

# Accuracy of Triple Assessment in Diagnosis of Breast Cancer in Women More than 40 Years of Age

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## Abstract

**Background:** To determine the diagnostic accuracy of triple assessment in diagnosis of breast cancer in women more than 40 years keeping histopathology as gold standard.

**Methods:** In this cross sectional study, women with a breast lump or change in the texture of breast with an age range of 40-70 years were included. Detailed physical and breast examination and mammography followed by FNAC were performed. Mammography of breast consists of two standard views, i.e., lateral oblique (MLO) and a craniocaudal view (CC). Sensitivity, specificity, positive predictive value and negative predictive value and accuracy of triple assessment were calculated.

**Results:** There were 49.5% patients who were labelled as malignant. Mammogram showed 69.7% as malignant. On FNAC 64.8% were labelled as malignant. Results of triple assessment showed 72.4% as malignant. Histopathology results showed 73.3% as malignant, thus showing that in overall study population 71.5% were true positives, 25.7% were true negatives, 1% were false positives and 2.0% were false negatives. The study findings revealed that sensitivity, specificity, PPV, NPV and accuracy of triple assessment in diagnosing breast cancer is 97.4%, 96.4%, 98.7%, 93.1% and 97.2% respectively.

**Conclusion:** Triple assessment allows detection of malignancy in palpable breast lumps with acceptable sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

**Key Words:** Breast cancer, Triple assessment, Mammography, Fine needle aspiration cytology

## Introduction

Breast malignancy is one of the major health issues affecting women all over the globe. Globally, it is the second most common malignancy.<sup>1</sup> In Pakistan; it is the commonest malignancy in women with a prevalence of 34.6%.<sup>2</sup> A prompt and accurate diagnosis followed by timely intervention can be

lifesaving in managing patients with breast malignancy.<sup>1</sup> There are various non-invasive imaging modalities for diagnosing breast lesions e.g. ultrasonography, mammography, MRI, Doppler scanning, contrast enhanced ultrasound, etc but alone none of these is reliable.<sup>1</sup> Their cost and availability also limit their use. There are three pathological procedures for diagnosing breast cancer, i.e., fine needle aspiration cytology, core needle biopsy and surgical biopsy.<sup>3</sup> FNAC has an advantage over core needle biopsy as it is more cost effective and both have comparable predictive values.<sup>3</sup> FNAC is minimally invasive causing pain similar to prick for blood sampling.

Open/surgical biopsy is regarded as a gold standard in diagnosing breast cancer. It is invasive, time consuming, associated with significant patient anxiety and exposes patient to more than one surgical procedure.<sup>1</sup> Open biopsy is unlikely to be an initial diagnostic approach, unless percutaneous or image-guided biopsy is not possible. It may become necessary to further investigate discordant findings.<sup>4-6</sup> Major disadvantages of FNAC is its inability to distinguish between CIS (carcinoma in situ) and invasive malignancy along with a high rate of insufficient samples.<sup>7</sup> Hence it is necessary that a diagnostic tool be employed for pre-operative diagnosis of breast cancer which is least invasive, cost effective and readily available with accuracy comparable to conventional surgical biopsy.<sup>1</sup>

A combination of three modalities called as triple assessment is currently employed in diagnosing all the breast lesions. It includes physical examination, radiological imaging (mammography) and pathology (FNAC).<sup>8,9</sup> It is a simple and affordable test with modalities used being non-invasive or minimally invasive. It is performed on OPD basis and requires no hospitalization.<sup>8</sup> Furthermore, it is a readily available and reliable diagnostic tool with a sensitivity of 93% and specificity of 95.2%.<sup>10</sup>

## Patients and Methods

In this cross sectional study, conducted in Department

of Radiology, RMC and Allied Hospitals, Rawalpindi, in collaboration with Pathology department of the same hospital, women with a breast lump or change in the texture of breast with an age range of 40-70 years were included. Women with breast abscess, anti-bioma, mastitis, infected cyst, mammary fistula and diagnosed cases of malignancy were excluded. Sample size (n=105) was calculated by using sensitivity specificity sample size calculator taking sensitivity 93%, absolute precision 7%, specificity 95.2%, absolute precision 4.8%, expected prevalence 34.6% and confidence level as 95%.<sup>10</sup> Mammography of breast consists of two standard views, i.e., lateral oblique (MLO) and a craniocaudal view (CC). The lateral oblique view was done by angulating the tube at 45 degrees to the horizontal. Depending on the patients build tube angulations was changed by 30 to 60 degrees to the horizontal. For adequate visualization, breast was lifted and compression was applied in order to spread the breast tissue evenly between the film holder and compression plates. No skin folds were superimposed on the breast. The craniocaudal view (CC) demonstrated subareolar, medial and lateral portions of breast. All the patients were sent to pathology department for FNAC. The results of physical examination, mammography and FNAC were classified as benign and malignant and compared to histopathological report of biopsies from specimens obtained at time of definitive surgery. A 2x2 table was used to calculate sensitivity, specificity, PPV, NPV and accuracy of triple assessment for diagnosing breast cancer using the findings of histopathology as gold standard.

