

# DIAGNOSTIC VALUE OF FINE NEEDLE ASPIRATION CYTOLOGY FOR BREAST TUMORS

Josip Mišković<sup>1</sup>, Andrea Zorić<sup>2</sup>, Helena Radić Mišković<sup>3</sup> and Violeta Šoljić<sup>4,5</sup>

<sup>1</sup>Clinical Department of Surgery, <sup>2</sup>Clinical Department of Internal Medicine, <sup>3</sup>Clinical Department of Gynecology and Obstetrics, <sup>4</sup>Clinical Department of Pathology, Cytology and Forensic Medicine, Mostar University Hospital; <sup>5</sup>University Department of Histology and Embryology, School of Medicine, University of Mostar, Mostar, Bosnia and Herzegovina

**SUMMARY** – Breast cancer is the most frequently diagnosed cancer and the leading cause of death from cancer in women. The accuracy of diagnosis can be increased with a combination of clinical examination, imaging diagnostics, and fine needle aspiration cytology (FNAC) or core needle biopsy, also known as triple test. The aim of the study was to evaluate the sensitivity and specificity of FNAC in the diagnosis of breast tumors in our institution by correlating it with histopathology findings. We assessed the accuracy of 124 FNAC findings by comparing cytological diagnosis of breast masses with the diagnoses from histopathology reports obtained by surgery. Statistical analysis showed 95.1% accuracy, 97.7% sensitivity, 89.1% specificity, 95.5% positive predictive value and 94.2% negative predictive value of FNAC. Study results indicated that FNAC could be used as a highly reliable tool in the differential diagnosis of breast tumors, in combination with clinical and imaging findings, especially in developing countries with limited financial resources.

**Key words:** *Fine needle aspiration cytology; Breast; Tumors; Histopathology*

## Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of death from cancer in women. Breast cancer survival rates tend to be poorer in developing countries, most likely because of a combination of late diagnosis and limited access to timely and appropriate treatment<sup>1</sup>. The accuracy of diagnosis can be increased with a combination of clinical examination, imaging diagnostics, and fine needle aspiration cytology (FNAC) or core needle biopsy, also known as triple test<sup>2</sup>. FNAC is a minimally invasive, simple, cost-effective, safe and sensitive method for breast tumor diagnosis<sup>3</sup>. Many authors have shown that FNAC is highly accurate in the diagnosis of breast tumors<sup>4,5</sup>.

Using the ultrasound guided method, FNAC has been used more widely for non-palpable breast tumors<sup>6,7</sup>. Although core biopsy is preferred to FNAC in most developed countries, its procedure is more expensive and time consuming as compared to FNAC<sup>8-10</sup>.

This study was conducted to evaluate the sensitivity and specificity of FNAC in the diagnosis of breast tumors in our institution by correlating it with histopathology findings.

## Materials and Methods

This retrospective study was conducted at the Clinical Department of Pathology, Cytology and Forensic Medicine, Mostar University Hospital in Mostar, Bosnia and Herzegovina. Data were collected from the archives of our institution for women with breast masses having received FNA cytological diagnosis and histopathologic evaluation during the period from January 2012 to December 2013. We assessed the ac-

Correspondence to: *Josip Mišković, MD, PhD*, Clinical Department of Surgery, Mostar University Hospital, Kralja Tvrtka bb, 88000 Mostar, Bosnia and Herzegovina

E-mail: [josip\\_miskovic@yahoo.com](mailto:josip_miskovic@yahoo.com)

Received June 9, 2016, accepted June 16, 2016

curacy of FNA findings by comparing cytological diagnoses of breast masses to the diagnoses from histopathology reports obtained by surgery. FNA was obtained through a 22-24-gauge needle; the aspirated content was then smeared on a glass slide, air-dried and stained with May-Grünwald-Giemsa for 30 min. Cytological diagnoses were classified into 3 categories: benign, suspect and malignant. Benign category includes poor cellularity, good cohesion and flat sheets of cells, and smooth or fine chromatin with no nuclear irregularity. Malignant category includes high cellularity, poor cohesion and three-dimensional arrangement of cells, clumped chromatin with variable nuclear size and pleomorphism. Suspect category should be used when the cytologist is almost certain that they come from a malignant lesion, although a confident diagnosis cannot be made.

