ELSEVIER

Canadian Association of Radiologists Journal 63 (2012) 146–152

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Breast Imaging / Imagerie du sein

Is Ductal Carcinoma In Situ With "Possible Invasion" More Predictive of Invasive Carcinoma Than Pure Ductal Carcinoma In Situ?

Tal Arazi-Kleinman, MD[a,b,*], Petrina A. Causer, MD[a], Sharon Nofech-Mozes, MD[c], Roberta A. Jong, MD[a]

[a]*Department of Medical Imaging, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada*
[b]*Department of Medical Imaging, Edith Wolfson Medical Center, Holon, Israel*
[c]*Department of Pathology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada*

Abstract

Objectives: To compare the underestimation of ductal carcinoma in situ (DCIS) vs DCIS with "possible invasion" at breast biopsy and to determine if any factors related to clinical indication, imaging abnormality, biopsy, or DCIS-grade affected the likelihood of underestimation.
Methods: Of 3836 consecutive lesions that were biopsied by using a 14-gauge needle, 117 lesions revealed DCIS. Surgical pathology results of invasive carcinoma were compared with needle biopsy results of DCIS or DCIS with possible invasion. Clinical indication, imaging abnormality, biopsy guidance modality, sample number, and histologic grade were recorded. Yates corrected χ^2 and Fisher exact tests were used to determine differences between groups.
Results: A total of 101 lesions were DCIS and 16 were DCIS with possible invasion at biopsy. Thirty-six of 117 lesions (31%) revealed invasive carcinoma at resection pathology. Invasive carcinoma was present more often when DCIS with possible invasion was diagnosed compared with pure DCIS (7/16 [44%] vs 29/101 [29%], $P = .36$). No factor, including clinical indication, imaging abnormality, biopsy guidance method, sample number, or grade, was found to significantly affect the likelihood of underestimation for lesions diagnosed as DCIS vs DCIS with "possible invasion." The likelihood of pure DCIS underestimation significantly increased when lesions were high grade compared with either intermediate or low grade (18/44 [41%] vs 9/44 [21%] vs 2/10 [20%], $P = .03$).
Conclusion: For lesions biopsied by using a 14-gauge needle, there is a trend towards underestimation of the presence of invasive carcinoma when pathology reveals DCIS with possible invasion compared with pure DCIS. High-grade DCIS was significantly more likely to be underestimated.

Résumé

Objectifs : Comparer le taux de sous-estimation des carcinomes canalaires in situ (CCIS) par rapport à celui des CCIS avec « invasion possible » lors des biopsies du sein et déterminer si tout facteur se rapportant aux indications cliniques, à des anomalies relatives à l'imagerie, à la biopsie ou au grade du CCIS avait une incidence sur la probabilité de sous-estimation.
Méthodes : Sur 3 836 lésions consécutives biopsiées au moyen d'une aiguille de calibre 14, 117 lésions correspondaient à des CCIS. On a comparé les résultats pathologiques chirurgicaux des carcinomes invasifs avec ceux des biopsies à l'aiguille des CCIS ou des CCIS avec invasion possible. On a consigné les indications cliniques, les anomalies relatives à l'imagerie, les lignes directrices en matière de biopsie, le numéro d'échantillon et le grade histologique. On a utilisé la correction de Yates au calcul du chi carré (χ^2) et la méthode exacte de Fisher pour déterminer les différences entre les groupes.
Résultats : Au total, 101 lésions correspondaient à des CCIS et 16 à des CCIS avec invasion possible selon les résultats de la biopsie. Trente-six des 117 lésions (31 %) comportaient un carcinome invasif lors de l'examen pathologique de résection. Les carcinomes invasifs étaient plus fréquents dans le cas d'un diagnostic de CCIS avec invasion possible que dans celui d'un diagnostic de CCIS pur (7/16 [44 %] par rapport à 29/101 [29 %], $P = 0{,}36$). Les facteurs comme les indications cliniques, les anomalies relatives à l'imagerie, les lignes directrices en matière de biopsie, le numéro d'échantillon ou le grade histologique n'avait une incidence considérable sur la probabilité de sous-estimation des lésions ayant fait l'objet d'un diagnostic de CCIS pur, comparativement aux diagnostics de CCIS avec « invasion possible ».

