Original Article

Comparing core needle biopsy and surgical excision in breast cancer diagnosis: implications for clinical practice from a retrospective cohort study

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Background: Preoperative ultrasound-guided core needle biopsy (CNB) is currently the standard procedure for managing breast illnesses. However, the differences in outcomes between CNB and surgical excision (SE) have not been thoroughly assessed. This study aimed to explore the disparities in pathological outcomes between these two procedures, using a large sample dataset.

Methods: This retrospective study consecutively included patients who underwent CNB and SE at Shenzhen People's Hospital from May 2016 to June 2023. Immunohistochemistry (IHC) was utilized to determine the status of estrogen receptor (ER), progesterone receptor (PgR), human epidermal growth factor receptor-2 (HER2), and Ki-67. Patients presenting with HER2 IHC 2+ underwent additional fluorescence in situ hybridization (FISH) examination. The cutoff value for high Ki-67 expression was established at 14%. Molecular subtypes were classified into four groups (Luminal A, Luminal B, Triple-negative, and HER2-positive) and five groups [Luminal A, Luminal B+ (HER2-positive), Luminal B– (HER2-negative), Triple-negative, and HER2-positive], based on different criteria.

Results: A total of 4,209 patients were included in this study. Post-surgical confirmation revealed 2,410 cases as benign and 1,799 as malignant. Among the malignant cases, 334 were excluded due to either not having undergone direct surgery or having incomplete IHC results. The remaining 1,465 cases underwent IHC testing. CNB demonstrated a 97% concordance rate (CR) in diagnosing benign cases. The CRs for diagnosing invasive breast cancer (IBC) and carcinoma in situ (CIS) were 92% and 54%, respectively. ER, PgR, HER2, and Ki-67 exhibited CRs of 94%, 91%, 98%, and 84%, respectively. In the four-group classification, the overall diagnostic CR was 82%, with CRs for Luminal A, Luminal B, HER2-positive, and triple-negative breast cancer (TNBC) being 84%, 82%, 78%, and 85%, respectively. Under the five-group classification, the overall diagnostic CR was also 82%, with CRs for Luminal A, Luminal B+, Luminal B–, HER2-positive, and TNBC being 86%, 85%, 94%, 88%, and 92%, respectively.

Conclusions: This study demonstrates that CNB is highly accurate in differentiating benign from malignant breast lesions, particularly showing significant consistency in the diagnosis of molecular subtypes, providing a reliable reference for clinical diagnosis.

Keywords: Breast cancer (BC); surgical excision (SE); core needle biopsy (CNB); molecular subtypes

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Introduction

Breast cancer (BC) stands as a prevalent malignant tumor with substantial implications for the physical and psychological well-being of affected individuals (1). Preoperative core needle biopsy (CNB) is widely acknowledged as the gold standard procedure for managing breast diseases, utilizing various guidance methods such as ultrasound, magnetic resonance imaging (MRI), and mammography (2-4). Ultrasound-guided breast biopsy is widely used in clinical practice due to its convenience and radiation-free advantage (4,5). By obtaining samples of breast tissue for pathological examination, it becomes possible to determine the tumor type, grade, and molecular subtype, which are crucial elements in devising an optimal treatment plan (6).

The method of CNB is not devoid of inherent limitations. Tumor heterogeneity, inadequate sampling, and sampling bias can lead to inaccuracies in CNB pathology results (7,8). These issues stem from the reliance on examining a small tissue sample to ascertain tumor type and grade. Insufficient sample size or the presence of sampling bias may lead to incorrect diagnoses. Potential concerns include the risks of misdiagnosing benign and malignant tumors, inaccuracies in identifying molecular subtypes, and the possibility of underestimating the pathological grade (9-12).

This study endeavored to investigate the concordance between surgical pathology and CNB pathology, thereby elucidating the factors underlying any discrepancies noted. We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-198/rc).

Methods

Patient population

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Review Board of Shenzhen People's Hospital (Approval No. LL-KY-2023120102; Approval Date: 1 December 2023). The requirement for individual consent for this retrospective analysis was waived. This study was conducted on all patients who had undergone CNB in the Ultrasound Department of Shenzhen People's Hospital from May 2016 to June 2023. All CNB procedures were performed under the guidance of ultrasound. The inclusion criteria were as follows: (I) the biopsy was ultrasound-guided and carried out at this center. (II) No treatment was administered prior to CNB. (III) Surgery was ultimately conducted, and surgical pathology results were obtained. (IV) For malignant lesions, immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) results were required, with additional FISH testing performed if human epidermal growth factor receptor-2 (HER2) IHC 2+ was indicated. The exclusion criteria were as follows: (I) patients who underwent biopsy but did not undergo surgery within two weeks. (II) Patients with malignant biopsy results who did not undergo IHC testing. (III) Patients with malignant surgical pathology results who did not undergo IHC testing.

