Annals of Surgical Oncology, **10**(7):748–753
DOI: 10.1245/ASO.2003.11.011

The Finding of Invasive Cancer After a Preoperative Diagnosis of Ductal Carcinoma-In-Situ: Causes of Ductal Carcinoma-In-Situ Underestimates With Stereotactic 14-Gauge Needle Biopsy

Lidewij E. Hoorntje, MD, Marguerite E. I. Schipper, MD, Petra H. M. Peeters, MD, PhD, Frank Bellot, MD, Remmert K. Storm, MD, and Inne H. M. Borel Rinkes, MD, PhD

Background: For the evaluation of nonpalpable lesions of the breast, image-guided 14-gauge automated needle biopsy is increasingly replacing wire-localized excision. When ductal carcinoma-in-situ (DCIS) is diagnosed at core biopsy, invasive cancer is found in approximately 17% of excision specimens. These so-called DCIS underestimates pose a problem for patients and surgeons, because they generally cause extension of treatment. We evaluated DCIS underestimates in detail to assess reasons for missing the invasive component at core biopsy. This evaluation also included a histological comparison with true DCIS (DCIS at core biopsy and excision).

Methods: Between 1997 and 2000, DCIS was diagnosed at 14-gauge needle biopsy in 255 patients. In 41 cases (16%), invasive cancer was found at excision. We performed a thorough histopathological and radiological review of all these DCIS underestimates, including a histological comparison with core biopsy specimens of 32 true DCIS cases. We assessed the main reason for missing the invasive component at core biopsy.

Results: Causes for DCIS underestimates were categorized into "mainly radiological" (n = 20), "mainly histopathological" (n = 15), and "histological disagreements" (n = 6). High-grade DCIS and periductal inflammation in core biopsies made a DCIS underestimate 2.9 and 3.3 times more likely, respectively.

Conclusions: A variety of radiological and histopathological reasons contribute to the DCIS underestimate rate. Approximately half of these are potentially avoidable.

Key Words: Breast cancer—Ductal carcinoma-in-situ—Large-core needle biopsy—Nonpalpable—DCIS underestimate rate.

Ductal carcinoma-in-situ (DCIS) diagnosed at image-guided core biopsy of the breast may turn out to be underestimated at subsequent surgical excision biopsy. In roughly 17% of cases, an invasive component is found at surgery.[1] These so-called DCIS underestimates are undesirable for various reasons. Because most surgeons do not perform axillary lymph node dissection or sentinel node biopsy (SNB) for DCIS, a DCIS underestimation will result in axillary dissection or SNB at a later date. This not only implies a delay in the definitive diagnosis and, hence, the appropriate treatment, but is also associated with higher costs. Furthermore, it has been suggested by several authors that SNB, the preferred axillary approach in small-size invasive breast cancer, is less accurate after prior breast surgery.[2,3] Finally, DCIS underestimates can be expected to be psychologically distressing for the patient. Therefore, decreasing the DCIS underestimate rate after image-guided breast biopsy is desirable.

Various studies have tried to find determinants of DCIS underestimates. Factors related to the underestimate rate include the size of the mammographic lesion (i.e., there is more sampling error with a larger lesion),

Received November 13, 2002; accepted April 21, 2003.

From the Department of Surgery (LEH, IHMBR), Department of Pathology (MEIS, FB), Clinical Epidemiology, Julius Center for Health Sciences and Primary Care (LEH, PHMP), and Department of Radiology (LEH, RKS), the University Medical Center Utrecht, Utrecht, The Netherlands.

Address correspondence and reprint requests to: I. H. M. Borel Rinkes, MD, PhD, University Medical Center Utrecht, Department of Surgery (G04.228), Heidelberglaan 100, 3584 CX Utrecht, The Netherlands; Fax: 31-30-254-1944; E-mail: i.h.m.borelrinkes@azu.nl.

the extent and distribution of the calcifications (i.e., a larger area of calcifications turns out to represent an invasive tumor more often), and the presence of a mass (a mammographic mass is often associated with an invasive carcinoma).[4–8] Histological factors reported to be associated with a higher likelihood of invasiveness or microinvasiveness include a high grade of nuclear atypia, a comedo subtype, and larger size.[6,8–12] However, these findings have not led to generally accepted recommendations for decreasing the DCIS underestimate rate.

