Preoperative ultrasound guided percutaneous axillary biopsy in breast cancer patients: fine needle aspiration cytology versus core biopsy

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Preoperative ultrasound guided percutaneous axillary biopsy in breast cancer patients: fine needle aspiration cytology versus core biopsy.

AIM: *The aim of this study is to compare the diagnostic accuracy in detecting axillary node metastases between preoperative ultrasound with percutaneous core biopsy or fine needle aspiration cytology, in patients with breast cancer.*
MATERIAL AND METHODS: *All cases with newly diagnosed ipsilateral primary breast cancer that underwent axillary ultrasound guided biopsies in a 2 year period were reviewed and the biopsy outcome was compared to the final histopathology from sentinel lymph node biopsy or axillary node dissection. Comparison was also attempted in a subgroup including only patients who underwent one method and in a second subgroup of patients who had both techniques performed.*
RESULTS*: Within the total population results are in favor of core biopsy which correlates statistically significantly with the final histology after excluding neoadjuvant related false negatives. Within the single modality subgroup results are again in favor of core biopsy which again correlates statistically significantly with the final histology. Within the combined modality subgroup results demonstrate equal diagnostics but neither method demonstrates statistically significant diagnostic success.*
DISCUSSION: *The results of the study are generally in favour of core biopsy which tends currently to override fine needle aspiration cytology. Only few studies have directly compared the two methods and a great variability exists in the results of the different studies.*
CONCLUSIONS: *A case-match cohort study is advised to accurately compare the diagnostic value of the two methods. Until then the decision will be based on the radiologist's experience.*

KEY WORDS: Breast cancer, Diagnostic accuracy, Percutaneous axillary biopsy

Introduction

Since 1990s the development of sentinel lymphnode biopsy (SLNB) resulted in improved staging accuracy with notable reduction in morbidity compared to complete axillary node dissection (AXND) for patients with breast cancer [1,2]. However SLNB itself is not without morbidity and usually requires that patients undergo two procedures [3]. Physical examination by itself has a low sensitivity (34-76%)[4]. Several imaging techniques aim to identify patients with high or low risk of axillary metastases for whom AXND and sampling or SLNB would be indicated respectively [5]. Ultrasound (US) is the most widely used [6] however an overlap between malignant and benign morphological lymphnode features exists. Tissue

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diagnosis remains the gold standard [1, 2]. For breast lesions US guided core biopsy (CB) is more accurate and easier to interpret than fine needle aspiration cytology (FNAC) and is now the diagnostic procedure of choice, but according to a recent meta-analysis the difference in sensitivity between the two methods with regards to detection of axillary node metastases was not significant [7] and recent publications have supported the role of FNAC with regards to accuracy, complication rate and cost [2,8,9]. Preoperative axillary US with either FNAC or CB of suspicious nodes are nowadays a routine practice regardless of the clinical status [10]. The choice is largely institution or operator dependent and most studies report results with either only FNAC or CB. The aim of this study was to determine if there is any difference in the diagnostic accuracy between CB and FNAC in detecting axillary node metastases in patients with newly diagnosed ipsilateral primary breast cancer.

Material and Method

The medical records of all patients that underwent axillary US guided biopsies in a 2 year period in a single centre were retrieved. Only patients with newly diagnosed ipsilateral breast cancer confirmed by biopsy of the primary tumour were included. Patients without histological confirmation of the primary or patients with recurrent disease were excluded. Patients in whom the axillary biopsy has revealed a type of malignancy different from the primary breast disease and patients with axillary biopsy demonstrating the presence of multifocal primary breast cancer in the axilla or cancer of the axillary tail were also excluded. Data collected from the aforementioned records included diagnostic procedures performed (FNAC, CB) and their results (positive/negative/ inconclusive), as well as final histopathology where available, including grade and histological type. Finally patients' age and administration of neo-adjuvant chemotherapy were also recorded. The diagnostic algorithm for management of the axilla described in Fig. 1 was applied on all patients and is in accordance with the Surgical Guidelines in the Management of Breast Cancer [11]. Patients diagnosed with ipsilateral breast cancer always undergo US of the axilla with or without percutaneous biopsy of suspicious lymphnodes. US of the axilla is also performed at the same time with the breast imaging in all patients with an ipsilateral breast lesion classified as M4/M5 on mammogram and/or U4/U5 on US (Royal College of Radiologists Breast Group Breast Imaging Classification) [12]. The investigators of this study follow the Best Practice Diagnostic Guidelines for Patients Presenting with Breast Symptoms [13] and the NHS BSP Clinical Guidelines for Breast Cancer Screening Assessment [14]. Morphologic criteria rendering a node suspicious included the increased size, an entirely hypoechoic node, the shape (short-long axis ratio >0.5), a focal cortical bulge or cortical thickening >2mm, an absent fatty hilum .On rare occasions colour Doppler was used as auxiliary technique. US guided biopsy was performed by dedicated breast imaging radiologists after administration of local anaesthesia with 1% xylocaine.