Ultrasound-guided biopsy

Prior to performing CNB, a comprehensive examination of the breast lesion was meticulously conducted, followed by the formulation of distinct biopsy protocols based on the mass type: (I) for masses with an anteroposterior diameter greater than 15 mm, a protocol of three biopsies was employed, progressing methodically from deep to shallow. (II) For masses with an anteroposterior diameter less than 15 mm, the protocol focused exclusively on the central part of the mass. (III) In cases of cystic-solid masses, the solid component was specifically targeted. (IV) Predominantly cystic masses underwent sampling primarily on the cyst wall. The entire biopsy procedure was collaboratively performed by two senior doctors, each with over a decade of expertise in ultrasound-guided interventions. All CNB are conducted using a 14 g TSK automatic biopsy gun (TSK Laboratory, Oisterwijk, the Netherlands). For each breast lesion, a minimum of three 14-gauge cores were extracted for subsequent pathological examination.

Surgical methods

Different surgical approaches were selected based on the results of the biopsy, encompassing a range of methods. These included fibroadenoma excision, segmental resection, breast-conserving surgery, and radical mastectomy for BC.

Pathology, IHC, and molecular subtypes

Surgical pathology findings served as the definitive diagnosis, classified according to the 2011 St. Gallen BC consensus as follows (6):

(I) Luminal A: hormone receptor-positive (HR+), HER2 (–), and Ki-67 (<14%);
(II) Luminal B–: HR (+), HER2 (–), and Ki-67 (>14%);
(III) Luminal B+: HR (+), HER2 (+), and any Ki-67;
(IV) HER2 positive: HR (–) and HER2 (+);
(V) Triple-negative breast cancer (TNBC): HR (–) and HER2 (–).

HR+ status was characterized by the presence of either estrogen receptor (ER) or progesterone receptor (PgR), where the percentage and intensity of stained cells exceed 1%. Conversely, when these criteria fell below this threshold, the status was categorized as hormone receptor-negative (HR–). To align with real-world clinical scenarios and ensure applicability, a Ki-67 cutoff of 14% was utilized to distinguish between Luminal A and B subtypes. Within the Luminal B subtype, further classification into Luminal B+ and Luminal B– was based on the HER2 status. In cases of HER2 where HER2 IHC is 2+, confirmation through FISH examination was required. This criterion reflects the average value for HR+/HER2– patients in CNB samples and the median value across all patients, thereby enhancing its practical utility.

Statistical analysis

All analyses were performed using the software SPSS 25.0 (IBM Corp., Armonk, NY, USA) and RStudio v2023.09.1+494 (SAS Institute, Inc., Cary, NC, USA). Figures were created using Illustrator CS6software (Adobe, San Jose, CA, USA). The *t*-test was utilized for numerical variables with a normal distribution, whereas the Chi-squared test was applied to categorical variables with a normal distribution. For variables with a non-normal distribution, the rank sum test was employed. Statistical significance was acknowledged at $P<0.05$.

The concordance rates (CRs) between CNB and surgical pathology for diagnosing the benign or malignant nature of breast lesions, as well as for evaluating receptor status and molecular subtypes, were assessed using the Kappa-value. Kappa-values were interpreted as follows: below 0.20 indicated poor agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.81–1.00 very good agreement. P values were determined using the chi-square test or Fisher's exact test, with values below 0.05 considered significant in two-tailed tests.

Results

Patient characteristics

A retrospective analysis was performed on all female patients who had undergone CNB in our department from January 2016 to June 2023, encompassing a total of 4,209 cases. Of these cases, 2,410 were diagnosed with benign conditions, and 1,799 were identified as having malignancies through surgical excision (SE). Among the malignant cases, 384 patients were excluded, with 334 due to either the absence of direct surgery or incomplete IHC results, and 50 cases where CNB misdiagnosed malignancies as benign. Comprehensive results from both IHC and FISH tests were available for the remaining 1,415 patients with malignancies (*Figure 1*, *Table 1*). There was no statistically significant difference in age, height, weight, or tumor location.

CNB in diagnosing benign or malignant tumors

In this study, out of 1,799 patients confirmed to have malignant tumors through surgery, the initial CNB accurately identified 1,749 BC patients but failed to detect cancer in 50 cases. The CR of CNB in this context was 0.98, as shown in *Table 2*.

CNB to distinguish between invasive cancer and carcinoma in situ (CIS)

In this study, CNB initially diagnosed 256 cases as CIS; however, subsequent surgical pathology confirmed that 118 of these cases were actually invasive cancer. The rate of upgrade to invasive cancer diagnosis was 0.46, as detailed in *Table 2*.

