An Advocacy for Core Needle Biopsy (CNB) in The Diagnosis of Breast Lesions in Tertiary Health Institutions in Nigeria

[1]T.O. Erameh, [1, 2]B.E. Odigie*
[1]Department of Medical Laboratory Science, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Nigeria
[2]Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, University of Nigeria, Enugu Campus, Nigeria

ABSTRACT
Fine-needle aspiration cytology (FNAC) is the current method of choice for breast lesion diagnosis in Nigeria. The need to reappraise and advocate for the use of Core Needle Biopsy (CNB) in our tertiary health institutions is warranted by its adoption worldwide. A literature search using MEDLINE, Google SCHOLAR, PubMed and Acta cytological journal site are used in the reappraisal of the technique. Detailed evidence-based literature is used to discuss and review the modalities preferable for breast lesion diagnosis. Though, FNAC is easier to perform, but the interpretation requires vast experience, and it is often inconclusive. Specificity of CNB is higher as well as the positive predictive value for suspicious and especially atypical and fibroepithelial lesions. CNB is very sensitive and accurate, especially for lesions which are not definitively benign or malignant, non-palpable and/or calcified. It is, therefore, imperious that CNB is familiarized appropriately in our health institutions in Nigeria, so as to assuage the performance and dominance of FNAC in diagnosing breast lesions.

KEYWORDS: Aspirates, Biopsy, Breast lesion, Core needle and Fine needle.

***Correspondence:** bolaji.odigie@uniben.edu; bolaji.odigie@yahoo.com ;+234-8023345132

INTRODUCTION
Breast lesion is known to be associated with extreme loss of tissue integrity. Therefore, it requires the use of a core needle biopsy (CNB) or fine needle aspiration cytology (FNAC) for a proper diagnosis. There is a need for the establishment of a national breast-screening program by the federal ministry of health in Nigeria so as to increase the detection of small or impalpable breast lesions. However, the ability to achieve an accurate histopathology diagnosis of these lesions is crucial to the screening program. Core needle biopsy (CNB) is referred to a procedure used to withdraw small cylinders (or cores) of tissue from an abnormal area in the breast. Fine needle aspiration cytology (FNAC) is widely used in Nigeria for pathological diagnosis, with its distinct advantages and limitations (1).

Obtaining cell or tissue specimens for pathological diagnosis often requires fine-needle or core-needle biopsy procedures, to obtain samples from patients (2). For example, FNAC is a standard procedure performed on thyroid masses detected by physical examination or ultrasound imaging. However, CNB removes larger tissue cores so as to maintain tissue architecture, and is frequently guided by ultrasound imaging, stereotactic x-ray imaging, or magnetic resonance imaging (2). This technique is used in evaluating breast masses found on X-ray or MR

mammography. Lung nodules found on same chest x-ray images are often biopsied with core needles under x-ray CT guidance in Europe, America, and other advanced countries of the world (2). According to Kooistra et al. (3) the inability to clearly distinguish in situ carcinoma from invasive disease and Willems et al. (1) the high insufficiency rates in FNAC samples in most hospitals, necessitated the calls for CNB advocacy, coupled with the inconclusive nature of most FNAC procedures (1, 3). It has led to the dominance of CNB over FNAC in many advanced countries in the world within the last decade (3).

Also; lack of immediate assessment of the radiologists and clinicians in the western world facilitated the shift from the use of FNAC for a histological diagnosis (CNB) (3). Studies on FNAC and CNB for breast lesion diagnosis are very common. A comparison involving method related issues, diagnostic performance indices, possibilities for additional prognostic and predictive tests, and cost effectiveness are well documented (1, 3, 4). Nonetheless, there paucity of information about comparative advantage of the two procedures in Nigeria, while the available ones are global in focus, leaving the sub-regional aspect abandoned. Therefore, this paper aimed at (i) advocating the use of CNB in tertiary health institutions in Nigeria. (ii) proclaiming the importance of CNB over FNAC for the diagnosis of breast lesions that are lacking in this part of the world (Nigeria).

METHODS

Detailed evidence-based literature is used to discuss the modalities preferable for breast lesion diagnosis in Nigeria. Literature reviews are conducted using the following sources: MEDLINE (January 1990 to March 2015), EMBASE, CAB Direct, Google SCHOLAR, ScienceDirect, PubMed and related journals like the Annals of Internal Medicine. A manual search of references to identify studies and relevant papers to determine necessary articles on CNB and or FNAC are also adopted. Search terms include core needle biopsy, fine needle aspiration cytology, patients safety, cost effectiveness, accuracy, specificity, and time.

