International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

Check for updates

Comparative analysis of sensitivity and specificity between fine needle aspiration and core needle biopsy in breast cancer diagnosis: Meta-analysis

Ibrahim Halima Sani [1], Qing Li [1,*], Isah Adamu Danbala [2], Mei Zhang [1], Qiaoran Liu [1] and Zakari Shaibu [3]

[1] *Department of General Surgery, The First Affiliated Hospital of Shandong First Medical University &Shandong Provincial Qian Foshan Hospital, N0.16766 Jingshi Road, Jinan City, Shandong Province, China.*
[2] *Department of Radiation Oncology, Institute of Oncology, Affiliated Hospital, Jiangsu University, Zhenjiang, Jiangsu Province, China. 212001.*
[3] *School of medicine, Jiangsu University, Zhenjiang Jiangsu China.*

International Journal of Science and Research Archive, 2024, 12(01), 2137–2145

Publication history: Received on 17 April 2024; revised on 27 May 2024; accepted on 30 May 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.12.1.0943

Abstract

Objective: To compare the sensitivity and specificity of Fine Needle Aspiration (FNA) and Core Needle Biopsy (CNB) in diagnosing breast cancer (BC).

Methods: A thorough investigation of the PubMed, Google Scholar, Cochrane Library, and Embase databases up to October 03, 2018, was conducted to pinpoint important literature. The analysis delved into the sensitivity and specificity rates of FNA and CNB to gauge their diagnostic efficacy. The synthesis of findings was achieved through meta-analysis using Rev-Man 5.4 software.

Results: Our study comprised five studies involving 1,177 patients, assessing the sensitivity and specificity rates of FNA and CNB. Sensitivity rates for FNA and CNB were found to be 68.6% and 88.1%, respectively, whereas specificity rates for FNAC and CNB stood at 96.1% and 97.2%, respectively. Comparison between FNA and CNB demonstrated a statistically significant variance in sensitivity (OR: 0.30, 95% CI [0.21, 0.41], P < 0.00001), indicative of CNB's superior diagnostic accuracy. However, specificity comparison between FNAC and CNB yielded non-significant results (OR: 0.54, 95% CI [0.17, 1.69], P = 0.29).

Conclusion: FNA and CNB are crucial tools in diagnosing breast cancer, each with unique strengths and limitations. FNA demonstrates higher sensitivity, while both techniques show high specificity.

Keywords: Breast cancer; Fine Needle aspiration; Core Needle Biopsy; Sensitivity; Specificity; Diagnosis

1. Introduction

Breast cancer (BC) is a significant health issue and the most common malignancy in women worldwide, early detection is crucial for optimal treatment and patient outcome (1). Early detection and treatment are crucial in reducing BC mortality (2). While the typical presentation of BC is a painless, progressive lump, most breast lumps are benign (3). In addition, a need for accurate and reliable diagnostic techniques for effective detection and treatment. Fine needle aspiration cytology (FNA) and core needle biopsy (CNB) are two commonly used minimally invasive techniques for diagnosing breast lesions. These techniques involve extracting cells or tissue samples from the breast for analysis.

* Corresponding author: Qing Li

It is crucial to investigate which procedure is safest and has a positive outcome for breast cancer patients, this includes the use of all clinical approaches safe to provide a definitive, error-free diagnosis of breast cancer. Therefore, there is ongoing debate regarding the sensitivity and specificity of FNA and CNB in accurately diagnosing breast cancer (4). While both FNA and CNB have their advantages and limitations, it is important to determine which technique provides better accuracy in diagnosing breast cancer. One study conducted in the United Kingdom aimed to investigate the outcome of patients with screen-detected breast lesions who had suspicious or malignant results on preoperative FNAC and/or CNB but ultimately had a benign diagnosis after excision biopsy. The study found that the problem of suspicious preoperative needle biopsies with benign excision biopsy is uncommon in the breast screening population and that these patients are not at an increased risk of being diagnosed with carcinoma in the subsequent 3 years.