Comparison of CNB and SE for ER, PgR, HER2 status, and Ki-67 results

In the CNB samples, levels of HR expression and *HER2*

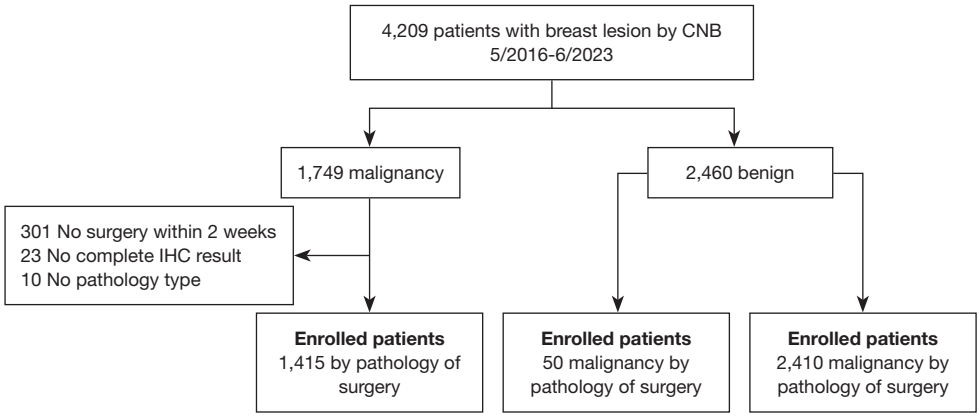

Figure 1 Flow chart. CNB, core needle biopsy; IHC, immunohistochemistry.

Table 1 Baseline patient characteristics

Variables	Total (n=4,209)	Benign (n=2,410)	Malignancy (n=1,799)	P value
Age (years), median (Q1, Q3)	44 (36, 52)	40 (32, 47)	49 (43, 58)	<0.001
Height (cm), median (Q1, Q3)	158 (154, 162)	158 (154, 162)	158 (154, 162)	0.66
Weight (kg), median (Q1, Q3)	57 (55, 60)	57 (55, 60)	57 (54, 60)	0.34
BI-RADS, n [%]				<0.001
3	680 [16]	666 [28]	14 [1]	
4a	1,738 [41]	1,560 [65]	178 [10]	
4b	561 [13]	159 [7]	402 [22]	
4c	875 [21]	25 [1]	850 [47]	
5	355 [8]	0 [0]	355 [20]	
Side, n [%]				0.76
Left	2,191 [52]	1,260 [52]	931 [52]	
Right	2,018 [48]	1,150 [48]	868 [48]	
Max, median (Q1, Q3)	18 (11, 28)	14 (10, 22)	23 (15, 34)	<0.001
Vertical, median (Q1, Q3)	14 (9, 21)	11 (8, 17)	18 (12, 25)	<0.001
Thickness, median (Q1, Q3)	9 (6, 14)	7 (5, 10)	13 (9, 17)	<0.001
Tissue composition, n [%]				<0.001
A	573 [14]	201 [8]	372 [21]	
B	3,157 [75]	1,953 [81]	1,204 [67]	
C	479 [11]	256 [11]	223 [12]	

Q1, first quartile; Q3, third quartile; BI-RADS, Breast Imaging Reporting and Data System.

gene expression consistently achieved a CR exceeding 0.9, with balanced accuracy (BA) results also surpassing the 0.9 threshold. It is noteworthy that a concordance rate of 0.99 was reached for HER2, demonstrating an exceptionally high level of agreement. Kappa-values were consistently above 0.8, indicating robust consistency in the assessments. However, a slightly diminished concordance was observed in the Ki-67 results, evidenced by a CR of 0.85, a BA value

Table 2 Concordance between CNB and SE for benign and malignant, CIS and IBC

Pathology type	CNB, n (%)	SE, n (%)	BA	CR	95% CI	Kappa	P value
Pathology category			0.98	0.99	0.98–0.99	0.97	<0.001
Benign	2,460 (58.45)	2,410 (57.26)					
Malignant	1,749 (41.55)	1,799 (42.74)					
Pathology grade			0.95	0.92	0.90–0.93	0.66	<0.001
CIS	256 (18.09)	138 (9.75)					
IBC	1,159 (81.91)	1,277 (90.25)					

CNB, core needle biopsy; SE, surgical excision; CIS, in situ carcinoma; IBC, invasive breast cancer; BA, balance accuracy; CR, confidence rate; CI, confidence interval.

Table 3 Concordance between CNB and SE for ER, PgR, HER2, and Ki-67 results

CNB	SE		BA	CR	Kappa	P value
	Neg	Pos				
ER			0.94	0.97	0.9	<0.001
Neg	262	17				
Pos	28	1,108				
PgR			0.91	0.94	0.84	<0.001
Neg	278	31				
Pos	49	1,057				
HER2			0.98	0.99	0.95	<0.001
Neg	1101	12				
Pos	10	292				
Ki-67			0.84	0.85	0.63	<0.001
≤14%	287	147				
>14%	63	918				

CNB, core needle biopsy; SE, surgical excision; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor-2; Neg, negative; Pos, positive; BA, balance accuracy; CR, confidence rate.

of 0.84, and a kappa value of 0.63, as reported in *Table 3*.