* Address for correspondence: Arazi-Kleinman, MD, Department of Medical Imaging, Edith Wolfson Medical Center, 62 HaLohamim Street, PO Box 5, Holon 58100 Israel.
E-mail address: t_arazikleinman@yahoo.com (T. Arazi-Kleinman).

doi:10.1016/j.carj.2010.10.002

La probabilité de sous-estimation des CCIS était beaucoup plus élevée dans le cas de lésions de haut grade que dans le cas de lésions de grade intermédiaire ou de bas grade (18/44 [41 %] par rapport à 9/44 [21 %] et 2/10 [20 %], $P = 0{,}03$).
Conclusion : En ce qui concerne les lésions biopsiées au moyen d'une aiguille de calibre 14, la tendance à la sous-estimation de la présence de carcinomes invasifs est supérieure lorsque l'examen pathologique permet de déceler un CCIS avec invasion possible, comparativement à un CCIS pur. Les CCIS de haut grade étaient beaucoup plus sujets à la sous-estimation.

Key Words: Breast; Biopsy; Carcinoma; Ductal; Ductal carcinoma in situ

Introduction

Histologic underestimation occurs when percutaneous breast needle biopsy reveals pure ductal carcinoma in situ (DCIS), and upon subsequent excision of the same lesion, invasive cancer is diagnosed. This scenario likely occurs because of undersampling of a lesion that contains both DCIS and invasive components. Patient management is compromised when DCIS underestimation occurs on percutaneous biopsy and is not diagnosed until final surgical pathology results are available, because a second operation, not routinely performed for noninvasive cancer, is then required to stage the axillary lymph nodes [1].

At pathology, percutaneous breast biopsy specimens are reported as "DCIS with possible invasion" or "at least DCIS," when the stromal epithelial interface is not demonstrable (ie, when dissociated malignant cells are noted), whenever the suspicious invasive focus does not appear at the plane of deeper sections or immunohistochemistry cases are not resolvable. By using a 9-gauge vacuum-assisted biopsy (VAB) device under magnetic resonance imaging (MRI) guidance, Lee et al [2] reported an 81% underestimation rate for lesions diagnosed as DCIS with possible invasion, compared with a 17% rate for pure DCIS lesions, and is the factor with the greatest affect on reported underestimation rates.

The remaining underestimation rate data available come from stereotactic- and ultrasound-guided biopsy literature [3–10]. Because DCIS traditionally is detected by mammographic calcifications, the underestimation rate literature is predominantly based on stereotactic-guided breast biopsy. At stereotactic biopsy, the reported DCIS underestimation rates range between 10%–36%, increasing when the biopsy was performed by using a 14-gauge core vs an 11-gauge VAB needle (20% vs 11%, $P < .001$), when the target lesion was a mass vs calcifications (24% vs 12%, $P < .001$), and when fewer than 10 samples were retrieved (18% vs 12%, $P < .02$) [4,9].

When using ultrasound as guidance for 11- or 14-gauge percutaneous needle biopsy, Lee et al [6] reported DCIS underestimation in nearly 42% of cases. Underestimation rates were higher for palpable lesions (60%) and for lesions with correlated mass seen on mammography (55%).

The impact of biopsy pathology yielding DCIS with possible invasion on the surgical outcome has not been previously reported for stereotactic- or ultrasound-guided breast biopsies by using a 14-gauge needle. The aims of this study were to compare the frequencies of histologic underestimation of invasive breast carcinoma that occurs when percutaneous breast biopsy performed by using an automated 14-gauge needle revealed pure DCIS vs DCIS with possible invasion, according to the clinical indication for imaging, imaging abnormality, biopsy guidance method, number of samples obtained, and DCIS pathologic grade.

Materials and Methods

With institutional review board approval, a retrospective review was performed of 3836 consecutive lesions that underwent image-guided percutaneous breast biopsy in our medical imaging department over a period of 4 years (September 2003 until August 2007). Inclusion criteria for the study were the following: biopsy performed by using an automated 14-gauge needle; diagnosis of DCIS or DCIS with possible invasion, without the presence of invasive cancer; no synchronous lesion in the same breast diagnosed as invasive cancer; and the lesion surgically excised, with surgical pathology reviewed at our institution. Clinical, imaging, and pathology findings were reviewed.