DIAGNOSIS USING FNAC

TECHNIQUE: A 21-gauge (green) needle is used most frequently, although, in expert hands, a 23-gauge (blue) needle can yield as much information (1), with less discomfort and bruising (3). Some clinicians opt for a hand-held 10-mL syringe, whereas others prefer a 20-mL syringe used with a syringe holder. Syringe holders allow a vacuum to maintain easily, but can make control of the needle tip less precise (4). Disinfection of the skin should be with an alcohol wipe and the needle passed through the lesion for an amount of time while maintaining suction and steadying the breast tissue with the other hand (4). The needle must be right-angled tangentially to the chest wall. Continue sampling until aspirate is observed at the bottom of the plastic portion of the needle. After that, transfer the aspirate to slides. Spread the aspirate thin enough to visualize individual cells (4). The slides may be air-dried or fixed according to the preference of the local laboratory. Though, the success of FNAC depends heavily on accurate localization and expertise of the cytologist (4).

Figure 1: A physician's hands are performing a needle biopsy to determine the nature of a lump either a fluid-filled cyst or solid tumor. Source: Bartlett, L. (5).

The skin above the area for biopsy is swabbed with an antiseptic solution and draped with sterile surgical towels. The skin, underlying fat, and muscle may be numbed with a local anesthetic, although this is often not necessary to ignorant masses. A special needle of very fine diameter passed into the mass, after locating the mass for biopsy, by x-rays or palpation. The needle may be inserted and withdrawn several times. There are many reasons for this: (i) one needle may serve as a guide, with the other needles placed along it to achieve a more precise position. (ii) Sometimes, several passes may be needed to obtain enough cells for the intricate tests that the cytopathologists perform. After the needles are into the mass, cells are withdrawn by aspiration with a syringe and spread on a glass slide (5).

Figure 2: Materials used for FNAC procedures (Source: Histopathology Laboratory, Department of Medical Laboratory Science, University of Benin, Nigeria).

DIAGNOSIS USING CNB

TECHNIQUES: Core needle biopsy uses a hollow-core needle, ranging in size from 11 to 16 gauges, to remove one or more pieces of breast tissue (4). The operator either aims the needle directly to the area of a palpable lesion (freehand biopsy) or uses an imaging technique to localize the target lesion (6). The imaging techniques include stereotactic radiography, ultrasound, and magnetic resonance imaging (2, 6). Methods to extract the biopsy specimen include automated gun and vacuum assistance. There is no consensus on which of these techniques is preferable for attaining the highest accuracy and lowest rate of harm for CNB (5).

Wei-Cheng et al. (2) stated that the standard vacuum assisted CNB handpiece mechanically operates via pneumatic pressure and vacuum (Figure 4). When attached to the system console and armed, pneumatic motor drives the cutting cannula forward to cover the biopsy channel. Moreover, it produces a smooth outer needle barrel before insertion into tissues. As soon as the needle tip is in a position, at the tissue site for biopsy (typically guided by an external imaging by stereotactic x-ray or ultrasound imaging). A foot pedal switch initiates a vacuum to draw the cutting cannula back, thereby exposing the biopsy channel, and allowing a small region of tissue to be drawn by vacuum into the biopsy channel region. The biopsy extraction modified in sequence, by putting a manual break between the opening of the cutting cannula with the applied vacuum and the closing of the cutting cannula. Following an activation switch, the outer cutting cannula closes with a rotating/spinning motion and shears off the tissue (specimen). A second manual break is also included in the process before the tissue is subsequently drawn back into a tissue collection trap by the applied vacuum; where it can be retrieved later and placed in formalin for tissue processing histologically (2).