Comparison of CNB and SE for molecular subtypes

In the five-category molecular subtyping, an overall diagnostic CR of 0.83 was observed, along with a BA of 0.82. Notably, two subtypes exhibited BA values exceeding 0.9: TNBC and Luminal B+ with respective values of 0.92 and 0.94. Additionally, the BA values for Luminal A, Luminal B– (B minus), and HER2-positive (HER2+) were 0.86, 0.85, and 0.88, respectively. This resulted from surgical confirmation that some cases of Luminal A had transitioned to Luminal B–, and some HER+ cases had evolved into the Luminal B+ subtype. In the four-category molecular subtyping, the overall diagnostic CR remained at 0.83, with a consistent BA of 0.82. Among these subtypes, three surpassed the 0.8 threshold: Luminal A, Luminal B, and TNBC, with BA values of 0.84, 0.82, and 0.85, respectively. The BA value for the HER2+ subtype was recorded at 0.78, primarily due to the surgical confirmation of HER2+ status transitioning to Luminal B (*Table 4*, *Figures 2*,*3*).

Discussion

CNB represents the predominant technique for histological assessment of abnormal breast tissue (13,14).

Table 4 Concordance rates for molecular subtypes between CNB and SE (five subtypes, four subtypes)

CNB	SE					BA	CR	Kappa	P value
	Luminal A	Luminal B		HER2	TNBC				
		B–	B+						
Five subtypes						0.82	0.82	0.74	<0.001
Luminal A	276	127	2	0	2	0.86			<0.001
Luminal B									
B–	51	518	6	1	15	0.85			<0.001
B+	0	3	165	23	0	0.94			<0.001
HER2	1	3	12	94	1	0.88			<0.001
TNBC	1	6	0	3	105	0.92			<0.001
Four subtypes						0.82	0.83	0.70	<0.001
Luminal A	276	129		0	2	0.84			<0.001
Luminal B	51	692		24	15	0.82			<0.001
HER2	1	15		94	1	0.78			<0.001
TNBC	1	6		3	105	0.85			<0.001

CNB, core needle biopsy; SE, surgical excision; HER2, human epidermal growth factor receptor-2; TNBC, triple negative breast cancer; BA, balance accuracy; CR, confidence rate.

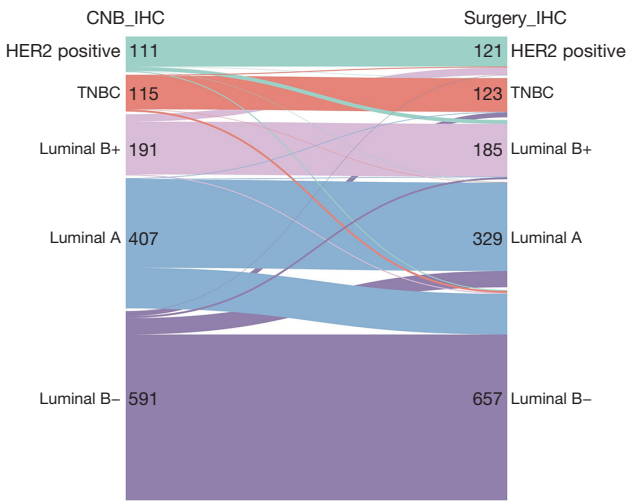

Figure 2 Sankey diagrams illustrating concordance for molecular subtypes in five subtypes between CNB and SE. CNB, core needle biopsy; IHC, immunohistochemistry; HER2, human epidermal growth factor receptor2; TNBC, triple negative breast cancer; SE, surgical excision.

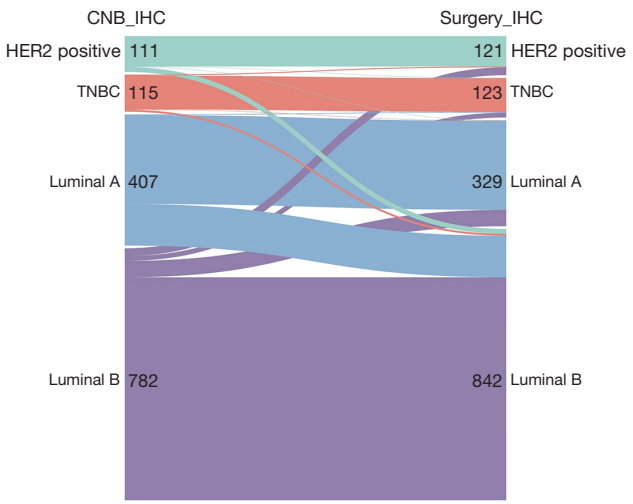

Figure 3 Sankey diagrams illustrating concordance for molecular subtypes in four subtypes between CNB and SE. CNB, core needle biopsy; IHC, immunohistochemistry; HER2, human epidermal growth factor receptor2; TNBC, triple negative breast cancer; SE, surgical excision.

