Breast fibroepithelial tumors

Diagnosis in breast mass

- The “triple” test
- Diagnosis is based on the combination of clinical examination, imaging, and tissue diagnosis(FNA-CNB-OPEN Bx)

Fibroadenoma

- Fibroadenomas (FAs) most often have a characteristic clinical presentation with an easily movable mass, seemingly unfixed to surrounding breast tissue.
- The gross appearance is usually characteristic.
- The sharp circumscription and smooth interface with surrounding breast tissue, usually producing an elevation of the FA on cut section, is also characteristic.

Fibroadenoma

- Autopsy studies demonstrate that fibroadenomas are present in approximately 10% of women.
- The peak incidence occurs between the second and third decades of life.
- these lesions are occasionally seen in the elderly.
- They are often solitary lesions, but 50% of patients will present with multiple masses.

- They are a subset of fibroepithelial tumors that comprise stromal and epithelial components.
- The histologic pattern depends on which of these components is predominant.
- Fibroadenomas are very responsive to hormonal stimulus and may enlarge premenstrually or during pregnancy.

- FAs that are allowed to grow after initial detection usually cease to grow when they reach 2 to 3 cm in diameter.
- Infarcts of the breast may occur during pregnancy or lactation with a resultant discrete mass.
- Approximately 1 of 200 FAs shows infarction.
- Pain and tenderness may occur during pregnancy, and an inflammatory reaction may be accompanied by lymphadenopathy, leading to the clinical impression of carcinoma.

- The incidence of carcinoma arising in a fibroadenoma is approximately 0.1% to 0.3%, with invasive carcinomas more frequently of the lobular type.
- one study reported that, overall, FAs were found to be associated with a slight increased relative risk of later cancer.

Diagnosis

- Diagnosis is based on the combination of clinical examination, imaging, and percutaneous tissue aspiration or biopsy (the “triple” test).
- A clinical diagnosis of fibroadenoma alone is unreliable and does not exclude malignancy, even in younger women.
- Ultrasound, in combination with mammography in select patients, should be performed

- A subsequent core needle biopsy is the most accurate means of establishing the diagnosis.
- Because of the heterogeneity of fibroadenomas and the overlapping features of fibroepithelial tumors, an accurate diagnosis from core needle biopsy can be challenging.
- Any atypical epithelial proliferation or unusual stromal changes on biopsy should prompt complete excision to rule out malignant transformation or phyllodes tumor.

- Gene expression profiling may prove useful in discerning these differences along the spectrum of fibroepithelial lesions. In a recent study, the levels of expression of proliferation-related genes (e.g., CCNB1 and MKI67) and mesenchymal/epithelial-related genes (e.g., CLDN3 and EPCAM) were used to distinguish fibroadenoma from malignant phyllodes tumor.

Treatment

- Traditionally, symptomatic fibroadenomas, as well as those greater than 2 to 3 cm, have been treated by surgical excision.
- Currently, alternatives to surgical excision include percutaneous removal radiofrequency ablation or cryoablation.
- Core biopsy–proven fibroadenomas in young women (<35 years) that are mobile, less than 2.5 cm, and otherwise clinically benign can be safely observed.