The purpose of this study was to provide a detailed evaluation of DCIS underestimates and to assess reasons for missing the invasive component at core biopsy. It included a histological comparison with core biopsy samples of patients with true DCIS (i.e., DCIS at core biopsy and excision).

MATERIALS AND METHODS

Study Population

From April 1997 to January 2001, 1179 stereotactic 14-gauge needle biopsies were performed in 1113 patients. In 255 patients, DCIS was diagnosed at needle biopsy, and all underwent surgical excision. At excision, invasive carcinoma was diagnosed in 41 (16%) of the 255 patients. These cases are referred to as DCIS underestimates. If no invasive cancer was found at excision, these cases were labeled true DCIS (n = 214). A random sample was taken from the true DCIS group (n = 32) for comparative purposes.

Biopsy Procedure

Since 1997 we have used stereotactic 14-gauge core needle biopsies in five institutions (Antoni van Leeuwenhoek Hospital, Amsterdam; Bosch Medicentrum, Den Bosch; Martini Hospital, Groningen; Dr. Daniel den Hoed Clinic, Rotterdam; and University Medical Center, Utrecht) to evaluate patients with nonpalpable breast lesions suggestive of carcinoma. All local institutional review boards approved the study protocol.

Biopsies were performed in all centers with a 14-gauge core needle and a long-throw (2.2-cm excursion) automated biopsy device with multiple passes (C. R. Bard Inc., Covington, GA) with the patient prone on a table (Fisher Imaging, Denver, CO). Lesions were localized with digital mammography. Our protocol advises taking at least eight core biopsy samples in cases of calcifications and five in cases of density or architectural distortion. In case of calcifications or microcalcifications, a specimen radiograph was obtained and the biopsy procedure was said to be representative if some of these calcifications or microcalcifications were shown in the specimen. In all cases, histopathological findings were correlated with the mammographic features at our weekly multidisciplinary meeting, which was attended by the radiologist performing stereotactic breast biopsies, a breast pathologist, and a surgeon. Our diagnostic protocol has been described in detail elsewhere.[13] Lesions at each of the five institutions were accrued sequentially. Ultrasonographically guided percutaneous biopsy findings were not included.

Data Collection

Characteristics of participants were collected through questionnaires before the 14-gauge needle biopsy and were compared between the true DCIS group (n = 214) and the DCIS underestimate group (n = 41). These included patient factors (age at needle biopsy procedure, history of benign or malignant breast disease, hormone-replacement therapy, and parity). Furthermore, radiological characteristics were noted by the radiologist who performed the biopsy (type of mammographic lesion [mass, calcifications, or architectural distortion]; radiological classification [probably benign, suggestive of malignancy, or radiologically malignant]; the largest diameter of the area of calcifications; accuracy of the localization of the lesions with digital imaging and of the biopsy procedure; and the total number of biopsy specimens obtained). Histopathological characteristics included tissue diagnosis and the type and grade of the tumor. The grade of DCIS (I, well differentiated; II, moderately differentiated; III, poorly differentiated) was determined by using the classification proposed by Holland et al.[14]

Radiological and Histopathological Review

An extensive review of the radiological and histopathological material of all DCIS underestimate cases (n = 41) was performed to find reasons for missing the invasive cancer at core biopsy. All mammograms, x-rays taken during the biopsy procedure, and specimen radiographs were reassessed by a radiologist with experience in stereotactic breast biopsy procedures.