The pathological findings derived from CNB play a pivotal role in guiding clinical treatment approaches and surgical planning (15). This study focused on the concordance between 14-gauge CNB and surgical pathology. It demonstrated a notable accuracy level of 0.98 in differentiating benign from malignant lesions, indicating

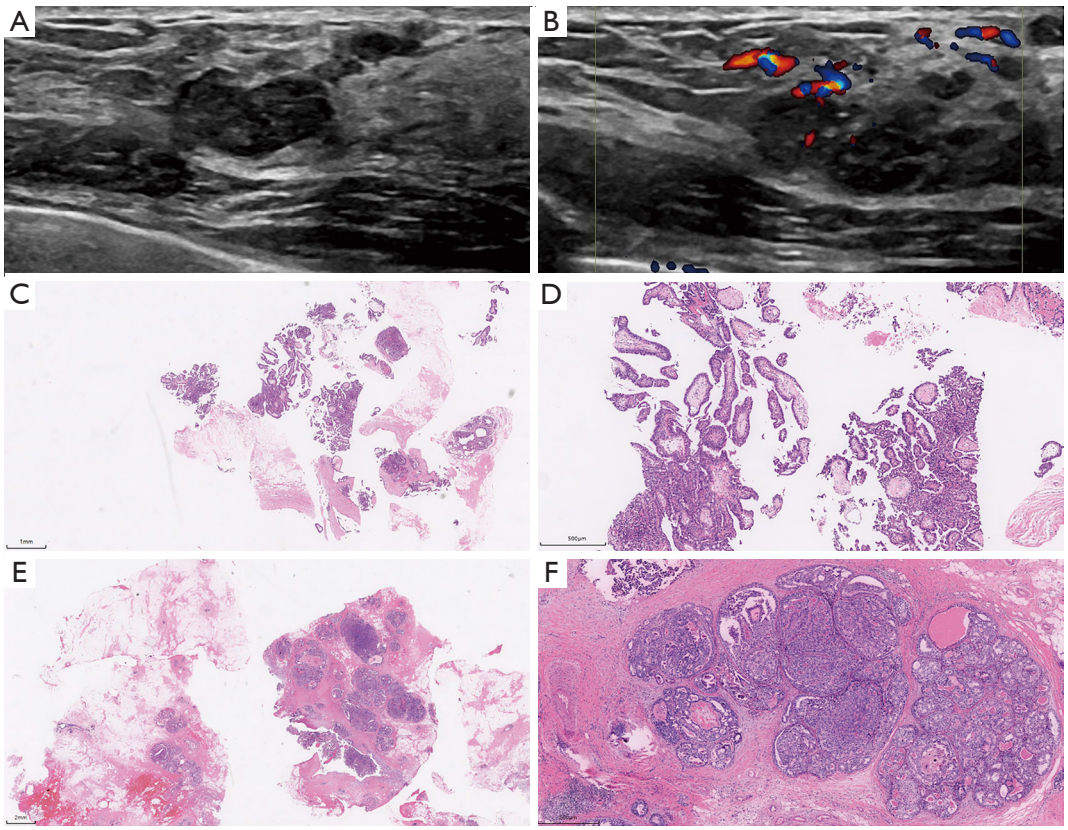

Figure 4 A 48-year-old female with a BI-RADS classification of 4a. (A) Grayscale ultrasound image of the lesion, demonstrating an intraductal papilloma. (B) CDFI ultrasound image of the lesion. (C-F) CNB and surgical pathology results at different magnifications, all stained with H&E: (C) CNB pathology result (1 mm), (D) CNB pathology result (500 μm), (E) surgical pathology result (2 mm), (F) surgical pathology result (500 μm). BI-RADS, Breast Imaging Reporting and Data System; CDFI, color Doppler flow imaging; CNB, core needle biopsy; H&E, hematoxylin and eosin.

significant consistency. The diagnostic precision for invasive cancers was recorded at 0.92. However, the accuracy in identifying CIS via CNB was notably lower, at 0.54. In terms of molecular subtype diagnosis, the four subtypes and five subtypes methods yielded an accuracy rate of 0.82 each.

CNB demonstrates high consistency in diagnosing benign and malignant lesions, with few cases of misdiagnosis observed. Our experiments suggest that misdiagnoses predominantly involve atypical ductal hyperplasia (ADH) or a combination of ADH and intraductal papilloma. Subsequent surgical pathology frequently reveals low-grade ductal carcinoma in situ (DCIS) or intermediate-grade DCIS, with rare progression to invasive cancer. Ultrasound imaging often lacks typical malignant features, and the maximum diameter of the mass is generally under 2 cm, presenting a lobulated shape with distinct margins. Some nodules may be associated with ductal alterations (16) (*Figure 4*).