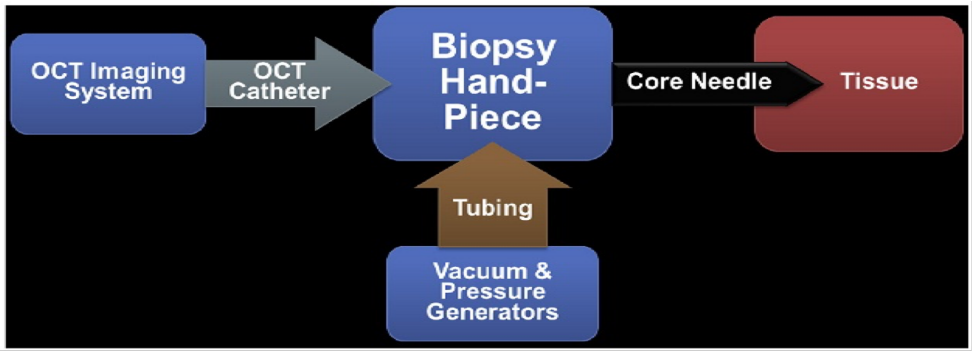

Figure 3: Representation of a 3-D optical coherence tomography OCT-guided vacuum-assisted core needle biopsy outline (2).

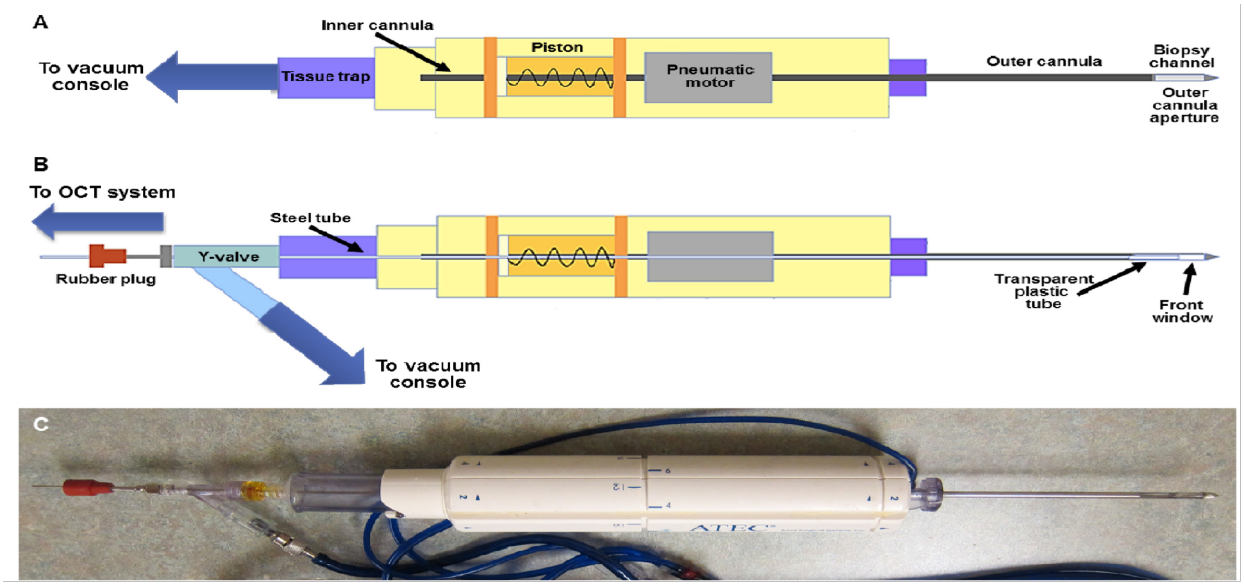

Figure 4: Schematics and photograph of the modified vacuum-assisted core needle biopsy handpiece for 3-D Optical coherence tomography OCT-guided procedures (2).

The working procedure is depicted in Figure 4, starting with the original hanpiece and ending with an integrated system.

(A)\Original handpiece components. The unit mechanically opens and closes by the action of pressure and a vacuum. The equipment makes use of a cutting cannula and a vacuum. They both draw tissues into the biopsy channel and to bring biopsied tissue back into a tissue trap for retrieval.

(B) Modified handpiece that includes the addition of a transparent front window for real-time OCT guidance and the addition of a long steel/plastic tube to allow the insertion of the OCT catheter. While, a Y-valve allows both the linear access for the OCT catheter and the vacuum/pressure tube connection.

(C) An integrated system (modified version). The integrated system is designed to leverage the advantages of commercial systems, yet a new design and concept for a core needle biopsy handpiece can be optically-guided in real-time by OCT. The expected operation and use of the 3-D OCT image-guided needle biopsy system have been summarized (2).

