

Editorial

The Density Factor: The Enigma of Dense Breast

In a recent article in the Wall Street Journal entitled “The latest Mammogram Controversy: Density,” Ms. Melinda Beck has brought out a few pertinent points with regard to the current practice of breast cancer screening with mammograms.^[1] Currently *mammography* is the gold standard for screening in the detection of early breast cancer, since it has proven to reduce mortality by about 30% (USA Data). The efficacy of mammography depends on the technical quality of the mammogram, the expertise of the interpreting radiologist, and proper implementation of a screening program. Mammography relies on the relative densities of breast tissues to differentiate normal from abnormal tissue. Breast density is the most significant independent predictor of mammographic sensitivity at any age. In the fatty breast, sensitivity is 98%; in the very dense breast, the sensitivity goes down to as low as 48%. This (low sensitivity) also holds good for women with breast implants, or in the post-surgical breast. In general, the technique is less reliable for detecting lesions in women younger than 50 years in whom dense, glandular breasts are a common radiographic finding yielding a high false-negative rate (25–45%) leading to frequent delays in the diagnosis of breast cancer associated with significantly shorter survival. Besides, the positive predictive value of mammography is reported to be less than 40% resulting in a high number of unnecessary biopsies. The incidence of breast cancer is at its peak during the 5th decade of women’s life in most countries/regions of the world. Paradoxically most women belonging to that age group will have dense breasts. Hence, it appears that a significant percentage of mammograms performed on women will be indeterminate because of dense breasts.

As an alternative, some physicians advocate that women with dense breasts should have regular ultrasound screening or magnetic resonance imaging (MRI) studies to reach a more definitive diagnosis or rule out malignancy. It may be noted that ultrasound and MRI have their own sets of limitations.

Interestingly, there is a passing mention of “Molecular Breast Imaging” in Ms. Beck’s article, which is extremely important in the management of breast cancer and for that matter any cancer. A number of radionuclide-based molecular imaging procedures are available today; most of them are routinely available in most standard nuclear medicine departments around the world. These procedures are independent of limiting factors like dense breast. These include: Scintimammography (Tc-99m MIBI), Breast Specific Gamma Imaging (BSGI), Positron Emission Tomography (PET), and Positron Emission Mammography (PEM). Scintimammography is perhaps the simplest and most cost-effective molecular imaging procedure for the diagnosis of breast cancer. It is the molecular imaging study of the breast performed with single-photon radiopharmaceuticals, such as ^{99m}Tc-Sestamibi which is a tumor localizing agent having the ability to specifically localize within viable malignant cells of breast cancer. The retention of Tc-99m Sestamibi in breast is specifically restricted to biologically viable regions of the cancer and is related to the negative ion potential on the mitochondrial membrane. The procedure is not new; it was first introduced by Khalkhali *et al.* in 1994,^[2,3] and can be performed with very basic nuclear medicine imaging equipment – a simple planar gamma camera and a scintimammography positioning pad [Figure 1]. The radiopharmaceutical used is also not new; it is routinely used for cardiac perfusion studies. The procedure offers a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of 85.2%, 86.6%, 88.2%, 81.8%, and 86%, respectively [Figure 2]. Despite these very encouraging results suggesting that scintimammography could be a useful

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Figure 1: Scintimammography procedure being carried out using a conventional gamma camera with a scintimammography positioning pad

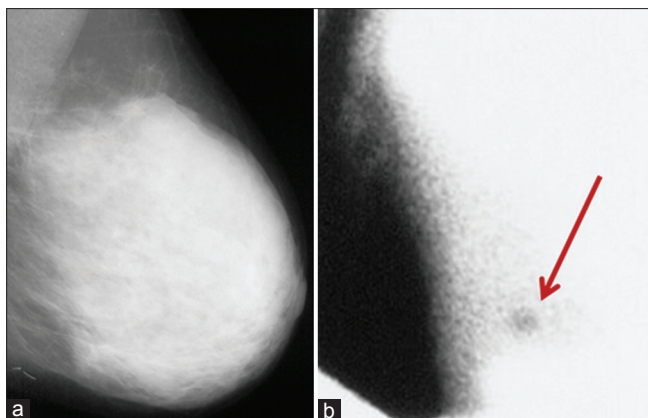


Figure 2: Woman with palpable node in right breast inferior outer quadrant. (a) X-ray mammogram is of no value due to dense breast. (b) Scintimammography with Tc-99m Sestamibi unequivocally demonstrates a small, discrete focus of increased radiotracer uptake in the right breast, consistent with breast cancer. Histopathology: Ductal infiltrating carcinoma

tool in the management of breast cancer, the procedure has never found its rightful place in the algorithm of breast cancer diagnosis. In recent years, the procedure of scintimammography has been upgraded to BSGI with the introduction of a dedicated high-resolution portable small field of view gamma camera. This offers imaging at the point of care, multiple acquisition angles; scope for duplicating standard mammographic views for easy comparison, and helps in selectively studying “hard-to-reach” spots such as the medial aspect of the breast with high-resolution image up to the chest wall. These improve lesion contrast for detection of earlier stage cancers, as small as 3–5 mm. It is encouraging to see that one of the first publications on BSGI was in a surgical journal (*American Journal of Surgery*), where the lead author is a surgeon.^[4] The authors reported that of the 176 initial patients in their study, clinical management was changed significantly in 14.2%, with another 6.3% in whom a negative BSGI could have prevented a biopsy. They concluded that BSGI has played an important role in their clinical management of breast patients with complex breast tissue. There could be several indications for scintimammography and/or BSGI. These include: Radio-dense breast tissue, indeterminate mammograms, postoperative or post-therapeutic evaluation, evaluation of multiple lesions, palpable mass not demonstrated on mammogram or US, for use in patients where MRI is indicated but not positive, patients who are claustrophobic, patients with breast implants, examining the axillary region for nodal status, determining the extent of the primary tumor for surgical/radiotherapy planning, predicting chemotherapy response, and monitoring tumor response.

The main objective of this editorial is not to argue against doing a mammogram or making a case for scintimammography or BSGI. Nevertheless, in our opinion, scintimammography remains probably one of the most underutilized nuclear medicine procedures. We are not advocating that every individual with a breast lump be subjected to a scintimammography procedure. Scintimammography can never be accepted as a screening procedure, nor should it be promoted as one. But it can always be offered as the next step to X-ray mammography, where the mammogram is indeterminate because of dense breast.

In terms of sensitivity, specificity, NPV, PPV, and accuracy, scintimammography and BSGI offer better value for money. When combined with X-ray mammography, it would have a greater synergistic value. Mammogram screening will continue to be used more and more widely around the world, and rightly so. But this should not preclude the use of other diagnostic tools like scintimammography. What is required is a change in mindset. It is time for the oncologists, surgeons, radiologists, and nuclear medicine physicians to realize that here is a radionuclide technique, which if applied judiciously can lead to a much better, cost-effective, and more logical and scientific management of breast cancer. Interestingly enough, one does not have to spend millions of dollars to buy new equipment or build new infrastructure. There may be a solution for the “Density Factor” – one has to just look round the corner.

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