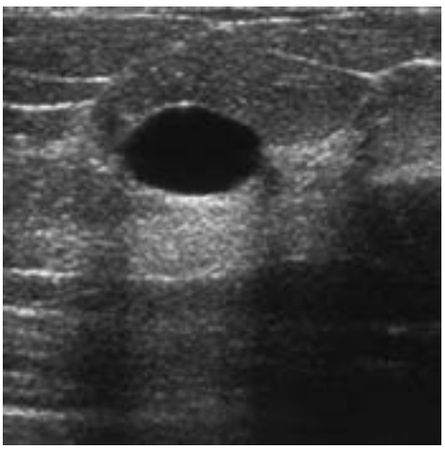
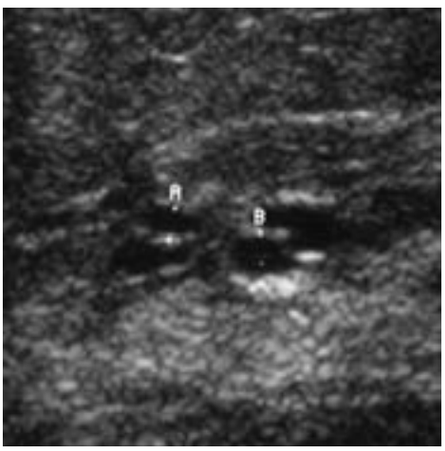


Shape	Oval
Size	11 mm diameter
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

Comment:
Typical cysts can be identified with ultrasound and usually do not require aspiration or biopsy unless they are causing complaints or subjectively unpleasant nodularity.

Fig. 7.1 **Typical sonographic features of a cyst (13-MHz transducer).**



Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

Comment:
The high resolution permits analysis of the diagnostic criteria even in small microcysts.

Fig. 7.2 **Microcystic disease.** Magnified view of a 20 × 20-mm area (13-MHz transducer) demonstrates a focal lesion composed of several microcysts, each 1–2 mm in diameter.

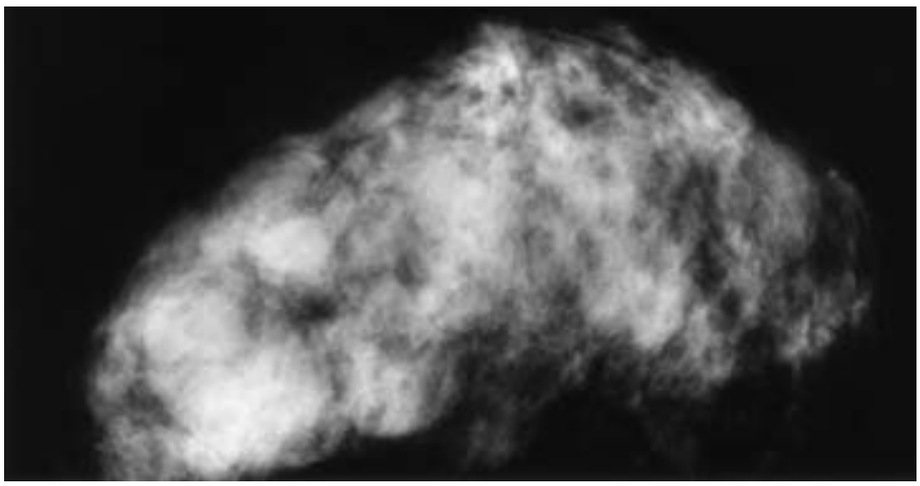
Complicated Cysts

The diagnostic criteria for complicated cysts and complex cystic masses are summarized in **Table 7.5**.

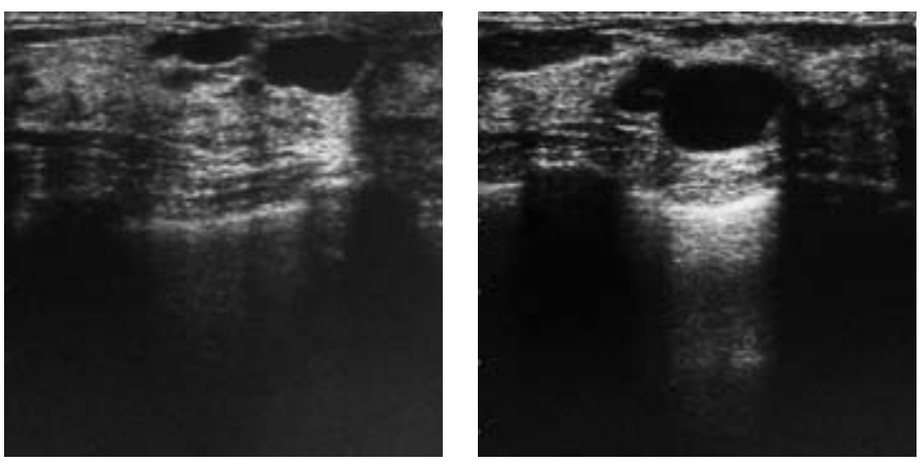
Internal Echoes and Posterior Features

The high reflectivity of the anterior cyst wall often gives rise to *reverberations* (**Figs. 7.6 a, b; 7.7 a, b**), a band of echoes from the cyst wall that project into the interior of the cyst. These artifacts may be mistaken for solid areas of wall thickening. By moving the transducer and alternating compression and decompression, or by changing the angle of the transducer against the breast tissue or altering the patient's position somewhat, the examiner can cause the reverberations to shift their position within the cyst and confirm them as artifacts. In addition, reverberations can be reduced by lowering the gain or power settings. Because the focal zone setting represents the highest concentration of acoustic energy, shifting the focal zone to a deeper level may also diminish the reverberations.