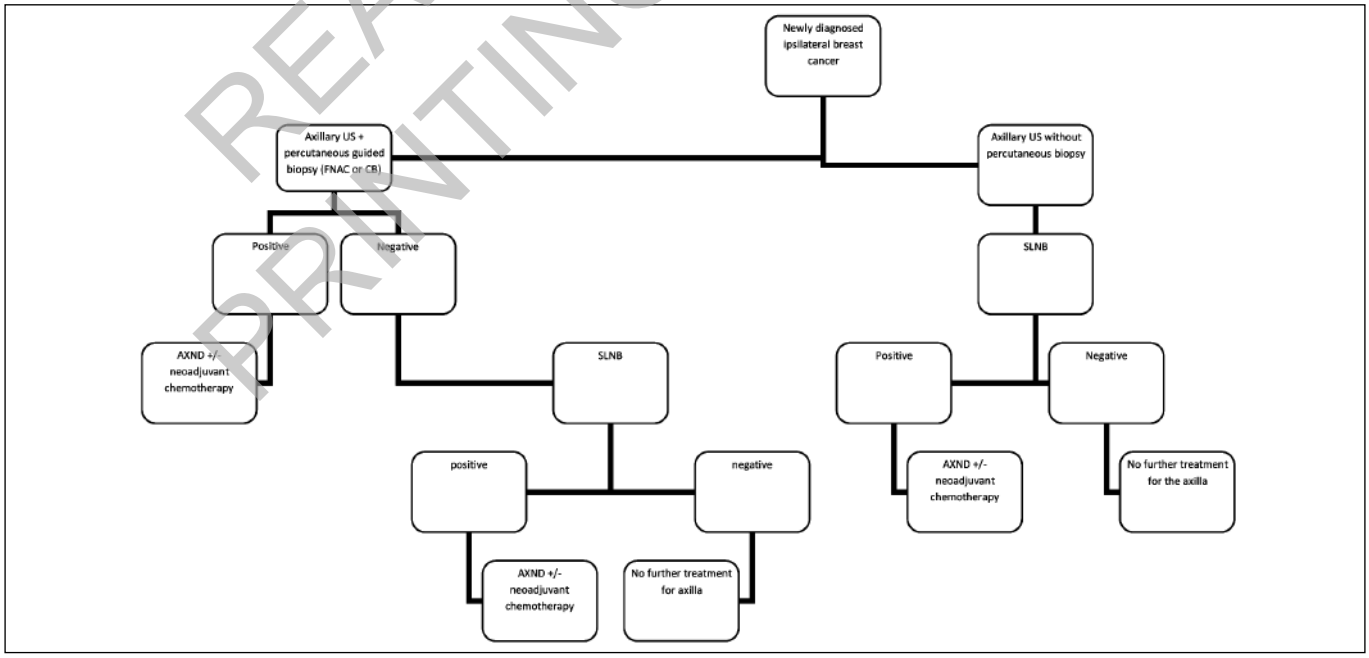

Fig. 1: Diagnostic algorithm of management of the axilla in patients diagnosed with ipsilateral primary breast cancer.