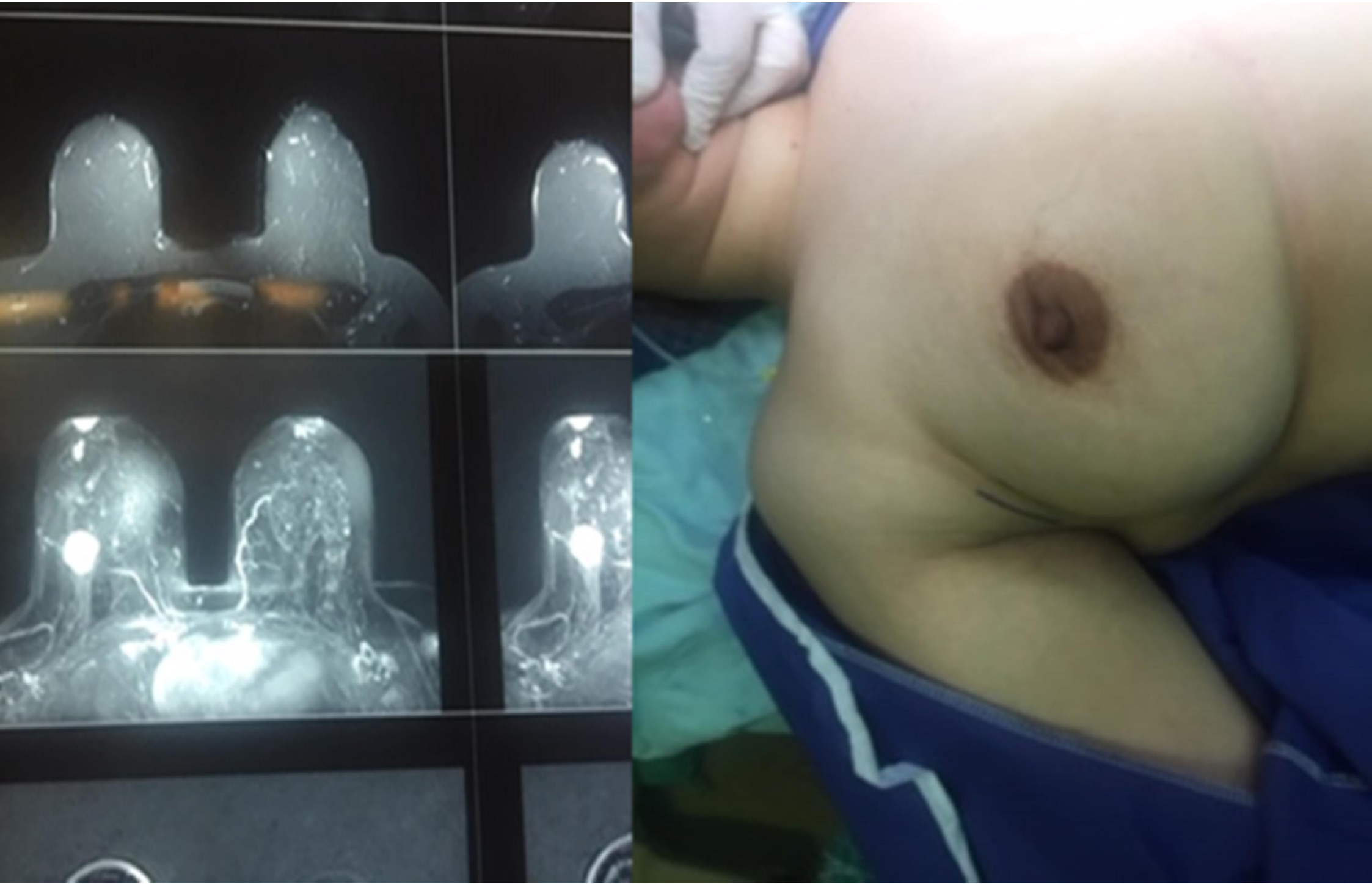
Complex Fibroadenoma

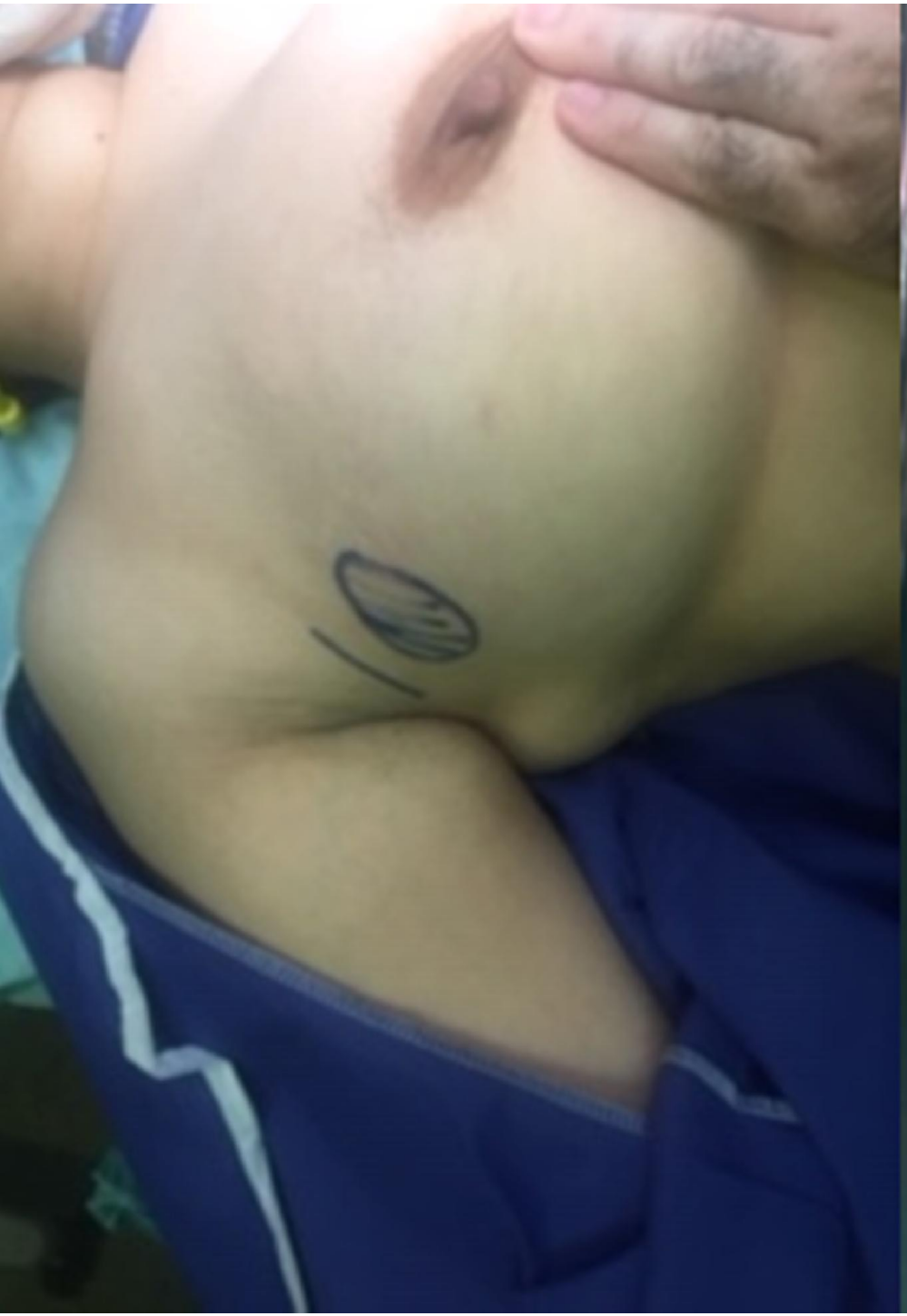
- Complex fibroadenomas are fibroadenomas harboring one or more complex features including epithelial calcifications, apocrine metaplasia, sclerosing adenosis, or cysts greater than 3 mm.
- Imaging features that can help distinguish complex fibroadenomas include ***irregular shape, noncircumscribed borders, complex echo structure, microcalcifications, and posterior acoustic enhancement.***
- The risk of invasive carcinoma developing in women with complex fibroadenoma was found to be ***three times*** that of the general population.
- The literature supports ***excision*** of complex fibroadenomas

