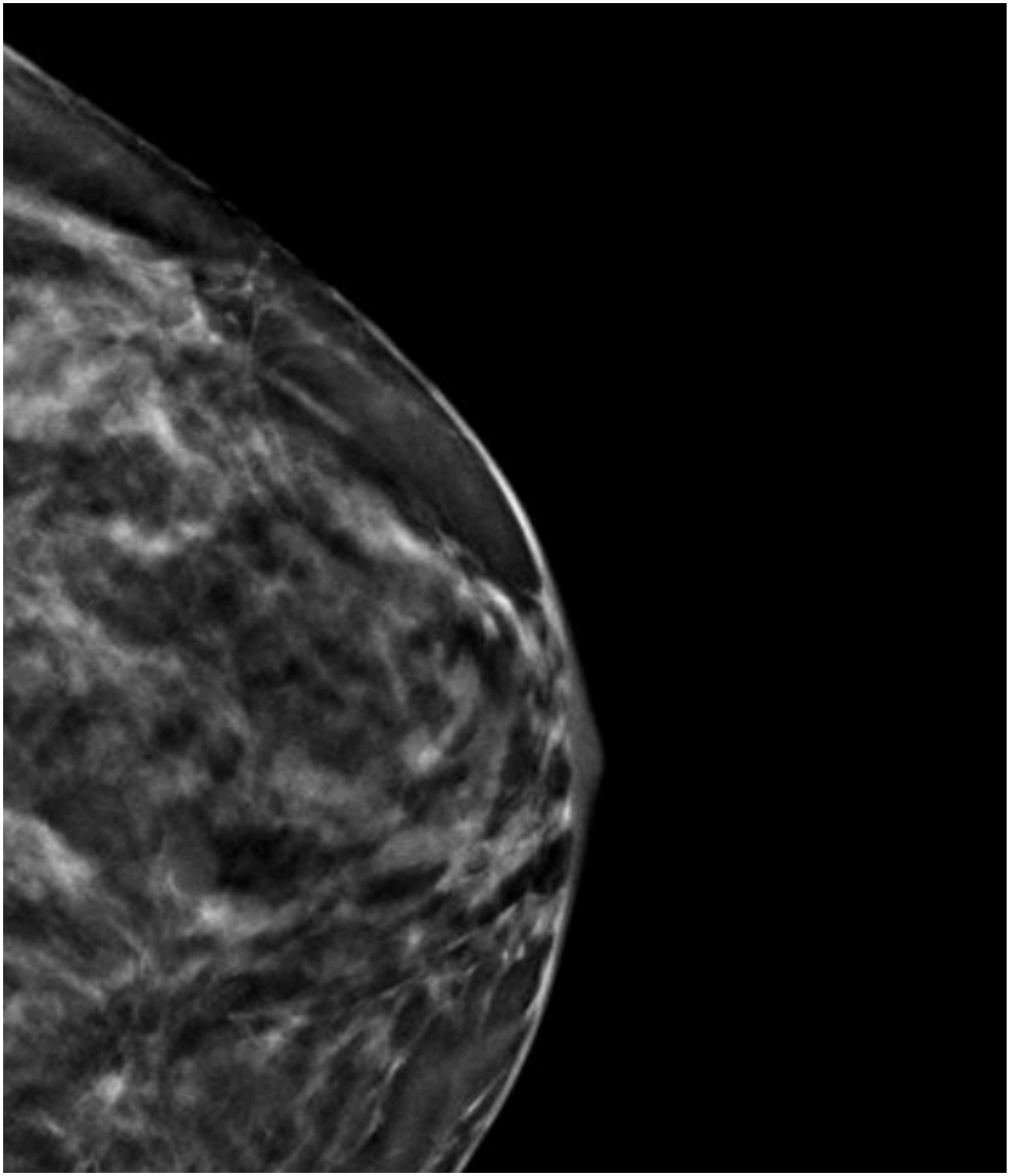


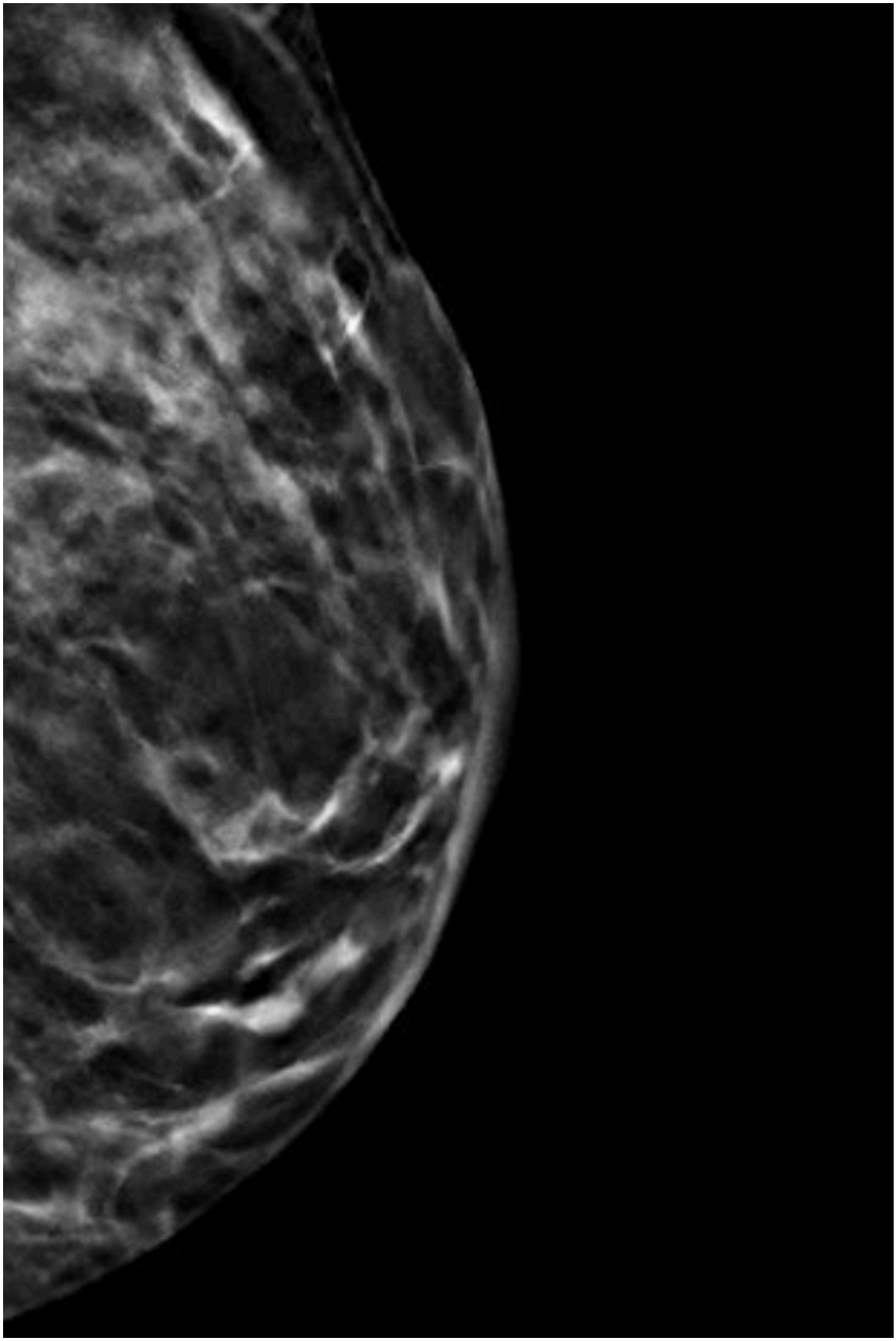
This is an example of a small cancer in a mammographically lucent (B density) breast with good contrast between the soft tissue density of the tumour mass and the adjacent fatty breast tissue. These are tomosynthesis slice images with the small circular focused images representing tomosynthesis spot compression views. I decided I didn't need to put an arrow on the mass. I wish my job was always this easy!