There were no specific criteria for choosing one method over another. The device used for imaging is LOGIQE9 (GE Healthcare Biosciences, Pittsburgh, USA), with a 15 MHz transducer. The size of the needle was 16 gauge for core biopsy or 21 gauge for FNA. One or two throws were usually performed for a core biopsy (one throw and then "eyeballing" the sample).More biopsies were performed at the discretion of the radiologist. When more than one abnormal node was identified the one involving the most suspicious characteristics was biopsied. The total number of biopsies and possible complications were recorded. In case of an FNA once the needle was in good position continuous suction moving the needle around was used until a sufficient sample was obtained. The number of needle entries and intracortical excursions was not documented. A pathologist was not present at the time of the procedure to evaluate the adequacy of the samples. Core biopsy samples were embedded in formalin. Aspirated material from FNA was placed on slides in alcohol. Results for both FNA and CB were classified as positive for malignancy, negative for malignancy and inadequate (insufficient samples have also been classified as inadequate). Inadequate FNA procedures were followed either by a CB or by a SLNB according to the following multidisciplinary team (MDT) decision. There was only one case of inadequate CB (insufficient sample) but has not been included in the study as the patient presented lung metastases and did not undergo surgery. In addition CBs were routinely reviewed by breast pathologists at the MDT meeting. The outcome of percutaneous biopsy was compared to histology from SLNB or AXND, considering the surgical pathology result as the gold standard. The demographics, grade and type of the primary tumour and histology of the tumour were documented in addition to the administration of neoadjuvant chemotherapy.

Data Analysis

Statistical process of data was conducted using SPSS v20 software (IBM Corporation, USA). Bivariate correlations were assessed with Chi square, Fischer's exact, Mann-Whitney U, Independent Samples Median test and Spearman's correlation as appropriate. Sensitivity and Specificity of each approach was assessed using the receiver operating characteristic (ROC) curve function. A p value of <0.05 was considered statistically significant and a p value between 0.1 and 0.05 was considered suggestive.Comparison of methods' diagnostic value was also attempted in two special subgroups: in the first subgroup only the pure CB and FNAC populations were analyzed, excluding the group of patients who had both techniques. In the second subgroup only patients who had both FNAC and CB were analyzed, excluding the patients who had only one of the two methods. All patients had consented for archiving and use of tissue for research purposes and approval from local ethical committee was not required as the study involved only retrospective analysis of clinical data associated with procedures performed without any deviation from institute's local guidelines.

Results

Total Population

During a two-year period, 71 patients diagnosed with breast cancer underwent core and/or FNA biopsy of lymph nodes under ultrasound guidance for preoperative assessment of lymph node involvement. Patients with lack of surgical histopathological correlation for different reasons (unfitness for surgery, surgery elsewhere, opted for endocrine treatment) were excluded.For 11 of these patients there was no histology available (10 not operated for various reasons and 1 patient operated elsewhere – no access to final histology). Total population consisted of 60 patients. Within the total population, 49 CBs have been performed of which 25 (51%) were positive for cancer. None of the CBs was inadequate. In the same total population 24 FNACs have been performed including 5 inadequate ones (20.83%) and 11 positive for malignancy (57.9% among the adequate ones). Eleven of these 60 patients (18.33%) had both CB and FNAC. One of the FNACs was inadequate. Five patients had both FNAC and CB reported as negative, 4 patients had both procedures reported as positive for cancer and 1 case was positive on FNAC and negative on CB. There were no cases with negative FNAC and positive CB. In the total population the median number of CBs for each patient was 2 (range 1-5). Table I shows the distribution in the total population. Documentations regarding neoadjuvant chemotherapy of 13 patients were missing (21.67%). Among the 38 patients who had neoadjuvant chemotherapy, 2 patients initially assessed positive on both CB and FNAC were found to be negative on the final histology following neoadjuvant. Four patients assessed positive on CB were negative on final histology following neoadjuvant. There were no false positives in patients who didn't have neoadjuvant. Two different evaluations of the total population regarding the sensitivity and specificity of the two methods were performed; one including neoadjuvant-related false negative results (Fig. 2A) and one excluding them (Fig. 2B).

Single Modality CB or Fnac Subgroups

Out of a total of 60 patients, 11 patients had both procedures performed. However one of these 11 patients had an inadequate FNAC therefore has been included in this population as a CB patient. The remaining 10

