Original Article

False Negative and Histologic Underestimation Rates of Stereotactic 14-Gauge Automated Core Needle Breast Biopsy in Phramongkutklao Hospital

Jungmeechoke K, MD[1], Chindamporn N, MD[1], Saengruang-orn S, PhD[1]

[1] Department of Radiology, Phramongkutklao Hospital, Bangkok, Thailand

Objective: To determine the false negative and underestimation rates of stereotactic 14-gauge automated core needle breast biopsy (CNB) in Phramongkutklao Hospital.

Materials and Methods: A retrospective review of 124 breast lesions receiving stereotactic 14-gauge automated CNB, with either subsequent surgical excision or complete 2-year mammographic follow-up to confirm benignity was performed. The false negative rate and underestimation rate of both high-risk lesions and ductal carcinoma in situ (DCIS) were calculated.

Results: The 124 lesions presented as microcalcifications. CNB revealed 80 benign, 13 high risk (seven papillomas, five atypical ductal hyperplasia, and one atypical gland proliferation), and 31 malignant lesions. One of the 37 lesions that had a final diagnosis of carcinoma was benign at CNB, a false negative rate of 2.7%. Three of the five atypical ductal hyperplasia (60%) and two of the seven papillomas (28.6%) turned out to be cancer at surgical excision, while two of the 20 DCIS (10%) had invasive component at final diagnosis.

Conclusion: The false negative rate of stereotactic 14-gauge automated CNB of microcalcifications in Phramongkutklao Hospital was 2.7%. The underestimation rates of atypical ductal hyperplasia, papilloma, and DCIS were 60%, 28.6%, and 10%, respectively.

Keywords: Stereotactic biopsy, 14-gauge automated core needle, breast lesions, breast cancer, false negative rate, underestimation rate.

J Med Assoc Thai 2019;102(12):1302-8
Website: http://www.jmatonline.com
Received 5 Apr 2019 | Revised 4 Sep 2019 | Accepted 9 Sep 2019

In Thailand, breast cancer has had the highest incidence of female cancers for several years and is expected to remain the highest until 2025[1]. It will contribute substantially to the national cancer burden in the future.

Imaging play an important role in screening, diagnosis, and management of breast cancer. Image-guided percutaneous biopsy, primarily by ultrasound or stereotactic guidance, is a minimally invasive technique for histopathological assessment of breast lesions. It provides an accurate pre-operative diagnosis of malignancy and avoidance of an open surgical procedure for benign lesions. It can be done both with automated biopsy needle, usually 14-gauge, or vacuum-assisted needle, 11-gauge or larger, for more tissue acquisition. The latter now becomes preferable, particularly for stereotactic guided biopsy, because there are many studies reporting decreasing false negative and underestimation rates of breast cancer diagnosis[2-5]. However, this benefit comes with the high cost. Vacuum-assisted device is 10 to 15 times more expensive than 14-gauge automated needle.

At Phramongkutklao Hospital, all stereotactic guided breast biopsies were done with 14-gauge automated needles because vacuum-assisted devices could not be reimbursed from the Comptroller General's Department. The purpose of the presented study was to evaluate the accuracy of stereotactic 14-gauge automated core needle breast biopsy (CNB) in Phramongkutklao Hospital by determining

Correspondence to:

Jungmeechoke K.

Department of Radiology, Phramongkutklao Hospital, 315 Rajavithi Road, Thung Phaya Thai, Khet Ratchathewi, Bangkok 10400, Thailand.

Phone & **Fax**: +66-2-3545243

Email: k_jungmeechoke@hotmail.com

How to cite this article: Jungmeechoke K, Chindamporn N, Saengruang-orn S. False Negative and Histologic Underestimation Rates of Stereotactic 14-Gauge Automated Core Needle Breast Biopsy in Phramongkutklao Hospital. J Med Assoc Thai 2019;102:1302-8.

retrospectively the false negative and underestimation rates.

Materials and Methods

The presented study was approved by the Institutional Review Board of Royal Thai Army Medical Department.