Cysts occasionally contain low-level internal echoes if the cyst fluid is inspissated, if the fluid contains hemosiderin, or if the cellularity of the fluid is increased (**Fig. 7.8 a, b**). This type of cyst, a *complicated cyst* in BI-RADS nomenclature, may resemble a fibroadenoma, especially when a transducer of 10 MHz or higher frequency is used. If doubt exists, cyst/solid differentiation can be accomplished by ultrasound-guided aspiration (**Fig. 7.8 a, b**). Despite their internal echoes, these cysts usually show an enhanced pattern of sound transmission. The cyst contents may also cause sound attenuation, producing a posterior acoustic shadow that creates the impression of a suspicious solid mass (**Figs. 7.9 a, b; 7.10 a, b**). This effect is common in cysts that contain milk of calcium and inflammatory cysts. The shadowing is most conspicuous when a high-frequency transducer is used.



a

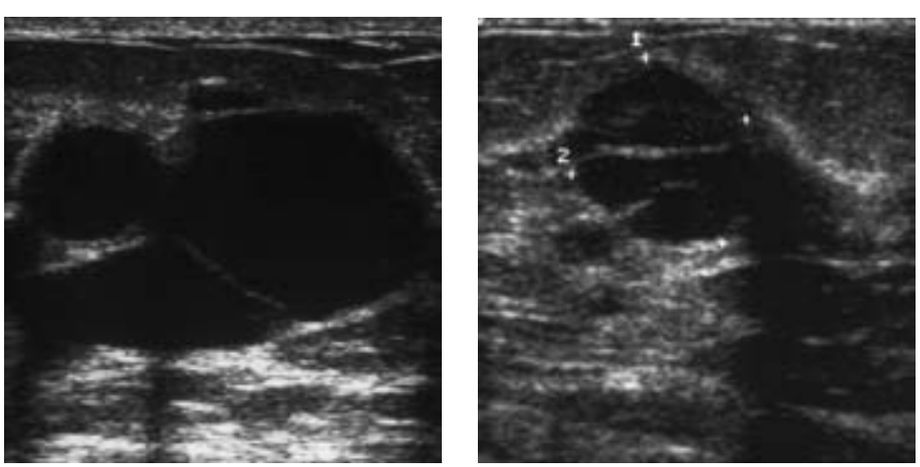


b, c

Fig. 7.3 a–c **Macrocystic disease.** **a** Mediolateral mammogram shows several rounded opacities in a dense breast. **b, c** Ultrasound reveals several macrocysts 4–20 mm in diameter (7.5-MHz transducer).

Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

Comment:
The presence of multiple cysts does not signify increased proliferation. All focal lesions should be carefully examined, however, to ensure that solid tumors and subtle abnormalities are not missed. Mammography alone does not permit an adequate evaluation.



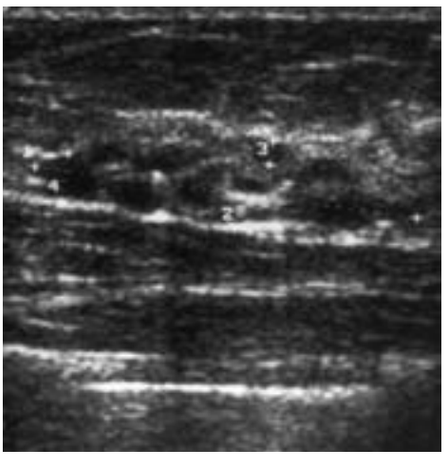
a, b

Fig. 7.4 a, b **Cysts with multiple septations.** **a** Multiple septa within a cystic area 40 × 25 mm in size (7.5-MHz transducer).
b Two septa in a cyst measuring 16 × 17 mm.

Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic, septate
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

Comment:
The large cysts (**a**) are clearly defined. The unilateral edge shadow (**b**) arises from a Cooper ligament that is oblique to the beam direction. Behind and to the left of the cyst is a smaller cyst (3 mm in diameter) cut off-center by the scanning plane. Because of this eccentricity, the cyst walls appears indistinct. Because of the multiple septa, the internal structure of the cyst is unclear (**b**). The fibrous changes in the surrounding tissue cause increased scattering and refraction, making it difficult to evaluate the septa and wall contours.

a, b



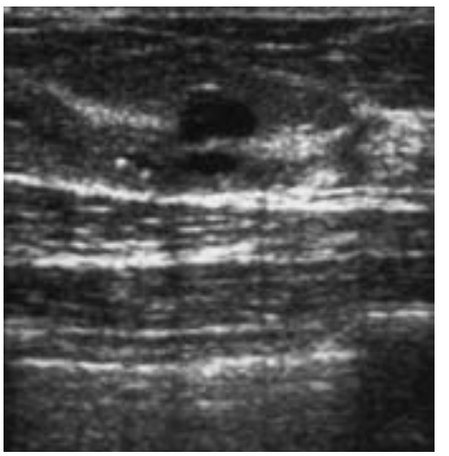
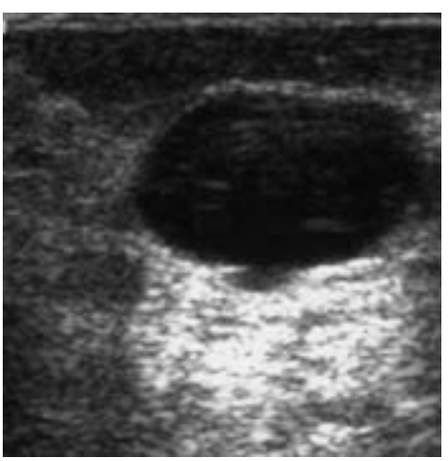


Fig. 7.5 a, b **Microcystic lesions in a parenchymal area measuring 33 × 8 mm in the sagittal plane.** The area contains multiple microcysts 1–4 mm in diameter (10-MHz transducer). Because mammograms showed clustered pleomorphic microcalcifications, the lesion was excised. Histology revealed grade II fibrocystic change.

Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	Microcalcifications in mass
Vascularity	Not assessed

! Comment:
The scans show a somewhat lobular but circumscribed focal lesion composed of an aggregation of multiple microcysts. The axial orientation of the individual cysts and the overall complex is horizontal. There are several bright, punctate mural echoes that represent microcalcifications.

a, b



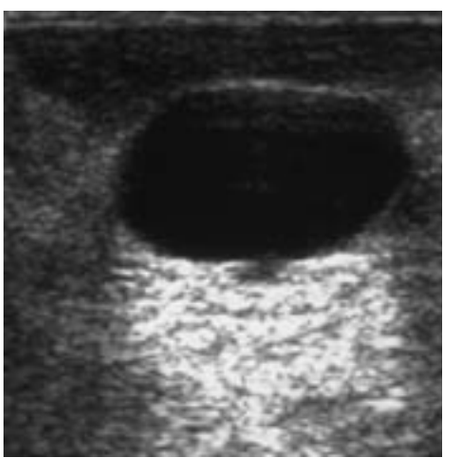


Fig. 7.6 a, b **Intracystic reverberations.** **a** Focus in the near field at 7 mm, **b** Focus shifted 5 mm deeper (10-MHz transducer).

Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

! Comment:
Focusing in the near field concentrates the sound energy in that region. Moving the focal zone distally diffuses the sound energy in the near field, reducing the intensity of the artifacts.

a, b

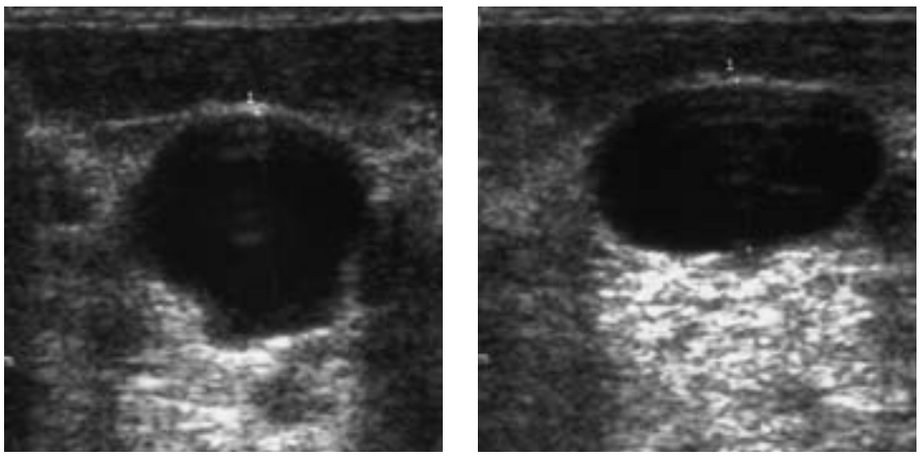


Fig. 7.7 a, b Intracystic reverberations.
a Without compression, anteroposterior diameter 15 mm.
b Light compression with the transducer, anteroposterior diameter 11 mm (10-MHz transducer).

Shape	Oval
Orientation	Parallel (under compression)
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

Comment:
Reverberations appear under compression and in the noncompression scans. Real-time scanning with dynamic compression identifies the echoes as reverberations rather than intracystic structures. As pressure is applied and released, the echoes move up and down within the cyst as the transducer moves closer to and farther from the anterior cyst wall. As compression is increased, the layer of subcutaneous fat becomes thinner and the transducer moves closer to the cyst, causing the reverberations to appear closer together.

a, b

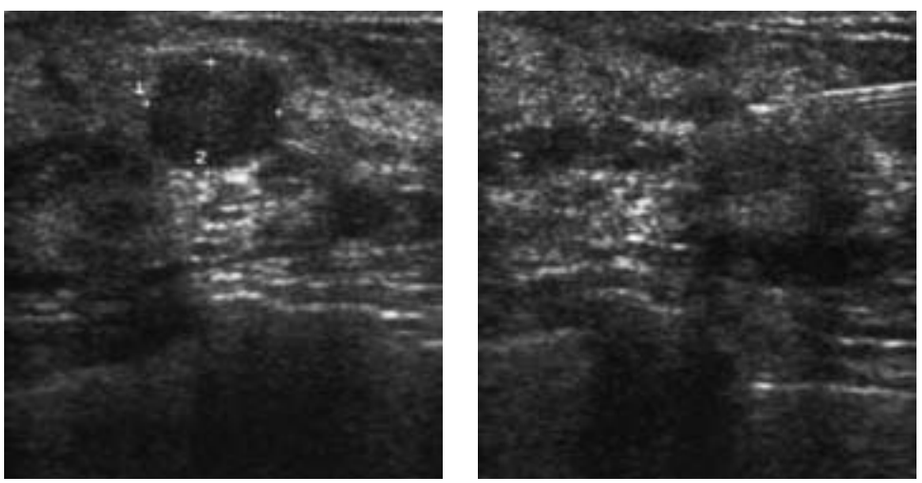


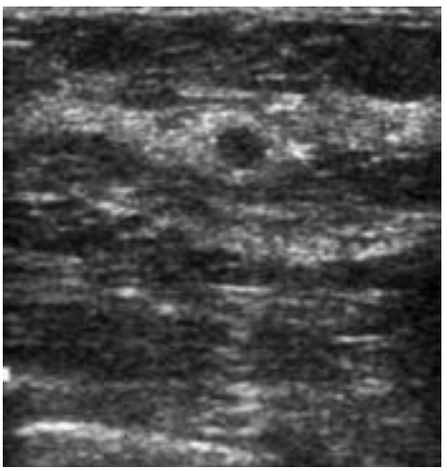
Fig. 7.8 a, b Echogenic cyst.
a Before aspiration.
b After aspiration, with the needle still in place (10-MHz transducer).

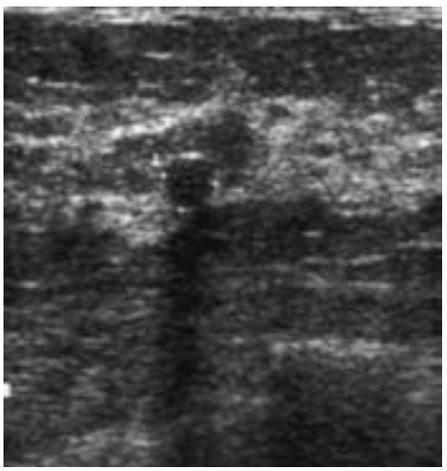
Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Hypoechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not present

Comment:
The ultrasonic image resembles a fibroadenoma. It cannot be classified as cystic or solid by its imaging features alone, and aspiration is necessary to exclude a solid, potentially proliferative tumor. Aspiration identified the lesion as an inspissated cyst.

Aspiration can establish whether a lesion is cystic or solid and, in the case of a simple cyst, can avoid unnecessary surgery.

a, b



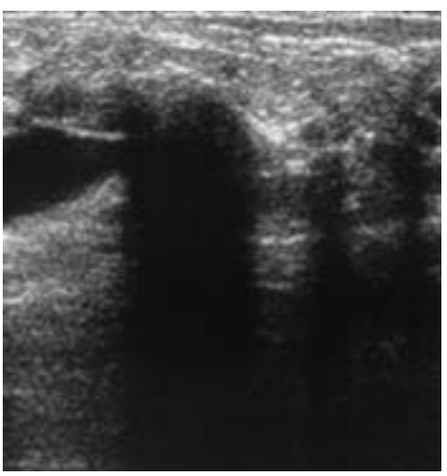


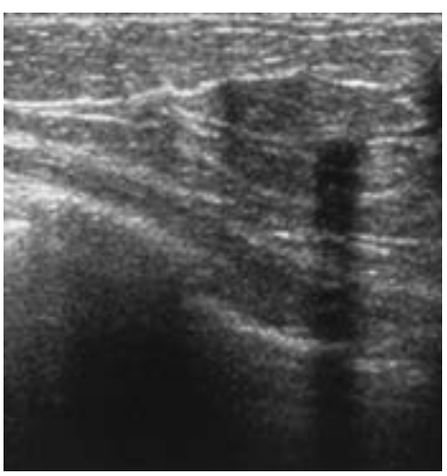
Shape	Round
Orientation	Not parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Hypoechoic
Posterior acoustic features	(**a**) none, (**b**) shadowing
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not present

Fig. 7.9 a, b **Hemosiderin-containing cyst.**
a No shadowing or enhancement.
b Posterior acoustic shadow (10-MHz transducer).