Statistical analysis to determine sensitivity, specificity, positive predictive value and negative predictive value with their 95% confidence intervals was performed using the SPSS 13.0 for Windows statistical software (SPSS Inc., Chicago, Illinois, USA). All values were calculated for the benign and malignant groups only, and for the benign, malignant and suspect groups together. The suspect and malignant cases were grouped together, based on the assumption for suspect cases to be positive for malignancy.

The study was approved by the Ethics Committee of the Mostar University Hospital and in accordance with the Helsinki Declaration<sup>11</sup>.

## Results

In this study, we collected 124 FNA diagnoses and histopathology reports. Median age was 46 (range 16-88) years. Out of 124 cases according to FNA, there were 35 (28.2%) benign, 83 (66.9%) malignant and 6 (4.8%) suspect cases. Out of the 85 confirmed malignant cases, 80 cases were malignant on cytology, 5 cases were suspect of malignancy, and 2 cases were benign. There were 3 benign cases confirmed by histology which were classified as malignant by cytology report (Table 1). The most common causes of false-positive cytological diagnosis were atypical lobular hyperplasia, papilloma and spreading artifacts. The most common cause of false-negative cytological diagnosis was inadequate aspiration. Table 2 summarizes data on the overall accuracy, sensitivity, specificity, pos-

*Table 1. Comparison of fine needle aspiration cytology (FNAC) and histopathology findings*

FNAC	Histopathology		Total N (%)
	Benign, n (%)	Malignant, n (%)	
Benign	33 (97.1) (TN)	2 (2.9) (FN)	35 (100)
Suspect	1 (33.3) (FP)	5 (66.7) (TP)	6 (100)
Malignant	3 (4.8) (FP)	80 (95.2) (TP)	83 (100)
Total	39 (100)	85 (100)	124 (100)

FN = false negative; FP = false positive; TN = true negative; TP = true positive

*Table 2. Diagnostic values of fine needle aspiration cytology in correlation with histopathology findings*

	Value (%) n=118	Value (%) n=124
Accuracy	95.7	95.1
Sensitivity	97.5	97.7
Specificity	91.6	89.1
Positive predictive value	96.3	95.5
Negative predictive value	94.2	94.2

itive predictive value and negative predictive value of FNA.

## Discussion

Accurate diagnosis of breast tumors can help avoid unnecessary surgical procedures and plan correct treatment options. Every patient with breast tumor should undergo triple test to make early and accurate diagnosis. FNA is widely used in the differential diagnosis of breast tumors because of the high level of accuracy, rapid results, and for being a less invasive procedure than tissue biopsy<sup>12,13</sup>. The accuracy, sensitivity and specificity found in our study showed FNA of breast tumors to be a reliable method for differential diagnosis of benign from malignant masses. Our study findings are consistent with those reported in the literature<sup>1,4,14</sup>. We had 4.8% of suspect FNA diagnoses. These findings are in line with previous reports<sup>15</sup>. According to various studies, the false-positive rate ranges from 0 to 2.5%, which is slightly lower than 3.2% found in this study<sup>4,5,15</sup>. The false-negative rate in our study was 1.6%, which is lower in comparison to other

