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Solid Breast Nodules: Use of Sonography to Distinguish between Benign and Malignant Lesions[1]

PURPOSE: **To determine whether sonography could help accurately distinguish benign solid breast nodules from indeterminate or malignant nodules and whether this distinction could be definite enough to obviate biopsy.**

MATERIALS AND METHODS: **Seven hundred fifty sonographically solid breast nodules were prospectively classified as benign, indeterminate, or malignant. Benign nodules had no malignant characteristics and had either intense homogeneous hyperechogenicity or a thin echogenic pseudocapsule with an ellipsoid shape or fewer than four gentle lobulations. Sonographic classifications were compared with biopsy results. The sensitivity, specificity, and negative and positive predictive values of the classifications were calculated.**

RESULTS: **Benign histologic features were found in 625 (83%) lesions; malignant histologic features, in 125 (17%). Of benign lesions, 424 had been prospectively classified as benign. Two lesions classified as benign were found to be malignant at biopsy. Thus, the classification scheme had a negative predictive value of 99.5%. Of 125 malignant lesions, 123 were correctly classified as indeterminate or malignant (98.4% sensitivity).**

CONCLUSION: **Sonography can be used to accurately classify some solid lesions as benign, allowing imaging follow-up rather than biopsy.**

Index terms: Breast neoplasms, diagnosis, 00.1298 • Breast neoplasms, US, 00.30 • Breast, US, 00.1298

Radiology 1995; 196:123–134

For appropriately selected patients, diagnostic breast ultrasonography (US) can improve the specificity of clinically and mammographically detected abnormalities. Its most readily accepted use in the United States has been in distinguishing a simple cyst from a solid lesion. When all criteria for a simple cyst are strictly adhered to, the accuracy of US is 96%–100% (1). However, cysts constitute only 25% of all palpable or mammographically detected lesions (2). This leaves a tremendous number of lesions that fall into the indeterminate or solid nodule categories. In general, these lesions require aspiration or biopsy, with use of excisional or large-core techniques. Although well tolerated, these procedures do have some risk, induce patient discomfort and anxiety, and increase costs in terms of both patient recovery and overall health care expense.

The emphasis on early detection of breast cancer, the desire not to miss a malignant lesion in the early stage of disease, and the current medicolegal environment encourage an aggressive biopsy approach to breast problems. With such an approach, a large majority of the palpable and mammographically detected nonpalpable breast lesions on which biopsies are performed will be benign. The positive biopsy rate for cancer is low, between 10% and 31% (3–5). This means that 70%–90% of breast biopsies are performed in women with benign disease (a negative-to-positive biopsy ratio of between 9:1 and 2.3:1). Both mammographic and sonographic methods have been used in attempts to reduce the negative-to-positive biopsy ratio, and therefore, the cost to society. Mammographic surveillance rather than surgical excision is an acceptable method for follow-up of mammographically "probably benign" lesions (6). Because not all benign lesions can confidently be placed in this category, some investigators have evaluated the characteristics of individual sonographic, spectral Doppler, and color Doppler imaging for distinguishing benign from malignant solid nodules (7–42).

The considerable overlap between benign and malignant lesion characteristics found in these studies has so disappointed some authors that they have recommended that sonography be used only to determine whether a lesion is cystic or solid and/or for needle guidance (7–23). On the basis of some of these reports, the recommendation has been made that biopsies should be performed on all solid nodules, regardless of their sonographic appearance (2,9–11,15,24,25, 34–37). Despite many positive reports on sonographic distinction between benign and malignant solid nodules (24–33), it is our impression that the vast majority of radiologists in the United States have not accepted these reports and act on the principle that biopsies should be performed on all solid nodules.

Since the initial sonographic studies were performed and published, the near-field imaging capability of sonographic equipment has markedly improved. Because of this, we decided to revisit the sonography issue and evaluated a battery of sonographic characteristics, combining both previously published (9–11,15,16,18,19,24–28,31,32,34) and new criteria, to determine our current ability to distinguish benign from malignant solid breast

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See also the editorial by Jackson (pp 14–15) in this issue.

Abbreviations: BI-RADS = Breast Imaging Reporting and Data System, CMAP = Colorado Mammography Advocacy Program, DCIS = ductal carcinoma in situ.

lesions with sonography. Despite the known overlap between benign and malignant features in some lesions, we were especially interested in determining whether we could identify a subgroup of solid nodules with sonographic characteristics so definitively benign that their presence might obviate biopsy.

MATERIALS AND METHODS

From March 1989 through July 1993, sonography was used to prospectively classify 750 sonographically solid breast nodules in 622 women into one of three categories: benign, indeterminate, or malignant. The mean age of the women was 47 years, with a range of 18–88 years. For the 750 nodules, the indications for breast sonography were nonspecific mammographic abnormality in 442 (59%), palpable abnormality in 278 (37%), follow-up of a sonographic lesion in 15 (2%), nipple secretion with unsuccessful ductography in eight (1%), and other indications in seven (1%). Nonspecific mammographic abnormalities included circumscribed nodules and partially circumscribed, partially obscured nodules; focal asymmetries present in two views; architectural distortions; and masses with indistinct borders. Lesions that were obviously mammographically malignant were not scanned sonographically, except for US-guided needle localization or large-core needle biopsy, and were not included in this study.

All patients were examined with high frequency, 7.5–10.0-MHz electronically focused near-field imaging probes with US equipment from Diasonics Spectra (Milpitas, Calif), Advanced Technology Laboratories (High Definition Imaging; Bothell, Wash), or Acoustic Imaging (model 5200; Phoenix, Ariz). In the vast majority of cases, no acoustic standoff pad was used. In the rare instances when the leading edge of the nodule was within 5 mm of the skin and poorly seen or when the palpable abnormality was "pea-sized" or smaller, a 1-cm-thick pad or a glob of acoustic jelly was used for a standoff. In addition to focused examination of the suspicious area in the breast in both longitudinal and transverse planes, particular attention was also given to scanning patients in radial and antiradial planes. These planes were defined like the spokes in a wheel, with the nipple being analogous to the hub and the radial axis along the line of the spokes. The antiradial plane was defined as perpendicular to the radial axis. Because the ductal system of the breast generally courses in a radial direction toward the nipple, tumors that extend along the duct are best visualized in this plane. The maximum diameter of the nodule was measured and defined as the greatest dimension of the nodule in any plane.

The prospective classification of the nodules into benign, indeterminate, or malignant categories was performed by five radiologists. The classification was included in their sonographic reports. Classification data were collected from the review of these reports and entered into a database. Classification was based on previously published criteria and nonpublished criteria from our retrospective study of 411 patients (9–11,15,16,18,19,24–28,31,32,34). None of the nodules in the retrospective study were included in the prospective study.

Individual sonographic characteristics that had less than a 5% association with malignancy in the retrospective study were considered benign findings for the prospective study. Findings associated with a 5%–49% chance of malignancy were considered indeterminate. Those with 50% or greater chance of malignancy were considered malignant. Individual benign, indeterminate, and malignant sonographic characteristics for solid lesions used in this study are listed in Table 1. Descriptions of the individual characteristics can be found at the end of this section.

Although five individual benign findings exist, a combination of individual benign findings was required to classify a nodule as benign. Only three combinations of benign findings resulted in a nodule's classification as benign: (*a*) lack of any malignant findings plus (*b*) intense and uniform hyperechogenicity; (*c*) ellipsoid shape plus a thin, echogenic capsule; and (*d*) gentle lobulations (two or three) plus a thin echogenic capsule.

To prospectively classify the nodules, the findings were used in the following manner. First, malignant findings for each nodule were sought. If even a single malignant feature was present, the nodule was excluded from the benign classification. If no malignant features were found, one of the three combinations of benign characteristics was sought. If one of the three combinations was found, the lesion was classified as benign. If no malignant features were found and none of the combinations of benign characteristics was found, the lesion was classified, by default, as indeterminate. This classification algorithm, with combinations of benign findings required for benign classification and with the absence of specific benign findings resulting in an indeterminate classification, was designed to err on the side of caution—to minimize the risk of false-negative sonographic findings at the expense of obtaining false-positive findings.

In addition to the prospective classification of nodules into benign, indeterminate, or malignant categories, each of the nodules was reassessed for its individual sonographic characteristics by one of the authors (A.T.S.), who was blinded to follow-up and histologic findings. The presence or absence of individual findings was recorded for each nodule and entered into the database.

Mammograms in patients with a malignant lesion were classified into one of five groups, based on the original dictated and transcribed reports, and compared with prospective sonographic classification to determine whether sonography altered the suspicion of malignant disease. The mammographic groups were negative, probably benign abnormality, indeterminate abnormality, probably malignant abnormality, and malignant abnormality.

Table 1
Individual Sonographic Characteristics

Characteristics		
Malignant*	Benign†	Indeterminate‡
Spiculation	Absent malignant findings	Maximum diameter§
Angular margins	Intense hyperechogenicity	Isoechogenicity
Marked hypoechogenicity	Ellipsoid shape	Mild hypoechogenicity
Shadowing	Gentle bi- or trilobulations	Normal sound transmission
Calcification	Thin, echogenic pseudocapsule	Enhanced transmission
Duct extension		Heterogeneous texture
Branch pattern		Homogeneous texture
Microlobulation		

* If even a single malignant feature is present, the nodule is excluded from benign classification.
† Individual benign features. For a nodule to be classified as benign, however, a combination of findings was required. The following three combinations of findings could result in a benign classification: (*a*) intense and uniform hyperechogenicity, (*b*) ellipsoid shape plus thin echogenic capsule, (*c*) gentle lobulations (two or three) plus a thin echogenic capsule.
‡ Odds ratios were nearly 1.0, indicating no substantial predictive value.
§ Maximum diameter equals the largest dimension in any plane.