**Table 1: Two × Two Table**

Triple assessment (Physical exam, Mammography, FNAC)	Histopathology		Total
	Malignant	Benign	
Malignant	True Positive (a)	True Negative (b)	a + b
Benign	False Negative (c)	False Positive (d)	c + d
Total	a + c	b + d	a + b + c + d

### Results

Mean age of patients (n=105) was 49.9 years ± 6.7, with a range of 41 years to 69 years. On physical examination 49.5% of patients were labeled as malignant. Mammogram results showed there were

65.7% patients who were labeled as malignant. FNAC results showed there were 64.8% patients who were labeled as malignant (Table 2). Results of triple assessment showed that there were 72.4% of patients who were labeled as malignant. Histopathology results showed that 73.3% of patients were malignant (Table 3). 2 × 2 tables showed the numbers of cases who were malignant on triple assessment scan and were also malignant on Histopathology (true positives), who were malignant on triple assessment scan positive but were benign on histopathology (false positives), who were benign on triple assessment scan but were malignant on histopathology (false negatives) and who were benign on triple assessment scan and were also benign on histopathology (true negatives). Our study results showed that in overall study population 71.5% were true positives, 25.7% were true negatives, 1% were false positives and 2.0% were false negatives (Table 4). Results depicted that sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of triple assessment in diagnosing breast cancer is 97.4%, 96.4%, 98.7%, 93.1% and 97.2% respectively.

**Table 2: Results of Physical Examination, Mammogram and FNAC**

Modality	Benign (%)	Malignant (%)
Physical examination	50.5	49.5
Mammography	34.3	65.7
FNAC	64.8	35.2

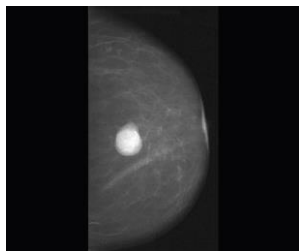
**Table 3: Results of Triple Assessment & Histopathology**

Modality	Benign (%)	Malignant (%)
Triple assessment	27.6	72.4
Histopathology	26.7	73.3

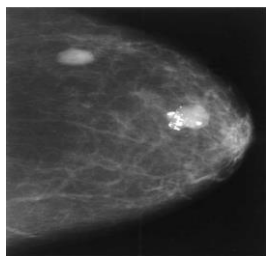
**Table 4: Cross-tabulation of Triple assessment and histopathology results**

Triple assessment	Histopathology		total
	Malignant	Benign	
Malignant	75 (True positives)	1 (False positives)	76
Benign	2 (False negatives)	27 (True Negatives)	29
Total	77	28	105

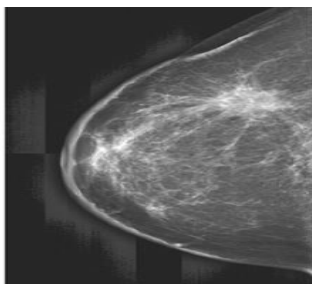
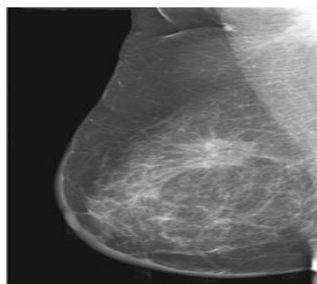
Sensitivity: 97.4%, Specificity: 96.4%, Positive Predictive Value: 98.7%, Negative Predictive Value: 93.1%, Over all Accuracy: 97.2%



**Figure 1:**Craniocaudal view of breast showing well defined rounded radio-opacity with coarse calcification suggesting a benign lesion



**Figure 2:**Craniocaudal view of breast showing well circumscribed lobulated mass with coarse calcification typical of fibroadenoma



**Figure 3:**Mediolateral oblique and craniocaudal view of breast shows an ill defined, irregular spiculated mass in upper outer quadrant of breast causing architectural distortion

