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Original article

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

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ABSTRACT

Introduction: Core needle biopsy (CNB) has progressively replaced fine needle aspiration cytology (FNAC) in the diagnosis of breast lesions. Less information is available on how these tests perform for biopsy of ultrasound (US) visible breast lesions. This study examines the outcomes of CNB and FNAC in a large series ascertained with surgical histology or clinical-imaging follow-up.

Materials and methods: Retrospective five-year audit of 3233 consecutive US-guided needle samplings of solid breast lesions, from self-referred symptomatic or asymptomatic subjects, performed by six radiologists in the same time-frame (2003–2006): 1950 FNAC and 1283 CNB. The probability of undergoing CNB as a first test instead of FNAC was evaluated using logistic regression. Accuracy and inadequacy were calculated for each of CNB and FNAC performed as *first* test. Accuracy measures included equivocal or borderline/atypical lesions as positive results.

Results: The probability of CNB as a first test instead of FNAC increased significantly over time, when there was a pre-test higher level of suspicion, in younger (relative to older) women, with increasing lesion size on imaging, and for palpable (relative to impalpable) lesions. Inadequacy rate was lower for CNB (B1 = 6.9%) than for FNAC (C1 = 17.7%), $p < 0.001$, and specifically in malignant lesions (B1 = 0.9% *vs.* C1 = 4.5%; $p < 0.001$). False negative rate was equally low for both CNB and FNAC (1.7% each test). CNB performed significantly better than FNAC for absolute sensitivity (93.1% *vs.* 74.4%; $p < 0.001$) and complete sensitivity (97.4% *vs.* 93.8%; $p = 0.001$), however specificity was lower for CNB than FNAC (88.3% *vs.* 96.4%; $p < 0.001$). Absolute diagnostic accuracy was higher for CNB than FNAC (84.5% *vs.* 71.9; $p < 0.001$) while FNAC performed better than CNB for *complete* diagnostic accuracy (95.4% *vs.* 93.2; $p < 0.008$). In the small subgroup assessed with CNB after an inconclusive initial FNAC (231 cases) there was improved complete sensitivity (from 93.8% to 97.0%) however this also increased costs.

Conclusion: FNAC and CNB were generally performed in different patients, thus our study reported indirect comparisons of these tests. Although FNAC performed well (except for relatively high inadequacy), CNB had significantly better performance based on measures of sensitivity, but this was associated with lower specificity for CNB relative to FNAC. Overall, CNB is the more reliable biopsy method for sonographically-visible lesions; where FNAC is used as the first-line test, inadequate or inconclusive FNAC can be largely resolved by using repeat sampling with CNB.

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Introduction

Preoperative diagnosis based on triple assessment inclusive of non-surgical (needle) biopsy has replaced diagnostic surgical biopsy, the latter being associated with low positive predictive value and high costs[1,2] and accounting for as much as 32% of breast screening program cost.[3] In Europe fine needle aspiration cytology (FNAC) was initially used and achieved high sensitivity.[4] Nevertheless FNAC has major limitations, including inadequate samplings, substantial false negative rates in some reports,[4–8] and operator-dependent accuracy[9]; it also provides limited information on tumour histologic features.[10] For these reasons core needle biopsy (CNB) has been increasingly replacing FNAC since the 1980's and in particular in assessment of screen-detected lesions. Following the introduction of ultrasound-guided CNB of breast lesions almost two decades ago,[11] many centres have adopted this approach for both screen-detected and symptomatic lesions, and studies have confirmed CNB high sensitivity.[12–17]

Studies comparing FNAC and CNB accuracy in biopsy of breast lesions that are visible on ultrasound (US) are invariably affected by selection to initial needle biopsy test, and there is limited information from high-quality controlled studies. We report an audit of needle biopsy accuracy from a major Italian breast diagnostic service, where both FNAC and CNB were applied by experienced operators over the same time-frame. The study center has established experience with US-guided FNAC but with increasing use of CNB in the diagnosis of solid breast lesions visible on ultrasound. The purpose of the audit was to examine the relative accuracy of FNAC and CNB in a large consecutive series of needle samplings, and to determine factors driving choice of first needle test as well as whether one test is superior to the other in this clinical setting.