The indications of stereotactic breast biopsy were suspicious findings seen only on mammogram, mainly microcalcifications. At Phramongkutklao Hospital, it was performed with the patient on a prone table (Multicare Platinum, Hologic) by using 14-gauge needle and biopsy gun (Bard, Magnum). There was only one radiologist performing this procedure, with experience of more than five years. Radiograph of specimens were taken in every case to confirm the retrieved microcalcifications. Twelve core samples were routinely obtained. If specimen radiograph failed to show microcalcification, more core samples were attempted. If the patient did not tolerate the procedure well or the target was tiny group of microcalcifications, fewer core samples were accepted. After the biopsy, the breast surgeons were the ones who evaluated the imaging-pathology correlation. If the result was benign concordance, interval follow-up by mammograms with ultrasound breasts for at least two years were recommended to confirm benignity. If the result was imaging-pathology discordance or pathology revealed high risk lesion or cancer, surgical excision was recommended.

During the three-year period between December 2013 and November 2016, 152 patients received stereotactic 14-gauge automated CNB at the Department of Radiology, Phramongkutklao Hospital. Sixteen patients were lost to follow-up and 15 cases had not yet completed the 2-year follow-up to ensure benignity. Five patients were referred back to their hospitals for operations. These 36 cases were excluded from the study. The remaining 116 patients had 124 lesions with either complete 2-year mammographic follow-up or pathological report of surgical excision. Retrospective review of these 124 lesions was done from medical records, mammographic reports, and pathological reports.

Continuous variables were summarized as mean with standard deviation, while categorical variables were done as counts and percentages.

False negative case was defined as a surgical proven cancer while stereotactic CNB yielded benign pathological result. False negative rate was obtained by dividing the number of false negative cases by the number of all cancer cases.

High-risk lesions are breast lesions that have a high prevalence of carcinoma at surgical excision or carry an increased risk for the future cancer development. These included atypical ductal hyperplasia (ADH), atypical lobular hyperplasia, lobular carcinoma in situ, flat columnar atypia, papillary lesions, and radial scar. The management of ADH is excision because of high underestimation rate while that of the other high-risk lesions are still controversial.

A diagnosis of high-risk lesion from CNB was considered to be histologic underestimate if the surgical excisional specimen contained carcinoma. Underestimation rate for each histologic type of high-risk lesion was determined by dividing the number of high-risk lesions that contained cancer at surgical excision by the number of high-risk lesions from CNB result.

Ductal carcinoma in situ (DCIS) underestimation means the underestimation of invasive cancer in cases where CNB shows DCIS. As underestimated DCIS at CNB is upgraded to invasive carcinoma at surgery and axillary node management is required at a later date, thus resulting in a two-stage therapeutic surgical procedure. Rate of DCIS underestimation was obtained by dividing the number of DCIS cases with invasive carcinoma on surgical specimen by the number of all DCIS from CNB result.

All statistical analyses were performed using SPSS version22.

False negative cases were reviewed in detail.

Results

One hundred twenty-four lesions were found in 116 patients with mean age of 55 years (SD 10.2), ranging from 28 to 79 years. The 28-year-old case did mammogram because of a mass in the other breast. Most of the patients (82.3%) showed extremely dense or heterogeneously dense breast density on mammogram, as shown in Table1. Indications of breast biopsy were abnormal microcalcifications in all cases, with group distribution being the most common, (79.8%). Most of the lesions were BI-RADS4A (46%) and BI-RADS4B (38%). There was one BI-RADS2 case in the presented study because of high anxiety of the patient (the final diagnosis in this case was fat necrosis). The details of the mammographic findings are shown in Table 1.

The number of core samples ranged from 3 to 25 (mean 12, SD 3.51). All cases showing micro-calcifications on specimen radiograph with calcified specimens ranged from 1 to 10 (mean 4.18, SD 1.9).

Out of 124 lesions, stereotactic CNB yielded

Table 1. Mammographic findings (n=124)

Characteristics and findings	n (%)
Mammographic grade of breast density	
Scattered fibroglandular densities	22 (17.7)
Heterogeneously dense	88 (71.0)
Extremely dense	14 (11.3)
Distribution of microcalcifications	
Group	99 (79.8)
Regional	6 (4.8)
Segmental	13 (10.6)
Linear	6 (4.8)
BI-RADS categories	
2	1 (0.8)
3	2 (1.6)
4A	57 (46.0)
4B	47 (37.9)
4C	9 (7.2)
5	8 (6.5)

BI-RADS=breast imaging reporting and data system

benign disease in 80 lesions (64.5%), high risk lesions in 13 (10.5%), DCIS in 20 (16.1%), and invasive cancer in 11 (8.9%).

