ORIGINAL ARTICLE

Impact of scintimammography in management of breast cancer

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Abstract

Mammography is the most widely used diagnostic imaging method for screening and diagnosing breast cancer. Nevertheless, this technique has some limitations in that not all breast cancers are evident on mammograms, especially in dense or dysplastic breasts, patients with breast prosthesis or if the patient has previously undergone radiation, surgery or biopsy. Scintimammography (SM) is the functional imaging study of the breast with radiopharmaceuticals, such as ^{99m}Tc-labelled methoxyisobutylisonitrile (^{99m}Tc-MIBI). SM is currently used as a complementary test to mammography in patients with suspected breast cancers. This study was undertaken to evaluate the impact of SM on the management of patients with a suspicious lesion detected by palpation or mammography.

Methods. We performed a prospective study of 53 patients with a suggestion of breast cancer, either on palpation or mammography. Planar imaging was performed after injection of ^{99m}Tc-MIBI. Results were compared with histopathological analysis in all cases.

Results. Breast cancer was proven in 11 cases. SM had a sensitivity of 90.9% and a specificity of 97.6%. SM correctly evaluated multicentricity or bilaterality in 3 of 11 patients and detected axillary lymph node in 1 patient. SM made the diagnosis of benign lesions in 41 cases with doubtful diagnosis, thus potentially avoiding biopsy in 77% of cases.

Conclusion. SM is a useful complementary tool for the diagnosis and evaluation of disease extent in patients with an inconclusive diagnosis and can decrease the number of negative breast biopsies.

Introduction

In South Africa breast cancer is one of the leading causes of disease-related mortality. One woman in 10 will suffer from breast cancer in her lifetime, and 1 woman in 20 will die from breast cancer. Several imaging techniques are used to evaluate women for breast cancer. Mammography is the most frequently used screening method, and a decrease in mortality of 21% has been observed for breast cancer in women who have undergone mammographic screening.[1] Mammographic screening in women older than 40 years provides an effective early diagnosis. Subsequent prompt treatment reduces the mortality rate. However, this technique has limitations with regard to sensitivity and specificity,[2,3] especially in dense breasts, lumpy breasts, fibrocystic breasts, previous breast surgery, breast implants, and multifocal or multicentric lesions. All of these situations make other tests necessary to confirm the nature of the lesion observed on the screening mammogram.

Approximately 1 in 4 women undergo surgical biopsy to rule out malignant breast lesion, but most of these women will not have cancer. For this reason, additional techniques are required to obtain a more accurate diagnosis, that differentiates between malignant and benign masses.[4]

Breast cancer, like other cancers, shows significant affinity for the radiopharmaceutical technetium-99m methoxyisobutylisonitrile (^{99m}Tc-MIBI), with high tumour/non-tumour ratios.[5] ^{99m}Tc-MIBI is a lipophilic agent and is furthermore a substrate of P-glycoprotein (Pgp), which is considered one of the multi-drug resistant (MDR) agents.[6] SM has been demonstrated to be useful in the diagnosis of primary breast tumours in patients with dense breasts,[7] and its value has been especially emphasised in the evaluation of therapeutic response.[8,9] Moreover, scintimammography (SM) may be considered a non-invasive method for the identification of MDR-positive patients, assisting in the choice of the most suitable therapy.[8-10]

Objective

The aim of this study was to review the diagnostic accuracy of SM using ^{99m}Tc-MIBI as a marker and its place in the diagnostic algorithm of breast cancer management.

Materials and methods

We examined 53 consecutive patients (age range 20 - 79 years, mean age 53 years) with a suspicious breast lesion detected by self-examination, physical examination or screening mammography. Afterwards most patients underwent ultrasound (US). Mammography and US were performed according to standard procedures. All patients underwent SM prior to fine-needle aspiration biopsy (FNAB). The patients with breast cancer at FNAB underwent surgery.

Mammograms were performed on dedicated mammography machines: a digital mammography unit. Mammography was performed with both mediolateral oblique and craniocaudal views in every case, and an additional lateromedial oblique view if indicated.

US was performed using the direct contact method with real-time equipment and a broadband linear probe (6 - 12 MHz). US-guided FNAB was performed freehand with a syringe holder connected to a 10 ml syringe and a 22-gauge needle.