We identified 117 consecutive lesions that met our inclusion criteria, 36 lesions (31%) revealed invasive cancer at subsequent resection pathology, 77 lesions (66%) revealed DCIS, and 4 lesions (3%) were benign (with no residual DCIS) at subsequent resection pathology. Eighty of 117 lesions (68%) presented as mammographic calcifications, 20 of 117 (17%) were mass only, and 17 of 117 (15%) were a mass with calcifications.

Biopsy Method

Lesions were biopsied according to the best method of imaging visualization for guidance. Calcifications were biopsied under stereotactic guidance, and masses or hypoechoic areas that were detected by ultrasound were sampled by using ultrasound guidance. If a mass is suspected based on mammographic findings, then the usual practice at our institution is to perform an ultrasound (ie, a mammographic mass or asymmetry or concerning calcifications in dense breast tissue).

In our practice, almost all lesions are biopsied with a 14-gauge needle by using ultrasound guidance and most by using stereotactic guidance. The 14-gauge needle biopsies under stereotactic guidance are performed on a dedicated table (stereoGuide; Lorad, Danbury, CT), with digital spot

mammography, by using an automated spring-loaded device (Manan Promag biopsy gun [Manan Medical Products Inc, Wheeling, IL] or Bard MAGNUM Reusable core biopsy instrument [Bard Biopsy Systems Inc, Tempe, AZ]). Ultrasound-guided breast biopsies are also performed by using the same 14-gauge automated spring-loaded devices and imaged by using a linear 5-12 MHz transducer (HDI 5000; Philips Healthcare Inc, Andover, MA). Biopsies were performed or supervised by 1 of 6 radiologists who specialize in breast imaging. All biopsies performed by trainees were directly supervised by an attending specialist. The biopsy accuracy was confirmed by the attending radiologist who was supervising the biopsy and observing in the room. If any question remained regarding sampling, then our practice was for the attending physician to perform additional passes during the biopsy. All attending radiologists had prior experience in breast imaging and percutaneous biopsies.

Pathology Methods and Definitions

Pathology reports of percutaneous breast biopsies and surgical specimens were reviewed. At the time of diagnosis, all specimens were signed out by a group of 5 pathologists with a focused practice in the area of breast pathology. Cases were classified as DCIS when malignant proliferation was contained within the basement membrane of native ducts or lobules and surrounded by myoepithelial cells [11]. Nuclear grade was determined by using the Holland classification [12]. When nuclear grade was low, cases were classified as: low-grade DCIS, only when the neoplastic proliferation replaced the entire duct; and atypical ductal hyperplasia, when there was incomplete involvement of the duct by cells indistinguishable from low-grade DCIS [12,13]. DCIS with microinvasion was defined as tumour cells, singly or in clusters, infiltrating the periductal stroma, or occasionally as a projection of neoplastic cells through a disrupted basement membrane in continuity with the DCIS, measuring equal to or less than 1 mm in greatest dimension [12]. Foci of stromal invasion tend to be accompanied by a desmoplastic reaction characterized by scattered chronic inflammatory cells arranged with pale staining loose arrays of new collagen.

Definitive diagnosis of stromal invasion may be difficult, and serial sections and immunohistochemical studies with myoepithelial markers are used in these cases [14,15]. However, when the stromal epithelial interface is not demonstrable (ie, when dissociated malignant cells are noted), or whenever the suspicious invasive focus does not appear at the plane of deeper sections or immunohistochemistry cases are not resolvable, these equivocal cases were reported as ''DCIS with possible invasion'' or ''at least DCIS'' (refer to Figure 1). Invasive carcinoma was reported whenever there were unequivocal features of stromal invasion. A DCIS underestimation was defined as a lesion that yielded DCIS without frank microinvasion or invasion at percutaneous breast biopsy, and with microinvasion or invasive cancer at the resection pathology.

All tissue samples were routinely fixed in 4% neutral buffered formalin and embedded in paraffin. Up to 3 cores were embedded in each block, and at least 2 hematoxylin and eosin–stained slides were obtained for microscopic evaluation. Additional sections and special stains were ordered at the pathologist's discretion. Excisional biopsy specimens were oriented by the surgeon, and the margins were inked by the pathologist. Specimens were serially sectioned. In general, lumpectomies that could fit in 30 blocks were entirely submitted, and larger specimens were sampled based on specimen radiography and gross abnormalities.

