Breast Imaging Vision by 2025 and Beyond: Vision on Breast Cancer Screening

Dr. Paolo Giorgi Rossi, PhD

If we observe the largest ongoing or recently concluded trials on breast cancer screening, we can distinguish two main areas of research:

1. Increasing sensitivity of the first level test
2. Personalization of the screening protocol according to individual risk and breast density

In the first area, tomosynthesis is the most studied tool and probably the only one that can reasonably be proposed for the entire target population of the screening. It showed higher sensitivity and equal or better specificity than 2D mammography[1]. Nevertheless, there are still uncertainties about its real efficacy. The scarce or null impact on interval cancers observed in most studies[2], including two[3,4] of the three[5] randomized trials that already published follow-up results, suggests that tomosynthesis is more sensitive than 2D in identifying small but slowly growing lesions and not the fastest ones. Despite the non-negligible impact on the reading time[6,7], which impacts overall screening costs, and the uncertainty about the final effect on patient-relevant outcomes, tomosynthesis is now recommended by the European guidelines as an alternative to 2D mammography in screening[8].

The studies on personalized screening adopted two main strategies: adding more sensitive (usually less specific and more costly) tests in women with a dense beast; adopting more or less intense screening protocols according to the individual risk of the woman; screening intensity is modulated by changing the age to start screening and intervals between screening tests, but also adding more sensitive tests.

The first strategy obtained promising results with the use of MRI in two large studies[9,10], showing a reduction of interval cancers. The detection obtained with MRI is so higher than that observed with mammography that a very long follow-up will be necessary to assess if part of these cancers is overdiagnosed; furthermore, if we will assess that overdiagnosis is acceptably small, this very high sensitivity probably implies that much longer intervals should be adopted. European guidelines suggest that tomosynthesis should be used in dense breasts instead of 2D mammography [11] and the Independent Expert Report by the Group of Chief Scientific Advisors, in 2022, proposed the European Commission introduce MRI for screening dense breasts [12]. Furthermore, European guidelines suggest using contrast enhanced mammography (CESM) instead of MRI when pre-surgical assessment is needed[13]; if equal safety and efficacy of CESM and MRI would be shown also for screening dense breasts, this would be a great opportunity to increase the sustainability of the intervention.

The second strategy is well represented by MyPeBS, a study funded by European Commission[14]. This international trial randomizes women to usual screening or to personalized screening based on risk: women with an estimated risk lower than that of women 40 years old are referred to new mammography in 4 years, those with an average risk are referred at 2 years as usual and, if they have dense breast, receive US, those with a risk that is higher than the average are referred to annual screening with US if have dense breast, and those with a risk comparable to a BRCA2 mutation are referred to MRI. To estimate the risk, the investigators use age, familial and biopsy history, density, and a genetic risk score based on 313 single nucleotide polymorphisms[15]. The trial will give results in 2028.

Most of the research results in both areas, if implemented, will inevitably increase the invasiveness and costs of the screening. Nevertheless, the balance of desirable and undesirable effects of screening programs is fragile, as well as their sustainability. Particularly when we work on stratifying women by risk, if we find a group at higher risk, the remaining population has a decreased risk compared to the average. Intensifying the intervention for the high-risk group without de-intensifying the intervention for the low-risk group probably does not optimize the balance between desirable and undesirable effects.

The future of screening must be defined through research focused on optimizing the balance, working on both the weighting plates: decreasing undesirable effects and increasing desirable effects. Focusing all the efforts on increasing cancer detection and forgetting that we are dealing with healthy women but in a sick health system may cause the end of equitable screening programs.

References:

1. Alabousi M, Wadera A, Kashif Al-Ghita M, et al. Performance of Digital Breast Tomosynthesis, Synthetic Mammography, and Digital Mammography in Breast Cancer Screening: A Systematic Review and Meta-Analysis. J Natl Cancer Inst. 2021 Jun 1;113(6):680-690. doi: 10.1093/jnci/djaa205.
2. Houssami N, Zackrisson S, Blazek K, et al. Meta-analysis of prospective studies evaluating breast cancer detection and interval cancer rates for digital breast tomosynthesis versus mammography population screening. Eur J Cancer. 2021 May;148:14-23. doi: 10.1016/j.ejca.2021.01.035.
3. Pattacini P, Nitrosi A, Giorgi Rossi P, et al. A Randomized Trial Comparing Breast Cancer Incidence and Interval Cancers after Tomosynthesis Plus Mammography versus Mammography Alone. Radiology. 2022 May;303(2):256-266. doi: 10.1148/radiol.211132.
4. Armaroli P, Frigerio A, Correale L, et al. A randomised controlled trial of digital breast tomosynthesis vs digital mammography as primary screening tests: Screening results over subsequent episodes of the Proteus Donna study. Int J Cancer. 2022 Jun 11. doi: 10.1002/ijc.34161.
5. Hofvind S, Moshina N, Holen ÅS, et al. Interval and Subsequent Round Breast Cancer in a Randomized Controlled Trial Comparing Digital Breast Tomosynthesis and Digital Mammography Screening. Radiology. 2021 Jul;300(1):66-76. doi: 10.1148/radiol.2021203936.
6. Pattacini P, Nitrosi A, Giorgi Rossi P, et al. Digital Mammography versus Digital Mammography Plus Tomosynthesis for Breast Cancer Screening: The Reggio Emilia Tomosynthesis Randomized Trial. Radiology. 2018 Aug;288(2):375-385. doi: 10.1148/radiol.2018172119.
7. Iotti V, Giorgi Rossi P, Nitrosi A, et al. Comparing two visualization protocols for tomosynthesis in screening: specificity and sensitivity of slabs versus planes plus slabs. Eur Radiol. 2019 Jul;29(7):3802-3811. doi: 10.1007/s00330-018-5978-x.
8. European Commission Initiative on Breast Cancer Guidelines Developing Group. Use of Tomosynthesis. Available at: (last access 17/09/2022) https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/screening-tests
9. Bakker MF, de Lange SV, Pijnappel RM, et al. Supplemental MRI Screening for Women with Extremely Dense Breast Tissue. N Engl J Med. 2019 Nov 28;381(22):2091-2102. doi: 10.1056/NEJMoa1903986.
10. Comstock CE, Gatsonis C, Newstead GM, et al. Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening. JAMA. 2020 Feb 25;323(8):746-756. doi: 10.1001/jama.2020.0572.
11. European Commission Initiative on Breast Cancer Guidelines Developing Group. Women with high breast density. Available at: (last access 17/09/2022) https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/dense-breast
12. Cancer screening in the European Union Group of Chief Scientific Advisors European Commission Directorate-General for Research and Innovation Unit 03 — Science Policy, Advice & Ethics, February 2022.
13. European Commission Initiative on Breast Cancer Guidelines Developing Group. Planning surgical treatment. Available at: (last access 17/09/2022) https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/surgical-planning
14. https://www.mypebs.eu/
15. Mavaddat N, Michailidou K, Dennis J, et al. Polygenic Risk Scores for Prediction of Breast Cancer and Breast Cancer Subtypes. Am J Hum Genet. 2019 Jan 3;104(1):21-34. doi: 10.1016/j.ajhg.2018.11.002.

NOTES