SM was performed with a single head gamma camera, equipped

with a parallel-hole, low-energy, high-resolution collimator. The test was performed using the standard technique: 740 MBq ^{99m}Tc-MIBI was injected intravenously in the opposite arm to the breast with the suspected lesion. In all patients, planar imaging was performed using a 256 × 256 matrix with an acquisition time of 10 - 15 minutes, in both lateral and anterior views, at 20 - 30 minutes after injection. Patients were examined in the prone position using an imaging table with breast 'cut-outs'. To avoid interference from the opposite breast, a layer of lead was used as a shield. The SM images were classified based on visual interpretation. Focal tracer accumulation in the breast was interpreted as suspicious or probably malignant and such scintigrams were classified as positive. The suspicious or probably malignant images were considered true positive when confirmed by histopathology. The SM was interpreted as true negative if the images and histopathology excluded breast cancer.

SM images were interpreted separately by 3 expert nuclear medicine physicians who worked independently. They were blinded to the results of mammography, US and physical examination.

Results

A total of 53 patients were investigated. Ten of 11 histopathologically proven malignant tumours could be detected by SM with ^{99m}Tc-MIBI. In 1 case, scintigraphy was false-negative. There were 41 benign lesions of the breast, with 1 being false-positive. This gives an outstanding sensitivity of 90.9%, a specificity of 97.6%, a positive predictive value (PPV) of 90.9%, and a negative predictive value (NPV) of 97.6%. The lesion size in the entire patient group ranged from 0.1 cm to 15 cm, with a mean of 1.3 cm. The smallest detectable tumour had a size of 1.2 cm. Fig. 1 shows a true negative scan while Fig. 2 demonstrates cancer in a patient in whom mammography was negative.

Axillary lymph node metastases were histopatologically confirmed in 2 patients. Scintigraphy with ^{99m}Tc-MIBI was positive in the axillary region in 1 case (Fig. 3).

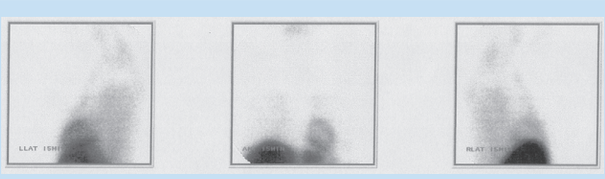

Fig. 1. Normal biodistribution of ^{99m}Tc-MIBI SM on both anterior and lateral images.

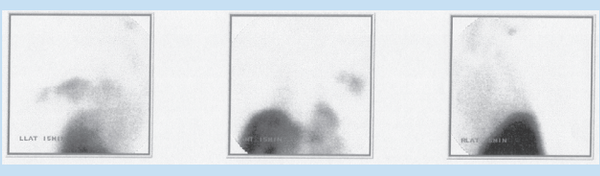

Fig. 2. A 52-year-old woman with inclusive mammography where planar anterior and left lateral SM clearly shows carcinoma with two adjacent sites of abnormal accumulation in the left breast.

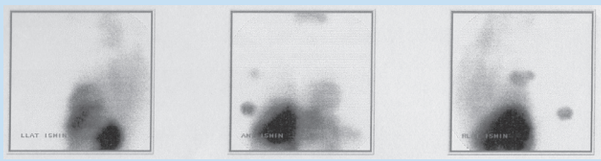

Fig. 3. Anterior and right lateral SM shows a single area of increased abnormal uptake in the right breast and also focal uptake in the right axilla of a 34-year-old patient.

Discussion

In accordance with numerous previous studies, our results showed high sensitivity and specificity of SM for detection of breast cancer. In our study, 90.9% of carcinomas with a diameter of 1.2 cm could be detected. Our results show that 1 case of fibroadenoma presented as a false positive. In comparison with mammogragraphy, SM showed a better diagnostic accuracy. This supports the numerous studies that have been published on the clinical usefulness of SM. The aggregated overall summary estimates of a recent meta-analysis selecting 64 unique studies,[11] with data on 5 340 patients, including 5 354 breast lesions, showed a sensitivity of 85.2%, specificity of 86.6%, NPV of 81.8%, a PPV of 88.2% and accuracy of 85.9%. It is worth noting that 80% of the studies yielded sensitivity and specificity values of > 80%, and nearly half of them were values of > 90%. Moreover, in > 5 660 cases reported to date, the sensitivity and specificity of ^{99m}Tc-sestamibi SM in detecting primary breast cancer were 83.8% and 86.4%, respectively.[12]

A comprehensive review of SM indications was published in 2004 documenting the impressive performance of this modality in the management of breast cancer. Table I lists appropriate clinical indications for SM.