! Comment:
Screening mammograms in this 60-year-old woman showed two densities in the left breast. When ultrasound revealed internal echoes, the patient was hospitalized for surgery. Ultrasound-guided aspiration yielded hemosiderin-containing fluid with no evidence of proliferation.

a, b





Shape	Oval
Orientation	–
Margin	Indistinct
Lesion boundary	Abrupt interface
Echo pattern	Hypoechoic
Posterior acoustic features	Shadowing
Surrounding tissue	Architectural distortion
Calcifications	None
Vascularity	Not present

Fig. 7.10 a, b **Bilateral milk of calcium cysts with acoustic shadows.**
a Upper outer quadrant of the right breast.
b Upper left breast (12-MHz transducer).

! Comment:
The axial orientation of the lesions is indeterminate because of acoustic shadowing (only the horizontal dimension can be measured). Similarly, compressibility cannot be assessed because the posterior wall is not defined. The lack of sound transmission through the cysts makes it impossible to evaluate the surrounding structures, and so the architecture is uninterpretable.

Sound absorption by the dense fluid gives rise to a suspicious ultrasound pattern, but aspiration promptly identified the lesions as cysts. If the mammograms were also suspicious, core biopsy or primary excision would have been indicated.

Table 7.5 Criteria for the diagnosis of complicated cysts and complex cystic masses

Shape	Oval, round or lobulated
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echo pattern	Complicated: low-level internal echoes or fluid–fluid level Complex: cystic and solid components
Posterior acoustic features	Variable
Surrounding tissue	No changes
Calcifications	Microcalcifications may be present
Vascularity	Not present *

* Assessment of vascularity is not required if lesions show typical cystic characteristics and if proliferative changes are not suspected.

Fluid Levels and Oil Cysts

Fluid levels develop in cysts that contain liquids with different specific gravities (**Fig. 7.11**). Fluid levels often form when immiscible oily and watery fluid phases coexist in the same cyst. The oily phase, which is usually more echogenic, floats on top of the watery phase and creates a fluid–fluid level. This phenomenon is also seen in galactoceles, milk collections found in lactating women where the hyperechoic, high-fat cream layer is found anteriorly while the anechoic, watery component of milk occupies the deeper portion of the cystic lesion. When the patient is moved from the supine to a sitting position, the level will gradually shift in response to gravity. A layering effect also occurs when cyst fluid becomes inspissated and the more echogenic material settles to the cyst floor.

When the cysts contain only liquefied fat or oil (fat necrosis), the mass may appear anechoic or hypoechoic, and either posterior enhancement or shadowing may be associated with it. The clinical history of accidental or surgical trauma may support the diagnosis and correlating the sonographic finding with a circumscribed radiolucent mammographic mass will establish the benign etiology without need for intervention.

Clustered Microcysts

Multiple microcysts that are aggregated in a cluster may form a palpable mass with indistinct margins that is difficult to evaluate clinically. An area of increased soft tissue density, at times partially circumscribed, may be the only mammographic manifestation. The tiny individual cystic components are poorly resolved, and only an ill-defined hypoechoic mass may be seen using lower-frequency transducers or ultrasound systems of poor quality. High-resolution scanners can usually define the individual microcysts that comprise the lesion (see **Fig. 7.2**). Occasionally, these microcysts, dilated lobular acini, contain small, bright, punctate mural echoes that correlate with microcalcifications (see **Fig. 7.5 a, b**). Ultrasound is not a suitable modality for the primary detection of microcalcifications, but once microcalcifications have been identified on mammograms, ultrasound can help identify their source when they are located in microcysts. These microcystic conglomerations should be carefully interrogated sonographically to identify or exclude a solid component. If there is no solid component, clustered microcysts can be considered probably benign with two initial short interval follow-up visits (commonly at 6-month intervals) with annual follow-ups thereafter.

If a solid component is found, ultrasound should be used to guide core biopsy. If proliferative changes or atypical cells are reported from fine-needle aspiration cytology, core biopsy or excision of the lesion would be the next step.

The microcalcifications associated with microcysts are rounded, punctuate, and adenosic. If mammograms reveal pleomorphic or dot-dash microcalcifications suggestive of malignancy in an area where benign-appearing microcysts are found with ultrasound, the higher level of suspicion for malignancy associated with the microcalcifications will override the microcystic lesion's benign assessment. The microcalcifications will require a histologic diagnosis, most commonly obtained with stereotactic guidance.

Complex Cystic Masses

Intracystic Papillomas and Cyst Wall Proliferation

Ultrasound is ideally suited for its ability to evaluate intracystic structures and cyst walls (**Figs. 7.12, 7.13**). Thus, a thorough examination requires that every cyst be imaged in real-time in at least

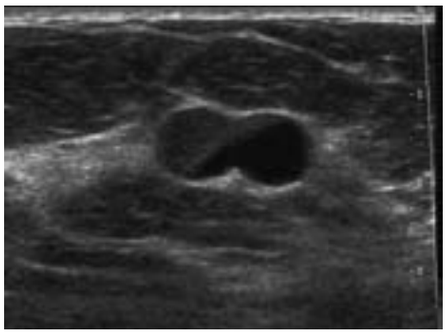
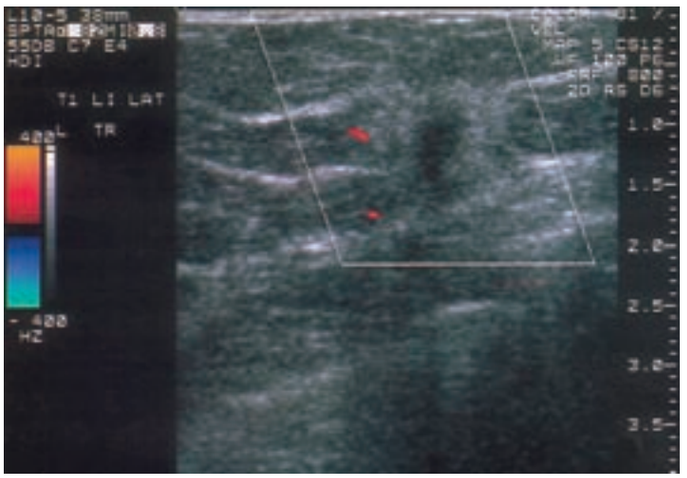