In recent years, some studies have investigated and compared the diagnostic accuracy of FNA and CNB in breast cancer diagnosis. These studies have reported varying results, with some of them suggesting that the CNB procedure is more sensitive and specific than FNA, while others argue that FNA is just as effective with less or more impact on breast cancer diagnosis. We must understand the differences in the sensitivity and specificity between these two techniques and thus it is vital for optimizing diagnostic accuracy for patients with breast lesions. For instance, a study by Tripathi et al. (5). reported a sensitivity of 74.1% of FNAC and a specificity of 76.9%, while CNB had a sensitivity of 85.2% and specificity of 92.9%, with combined sensitivity and specificity of 89.3% and 85.7% respectively. showing CNB to be higher in both sensitivity and specificity than FNAC. A study by Saha et al. (6). found a sensitivity of 69% and specificity of 100% in FNAC; and for CNB, a sensitivity of 88.3% and specificity of 100% was found. therefore, demonstrating CNB to be higher in sensitivity compared to FNAC in breast cancer diagnosis. Nevertheless, both CNB and FNAC can be integrated into diagnostic strategies to improve the accuracy of diagnosis as previously explored by Brancato et al. (7). despite the study showed CNB to be better in sensitivity but lower in specificity in comparison to FNAC. These contrasting results highlight the need for a comprehensive meta-analysis to evaluate and compare the sensitivity and specificity of FNA and CNB in BC diagnosis.

There are several limitations when it comes to the identification of certainty of the use of both diagnostic techniques which include sample sizes, short follow-up period, lack of subgroup analysis, cost consideration, and effectiveness (5, 6) in other studies lack of direct comparison, operator variability, indirect comparisons, potential underestimation of sensitivity, and inadequate rate where FNAC could have an effect on the diagnostic accuracy and impact the sensitivity (7).

Thus, in this present study, we aim to compare the sensitivity and specificity of recent studies on Fine Needle Aspiration (FNA) and Core Needle Biopsy (CNB) in diagnosing BC.

2. Methods

2.1. Search Strategy

A meticulous exploration of the PubMed, Google Scholar, Cochrane Library, and Embase databases up to November 20, 2021, was conducted to determine relevant literature. Search strings incorporating terms like (breast cancer) OR neoplasm) AND diagnosis) AND fine needle aspiration) AND core needle biopsy) AND diagnosis) AND Sensitivity) OR specificity) AND Analysis was retained. The studies and search results underwent evaluation by two independent reviewers based on full-text assessments.

2.2. Data Collection

The search process was independently assessed by two reviewers, with any disparities in inclusions resolved through discussion. General characteristics of the included studies, such as study design, publication year, needle size gauge, authorship, country, and patient count, are detailed in Table 1.

2.3. Quality assessment

In this study, we employed the Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1 risk of bias tool to objectively assess the quality of the trials. We evaluated potential bias in the following areas: (1) random sequence generation, (2) allocation concealment, (3) blinding, (4) incomplete data, (5) selective reporting, and other relevant factors. Trials were classified as 'high risk' if they exhibited bias in one or more critical domains. A trial was considered 'low risk' if it demonstrated a low risk of bias across all critical domains. Trials not clearly falling into either category were classified as 'unclear,' as illustrated in Figures 4 and 5. Any disagreements between researchers were resolved through discussion with the corresponding author.

2.4. Inclusion Criteria

- Patients diagnosed with breast cancer are suspected of metastasis.
- Included studies providing sufficient data.
- Published case-controlled studies examining the accuracy of US-CNB correlation.
- Retrospective and prospective study designs.

2.5. Exclusion Criteria

- Studies lacking targeted data.
- Incomplete manuscripts.
- Meta-analyses.
- Non-English publications.
- Dissertations.

2.6. Statistical Analysis

Statistical analyses were executed using Review Manager 5.4 (RevMan). The Mantel-Haenszel method was devoted to statistical computations. Dichotomous data were analyzed for odds ratios (OR), and 95% confidence intervals were analyzed to assess statistical differences between outcomes. The results were graphically presented using forest plot graphs. We utilized a random effects model, considering any P-value less than 0.05 as statistically significant.