All core and surgical biopsy specimens were reviewed by an expert breast pathologist. In addition, we compared the histopathological findings at core biopsy of a nonselective sample of 32 true DCIS cases with those of the 41 DCIS underestimate cases. All tissue obtained at core biopsy was embedded in paraffin and serial-sectioned in slides of 5 μm, and every 10th slide was stained with hematoxylin and eosin. Slides of the core specimens were scored on the technical quality of the slide, fixation, and the staining (hematoxylin and eosin). The quality of the tissue and the damage induced by the biopsy proce-

dure were noted. The total length of the core biopsies was registered. The presence, type (dystrophic or psammomatous), and location (in malignant or benign tissue) of calcifications were noted. Furthermore, periductal stromal reaction—e.g., fibrosis and inflammatory infiltrate—was quantified as a potential predictor of invasive carcinoma.[5] All surgical excision specimens were reviewed along the same criteria, including a description of the type, size, location, and multifocality of the invasive carcinoma.

Finally, for each of the 41 DCIS underestimate cases, the pathologist and the radiologist decided what the most likely reason was for missing the invasive component at core biopsy. These reasons were subsequently classified into the categories "mainly radiological" and "mainly histopathological" reasons and "histological disagreements."

Statistical Analysis

Characteristics for DCIS underestimates were compared with true DCIS characteristics. Categorical characteristics are presented as percentages, and the χ^2 test was used to compare proportions. Statistical analysis was performed with SPSS 9.0 (SPSS Inc., Chicago, IL).

RESULTS

Baseline Characteristics

Patient characteristics are listed in Table 1. Apart from a lower frequency of nulliparity (10% vs. 25%; $P < .05$) and a higher frequency of postmenopausal women (71% vs. 10%; $P < .05$) in the DCIS underestimate group, the results were not significantly different from those of true DCIS patients. In the 41 DCIS underestimate cases, the mean ± SD diameter of the invasive component was 8.3 ± 6.3 mm. Eight patients had axillary metastases (range, 1–11 tumor-positive lymph nodes; median, 7).

TABLE 1. *Patient characteristics*[a]

Variable	DCIS underestimates (n = 41)	True DCIS (n = 214)
Age, y (mean ± SD)	59.2 ± 10.0	57.7 ± 10.1
History of breast cancer	8 (20)	26 (12)
History of benign breast disease	10 (24)	58 (27)
Family history of breast cancer	11 (27)	60 (28)
Nullipara	4 (10)[b]	53 (25)[b]
Hormone-replacement therapy use	18 (44)	111 (52)
Postmenopausal	29 (71)[b]	21 (10)[b]
Referral by national screening program	21 (51)	135 (63)

DCIS, ductal carcinoma-in-situ.
[a] Data are n (%) unless otherwise marked.
[b] $P < .05$.

Radiological Characteristics

The radiological characteristics are listed in Table 2. Both in the DCIS underestimate and the true DCIS group, the radiologist documented the lesion localization and biopsy procedure to be correctly executed in 95% of cases. The average extent of microcalcifications for the entire group of lesions consisting of calcifications (n = 236) was 16.4 mm.

Histopathological Review

The average length of the sum of all core biopsy specimens per patient was 53.2 ± 19.3 mm in the DCIS underestimate group vs. 54.3 ± 29.7 mm for the true DCIS group ($P > .05$). Calcifications were never found in the center of the invasive tumor in the excision specimen, but were found in the peripheral ducts containing DCIS or in adjacent benign mammary tissue (Fig. 1).

The results of the histopathological review are listed in Table 3. Periductal stromal fibrosis was not related to invasiveness. A poorly differentiated DCIS in the core biopsy specimen was 2.9 times more likely to be a DCIS underestimate than a true DCIS when compared with well-differentiated or moderately differentiated DCIS, and if a periductal inflammatory infiltrate was seen, this was 3.3 times more likely to be associated with invasiveness.