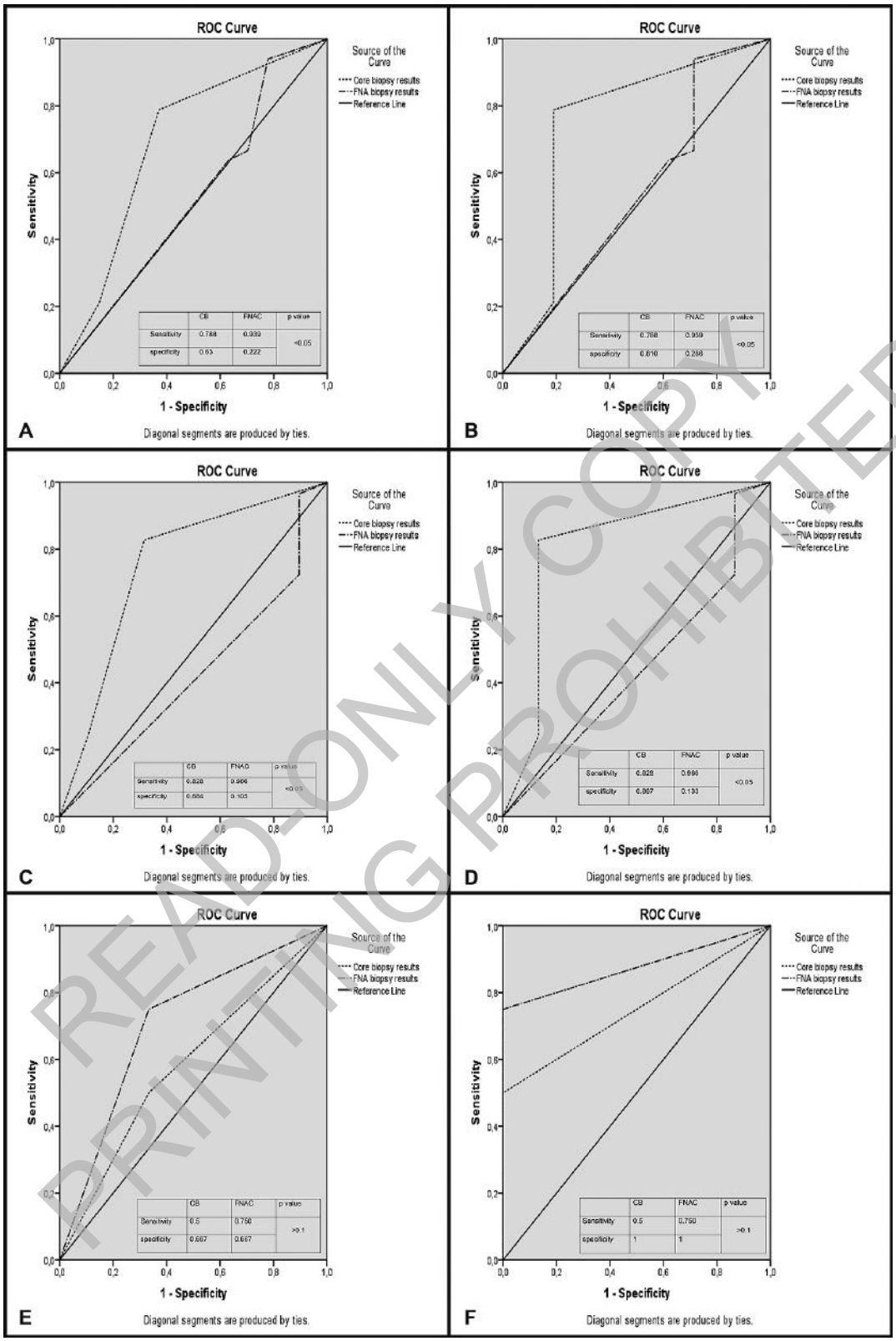

Fig. 2: ROC curves comparing sensitivity and specificity for each procedure across studied subgroups. **A**: Total population including all patients, regardless neoadjuvant chemotherapy administration. **B**: Total population excluding patients that received neoadjuvant chemotherapy. **C**: Subgroup of patients subjected to only one of the two studied procedures, regardless neoadjuvant chemotherapy administration. **D**: Subgroup of patients subjected to only one of the two studied procedures excluding those that received neoadjuvant chemotherapy. **E**: Subgroup of patients subjected to both studied procedures, regardless neoadjuvant chemotherapy administration. **F**: Subgroup of patients subjected to both studied procedures excluding those that received neoadjuvant chemotherapy.

patients have been excluded from the total population. Two more patients have been excluded as they had inadequate FNAC only, without CB. Therefore, single modality CB or FNAC subgroup consists of 48 patients. Thirty-nine patients had CBs, 21 of which (53.8%) were positive for malignancy. No inadequate CBs have been documented. On the other hand 10 patients had FNACs one of which was inadequate (10%) and 6 of which were positive for malignancy (66.7% among the adequate ones). The median number of CBs was 2 (range 1-5). Table I shows the distribution in the single modality subgroup. Documentations regarding neoadjuvant chemotherapy of 11 patients were missing (22.92%). Two different diagnostic evaluations of the single modality subgroup were performed regarding the sensitivity and specificity of the two methods, one including neoadjuvant-related false negative results (Fig. 2C) and one excluding them(Fig. 2D).