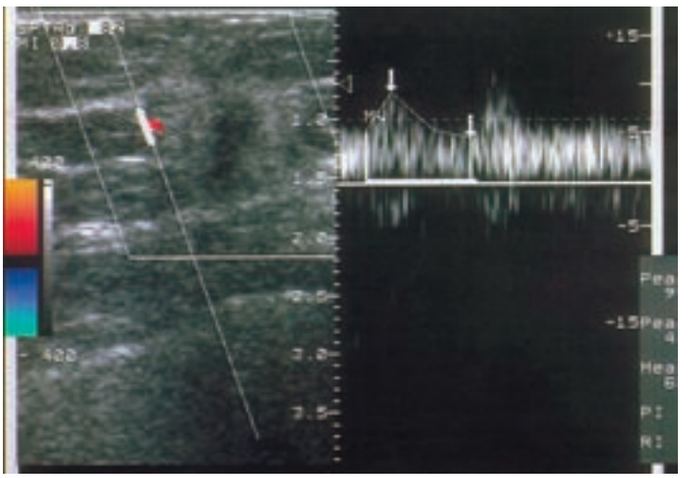
Fig. 7.11 Oil cyst with a fluid level between the aqueous and oily phases (12-MHz transducer).

Shape	Oval
Orientation	Parallel
Margin	Circumscribed
Lesion boundary	Abrupt interface
Echogenicity	Hypoechoic/anechoic
Posterior acoustic features	Enhancement
Surrounding tissue	No changes
Calcifications	None
Vascularity	Not assessed

! Comment:
Inspissated, hemosiderin-containing, fatty or cellular cyst fluid is more echogenic than water. Because fat is lighter than water and is immiscible with it, a fluid–fluid level is formed. Aspiration yielded a fatty, viscous fluid with no signs of proliferation.



a



b

Fig. 19.10 a, b **Invasive ductal carcinoma with low blood flow.**
a Color Doppler display of vessels.
b Duplex flow velocity measurement.

If morphology shows a suspicious pattern, but the vascularity is sparse, one should not be dissuaded from a working diagnosis of carcinoma or from biopsy.

Possible Applications

Smoothly Marginated Carcinomas

The cases in **Figures 19.1–19.3** illustrate that cellular carcinomas, which may be mistaken for benign tumors in imaging studies, show conspicuous abnormalities on color Doppler images. Doppler ultrasound is particularly useful for confirming the suspicious nature of these tumors.

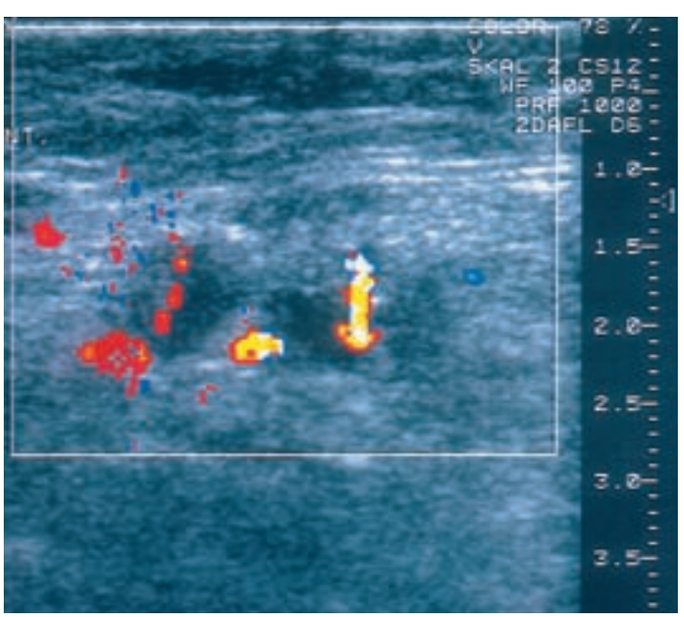


Fig. 19.11 **Multifocal breast cancer.** Color Doppler shows two small tumor masses, each of which is associated with a radial pattern of tumor vessels.

Proliferative Fibroadenomas

The proliferative activity of highly vascularized fibroadenomas can be predicted with Doppler ultrasound (**see Fig. 19.7**). Observations of these tumors following cytologic confirmation have confirmed their proliferative tendency. The histologic and cytologic analysis of these tumors consistently show proliferative changes, and therefore surgical excision can be recommended when a hypervascular fibroadenoma is found.

Multifocal and Multicentric Tumors

The detection of multifocality and multicentricity is an important part of preoperative diagnosis. Multifocal lesions can be difficult to identify mammographically, especially in women with dense breasts. If the decision between breast-conserving surgery and mastectomy must be based on ultrasound findings alone, it is very helpful if the diagnosis of multiple tumor masses is confirmed by demonstrating multiple vascularized lesions with color Doppler (**Fig. 19.11**).

Scars

In the follow-up of patients who have undergone breast-conserving surgery, major difficulties can arise in the exclusion of recurrent disease. It is advantageous in these cases to exclude a recurrence by noninvasive means (**Fig. 19.12**). Postsurgical scars generally have a low blood supply. Even so, much experience is required in differentiating a scar from a recurrence, because many recurrent tumors are hypovascular, especially after prior radiotherapy. If doubt exists concerning recurrence in a mature scar, contrast-enhanced breast MRI can be helpful in excluding recurrence. With an area of enhancement in or near the tumor, local recurrence is suspected, and image-guided percutaneous core biopsy should be directed to the area to confirm the diagnosis. Use of an

ultrasound contrast agent, not yet FDA-approved in the United States, may help accomplish this goal (see below).

Lymph Node Evaluation

The detection of nodal metastases plays an increasingly important role in preoperative planning. In metastatic lymph nodes that do not display some of the typical ultrasound findings, usually focal changes in the cortex of the node, color Doppler can advance the diagnosis by demonstrating a reactive pattern in enlarged lymph nodes. A concomitant increase in blood flow implies a higher index of suspicion for metastasis (**Fig. 19.13**). Inflammatory changes can also cause a slight increase in vascularization, but usually this is detectable in the hilar area of the node.