The pathological diagnosis of ADH presents challenges, especially in differentiating it from low-grade DCIS. The distinction between ADH and low nuclear grade DCIS typically depends on criteria such as a lesion size of 2 mm or the involvement of two intact ducts. Specifically, a diagnosis of low nuclear grade DCIS is considered when ADH cells fill two or more intact ducts, or when the lesion exceeds 2 mm in size. These criteria are pivotal in enhancing diagnostic accuracy between ADH and low-grade DCIS, significantly influencing treatment decisions. It is crucial to acknowledge the challenges in pathological differentiation, underlining the necessity of comprehensive consideration of various clinical and pathological factors for precise diagnosis.

Although CNB exhibits high accuracy in diagnosing benign and malignant breast tumors, the evolving landscape of BC treatment strategies, advancements in

surgical techniques, and the introduction of novel adjuvant therapies have rendered a binary benign-malignant diagnosis insufficient for meeting contemporary clinical demands (17). For effective treatment planning, precise pathological grading is imperative, as different pathological grades necessitate varied therapeutic approaches (18). In managing breast diseases, there are notable distinctions in the treatment modalities for *in situ* and invasive carcinomas.

For invasive carcinomas, emphasis is placed on the employment of new adjuvant treatment methods (19-23). Conversely, for CIS, SE is generally the favored treatment modality (19,24,25). Given the heightened risk of underestimation by biopsy, intraoperative evaluation of sentinel lymph nodes is commonly undertaken. Since CIS does not penetrate the basement membrane and lacks metastatic potential, enhancing the diagnostic precision of *in situ* carcinoma is pivotal. This advancement helps in circumventing excessive axillary lymph node biopsies and mitigates unwarranted harm (26).

If pathological upgrading of a lower-grade lesion occurs during surgery, it may necessitate alterations in surgical tactics, such as widening the excision margins (27). This scenario can lead to patients forfeiting the option of breast-conserving surgery or enduring adverse outcomes such as secondary surgeries, thus diminishing the overall therapeutic benefits (24).

In our research, we observed that CNB was associated with increased tumor sizes and elevated Breast Imaging Reporting and Data System (BI-RADS) grades in patients with CIS undergoing surgical upgrades. Additionally, breast lesions manifesting as non-mass-like abnormalities demonstrated a higher propensity for pathological upgrading during surgery. Some studies suggest that enhancing the frequency of CNB or employing vacuum-assisted biopsy (VAB) instead may augment diagnostic precision in lesions with calcifications or heterogeneous internal echoes, consequently diminishing the incidence of pathological upgrades (28-31).

The introduction of neoadjuvant chemotherapy (NAC) in recent years has markedly enhanced the 5-year survival and breast conservation rates among BC patients, heralding a significant advancement in treatment (32-35). The application of NAC frequently relies on the IHC results derived from CNB. In our study assessing the diagnostic concordance of molecular subtypes, the rates for five and four subtypes were found to be 81.8% and 82.5%, respectively. Notably, the concordance rate for HER2 reached a remarkable 98%. We adhered to the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) HER2 testing guidelines by conducting FISH testing on IHC 2+ cases, which yielded high consistency in HER2 outcomes. Regarding the diagnosis of HR levels, the concordance rates for ER and PgR were 0.94 and 0.91, respectively, indicating high consistency. This can be attributed to our use of a cutoff value of 0.01 for tumor nuclear immunoreactivity, aligning with findings from previous studies. Although the consistency for Ki-67 was slightly lower than that for HER2, PgR, and ER, it still reached 0.84, with a Kappa-value of 0.63.

In analyzing the discrepancies in molecular subtyping between CNB and SE, sample size emerges as a primary factor. Ki-67 antigen, indicative of BC proliferative activity, often exhibits variance in diagnosis due to inadequate sampling. Studies have indicated that Ki-67 values obtained from surgical pathology are generally higher compared to those from CNB (14,36). In our study, of the 210 cases with inconsistent Ki-67 diagnoses, 63 were overestimated, and in 147 cases, Ki-67 levels were upgraded post-surgery. Literature suggests that increasing the number of CNB cores can enhance the consistency of Ki-67 diagnosis, yet this consistency plateaus at around six cores. Alternatively, switching from CNB to VAB may also improve Ki-67 diagnostic consistency. In ultrasound imaging, although breast lesions with high Ki-67 are typically larger than those with low Ki-67, the size difference is not statistically significant. Lesions with high Ki-67 often display characteristic spiculated features and thicker hyperechoic halos, aligning with prior research findings (*Figure 5*). High Ki-67 is associated with the hyperechoic halo around breast tumors, indicating infiltrative growth of tumor cells, which may lead to perifocal edema. This reflects rapid proliferation and invasiveness of tumor cells, with Ki-67 commonly used to assess this proliferative activity in clinical settings (37). ER and PgR diagnoses demonstrate high consistency, with some studies even suggesting higher positivity rates in CNB over SE for ER and PgR. This could be attributed to the slower or incomplete penetration of formalin in larger SE specimens, leading to reduced epitope detection. The ASCO/CAP guidelines advocate for CNB testing for ER and PgR (36).