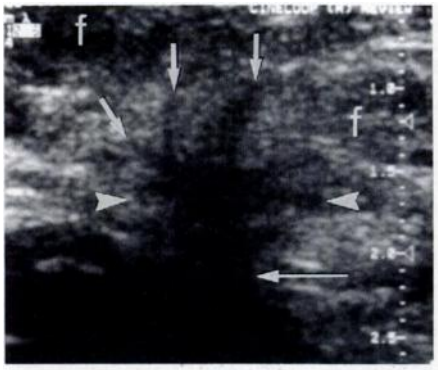


Figure 1. US image shows a malignant nodule with anechoic spiculations (short arrows), angular margins (arrowheads), posterior shadowing (long arrow), and a very hypoechoic center compared with fat (*f*).

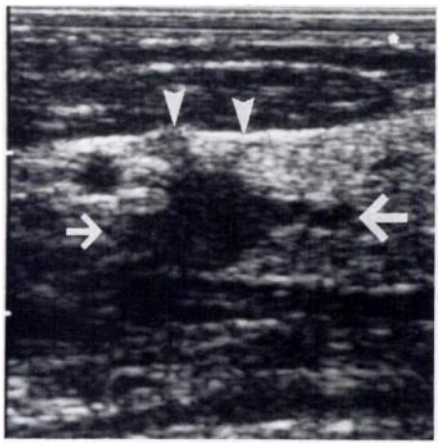


Figure 2. US image reveals a nodule with multiple malignant characteristics, including duct extension (large arrow), branch pattern (small arrow), and hypoechoic spiculations (arrowheads). (Display markers on the left are 1 cm apart.) Histologic findings were mixed infiltrating ductal carcinoma and ductal carcinoma in situ (DCIS); Bloom and Richardson score = 4 (grade I).

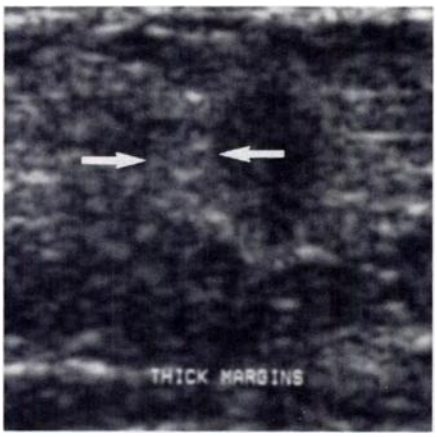


Figure 3. US image demonstrates a small malignant nodule, taller than wide, with a thick, ill-defined echogenic left border (between arrows) that indicates infiltration of surrounding tissues.

(This classification system was based on the Colorado Mammography Advocacy Program [CMAP] and preceded the American College of Radiology Breast Imaging Reporting and Data System [BI-RADS] classification by several years. The "probably benign" category in the CMAP system closely corresponds to the "probably benign finding" in the BI-RADS lexicon. The "negative" classification in the CMAP system includes both "negative" and "benign finding" categories of the BI-RADS. The "indeterminate" CMAP category corresponds to the "assessment incomplete category" of the BI-RADS. The "probably malignant" category in the CMAP system corresponds to the "suspicious abnormality" category of the BI-RADS lexicon. Finally, the "malignant" category of the CMAP system corresponds to the "highly suggestive of malignancy" category of the BI-RADS.)

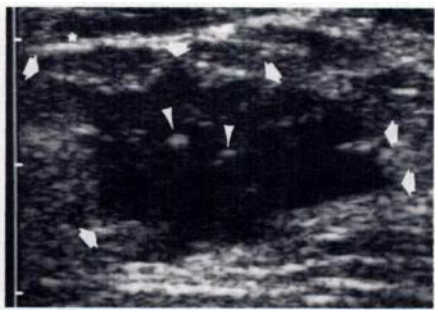


Figure 4. US image of a tender, palpable malignant nodule shows angular margins (arrows), a markedly hypoechoic texture, and internal calcifications (arrowheads). Also note the enhanced through-transmission. (Markers on the left are 1 cm apart.) Histologic examination showed medullary carcinoma with extensive lymphocytic infiltrate. Medullary carcinomas typically are markedly hypoechoic and show enhanced through-transmission, probably due to associated lymphocytic infiltrates. Although medullary carcinomas are reported to often have smooth margins, angular margins were found in all five medullary carcinomas in this series.

Biopsies were performed in all of the solid nodules, with 416 (55%) nodules undergoing 14-gauge large-core needle biopsy and 334 (44%) undergoing excisional biopsy. (Percentages do not add to 100% because of rounding.) The results of the prospective mammographic and sonographic classifications and the presence or absence of individual sonographic features were then compared with the histologic results.

The sensitivity, specificity, and predictive values of a negative and a positive result, and overall accuracy were calculated for the prospective nodule classification and for each individual sonographic characteristic. Odds ratios were also calculated.

The odds ratio shows how the risk of malignancy is altered by the presence of a given finding. It is calculated by dividing the posttest probability by the pretest probability. In these 750 solid breast nodules, the pretest probability is the prevalence of malignancy, 16.7%. For malignant findings, the posttest probability is the positive predictive value. Findings that are associated with increased risk of malignancy have odds ratios greater than 1.0. For example, an odds ratio of 3.0 triples the risk of malignancy over the underlying prevalence of disease. With a prevalence of 16.7%, an odds ratio of 3.0 also indicates a 50% or greater risk of malignancy, the definition of a malignant finding in this study. For benign lesions, the odds ratio represents 1.0 minus the negative predictive value divided by the prevalence. The odds ratio necessary for a finding to be considered benign, therefore, depends on the prevalence of malignancy and the "acceptable" rate of false-negative findings. Although in the retrospective study individual benign findings were originally defined as those with 5% or less chance of malignancy, we and others currently believe, on the basis of recent mammography reports, that a 2% or less chance of malignancy is necessary to consistently avoid biopsy (6,43–45). In this population of solid nodules (with a 16.7% prevalence of malignancy), an odds ratio of 0.3 would reduce the risk of malignancy to 5% and an odds ratio of 0.12 would reduce the risk to 2%.

Malignant Characteristics

"Sonographic spiculation" is similar to mammographic spiculation (46). It consists of alternating hyperechoic and hypoechoic straight lines that radiate perpendicularly from the surface of the solid nodule. In lesions surrounded by intensely echogenic fibrous tissue, only the hypoechoic spiculations are sonographically visible (Figs 1, 2). In spiculated nodules surrounded by fat, only the echogenic spiculations are sonographically visible. A thick echogenic "halo," best seen around the lateral edges of a malignant nodule, also represents hypoechoic spiculations (Fig 3).

"Taller than wide" indicates that a part or all of the nodule is greater in its anteroposterior dimension than in either the sagittal or transverse dimension. We considered this finding to be positive if any part of the nodule was taller than wide (Fig 3).

"Angular margins" refers to the junction between the relatively hypoechoic or isoechoic central part of the solid nodule and the surrounding tissue. These angles may be acute, obtuse, or 90°. Angular margins should be distinguished from round or gently lobulated borders of a solid nodule with the surrounding tissue (Figs 1, 4).

"Markedly hypoechoic" nodules are very black when compared with the surrounding isoechoic fat (Figs 1, 4, 5).

"Shadowing" exists when an area has relatively less through-transmission of sound than is present in surrounding tissues. Shadowing is considered to be present even when it is mild or is found behind only part of the nodule (Fig 1).

"Punctate calcifications" that are sonographically visible within solid nodules are more likely to be associated with malignant than benign lesions (Figs 1, 4, 6).

"Duct extension" is a projection from the nodule that extends radially within or around a duct and courses toward the nipple (Fig 2).

"Branch pattern" is defined as multiple projections from the nodule within or around ducts extending away from the nipple (Fig 2).

"Microlobulation" is analogous to the mammographic finding and is recognized by the presence of many small (1–2 mm) lobulations on the surface of the solid breast nodule (Fig 5).

Only if there were no malignant criteria were benign criteria sought.

Benign Characteristics

"Markedly hyperechoic" tissue (as compared with the echogenicity of fat) that is well circumscribed and of uniform echogenicity represents fibrous tissue. If the

echotexture is not uniform or if it contains hypoechoic areas (other than fat lobules) that are larger than normal ducts or terminal ductal-lobular units (> 4 mm), then the lesion is not classified as markedly hyperechoic (Fig 7).

"Ellipsoid shape" (wider than tall) indicates that the sagittal and transverse dimensions are greater than the anteroposterior dimension (Figs 8, 9). It is considered a benign finding.

"Well-circumscribed lobulations" that are gently curving, smooth, and number three or less and that occur in a nodule wider than it is tall are considered benign. They are distinguished from the more numerous and smaller (1–2 mm) microlobulations that increase the likelihood of malignancy (Fig 9).

A "thin, echogenic pseudocapsule" that is well-circumscribed suggests a slowly growing, noninfiltrating lesion typical of benign lesions (Figs 8, 9). Demonstration of a complete capsule usually requires scanning the entire nodule in real time in multiple planes and rocking the probe along both its short and long axes, since the capsule is well seen only on the portions of the nodule that are nearly perpendicular to the beam on any single image.

