New evidence for digital mammography plus tomosynthesis in breast cancer screening

By Dr S Muller

Breast cancer accounts for 1 in 3 cancers in women in the European Union (EU), making it the leading cause of cancer among women throughout the continent. With a mean incidence rate of 160.2 per 100,000, western Europe also has one of the highest incidences of breast cancer in the world [1]. Screening is the mainstay of breast cancer detection, with numerous studies having found that early detection translates into substantially reduced mortality rates [2-4]. Screen-film mammography was the standard for decades until the advent of full-field digital mammography (FFDM) in 2000 [5]. However, these traditional technologies have several shortcomings. One of the most common is a relatively high false-positive recall rate, leading to unnecessary testing and biopsy [6,7]. False positive diagnosis causes anxiety and fear, and women who receive such results are more likely to delay their next mammogram [8].

Another common shortcoming is the lower sensitivity of mammography in dense breasts, mainly due to normal parenchyma hiding small lesions in 2D projected images [9]. False-negative diagnosis increases the number of interval cancers with the potential danger and risk that breast cancer treatment may be delayed [10].

In mammography, there is also significant inter- and intra-observer variability resulting from, in part, radiologist and technician expertise and practice patterns [5, 11-15]. A multicentric study, for instance, found substantial observer variability for both screen-film mammography and FFDM between 6 radiologists who interpreted the mammograms of 232 cases obtained with both techniques [14]. Digital breast tomosynthesis (DBT), the latest generation in breast imaging, uses a limited-angle tomographic breast imaging technique to provide multiple low-dose projection views of the breast, thus reducing interference from overlapping tissues. A stack of slices (at typically 1-mm spacing) is then reconstructed to provide a three-dimensional view of the breast.

Numerous observational and clinical studies support the improved performance DBT offers compared to FFDM alone, whether used as an adjunct to digital mammography (DM) or to synthetic 2D mammography, or as a stand-alone screening technique. Several studies have found that the use of DBT can reduce recall rates while improving cancer detection, particularly for invasive cancers, and provide better lesion characterization [7, 16-21]. The combination of DBT and DM, while providing greater sensitivity than DM alone, initially required an increased radiation dose compared to DM only. Skaane et al later demonstrated comparable results between DBT combined with synthetically reconstructed two-dimensional images and DBT plus DM, enabling the use of lower radiation doses [20]. This is now becoming more common in centers using DBT as a screening modality.

The European Society of Breast Imaging (EUSOBI) in its most recent position paper on screening mammography concluded that DBT is set to become “routine mammography” in the screening setting in the near future, but also noted there are several unanswered questions around the technology [22]. The European Commission Initiative on Breast Cancer is also cautious in its recommendations for its use, as are the American Cancer Society and the US Preventive Services Task Force [23 – 25].

Areas for research include data on the challenges of implementing DBT-based screening programs; cost-effectiveness; rates of overdiagnosis; and, most important, the ability of DBT to improve prognosis and reduce mortality and morbidity [23]. Thus, DM still remains the standard for organized mammography screening in Europe.

REGGIO EMILIA TOMOSYNTHESIS RANDOMIZED TRIAL

Recently published preliminary results of the Reggio Emilia Tomosynthesis Randomized Trial provide additional evidence regarding the strengths of DBT plus DM versus DM alone. This 2-arm, test-and-treat prospective randomized trial is comparing DM plus DBT (experimental arm) to DM alone (control arm) in 19,560 women aged 45-70 who had previously received 1 round of screening and had no familial risk of breast cancer. All screening mammograms were conducted using GE Healthcare digital mammography systems, 4 of which were equipped with tomosynthesis [26].

The authors report a detection rate 90% higher in the DBT arm than in the control arm (8.6 per 1,000 women screened vs 4.5 per 1,000 in a population previously screened with DM) across all age groups, with similar recall rates. The detection rate was higher for ductal carcinoma in situ (DCIS) than invasive cancer. Although there is debate regarding the increased rate of DCIS diagnosis that has occurred with screening mammography, there is also substantial evidence that some DCIS are precursor to invasive cancer and therefore should be detected during screening [27, 28].

The detection rate was also higher for invasive cancers <10 mm (94% increase) and for cancers 10-20 mm (122% increase), corresponding to lesion size ranges that are most beneficial in the early diagnosis of breast cancer. The detection rate was also higher for grade 1 or 2 cancers. There was no difference between the 2 arms for larger or grade 3 cancers.

The investigators also reported a 12% lower rate of false-positive results in the experimental group than in the control group.

The overall detection rate seen with DBT in this study is slightly higher than that seen in recent European studies, and significantly higher than those seen in US observational studies [5, 16, 19, 29-31]. Finally, the study demonstrated a 70% longer reading time for DBT plus DM versus DM alone. The difference observed in reading time

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was related to negative cases, suggesting the longer time was primarily due to multiple image reviews and not to the interpretation itself. Moreover, variability between readers was similar in both arms. This result confirms the need for efficient image review protocols and software and may also be related to the radiologist learning curve in reading images of a new imaging modality.

Most of the gain in invasive cancer detection observed in the experimental arm was due to increased detection with DBT alone. Thus, the use of DBT alone may have the potential to reduce the higher dose in the experimental arm while preserving most of the clinical performance benefit. The use of synthetic 2D in addition to DBT is another attempt to provide a lower dose compared to DBT plus DM and preserve the performance of DBT plus DM. Advances in the ability of synthetic 2D images to improve their current lower specificity are expected. [32].

CONCLUSION

The body of evidence for DBT's ability to identify in a screening environment significantly more cancers with similar recall rates compared to DM continues to expand.[21 – 33]. The gain in detection for small cancers (<20mm in diameter) and early stage lesions (stage I) shown in the Reggio Emilia study should prove beneficial for the early detection of breast cancer in mammography screening. However, data from following screening rounds are required to understand how this higher detection rate will impact interval cancers and overdiagnosis compared with digital mammography. In addition, the expected benefit of DBT versus DM in dense breasts has not yet been realized. Therefore, alternative approaches such as contrast-enhanced spectral mammography (CESM), possibly combined with DBT, may have a future role to play in screening women with dense breasts [34].

Finally, synthetic 2D mammograms as an adjunct to DBT have the potential to reduce the dose of a DBT plus DM exam while preserving the clinical performance of DBT plus DM, but needs further technological improvement and generation of clinical evidence. Several large, multicenter clinical trials are currently underway that will, hopefully, answer some of the remaining questions currently preventing greater uptake of DBT in the clinical setting.

REFERENCES