Materials and methods

This is a retrospective study of 3233 consecutive needle biopsies (1950 FNAC and 1283 CNB) performed by six experienced radiologists on solid, palpable or impalpable, sonographically-visible breast lesions. Needle biopsies were from self-referred (symptomatic or asymptomatic) women who were investigated at the study centre from October 2003 to September 2006. Level of suspicion at palpation and imaging was recorded before FNAC or CNB, according to a categorical scale used in European guidelines: R2 = probably benign, R3 = indeterminate, R4 = suspicious, R5 = malignant.[18]

FNAC employed 22–23-gauge needles without aspiration.[19] Cytological smears were fixed in 95° alcohol and stained with Papanicolaou technique. CNB was performed with automated or semi-automated devices using 14-gauge needles, collecting at least two cores from each lesion. FNAC and CNB specimens were examined by dedicated breast cyto-pathologists and pathologists each with at least 15 years experience in breast diagnostics. FNAC was reported according to five categories (C1 = inadequate, C2 = benign, C3 = atypia, C4 = suspicious of malignancy, C5 = malignant). CNB was reported according to five categories (B1 = normal tissue/inadequate sample, B2 = benign lesion, B3 = lesion of uncertain malignant potential, B4 = suspicious of malignancy, B5 = malignant) as recommended by European guidelines.[18] Reference standard was surgical histology or clinical/imaging follow-up for lesions diagnosed as benign and those not undergoing surgery (follow-up mean = 1.44 years, median = 1.30 years). Benign lesions with <6 months follow-up were ineligible for this analysis. Follow-up data were available for 3233 cases (FNAC = 1950; CNB = 1283) which were included in this analysis.

Statistical analysis

The probability of undergoing CNB instead of FNAC (referent) as the first test was estimated as an odds ratio (OR) using logistic regression analysis. The effect of each considered variable (calendar year, pre-needle biopsy level of suspicion, age-group, size of the lesion on imaging, palpability) was examined in univariate analysis and also by adjusting for other variables in multivariate analysis.

Analysis of FNAC and CNB outcomes included the following measures: overall inadequacy rate (C1 or B1), inadequacy rate amongst cancers, false benign reports (C2 or B2) amongst cancers, absolute sensitivity (C5 or B5 in cancers), complete sensitivity (C3–C5 or B3–B5 in cancers), diagnostic conclusiveness (conclusive report rate: C2 + C5 or B2 + B5), specificity (true negative C1 + C2 or B1 + B2 in negative), absolute and complete diagnostic accuracy. Inadequate samples were included in the calculation of these parameters to reflect the results of the whole diagnostic procedure. Pearson Chi^2 test was used to evaluate differences between proportions. Statistical significance was set at $p < 0.05$ level.

The methods and reporting of this study considered the STARD recommendations (Statement for Reporting studies of Diagnostic accuracy).[20]

Results

For all needle biopsies included in this study (3233) CNB use increased over time relative to FNAC: 28.8% *vs*. 71.2% in 2003; 30.4% *vs*. 69.6% in 2004; 43.5% *vs*. 56.5% in 2005; 59.8% *vs*. 40.2% in 2006 (p for trend <0.01). Table 1 shows the distribution of first test FNAC and CNB – according to pre-test level of suspicion, age-groups, diameter and palpability – including estimates of the probability (OR) of undergoing as *first* test CNB instead of FNAC. The effect of each variable is expressed in terms of both crude OR (single variable effect) and also adjusted OR assuming the same distribution of all the other variables between FNAC and CNB cases. We found an independent effect of the annual interval, with an increasing probability over time for CNB of more than 60% for each of the years included. For all lesions, if the pre-test suspicion was R3 or greater,

Table 1
Probability (Odds Ratio, OR) of undergoing CNB as the first test instead of FNAC (referent).

	FNAC (1950)	CNB (1283)	Crude OR (95% CI)	Adjusted[a] OR (95% CI)
Year			1.68 (1.54–1.83)	1.61 (1.46–1.77)
Pre-needle biopsy level of suspicion				
R2	913	239	1	1
R3–R4	612	754	4.71 (3.94–5.62)	4.79 (3.95–5.80)
R5	425	290	2.61 (2.12–3.20)	2.38 (1.85–3.06)
Age-group				
≥80	169	69	1	1
70–79	202	132	1.60 (1.12–2.84)	1.77 (1.21–2.58)
60–69	189	142	1.84 (1.29–2.62)	2.56 (1.54–3.31)
50–59	253	212	2.05 (1.47–2.87)	3.17 (2.19–4.59)
<50	1137	728	1.57 (1.17–2.11)	3.19 (2.28–4.46)
Lesion size on imaging (mm)				
<10	1101	600	1	1
10–19	627	376	1.10 (0.94–1.29)	1.15 (0.97–1.38)
20–29	162	153	1.73 (1.36–2.21)	1.76 (1.34–2.30)
30–39	33	41	2.80 (1.43–3.64)	2.77 (1.67–4.62)
≥40	27	113	7.68 (4.99–11.82)	6.68 (4.21–10.60)
Palpability				
No	708	330	1	1
Yes	1242	953	1.63 (1.40–1.92)	1.38 (1.15–1.65)

(FNAC = fine needle aspiration cytology; CNB = core needle biopsy; OR = Odd Ratio; 95% CI 95% Confidence intervals; R2 = probably benign; R3 = indeterminate; R4 = suspicious; R5 = malignant).
[a] Adjusted for the other variables.