Because some ellipsoid or gently lobulated malignant lesions do not have well-circumscribed, thin pseudocapsules and some purely intraductal malignant lesions have thin, echogenic walls, a combination of either an ellipsoid shape with a thin, echogenic pseudocapsule or gentle lobulation with a thin, echogenic pseudocapsule was required for benign classification. A capsule did not need to be demonstrated for hyperechoic lesions to be classified as benign, since an echogenic capsule is indistinguishable from similarly internal echogenic fibrous tissue.

RESULTS

Of the 750 solid nodules, 625 (83%) were benign and 125 (17%) were malignant. The overall negative-to-positive biopsy ratio was 5:1. The malignant lesions included infiltrating ductal carcinoma (n = 102 [81.6%]), infiltrating lobular carcinoma (n = 6 [4.8%]), medullary carcinoma (n = 5 [4.0%]), mucinous carcinoma (n = 2 [1.6%]), metastasis (n = 2 [1.6%]), other infiltrating malignant lesions (n = 3 [2.4%]), and DCIS (n = 5 [4.0%]). Of the 125 malignancies, 85 (68%) had 1.5-cm maximum diameter or less. The results of axillary lymph node dissection were available in 78 patients with cancer. The majority of these patients (n = 52) (67%) had negative findings for the axillary lymph nodes. In eight (10%) of the patients, only one lymph node was positive; in two (2%), two nodes were positive, and in 16 (20%), three or more lymph nodes were positive for cancer.

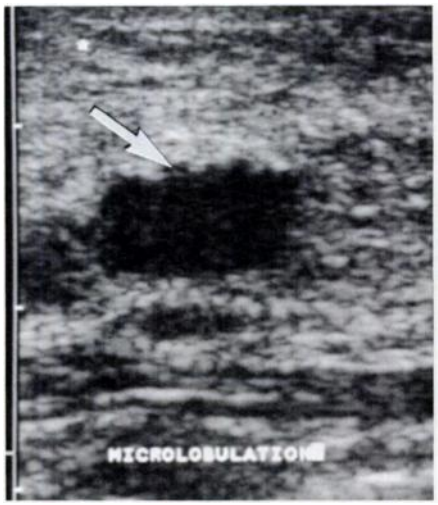


Figure 5. US image shows a markedly hypoechoic and microlobulated (arrow) malignant nodule. Microlobulations are 1–2 mm in diameter. Sound transmission is normal. (Display markers on the left are 1 cm apart.) Histologic findings showed infiltrating ductal carcinoma; Bloom and Richardson score = 6 (grade II).

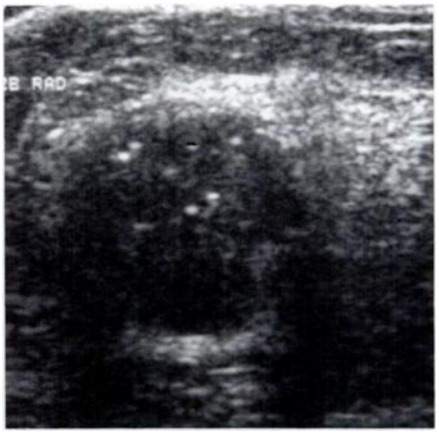


Figure 6. US image reveals a malignant nodule that contains internal calcifications. It is difficult to determine exact size from this image. Because of beam width, volume averaging, and sonographic bloom, sizes appear larger than they really are. Although larger individual calcifications appear to be 1–2 mm, they are actually 1 mm or smaller at mammography. Although large enough to cause reflection of the ultrasound beam, these calcifications are smaller than beam width; therefore, they do not cast shadows. (Note that there is enhanced through-transmission.) Histologic findings showed infiltrating ductal carcinoma; Bloom and Richardson score = 8 (grade III).

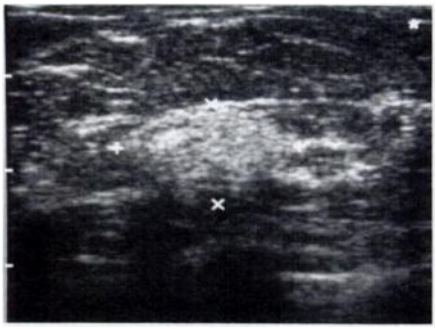


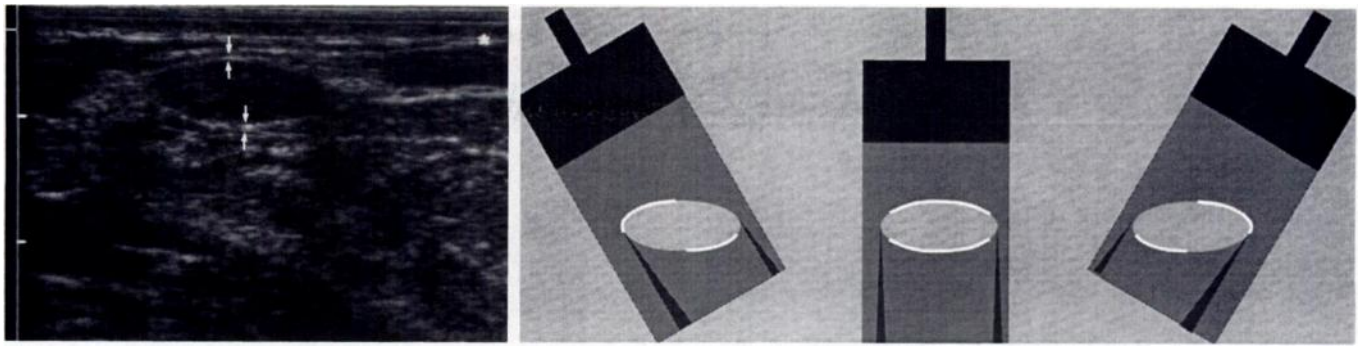
Figure 7. US image shows uniformly hyperechoic nodule (calipers) that caused a mammographic mass. At biopsy, the mass proved to be normal fibrous breast tissue. (Display markers on the left are 1 cm apart.)

The most common benign diagnosis was fibroadenoma (n = 338 [54%]). Other benign conditions were fibrosclerosis (n = 81 [13%]), papillary duct hyperplasia (n = 25 [4%]), sclerosing adenosis (n = 19 [3%]), and miscellaneous fibrocystic change (n = 131 [21%]). The remaining lesions were intraductal papillomas (n = 16 [2.6%]) and intramammary lymph nodes (n = 15 [2.4%]). The majority of the benign lesions were also small; 481 (77%) were 1.5 cm or less in maximum diameter.

There was little difference between the sizes of benign and malignant lesions. Figure 10 shows the percentage of benign and malignant nodules for each size group.

Mammographic correlations were available for 726 (97%) of the nodules in this series. In 16 (2%) of the patients, mostly women younger than 30 years of age and pregnant women, mammography was not performed. For eight (1%) of the patients, mammograms and/or interpretations were not available at sonography.

Mammographic interpretations for all sonographically detected nodules that had mammograms available for comparison (726 of 750 nodules [97%]) were negative for 174 (24%) of the nodules, probably benign for 189 (26%), indeterminate for 313 (43%), probably malignant for 36 (5%), and malignant for 14 (2%). Of the 125 nodules proved to be malignant at biopsy, the mammograms were classified as negative for 24 (19%) of the nodules, probably benign for five (4%), indeterminate for 59 (47%), probably malignant for 25 (20%), and malignant for 12 (10%). A comparison of the sonographic and mammographic classifications for all malignant nodules (palpable and nonpalpable) is shown in Table 2. Sonography helped correctly classify 100 nodules as malignant in comparison to 38 classified as malignant with mammography. For 71 of 125 (57%) malignant nodules, sonography increased the certainty of malignant diagnosis when compared with the mammographic results. The sonographic classification was indeterminate or malignant for 27 malignant nodules classified as negative or probably benign with



a. b.

Figure 8. **(a)** US image reveals ellipsoid-shaped fibroadenoma with no malignant characteristics. It is smooth and well circumscribed; is wider than it is tall; and has a thin, echogenic pseudocapsule (between arrows). The capsule is best seen on anterior and posterior surfaces, where it is parallel to the probe and perpendicular to the beam. It is less well seen on the curving lateral edges of the nodule, which are parallel to the beam, due to beam refraction and reflection related to the oblique angles of incidence and its dependence on poorer lateral resolution (as compared with axial resolution) for demonstration. The entire capsule can be seen only by sweeping the nodule in real time, rocking and heeling and toeing to create an angle of incidence more nearly perpendicular to portions on the lateral edges of the nodule. It is difficult to show the entire capsule on a single freeze-frame image. Demonstration of the capsule depends strongly on axial resolution, which is best with high-frequency, broad bandwidth, short pulse-length probes. (Display markers on the left are 1 cm apart.) **(b)** Thin, echogenic pseudocapsule around fibroadenomas and other benign solid nodules is best seen where it is parallel to the probe surface and perpendicular to the ultrasound beam. Therefore, the capsule is best seen on anterior and posterior surfaces of the nodule and less well seen along the lateral edges on routine individual freeze-frame images. It is necessary to show a thin capsule around the entire nodule, which requires sweeping the entire nodule in real time, as well as rocking and heeling and toeing the probe to create more perpendicular angles of incidence along the lateral edge of the nodule.