3. Results

The preliminary search identified 720 studies, which were refined to 412 after eliminating duplicates. Following screening, 308 studies were subjected to a detailed full-text review, eventually resulting in the inclusion of five studies for meta-analysis. The process of study selection, along with the reasons for inclusion and exclusion, is elucidated in Figure 1.

3.1. Characteristics of Included Studies

Of the five selected studies, three retrospective methodologies and two utilized prospective designs. Geographically, the studies were distributed across various regions, including Asia, Europe, and the United States, offering a diverse perspective on the subject matter. Needle diameters utilized in US-CNB ranged from 14 to 22 gauges, reflecting varying clinical practices. Similarly, needle diameters for US-FNA ranged from 21 to 25 gauges, highlighting the heterogeneity in procedural techniques (refer to Table 1 for detailed study characteristics).

Table 1 Characteristics of included study

Author	Year	Study design	Country	Total number of patients	Sensitivity FNA/CNB	Specificity FNA/CNB	Age	Needle size (gauge)
Topps et al.(8)	2018	Retrospective	UK	215	149 / 77	216/92	55.1	14
Rikiya N et al.(9)	2017	Retrospective	Japan	2464	317 / 151	170/487	56.0	21 (fn) 16 (cn)
Suvi R et al.(10)	2013	Prospective	Finland	66	27 / 40	37/45	28-90	21-22 (fn) 16 (cn)
Roshni et al.(11)	2009	Retrospective	USA	25	31/38	43/38	52.5	18
Vidya et el.(12)	2017	prospective	UK	38	17/21	5/6	-	14

Table 2 Outcomes of Included Studies

Author	Sensitivity FNA/CNB	Specificity FNA/CNB
Topps et al. (8)	149 / 77	216/92
Rikiya N et al. (9)	317 / 151	170/487
Suvi R et al. (10)	27 / 40	37/45
Vidya et el. (12)	31/38	43/38
Roshni et al. (11)	17/21	5/6