## Discussion

A definite diagnosis of a woman presenting with breast lump is highly crucial for the surgeon in order to decide final treatment thus saving the female from unnecessary burden of psychosocial, physical and emotional trauma.<sup>11, 12</sup> Although majority of breast lumps in women of 20-50 years of age group are benign, but still it is very important to exclude malignancy.<sup>13</sup> A combination of three tests/ modalities is devised to approach women presenting with breast problems. It is called as triple assessment or triple test and includes clinical examination, radiological imaging (mammography) and pathology. These modalities when employed alone give variable results but together they have sensitivity of 99%.<sup>14</sup> If any one out of three components is positive, then triple assessment is also considered positive but all the three components should be negative for triple assessment to be negative. Regarding pathology, FNAC is taken as a component of triple assessment rather than core needle biopsy since it is minimally invasive and cost effective, moreover in settings where a trained cytopathologist is available it has predictive value comparable to core needle biopsy.<sup>3,14</sup> Breast of young

patients are very sensitive to radiation but if there is high suspicion of malignancy along with a strong family history, mammography can be done.<sup>15</sup> On mammography most of breast cancers appear as spiculated masses, others being masses with irregular margins, oval, round lobulated lesions, well defined masses or areas of architectural distortion.<sup>16</sup>

Ghimire B. et al showed that triple assessment had an accuracy of 98% with sensitivity of 100% and specificity being 95.2%. Morris KT, et al also evaluated the accuracy of triple assessment by devising a modified triple assessment score.<sup>18</sup> 113 patients were included in the study. All the benign lesions were given a score of 1, suspicious lesions 2, and malignant lesions 3 on each modality. Sum of these 3 score gave the final score. Results were then correlated with biopsy. It was found that triple assessment had an accuracy of 100%. They further suggested that lesions having less than four score are benign, those with five score should undergo biopsy and those with six and higher score should undergo definitive treatment. This approach thus avoided unnecessary biopsies.

Morris A, et al also evaluated accuracy of triple assessment in evaluating breast lumps to avoid unnecessary biopsies.<sup>19</sup> The study included 261 female patients. All the benign lesions were given a score of 1, suspicious lesions 2, and malignant lesions 3 on each modality. Sum of these 3 score gave the final score. Results were then correlated with biopsy. It was found that triple assessment had an accuracy of 100%.

Mansoor I, et al conducted a similar study on non-diagnostic FNACs of palpable breast masses and compared the results with the available literature.<sup>20</sup> All malignant cases had scores of above 6 except one that scored 5. Two benign cases had scores of 1 and 3. They concluded that triple assessment can be used to achieve diagnostic accuracy for breast FNACs and management of breast lumps.

Kachewar SS, et al conducted a prospective study to calculate accuracy of triple assessment in diagnosing breast lumps.<sup>21</sup> Triple assessment was done in 200 cases out of 225 FNACs. Out of 124 cases, 123 had concordant triple assessment score and 3 discordant. Of 62 malignant cases on FNAC, only one had discordant triple assessment score. Biopsy was done only in seventy patients, out of which forty two were malignant and twenty eight benign. This gave triple assessment a sensitivity of 97.44% and specificity of 100%.

Kaufman Z, et al also conducted a similar study determining accuracy of triple assessment.<sup>22</sup> The study included 234 patients which were labelled as benign,

suspicious and malignant on triple assessment followed by histopathology. The sensitivity and specificity of the each test was less than triple assessment which turned out to be 100% and 57% respectively. They concluded that breast lesions can be diagnosed with accuracy by triple assessment, thus obviating the need for invasive procedure (open biopsy).

Ahmed I, et al also determined the accuracy of triple assessment in characterizing breast lesions.<sup>23</sup> They scored results of triple assessment as concordant and non-concordant. If all elements were either benign or malignant then findings were considered as concordant and non-concordant if the elements were neither all malignant nor benign. The study concluded that triple assessment is less time consuming, minimally invasive and cheap, however, it should only be employed in settings where good imaging modalities and trained staff are available. A study by Salami N, et al concluded that triple assessment can be used with high diagnostic accuracy to evaluate breast lumps.<sup>24</sup> Kharkwal S, et al conducted a prospective study to calculate accuracy of triple assessment in diagnosing breast cancer.<sup>25</sup> It was found that all these modalities had less accuracy when employed alone but in combination triple assessment gave 100% sensitivity and specificity.

### **Conclusion**

Triple assessment allows detection of malignancy in palpable breast lumps with sensitivity, specificity, PPV, NPV and accuracy of 97.4%, 96.4%, 98.7%, 93.1% and 97.2% respectively.