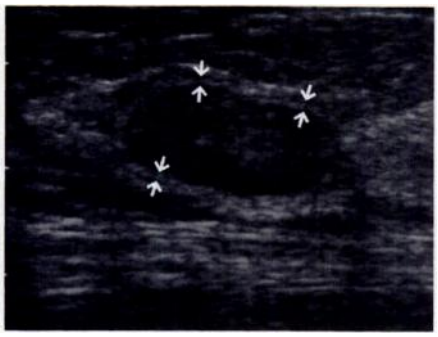


Figure 9. US image reveals a gently lobulated, bilobed fibroadenoma that is wider than it is tall; is well circumscribed; and has a thin, echogenic pseudocapsule (between arrows). (Display markers on the left are 1 cm apart.)

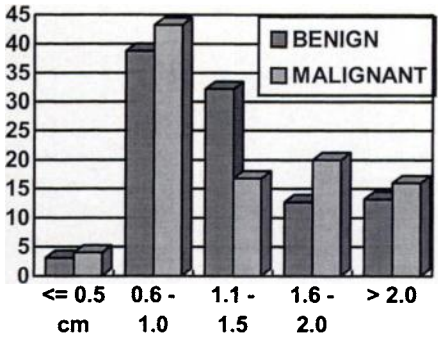


Figure 10. Bar graph shows the percentage of benign and malignant nodules for each size group.

mammography. The sonographic classification was malignant for 44 nodules classified as indeterminate mammographically. In no case was a nodule classified as both mammographically malignant and sonographically benign.

The sonographic versus mammographic classifications for palpable malignant nodules are shown in Table 3. Sonographic classification gave a higher certainty of malignant diagnosis than mammography for 37 of 44 (84%) palpable malignant nodules. Sonographic classification was indeterminate or malignant for 21 malignant nodules classified as negative or probably benign mammographically. Sonography helped classify as malignant 16 nodules that were mammographically indeterminate.

There were 44 solid nodules that were neither palpable nor mammographically visible. Of these nodules, 11 were found to be malignant. These nodules were incidental findings, separate from the lesion for which US was performed, and usually were additional nodules found during sonography. These nodules constituted 44 of 750 (5.9%) of all nodules, 11 of 125 (8.8%) malignant nodules, 21 of 338 (6.2%) fibroadenomas, one of 16 (6.2%) papillomas, and six of 131 (4.6%) fibrocystic changes. However, of 11 nonpalpable and mammographically negative malignant nodules, five were second malignant lesions in patients who had multicentric or multifocal cancer.

The sonographic-histologic correlation is shown in Table 4. The category of "not benign" is the total number of the sonographic classifications, malignant plus indeterminate. This represents the total number of lesions requiring biopsy according to their sonographic classification. Thus, the sensitivity of breast US for malignancy was 98.4%, the specificity was 67.8%, the overall accuracy was 72.9%, the positive predictive value was 38%, and the negative predictive value was 99.5%.

Table 5 shows the number of nodules, percentage of total number of solid nodules in each sonographic classification, and percentage of malignant diagnoses for each classification. Of all solid nodules, over half (426 of 750, 57%) were classified as benign and only two of the 426 (0.5%) were malignant. One of the false-negative nodules was a metastatic lung cancer, and the other was a small infiltrating ductal cancer. Of the 625 solid nodules that had benign histologic findings after biopsy, 424 (68%) were correctly classified sonographically as benign. Of the 187 nodules classified as indeterminate, 23 (12.3%) were malignant. Of the 137 nodules classified sonographically as malignant, 100 (73%) were histologically malignant.

Tables 6 and 7 summarize the sensitivity, specificity, positive and negative predictive values, overall accuracy, and odds ratios for the individual sonographic criteria for malignant and benign nodules, respectively. Most malignant nodules had multiple positive sonographic findings. The mean number of malignant findings per malignant nodule was 5.3.

Note that all the malignant findings in Table 6 have odds ratios of 2.9 or greater. Microlobulation is the only

malignant finding with an odds ratio of less than 3.0. However, we calculated the positive predictive values and odds ratios for each of the findings at various times during the study. During these multiple evaluations, the odds ratio for microlobulation varied between 2.9 and 3.1. Therefore, we have included it as a malignant finding.

All of the selected benign findings in Table 7 have odds ratios of less than 0.12. Therefore, given the underlying prevalence of malignancy of 16.7%, each benign finding indicates less than a 2% chance of malignancy. In Table 7, the negative predictive values for the benign findings ranged from 98.8% to 100%, and the sensitivities for malignancy when these findings were absent ranged from 95.2% to 100%.

Several individual sonographic characteristics were not useful for classification of nodules into either benign or malignant categories. Maximum diameter, heterogeneous texture, homogeneous texture, isoechogenicity compared with fat, and normal or enhanced sound transmission criteria were not helpful. Figure 9 shows a chart that compares the maximum diameter for benign and malignant nodules. The distribution of benign and malignant nodules is similar in all size groups except the 1.0–1.4-cm group.

Of the benign nodules, 137 of 625 (21.9%) were heterogeneous, as were 33 of 125 (26.4%) of the malignant nodules. The positive predictive value of heterogeneity as a malignant finding was 19.3%. The odds ratio for heterogeneity as a malignant finding was only 1.16. The negative predictive value of homogeneity as a benign finding was 84.1%. The odds ratio for homogeneity as a benign finding was 0.95. Odds ratios close to 1.0 indicate little change in the risk of malignancy based on internal heterogeneous or homogeneous texture.

Normal or increased through-transmission was present in 596 of 625 (95.4%) of the benign nodules and 52 of 125 (41.6%) of the malignant nodules. The negative predictive value of normal or enhanced through-transmission was 91.8%. The odds ratio as a benign finding was 0.49.

Echogenicity equal to fat or very slightly hypoechoic relative to fat was present in 527 of 625 (84.3%) of the benign nodules and 38 of 125 (30.4%) of the malignant nodules. The negative predictive value of isoechogenicity or very mild hypoechogenicity was 93.3%. The odds ratio as a benign finding was 0.4.

Table 2
Mammographic versus Sonographic Classification of 125 Malignant Nodules

US Findings	Mammographic Findings		
	Benign*	Indeterminate	Malignant†
Benign	1	1	0
Indeterminate	7	14	2
Malignant	20	44	36

* Negative findings plus probably benign.
† Probably malignant plus malignant.

Table 3
Mammographic versus Sonographic Classification of 44 Palpable Malignant Nodules

US Findings	Mammographic Findings		
	Benign*	Indeterminate	Malignant†
Benign	1	0	0
Indeterminate	5	1	0
Malignant	16	16	5

* Negative plus probably benign.
† Probably malignant plus malignant.

DISCUSSION

Despite some encouraging early reports, US has more recently been portrayed in the United States as being useful only for differentiation of cysts from solid nodules (2,9–11,15,24,25, 34–37). It is our experience and the experience of others, however, that breast US is capable of doing much more than that and is an essential problem-solving tool in the breast radiologist's armamentarium (24–33). This study reinforces that belief by demonstrating that high-resolution US of the breast can successfully help distinguish many benign from malignant solid nodules. The negative predictive value for a sonographically benign classification was 99.5%. Only 1.6% of malignant lesions were misclassified as benign. Although individual malignant findings had low-to-moderate sensitivity, there was a mean of 5.3 malignant findings per malignant nodule. The chances of a malignant nodule having at least one malignant finding was very high. By excluding any nodule with even a single finding of malignancy from the benign category, the sensitivity for cancer was 98.4%. These results, if widely reproducible, could have a substantial impact on the evaluation of breast disease and the cost of care in patients undergoing breast evaluation.

Among the sonographic findings of malignancy, the one with the highest positive predictive value is spiculation. Spiculation has infrequently been reported in the literature (47), but similar and related findings have been reported often as a "thick, echogenic halo" (24,31,32,48–52) or indistinct margins (28,31,48,53) which, like spiculation, are imaging manifestations of infiltrating tentacles of tumor that extend into the surrounding tissues. The hypoechoic spiculations within the fibrous tissue surrounding a cancer may be inconspicuous mammographically because both the spiculations and the adjacent fibrous tissue have the density of water. Sonography can be very helpful in such cases. Most of the spiculated le-

Table 4
Comparison of US Classification with Histologic Findings in 750 Solid Nodules

US Classification	Histologic Findings		
	Benign	Malignant	Total
Benign	TN, 424	FN, 2	426
Not benign*	FP, 201	TP, 123	324
Total	625	125	750

Note.—FN = false negative, FP = false positive, TN = true negative, TP = true positive. Sensitivity = TP/(TP + FN) = 123/125 (98.4%). Specificity = TN/(TN + FP) = 424/625 (67.8%). Positive predictive value = TP/(TP + FP) = 123/324 (38.0%). Negative predictive value = TN/(TN + FN) = 424/426 (99.5%). Accuracy = (TP + TN)/(TP + TN + FP +FN) = 547/750 (72.9%).
* Malignant plus indeterminate.