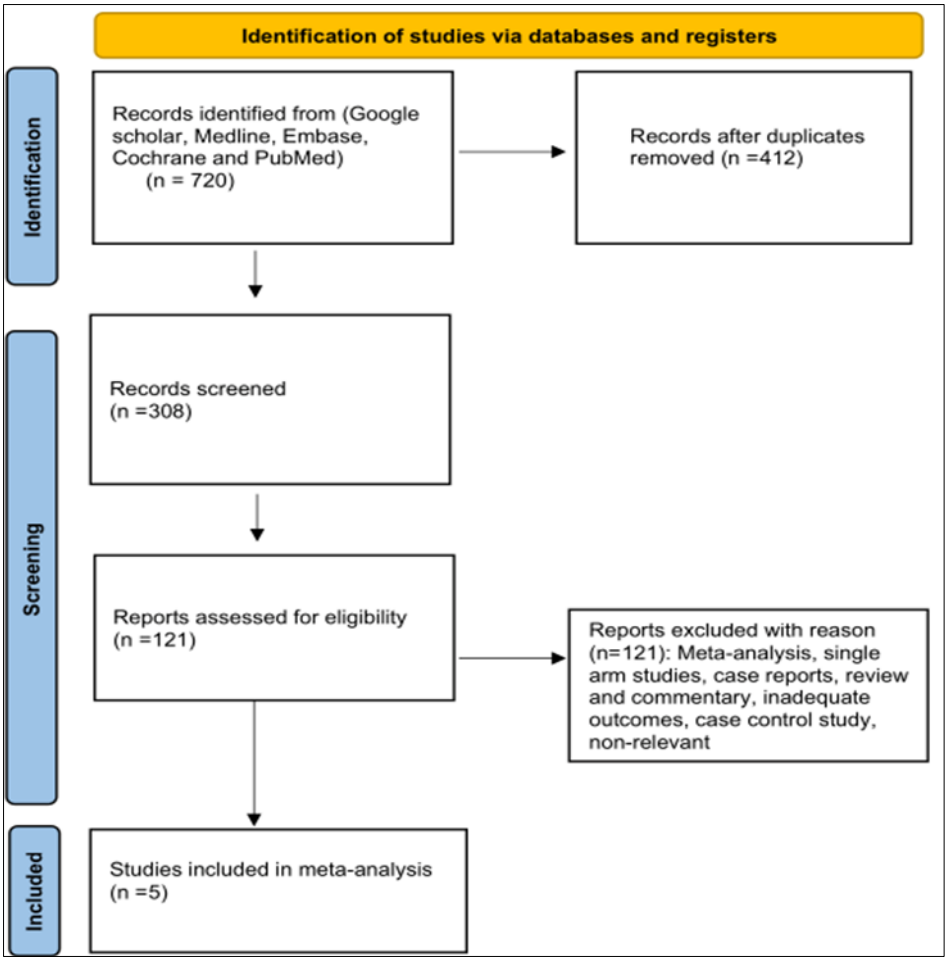

Figure 1 Prisma flow of selected studies

Sensitivity was assessed regarding FNA and CNB, resulting in rates of 68.6% and 88.1%, respectively. An analysis of five studies involving a total of 1,177 patients revealed that 541 patients underwent FNA, while 397 underwent CNB. The comparison between FNA and CNB demonstrated statistically significant findings, with an OR of 0.30 (95% CI [0.21, 0.41], $P < 0.00001$), indicating a substantial variance in diagnostic accuracy between the two-biopsy methods Figure 2.

Specificity for FNA was found to be 96.1%, while CNB demonstrated a specificity of 97.2%. In the analysis of diagnostic procedures across five studies encompassing 1,177 patients, 471 patients underwent FNAC, and 668 patients underwent CNB. The comparison between FNAC and CNB revealed non-significant findings, with an OR of 0.54 (95% CI [0.17, 1.69], $P = 0.29$) Figure 3.

