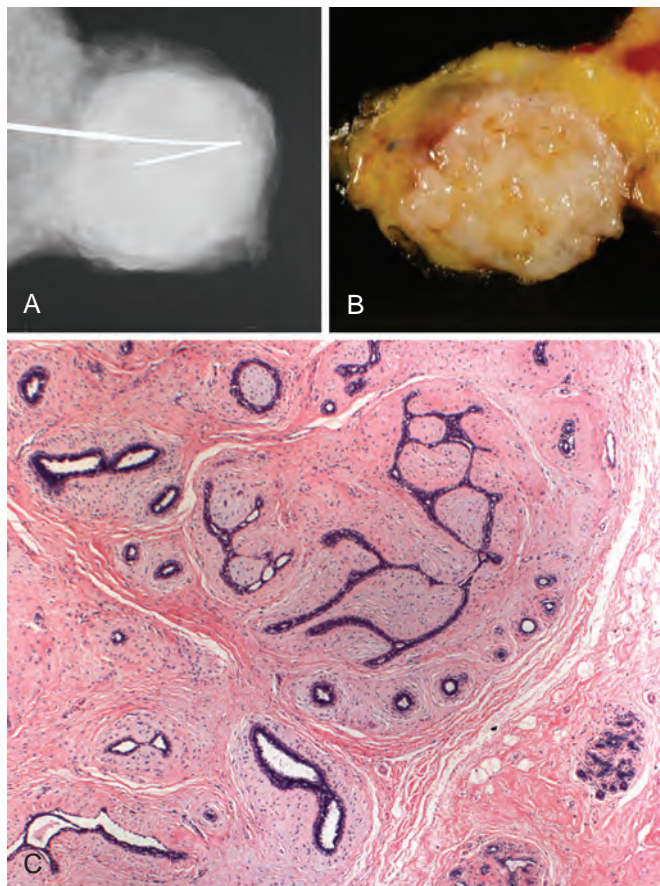


specialized stroma may elaborate growth factors for epithelial cells, resulting in the proliferation of the non-neoplastic epithelial component of these tumors. Interlobular stroma is the source of the same types of tumors found in connective tissue in other sites of the body (e.g., lipomas and angiosarcomas) as well as tumors arising more commonly in the breast (e.g., pseudoangiomatous stromal hyperplasia, myofibroblastomas, and fibrous tumors).

## Fibroadenoma

**Fibroadenomas are the most common benign tumor of the female breast.** Most occur in women in their 20s and 30s, and they are frequently multiple and bilateral. Young women usually present with a palpable mass and older women with a mammographic density (Fig. 23-27A) or clustered calcifications. The epithelial component is hormonally responsive and there is typically an increase in size due to lactational changes during pregnancy. Such increases in size may be complicated by infarction and inflammation, and may raise a false suspicion of carcinoma.



**Figure 23-27** Fibroadenoma. **A**, The radiograph shows a characteristically well-circumscribed mass. **B**, Grossly, a rubbery, white, well-circumscribed mass is clearly demarcated from the surrounding yellow adipose tissue. The absence of adipose tissue accounts for the radiodensity of the lesion. **C**, The proliferation of intralobular stroma surrounds, pushes, and distorts the associated epithelium. The border is sharply delimited from the surrounding tissue.

## MORPHOLOGY

Fibroadenomas vary in size from less than 1 cm to large tumors that replace most of the breast. The tumors are well-circumscribed, rubbery, grayish white nodules that bulge above the surrounding tissue and often contain slitlike spaces (Fig. 23-27B).

The delicate and often myxoid stroma resembles normal intralobular stroma. The epithelium may be surrounded by stroma (pericanicular pattern) or compressed and distorted by it (intracanicular pattern) (Fig. 23-27C). In older women, the stroma typically becomes densely hyalinized and the epithelium atrophic.

Many fibroadenomas are polyclonal hyperplasias of lobular stroma. For example, almost half of women receiving cyclosporin A after renal transplantation develop multiple and bilateral fibroadenomas that regress after cessation of treatment. Other fibroadenomas are benign neoplasms associated with clonal cytogenetic aberrations that are confined to the stromal component. No consistent cytogenetic changes have been found.

Fibroadenomas are grouped with “proliferative changes without atypia” in conferring a mildly increased risk of subsequent cancer. However, in one study the increased risk was limited to fibroadenomas associated with cysts larger than 0.3 cm, sclerosing adenosis, epithelial calcifications, or papillary apocrine change (“complex fibroadenomas”) (Table 23-1).

## Phyllodes Tumor

Phyllodes tumors, like fibroadenomas, arise from intralobular stroma, but are much less common. Although they can occur at any age, most present in the sixth decade, 10 to 20 years later than the peak age for fibroadenomas. The majority are detected as palpable masses, but a few are found by mammography. *Cystosarcoma phyllodes* is a term sometimes used for these lesions. However, *phyllodes tumor* is preferred, since most behave in a relatively benign fashion and are not cystic.

Phyllodes tumors are associated with clonal acquired chromosomal changes, with gains in chromosome 1q being the most frequent. Increased numbers of chromosomal aberrations and overexpression of the homeobox transcription factor HOXB13 are associated with higher tumor grade and more aggressive clinical behavior.

## MORPHOLOGY

The tumors vary in size from a few centimeters to massive lesions involving the entire breast. The larger lesions often have bulbous protrusions (*phyllodes* is Greek for “leaflike”) due to the presence of nodules of proliferating stroma covered by epithelium (Fig. 23-28). In some tumors these protrusions extend into a cystic space. This growth pattern can also occasionally be seen in larger fibroadenomas and is not an indication of malignancy. Phyllodes tumors are distinguished from fibroadenomas on the basis of higher cellularity, higher mitotic rate, nuclear pleomorphism, stromal overgrowth, and infiltrative borders. Low-grade lesions resemble fibroadenomas but are more