Table 5
Classification of Solid Nodules

Sonographic Classification	No. of Nodules	Percentage of Nodules	Percentage of Malignant Nodules
Benign	426	57.0	0.5
Indeterminate	187	25.1	12.3
Malignant	137	18.2	73.0

Table 6
Malignant Sonographic Characteristics versus Malignant Histologic Findings

Characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Odds Ratio
Spiculation	36.0	99.4	91.8	88.6	88.8	5.5
Taller than wide shape	41.6	98.1	81.2	89.4	88.7	4.9
Angular margins	83.2	92.0	67.5	96.5	90.5	4.0
Shadowing	48.8	94.7	64.9	90.2	87.1	3.9
Branch pattern	29.6	96.6	64.0	87.3	85.5	3.8
Hypoechogenicity	68.8	90.1	60.1	93.6	87.2	3.6
Calcifications	27.2	96.3	59.6	86.9	84.8	3.6
Duct extension	24.8	95.2	50.8	86.4	79.3	3.0
Microlobulation*	75.2	83.8	48.2	94.4	82.4	2.9

Note.—In order of positive predictive value (PPV): prevalence = pretest probability (16.7%), PPV = posttest probability, odds ratio = PPV/prevalence, specificity = percentage of benign nodules without any malignant findings, negative predictive value (NPV) = percentage of chance of benignancy when there are no malignant findings.
* PPV for microlobulation varies between 48% and 52% as nodules are added to the database.

Table 7
Benign Sonographic Characteristics versus Benign Histologic Findings

Characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Odds Ratio
Hyperechogenicity	100.0	7.4	17.8	100.0	22.8	0.00
Two or three lobulations	99.2	19.4	19.7	99.2	32.7	0.05
Ellipsoid shape	97.6	51.2	28.6	99.1	59.2	0.05
Thin capsule	95.2	76.0	44.2	98.8	79.2	0.07

Note.—In order of negative predictive value (NPV): prevalence of malignancy = pretest probability (16.7%), sensitivity = percentage of malignancies without benign findings, positive predictive value (PPV) = percentage of the chance of malignancy when there are no benign findings. Classification of a solid nodule as benign requires (*a*) a lack of malignant characteristics, plus (*b*) hyperechogenicity, or (*c*) a thin echogenic capsule plus ellipsoid shape, or (*d*) a thin echogenic capsule plus two or three gentle lobulations.

sions in this series had hypoechoic spiculations. The echogenic spiculations in lesions surrounded by fat are conspicuous mammographically. Sonography is not often necessary for diagnosis of such nodules, but it may be useful for guiding needle biopsy and/or localization procedures and for determining the true size of malignant lesions.

It has been reported that nodules that are taller than they are wide (larger anteroposteriorly than horizontally) are likely to be malignant (24,25,31,32,54). This is a worrisome finding because it suggests growth across normal tissue planes, which are horizontally oriented in patients scanned in the supine position (24). Growth of most fibroadenomas remains within normal tissue planes; therefore, they are usually wider than they are tall (25). The flatter shape of fibroadenomas relative to malignant lesions may also be a reflection of the greater compressibility of benign lesions with normal probe pressure (32). In addition, Nishimura et al (54) have postulated that the lateral edges of infiltrating tumors appear echogenic and therefore are often not measured as part of the nodule, which results in artificially high anteroposterior to transverse measurements of the nodule. We had previously found that this finding had relatively low sensitivity but a high positive predictive value. In an attempt to increase sensitivity, we modified the finding by considering it positive if any part of the nodule was taller than wide rather than requiring the entire nodule to be taller than wide. This improved sensitivity somewhat but also decreased the positive predictive value.

Our angular margins characteristic is similar to what has previously been described as jagged or irregular margins. Angular margins should be distinguished from gently curving lobulations. In our study, the presence of angular margins had the greatest individual sensitivity and overall accuracy. Historically this has been the most frequently reported finding and one of the most reliable findings for malignancy (12,16,19,23,26–29,31,32,48,49,55–57).

Markedly hypoechoic nodules should be defined as being much less echogenic than the relatively homogeneous medium-level echogenicity of fat. Previous studies have mentioned hypoechogenicity as a malignant finding (12,16,19,23,24,28,29,56). It is important to compare the echogenicity of the nodule to that of normal breast fat rather than to that of intensely echogenic fibrous tissue. Because hyperechoic fibrous tissue is more echogenic than anything in the breast except calcification, we do not believe that comparison to fibrous tissue provides much useful information. More useful information can be gained by comparing nodule echogenicity to a structure that has an echogenicity near the middle of the gray-scale spectrum. In the breast, periductal elastic tissue, breast terminal ductal-lobular units, and fat have an echogenicity near the middle of the gray-scale spectrum. Of these, only fat is uniformly present in all patients. Therefore, we have found fat to be the tissue against which the echogenicity of solid nodules can most consistently be compared from patient to patient.

To compare the echogenicity of solid nodules to fat, sonographic parameters must be set so that fat is portrayed as gray rather than black. In some previous studies, fat has been either displayed and/or described as hypoechoic (19,23,33,58,59). We and others believe that use of such sonographic scanning parameters decreases the chances of accurately assessing the echogenicity of a solid nodule and also increases the chance of not identifying some solid nodules (16,23,60). Use of broadband high-frequency transducers (7.5 MHz or greater) is important for the identifi-

cation of some fat-surrounded nodules and for assessment of their echogenicity (23,31,60,61). We have found that most fibroadenomas are isoechoic or mildly hypoechoic relative to fat, whereas about two-thirds of malignant nodules are markedly hypoechoic compared with fat. However, about one-third of malignant nodules are nearly isoechoic or only mildly hypoechoic. Therefore, even though marked hypoechogenicity is a worrisome finding for malignancy, isoechogenicity and mild hypoechogenicity are not necessarily reassuring and should be considered indeterminate findings.

Shadowing has previously been reported to be present in a variable percentage of malignant nodules (9,12,16,19,23,24,25,27–29,31,32,48,56,62–67). Shadowing is the result of attenuation of the sound beam by desmoplastic host response to breast cancer rather than being due to the tumor itself (9,17,26,27,31,62,67). In our experience, shadowing is most commonly seen in low-grade infiltrating ductal carcinomas and tubular carcinomas probably because they grow slowly enough to allow the intensely shadowing desmoplastic reaction to occur. Highly cellular special-type tumors such as papillary or medullary carcinoma, tumors that contain mucin (eg, colloid carcinoma), and necrotic infiltrating ductal carcinomas are often associated with normal to enhanced through-transmission of sound rather than shadowing (7,9,16,17,26–28,31,32,56,62,66). Because high-grade infiltrating ductal carcinomas are more cellular, more likely to have associated lymphocytic infiltrates, and also more likely to have necrosis than lower-grade tumors, we have often found them to have enhanced through-transmission. Therefore, although the presence of shadowing is worrisome for malignancy, we and others believe that neither normal sound transmission nor increased through-transmission is necessarily reassuring. Both normal and enhanced through-transmission should be considered indeterminate findings (28,32).

US is less sensitive for demonstration of microcalcifications than is mammography (16,60,68,69). The smaller the calcifications, the lower the sensitivity of US for showing them (16,69). However, the currently used high-frequency transducers can show a higher percentage of mammographically visible calcifications than could the previously used lower-frequency transducers (60,68,70). Malignant calcifications within DCIS and microscopically invasive ductal carcinoma, which do not have associated sonographically demonstrable masses, are difficult to identify sonographically (16,68,69). Finding such tumors is the goal of mammographic screening. US cannot compete with mammography in that arena, and therefore has virtually no role in breast cancer screening. However, calcifications that occur within masses are more likely to be seen sonographically (60,68,69). Furthermore, typical malignant microcalcifications as small as 100–500 μm can be shown within malignant masses with current US equipment, even though demonstration of such calcifications exceeds the theoretic limits of sonographic resolution. Such calcifications appear as bright punctate echoes that appear larger than their true size, but they are not large enough to create acoustic shadowing (70). We have found that the majority of malignant solid nodules provide either a very hypoechoic or a mildly hypoechoic and relatively homogeneous background that enhances our ability to identify the bright punctate calcification echoes. Therefore, punctate echogenic calcifications within such malignant nodules are very conspicuous. Conversely, because normal breast tissue includes a large amount of hyperechoic and heterogeneous fibrous tissue, benign calcifications within such a background are sonographically difficult to detect (70). The net result is that a larger percentage of malignant than benign calcifications are visible sonographically. Therefore, even though the sensitivity of sonography for calcifications is very low when compared with that of mammography, our experience indicates that the calcifications that are seen sonographically within a solid mass are more likely to be malignant.

The finding of either duct extension or a branch pattern suggests that a process is spreading along the ductal system and increases the likelihood of malignancy. Duct extension is defined as progression toward the nipple and branch pattern as progression away from the nipple. One previous study has reported a branching pattern in larger tumors (71). Radial scan planes are necessary in most cases to show such extensions from the tumor. Demonstration of such findings can be helpful in two situations. First, it may indicate an extensive intraductal component in nodules that have other malignant characteristics. Second, it may prevent false-negative classification of DCIS and small infiltrating tumors as benign. However, such extensions may indicate the presence of an invasive tumor around the duct as well as an intraductal tumor. These findings have low sensitivity but high specificity. With duct extension, usually only a single duct is involved, whereas a branch pattern generally involves multiple ducts.

Microlobulation is similar to the mammographic finding. These are numerous, small (1–2-mm) lobulations. The risk of malignancy increases as the number of lobulations increases (31,72,73). Microlobulation can also occur in fibroadenomas, becoming more frequent as size of the fibroadenoma increases. Microlobulations are often best seen in the peripheral part of the nodule in an antiradial plane. They can represent several different types of tumor involvement on the periphery of a malignant nodule: intraductal tumor extensions, cancerization of lobules, or small fingers of infiltrating cancer.