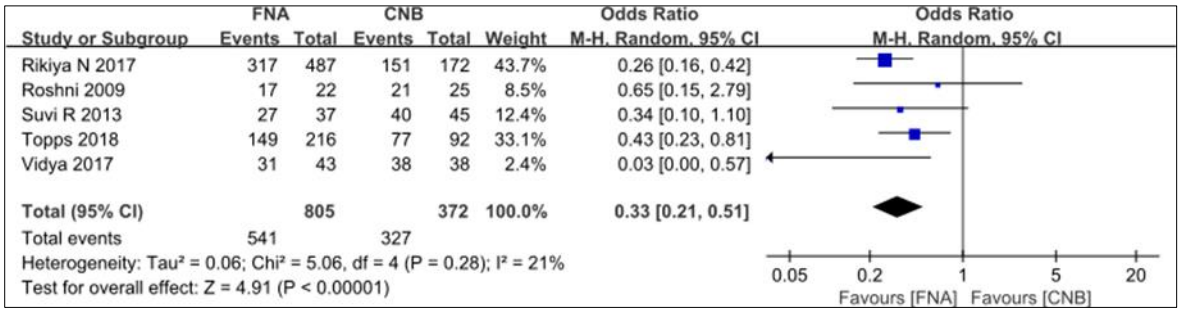

Figure 4 Forest plot of sensitivity between FNA and CNB

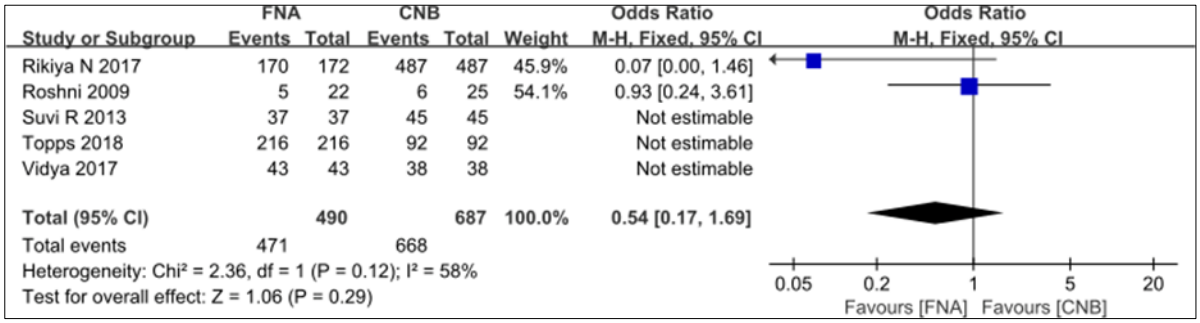

Figure 5 Forest plot of specificity between FNA and CNB

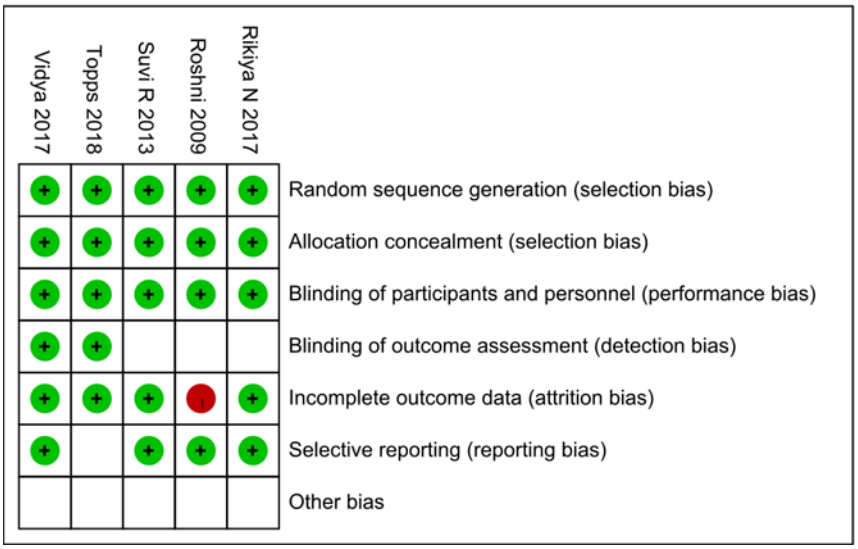

Figure 6 Risk of bias summary: review authors' judgments about each risk of bias item for each included study

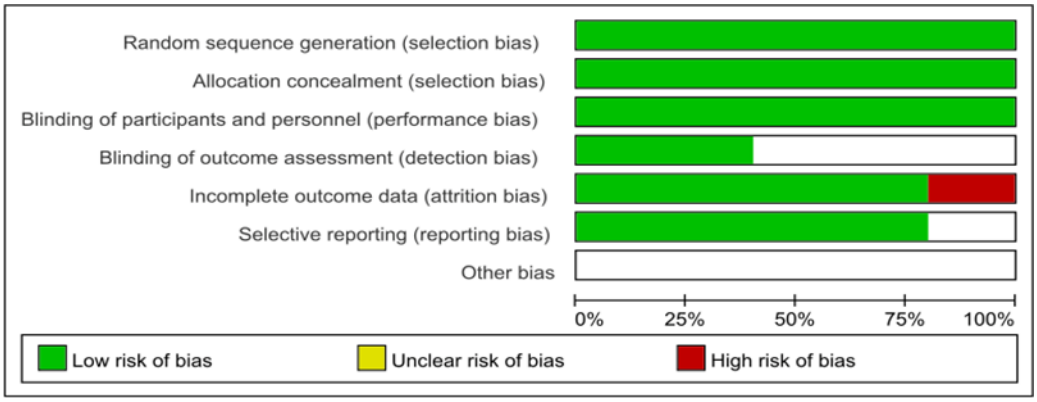

Figure 7 Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies

4. Discussion

Breast cancer remains a prevalent and potentially lethal disease among women globally. Modern diagnostic techniques such as FNAC and CNB are widely employed, particularly in the early stages of BC (13). Numerous studies have compared the efficacy of FNAC and CNB(14, 15).

Imaging techniques are effective for screening, but minimally invasive procedures like FNAC and CNB guide most treatments, offering high accuracy comparable to histopathological outcomes (16). The debate over whether cytological or tissue-level changes are more clinically accurate continues, with mixed results from various studies (17, 18). In the recent past, several studies have tried to resolve this debate. This underscores the need for individual clinical experience in assessing the effectiveness of these diagnostic methods (19).