Combined Modality Subgroup

In the final analysis considering only the group of patients who had both FNAC and CB and excluding the patients who had one of the two methods, out of the total population of 60 patients 11 patients had both procedures but one of them had an inadequate FNAC therefore was excluded. The number of patients in the combinedmodality subgroup of FNAC and CB was 10 patients. Four out of 10 CBs were positive (40%) and 5 out of 10 FNACs were positive (50%). The median number of CBs was 4 (range 2-4). Table I shows the distribution in the combined modality subgroup. Two different diagnostic evaluations of this subgroup regarding the sensitivity and specificity of the two methods were performed; one including neoadjuvant-related false negative results (Fig. 2E) and one excluding them (Fig. 2D).

Discussion and Commentary

Preoperative diagnosis by axillary US guided biopsy can eliminate unnecessary SLNB procedures and reduce false negative rates of SLNB (1-15%) [15, 16], being also performed in conjunction with the biopsy of the primary breast lesion. SLNB is still offered when US guided biopsy has been negative and meta-analyses have shown that 25% of women with negative US biopsy will be proven to have positive axillary lymphnodes [17]. US guided FNAC is useful for evaluation of metastatic disease with sensitivities varying from 44 to 100% due to patient selection. However it requires cooperation of a highly experienced practitioner and cytologist [18] and often leads to inadequate sampling. The question of whether CB is a safe and effective procedure in this context has been raised by breast specialists [1,10], however only a few studies have compared directly the two methods [1,2,10,19].
In the present study FNAC demonstrates higher sensitivity, especially in cross-checked population, but this is not statistically significant. This is in contrast to studies who demonstrated greater sensitivity for CB but again not statistically significant: (87.1% vs. 78.6%) [1],

Table I - *Age, grade, type, final histology and administration of neoadjuvant chemotherapy across procedures for each studied subgroup.*

	Total population				Single modality subgroup				Combined modality subgroup
	Total	**FNAC**	**CB**	**p value**	**Total**	**FNAC**	**CB**	**p value**	**Total**
Age (years), median (range)	52(34-88)	52(34-88)	54(34-82)	>0.1	57(37-88)	57(48-88)	56(37-82)	>0.1	47(34-70)
Grade, n (%)									
I	2(3.3%)	1(5.3%)	1(2%)	>0.1	2(4.2%)	1(11.1%)	1(2.6%)	>0.1	0
II	27(45%)	7(36.8%)	24(49%)		21(43.8%)	2(22.2%)	19(48.7%)		5 (50%)
III	31(51.7%)	11(57.9%)	24(49%)		25(52.1%)	6(66.7%)	19(48.7%)		5 (50%)
Type, n (%)									
IDC	54(90%)	17(89.5%)	45(91.8%)	0.008	42(87.5%)	7(77.8%)	35(89.7%)	0.008	10(100%)
ILC	4(6.7%)	0	4(8.2%)		4(8.3%)	0	4(10.3%)		0
DCIS	2(3.3%)	2(10.5%)	0		2 (4.2%)	2(22.2%)	0		0
Positive Hx, n (%)	33 (55%)	11 (57.9%)	26 (53.1%)	>0.1	29 (60.4%)	7 (77.8%)	22 (56.4%)	>0.1	4 (40%)
Administered Neoadjuvant, n (%)	38 (80.9%)	13 (81.2%)	32 (78%)	>0.1	31 (83.8%)	6 (100%)	25 (80.6%)	>0.1	7 (70%)