It is very important to detect metastatic involvement of the internal mammary nodes, because that region is not routinely included in lymphadenectomy. Color Doppler has a critical role in the surgical planning of these cases because of the proximity of these nodes to the pleura and internal thoracic vessels. Detecting or excluding direct vascular connections during the planning phase can reduce the subsequent risk of surgical complications (**Fig. 19.14**).

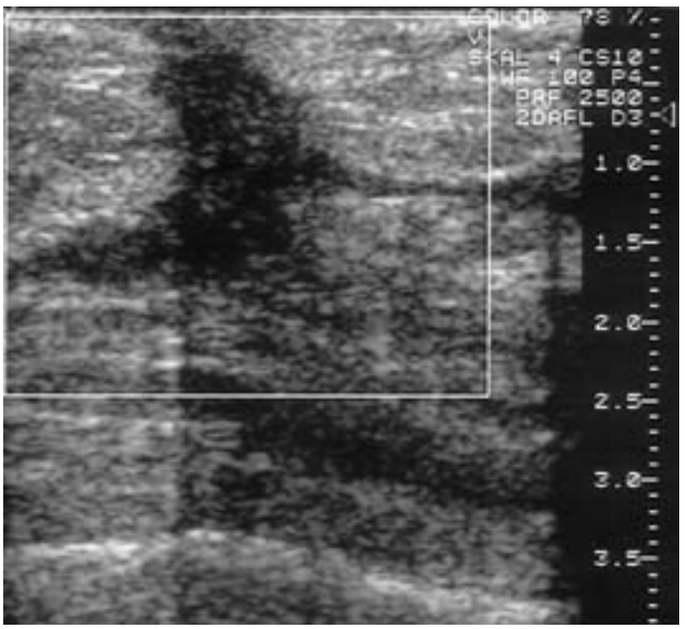


Fig. 19.12 **Postsurgical scar following local excision of breast carcinoma.** The scar appeared suspicious at ultrasound, but color Doppler shows no abnormal increase in vascularity, suggesting that the lesion is benign.

Prognostic Evaluation

Pathologic studies have shown that a correlation exists between tumor angiogenesis and disease prognosis. This type of study requires a large population to make a prognostic evaluation. The follow-up period in women examined by color Doppler ultrasound is not yet sufficient to make a definitive evaluation. We were able to make a tentative assessment, however, by comparing the numbers of tumor vessels and total blood flow (sum of flow velocities) in 51 patients with nodal metastases and 82 patients without nodal metastases. We found a significant difference with regard to the number of tumor vessels ($p < 0.01$) in both groups. Measurements of total blood flow showed a tendency toward higher blood flow when metastases were present ($p < 0.062$). Thus, there is evidence that blood flow measurements can provide at least a crude prognostic assessment in that tumors with less blood flow correlate more frequently with an absence of metastases (**Fig. 19.15 a, b**).

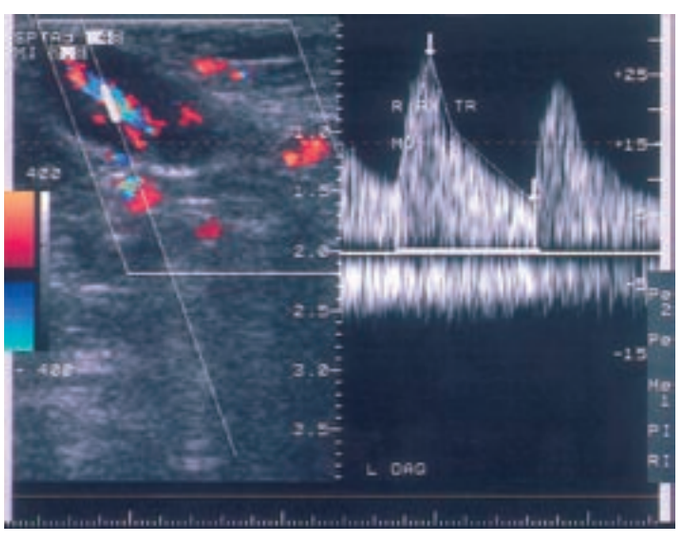


Fig. 19.13 **Axillary lymph node metastasis with a rich vascular supply.**

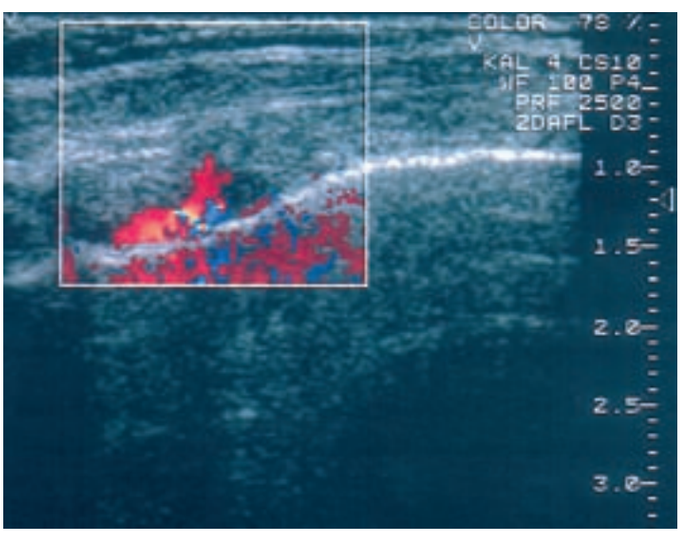
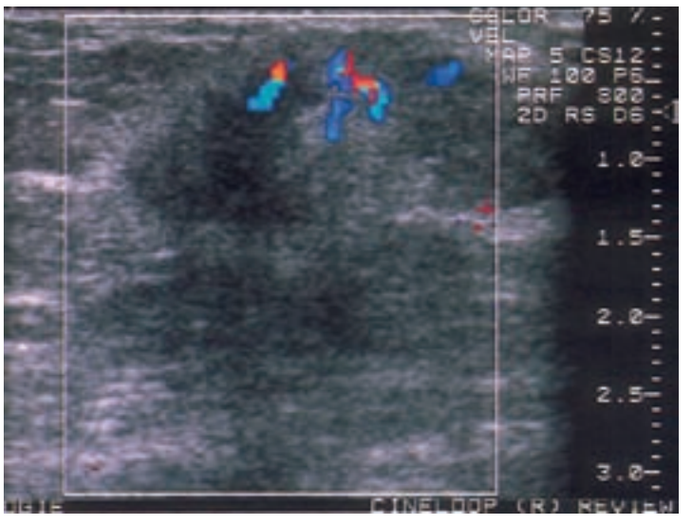
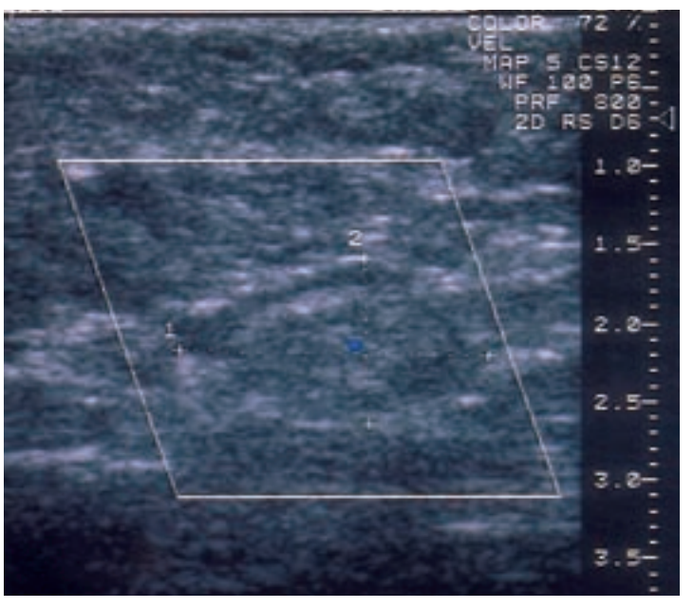