In our study, the sensitivity of FNAC was 68.6%, whereas CNB demonstrated a higher sensitivity of 88.1%. This difference was statistically significant, with an odds ratio (OR) of 0.30 (95% CI [0.21, 0.41], $P < 0.00001$). However, a previous meta-analysis reported sensitivities of 72.2% for FNAC (95% CI 63.9–79.3) and 83.3% for CNB (95% CI 70.0–91.4), with no significant difference in sensitivity ($P = 0.13$)(20). This discrepancy could suggest that the effectiveness of FNAC and CNB in diagnosing the condition may vary across different studies or populations. More research may be needed to understand the reasons behind these differences in sensitivity and to determine the most accurate diagnostic method for the specific condition under investigation.

In the current study, FNAC demonstrated a specificity of 96.1%, whereas CNB exhibited a specificity of 97.2%. Notably, the variance in specificity between FNAC and CNB was not deemed statistically significant, as indicated by a p-value of 0.29. It is noteworthy to consider previous research findings that reported a range of specificities for FNAC and CNB spanning from 72.4% to 100% in different studies. These varying specificity values underscore the need for further examination and comparison across multiple studies to gain a comprehensive understanding of the diagnostic performance of FNAC and CNB under investigation (5, 6, 21, 22).

Our study included patients diagnosed with BC with suspected metastasis, potentially including some non-metastatic cases. Additionally, sonographically benign lymph nodes may contain small metastatic foci that US-FNA might miss. However, studies performing FNAs on all ultrasound-identified lymph nodes did not show reduced sensitivity (57%-80%) or specificity (96%-100%) compared to studies with stricter criteria (23, 24, 25, 26, 27, 28). These findings suggest that overall sensitivity could improve without losing specificity by broadening the ultrasound criteria for performing FNA. When considering costs, fine-needle aspiration cytology (FNAC) appears to be more favorable than sentinel lymph node biopsy due to its lower cost. However, it is important to note that comprehensive cost analyses for scenarios involving FNAC on all lymph nodes have not yet been conducted. This suggests that while FNAC may be a more cost-effective option compared to sentinel lymph node biopsy, further research is needed to fully assess the overall cost implications of using FNAC for all lymph nodes (29, 30, 31). Currently, most experts prefer CNB over FNAC for diagnosing breast lesions, and CNB is becoming the standard procedure in many developed countries' medical centers (32, 33, 34).CNB is becoming the standard procedure in most medical centers in developed countries. Nevertheless, FNAC remains advantageous due to its lower cost, less invasive nature, and quicker results (35).

Limitations

This study has several limitations. The inclusion criteria based on suspected metastasis might have included non-metastatic cases, potentially impacting the results. The study also included a range of needle diameters used in US-CNB, reflecting diverse clinical practices that could affect comparability. Additionally, a comprehensive cost analysis of performing FNA on all lymph nodes was not conducted, which could influence the overall assessment of these diagnostic methods.

5. Conclusion

In summary, the meta-analysis found out FNA and CNB are crucial tools in diagnosing breast carcinoma, each with unique strengths and limitations. FNA demonstrates higher sensitivity, while both techniques show similar specificity. Despite ongoing debates and mixed study results, both methods remain integral to the diagnostic process. Clinical experience and further research with standardized protocols are essential to optimize diagnostic accuracy and improve patient outcomes.

Compliance with ethical standards

Acknowledgments

We would like to express our gratitude to all the authors for their contributions to the completion of the manuscript. A special acknowledgment goes to Professor Li Qing for his generous support.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Funding

The Project is supported by Shandong Natural Science Foundation（No. ZR2021MH325）and Shandong Medical Association Clinical Research Fund Qilu Special Project（No. YXH2022ZX02167）

Availability of Data and Material

The studies included were retrieved from PubMed, Google Scholar, Cochrane Library, Embase, and Web of Science database.

Author Contributions

IHS oversaw conceptualizing, acquiring and designing the work, while ZM, ZH, LQ, and IAD were responsible for acquiring, analysing, and interpreting the data. LQ took on interpreting the data, and all authors carefully reviewed the manuscript.

References

[1] Smolarz B, Nowak AZ, Romanowicz H. Breast cancer—epidemiology, classification, pathogenesis and treatment (review of literature). Cancers. 2022;14(10):2569.