(82% vs. 75%)[2], (77% vs. 73%)[19], (83.3% vs. 72.2%)[7]. One more author [10] demonstrated a statistically significant greater sensitivity for CB (88.25% vs. 72.5%) but the small sample size is of concern. Another author [2] found an unexpected similar sensitivity between the two methods, explained by the higher number of FNAC passes. Although it has been previously otherwise reported [1], in our results the number of CB attempts has not affected the sensitivity; when the median number of CB was higher, sensitivity was actually lower (combined modality subgroup). FNAC demonstrates statistically significantly lower specificity in the total and the single modality subgroup. In other studies specificity was equal between the two methods (100%)[2,10,19]. These results might be affected by the type of tumors assessed with FNAC rather than with CB, namely more ductal carcinomas in situ (DCIS) and less invasive lobular carcinomas (ILC).Some authors take into consideration the types of primary tumour in their population [4-6,8,9,16]. Another investigator [9] did not find any correlation of CB sensitivity with tumor type although he did with tumor grade and lymphovascular invasion, while one study [8] demonstrated a strong positive correlation of FNAC sensitivity only with tumor grade and size. They both considered though the tumor type in the total breast cancer population studied and not in the sample that had actually undergone axillary biopsy. Another investigator [5] demonstrated a correlation for both methods with size, grade and axillary metastatic burden, but like others, did not focus on the type of tumor [4,6], while no correlations were found in one other study [16]. In the present analysis in all different subgroups the sensitivity and specificity of the two methods ranged 0.5-0.828 for CB sensitivity, 0.75-0.966 for FNAC sensitivity, 0.63-0.1 for CB specificity, 0.105-1.0 for FNAC specificity. Relevant literature includes grossly varying reported sensitivities (52-94% for CB and 28-100% for FNAC), consistent CB specificity (97-100%) and a solid 100% specificity for FNAC [4,6,8,9,18,20-24].

It is generally difficult to compare different studies because of their heterogeneity [16]. Some include patients without final surgical histological result considering that final histology would have been positive as both preoperative FNA and CB were positive [1]. This is in accordance with other authors' view on complete neoadjuvant response [3,4,6,9,21]. Others exclude not surgical patients [5]. In the present study all patients with lack of final surgical pathology were excluded. Different units use different morphologic criteria for biopsy and preparation modalities for cytology [8]. Techniques generally vary and are operator dependent [9,20]. Length of procedure, number of slides, number of CB excursions, non-uniform use of biopsy needles, absence of pathologist during the procedure, can all also explain the different results [1]. Study design and indication for biopsy (morphology) could also justify the different rates, although some differences are still unexplained [17]. In some studies, clinically positive axillas were excluded [3,20,25], while included in others [5,10,16,22]. One investigator has included only clinical abnormal nodes [4]. In literature, FNAC demonstrates inadequate samples in a range of 0-53% [10] which can also add to the heterogeneity of results. A study [18] revealed a decrease from 88.46% to 76.66% in FNAC sensitivity by including inadequate aspirations. In the total population of the present analysis 5 cases (20.83%) of FNAC were inadequate and have all been excluded. The exclusion of false-negatives attributed to neo-adjuvant chemotherapy remains a statistical concern, but appears that conveys equivalent increase in tests' specificities, thus can be excluded as a confounding factor. This is supported also by a study [1] which included neoadjuvant chemotherapy as it affected equally the two procedures. Neoadjuvant chemotherapy patients have also been included by different authors [2-4, 9,21], while others [19, 20] have excluded them. Some studies do not make any comment on this [5,6,8,10,16,18,25]. The subgroup analysis performed in the current study has attempted to overcome this point. The authors have included patients with ILC in the analysis as the use of percutaneous biopsy in this setting has been previously validated [2,22].

Possible limitations of the present study include small sample size of the total population, the combined diagnostic approach group and the FNACs, issue which is often encountered in literature [1,2,5,10]. There was also an unequal distribution of tumour type across the approaches, but the numbers were too small to stratify. The assessment of factors affecting the diagnostic value of each approach individually was outside the scope of this study, thus not attempted.

There is no doubt that both methods have led to reduction of unnecessary SLNB [3,8,18,21] and in modern practice their use is expanding. In literature there is no clear advantage between the two methods and although CB is criticized for being more invasive [2,5] it is generally considered safe, effective and less operator dependent [4-6,9]. In the present study, only CB demonstrates statistically significant correlation with histology, and this is confirmed in the pure population and the total population excluding neo-adjuvant false negatives.

Conclusions

The results of this study are generally in favor of CB; however a case-match cohort study is advised to assess tumor type as a confounding factor and to accurately compare the diagnostic value. Until then the decision needs to be based on radiologist's experience and preference.