It must be emphasized that in this study even a single malignant characteristic absolutely excluded a nodule from being classified as benign. The classification system required that benign characteristics be sought only after a thorough search failed to demonstrate any malignant features. Specific benign sonographic findings were less numerous than the number of different malignant characteristics. However, by first excluding the presence of any malignant findings, then using these few benign characteristics, we found that biopsy can potentially be avoided in over half of all solid nodules and almost 70% of benign nodules.

The benign characteristic with the highest negative predictive value, marked hyperechogenicity, represents normal fibrous tissue or focal fibrous change. In this series, there were 42 biopsies of hyperechoic lesions, about 7% of all of the nodules classified as benign. All of these lesions proved to be benign, and the negative predictive value was, therefore, 100%. We have never seen a single malignant nodule that was as homogeneously hyperechoic as normal fibrous tissue, and others agree (19,24). Leucht et al (28) found hyperechoic malignant lesions to be very rare. It is important to understand that if areas of isoechogenicity or hypoechogenicity exist within the fibrous tissue that are larger than normal ducts or terminal ductal-lobular units and are not entrapped fat lobules, the tissue should not be consid-

ered homogeneously hyperechoic. Such areas could be small malignant nodules. Similarly, the margins of the hyperechoic tissue should be well defined. We have seen some small malignant nodules that have a very small isoechoic or hypoechoic central nidus of 5 or 6 mm and a thick, hyperechoic, ill-defined halo.

A thin capsule has been reported as a benign finding mammographically in fat-containing lesions (46,74). It has also been reported sonographically (10,19), although in one study no fibroadenoma had a demonstrable thin capsule (25). A thin, echogenic capsule is well circumscribed on both its inner and outer surfaces. Such a capsule is usually a pseudocapsule of compressed adjacent normal breast tissue. Visualization of such a capsule is reassuring, because it indicates that the leading edge of the nodule is pushing rather than infiltrating. The capsule is best seen where it is perpendicular to the US beam, on the anterior and posterior surfaces of the nodule, and least well seen on the lateral edges of the nodule where it is parallel to the beam. Demonstration of the entire capsule on any one hard-copy image is difficult. It is necessary to sweep the entire nodule in real time and to rock and heel and toe the probe to show the entire nodule. Demonstration of the thin capsule is also highly dependent on axial resolution, which, in turn, depends on probe frequency, bandwidth, and pulse length. It is best demonstrated with higher frequency, broader bandwidth probes that use shorter pulse lengths. Some higher frequency probes use only a narrow portion of the bandwidth and longer pulse lengths and, therefore, do not as readily demonstrate the capsule.

The classical fibroadenoma has smooth margins and is ellipsoid or oval in shape (9,10,15,23,25–28,75). Many fibroadenomas are also smoothly marginated and gently lobulated (10,19,23,25,27). Typical fibroadenomas are wider than they are tall (25). The larger a fibroadenoma becomes, however, the more lobulated and irregular in shape it is likely to become (28). Consequently, some fibroadenomas are not ellipsoid or gently lobulated.

Some malignant nodules have a thin, echogenic capsule, but shapes other than ellipsoid or gently lobulated, and some small malignant nodules are ellipsoid but do not have a demonstrable echogenic capsule. Therefore, we required that the presence of a thin, echogenic capsule be combined with an ellipsoid shape or a gently bilobed or trilobed shape to be considered a benign finding. For ellipsoid or gently lobulated nodules, the presence of a thin, echogenic capsule increases the certainty of benignity. About 75% of all benign nodules had a thin, echogenic pseudocapsule. An ellipsoid shape; two or three gentle lobulations; and a thin, echogenic pseudocapsule had about a 99% negative predictive value each.

Other characteristics listed in Table 1 were found not to be helpful in the differentiation of benign from malignant solid nodules. Heterogeneity and homogeneity of texture were indeterminate findings in this study. We found that about the same percentage of benign and malignant nodules were heterogeneous. We found heterogeneous texture in 33 of 125 (26.4%) malignant nodules and in 137 of 625 (21.9%) benign nodules. Therefore, the odds ratios for heterogeneity and homogeneity approximate 1.0 in this study. This contradicts most of the published literature, in which homogeneity has been associated with benign nodules (10,23,25–28) and heterogeneity has been found to be a major predictor of malignancy (16,19,23,24,26,28,31,48).

There are several possible explanations for this discrepancy. First, calcifications may be a cause of heterogeneity (24). We classified hypoechoic nodules that contained calcifications as homogeneous and considered the calcifications as a separate category. Calcifications were visible in 27% of the malignant nodules. If calcifications had not been considered separately, 53% of malignant nodules would have been considered heterogeneous and heterogeneity would have been a major predictor of malignancy. Second, with the use of higher frequency 7.5–10.0-MHz probes, the internal texture of intensely shadowing nodules could not be evaluated due to echo dropout. In this series, intensely shadowing nodules were classified as homogeneous. In studies in which lower-frequency probes were used, some internal texture may have been appreciated, even in the presence of shadowing. Ueno (31) used high-frequency probes and also found heterogeneity not helpful in shadowing scirrhous lesions. Third, we interpreted some areas of increased echogenicity within the substrate of hypoechoic nodules to be normal tissue between duct extensions or a branch pattern and the main nodule rather than internal heterogeneity. Finally, the solid nodules in this series were smaller than the nodules in at least one of the earlier studies (26). It is probable that smaller malignant nodules are less likely to be heterogeneous than larger nodules. Fornage (24), in a series of malignant nodules smaller than 1 cm^3, found only 41% of the nodules to be heterogeneous as compared with 66% and 70% in the series of Leucht et al (28) and Harper et al (26), respectively. Because many of the malignant nodules in our series were small, it is likely that fewer actually had heterogeneous echotexture.

Normal and enhanced through-transmission were not helpful characteristics, since many high-grade infiltrating ductal tumors with necrosis and highly cellular special-type tumors, such as medullary carcinoma (Fig 4), papillary carcinoma, and colloid carcinoma, demonstrated such sound transmission in this and many other series (7,9,16,17,26–28,31,32,56, 62,76).

Isoechogenicity and mild hypoechogenicity were also indeterminate findings, since about one-third of the malignant nodules in this series had one of these characteristics.

It was surprising that maximum diameter was also an indeterminate finding. Figure 10 shows that size distribution of benign and malignant nodules nearly parallel each other, except in the 1.1–1.5-cm range, where benign lesions predominate.

It is important to note that the 98.4% sensitivity for malignancy in this series was not achieved simply because the malignant nodules were all large, late-stage lesions, with little chance of cure. Instead, the nodules were typical of those seen in everyday practice. Most were relatively small, early lesions. Just over two-thirds of the malignant lesions were 1.5 cm or smaller in maximum diameter. Lesions of this size have an excellent prognosis (77). Furthermore, 67% of the malignant lesions did not have involvement of the axillary lymph nodes. Thus, most of the sonographically detected and correctly classified lesions in this series were potentially curable.

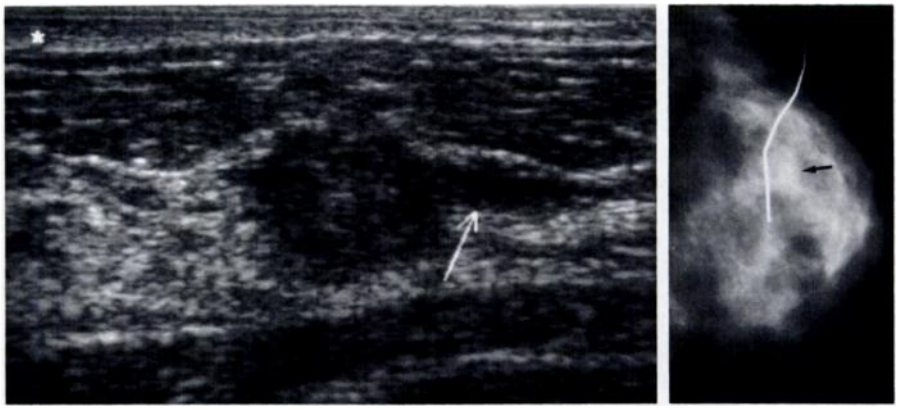
The percentage of malignant solid nodules that were DCIS (five of 125 [4%]) was much lower than that reported in screening mammography series (15%–20%) (78–80). This is not surprising, since detection of DCIS is based mainly on microcalcifications, for which mammography is much more sensitive than sonography. In addition, the indications for sonography (a palpable lump or nonspecific

mammographic abnormality) tend to preselect patients who have more than isolated, clustered calcifications. The prevalence of DCIS is lower in women who have palpable abnormalities (81). Finally, the vast majority of patients with worrisome calcifications but no other findings undergo stereotaxic large-core biopsy or needle-localized excisional biopsy and do not undergo sonography. Therefore, DCIS is preselected out of the population undergoing sonography.

Many specific indications for breast US have been enumerated, including (*a*) evaluation of a palpable mass incompletely evaluated at mammography; (*b*) differentiation of a cyst from a solid nodule; (*c*) evaluation of palpable lesions with associated mammographic asymmetry, no mammographic findings, the presence of implants, or a history of lumpectomy or segmentectomy. The overriding general goal of sonography, however, is to improve specificity and diagnostic accuracy of the clinical and mammographic findings in these selected patients. This goal was met in a large percentage of patients in this series.