Among 80 benign lesions from stereotactic CNB (including three cases of BI-RADS2 and BI-RADS3), 54 of them had complete 2-year follow-up with stable mammographic findings. Twenty-five had imaging-pathology discordance. Surgical excision was undertaken with final diagnosis of benign in 21 lesions and high-risk in four, being two papillomas and two ADH. The last lesion was considered as benign concordance as mammographic follow-up suggested. At about 1-year follow-up, there was increased microcalcifications at the biopsy site. This led to surgical excision with final diagnosis of high-grade DCIS. This was a false negative case.

Thirteen high-risk lesions from stereotactic biopsy consisted of five ADH, seven papillomas, and one atypical gland proliferation. All were suggested to do surgical excision, but one patient with papilloma denied surgery and did mammographic follow-up, which showed stable result for two years. Surgical excision was not performed in one case of ADH because there was no remaining microcalcifications and mammographic follow-up at two-years was still normal. Eleven cases received surgical excisions. Three cases of ADH and two papillomas (Figure 1) turned out to be five DCIS, with minimally invasive component in one case with a size of 0.1cm. Two cases showed benign disease at excision, but these were still categorized as high-risk because of possible total removal at CNB.

Two cases of DCIS showed invasive component

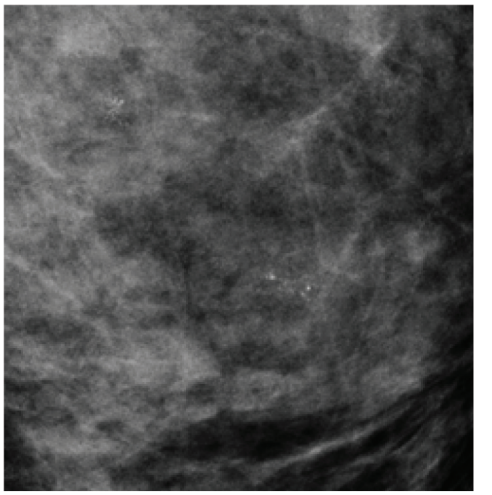

Figure 1. Pathology underestimation of papilloma. Mammogram showed two groups of amorphous and pleomorphic microcalcifications, BI-RADS4B. CNB of both lesions showed papillomas, while later excision showed DCIS.

Figure 2. Downgrade case. Magnification CC view showed linear microcalcifications in linear distribution, BI-RADS5. CNB showed infiltrative ductal carcinoma, microinvasion, with microcalcifications. Left mastectomy was done and showed only DCIS.

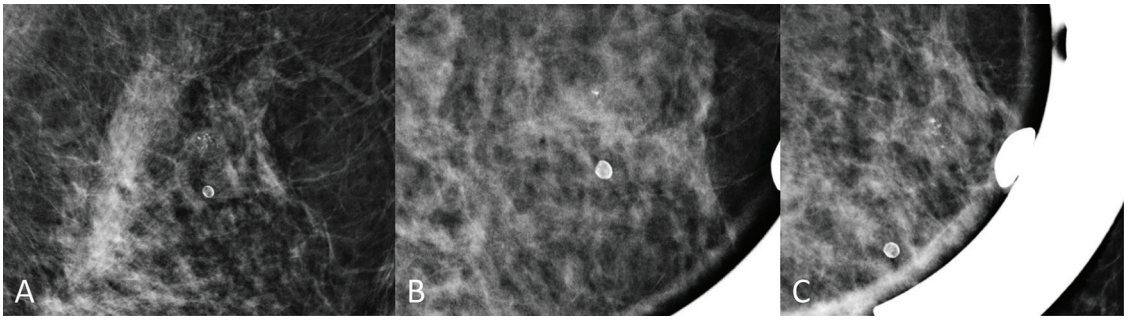

Figure 3. The missed cancer case. (A) Magnification MLO view showed a group of pleomorphic microcalcifications, BI-RADS4B. (B) At 6-month mammographic follow-up after benign CNB showed one microcalcification left at the biopsy site. (C) At 12-month mammographic follow-up showed interval increased pleomorphic microcalcifications, BI-RADS4B. Excision showed high-grade DCIS.