Fig. 19.14 **Lymph node metastasis 3 × 4 mm in diameter next to the internal thoracic artery.** A large, branched vascular pedicle runs directly from the artery into the lymph node. Parasternal transverse scan in the third intercostal space on the left side.

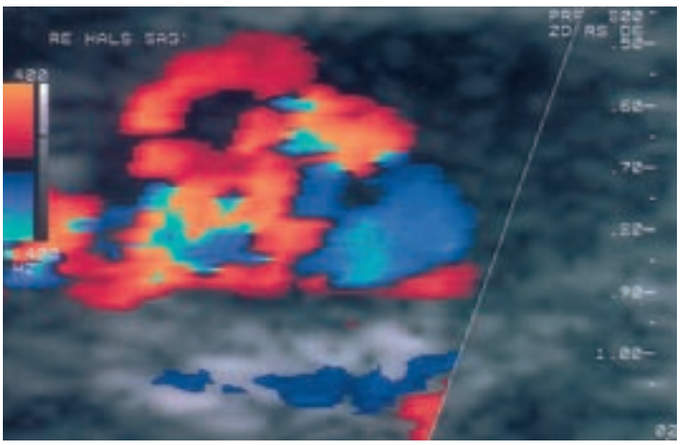


a

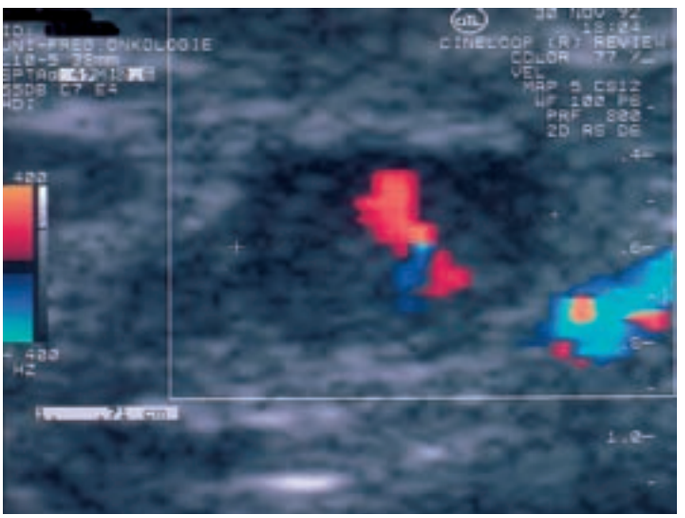


b

Fig. 19.15 a, b **Invasive ductal breast carcinoma.**
a Hypovascular primary tumor.
b Enlarged reactive lymph node with no abnormal vascularity in color Doppler. Histology showed no metastatic involvement of the node.



a



b

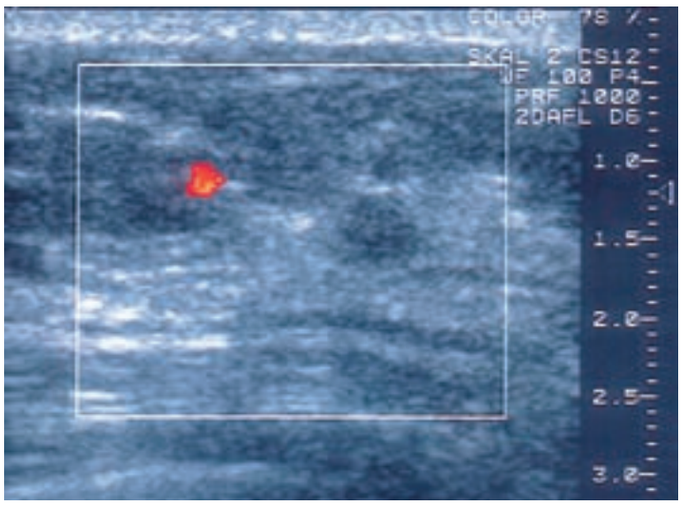
Fig. 19.16 a, b **Lymph node metastasis 1 cm in diameter after earlier primary treatment.**
a Initial image shows very high tumor blood flow. Chemotherapy with Taxol was initiated.
b The same lymph node 3 months after the start of treatment. The size of the node is unchanged, but the decrease in vascularity indicates significant tumor response.