studies<sup>4</sup>. False-negative and false-positive results occur due to physician experience<sup>16,17</sup>, sample quality<sup>18</sup> and certain histopathology diagnoses<sup>19</sup>. Using ultrasound guided FNAC increases specificity and sensitivity of FNA<sup>20,21</sup>. False-positive and false-negative results can mislead clinicians and therefore FNA should not be used as the only diagnostic tool in differential diagnosis of breast tumors. Results of FNAC should be interpreted in correlation to clinical and imaging findings, thus reducing the risk of missed diagnosis of breast cancer<sup>22-24</sup>. Even though diagnostic accuracy of core needle biopsy and FNA is similar<sup>24</sup>, many physicians prefer core needle biopsy as a technique superior to FNA because core needle biopsy can better detect ductal carcinoma *in situ* and offers better histopathologic and immunohistochemical evaluation of tumor tissues<sup>25,26</sup>. Evaluation of estrogen receptor can also be done in cytologic material, which is favorable for some patients, particularly those undergoing preoperative chemotherapy or irradiation, or those with inoperable primary tumor<sup>27-29</sup>. Because FNA is less traumatic and easier technique than core needle biopsy, it can be repeated in the same day in case of unsatisfactory samples. FNA is cost-effective even when followed by core needle biopsy or surgical excision<sup>8</sup>. Therefore, it is possible to introduce FNA procedure into smaller hospitals where physicians are less experienced with this technique<sup>30,31</sup>. This study indicated that FNA could be used as a highly reliable tool, in combination with clinical and imaging findings, in the differential diagnosis of breast tumors, especially in developing countries with limited financial resources.

## Conclusion

This study indicated FNA to be an accurate and highly reliable tool in the assessment of breast tumors. With high sensitivity and specificity, most breast tumors can be reliably diagnosed by FNA. It is a simple, safe, cost-effective and accurate method for the initial diagnosis and for guiding treatment. However, one must be aware of the possibility of false-positive and false-negative results. All patients with breast tumors should be diagnosed based on a combination of physical examination, radiological diagnostics and FNA. FNA is an acceptable and reliable procedure for the preoperative diagnosis of breast tumors, particularly in developing countries.

## References

- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011;61:69-90, <http://dx.doi.org/10.3322/caac.20107>
- Bukhari MH, Akhtar ZM. Comparison of accuracy of diagnostic modalities for evaluation of breast cancer with review of literature. *Diagn Cytopathol.* 2009;37:416-24, <http://dx.doi.org/10.1002/dc.21000>
- Nasuti JF, Gupta PK, Baloch ZW. Diagnostic value and cost-effectiveness of on-site evaluation of fine-needle aspiration specimens: review of 5,688 cases. *Diagn Cytopathol.* 2002;27:1-4, <http://dx.doi.org/10.1002/dc.10065>
- Chaiwun B, Thorner P. Fine needle aspiration for evaluation of breast masses. *Curr Opin Obstet Gynecol.* 2007;19:48-55, <http://dx.doi.org/10.1097/GCO.0b013e328011f9ae>
- Akcil M, Karaagaoglu E, Demirhan B. Diagnostic accuracy of fine-needle aspiration cytology of palpable breast masses: an SROC curve with fixed and random effects linear meta-regression models. *Diagn Cytopathol.* 2008;36:303-10, <http://dx.doi.org/10.1002/dc.20809>
- Evans WP, Cade SH. Needle localization and fine-needle aspiration biopsy of nonpalpable breast lesions with use of standard and stereotactic equipment. *Radiology.* 1989;173:53-6, <http://dx.doi.org/10.1148/radiology.173.1.2675189>
- Sterrett G, Oliver D, Frayne J, Ingram D, Sheiner H. Stereotactic fine needle aspiration biopsy (SFNB) of breast: preliminary results in Perth with the TRC mammo-test machine. Cytological aspects. *Pathology.* 1991;23:302-10, <http://dx.doi.org/10.1111/j.1445-2197.1992.tb07226.x>
- Rubin M, Horiuchi K, Joy N, *et al.* Use of fine needle aspiration for solid breast lesions is accurate and cost-effective. *Am J Surg.* 1997;174:694-6; discussion 697-8, [http://dx.doi.org/10.1016/S0002-9610\(97\)00192-X](http://dx.doi.org/10.1016/S0002-9610(97)00192-X).
- Berner A, Davidson B, Sigstad E, Risberg B. Fine-needle aspiration cytology *vs.* core biopsy in the diagnosis of breast lesions. *Diagn Cytopathol.* 2003;29:344-8, <http://dx.doi.org/10.1002/dc.10372>
- Lieu D. Value of cytopathologist-performed ultrasound-guided fine-needle aspiration as a screening test for ultrasound-guided core-needle biopsy in nonpalpable breast masses. *Diagn Cytopathol.* 2009;37:262-9, <http://dx.doi.org/10.1002/dc.20984>
- Williams JR. The Declaration of Helsinki and public health. *Bull WHO.* 2008;86:650-2, <http://dx.doi.org/10.1002/dc.20984>
- He Q, Fan X, Yuan T, *et al.* Eleven years of experience reveals that fine-needle aspiration cytology is still a useful method for preoperative diagnosis of breast carcinoma. *Breast.* 2007;16:303-6, <http://dx.doi.org/10.1016/j.breast.2006.12.006>.
- Lee HC, Ooi PJ, Poh WT, Wong CY. Impact of inadequate fine-needle aspiration cytology on outcome of patients with palpable breast lesions. *Aust N Z J Surg.* 2000;70:656-9, <http://dx.doi.org/10.1046/j.1440-1622.2000.01920.x>
- Yu YH, Wei W, Liu JL. Diagnostic value of fine-needle aspiration biopsy for breast mass: a systematic review and meta-

