Breast screening by mammography has increased awareness of breast cancer, which is the second most common cause of death in females.\(^1\) Screening mammography has led to increased discovery of localized breast cancer and has resulted in increase in number of biopsies with majority being performed under imaging guidance.\(^2\) The resultant diagnosis finally leads to early and appropriate patient care and subsequent neoadjuvant and surgical treatment in case of malignancy.\(^3\) The image guided percutaneous breast biopsy procedures are minimally invasive, cause less breast scarring, save time and money, and relieve the patient of the anxiety of going to the operation theatre.\(^4\)

Majority, i.e. 70 - 80% of image detected suspicious breast lesions biopsied under image guidance turn out to be benign thus obviating a need for a surgical procedure.\(^5\) In addition, patients who are diagnosed as having cancer undergo fewer operations as the disease is detected at a non-clinical earlier stage.\(^6,7\) Masroor et al. studied the cost effectiveness of percutaneous breast biopsy to open surgical biopsies, and reported that the cost saving per patient was 253 US dollars.\(^8\)

Similarly, other studies reported that core needle biopsy, in comparison to open surgical biopsy, lead to cost saving from 51 to 96%\(^,9,10\) Image guided vacuum-assisted core biopsy yields a high diagnostic accuracy predominantly of lesions with low to intermediate risk of malignancy. Approximately half of the cases obviate the need for surgical removal with resultant better cosmetic result.\(^11\)

The National Comprehensive Cancer Network (NCCN), in the most recent Clinical Practice Guidelines, has recommended percutaneous breast biopsy for lesions categorised as Breast Imaging Reporting and Data System (BI-RADS) 4 (suspicious abnormality); or BI-RADS 5 (highly suggestive of malignancy).\(^12\)

Indeed, breast program accrediting bodies recommend image guided biopsy as the standard of care, and recommend this as one of the measures of quality when accrediting breast imaging centres. A number of institutions in Pakistan are at present in the phase of setting up sections of breast imaging and intervention; and are faced with the challenges of learning how to perform image guided breast interventions. The options available for such interventions and the appropriate modality for image guidance are not widely known among many clinicians.

The objective of this review was to describe and discuss the different aspects of image guided biopsy techniques along with the authors' practices, their indications and contraindication along with their merits and demerits.

**METHODOLOGY**

Studies published in English language from 2000 to 2015 were searched by using key words “ultrasound guided biopsy, stereo-tactic biopsy, needle localization, MRI guided biopsy and sampling techniques” on PubMed, Medline and Google Scholar. Relevant publications describing the localizing and sampling techniques of breast lesions under various imaging modalities along with their technical aspects, cost efficacy and merits and demerits, were included. Overall
56 studies were selected after analysing and evaluating the papers. Historical details were collected from the older reviews. Results were described as localizing and sampling techniques.

**Localizing techniques:** The localization of suspicious breast lesions is performed under ultrasound, stereotactic and MRI guidance with ultrasound being the most commonly employed.

**Ultrasound:** Presently, ultrasound is being increasingly used for breast interventions which may be diagnostic like percutaneous biopsy of breast lesions/axillary lymphadenopathy and preoperative wire localization or therapeutic like cyst aspirations and abscess drainage. The ultrasound guided core needle biopsy is now the preferred method for performing most breast biopsies with sensitivity of 97.5%.\(^1\)

The advantages of ultrasound-guided biopsy are: short duration of the procedure, less discomfort, better tolerated by the patient, reduced cost, low risk of infection, high yield of accurate samples as the procedure is performed in real time, and lastly since this requires no radiation exposure or intravenous (IV) contrast, it is the localizing technique of choice in pregnant patients.\(^4\,^5\) This localizing technique is cost effective in comparison to biopsies under stereotactic guidance.\(^6\,^7\)

The equipment required for ultrasound-guided breast interventions are high frequency transducer and biopsy device.

Micro-calcifications detected on ultrasound in addition to mammography are more often malignant\(^1\) and can also be sampled using ultrasound, especially under circumstances when stereotactic biopsy is not feasible, e.g. due to limitations of patient positioning or breast size. The contraindications to ultrasound-guided breast biopsy include non-visualization of lesion sonographically, uncooperative patient etc.\(^1\)

For the procedure, the patient is comfortably positioned. Under ultrasound guidance and after usual preparation, the needle is advanced and inserted into the lesion and the required number of samples are obtained, (Figure 1) documenting the needle placement in 2 orthogonal planes.

