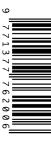
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Implications of Breast Density on Cancer Screening

Athina Vourtsis is the founder of Athena Medical, a Breast Imaging and Women's Health Centre in Athens, Greece, where she is the Head of the Radiology department and Chief Scientific Advisor. She is also the Founding President of the Hellenic Breast Imaging Society. Dr Vourtsis has shown special interest in supplemental screening methods and AI. Throughout her career, she has actively supported breast awareness programmes. As a member of the Medical Advisory Board and European Liaison of DenseBreast-Info.org, she has been working on expanding DBI's Educational Coalition into Europe.

What are the implications of breast density on cancer screening, and do you think it can impair the sensitivity of mammography?

Having dense breasts is a normal condition that over 40% of women have after the age of 40. However, breast density has become a challenging topic for both women and radiologists. Various studies have shown that breast density reduces the sensitivity of mammography due to the masking effect of uncalcified breast cancer. Therefore, in women with dense breasts, a normal mammography report does not exclude the possibility that a tumoural tissue is not hidden within the radiopaque (white) on mammography dense breast tissue. Also, many studies have shown that cancers diagnosed in this group of women are at a higher grade, larger in size, and often present with symptoms, leading to an increase in the interval cancer rate compared to women with non-dense breasts. In addition, breast density has been recognised as an independent risk factor for developing breast cancer. The denser the breast, the greater the risk. This explains why breast density has been integrated into many risk assessment models, playing an important role in shaping screening strategies.

How can breast screening be personalised for women with dense breasts?

Significant changes need to be made to adopt personalised breast cancer screening in women with dense breasts. This may involve organisational changes in healthcare systems and clinical settings. Automated density software for reliable breast density assessment and the integration of risk prediction models are necessary for the adoption of risk-based screening and prevention counselling in a primary care setting. This will lead to more precise management regarding personalised risk-based screening. At the same time, the accessibility to genetic counselling will provide opportunities to indicate related preventive measures and to determine the appropriate screening tests and at what age to begin. In addition, breast density is a modifiable risk factor that may need to be reassessed periodically. Essentially, the feasibility of implementing personalised screening in women with dense breasts may vary from country to country according to funding and the type of healthcare policies.

How do you think supplemental screening can be more effectively utilised keeping in mind the fact that there is a lack of consistent guidelines regarding this?

Increased knowledge of breast density implications has created the need to investigate various options to revise the current screening guidelines and to evaluate the possibility of adopting a personalised



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risk-based approach. Considering the benefits of supplemental screening in addition to mammography in women with dense breasts may aid in moving forward from a "one size fits all" strategy into the adoption of personalised screening for these women. Patient-increased awareness through various advocacy groups has played a fundamental role in educating women and influencing many educational organisations to issue position statements supporting supplemental screening for women with dense breasts. This transition has been a driving force for policymakers to comprehend the advancements of supplemental screening and to find resources to reshape screening strategies.

What breast imaging techniques do you recommend facilitating early diagnosis in women?

At our facility, we look at individual risk profiles and density using the Tyrer-Cuzick model to optimise personalised breast cancer screening for each woman separately. We have integrated tomosynthesis, and automated breast density volumetric assessment is used for more precise density measurement. In women with dense breasts, we perform supplemental automated breast ultrasound, and if there is any concern, a diagnostic hand-held breast ultrasound is followed during the same visit. The implementation of double reading of all tomosynthesis and automated breast ultrasound examinations has been adopted, and AI reading solutions are used for both systems. We have adopted the EUSOBI guidelines, and we recommend MRI in women with extremely dense breasts every two to

four years, whereas, in women who cannot tolerate MRI, contrast-enhanced mammography is offered. In women with >20% lifetime risk of breast cancer, MRI is considered, as well as in women with lobular carcinoma in situ or atypical hyperplasia. We also suggest annual screening MRI in addition to tomosynthesis in women with a personal history of breast cancer diagnosed by age 50 or with dense breasts.

What measures can be undertaken to help women make an informed choice on screening methods?

Most women in Europe do not have the choice to pursue supplemental screening independent of their healthcare providers or government-sponsored screening. Education and training of healthcare professionals may help in delivering clear and comprehensive information to women that will help them to make informed decisions. Understanding the benefits and risks of supplemental screening is essential in the informed decision-making process. DenseBreast-info.org (DBI), and subsequently DBI/ Europe, was launched to educate women and healthcare professionals about the screening and risk implications of breast density and the effect of supplemental screening.

Do you think breast cancer screening guidelines need to be reviewed/updated? What would you recommend in this regard?

Currently, there is a lack of consistent Europeanwide guidelines, resulting in unequal access to supplemental screening –with the potential for substandard care. However, recently, there has been a change in the paradigm of breast cancer screening in European women with extremely dense breasts. The results of the randomised DENSE trial published in the New England Journal of Medicine demonstrated that contrast-enhanced breast MRI identified another 16.5 cancers per 1000 women screened and that the interval cancer rate was reduced from 4.9/1000 to 0.8/1000 among women having supplemental MRI every other year, after negative mammography (Bakker et al. 2019). The results of this study have provided evidence supporting the EUSOBI recommendations, suggesting breast MRI every two to four years in women with extremely dense breasts. accounting for about 10% of the total screening population.

Additionally, further guidance is needed for screening women with heterogeneously dense breasts since they also have a high risk of masking effect of non-calcified cancer on mammography and of the higher incidence of interval cancer rate. However, widespread implantation of MRI in both women with extremely dense and heterogeneously dense breasts is unlikely with current resources and a lack of specialised technologists and radiologists on MRI in most healthcare systems widely throughout Europe. Therefore, at present, alternative approaches to personalised screening for women with dense breasts should be considered. Other feasible options are to replace 2D mammography with tomosynthesis and to apply supplemental automated or hand-held breast ultrasound. Both hand-held ultrasound and



automated breast ultrasound have been shown to improve breast cancer detection in women with dense breasts when added to mammography with an incremental CDR of 2.0-2.7 per 1000 women screened. Additionally, contrast-enhanced mammography has shown an incremental CDR equal to 10.7 per 1,000 women screened beyond 2D mammography (Berg et al. 2021). These results are promising, suggesting that contrast-enhanced mammography may be used as an alternative imaging tool for women who cannot tolerate breast MRI.

What role can Hologic play in increasing awareness and improving early cancer diagnosis? How can the Women's Health Index help?

Hologic can play a key role in raising awareness and improving breast cancer detection by using the Global Women's Health Index network to inform women on the implications of breast density and to promote supplemental screening options according to women's risk profile. Women who get screening truly believe if they develop cancer, it will be found at an early stage. Therefore, the benefits and potential risks of tomosynthesis and supplemental screening with ultrasound or MRI, as well as contrast-enhanced mammography, may thereby increase women's awareness, which may result in more effective and meaningful communication to reduce anxiety and to pursue supplemental examinations. The Global Women's Health Index has the potential to deliver information to women in the format of a questionnaire that will be clear and comprehensively presented based on the religion, ethnicity, education, and women's preferences for each country.

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