SUMMARY REVIEW OF LITERATURES

Due to the FNAC operational limits, CNB was introduced (6) to complement the assessment of calcification in a CNB, which is much more sophisticated than in FNAC. As a result, calcification can be seen in the tissue sections within the lesion while using CNB techniques. CNB technique enables a comparison of the pattern of calcification in the core needle with that observed on the x-ray. In UK breast screening program, recommendation on the use of CNB for the assessment of calcification has been adopted nationwide (1). In comparison, CNB is of a larger caliber than FNAC and are mounted onto a spring-loaded device that allows small cylinders of tissue to be cut and collected within the notch of the needle. Technically, the best CNB samples are obtained by using 14-gauge needles (4). The optimal number of passes required

varies according to the mammographic appearances of the lesions being sampled with fewer passes needed for solid lesions compared with microcalcifications (6). Several investigators have shown that a minimum of 5-6 passes is required for sampling microcalcifications to minimize sampling error (6).

CNB is an accurate method for the diagnosis of high-risk lesions such as atypical ductal hyperplasia, lobular carcinoma in situ, atypical papillomatosis, and columnar cell lesions (7). However, recognition of these lesions is necessary as they can mimic, and often associated with further advanced lesions (7), and indicate an increased risk of invasive cancer in follow-up cases (8). Increase in the use of vacuum-assisted biopsies and the complete biopsy procedures by which a semi-invasive mini-resection can perform has raised the question of whether an open surgical excision is always warranted for breast lesions (9). Sie et al. (9) further confirmed that an entire biopsy procedure differs from core devices in that it removes one spheroid specimen rather than smaller cylindrical cores. Also, it can perform safely and accurately and tends to have fewer underestimations of (ductal carcinoma in situ; DCIS) compared with CNB (9, 10).

Dahlstrom et al. (11) suggested that as for any diagnostic procedure, a high negative predictive value is important to minimize under treatment; while a high positive predictive value reduces the risk of overtreatment. Therefore, high sensitivity and specificity are crucial as they are the key determinants of both negative and positive predictive values. The overall sensitivity and specificity of FNAC and CNB in the classification of breast lesions depend on variables intrinsic to the techniques and also related to the radiological/clinical and histological features.Furthermore, the survey included only definitive benign and malignant lesions, ignoring the atypical and different categories and thus gives an account for up to 20% of breast lesions in the joint pathology. Studies comparing the exactitude of FNAC and CNB within the same patient populace are relatively scarce. According to Dahlstrom et al. (11) CNB has both higher sensitivity and specificity than FNAC in diagnosing benign and malignant lesions. Sensitivity, specificity, positive and negative predictive values for FNAC have been reported and therefore, corroborates the report from one of the highest studies ever (12). From the ongoing; CNB achieved higher performance indices when compared with FNAC across different parameters.

Kwok et al. (13) reported that the increased use of neoadjuvant therapy has prompted the need for reliable preoperative assessment of histological and immunohistochemical prognostic and predictive features. Hence, the grading of malignant breast tumors is an independent prognostic factor. Cytological grading of FNAC correlates quite well with histological grading of a CNB while morphometric indices of FNAC have been shown to be very reliable (14). Again, FNAC cannot reliably discriminate between a ductal carcinoma in-situ (DCIS) and an invasive carcinoma, while the value of the cytological grading of a malignant FNAC remains relatively unclear. Therefore, the correlation in grading between CNB and excision specimens on H&E slides is limited (14). Sometimes with an underestimation on biopsy, but better concordance are obtainable by additional immunohistochemical markers. There is no overall agreement on cut-off values (13). However, despite some centers assessing histological grade on immunohistochemical / H&E staining, it is still not recommended, neither on FNAC nor CNB (1). Therefore, in the (neo) adjuvant setting, assessment of ER, progesterone receptor (PR) and HER2

status is crucial (15). Receptor status is determined routinely on (preoperative) biopsies in many pathology laboratories. It is acceptable that ER, PR, and HER2 are assessed on CNB but not on FNAC (15). The same holds true for proliferation assessment, which is a part of grading and is prognostically paramount (16). Looking at the introduction of small molecule inhibitors in the past decade, molecular profiling of (breast) tumour samples is increasingly important (15). In respect to the above, it becomes striking to note that CNB contains RNA/DNA in a significant amount and of sufficient quality for molecular testing (e.g., arrays). Whereas, this can be a problem in the case of FNAC, which typically yields limited samples during aspiration (1).