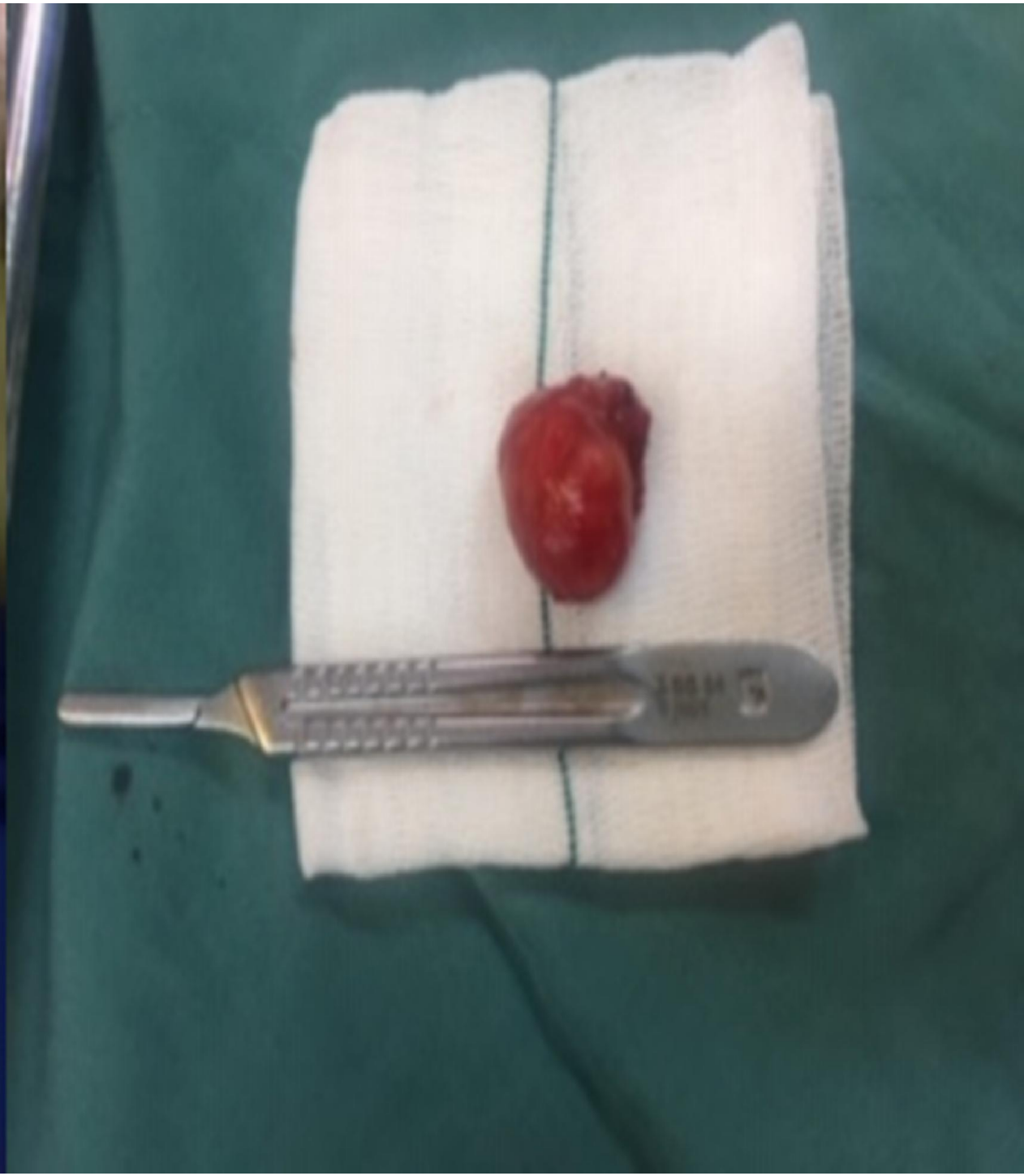
Fibroadenomatosis (Fibroadenomatoid Mastopathy).