Riassunto

L'ecografia preoperativa con biopsia percutanea (ago-biopsia,CB, oppure aspirazione citologica ad ago aspirato

sottile, FNAC) dei linfonodi del cavo ascellare è nei nostri tempi una prattica commune per pazienti con cancro della mammella. Comunque, non è chiaro quale tecnica offre i risultati migliori. Lo scopo di questo studio era di confrontare la precisione diagnostica tra CB e FNAC nell'individuare metastasi linfonodali in pazienti con cancro della mammella.

Si sono rivisti tutti i casi con neoplasie della mammella recentemente diagnosticate che hanno avuto una biopsia percutanea preoperativa omolaterale eco-guidata (CB o FNAC) del cavo ascellare, in un periodo di 2 anni in un singolo centro. Il risultato della biopsia è stato confrontato con il risultato istopatologico finale della biopsia del linfonodo sentinella (SLNB) oppure della dissezione linfonodale ascellare. I dati raccolti includono il tipo della procedura, i risultati (positivi/negativi/ inconcludenti),la istopatologia finale includendo il grado e il tipo istologico, l'età e la somministrazione di chemioterapia neoadiuvante. Comparazione è stata anche fatta in un sottogruppo comprendente pazienti che avevano avuto soltanto una delle due metodi ed anche in un altro sottogruppo contenendo pazienti che avevano avuto entrambi i metodi.

Nella popolazione totale (60 pazienti) i risultati sono a favore della CB che è in correlazione statisticamente significativa con la istologia finale(p=0.003) dopo aver escluso i falsi negativi connessi con la chemioterapia neoadiuvante. Nel sottogruppo dei pazienti che avevano avuto soltanto uno dei due metodi, riguardante 48 pazienti , i risultati sono di nuovo a favore della CB che di nuovo è in correlazione statisticamente significativa con la istologia finale. Nel sottogruppo di pazienti che avevano avuto entrambi i metodi , riguardante 10 pazienti, i risultati sono pari dal punto di vista diagnostico, pero' nessuna tecnica mostra un successo diagnostico statisticamente significativo.

I risultati dello studio sono generalmente a favore della ago biopsia che attualmente tende di superare la FNAC. In literattura soltanto pochi studi hanno direttamente confrontato le due tecniche, esiste una grande variazione di risultati e non esiste un vantaggio chiaro tra i due metodi.

Comunque, per confrontare con precisione il valore diagnostico della CB e della FNAC, un cohort case-match studio dovrebbe essere effetuato. Fino ad allora la decisione dovra' essere basata sulla esperienza e le preferenze del radiologo.

References

1. Ganott MA, Zuley ML, Abrams GS, et al.: *Ultrasound guided core biopsy versus fine needle aspiration for evaluation of axillary lymphadenopathy in patients with breast cancer*. ISRN Oncol, 2014; 2014; 703160.

2. Rao R, Lilley L, Andrews V, et al.: *Axillary staging by percutaneous biopsy: Sensitivity of fine-needle aspiration versus core needle biopsy*. Ann Surg Oncol, 2009; 16(5):1170-175.

3. Holwitt DM, Swatske ME, Gillanders WE, et al.: *Scientific Presentation Award: The combination of axillary ultrasound and ultrasound-guided biopsy is an accurate predictor of axillary stage in clinically node-negative breast cancer patients*. Am J Surg, 2008; 196(4):477-82.

4. Topal U, Punar S, Tasdelen I, Adim SB: *Role of ultrasound-guided core needle biopsy of axillary lymph nodes in the initial staging of breast carcinoma.* Eur J Radiol, 2005; 56(3):382-85.

5. Damera A, Evans AJ, Cornford EJ, et al.: *Diagnosis of axillary nodal metastases by ultrasound-guided core biopsy in primary operable breast cancer*. Br J Cancer, 2003; 89(7):1310-313.

6. Torres Sousa MY, Banegas Illescas ME, Rozas Rodriguez ML, et al.: *Preoperative staging of axillary lymph nodes in breast cancer: Ultrasonographic parameters and ultrasound-guided core needle biopsy*. Radiologia, 2011; 53(6):544-51.

7. Houssami N, Ciatto S, Turner RM, Cody HS, 3rd, Macaskill P: *Preoperative ultrasound-guided needle biopsy of axillary nodes in invasive breast cancer: Meta-analysis of its accuracy and utility in staging the axilla.* Ann Surg, 2011; 254(2):243-51.

