

Evolving role of radiological imaging in early detection of breast cancer: beyond 2D mammography

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Introduction

Breast imaging is targeted at two main indications: screening for breast cancer and assessment of suspected pathology. Even though two view mammography is the standard tool for screening of breast cancer, the sensitivity of 2D mammography varies widely and is dependent on a number of factors [1]. Beyond 2D mammography, a number of new advances have emerged in breast imaging with prospects for increasing early detection of breast cancer.

Digital Breast Tomosynthesis (DBT) is a new technical advance in breast imaging which enables imaging of 1mm thin slices of breast in the same orthogonal planes to 2D mammography. DBT obtained US Food and Drug Administration (FDA) approval for clinical use in 2011. Currently it is utilized for breast screening in combination with 2D digital mammography in some centres. 2D synthetic mammography is a further advancement of DBT which enables reduction of dose to the patient in DBT and 2D combined protocols.

MRI has high sensitivity for breast cancer detection and is selectively utilized in breast screening. The role of MRI in the screening of younger women at high risk for breast cancer is widely discussed.

Ultrasound scanning (USS) is a very useful imaging modality used for the assessment of breast pathology. However, its place as a breast screening modality is not affirmed. The options for utilizing USS as an adjunct screening modality for selected subgroups of women is discussed by many.

While some of the new advances are in the form of new technology, some are revised or new protocols for breast screening using existing imaging modalities. The role of these new imaging modalities and protocols in breast screening continues to be defined mostly in light of evidence and cost effectiveness.

Further new concepts being investigated for a supplementary

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role in breast screening such as automated whole breast USS, positron emission mammography and positron emission tomography, and the role of image guided intervention in the early diagnosis of breast cancer are not discussed in this article.

Digital Breast Tomosynthesis

Digital breast tomosynthesis (3D mammography) is an imaging modality which uses X-rays similar to mammography (2D mammography). Unlike 2D mammography however, a selected view of the breast (i.e. CC, MLO etc.) is acquired in multiple angles followed by reconstruction of the acquired data to form a series of thin cross sectional images in the acquired plane. Images can be viewed individually or as a cine loop. One mm thin slices are imaged in CC and MLO views in a routine study. A cross sectional approach in DBT helps to overcome the issue of tissue overlap and is expected to increase the sensitivity and specificity of breast imaging when compared to 2D mammography.

The efficacy of DBT in breast cancer detection

Gilbert et al (2015) conducted a multicentre retrospective reading study recruiting 8869 women in the NHS Breast screening Programme, United Kingdom, to compare the efficacy of DBT with standard 2D digital mammography (TOMMY trial). The trial targeted a cancer rich population including patients recalled for a mammographic abnormalities detected in a routine 2D screening session, and cases with a family history undergoing annual mammographic screening.

Results of the TOMMY trial highlighted that adding DBT to 2D mammography significantly increases the specificity of depicting breast cancer as compared to a 2D mammogram alone for all subgroups of women [2]. Sensitivity does not achieve a level of significance when the total screening population is considered, but a statistically significant higher sensitivity was observed for the sub group of women with >50% dense breasts, and for women of the 50- 59 age group when DBT was added to 2D mammography [2].

The trial also concurs with other reported studies that DBT is better at detecting breast masses rather than

microcalcifications [2].

Place of DBT in breast screening

As the TOMMY trial is not a screening trial but was done in a cancer rich cohort, the place of DBT in screening is better discussed by other trials done in screening populations.

The STORM trial (Screening with Tomosynthesis OR standard Mammography) compared paired screen reading findings between 2D alone and 2D combined with DBT in a prospective study including 7292 women attending a breast screening programme in Italy in 2011/2012. They found that there is an increment of 2.7 cancers detected per 1000 screens in the combination method (2D alone detects 5.3 per 1000 screens while 2D combined with DBT detects 8.1 per 1000 screens). The STORM trial concludes that adding DBT to 2D mammography improves breast cancer detection by 34% and reduces false positive recalls for assessment by 17% [3].

A similar population based screening trial (Oslo Tomosynthesis screening study) compared findings of 2D mammography alone against 2D mammography combined with DBT in 12,631 women consenting from the Oslo Breast Screening Programme, Norway in 2010/2011. The Oslo trial reported an increment of 27% in cancer detection and a reduction of 15% in false positive recalls by the combined method. No increment was detected for ductal carcinoma in situ by the combined method compared to 2D mammography alone [4].

Both the STORM and Oslo trials conclude that combining DBT to 2D mammography significantly increases cancer detection in a population based screening program in addition to reducing the number of false positive recalls.

Dose of radiation to the patient when DBT is combined to 2D mammography

DBT technology can be used on its own as a standalone sole modality for breast imaging or in combination with 2D mammography. The current evidence supports its use in combination with standard 2D digital mammography. However, this incurs an obvious almost double dose of ionizing radiation to the patient [2, 5].

2D synthetic mammography

More recent technology allows the synthesis of 2D images from the same data acquired from DBT without exposing the patient to an additional 2D mammogram. The synthesized 2D images can be combined with DBT instead of an originally acquired 2D mammogram, evading the extra dose of radiation from an additional 2D mammogram. The efficacy of the synthetic plus BDT combination and accuracy of the synthetic images compared to standard 2D images have been studied by various authors.

The TOMMY Trial reports synthetic mammography to be inferior for detecting microcalcifications and small masses of 11mm to 20 mm in size. Also the observed increase in sensitivity for women aged 50- 59 years and for women with >50% dense breasts in the standard 2D plus DBT combination method is not detected by the synthetic 2D plus DBT combination [2].

Even with the above specific shortcomings in the synthetic protocol it is reported that there is no significant difference in the overall sensitivity and specificity between the combinations of standard 2D plus DBT and synthetic 2D plus DBT when the whole study population is considered [2].