Table 2. CNB results and final diagnosis (n=124)

Characteristics and findings	n (%)
CNB result	
Benign	80 (64.5)
High risk	13 (10.5)
Carcinoma	31 (25.0)
Final diagnosis	
Benign	75 (60.5)
High risk	12 (9.7)
Carcinoma	37 (29.8)

CNB=core needle breast biopsy

Table 3. Correlation of CNB result and final diagnosis

CNB result	Final diagnosis				Total
	Benign	High risk	DCIS	IDC	
Benign	75	4	1	0	80
High risk	0	8	4	1	13
DCIS	0	0	18	2	20
IDC	0	0	1	10	11
Total	75	12	24	13	124

CNB=core needle breast biopsy; DCIS=ductal carcinoma in situ; IDC=invasive ductal carcinoma

at surgical excision with a size of 0.6 cm and 0.8 cm. One invasive cancer from biopsy turned out to be the only DCIS at surgical excision (Figure 2).

The details and correlation of stereotactic CNB result and final diagnosis are shown in Table 2 and 3.

The false negative rate in the presented study was 2.7% (one missed cancer from the 37 pathological proven cancers). This missed case presented as a group of pleomorphic microcalcifications, BI-RADS4B, with positive microcalcifications on specimen radiograph in four core samples from 14 samples. Pathology reported benign breast tissue but did not mention microcalcification. There was progression of microcalcifications at 12-month mammographic follow-up with final diagnosis of DCIS at surgical excision (Figure 3).

The underestimation rates of ADH, papilloma and DCIS were 60% (three out of five lesions), 28.6% (two out of seven lesions), and 10% (two out of twenty lesions), respectively.

Discussion

The false negative rate of stereotactic 14-gauge CNB in the presented study was 2.7%, which was in the range of prior studies, 1.2% to 7.8%[2,6]. It was slightly higher than 11-gauge vacuum-assisted one, of which the false negative rates were near zero in some studies, but also ranged from 0.16% to 6%[2-4,7]. False negative rate of breast biopsy depends on multiple factors including the number and characteristic of research population, experiences of radiologist and radiographer, quality of machine, and gauge of the biopsy needle[2,8]. The 11-gauge vacuum-assisted biopsy obtains larger tissue volume than the 14-gauge needle, leading to more accurate tissue diagnosis.

The missed cancer case in the presented study showed no microcalcification on CNB pathological report. In this scenario, review with pathologist to find microcalcification is needed, and if no microcalcification was found, re-biopsy or surgical excision should be done. Mammographic follow-up after CNB also plays a role in detecting missed breast cancer at a later date. There were 15 cases of

exclusion of the presented study because of no follow-up. Encouraging the patient to do mammographic follow-up after biopsy is thus important in patient care.

The underestimation rate of ADH in the presented study was 60%, which was similar to the 31% to 88% rate found in other studies[6,9]. However, it was higher than the rate of 11-gauge vacuum-assisted biopsy, which ranged from 13% to 50%[3,5,7,10]. ADH and DCIS share some pathological features and size of the abnormality are important for their differentiation. In addition, DCIS and ADH are often found in scattered ducts, so DCIS can be missed by needle biopsy. The 11-gauge vacuum-assisted biopsy enables larger volume of tissue sample retrieved, therefore, more accurate diagnosis and less underestimation rate are obtained. However, it seems that underestimation of ADH cannot be eliminated as Penco et al[11] reported underestimation rate of 6.6% when the mammography target was completely removed. Surgical excision is still the standard management for ADH.

The underestimation rate of papilloma in the presented study was very high, 28.6%. This was partly because of the small number of papillomas in the study. The previous studies using 14-gauge CNB, most of them with ultrasound guidance, showed the upgrade rate of 2.6% to 11%[12-14], while using 11-gauge vacuum-assisted needle showed the rate of 0% to 3%[12,14,15]. Management of benign papilloma is controversial, with follow-up recommended in some cases and excision in others. There were several studies trying to find factors associated with high underestimation rate[13-20] to select some cases to excision but a conclusion has not yet been reached. Some reported the smaller size of the needle[14,16], calcifications, or positive finding on mammogram[15,17], BI-RADS4B-5 category[13], or imaging-pathology discordance[20] associated with high underestimation rate. The result of the presented study also suggested that benign papilloma with suspicious microcalcifications and diagnosed by stereotactic 14-gauge CNB should be regarded as high-risk lesion and managed with excision, either by open surgery or vacuum assisted device.