Correlation Between Histopathology and Radiology

On combined review of the histopathological and radiological findings, the radiologist and pathologist for-

TABLE 2. *Radiological characteristics of DCIS underestimates and true DCIS*[a]

Radiological characteristics	DCIS underestimates (n = 41)	True DCIS (n = 214)
Radiological classification		
Probably benign	6 (15)	43 (20)
Suggestive of maligancy	27 (66)	141 (66)
Radiologically malignant	8 (19)	30 (14)
Lesion type		
Density only	2 (5)	17 (8)
Density with calcifications	6 (15)	32 (15)
Calcifications only	33 (80)	165 (77)
Largest-diameter calcification area (mm)	23.2[b]	15.0[b]
Largest diameter ≥10 mm	33 (85)	155 (79)
Largest diameter ≥25 mm	13 (34)[b]	26 (13)[b]
Largest diameter ≥50 mm	6 (15)[b]	4 (2)[b]
Accuracy of biopsy procedure		
Sampling of the lesion certain	39 (95)	201 (94)
Uncertain sampling of the lesion	2 (5)	13 (6)
No. of core biopsies, median (range)	6 (5–13)	7 (1–18)

DCIS, ductal carcinoma-in-situ.
[a] Data are n (%) unless otherwise marked.
[b] $P < .05$.

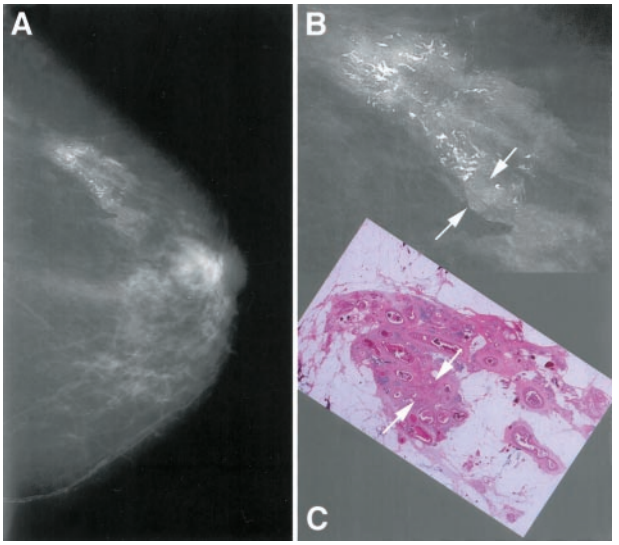

FIG. 1. (**A**) Representative mammogram with suggestive calcifications. (**B**) Detail of area with calcifications and density. Arrows indicate the density. (**C**) Detail of histological slide corresponding to (**B**). Arrows indicate the invasive component.

mulated the most likely reason for missing the invasive carcinoma at core biopsy for each of the 41 DCIS underestimate cases (Table 4). The reasons were categorized into three groups. The first category was "mainly radiological" problems. This included four cases in which the invasive component was missed because the mammographic lesions consisted of such a large area (30, 45, 60, and 95 mm) of calcifications that only part of the lesion was sampled, which turned out not to be the invasive component (sizes of the invasive tumors were 16, 6, 9, and 2 mm, respectively). In nine cases, the mammographic lesion consisted of calcifications and an accompanying density, but only calcifications were sampled. At review, the invasive component found at excision turned out to be the mammographic density. Seven other cases were underestimated because of different sampling difficulties. The second category was "mainly histopathological" problems—e.g., nine cases were suggestive of invasive cancer, but the diagnosis could not be made with sufficient certainty. Most of these cases involved intermediately or poorly differentiated DCIS. In three other cases, the combination of a poor quality of the slide itself, the fixation, or the staining negatively affected the microscopic examination and subsequent accuracy of the histopathological diagnosis of the core biopsy specimen. In these other cases, suggestion of invasive or microinvasive carcinoma was seen, but because of the lack of quality of the slide, there was not enough convincing evidence for an invasive carcinoma diagnosis at core biopsy. In three cases, the findings of invasive tumor at excision were coincidental.

The third category consisted of "histological disagreements." Two cases seemed to have been misdiagnosed by the pathologist who originally examined the core biopsy sample. Invasive cancer was already present in the core biopsy specimen but was missed. In an additional four cases, no invasive cancer was diagnosed in the excision specimen at revision, which implies that these had been incorrectly defined and treated as DCIS underestimates.