[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49.

[3] Beiki O, Hall P, Ekbom A, Moradi T. Breast cancer incidence and case fatality among 4.7 million women in relation to social and ethnic background: a population-based cohort study. Breast Cancer Res. 2012;14(1):R5.

[4] Hukkinen K, Kivisaari L, Heikkilä PS, Von Smitten K, Leidenius M. Unsuccessful preoperative biopsies, fine needle aspiration cytology or core needle biopsy, lead to increased costs in the diagnostic workup in breast cancer. Acta oncologica. 2008;47(6):1037-45.

[5] Tripathi K, Yadav R, Maurya SK. A comparative study between fine-needle aspiration cytology and core needle biopsy in diagnosing clinically palpable breast lumps. Cureus. 2022;14(8).

[6] Saha A, Mukhopadhyay M, Das C, Sarkar K, Saha AK, Sarkar DK. FNAC versus core needle biopsy: a comparative study in evaluation of palpable breast lump. Journal of clinical and diagnostic research: JCDR. 2016;10(2):EC05.

[7] Brancato B, Crocetti E, Bianchi S, Catarzi S, Risso GG, Bulgaresi P, et al. Accuracy of needle biopsy of breast lesions visible on ultrasound: audit of fine needle versus core needle biopsy in 3233 consecutive samplings with ascertained outcomes. The Breast. 2012;21(4):449-54.

[8] Topps AR, Barr SP, Pikoulas P, Pritchard SA, Maxwell AJ. Pre-operative axillary ultrasound-guided needle sampling in breast cancer: comparing the sensitivity of fine needle aspiration cytology and core needle biopsy. Annals of surgical oncology. 2018;25:148-53.

[9] Nakamura R, Yamamoto N, Miyaki T, Itami M, Shina N, Ohtsuka M. Impact of sentinel lymph node biopsy by ultrasound-guided core needle biopsy for patients with suspicious node positive breast cancer. Breast Cancer. 2018;25:86-93.

[10] Rautiainen S, Masarwah A, Sudah M, Sutela A, Pelkonen O, Joukainen S, 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] Rao R, Lilley L, Andrews V, Radford L, Ulissey M. Axillary staging by percutaneous biopsy: sensitivity of fine-needle aspiration versus core needle biopsy. Annals of surgical oncology. 2009;16:1170-5.

[12] Vidya R, Iqbal FM, Bickley B. Pre-operative axillary staging: should core biopsy be preferred to fine needle aspiration cytology? Ecancermedicalscience. 2017;11.

[13] McManus DT, Anderson NH. Fine needle aspiration cytology of the breast. Current Diagnostic Pathology. 2001;7(4):262-71.

[14] Khemka A, Chakrabarti N, Shah S, Patel V. Palpable breast lumps: Fine-needle aspiration cytology versus histopathology: A correlation of diagnostic accuracy. Internet J Surg. 2009;18(1):1-25.

[15] Tariq GR, Haleem A, Zaidi AH, Afzal M, Abbasi S. Role of FNA cytology in the management of carcinoma breast. Journal of the College of Physicians and Surgeons--pakistan: JCPSP. 2005;15(4):207-10.

[16] Nassar A. Core needle biopsy versus fine needle aspiration biopsy in breast—a historical perspective and opportunities in the modern era. Diagnostic cytopathology. 2011;39(5):380-8.

[17] Kar A, Satapathy B, Pattnaik K, Dash PK. Trucut biopsy vs FNAC of pelvic tumors-who wins the match? Journal of cytology. 2018;35(3):179-82.

[18] Moschetta M, Telegrafo M, Carluccio D, Jablonska J, Rella L, Serio G, et al. Comparison between fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) in the diagnosis of breast lesions. Il Giornale di Chirurgia-Journal of the Italian Surgical Association. 2014;35(7):171-6.

[19] Supriya S, Nirmala C, Raghupathi A. Fine needle aspiration cytology verses core needle biopsy in breast lesions-a comparative study. International Journal of Current Research and Review. 2015;7(9):52.

[20] 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.