The second major factor influencing the variance in molecular subtyping between CNB and SE is tumor heterogeneity. Research has indicated that HER2 heterogeneity in breast tumors can reach as high as 34% (38). In our study, 12 patients were deemed HER2– by CNB but positive by SE, whereas another 10 were HER2+ by CNB

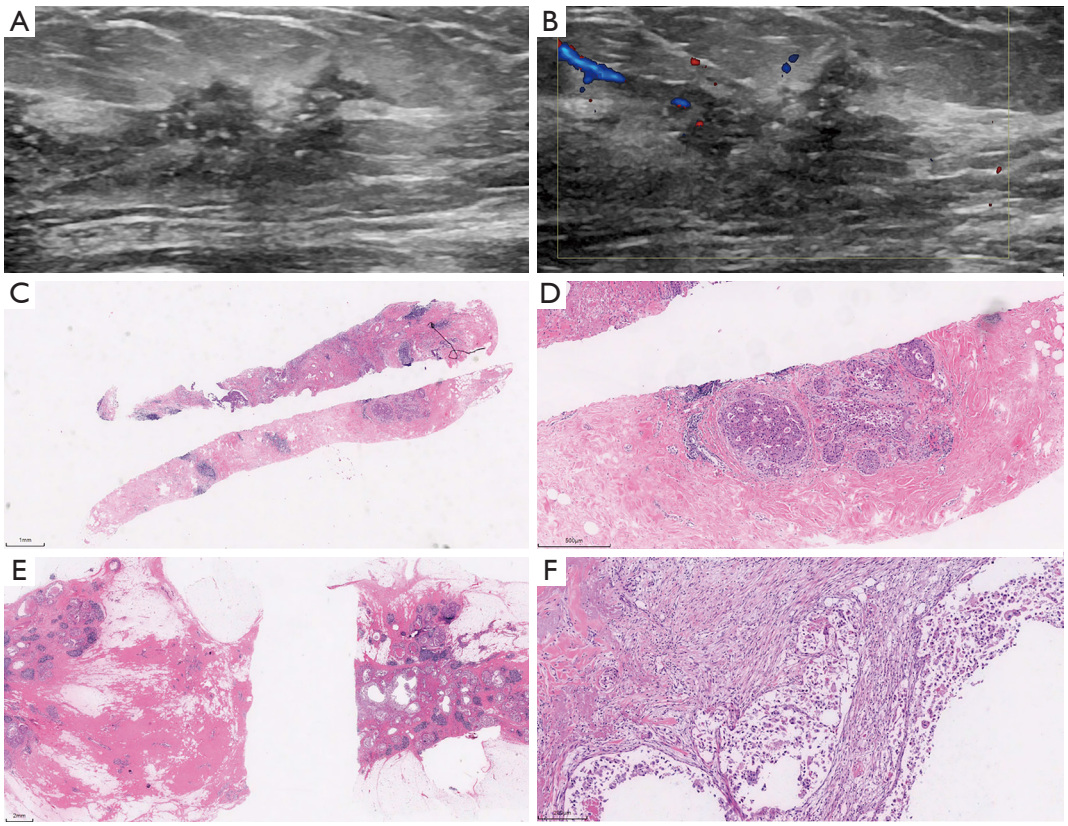

Figure 5 A 61-year-old female with a BI-RADS classification of 4b. (A) Grayscale ultrasound image of the lesion, with a hyperechoic halo surrounding the mass. (B) CDFI ultrasound image of the lesion. (C-F) CNB and surgical pathology results at different magnifications, all stained with H&E: (C) CNB pathology result (1 mm), (D) CNB pathology result (500 μm), (E) surgical pathology result (2 μm), (F) surgical pathology result (200 μm). BI-RADS, Breast Imaging Reporting and Data System; CDFI, color Doppler flow imaging; CNB, core needle biopsy; H&E, hematoxylin and eosin.

but negative post-surgery. Among these 22 patients with inconsistent diagnoses, over half had a mix of infiltrating and *in situ* carcinoma, exhibiting divergent expression patterns between the two. Three cases displayed a combination of lobular and ductal carcinoma. Furthermore, when CNB identifies *in situ* carcinoma with HER2 (2+), continuing FISH testing is often deemed unnecessary. However, our findings reveal that 40% of CNB-diagnosed DCIS experienced pathological upgrades during surgery. In such instances, CNB underestimates the pathological grade, and omitting additional FISH testing can lead to inaccuracies in molecular subtyping, potentially resulting in erroneous treatment strategies and impacting patient outcomes. Ultrasound images in patients with inconsistent HER2 expression commonly exhibit a blend of mass and non-mass lesions, featuring heterogeneous echogenicity and multiple fine calcification (39-41) (*Figure 6*).