Data Collection and Analysis

Data collected for this study was as follows: indication for initial breast imaging, including routine screening; high-risk screening (BRCA1 or 2 mutation carriers, family history or prior personal history of breast cancer, prior mantle radiation, and risk markers on prior biopsy); clinical finding (palpable mass, pain, or nipple symptoms [discharge, inversion, Paget disease]); patient age, breast side, and lesion location; biopsy date; imaging abnormality (calcifications or mass with or without calcifications); biopsy imaging guidance method; the number of samples obtained; and DCIS pathologic grading of the biopsy specimen and the resection pathology.

Data were entered into a computerized spreadsheet (Excel; Microsoft Corporation, Redmond, WA). The likelihood of DCIS underestimation was calculated separately for each biopsy method, imaging abnormality, number of samples obtained per lesion, DCIS grade as determined on the core biopsy, and indication for initial breast imaging. Tests for statistical significance were performed with computerized statistical software by using the Yates corrected χ^2 and Fisher exact tests, with $P < .05$ considered significant [16]. The 95% confidence intervals were calculated by using the exact binomial and Poisson distributions [17].

Results

One hundred and seventeen lesions in 109 women were identified with a diagnosis of DCIS on percutaneous biopsy and subsequently underwent surgical excision with resection pathology reviewed at our institution. The mean age of the patients was 57 years (range, 33–84 years). The lesions were found in 112 breasts (59 left and 53 right breasts). Three patients had bilateral lesions, and 5 patients had biopsies of different lesions in the same breast.

Of 117 lesions, 101 were DCIS vs 16 DCIS with possible invasion at percutaneous biopsy performed by using an automated 14-gauge needle. Most (77/117 [66%]) of the lesions yielded pure DCIS at the resection pathology, followed by 36 (31%) which revealed invasive cancer, and 4 lesions (3%) yielded benign tissue. The likelihood of DCIS underestimation was higher for the lesions that yielded DCIS with possible invasion vs DCIS on biopsy pathology (44% vs 29%, $P = .36$). Refer to Table 1 for final excisional pathology