Frankel et al. (17) conducted a cross-sectional, retrospective and descriptive study. The survey aimed at examining the accuracy of FNAC and of the CNB in diagnosing breast lumps and breast cancers; base on the review of medical records. FNAC and CNB are carried out sequentially according to the routine of the Mastology Service in Brazil, using both percutaneous procedures. Participation involves women aged 18-years or more with changes in the clinical and/or image examination of the breast or a family history of breast and/or ovarian cancer (17). The percentages of the agreement are Cohen's Kappa coefficient, sensitivity, specificity, positive and negative predictive values and the accuracy of FNAC and CNB forms the basis for compares. The research also considers the surgical biopsy performed as the gold standard. The results show that the diagnostic accuracy for CNB is higher (97.5%) than of FNAC (77.5%). Therefore, Frankel et al. (17) concludes that CNB shows a greater rate of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy than FNAC for palpable and non-palpable breast lumps which is of great interest in the present review (Table 1).

Table I: Advantages and limitations of both techniques.

	FNAC	CNB
Procedural (dis)advantages		
Accessibility of deep sites	Yes	No
Level of experience required	High	Average
Success rate	60-75%	99%
Complication rate	Very low	Low
Diagnostic performance dependent on clinical/radiological features		
Non-palpable tumours	Low	High
Palpable lesions	High	High
Size <10 mm or >40 mm	Low	High
Diagnostic Performance Dependent on Histological Features		
Distinction between in-situ and invasive cancer	No	Yes
Diagnosis of pre-invasive lesions (CCL, ADH)	Low	High
Diagnosis of papillary lesions	Low	Moderate
Distinction between fibroadenoma and phyllodes tumour	Moderate	High
Assessment of Prognostic and Predictive Biomarkers		
Grading	Low	Moderate
ER/PR assessment	Low	High
HER2 assessment	Low	High
Proliferation assessment	Moderate	High
DNA/RNA isolation for molecular test	Low	High
Cost/speed effectiveness		
Speed	High	Moderate
Costs	Very low	Low

The tabular representations above are further summarized and have been reported Willems et al. (1).