8. Baruah BP, Goyal A, Young P, Douglas-Jones AG, Mansel RE: *Axillary node staging by ultrasonography and fine-needle aspiration cytology in patients with breast cancer*. Br J Surg, 2010; 97(5):680-83.

9. Solon JG, Power C, Al-Azawi D, Duke D, Hill AD: *Ultrasound-guided core biopsy: An effective method of detecting axillary nodal metastases.* J Am Coll Surg, 2012; 214(1):12-17.

10. Rautiainen S, Masarwah A, Sudah M, et al.: *Axillary lymph node biopsy in newly diagnosed invasive breast cancer: Comparative accuracy of fine-needle aspiration biopsy versus core-needle biopsy.* Radiology, 2013; 269(1):54-60.

11. Association of Breast Surgery at B: *Surgical guidelines for the management of breast cancer*. Eur J Surg Oncol, 2009; 35 Suppl 1:1-22.

12. Maxwell AJ, Ridley NT, Rubin G, Wallis MG, Gilbert FJ, Michell MJ: *The Royal College of Radiologists Breast Group breast imaging classification.* Clin Radiol, 2009; 64(6):624-27.

13. Association of Breast Surgery: *Best practice diagnostic guidelines for patients presenting with breast symptoms.* In: Willet AM, Michell MJ, Lee MJ, editors. 2012.

14. NHS Breast Screening Programme: *Clinical guidelines for breast cancer screening assessment*. In: Liston J, Wilson R (eds): *NHS Cancer Screening Programmes.* 3rd ed. Sheffield 2010.

15. Alvarez S, Anorbe E, Alcorta P, Lopez F, Alonso I, Cortes J: *Role of sonography in the diagnosis of axillary lymph node metastases in breast cancer: A systematic review.* AJR Am J Roentgenol, 2006; 186(5):1342-348.

16. Mills P, Sever A, Weeks J, Fish D, Jones S, Jones P: *Axillary ultrasound assessment in primary breast cancer: An audit of 653 cases*. Breast J, 2010; 16(5):460-63.

17. Houssami N, Diepstraten SC, Cody HS, 3rd, Turner RM, Sever AR: *Clinical utility of ultrasound-needle biopsy for preoperative staging of the axilla in invasive breast cancer.* Anticancer Res, 2014; 34(3):1087-97.

18. Oz A, Demirkazik FB, Akpinar MG, et al.: *Efficiency of ultrasound and ultrasound-guided fine needle aspiration cytology in preop-*

erative assessment of axillary lymph node metastases in breast cancer. J Breast Cancer, 2012; 15(2):211-17.

19. Ahn HS, Kim SM, Jang M, et al.: *Comparison of sonography with sonographically guided fine-needle aspiration biopsy and core-needle biopsy for initial axillary staging of breast cancer*. J Ultrasound Med, 2013; 32(12):2177-184.

20. Yamashita M, Hovanessian-Larsen L, Sener SF: *The role of axillary ultrasound in the detection of metastases from primary breast cancers*. Am J Surg, 2013; 205(3):242-44; discussion 4-5.

21. Gilissen F, Oostenbroek R, Storm R, Westenend P, Plaisier P: *Prevention of futile sentinel node procedures in breast cancer: Ultrasonography of the axilla and fine-needle aspiration cytology are obligatory*. Eur J Surg Oncol, 2008; 34(5):497-500.

22. Boughey JC, Middleton LP, Harker L, et al.: *Utility of ultrasound and fine-needle aspiration biopsy of the axilla in the assessment of invasive lobular carcinoma of the breast*. Am J Surg, 2007; 194(4):450-55.

23. Krishnamurthy S, Sneige N, Bedi DG, et al.: R*ole of ultrasound-guided fine-needle aspiration of indeterminate and suspicious axillary lymph nodes in the initial staging of breast carcinoma.* Cancer, 2002; 95(5):982-88.

24. Hinson JL, McGrath P, Moore A, et al.: *The critical role of axillary ultrasound and aspiration biopsy in the management of breast cancer patients with clinically negative axilla*. Ann Surg Oncol, 2008; 15(1):250-55.

25. Deurloo EE, Tanis PJ, Gilhuijs KG, et al.: *Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer*. Eur J Cancer, 2003; 39(8):1068-73.