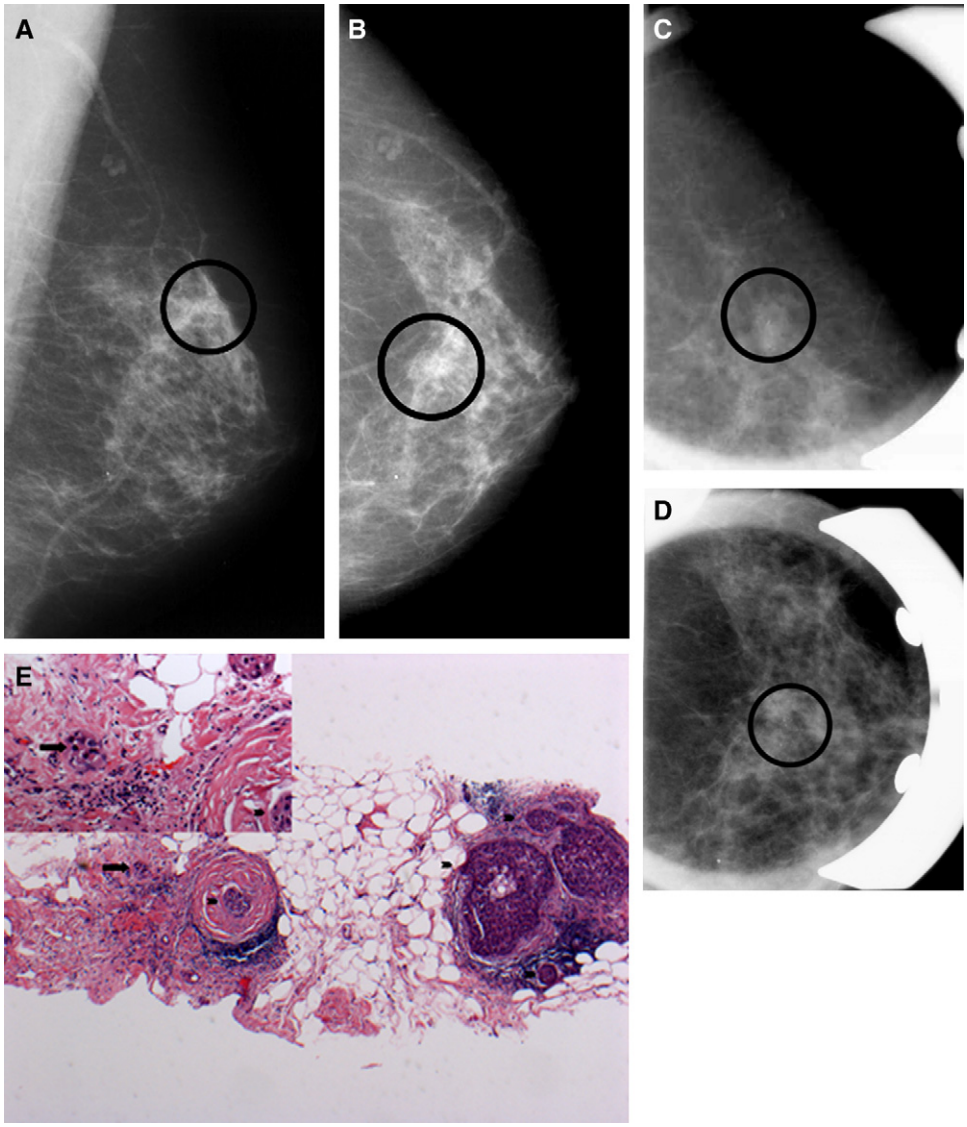

Figure 1. Mammographic and pathologic findings in a 65-year-old woman with prior right mastectomy. (A) Left mediolateral oblique and (B) Craniocaudate views demonstrate a new cluster of microcalcifications in the central upper left breast, without an associated mass (circle). (C) Lateral and (D) caudocranial spot compression magnification views characterize the calcifications as pleomorphic. (E) Low-power photomicrograph (hematoxylin and eosin stain), showing high-grade ductal carcinoma in situ (DCIS), solid type (arrow heads), diagnosed by stereotactic 14-gauge core needle biopsy. A small group of malignant cells are noted in the stroma (arrow) and appear to lack myoepithelial cells at its periphery (high-power photomicrograph insert). This focus does not appear on a deeper level, thus, immunohistochemistry to demonstrate the lack of myoepithelial cells and confirm stromal invasion is not feasible in this case. As a result, the lesion was designated as DCIS with possible invasion. Subsequent resection yielded a focus of 1 cm of invasive ductal carcinoma. This figure is available in colour online at http://carjonline.org/.

results for lesions that revealed DCIS vs DCIS with possible invasion on percutaneous biopsy.

The most frequent indication for imaging was routine screening (48/117 [41%]), followed by a history of breast cancer (37/117 [32%]), a clinical finding (20/117 [17%]), and screening of patients with high risk for breast cancer (12/117 [10%]). Patients with a mutation in the BRCA 1 or 2 gene or with a family history suggestive of hereditary breast cancer were considered high risk for breast cancer. See Table 2 for the underestimation rates of lesions diagnosed as DCIS with or without possible invasion according to clinical indication for lesion detection. Although there was no statistical difference in underestimation rates between lesions diagnosed as pure DCIS vs DCIS with possible invasion according to clinical indication for lesion detection, there was a trend towards a higher likelihood of underestimation DCIS with possible invasion when lesions presented as a clinical finding (3/6 [50%] vs 5/14 [36%], $P = .9$) and in patients with a history of breast cancer (3/7 [43%] vs 5/30 [17%], $P = .3$).

Most lesions were biopsied by using stereotactic guidance (80/117 [68%]), and the remainder were biopsied by using ultrasound guidance (37/117 [32%]). The final surgical pathology results in lesions that yielded DCIS or DCIS with possible invasion at core biopsy according to the biopsy guidance method are listed in Table 1. Due to the fact that all

Table 1
Resection pathology in lesions that yield DCIS at 14-gauge needle core biopsy according to biopsy guidance

Resection pathology				DCIS	Invasive cancer	Benign	Total
Stereotactic biopsy (N = 80)	Range of sample size: 4-14; average no. cores: 6	DCIS	No. lesions	52	18	4[a]	74
			% (95% CI)	70 (58-80)	24 (15-36)	6 (2-13)	100 (95-100)
		DCIS with possible invasion	No. lesions	3	3	0	6
			% (95% CI)	50 (12-88)	50 (12-88)	NA	100 (54-100)
Ultrasound biopsy (N = 37)	Range of sample size: 3-6; average no. cores: 4	DCIS	No. lesions	16	11	0	27
			% (95% CI)	59 (39-78)	41 (22-61)	NA	100 (87-100)
		DCIS with possible invasion	No. lesions	6	4	0	10
			% (95% CI)	60 (26–88)	40 (12–74)	NA	100 (69–100)
Total							
DCIS				101	68 (67%)	29 (29%)	4 (4%)	101/117 (86%)
DCIS with possible invasion				16	9 (56%)	7 (44%)	0	16/117 (14%)