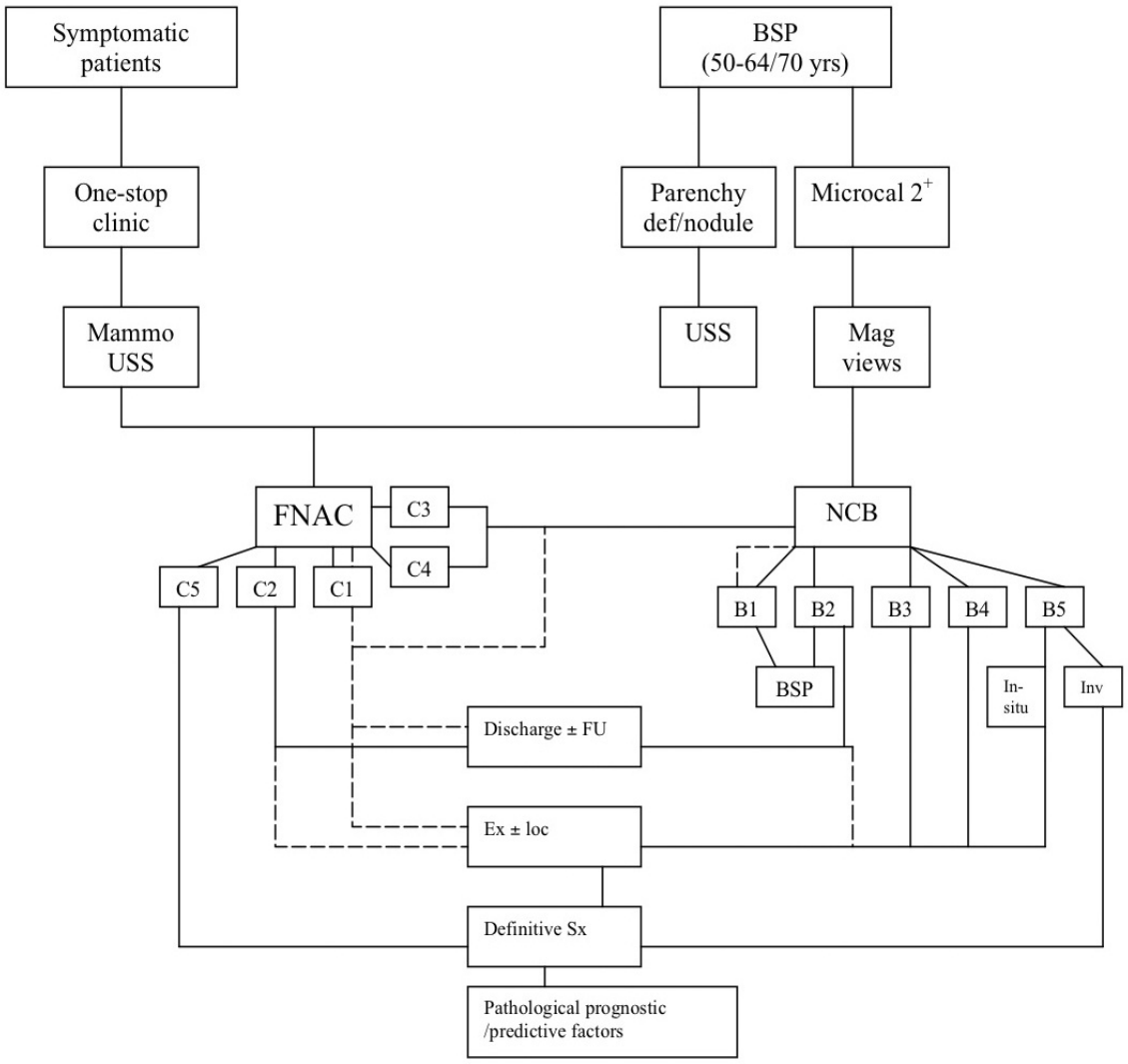

Figure 5: Summary of the algorithm of breast lesion (18).
Key: Sx – surgery • Inv – invasive • Ex – excision • FU – follow-up • Loc – localization • BSP – breast screening programme • Microcal 2+ – microcalcification • Mag – magnified • USS – ultrasound scan • C1 – inadequate material for diagnosis • C2 – benign lesions e.g. cyst, fibroadenoma, abscess, fat necrosis, fibrocystic change • C3 – atypical features but probably benign • C4 – atypical features but suspicious of malignancy • C5 – unequivocal malignant cells • B1 – normal tissue or inadequate material (no microcalcification present) • B2 – benign lesions e.g. fibroadenoma, sclerosing adenosis • B3 – radial scars, atypical epithelial hyperplasia, papillary lesions • B4 – epithelial proliferations which are suspicious but not diagnostic of malignancy due to either quantitative or qualitative reasons • B5 – (a) in-situ carcinoma (b) invasive disease.

We have attempted to demonstrate the size and location of some lesions may preclude the use of CNB techniques in this review. Small lesions either situated deeply near the chest wall or superficially or in the nipple/subareolar region may be more amenable to FNAC than core biopsy while both techniques (FNAC and CNB) are operator dependent. In buttress of the ongoing discuss, reports have it that centers with the lowest inadequate rates for FNAC have dedicated skilled

operators, in the likes of the clinicians, radiologists and/ or cytologists (3, 19). Serious complications are rare for both procedures while the crucial element is the feedback to the aspirator as to how good or poor the sample is, and how best to prepare the smears. CNB causes more traumas than FNAC and haematoma formation is more likely to occur (19, 20). Again, pneumothorax can also occur in both if the needle pushes in too deeply and is more liable to occur in women with small breasts (20).

It is imperative that CNB is introduced appropriately in Nigeria. It will help to alleviate the one stop FNAC performance and dominance in our tertiary health institutions nationwide. Therefore, we at this moment recommend the use of CNB to the generality of the tertiary health institutions in Nigeria. However, there is still a significant role for FNAC in providing a speedy and accurate diagnosis of not only breast cancers but also the majority of benign lesions mimicking malignancy.