- analysis. *BMC Cancer*. 2012;12:41, <http://dx.doi.org/10.1186/1471-2407-12-41>.
15. Chaiwun B, Settakorn J, Ya-In C, Wisedmongkol W, Rangdaeng S, Thorner P. Effectiveness of fine-needle aspiration cytology of breast: analysis of 2,375 cases from northern Thailand. *Diagn Cytopathol*. 2002;26:201-5, <http://dx.doi.org/10.1002/dc.10067>
  16. Ljung BM, Drejet A, Chiampi N, *et al.* Diagnostic accuracy of fine-needle aspiration biopsy is determined by physician training in sampling technique. *Cancer*. 2001;93:263-8, <http://dx.doi.org/10.1002/cncr.9040>
  17. Day C, Moatamed N, Fimbres AM, Salami N, Lim S, Apple SK. A retrospective study of the diagnostic accuracy of fine-needle aspiration for breast lesions and implications for future use. *Diagn Cytopathol*. 2008;36:855-60, <http://dx.doi.org/10.1002/dc.20933>
  18. Boerner S, Sneige N. Specimen adequacy and false-negative diagnosis rate in fine-needle aspirates of palpable breast masses. *Cancer*. 1998;84:344-8, [http://dx.doi.org/10.1002/\(SICI\)1097-0142\(19981225\)84:6<344::AIDCNCR5>3.0.CO;2-R](http://dx.doi.org/10.1002/(SICI)1097-0142(19981225)84:6<344::AIDCNCR5>3.0.CO;2-R)
  19. Park IA, Kim JS, Ham EK. Fine needle aspiration cytology of gastric epithelioid leiomyosarcoma metastasized to the liver. A case report. *Acta Cytol*. 1997;41:1801-6, <http://dx.doi.org/10.1159/00333190>
  20. Suzuki S, Moro-oka T, Choudhry NK. The conditional relative odds ratio provided less biased results for comparing diagnostic test accuracy in meta-analyses. *J Clin Epidemiol*. 2004;57:461-9, <http://dx.doi.org/10.1016/j.jclinepi.2003.09.017>
  21. Ishikawa T, Hamaguchi Y, Tanabe M, *et al.* False-positive and false-negative cases of fine-needle aspiration cytology for palpable breast lesions. *Breast Cancer*. 2007;14:388-92, <http://dx.doi.org/10.2325/jbcs.14.388>
  22. Negri S, Bonetti F, Capitanio A, Bonzanini M. Preoperative diagnostic accuracy of fine-needle aspiration in the management of breast lesions: comparison of specificity and sensitivity with clinical examination, mammography, echography, and thermography in 249 patients. *Diagn Cytopathol*. 1994;11:4-8, <http://dx.doi.org/10.1002/dc.2840110103>
  23. Chaiwun B, Sukhamwang N, Lekawanvijit S, *et al.* Atypical and suspicious categories in fine needle aspiration cytology of the breast: histological and mammographical correlation and clinical significance. *Singapore Med J*. 2005;46:706-9.
  24. Brenner RJ, Bassett LW, Fajardo LL, *et al.* Stereotactic core-needle breast biopsy: a multi-institutional prospective trial. *Radiology*. 2001;218:866-72, <http://dx.doi.org/10.1148/radiology.218.3.r01mr44866>
  25. Litherland JC, Evans AJ, Wilson AR, *et al.* The impact of core-biopsy on preoperative diagnosis rate of screen detected breast cancers. *Clin Radiol*. 1996;51:562-5, [http://dx.doi.org/10.1016/S0009-9260\(96\)80136-X](http://dx.doi.org/10.1016/S0009-9260(96)80136-X)
  26. Usami S, Moriya T, Amari M, *et al.* Reliability of prognostic factors in breast carcinoma determined by core needle biopsy. *Jpn J Clin Oncol*. 2007;37:250-5, <http://dx.doi.org/10.1093/jjco/hym021>
  27. Masood S. Prognostic and diagnostic implications of estrogen and progesterone receptor assays in cytology. *Diagn Cytopathol*. 1994;10:263-7, <http://dx.doi.org/10.1002/dc.2840100314>
  28. Masood S. Estrogen and progesterone receptors in cytology: a comprehensive review. *Diagn Cytopathol*. 1992;8:475-91, <http://dx.doi.org/10.1002/dc.284008050>
  29. Gong Y, Symmans WF, Krishnamurthy S, Patel S, Sneige N. Optimal fixation conditions for immunocytochemical analysis of estrogen receptor in cytologic specimens of breast carcinoma. *Cancer*. 2004;102:34-40, <http://dx.doi.org/10.1002/cncr.11906>
  30. Lannin DR, Silverman JF, Walker C, Pories WJ. Cost-effectiveness of fine needle biopsy of the breast. *Ann Surg*. 1986;203:474-80.
  31. Lau SK, McKee GT, Weir MM, Tambouret RH, Eichhorn JH, Pitman MB. The negative predictive value of breast fine-needle aspiration biopsy: the Massachusetts General Hospital experience. *Breast J*. 2004;10:487-91, <http://dx.doi.org/10.1111/j.1075-122X.2004.21496.x>