CI = confidence interval; DCIS = ductal carcinoma in situ; NA = not applicable.
[a] Resection pathology was benign in 4 lesions: 2 - yielded normal breast tissue, 1 - yielded radial scar, and 1 - yielded fibrocystic changes.

calcifications not associated with a mass were biopsied using stereotactic guidance and that all masses were biopsied using ultrasound guidance regardless if they were associated with calcifications or not, the results according to method of biopsy guidance (stereotactic or ultrasound) and the imaging abnormality (calcifications or mass) are equivalent. Although underestimation rates were not significantly different for pure DCIS compared with DCIS with possible invasion according to the presenting imaging abnormality or method of guidance used for biopsy, there was a trend for lesions presenting as calcifications, biopsied under stereotactic guidance to be underestimated when the biopsy yielded DCIS with possible invasion compared with pure DCIS (3/6 [50%] vs. 18/74 [74%], $P = .4$). There was a trend to a higher likelihood of pure DCIS underestimation when the lesion presented as a mass or when the biopsy was performed under ultrasound guidance compared with the lesion presenting as calcifications or biopsied under stereotactic guidance (11/27 [41%] vs 18/74 [24%], $P = .17$).

The number of samples taken at a biopsy ranged from 3-14 cores, with an average of 6 samples. Six or fewer samples were taken during the biopsy of most lesions (97/117 [83%]). Underestimation rates according to the number of samples taken and DCIS lesion type on initial core biopsy are shown in Table 1. Although the results were not statistically significant, there was a trend towards increased underestimation for lesions that yielded DCIS with possible invasion compared with pure DCIS when 6 or fewer samples were obtained (7/15 [47%] vs 25/82 [31%], $P = .4$).

Most lesions that yielded pure DCIS on the biopsy specimen were either high grade (44/101 [43.5%]) or intermediate grade (44/101 [43.5%]) followed by low grade (10/101 [10%]). Grading was not available for 3 biopsy specimens (3/101 [3%]). Although there was no statistical difference between the groups of pure DCIS vs DCIS with possible invasion according to nuclear grade, the likelihood of underestimation was significantly higher for the pure DCIS group when the nuclear grade was high (41%) compared with intermediate (21%) and low grade (20%), $P = .03$. See Table 2 for underestimation rates according to DCIS nuclear grade.

The size of the invasive component in the 36 lesions that yielded invasive carcinoma at surgery was known in 35 (97%) and ranged between microinvasion (less than 1 mm) to 4.0 cm, with an average of 0.63 cm. The invasive component was greater or equal to 1 cm but less than 5 cm (pT1c or pT2) for 25% of lesions (9/36), less than 1 cm but greater than 1 mm (pT1a or pT1b) for 50% of lesions (18/36), and less than 1 mm (pTmic) for 22% of lesions (8/36).

Discussion

DCIS underestimation on percutaneous breast biopsy compromises a patient's surgical management, because it necessitates a second surgery, not routinely performed for DCIS lesions, to assess the axillary lymph nodes. The effect of ''possible invasion'' being present when DCIS is diagnosed on 14-gauge needle biopsy performed by using

Table 2
Likelihood of invasion at surgery in lesions that yield pure DCIS vs DCIS with possible invasion at core biopsy according to method of biopsy guidance, number of samples, clinical indication, and nuclear grade

	DCIS (N = 101)		DCIS with possible microinvasion (N = 16)			
Factor	No. invasive surgery/no. lesions	%	No. invasive surgery/no. lesions	%	*P*	Total no. (%)
Modality						
Stereotactic biopsy	18/74	24	3/6	50	.4	80 (68)
Ultrasound biopsy	11/27	41	4/10	40	NA	37 (32)
No. cores						
≤6	25/82	31	7/15	47	.4	97 (83)
>6	4/19	21	0/1	NA	.6	20 (17)
Indication						
Routine screening	16/45	36	1/3	33	NA	48 (41)
High-risk screening[a]	3/12	25	0	NA	NA	12 (10)
History of breast cancer	5/30	17	3/7	43	.3	37 (32)
Clinical finding	5/14	36	3/6	50	.9	20 (17)
DCIS grade						
Unknown	0/3	NA	2/2	100	NA	5 (4)
Low	2/10	20	1/1	100	NA	11 (10)
Intermediate	9/44	21	1/3	33	NA	47 (40)
High	18/44	41	3/10	30	.8	54 (46)
Total	29/101	29	7/16	44	.4	