REFERENCES

1. Willems, S.M., van Deurzen, C.H.M. and van Diest, P.J. (2012). Diagnosis of breast lesions: Fine-needle Aspiration Cytology or core needle biopsy? A review. J Clin Pathol. 65:287-292.
2. Wei-Cheng, K., Jongsik, K., Nathan, D.S., Eric, J.C., Darold, R.S. (Jr) and Boppart, S.A. (2012). Real-time three-dimensional optical coherence tomography image-guided core-needle biopsy system. Biomedical Optics Express, 3(6): 1149-1161.
3. Kooistra, B., Wauters, C., Strobbe, L. and Wobbes, T. (2010). Preoperative cytological and histological diagnosis of breast lesions: a critical review. Eur J Surg Oncol. 36(10):934-940.
4. Hemant, S. (2013). Breast Stereotactic Core Biopsy/Fine Needle Aspiration. http://emedicine.medscape.com/article/1845123-overview#showall Retrieved: 12th July 2015.
5. Bartlett, L. (2015). Fine Needle Aspiration Cytology. http://en.wikipedia.org/wiki/fine-needle_aspiration. Retrieved: 19th August 2015.
6. Rich, P.M., Michell, M.J., Humphreys, S., Howes, G.P. and Nunnerley, H.B. (1999). Stereotactic 14G core biopsy of non-palpable breast cancer: what is the relationship between the number of core samples taken and the sensitivity for detection of malignancy? Clin Radiol. 54(6):384-9.
7. Dillon, M.F., Mcdermott, E.W., Hill, A.D., O'Doherty, A., O'Higgins, N. and Quinn, C.M. (2007). Predictive value of breast lesions of "uncertain malignant potential" and "suspicious for malignancy" determined by core needle biopsy. Ann Surg Oncol. 14:704-711.
8. Houssami, N., Ciatto, S., Ellis, I. and Ambrogetti, D. (2007). Underestimation of malignancy of breast core needle biopsy: concepts and precise overall and category-specific estimates. Cancer, 109:487-495.
9. Sie, A., Bryan, D.C., Gaines, V., Killebrew, L.K., Kim, C.H. and Morrison, C.C. et al. (2006). Multicenter evaluation of the breast lesion excision system, a percutaneous, vacuum-assisted, intact-specimen breast biopsy device. Cancer, 107:945-949.

10. Killebrew, L.K. and Oneson, R.H. (2006). Comparison of the diagnostic accuracy of a vacuum-assisted percutaneous intact specimen sampling device to a vacuum-assisted core needle sampling device for breast biopsy: initial experience. Breast J. 12:302-308.
11. Dahlstrom, J.E., Sutton, S. and Jain, S. (1996). Histological precision of stereotactic core biopsy in the diagnosis of malignant and premalignant breast lesions. Histopathology, 28:537-541.
12. Boerner, S., Fornage, B.D., Singletary, E. and Sneige, N. (1999). Ultrasound-guided fine-needle aspiration (FNA) of non-palpable breast lesions: a review of 1885 FNA cases using the National Cancer Institute-supported recommendations on the uniform approach to breast FNA. Cancer, 87:19-24.
13. Kwok, T.C., Rakha, E.A., Lee, A.H.S., Grainge, M., Green, A.R. and Ellis, I.O., et al. (2010). Histological grading of breast cancer on core needle biopsy: the role of immune-histochemical assessment of proliferation. Histopathology, 57:212-219.
14. cKee, G., Nicholson, A., D'Arcy, J., Jackson, P.A., Cook, M.G. and Kissin, M.W. (1999). Prognostic value of cytological grading of fine-needle aspirates from breast carcinomas. Lancet, 343:947-949.
15. Rakha, E.A. and Ellis, I.O. (2007). An overview of assessment of prognostic and predictive factors in breast cancer needle core biopsy specimens. J Clin Pathol. 60: 1300-1306.
16. van Diest, P.J., van Der, W.E. and Baak, J.P. (2004). Prognostic value of proliferation in invasive breast cancer: a review. J Clin Pathol. 57:675-681.
17. Frankel, P.P., Esteves, V.F., Thuler, L.C. and Vieira, R.J. (2011). Diagnostic accuracy of the fine needle aspiration cytology and core needle biopsy as a diagnostic method for breast lesions. Rev Bras Ginecol Obstet. 33(3):139-143.
18. Tong, F.L. (2007). The Role of Fine Needle Aspiration Cytology and Needle Core Biopsy in the Diagnosis and Management of Breast Cancer. Breast J. 1(6): 8-12
19. Dray, M., Mayall, F. and Darlington, A. (2000). Improved FNA cytology results with near-patient diagnosis service for breast lesions. J. Cytopathology, 11:32-37.
20. Dennison, G., Anand, R., Makar, S.H. and Pain, J.A. (2003). A prospective study of the use of FNAC and Core Needle Biopsy in the Diagnosis of breast cancer. Breast J. 9:491-493.