We also analyzed the variables in the errors associated with CNB, including age, height, weight, tumor size, tissue composition, and BI-RADS. We found that tumor size is a factor leading to CNB misdiagnosis; the larger the tumor, the more likely it is to result in a CNB diagnostic error (Tables S1-S5).

Despite being a single-center study with a large sample size, the possibility of sample imbalance persists, introducing a potential bias in our findings. We did not perform IHC grading, nor did we address the accuracy of CNB in diagnosing nuclear-level DCIS. Our study was limited to 14 g CNB and did not include comparisons with other biopsy methods.

Conclusions

CNB demonstrates significant reliability in differentiating

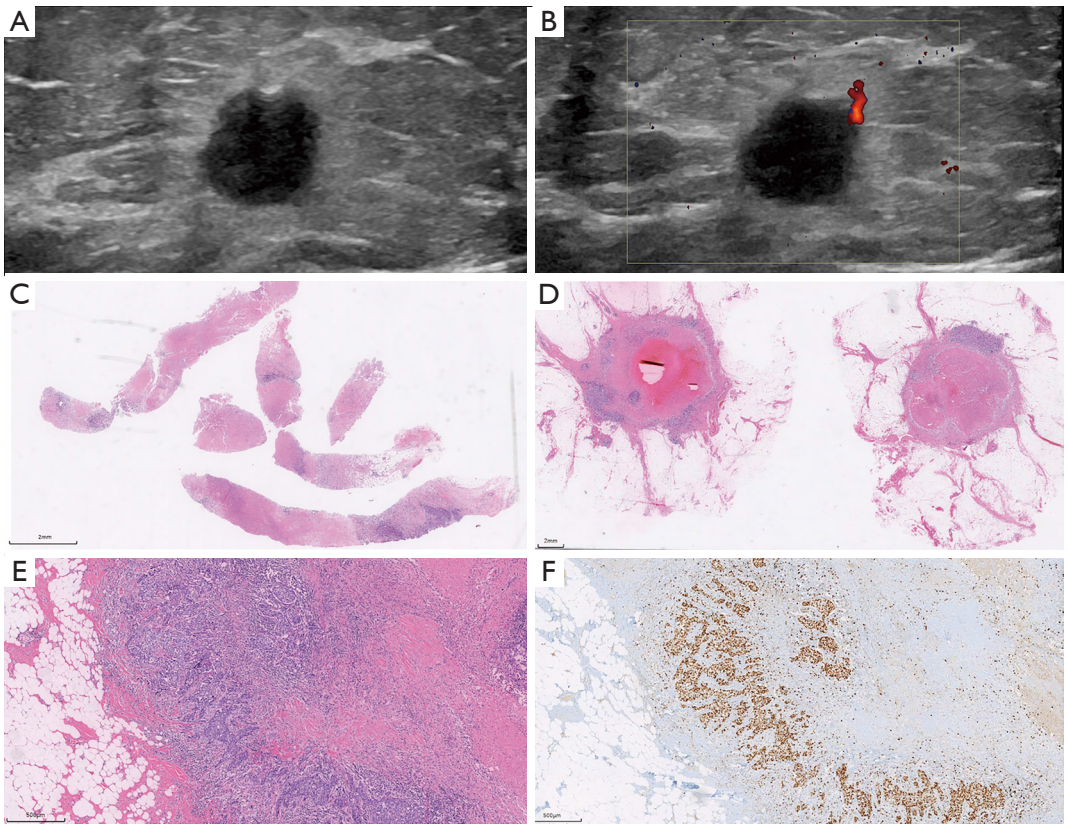

Figure 6 A 51-year-old female with a BI-RADS classification of 4c. (A) Grayscale ultrasound image of the lesion, demonstrating a non-mass lesion with calcifications. (B) CDFI ultrasound image of the lesion. (C-E) CNB and surgical pathology results at different magnifications, stained with H&E: (C) CNB pathology result (2 mm), (D) CNB pathology result (2 mm), (E) surgical pathology result (500 μm), (F) surgical pathology result (500 μm) stained with IHC. BI-RADS, Breast Imaging Reporting and Data System; CDFI, color Doppler flow imaging; CNB, core needle biopsy; H&E, hematoxylin and eosin; IHC, immunohistochemistry.

the characteristics of benign and malignant breast lesions. In diagnosing *in situ* and invasive carcinoma, there is a tendency to underestimate in CIS, particularly when it manifests as non-mass-like lesions in ultrasound imaging. Notably, CNB consistently exhibits high accuracy in molecular subtyping, effectively applicable in both four-group and five-group classifications.

Acknowledgments

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Footnote

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