**Stereotactic guidance:** The number of women diagnosed with ductal carcinoma in situ (DCIS) has increased in the past few years as a result of screening mammography. The commonest mammographic feature of DCIS is micro-calcification, which is conveniently sampled with stereotactic biopsy.\(^1\) The accuracy of stereotactic biopsy instrument is influenced by the sampling technique, i.e. core needle biopsy (CNB) versus vacuum assisted biopsy (VAB) with increasing accuracy ranging from 87% to 97% when larger samples are obtained. False negative rate being 1.2 - 5.4%.\(^2\)

The stereotactic devices were added on to the standard mammography units at its inception with the patient in upright sitting position (Figure 2). Prone biopsy units were introduced in mid-1980's with the patient lying prone for the procedure. This reduced patient movement, improved patient comfort, and eliminated syncope in addition to enabling the biopsy of lesions close to the chest wall due to the gravitational influence.\(^2\)

When micro-calcifications are sampled, the specimen radiography is performed to confirm the presence of representative calcifications. A minimum 3 flecks of calcification should be present in at least 2 cores and, if possible, 5 or more flecks in 3 cores.\(^2\)

For the procedure, initially scout images are achieved to confirm the presence of suspicious calcifications or lesion in the biopsy region, following which stereo images are obtained (Figure 2). The coordinates of the final 3 dimensions are derived by triangulation formulas making sure the presence of adequate stroke margin to avoid damage to the biopsy apparatus.
The breast is cleansed and draped to achieve asepsis; and under local anaesthesia, biopsy is performed after confirming accurate needle placement followed by specimen radiography, if suspicious calcifications were targeted. Radio opaque markers/clips are placed to mark the position of the biopsy site.21

The complication rates of stereotactic biopsy are low and include minimal pain, bruising, formation of hematoma and abscess with 0.1% requiring surgical drainage21 and seeding of tumour cells which does not appear to be of clinical implication.23 Communication with the patients and educating them regarding these complications before the procedure, helps diminish patients’ apprehension and anticipated pain.24

One of the limitations of the stereotactic biopsy is non-applicability in a thin or small breast, as adequate breast thickness is not available while in compression. For patients weighing more than 300 pounds, prone table cannot be used due to weight restrictions from most vendors. Another important limitation is related to the gauge of the biopsy device, i.e. CNB/VAC which may result in the upgrading of DCIS on definitive surgery.25

**Magnetic resonance imaging (MRI):** Due to the proven sensitivity and specificity of contrast enhanced MRI for the detection of breast lesions, especially those not detected on other imaging modalities,26 there is a resultant increase in demand for its utility in obtaining samples for histological evaluation.27 Once a lesion is categorized as BI-RADS 4 or 5 and only seen on MRI, then this warrants re-examination of mammograms and targeted ultrasound, i.e. second look to evaluate for a correlate. If initially obscured findings are visible on re-look mammography or ultrasound, then the MRI detected lesions should be biopsied under ultrasound or mammographic guidance. Up to 57% of lesions detected only on MRI can be sonographically correlated and hence biopsied.28 MRI guided biopsy is recommended only if no correlate detected on second-look ultrasound.

The MRI guided biopsy is technically more complex, costly, and time consuming due to reasons like the availability of MRI compatible biopsy device and patient to be moved in and out of the magnet bore during the procedure. After obtaining localization images, intravenous contrast is administered to locate suspicious lesion. Computerized calculations aid in determining the precise location of the lesion in relation to the grid. A co-axial technique is used for most MRI guided biopsies using MRI compatible needles (i.e. titanium).29

The limitation is the difficulty in localization of small lesions and that of time since the breast parenchyma shows gradual increase in enhancement, which may obscure the suspicious lesion with rapid contrast washout. The general limitations of MRI like claustrophobia and patient body habitus also apply for this procedure.

**Sampling Techniques:**

**Fine needle aspiration (FNA):** The technique is essentially unchanged since its inception in the 1930’s.30

This procedure diagnoses the breast lesions with high accuracy (72 - 94%), although it depends on operator's skill and experience.31-33 It has a miss-rate of 5%,34 requiring a repeat biopsy or further investigation.32

FNA being minimally invasive and cost effective35 was the most widely used technique for breast biopsy before the 1990s, but it had many limitations like operator dependency, non-availability of skilled cytopathologist for rapid interpretation of results at many centres. Thus making rapid evaluation impossible.36 The pathologist can only report benign or malignant cells in the aspirate and cannot comment on in situ or invasive carcinoma or on hormone receptor status.37 The advantages of CNB has led to overall decrease in its utilization.38 FNA is still invaluable for the evaluation of axillary lymph nodes or lesions adjacent to breast implants or lesions near pectoral muscles which are very close to chest wall.33
The technique involves utilization of aseptic technique and under ultrasound guidance 19 to 25-G needles are used. For maximum safety of the underlying structures, the needle is inserted at a shallow angle achieved by selecting the entry site of needle at a distance of 1 - 2 cm from the transducer. In most instances, 2 passes into the lesion at different angles and with moderate suction are sufficient. The radiologist prepares the smears from the aspirate by fixing in alcohol for Papanicolaou and Diff-Quik stain and preliminary diagnosis is provided by the on-site cytopathologist.