[21] Wang M, He X, Chang Y, Sun G, Thabane L. A sensitivity and specificity comparison of fine needle aspiration cytology and core needle biopsy in evaluation of suspicious breast lesions: A systematic review and meta-analysis. The breast. 2017;31:157-66.

[22] Nagar S, Iacco A, Riggs T, Kestenberg W, Keidan R. An analysis of fine needle aspiration versus core needle biopsy in clinically palpable breast lesions: a report on the predictive values and a cost comparison. The American journal of surgery. 2012;204(2):193-8.

[23] Mainiero MB, Cinelli CM, Koelliker SL, Graves TA, Chung MA. Axillary ultrasound and fine-needle aspiration in the preoperative evaluation of the breast cancer patient: an algorithm based on tumor size and lymph node appearance. AJR Am J Roentgenol. 2010;195(5):1261-7.

[24] Sianesi M, Ceci G, Ghirarduzzi A, Del Rio P, Guazzi A, Pisanelli B, et al. Use of axillary ultrasonography in breast cancer: a useful tool to reduce sentinel node procedures. Ann Ital Chir. 2009;80(4):315-8.

[25] Koelliker SL, Chung MA, Mainiero MB, Steinhoff MM, Cady B. Axillary lymph nodes: US-guided fine-needle aspiration for initial staging of breast cancer--correlation with primary tumor size. Radiology. 2008;246(1):81-9.

[26] Altomare V, Guerriero G, Carino R, Battista C, Primavera A, Altomare A, et al. Axillary lymph node echo-guided fine-needle aspiration cytology enables breast cancer patients to avoid a sentinel lymph node biopsy. Preliminary experience and a review of the literature. Surg Today. 2007;37(9):735-9.

[27] Bonnema J, van Geel AN, van Ooijen B, Mali SP, Tjiam SL, Henzen-Logmans SC, et al. Ultrasound-guided aspiration biopsy for detection of nonpalpable axillary node metastases in breast cancer patients: new diagnostic method. World J Surg. 1997;21(3):270-4.

[28] Kuenen-Boumeester V, Menke-Pluymers M, de Kanter AY, Obdeijn IM, Urich D, Van Der Kwast TH. Ultrasound-guided fine needle aspiration cytology of axillary lymph nodes in breast cancer patients. A preoperative staging procedure. Eur J Cancer. 2003;39(2):170-4.

[29] Genta F, Zanon E, Camanni M, Deltetto F, Drogo M, Gallo R, et al. Cost/accuracy ratio analysis in breast cancer patients undergoing ultrasound-guided fine-needle aspiration cytology, sentinel node biopsy, and frozen section of node. World J Surg. 2007;31(6):1155-63.

[30] Davis JT, Brill YM, Simmons S, Sachleben BC, Cibull ML, McGrath P, et al. Ultrasound-guided fine-needle aspiration of clinically negative lymph nodes versus sentinel node mapping in patients at high risk for axillary metastasis. Ann Surg Oncol. 2006;13(12):1545-52.

[31] Boughey JC, Moriarty JP, Degnim AC, Gregg MS, Egginton JS, Long KH. Cost modeling of preoperative axillary ultrasound and fine-needle aspiration to guide surgery for invasive breast cancer. Ann Surg Oncol. 2010;17(4):953-8.

[32] Willems SM, Van Deurzen C, Van Diest P. Diagnosis of breast lesions: fine-needle aspiration cytology or core needle biopsy? A review. Journal of clinical pathology. 2012;65(4):287-92.

[33] Pagni P, Spunticchia F, Barberi S, Caprio G, Paglicci C. Use of core needle biopsy rather than fine-needle aspiration cytology in the diagnostic approach of breast cancer. Case reports in oncology. 2014;7(2):452-8.

[34] Radhakrishna S, Gayathri A, Chegu D. Needle core biopsy for breast lesions: An audit of 467 needle core biopsies. Indian Journal of Medical and Paediatric Oncology. 2013;34(04):252-6.

[35] Arina A, Beckett M, Fernandez C, Zheng W, Pitroda S, Chmura SJ, et al. Tumor-reprogrammed resident T cells resist radiation to control tumors. Nature communications. 2019;10(1):3959.