The underestimation rate of DCIS in the presented study was 10%, lower than in previous studies, which ranged from 15% to 50%[6,9,21,22], but comparable to previous studies of 11-gauge vacuum-assisted biopsy, which ranged from 0% to 29%[3,5,9,10,22,23]. Underestimation of DCIS happens because of sampling error, so large volume of tissue sample decreases this underestimate rate. Other factors associated with higher underestimation of DCIS include the size and grade of the cancer, mammographic findings, and palpability as shown in the study of Brennon et al[24]. The low underestimation rate of DCIS in the presented study was possibly from the small size of the lesions, most of them being group in distribution, with less than 2 cm in size by definition.

There was one downgrade case from invasive cancer to DCIS at surgery. This was either from all invasive component removal at biopsy or from epithelial displacement. This might lead to non-necessary axillary management.

The limitations of the present study were retrospective study, large number of exclusions and no pathological slide reviewed.

Conclusion

The false negative rate of stereotactic 14-gauge automated CNB of microcalcifications in Phramongkutklao Hospital was 2.7%. The underestimation rates of ADH and papilloma were high, 60% and 28.6%, respectively while that of DCIS was 10%.

The accuracy of stereotactic 14-gauge automated CNB is sufficient for breast disease diagnosis. Imaging-pathological correlation and mammographic follow-up play important roles in detecting missed breast cancer. Because of the high underestimation rate, benign papilloma with suspicious microcalcifications and diagnosed by stereotactic 14-gauge CNB should be regarded as high-risk lesion and excision should be recommended.

What is already known on this topic?

The false negative rate of stereotactic 14-gauge CNB in the prior studies ranged from 1.2% to 7.8%, while that of 11-gauge vacuum-assisted one ranged from 0.16% to 6%.

The underestimation rate of benign papilloma by 14-gauge CNB varied from 2.6% to 11%, resulting in controversy in management, follow-up versus excision.

What this study adds?

The false negative rate of stereotactic 14-gauge automated CNB of microcalcifications in Phramongkutklao Hospital was 2.7%, slightly higher than 11-gauge vacuum- assisted one in good hand, suggesting that it is sufficient for breast disease diagnosis.

Excision is suggested for benign papilloma with suspicious microcalcifications and diagnosed by stereotactic 14-gauge CNB.