Chemotherapy and Follow-Up

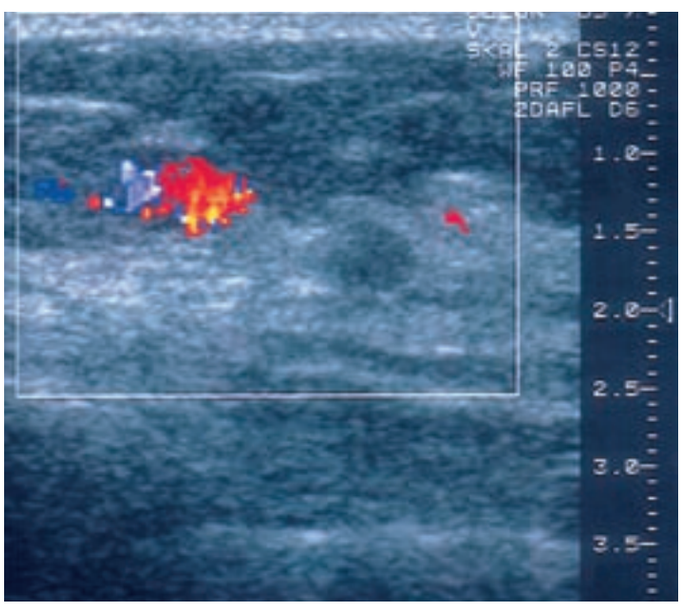
Malignant tumors vary greatly in their response to chemotherapy and often develop resistance during the course of treatment. It is very difficult to detect this clinically. We have already tested Doppler ultrasound in experimental animals and in various treatment modalities as a means of evaluating tumor response. Traditionally, tumor size measured clinically or by imaging has been the only parameter used to evaluate response. A constant tumor diameter is interpreted as "no change," and this may justify changing to a different therapy. But as **Figure 19.16 a, b** shows, a marked decrease in tumor blood flow may occur without an apparent change in tumor size. Thus, Doppler ultrasound provides a sensitive method for evaluating in vivo the chemotherapeutic response of tumors.

Use of Ultrasound Contrast Agents to Increase Doppler Signal

Ultrasound contrast agents are substances that increase the echogenicity of blood following intravenous injection. By improving the signal-to-noise ratio, these agents enhance the apparent echo contrast between hypervascular and hypovascular areas. Small vessels that were previously invisible can be detected following contrast administration. This technique can help differentiate a hypovascular carcinoma from scar tissue, whose morphology, for example, frequently mimics carcinoma at ultrasound.



a

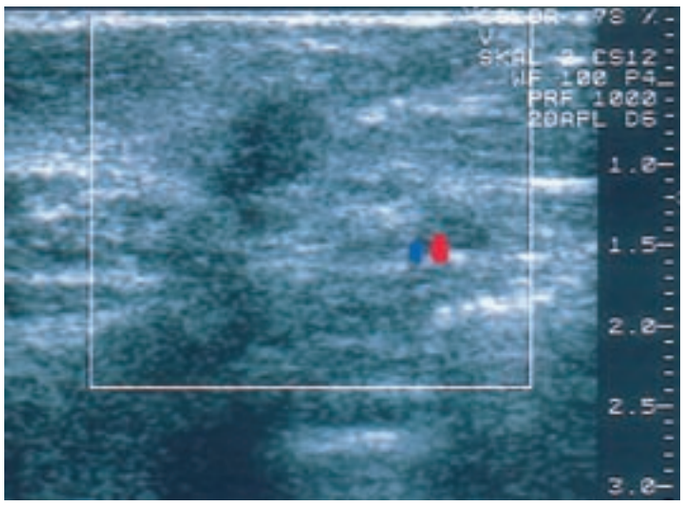


b

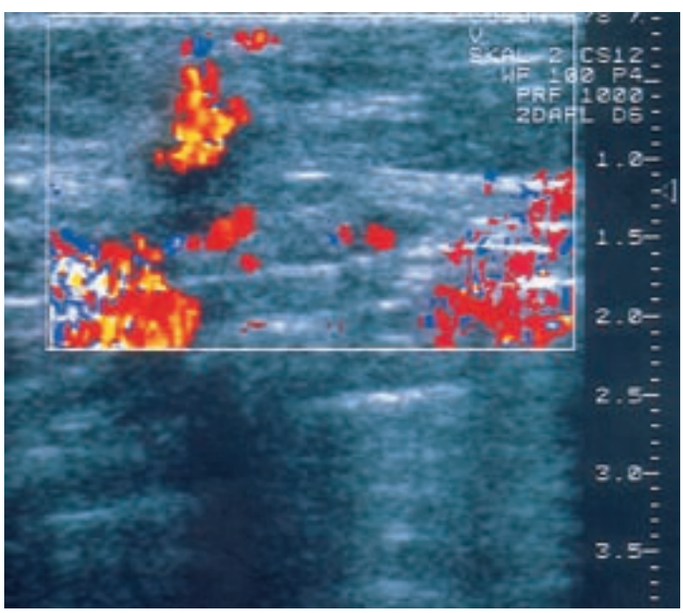
Fig. 19.17 a, b Scar granuloma 2 years after breast-conserving cancer surgery. Ultrasound showed a hypoechoic mass with ill-defined margins.

a Color Doppler prior to contrast administration shows a parenchymal vessel separate from the tumor.

b After the intravenous injection of 8 mL Levovist (400 mg/mL), the tumor still appears avascular but the parenchymal vessel is more clearly demonstrated.



a



b

Fig. 19.18 a, b Local recurrence 2 years after breast-conserving cancer surgery. Ultrasound showed a lesion similar to that in Fig. 19.17.

a The tumor itself is avascular, but a small parenchymal vessel is visible some distance away.

b Following contrast injection, the parenchymal vessel appears more prominent. But the major change is the increased signal intensity within the mass, indicating a high blood flow rate in the tumor.

Practical Application

Following intravenous injection of the echo-enhancing agent, it takes approximately 20–40 seconds for blood carrying the contrast material to reach the arterial bed. By increasing the echogenicity of the blood, the agent increases the amplitude of the Doppler signal while causing no significant increase in the frequency shift. Vessels that are faintly visualized in color Doppler become more conspicuous, and previously nonvisualized vessels can be seen. Vessels that were visible before contrast injection and are enhanced by the contrast agent should not be classified as suspicious (**Fig. 19.17 a, b**), but a focal increase of blood flow in an area that previously appeared avascular should raise suspicion of carcinoma (**Fig. 19.18 a, b**).

In our studies we employed the ultrasound contrast agent Levovist (Schering, Berlin), which is used primarily in cardiology, gastroenterology, and nephrology. The advantages of echo enhancement in breast tumors are currently being tested. The agent consists mainly of galactose granules that are stabilized with a special lipid-based preparation so that they will remain stable for a short time in the bloodstream. The particles are small enough to pass easily through the pulmonary capillary bed. We have observed no side effects other than an occasional warm or cold sensation at the injection site, and the agent may be administered