Although the main emphasis of this study has been to identify a population of nodules so likely to be benign that biopsy may be avoided, the importance of sonography in increasing the sensitivity and certainty of malignancy over mammography alone in *carefully selected patients* should not be underestimated. To illustrate this point, breast US increased our certainty of malignancy (higher classification on a scale of negative, probably benign, indeterminate, probably malignant, and malignant) over routine mammography alone in 71 of 125 (57%) malignant lesions. Sonography enabled classification as indeterminate or malignant in 27 malignant lesions (22%) that were either not visible or classified as probably benign at mammography. In these cases, sonography appropriately led to biopsy in situations in which a biopsy might not otherwise have been performed. Histologic examination was performed for confirmation of the more specific sonographic impression.

The sonographic classification of indeterminate has a clinical impact similar to that of the malignant classification, since both warrant biopsy. Of 54 malignant lesions mammographically classified as indeterminate, 42 were correctly classified as malignant with US. The effect of sonography on the classification of palpable malignant nodules was even more pronounced. Suspicion of malignancy was higher with sonography than with mammography in 37 of 44 (84%) palpable malignant nodules. This is important because not all palpable abnormalities are hard, fixed masses on which biopsies are automatically performed (Fig 11). Palpable abnormalities represent a spectrum of abnormalities, many of which are relatively unimpressive clinically. In such cases, sonographic results once again correctly demand biopsy. One should recognize that these data represent a careful preselection of patients in whom there was a concern about false-negative or indeterminate mammographic findings, based on clinical findings (ie, dense tissues in the area of the palpable abnormality at mammography), and are not an indictment of the overall sensitivity of mammography.



a. b.

Figure 11. **(a)** US image shows a soft, palpable malignant nodule with normal sound transmission, angular margins, and prominent duct extension toward the nipple (arrow). Histologic findings indicated invasive papillary carcinoma with extensive papillary DCIS. There was no cystic component. **(b)** Routine mediolateral oblique mammogram of the palpable malignant nodule in **a** shows focal nonspecific mammographic asymmetry (arrow in **b**). Localization for excisional biopsy was performed with US guidance.

The improvement in specificity for benign lesions potentially has even greater clinical importance. The negative predictive value of a benign classification was 99.5% in a population with a cancer prevalence of 16.7%. For solid nodules classified as benign, 200 negative biopsies were performed for each positive biopsy. From a medical and economic viewpoint, this is an unacceptably high negative-to-positive biopsy ratio. The need for continued biopsy of such lesions must be questioned. If biopsies had not been performed in the lesions meeting our strict criteria for benignancy, the overall negative-to-positive biopsy ratio in this series would have been reduced from 5:1 (625 negative to 125 positive nodules) to 1.6:1 (199 negative to 125 positive nodules). The number of unnecessary biopsies would have been reduced by 60%. Only two malignant nodules were missed in this series of 750 nodules, and one of these was a metastatic lung carcinoma in which a biopsy was performed to rule out a second primary lesion.

The potential reduction in the need for biopsy as a result of sonographic classification of solid breast nodules as benign has a bearing on cost. In this series, 426 nodules were classified as benign with sonography. These accounted for 57% of all solid nodules and nearly 70% of the benign nodules. In our area, the total cost for percutaneous large-core biopsy (including the technical component, the physician's fee, and the pathology fees) of a breast nodule with US guidance or stereotaxis is approximately $1,000. The total cost for an excisional breast biopsy (including operating room, anesthesia, surgeon's fees, pathology fees, and other items) is about $3,000 as an outpatient and $4,500 as an inpatient procedure.

With core needle biopsy, the least expensive biopsy method, $426,000 would have been saved in this small series by not performing biopsies on those nodules classified as sonographically benign. The estimated maximum savings would have been over $1.9 million. (The cost of sonography has not been included in this estimate because we assume that US would have been performed anyway to evaluate whether the nodule was cystic or solid.) If these numbers are extrapolated to the general population of women undergoing screening mammography and breast examination, the financial savings could be considerable. Furthermore, the morbidity associated with the biopsy procedure, including the lost time from work or other activities that occurs as

a result of biopsy, particularly excisional biopsy, could be markedly reduced.

We agree with previous studies that show a substantial overlap in sonographic characteristics between benign and malignant nodules. It is currently impossible to distinguish all benign from malignant solid nodules. However, we do not agree with previous assessments that, because of this overlap, it is inappropriate to use sonography for benign and malignant determination. On the contrary, it is not necessary to distinguish all benign from all malignant nodules. It is only necessary to identify a subgroup in which the certainty of malignancy is low enough that biopsy can be avoided. This precedent has been set with mammography, where follow-up studies rather than biopsy are advocated for mammographically benign nodules with a 2% or less chance of malignancy (6,43–45). The negative predictive value of over 99% in this study for a solid, benign classification is quite comparable to the negative predictive value of 98% in these mammographic studies for mammographically benign nodules.

In summary, this study shows that sonography is useful in the characterization of some solid breast masses. Sonography improves the specificity of the diagnosis for the majority of both malignant and benign solid breast nodules. It must be reemphasized that these results are predicated on valid targeted indications; excellent sonographic technique (including radial and antiradial scanning); optimal machine and transducer characteristics; and strict adherence to the criteria for a benign lesion, which require the absence of even a single malignant finding. With this approach, a population of benign solid breast lesions that does not require biopsy can be accurately defined. This could result in improved care and reduction of patient discomfort, morbidity, and health care cost. ■

References

1. Sickles EA. Detection and diagnosis of breast cancer with mammography. Perspect Radiol 1988; 1:36–65.
2. Hilton SW, Leopold GR, Olson LK, Wilson SA. Real-time breast sonography: application in 300 consecutive patients. AJR 1986; 147:479–486.
3. Gisvold JJ, Martin JK Jr. Prebiopsy localization of nonpalpable breast lesions. AJR 1984; 143:477–481.
4. Rosenberg AL, Schwartz GF, Feig SA, Patchefsky AS. Clinically occult breast lesions: localization and significance. Radiology 1987; 162:167–170.
5. Bassett LW, Liu TH, Giuliano AI, Gold RH. The prevalence of carcinoma in palpable vs impalpable, mammographically detected lesions (comment). AJR 1992; 158:688–689.
6. Sickles EA. Periodic mammographic follow-up of probably benign lesions: results in 3184 consecutive cases. Radiology 1991; 179:463–468.
7. Bassett LW, Kimme-Smith C, Sutherland LK, Gold RH, Sarti D, King W. Automated and hand-held breast ultrasound: effect on patient management. Radiology 1987; 165:103–108.
8. Bassett LW, Ysrael M, Gold RH, Ysreal C. Usefulness of mammography and sonography in women less than 35 years old. Radiology 1991; 180:831–835.
9. Cole-Beuglet C, Soriano RZ, Kurtz B, et al. Ultrasound analysis of 104 primary breast carcinomas classified according to histopathologic type. Radiology 1983; 147:191–196.
10. Cole-Beuglet C, Soriano RZ, Kurtz AB, Goldberg BB. Fibroadenoma of the breast: sonomammography correlated with pathology in 122 patients. AJR 1983; 140: 369–375.
11. Cole-Beuglet C, Soreano R, Pasto M, et al. Solid breast mass lesions: can ultrasound differentiate benign and malignant? In: Jellins J, Kobayahsi T, eds. Ultrasonic examination of the breast. New York, NY: Wiley, 1983; 45–55.
12. Dempsey PJ. Breast sonography: historical perspective, clinical application, and image interpretation. Ultrasound Q 1988; 6:69–90.
13. Feig SA. The role of ultrasound in a breast imaging center. Semin Ultrasound CT MR 1989; 10:90–105.
14. Bassett LW, Kimme-Smith C. Breast sonography. AJR 1991; 156:449–455.
15. Jackson VP, Rothschild PA, Kreipke DL, et al. The spectrum of sonographic findings of fibroadenoma of the breast. Invest Radiol 1986; 21:34–40.
16. Jackson VP. Sonography of malignant breast disease. Semin Ultrasound CT MR 1989; 10:119–131.
17. Jackson VP. The role of US in breast imaging. Radiology 1990; 177:305–311.
18. Kopans DB, Meyer JE, Steinbock RT. Breast cancer: the appearance as delineated by whole breast water-path ultrasound scanning. JCU 1982; 10:313–322.
19. Mendelson E. Breast ultrasound: 1994. In: Leopold GR, ed. 1994 AIUM syllabus for categorical course on women's imaging. Rockville, Md: American Institute of Ultrasound in Medicine, 1994; 83–88.
20. Rubin E, Miller VE, Berland LL, et al. Hand-held real-time sonography. AJR 1985; 144:623–627.
21. Sickles EA, Filly RA, Callen PW. Benign breast lesions: ultrasound detection and diagnosis. Radiology 1984; 151:467–486.
22. Sickles EA, Filly RA, Callen PW. Breast cancer detection with sonography and mammography. AJR 1983; 140:843–845.
23. Venta LA, Dudiak CM, Salomon CG, Flisak ME. Sonographic evaluation of the breast. RadioGraphics 1994; 14:29–50.
24. Fornage BD, Sneige N, Faroux MJ, Andry E. Sonographic appearance and ultrasound guided fine-needle aspiration biopsy of breast carcinomas smaller than 1 cm^3. J Ultrasound Med 1990; 9:559–560.
25. Fornage BD, Lorigan JG, Andry E. Fibroadenoma of the breast: sonographic appearance. Radiology 1989; 172:671–675.
26. Harper PA, Kelly-Fry E, Noe JS, Bies RJ, Jackson VP. Ultrasound in the evaluation of solid breast masses. Radiology 1983; 146: 731–736.
27. Kobayashi T. Diagnostic ultrasound in breast cancer: analysis of retrotumorous echo patterns correlated with sonic attenuation by cancerous connective tissue. JCU 1979; 7:471–479.
28. Leucht WJ, Rabe DR, Humbert KD. Diagnostic value of different interpretative criteria in real-time sonography of the breast. Ultrasound Med Biol 1988; 14(suppl 1):59–73.
29. Majewski A, Rosenthal H, Wagner HH. Results of real-time sonography and raster mammography of 200 breast cancers. ROFO Fortschr Nucleamed 1986; 144:343–350.
30. Smallwood JA, Guyer P, Dewbury K, Mengatti S, Royle GT, Taylor I. The accuracy of ultrasound in the diagnosis of breast disease. Ann R Coll Surg Engl 1986; 68:19–22.
31. Ueno E, Tohno E, Itoh K. Classification and diagnostic criteria in breast echography. Jpn J Med Ultrasonics 1986; 13:19–31.
32. Ueno E, Tohno E, Soeda S, et al. Dynamic tests in real-time breast echography. Ultrasound Med Biol 1988; 14(suppl 1):53–57.
33. Wadden NAT. Breast ultrasound. In: Wilson SR, Charboneau JW, Leopold GR, eds. 1993 ARRS ultrasound categorical course syllabus. Reston, Va: American Roentgen Ray Society, 1993; 199–204.
34. Heywang SH, Lipsit ER, Glassman LM, et al. Specificity of ultrasonography in the diagnosis of benign breast masses. J Ultrasound Med 1984; 3:453–461.
35. Jokich PM, Monticciolo DL, Adler YT. Breast ultrasonography. Radiol Clin North Am 1992; 30:993–1009.
36. Kopans DB, Meyer JE, Lindfors KK, Buchianeri SS. Breast sonography to guide cyst aspiration and wire localization of occult solid lesions. AJR 1984; 143:489–492.
37. Kopans DB. Breast imaging and the standard of care for the symptomatic patient. Radiology 1991; 187:608–611.
38. Schoenberger SG, Sutherland CM, Robinson AE. Breast neoplasms: duplex sonographic imaging as an adjunct in diagnosis. Radiology 1988; 168:665–668.
39. Dock W. Tumor vascularization: assessment with duplex sonography. Radiology 1991; 181:241–244.
40. Dock W. Duplex sonography of mammary tumors: a prospective study of 75 patients. J Ultrasound Med 1993; 12:79–82.
41. Adler DD, Carson PL, Rubin JM, Quinn-Reid D. Doppler ultrasound color flow imaging in the study of breast cancer: preliminary findings. Ultrasound Med Biol 1990; 16:553–559.
42. Jackson VP. Duplex sonography of the breast. Ultrasound Med Biol 1988; 14(suppl 1):131–137.
43. Hall FM, Storella JM, Silverstone DZ, et al. Non-palpable breast lesions: recommendations for biopsy based on suspicion of carcinoma at mammography. Radiology 1988; 167:353–358.
44. Moskowitz M. The predictive value of certain mammographic signs in screening for breast cancer. Cancer 1983; 51:1007–1011.
45. D'Orsi CJ. To follow or not to follow: that is the question (editorial). Radiology 1992; 184:306.
46. Sickles EA. Breast masses: mammographic evaluation. Radiology 1989; 173: 297–303.
47. Marquet KL, Funk A, Fendel H, Handt S. The echo-dense edge and hyper-reflective spikes: sensitive criteria for malignant processes in breast ultrasound. Geburtshilfe Frauendheilkd 1993; 53:20–23.
48. Bamber JC, De Gonzalez L, Cosgrove DO, Simmons P, Davey J, Mckinna JA. Quantitative evaluation of real-time ultrasound features of the breast. Ultrasound Med Biol 1988; 14:81–87.