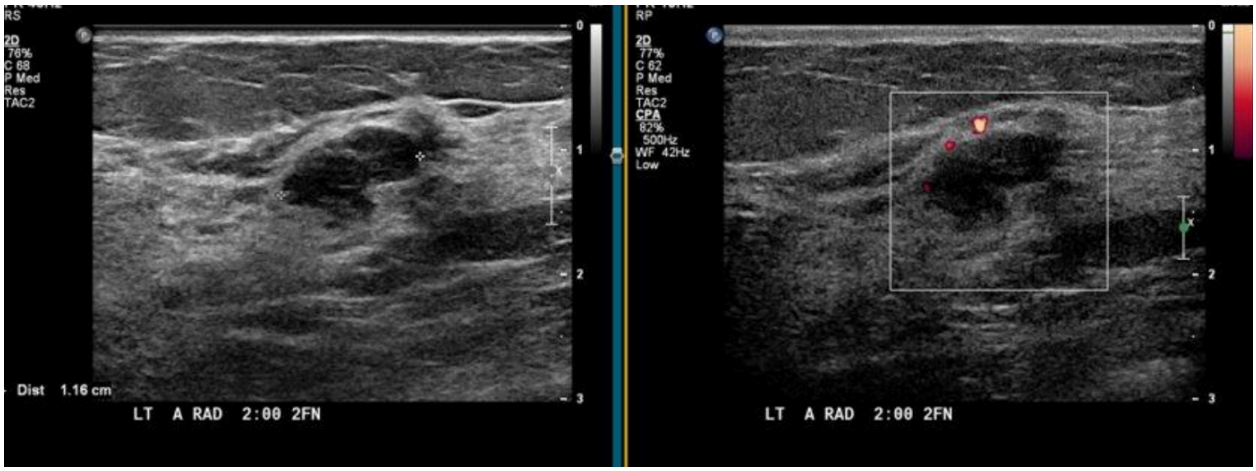


This is a patient with C density (heterogeneously dense) tissue. This patient has a 1.5 cm cancer on both tomosynthesis images. Can you see it? It’s much larger than the subcentimeter cancer above.





I must admit, I am unable to see the cancer on the mammographic images, even knowing it's there. The cancer was, however found on screening supplemental ultrasound. The patient was asymptomatic and had no risk factors aside from breast density. This woman is far likelier to do well with less aggressive treatment than if her cancer was found later, when it was large enough to be palpable with a higher likelihood of being node positive.



Along with a greater public awareness of the problem of increased incidence and missed cancers associated with dense breasts, there has been increasing legislation around reporting breast density in the radiologist report and/or in the women's result letter in both USA and Canada. Several provinces have enacted or are soon to enact legislation requiring density reporting in various forms, but access to and availability of supplemental screening remain limited in many regions. For further information, the CAR/CSBI Position Statement on Mammographic Breast Density and Supplemental Screening includes recommendations and references.

High Risk Screening

Women of any breast density who are at high risk for developing breast cancer due to family history of breast cancer, genetic risk of breast cancer, or a history of mantle radiotherapy should be identified as early as possible and should undergo high risk screening with MRI, starting around age 30, but no earlier than age 25. Breast MRI screening should be added for all high risk women - defined as lifetime risk above 20-25%. There are several risk calculators, but a simple online calculator can be found at ibis.ikonopedia.com.

Supplemental breast ultrasound should not replace breast MRI for women at high risk unless there is a contraindication or intolerance to MRI.

For further information on the current recommendations of breast experts, including breast imagers and breast surgeons in Europe and USA, I'll include several recent references with specific guidelines on density and high risk management.

Summary:

- **All** women should have risk assessment at age 25-30. For most women, this is a question or two about family history and chest radiotherapy history to rule out a need for early screening. If there are 2 or more close relatives with breast cancer, particularly premenopausal cancer, consider performing a risk calculation using an online tool, such as IBIS https://ibis.ikonopedia.com/

- **Average** risk women should be offered screening at age 40, every year from 40-49 and every 1-2 years from 50-74. Over 74, women may continue to screen as long as they are in good general health, but should stop when they have fewer than 7 years life expectancy.
- Women who have **dense** breast tissue, but no other risk factors, should be offered supplemental screening ultrasound, acknowledging the possibility of a higher chance or recall and biopsy. The intent of supplemental screening is to decrease the risk of interval cancers and the attendant poorer outcome predictors. Annual mammographic screening is also recommended as it may decrease the number of interval cancers. [1,2]
- Women of any breast density, but with **elevated risk** (gene mutation or untested first degree relative, mantle radiotherapy between ages 10 and 30, strong family history with calculated risk ≥ 20-25%) should be offered MRI screening. Ultrasound may be used if there are contraindications to MRI. Ultrasound is not needed in addition to MRI.
- Ultrasound is not a standalone screening method. Mammography remains the primary modality for breast screening.

References:

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Further guidelines:

- Lee, Carol H. et al. Breast Cancer Screening With Imaging: Recommendations From the Society of Breast Imaging and the ACR on the Use of Mammography, Breast MRI, Breast Ultrasound, and Other Technologies for the Detection of Clinically Occult Breast Cancer. Journal of the American College of Radiology, Volume 7, Issue 1, 18 – 27\
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- https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf
- https://www.breastsurgeons.org/docs/statements/Position-Statement-on-Screening-Mammography.pdf