- Fibroadenomatosis is a benign breast lesion with the composite histologic features of a fibroadenoma and fibrocystic changes that may represent a morphologic stage in the development of fibroadenomas.
- The lesion is characterized by microscopic fibroadenomatoid foci intermingled with dilated ducts, epitheliosis, and adenosis and was found in more than 10% of cases of BBD.
- Although there is no clear etiology of fibroadenomatosis, there have been case reports of cyclosporine-induced fibroadenomatosis in immunosuppressed patients after renal transplantation.

- Although traditionally the risk of subsequent carcinoma in patients with typical FA has not been considered to be higher than that for the general population, one study reported that, overall, FAs were found to be associated with a slight increased relative risk of later cancer.
- The level of risk varies, depending on the characteristics of the FA itself and the status of the adjacent epithelium.
- If the adjacent epithelium shows proliferative changes or if the FA is complex, defined as the presence of cysts, sclerosing adenosis, epithelial calcifications, or papillary apocrine changes within the FA, the risk is slightly higher than when these changes are absent.







Phyllodes tumor

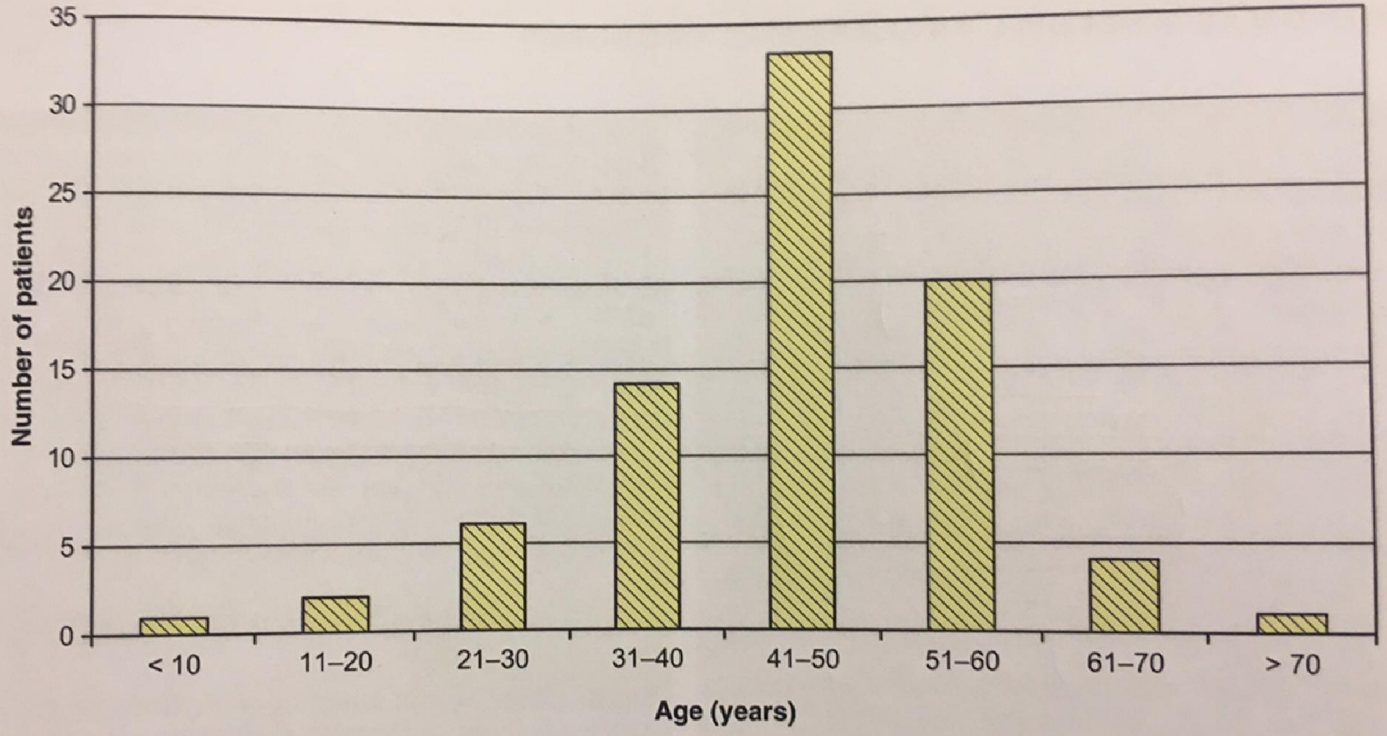


FIGURE 62-4 Age distribution of women diagnosed with phyllodes tumors. (Modified from Salvadori B, Cusumano F, Del Bo R, et al. Surgical treatment of phyllodes tumors of the breast. *Cancer* 1989;63(12):2532–2536.)