DISCUSSION

In our consecutive series of 255 cases in which DCIS was diagnosed at stereotactic 14-gauge-needle biopsy, invasive cancer was found in 41 cases (16%). This DCIS underestimate rate is comparable to rates reported in the literature.[1] Review showed that reasons for missing the invasive component at core biopsy were mainly radiological in 20 cases (49%), were mainly histopathological in 15 cases (36%), and were misdiagnoses (histological disagreements) in 6 (15%). Careful sampling, handling of biopsy specimens, and staining may prevent DCIS underestimates in up to 50% of cases. When core biopsy specimens were compared, the only difference we found was that high-grade DCIS and periductal inflammatory response were more often present in core specimens of DCIS underestimate cases than in true DCIS cases.

In an attempt to avoid radiological causes of DCIS underestimates, one has to realize that most DCIS lesions—in our series, 236 (95%) of 255 lesions—present as calcifications on the mammogram. Thorough sampling of a large area of calcifications is often impossible because of technical reasons of the stereotactic breast biopsy. However, the likelihood of an invasive carcinoma is greater in the presence of extensive calcifications.[15] It is interesting to note that we found the invasive component of the tumor never to be present in the area of calcifications; these areas usually represented DCIS, benign tissue, or both. If invasive carcinoma is present, it is most likely to be present as a mammographic density, and, hence, in composed lesions, both density and calcifications should be sampled. Because 14-gauge needle biopsy is a sampling method, the histopathological diagnosis can be made only on the tissue sampled, and this may be not representative of all pathological findings in a given case.

Decreasing the DCIS underestimate rate has been attempted by using biopsy devices that take larger biopsy specimens, such as 11-gauge vacuum-assisted biopsy.[4,16,17] DCIS underestimate rates for 11-gauge vacuum-

TABLE 3. *Histological features of DCIS underestimates and true DCIS*[a]

Variable	DCIS underestimates (n = 41)	True DCIS (n = 32)	Total
Histological grade of DCIS[b]			
Poorly differentiated (grade III)	20 (49)	8 (25)	28
Well- or intermediately differentiated (grade I or II)	21 (51)	24 (75)	45
Stromal periductal fibrosis[c]			
Yes	25 (61)	20 (63)	45
No	16 (39)	12 (38)	28
Periductal inflammatory infiltrate[d]			
Yes	26 (63)	11 (34)	37
No	15 (37)	21 (66)	36

DCIS, ductal carcinoma-in-situ; 95% CI, confidence interval.
[a] Data are n (%).
[b] Odds ratio, 2.9; 95% CI, 1.0–7.8.
[c] Odds ratio, .9; 95% CI, .4–2.4.
[d] Odds ratio, 3.3; 95% CI, 1.3–8.7.

assisted biopsy are reported to be 10.3% to 11.4%, in comparison to the 15.5% (95% confidence interval, 8%–26%) reported for 14-gauge automated core biopsy.[1] Of note, even with diagnostic excision biopsy, DCIS underestimates have been reported in up to 18% of cases.[18,19]

To decrease histopathological causes of DCIS underestimates, careful handling of the fragile material obtained at core biopsy is imperative. A sufficient number of slides should be made to gain adequate exposure of the tissue retrieved. We advocate serial sectioning of all core biopsy tissue. The histopathological assessment of 14-gauge breast biopsies may be more complicated when compared with open breast biopsy, because a smaller amount of tissue is obtained. The context of the surrounding tissue and topographic relationships of various structures is crucial for histologic analysis in many instances. Disagreements in histopathological diagnosis between pathologists do occur and may have a serious effect on therapeutic decisions. In this study, in six cases the diagnosis made at review differed from the original histopathological diagnosis. We therefore recommend that whenever a pathologist has doubts about the histopathological diagnosis at core biopsy (considering the consequences of repeated breast surgery), he or she should not hesitate to consult a colleague with extensive expertise in breast pathology.