Acknowledgement

The authors would like to thank Hansa Boonrat for her assistance with English language, manuscript.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Virani S, Bilheem S, Chansaard W, Chitapanarux I, Daoprasert K, Khuanchana S, et al. National and subnational population-based incidence of cancer in Thailand: Assessing cancers with the highest burdens. Cancers (Basel) 2017;9:pii: E108.
2. Pfarl G, Helbich TH, Riedl CC, Wagner T, Gnant M, Rudas M, et al. Stereotactic 11-gauge vacuum-assisted breast biopsy: a validation study. AJR Am J Roentgenol 2002;179:1503-7.
3. Kettritz U, Rotter K, Schreer I, Murauer M, Schulz-Wendtland R, Peter D, et al. Stereotactic vacuum-assisted breast biopsy in 2874 patients: a multicenter study. Cancer 2004;100:245-51.
4. Jackman RJ, Marzoni FA Jr, Rosenberg J. False-negative diagnoses at stereotactic vacuum-assisted needle breast biopsy: long-term follow-up of 1,280 lesions and review of the literature. AJR Am J Roentgenol 2009;192:341-51.
5. Burak WE Jr, Owens KE, Tighe MB, Kemp L, Dinges SA, Hitchcock CL, et al. Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. Arch Surg 2000;135:700-3.
6. Jackman RJ, Nowels KW, Rodriguez-Soto J, Marzoni FA Jr, Finkelstein SI, Shepard MJ. Stereotactic, automated, large-core needle biopsy of nonpalpable breast lesions: false-negative and histologic underestimation rates after long-term follow-up. Radiology 1999;210:799-805.
7. Wiratkapun C, Fusuwankaya E, Wibulpholprasert B, Lertsittichai P. Diagnostic accuracy of vacuum-assisted stereotactic core needle biopsy for breast lesions. J Med Assoc Thai 2010;93:1058-64.
8. Wiratkapun C, Wibulpholprasert B, Wongwaisayawan S, Pulpinyo K. Nondiagnostic core needle biopsy of the breast under imaging guidance: result of rebiopsy. J Med Assoc Thai 2005;88:350-7.
9. Darling ML, Smith DN, Lester SC, Kaelin C, Selland DL, Denison CM, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. AJR Am J Roentgenol 2000;175:1341-6.
10. Lourenco AP, Mainiero MB, Lazarus E, Giri D, Schepps B. Stereotactic breast biopsy: comparison of histologic underestimation rates with 11- and 9-gauge vacuum-assisted breast biopsy. AJR Am J Roentgenol 2007;189:W275-9.
11. Penco S, Rizzo S, Bozzini AC, Latronico A, Menna S, Cassano E, et al. Stereotactic vacuum-assisted breast biopsy is not a therapeutic procedure even when all mammographically found calcifications are removed: analysis of 4,086 procedures. AJR Am J Roentgenol 2010;195:1255-60.
12. Londero V, Zuiani C, Linda A, Battigelli L, Brondani G, Bazzocchi M. Borderline breast lesions: comparison of malignancy underestimation rates with 14-gauge core needle biopsy versus 11-gauge vacuum-assisted device. Eur Radiol 2011;21:1200-6.
13. Kim SY, Kim EK, Lee HS, Kim MJ, Yoon JH, Koo JS, et al. Asymptomatic benign papilloma without atypia diagnosed at ultrasonography-guided 14-gauge core needle biopsy: Which subgroup can be managed by observation? Ann Surg Oncol 2016;23:1860-6.
14. Seely JM, Verma R, Kielar A, Smyth KR, Hack K, Taljaard M, et al. Benign papillomas of the breast diagnosed on large-gauge vacuum biopsy compared with 14 gauge core needle biopsy - Do they require surgical excision? Breast J 2017;23:146-53.
15. Hawley JR, Lawther H, Erdal BS, Yildiz VO, Carkaci S. Outcomes of benign breast papillomas diagnosed at image-guided vacuum-assisted core needle biopsy. Clin Imaging 2015;39:576-81.
16. Holley SO, Appleton CM, Farria DM, Reichert VC, Warrick J, Allred DC, et al. Pathologic outcomes of nonmalignant papillary breast lesions diagnosed at imaging-guided core needle biopsy. Radiology 2012; 265:379-84.
17. Wen X, Cheng W. Nonmalignant breast papillary lesions at core-needle biopsy: a meta-analysis of underestimation and influencing factors. Ann Surg Oncol 2013;20:94-101.
18. Destounis S, Seifert P, Somerville P, Murphy P, Morgan R, Arieno A, et al. Underestimation of papillary breast lesions by core biopsy: correlation to surgical excision. Breast Cancer 2014;21:128-34.
19. Boufelli G, Giannotti MA, Ruiz CA, Barros N, Chala LF, Maesaka JY, et al. Papillomas of the breast: factors associated with underestimation. Eur J Cancer Prev 2018;27:310-4.
20. Youk JH, Kim EK, Kwak JY, Son EJ, Park BW, Kim SI. Benign papilloma without atypia diagnosed at US-guided 14-gauge core-needle biopsy: clinical and US features predictive of upgrade to malignancy. Radiology 2011;258:81-8.
21. Meyer JE, Christian RL, Lester SC, Frenna TH, Denison CM, DiPiro PJ, et al. Evaluation of nonpalpable solid breast masses with stereotaxic large-needle core biopsy using a dedicated unit. AJR Am J Roentgenol 1996;167:179-82.
22. Won B, Reynolds HE, Lazaridis CL, Jackson VP. Stereotactic biopsy of ductal carcinoma in situ of the breast using an 11-gauge vacuum-assisted device: persistent underestimation of disease. AJR Am J Roentgenol 1999;173:227-9.
23. Liberman L, Dershaw DD, Rosen PP, Morris EA, Abramson AF, Borgen PI. Percutaneous removal of malignant mammographic lesions at stereotactic vacuum-assisted biopsy. Radiology 1998;206:711-5.

24. Brennan ME, Turner RM, Ciatto S, Marinovich ML, French JR, Macaskill P, et al. Ductal carcinoma in situ at core-needle biopsy: meta-analysis of underestimation and predictors of invasive breast cancer. Radiology 2011;260:119-28.