Ultrasound Scan (USS)

Place of USS in Breast screening

Despite being less costly, free of radiation, widely available and better tolerated by patients than most imaging modalities, USS is operator dependant and demands time and skill [6]. USS is widely used to further evaluate mammographically detected/suspected breast pathology in screening recalled patients. Further to this defined role, the place of USS as a routine adjunct to screening mammography in selected subgroups has been looked into by various authors.

Is USS indicated for screening of dense breasts with normal mammogram?

Dense breasts have a strong positive association with breast cancer [7-9]. Higher mortality from breast cancer is reported in women with mammographically dense breasts [9]. Higher interval cancers, up to a six fold increase, are reported in women with extremely dense breasts [1]. Therefore, whilst increased breast density increases the risk of breast cancer such breasts also have less mammographic sensitivity presenting a constant challenge to mammographic breast screening. In fact, it is interesting to note that a number of states in America have passed legislations requesting radiologists to inform individual women of their breast density with a view to discussing optimum personalized screening strategies for women with dense breasts [6].

The use of USS as a routine adjunct to mammography to increase sensitivity of screening of the dense breast has been looked in to with varying results. Some authors report adding USS to mammography increases sensitivity of breast screening leading to increased cancer detection in dense breasts both in the normal population [10, 11] and among high risk subgroups [12]. The IARC work group on breast cancer (2014) however concludes that there is limited evidence to suggest that adding USS to screening mammography (in women with a dense breast and a negative mammogram) increases cancer detection in the normal population or in high risk groups. There is also insufficient evidence that this protocol reduces mortality from breast cancer or that it

reduces the interval cancer rates [13]. Conversely, there is a consensus that USS in this regard leads to higher false positive recall rates [12, 14] and only 11% positive predictive value [14]. There is sufficient evidence to conclude that adding USS to mammography leads to higher false positive screening outcomes [13].

Magnetic Resonant Imaging (MRI)

MRI has a proven higher sensitivity for breast cancer detection than mammography in women at high risk of breast cancer [15, 16]. Despite its high cost, MRI is recognized as cost effective for screening of high risk women [17]. However, there is insufficient evidence to conclude that MRI reduces mortality from breast cancer in women with BRCA 1 or BRCA 2 mutations [13]. MRI also has the disadvantage of lower specificity which leads to a high biopsy and follow up recommendations with more false positive outcomes [6].

Current place of MRI in Breast cancer screening programmes

Women at high risk of breast cancer are offered screening at an earlier age than the normal population when their breast density is likely to be higher than at the usual screening age, therefore rendering screening mammography less sensitive. MRI is recognized as a screening tool, either stand alone or more commonly as an adjunct to mammography, in screening of these selected subgroups of women by breast screening programmes. The NHS breast cancer screening programme, UK recommends surveillance imaging protocols specific for identified high risk categories after relevant genetic testing or after risk assessment by a geneticist. The program offers annual MRIs to the most high risk categories between 30-39 years and an annual MRI coupled with annual mammography for some high risk categories between 40-49 years of age [18]. The American cancer society recommends an annual screening MRI as an adjunct to mammography to selected high risk subgroups including women who are identified with BRCA mutations, those who are first degree relative of a BRCA carrier or to those who have at least a 20-25% higher risk than the normal population for breast cancer by risk assessment [19]. The role of the geneticist in risk assessment and risk prediction tools are duly identified by breast screening programmes.

Role of new imaging modalities/protocols in breast screening

The emergence of new technology and protocols demand an evidence based basis prior to implementation into practice. Whether the costly new advances lead to better mortality reduction rates with benefit to the individual patient and community needs discussion. The offered degree of sensitivity, specificity, number of false recall rates and tendency for unnecessary intervention are among some of the other variables to look at in this regard.

Currently 2D mammography remains the standard screening modality for breast cancer in the normal population. Paying due attention to breast density with a more individualized screening approach concurs with evidence when using other imaging modalities for screening.

In lower-middle-income countries like Sri Lanka where population screening is not established, protocols for identifying high risk groups and offering regular screening at least to these selected groups can be considered a priority.

The author discloses no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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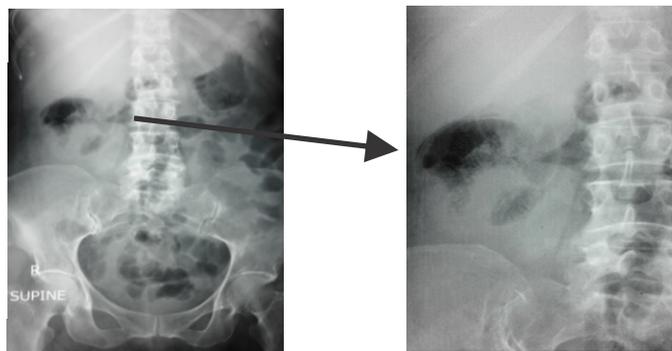
IMAGES IN SURGERY

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Case:

A 62 year old female with uncontrolled diabetes mellitus presented with a history of acute onset right sided flank pain, fever with chills and rigors for a duration of 1 day. On examination, she had significant right sided renal angle tenderness with gaseous distention of the abdomen. On investigation, she was found to have neutrophil leukocytosis (WBC: $22 \times 10^3/\text{mm}^3$ Neutrophils – 88%), and urinalysis revealed field full pus cells per high power field on microscopy. Ultrasonography revealed highly echogenic areas within the right kidney with a perinephric fluid collection in the right paracolic gutter. An X-ray KUB was performed and is shown below.

1. What is the radiological abnormality/clinical diagnosis shown?
2. What are the principles of management of a patient with this condition?



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