Core needle biopsy (CNB): A growing use of CNB technique was witnessed in the 1990’s on account of adequacy of sample and hence accurate differentiation of benign from malignant lesion.

After the identification of the lesion, the overlying skin is marked, cleansed and local anaesthesia is injected. A skin incision is given to allow insertion of core needle device in a spring loaded automated gun. Usually a 14-gauge needle is used. The biopsy gun retrieves small cores of tissue, thus allowing more adequate histological evaluation. Micro-califications require more cores than solid lesions. The needle is directed into the lesion parallel to chest wall in order to avoid damage to chest wall structures. After adequate samples have been taken, pressure is applied at biopsy site. Post-procedure specimen radiography is done, especially if the biopsy was done for suspicious micro-califications seen on mammogram. It is recommended to obtain a minimum of 4 non-fragmented specimens to enhance the yield of the procedure under ultrasound guidance.

A major limitation of CNB is under estimation of disease, such as with atypical ductal hyperplasia (ADH) and ductal carcinoma in situ (DCIS). The miss-rate for core needle biopsy has been reported as 8 - 12% and the under estimation rates of 3.4% to 100% have been reported.

Vacuum-assisted breast biopsy (VABB): The limitations of core biopsies lead to development of VABB in the late 1995. The initial technique has potentially reduced the under-estimation and false negative rates. It is same as CNB and under imaging guidance single insertion of an 8 or 11 gauge needle facilitates faster retrieval of large tissue volumes in contiguous specimens of tissue. VABB with an 11-G needle can be employed for complete resection of lesions that are 1.0 cm or less in diameter and an 8-gauge needle is capable of resecting breast lesions less than 3.0 cm in diameter. It is associated with complications like pain and haemorrhage but offers acceptable cosmetic outcome. The histopathological diagnosis after VABB is known to be reliable and almost equivalent to open surgical biopsy, as quoted in some studies.

Surgical excision following needle localization: The procedure is performed under image guidance, i.e. mammography, ultrasound, and MRI. After the usual preparation, a hook-wire is placed inside a rigid introducer needle and advanced into the suspicious lesion; and once its location within the lesion is confirmed, the needle is taken out and the hook wire is left in place. The hook wire is self-retaining and anchors to the tissue which prevents further advancement, withdrawal, and movement (Figure 3).

Mammographic images are provided to the surgeon and the radiologist describes the lesion location in relation to the wire. Specimen imaging should be obtained to verify the removal of suspicious lesions/califications (Figure 3). A working alliance among an experienced surgeon, radiologist and pathologist is crucial to achieve desired surgical results. Needle localization followed by open surgical biopsy provides an opportunity for rapid and precise excision resulting in minimal tissue damage with low miss-rates (~1.1%) and false negative rates (1.0%). The open surgical biopsy for initial diagnosis is an invasive test, hence it is not recommended by NCCN as an initial procedure.

Radio-opaque metallic marker/clip placement: Radio-opaque metallic markers/clips are placed after image guided biopsy in almost all cases, and mammograms obtained to confirm its position. A single clip should ideally be placed in the center of the lesion. It localizes the tumor bed with radio-opaque markers prior to the institution of chemotherapy and facilitates breast conservation surgery with excision of entire tumor bed even after complete clinical and radiological response (Figure 4).

The marker is also placed after biopsy of non-palpable or too small breast lesion with possibility of complete disappearance after biopsy. Post-deployment clip migration is a common complication associated with this procedure and may be seen immediately after the biopsy or on follow-up mammography. There are 3 categories of clip markers, i.e. commercial metallic markers, which include stainless steel and plain titanium clips, metallic markers covered with bio-absorbable substance, and markers that can be locally assembled by using the Montreal technique.

CONCLUSION

Percutaneous imaging guided biopsy can provide a diagnosis with minimum patient trauma as it is minimally invasive and also saves time. It provides an opportunity to the breast surgeon to discuss with the patient the surgical options, based on the histopathology results. A multi-modality approach, i.e. mammography, ultrasound, and magnetic resonance imaging can be utilized for optimum patient care and accurate diagnosis.

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