The presence of stromal fibrosis or a periductal inflammatory cell infiltrate are subtle signs of early invasion.[19,20] The etiology of the periductal inflammatory response in association with carcinoma is unknown, but it has been speculated to represent an immune response to (occult) basement membrane destruction and invasion or a response to a tumor-secreted or carcinogenic agent.[19,21,22] In this study, we found that when a periductal inflammatory infiltrate is present, the risk of finding invasion at excision is more than three times higher than when no inflammation is present. Also, poorly differentiated DCIS was associated with a 3-fold increased risk of invasion. A lesion with poorly differentiated DCIS and a periductal inflammatory response turned out to be a DCIS underestimate in 16 (70%) of 23 cases.

The diagnosis of subtle invasive carcinoma in a core biopsy specimen can be facilitated by obtaining deeper levels from the tissue block and/or by using immunohistochemical stains for the basement membrane (collagen IV and laminin) and myoepithelial cells (e.g., α–smooth muscle actin or heavy-chain myosin).[20] Cytokeratin immunostains are essential because they highlight individual invasive carcinoma cells that are beyond the bounds of the parent in situ carcinoma. These immunostains are also useful but not necessary in all cases for making the diagnosis of microinvasion.[23] Nevertheless, the α–smooth muscle actin and cytokeratin 14 immunostains we performed on our core biopsy specimens of DCIS underestimates revealed no confirmation of invasiveness. The value of these staining procedures is at least disputable.

The success of 14-gauge needle biopsy procedures and the validity of pathological diagnoses made on the core biopsy material are key determinants for the surgeon in planning the optimal management of nonpalpable breast lesions. Another option might be that when suspicion for invasion or microinvasion is high, treatment is directed as if invasive cancer were established at core biopsy. This may be appropriate for patients with a lesion presented by an area of microcalcifications $\geq$50 mm, because 60% of our cases turned out to be DCIS underestimates. Also, when the core biopsy specimen showed poorly differentiated DCIS with a periductal inflammatory response, we found invasive cancer at excision in 16 (70%) of 23 cases.

TABLE 4. *Reasons for missing the invasive carcinoma on core biopsy*

Variable	n
Mainly radiological problem	20
Mammographic lesion	
Large area of microcalcifications, no density	4
Large area of microcalcifications plus a density; only calcifications were sampled	9[a]
No density could be distinguished because breast tissue was very dense	2
Very small area of calcifications	1
Biopsy procedure	
Density could not be visualized clearly with digital imaging (technical problem)	2
Too few or nonrepresentative core specimens obtained	2[b]
Mainly histopathological problem	15
Poor quality of the slides/fixation/staining/too much damage induced by core biopsy to diagnose invasive cancer	3
Suspicion of (micro)invasive carcinoma	8
No invasive carcinoma in core biopsy but stromal response suggesting invasive cancer elsewhere in the DCIS area	1
Coincidental finding of a small invasive cancer at excision	3
Other reasons: histological disagreements	6
Invasive carcinoma already present in core biopsy, but missed by routine pathologist	2
No invasive carcinoma present in the excision specimen, only DCIS	4

DCIS, ductal carcinoma-in-situ.

[a] One patient had a density on ultrasound, but on the mammogram, only three clusters of calcifications were visible, and these were sampled.

[b] Core biopsy material showed only one and two ducts in total; all three had DCIS.

In conclusion, approximately 16% of DCIS diagnosed by stereotactic 14-gauge needle biopsy are invasive at excision. Reasons for missing the invasive component are mostly radiological (49%) or histopathological (36%), whereas histopathological disagreements account for 15% of DCIS underestimates. Poorly differentiated DCIS and periductal inflammation found at core biopsy increase the chances of finding an invasive component at excision by approximately 3-fold.

ACKNOWLEDGMENTS

The acknowledgments are available online at www.annalssurgicaloncology.org.