49. Baum G. Ultrasound mammography. Radiology 1977; 122:199–205.
50. Kasumi F, Fukami A, Kuno K, Kajitani T. Characteristic echographic features of circumscribed cancer. Ultrasound Med Biol 1982; 8:369–377.
51. McSweeney MB, Murphy CH. Whole-breast sonography. Radiol Clin North Am 1985; 23:157–167.
52. Teubner J. The echogenic border: an important diagnostic criterion in sonographic tumor diagnosis of the breast. In: Gill RW, Dadd MJ, eds. World Federation of Ultrasound in Medicine and Biology 1985. Oxford, England: Pergammon, 1985; 342.
53. Kobayashi, T. Gray-scale echography for breast cancer. Radiology 1977; 122:207–214.
54. Nishimura S, Matsusue S, Loizumi S, et al. Size of breast cancer on ultrasonography, cut-surface of resected specimen, and palpation. Ultrasound Med Biol 1988; 14(suppl 1):139–144.
55. Kobayashi T. Review: ultrasound diagnosis of breast cancer. Ultrasound Med Biol 1975; 1:383–391.
56. Meyer JE, Amin E, Lindfors KK, Lipman JC, Stomper PC, Genest D. Medullary carcinoma of the breast: mammographic and US appearance. Radiology 1989; 170:79–82.
57. Rotten D, Levaillant JM, Le Floch JP, Constancis E, Andre JM. Mass screening for breast cancer with sonomammography: a prospective study. Eur J Obstet Gynecol Reprod Biol 1988; 28:257–267.
58. Basset LW, Kimme-Smith C. Breast sonography: technique, equipment and normal anatomy. Semin Ultrasound CT MR 1989; 10:82–89.
59. Schenck CD, Lehman DA. Sonographic anatomy of the breast. Semin Ultrasound 1982; 3:13–33.
60. Jackson VP, Kelly-Fry E, Rothschild PA, Holden RW, Clark SA. Automated breast sonography using a 7.5 MHz PVDF transducer: preliminary clinical evaluation. Radiology 1986; 159:679–684.
61. Kelly-Frye E, Morris ST, Jackson VP, Holden RW, Sanghvi NT. Variation of transducer frequency output and receiver band-pass characteristics for improved detection and image characterization of solid breast masses. Ultrasound Med Biol 1988; 14:143–161.
62. Calderon C, Vilkomerson D, Mezrich R, Etzold FK, Kingsley B, Haskin M. Differences in the attenuation of ultrasound by normal, benign, and malignant breast tissues. JCU 1976; 4:249–254.
63. Cole-Beuglet C, Goldberg BB, Kurtz AB, Patchefsdy AS, Shaber GS, Rubin CS. Clinical experience with a prototype real-time dedicated breast scanner. AJR 1982; 139:905–911.
64. D'Astous FT, Foster FS. Frequency dependence of ultrasound attenuation and backscatter in breast tissue. Ultrasound Med Biol 1986; 12:795–808.
65. Egan RL, Egan KL. Detection of breast carcinomas classified according to histologic type. Radiology 1983; 147:191–196.
66. Hayashi N, Tamaki N, Honekura Y, Senda M, Yamamoto K, Torizuka K. Real-time sonography of palpable breast masses. Br J Radiol 1985; 58:611–615.
67. Kossoff G. Causes of shadowing in breast sonography. Ultrasound Med Biol 1988; 14(suppl):211–215.
68. Lambie RW, Hodgden K, Herman EM, Kipperman M. Sonomammographic manifestations of mammographically detectable breast microcalcifications. J Ultrasound Med 1983; 2:509–514.
69. Sickles EA. Sonographic detectability of breast calcifications. Proc SPIE 1983; 419: 51–52.
70. Kasumi F. Can microcalcifications located within breast carcinomas be detected by ultrasound imaging? Ultrasound Med Biol 1988; 14(suppl 1):175–182.
71. Stosiek U, Zedelius M. Correlations between sonographic and clinical findings in breast cancer. Ultraschall Med 1986; 7:185–188.
72. Adler DD. Breast masses: differential diagnosis. In: Feig SA, ed. ARRS categorical course syllabus on breast imaging. Reston, Va: American Roentgen Ray Society, 1988; 231–240.
73. Moskowitz M. Circumscribed lesions of the breast. In: Moskowitz M, ed. Syllabus: a diagnostic categorical course in breast imaging. Oak Brook, Ill: Radiological Society of North America, 1986; 31–33.
74. Hessler C, Schnyder P, Ozello L. Hamartoma of the breast: diagnostic observation. Radiology 1978; 126:95–98.
75. Adler DD. Ultrasound of benign breast conditions. Semin Ultrasound CT MR 1989; 10:106–118.
76. Egan RL, Egan KL. Automated water-path full-breast sonography: correlation with histology in 176 solid lesions. AJR 1984; 143:499–507.
77. Tabar L, Duffy SW, Burhenne LW. New Swedish breast cancer detection results for women aged 40–49. Cancer 1993; 72:1437–1448.
78. Andersson I. Breast cancer screening in Malmo. Recent Results Cancer Res 1984; 90:114–116.
79. Schmidt J, Silen W, Sadowsky NI, Connolly JL, Harris JR. Ductal carcinoma of the breast. N Engl J Med 1988; 318:898–903.
80. Verbeek ALM, Hendriks JHCL, Holland R, et al. Reduction of breast cancer mortality through mass screening with modern mammography: first results of the Nijmegen Project, 1975–1981. Lancet 1984; 1:1222–1224.
81. Stomper PC, Margolin FR. Ductal carcinoma in situ: the mammographer's perspective. AJR 1994; 162:585–591.