DCIS = ductal carcinoma in situ; NA = not applicable.
[a] BRCA1, BRCA2, family history, prior mantle radiation.

stereotactic or ultrasound guidance on underestimation rates has not been previously reported. In our study of 117 lesions that yielded DCIS at percutaneous breast biopsy performed by using an automated 14-gauge needle, the likelihood of invasive disease at surgery tended to be higher when the lesions revealed DCIS with possible invasion, compared with lesions that yielded pure DCIS (44% vs 29%, $P = .36$).

Our findings of a 44% underestimation rate for DCIS with possible invasion diagnosed by using a 14-gauge needle under stereotactic or ultrasound guidance is much lower than the 80% previously reported when using a 9-gauge VAB under MRI guidance [2]. The higher underestimation rate, despite obtaining a much greater volume of tissue when using a 9-gauge VAB device compared with a 14-gauge trucut needle, although counterintuitive, is most likely explained by the differences in lesion types visualized and targeted with MRI compared with either ultrasound or mammography. Because tumors detected when using MRI are visible based on biological activity related to lesion enhancement, this may be a more relevant indicator of the propensity of invasion compared with nonphysiologic imaging with mammography and ultrasound.

The overall underestimation for the study group was 31% (36/117), which is in the range reported in the literature (10%–42%) [3–10]. Our data demonstrated a statistically significant increase in the likelihood of invasive cancer at subsequent surgery for pure DCIS lesions with a high nuclear grade compared with intermediate- and low-grade lesions (18/44 [41%] vs 9/44 [21%] vs 2/10 [20%], $P = .03$). Our results are comparable with those of previous studies, finding one of the most consistent predictors of invasive disease to be high-grade DCIS, as reported underestimation rates for high-grade DCIS at 14-gauge core or 11-gauge VAB range from 13%–36% compared with 7%–13% for low- or intermediate-grade DCIS [18,19]. Small numbers in the subgroup of DCIS with "possible invasion" preclude statistical comparison between groups based on nuclear grade.

There was a trend towards pure DCIS lesions having a higher likelihood of underestimation when the lesion presented as a mass and was biopsied by using ultrasound compared with stereotactic guidance (11/27 [41%] vs 18/74 [24%], $P = .17$). Our findings support previously reported higher rates of DCIS underestimation for lesions biopsied under ultrasound compared with stereotactic guidance (36.5%–42% vs 10%–36%, respectively) [3–10]. No additional factors, including imaging abnormality, clinical indication for imaging, or number of samples, were found to have a statistically significant effect on underestimation rates of DCIS on 14-gauge core biopsy.

Four initial DCIS lesions yielded benign results in the final surgical specimen, including 1 radial scar, 2 normal breast tissue, and 1 fibrocystic change. In all cases, the biopsy site reaction was identified, and none of the DCIS lesions were low grade, therefore, the event of an initial false-positive pathology reading was very low. The likely explanation was that either the lesions were completely removed by the core needle biopsy procedure, or that the residual disease was so minute that it could not be demonstrated at the level of histopathologic sections, including the previous biopsy site.

This study is limited because it was performed at a single centre, with a relatively small number of biopsy specimens that yielded DCIS with "possible invasion" and hence does not have the power for significant statistics. Although some of the biopsies were performed by trainees, all biopsies were supervised by experienced breast radiologists who routinely

performed more biopsy samples as required to obtain a sufficient volume of lesional tissue. This factor, therefore, likely has little effect on the results, as supported by the similar underestimation rates reported in the literature.