#### Sažetak

### DIJAGNOSTIČKA VRIJEDNOST CITOLOŠKE PUNKCIJE TANKOM IGLOM KOD TUMORA DOJKE

*J. Mišković, A. Zorić, H. Radić Mišković i V. Šoljić*

Karcinom dojke je najčešći zloćudni tumor i vodeći uzrok smrti od zloćudne bolesti kod žena. Pravodobnost i točnost dijagnoze mogu se poboljšati kombinacijom kliničkog pregleda, radioloških pretraga i citološke punkcije tankom iglom ili *core* biopsije. Istraživanje je provedeno kako bi se utvrdila osjetljivost i specifičnost citološke punkcije tankom iglom tumora dojke u odnosu na patohistološki nalaz. U istraživanje je uključeno 124 nalaza citološke punkcije tankom iglom tumora dojke koji su uspoređeni s patohistološkim nalazom nakon kirurške resekcije. Statistička analiza je pokazala točnost od 95,1%, osjetljivost od 97,7%, specifičnost od 89,1%, pozitivnu prediktivnu vrijednost od 95,5% i negativnu prediktivnu vrijednost od 94,2%. Istraživanje je pokazalo da se citološka punkcija tankom iglom može koristiti kao veoma pouzdana pretraga u diferencijalnoj dijagnozi tumora dojke, u kombinaciji s kliničkim pregledom i radiološkim pretragama, pogotovo u zemljama u razvoju s ograničenim materijalnim sredstvima.

**Ključne riječi:** *Citološka punkcija tankom iglom; Dojka; Tumori; Patohistologija*