REFERENCES

1. Verkooijen HM, Peeters PH, Buskens E, et al. Diagnostic accuracy of large-core needle biopsy for nonpalpable breast disease: a meta-analysis. *Br J Cancer* 2000;82:1017–21.
2. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer—a multicenter validation study. *N Engl J Med* 1998;339: 941–6.
3. Feldman SM, Krag DN, McNally RK, Moor BB, Weaver DL, Klein P. Limitation in gamma probe localization of the sentinel node in breast cancer patients with large excisional biopsy. *J Am Coll Surg* 1999;188:248–54.
4. Jackman R, Burbank F, Parker S, et al. Stereotactic breast biopsy of nonpalpable lesions: determinants of ductal carcinoma in situ underestimation rates. *Radiology* 2001;218:497–502.
5. King TA, Farr GH Jr, Cederbom GJ, et al. A mass on breast imaging predicts coexisting invasive carcinoma in patients with a core biopsy diagnosis of ductal carcinoma in situ. *Am Surg* 2001; 67:907–12.
6. Wahedna Y, Evans AJ, Pinder SE, Ellis IO, Blamey RW, Geraghty JG. Mammographic size of ductal carcinoma in situ does not predict the presence of an invasive focus. *Eur J Cancer* 2001;37: 459–62.
7. Dinkel HP, Gassel AM, Tschammler A. Is the appearance of microcalcifications on mammography useful in predicting histological grade of malignancy in ductal cancer in situ? *Br J Radiol* 2000;73:938–44.
8. Bagnall MJ, Evans AJ, Wilson AR, et al. Predicting invasion in mammographically detected microcalcification. *Clin Radiol* 2001; 56:828–32.
9. Lagios MD, Westdahl PR, Margolin FR, Rose MR. Duct carcinoma in situ. Relationship of extent of noninvasive disease to the frequency of occult invasion, multicentricity, lymph node metastases, and short-term treatment failures. *Cancer* 1982;50:1309–14.
10. Holland R, Hendriks JH, Vebeek AL, Mravunac M, Schuurmans Stekhoven JH. Extent, distribution, and mammographic/histological correlations of breast ductal carcinoma in situ. *Lancet* 1990; 335:519–22.
11. Lagios MD. Duct carcinoma in situ. Pathology and treatment. *Surg Clin North Am* 1990;70:853–71.
12. Renshaw AA. Predicting invasion in the excision specimen from breast core needle biopsy specimens with only ductal carcinoma in situ. *Arch Pathol Lab Med* 2002;126:39–41.
13. Verkooijen HM. Diagnostic accuracy of stereotactic large-core needle biopsy for nonpalpable breast disease: results of a multicenter prospective study with 95% surgical confirmation. *Int J Cancer* 2002;99:853–9.
14. 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.
15. Liberman L, Abramson AF, Squires FB, Glassman JR, Morris EA, Dershaw DD. The breast imaging reporting and data system: positive predictive value of mammographic features and final assessment categories. *AJR Am J Roentgenol* 1998;171:35–40.
16. Darling ML, 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;175:1341–6.
17. Burak WE, Owens KE, Tighe MB, et al. Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. *Arch Surg* 2000;135:700–3.
18. Carter D, Smith RR. Carcinoma in situ of the breast. *Cancer* 1977;40:1189–93.
19. 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.
20. Hoda SA, Rosen PP. Practical considerations in the pathologic diagnosis of needle core biopsies of breast. *Am J Clin Pathol* 2002;118:101–8.
21. Azzopardi JG, Laurini RN. Elastosis in breast cancer. *Cancer* 1974;33:174–83.
22. Fisher ER, Sass R, Fisher B, Wickerham L, Paik SM. Pathologic findings from the National Surgical Adjuvant Breast Project (protocol 6). I. Intraductal carcinoma (DCIS). *Cancer* 1986;57:197–208.
23. Prasad ML, Osborne MP, Giri DD, Hoda SA. Microinvasive carcinoma (T1mic) of the breast: clinicopathologic profile of 21 cases. *Am J Surg Pathol* 2000;24:422–8.