In summary, lesions biopsied by using a 14-gauge needle under stereotactic or ultrasound guidance tended to underestimate the presence of invasive cancer when pathology revealed DCIS with possible invasion compared with pure DCIS, as surgical pathology revealed invasive disease in 44% of lesions that yielded DCIS with possible invasion compared with 29% of lesions that yielded pure DCIS. High nuclear grade significantly increased the likelihood of pure DCIS lesion histologic underestimation. Whereas DCIS is recognized as a heterogeneous disease whose biology remains elusive, the literature continues to evolve that identifies high-risk factors for DCIS. Although controversial, with the growing body of literature, there is a push to consider sentinel lymph node biopsy at the time of initial definitive lumpectomy for patients with high-risk DCIS to decrease the morbidity and cost associated with a second operation after invasive cancer is found [20]. Our results support recommendations by other researchers that high-grade DCIS is considered a high-risk factor and lymph-node sampling by sentinel node procedure may be appropriate at the first operation. The additional factor of ''possible invasion'' associated with DCIS at 14-gauge core biopsy could be considered a high-risk marker and be given similar considerations for sentinel lymph node sampling at the initial lumpectomy but requires further investigation.

References

[1] Liberman L, Goodsine SL, Dershaw D, et al. One operation after percutaneous diagnosis of non palpable breast cancer: frequency and associated factors. AJR Am J Roentgenol 2002;178:673−9.

[2] Lee J, Kaplan JB, Murray MP, et al. Underestimation of DCIS at MRI guided vacuum assisted breast biopsy. AJR Am J Roentgenol 2007; 189:468−74.

[3] Liberman L. Clinical management issues in percutaneous core breast biopsy. Radiol Clin North Am 2000;38:791−807.

[4] Jackman RJ, Burbank F, Parker SH, et al. Stereotactic breast biopsy of nonpalpable lesions: determinants of ductal carcinoma in situ underestimation rates. Radiology 2001;218:497−502.

[5] Pandelidis S, Heiland D, Jones D, et al. Accuracy of 11 gauge vacuum assisted core biopsy of mammographic breast lesions. Ann Surg Oncol 2003;10:43−7.

[6] Lee JW, Han W, Ko E, et al. Sonographic lesion size of ductal carcinoma in situ as a preoperative predictor for the presence of an invasive focus. J Surg Oncol 2008;98:15−20.

[7] Lourenco AP, Mainiero MB, Lazarus E, et al. 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.

[8] Lee CH, Carter D, Philpotts LE, et al. Ductal carcinoma in situ diagnosed with stereotactic core needle biopsy: can invasion be predicted? Radiology 2000;217:466−70.

[9] Darling MLR, Smith DN, Lester SC, 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;175:134−6.

[10] Schueller G, Jaromi S, Ponhold L, et al. US-guided 14-gauge core-needle breast biopsy: results of a validation study in 1352 cases. Radiology 2008;248:406−13.

[11] Tavassoli FA, Devilee P. Pathology and genetics of tumors of the breast and female genital organs. Lyon, France: IARC; 2002.

[12] Holland R, Peterse JL, Millis RR, et al. Ductal carcinoma in situ: a proposal for a new classification. Semin Diagn Pathol 1994;11:167−80.

[13] Ellis IO, Humphreys S, Michell M, et al. Best practice no 179. Guidelines for breast needle core biopsy handling and reporting in breast screening assessment. J Clin Pathol 2004;57:897−902.

[14] Silver SA, Tavassoli FA. Mammary ductal carcinoma in situ with microinvasion. Cancer 1998;82:2382−90.

[15] Padmore RF, Fowble B, Hoffman J, et al. Microinvasive breast carcinoma: clinicopathologic analysis of a single institution experience. Cancer 2000;88:1403−9.

[16] Joseph L. Fleiss. Statistical methods for rates and proportions. 2nd ed. New York: John Wiley & Sons; 1981:19−32.

[17] Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934;26:404−13.

[18] Wilkie C, White L, Dupont E, et al. An update of sentinel lymph node mapping in patients with ductal carcinoma in situ. Am J Surg 2005; 190:563−6.

[19] O'Flynn EA, Morel JC, Gonzalez J, et al. Prediction of the presence of invasive disease from the measurement of extent of malignant microcalcification on mammography and ductal carcinoma in situ grade at core biopsy. Clin Radiol 2009;64:178−83.

[20] Goyal A, Douglas-Jonaes A, Monypenny I, et al. Is there a role of sentinel lymph node biopsy in ductal carcinoma in situ? Analysis of 587 cases. Breast Cancer Res Treat 2006;98:311−4.