Because the uptake of the radiopharmaceutical by the breast is independent of the breast density, and the accuracy of SM is similar for fatty

Table I. Clinical indications for SM

Equivocal mammograms
Dense breast
Palpable abnormalities that cannot be imaged well with mammography
Axillary lymph node metastases of an adenocarcinoma of unknown primary origin
Breast implants
Parenchymal distortions of the breast
Doubtful microcalcifications
Assessment of multicentric disease
Breast iatrogenic architectural distortion
Suspected recurrent breast cancer
Monitoring the response to neoadjuvant chemotherapy

and dense breasts, scintigraphy is indicated for patients with a palpable mass not detected on mammography due to dense breast tissue - in particular, when the other diagnostic tests are inconclusive. Furthermore, SM is particularly useful in patients with doubtful microcalcifications or parenchymal distortions, in the presence of scar tissue after surgery or biopsy and in breasts with implants.[13] It is well known that mammography is less accurate in evaluating breasts that have previously been submitted to surgery, biopsy, radiation therapy, or chemotherapy. Cases where there is a scar within the breast due to these iatrogenic interventions are often difficult to interpret using mammographic imaging, whereas SM is not affected by these morphological changes.

Furthermore, a few studies[8-10] have shown this technique to be useful in predicting and monitoring the response to chemotherapy. ^{99m}Tc-MIBI is taken up by the tumour cells and stored in mitochondria and cytoplasm. Therefore, it is an appropriate indicator of cells with high metabolism, such as cancer cells. It is also a substrate for Pgp, the most widely studied multidrug-resistant factor, which actively transports ^{99m}Tc-MIBI and chemotherapeutic agents outside of the cell. A good correlation has been found between the efflux rate of ^{99m}Tc-MIBI and the cell content of Pgp. Thus, cells that show a high release of Tc-^{99m} MIBI would be less responsive to chemotherapy treatment.[10]

Despite these very encouraging results suggesting that SM could be a useful adjunct to mammography, the precise role of this technique in the algorithm of breast cancer diagnosis and its specific clinical indications are still being debated and have not been definitively assessed. One of the reasons is that it is well known that planar SM has a low sensitivity for non-palpable and ≤ 1 cm cancers, as indicated by several reports. In particular, in a multicentre study on 420 patients, Scopinaro *et al.*[14] reported a sensitivity of 62% for non-palpable tumours and of 46% for ones ≤ 1 cm, whereas the values for palpable and > 1 cm cancers were 98% and 96%, respectively. Therefore, increasing the sensitivity of planar SM for small-sized tumours is clinically very relevant, and the role of SPECT in this task could be significant. The main drawback of single photon emission computed tomography (SPECT) is that, despite its better contrast resolution, it can be difficult to obtain a precise definition of the sites of radiopharmaceutical uptake, whereas prone lateral planar views provide natural landmarks of breast contours, which are useful for the localisation of lesions. This limitation can be overcome by the recent availability of hybrid SPECT/CT systems which allow – through the co-registration of SPECT and CT – for the precise correlation of functional and anatomical data on the same image. The first clinical applications of this new technology in breast imaging indicate that SPECT/CT can increase the accuracy of SPECT by a more accurate anatomical assessment of the sites of abnormal activity.[15]

Conclusion

Breast scintigraphy is not a screening tool for breast cancer, but may supply important information, after a physical breast examination, mammography and US have been performed. SM studies may be particularly appropriate in the case of a suspicious breast lesion that requires a biopsy, thus decreasing the number of negative breast biopsies. Hence, the South African community should make SM part of the algorithm in the management of breast cancer.

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