### **References**

1. Ghimire B, Khan MI, Bibhusal T, Singh Y. Accuracy of Triple Test Score in the diagnosis of palpable breast lump. *J Nepal Med Assoc.* 2008;47:189-92.
2. Rashid MU, Zaidi A, Torres D, Sultan F. Prevalence of BRCA1 and BRCA2 mutations in Pakistani breast and ovarian cancer patient. *Int J Cancer.* 2006;119:2832-39.
3. Nagar S, Iacco A, Riggs T, Kestenberg W. Analysis of fine needle aspiration versus core needle biopsy in palpable breast lesions. *Am J Surg.* 2012;204:193-98.
4. Stomper PC, Winston JS, Proulx GM. Mammographic detection and staging of ductal carcinoma in situ: Mammographic-pathologic correlation. *Semin Breast Dis.* 2000;3:1-4.
5. Silverstein MJ, Recht A, Lagios MD. Consensus conference III. Image-detected breast cancer: state-of-the-art diagnosis and treatment. *J Am Coll Surg.* 2009;209:504-08.
6. Gutwein LG, Ang DN, Liu H. Utilization of minimally invasive breast biopsy for the evaluation of suspicious breast lesions. *Am J Surg.* 2011;202:127-30.
7. Pisano ED, Fajardo LL, Caudry DJ. Fine-needle aspiration biopsy of nonpalpable breast lesions. *Radiology.* 2001;219:785-88.
8. Jan M, Mattoo JA, Salroo NA, Ahangar S. Triple assessment in the diagnosis of breast cancer in Kashmir. *Indian J Surg.* 2010;72:97-103.
9. Clarke D, Sudhakaran N, Gateley CA. Replace fine needle aspiration cytology with automated core biopsy in the triple assessment of breast cancer. *Ann R Coll Surg Engl.* 2001;83:110-13.
10. KristoffersenWiberg M, Aspelin P, Perbeck L. Value of MR imaging in clinical evaluation of breast lesions. *ActaRadiol.* 2002;43:275-81.
11. Klein S. Evaluation of palpable breast masses. *Am Fam Physician.* 2005;71:1731-33.
12. Schoonjans JM, Brem RF. Fourteen-gauge ultrasonographically guided large-core needle biopsy of breast masses. *J Ultrasound Med.* 2001;20:967-71.
13. Elmore JG, Barton MB, Moceri VM. Ten-year risk of false positive screening mammograms and clinical breast examinations. *N Engl J Med.* 1998;338:1089-93.
14. Kocjan G. Needle aspiration cytology of the breast: current perspective on the role in diagnosis and management. *Acta Med Croatica.* 2008;62:391-401.
15. Wang LE, Han CH, Xiong P. Gamma-ray-induced mutagen sensitivity and risk of sporadic breast cancer in young women. *Breast Cancer Res Treat.* 2012;132:1147-50.
16. Stomper PC. Breast imaging. In: *Atlas of Breast Cancer.* Philadelphia: Mosby; 2000;54-62.
17. Jan M, Mattoo JA, Salroo NA, Ahangar S. Triple assessment in the diagnosis of breast cancer in Kashmir. *Indian J Surg.* 2010;72:97-103.
18. Morris KT, Vetto JT, Petty JK, Lum SS. A new score for the evaluation of palpable breast masses in women under age 40. *Am J Surg.* 2002;184:346-49.
19. Morris A, Pommier RF, Schmidt WA, Shih RL. Accurate evaluation of palpable breast masses by the triple test score. *Arch Surg.* 1998;133:930-34.
20. Mansoor I, Zahrani I. Analysis of inconclusive breast FNA by triple test. *J Pak Med Assoc.* 2002;52:25-29.
21. Kachewar SS, Dongre SD. Role of triple test score in the evaluation of palpable breast lump. *Indian J Med Paediatr Oncol.* 2015;36:123-27.
22. Kaufman Z, Shpitz B, Shapiro M. Triple approach in the diagnosis of dominant breast masses: combined physical examination, mammography, and fine-needle aspiration. *J Surg Oncol.* 1994;56:254-57.
23. Ahmed I, Nazir R, Chaudhary MY, Kundi S. Triple assessment of breast lump. *J Coll Physicians Surg Pak.* 2007;17:535-38.
24. Salami N, Hirschowitz SL, Nieberg RK. Triple test approach to inadequate fine needle aspiration biopsies of palpable breast lesions. *Acta Cytol.* 1999;43:339-43.
25. Kharkwal S, Sameer, Mukherjee A. Triple test in carcinoma breast. *J Clin Diagn Res.* 2014;8:NC09-11..