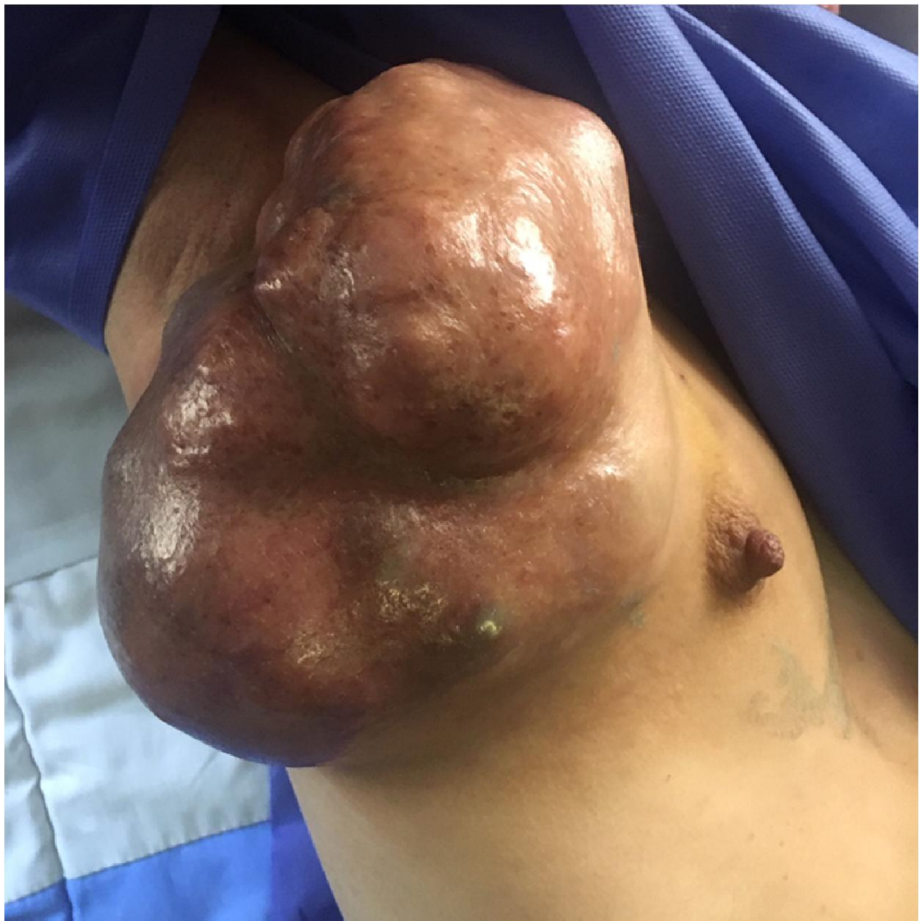
- Phyllodes tumors have been reported in males but are extremely rare, occurring in conjunction with gynecomastia and lobular development in male breast tissue .
- Phyllodes tumors are fibroepithelial breast tumors capable of a diverse range of biological behavior.

- Also termed “phylloides tumors” or “cystosarcoma phyllodes,” these lesions are similar to benign fibroadenomas in their least aggressive form, but with an increased propensity for local recurrence following excision.

- Phyllodes tumors in their most aggressive form, however, can recur locally and distantly, typically degenerating into a sarcomatous lesion lacking an epithelial component .
- Fortunately, this malignant form of phyllodes is uncommon, with fewer than 5% of lesions ever developing distant metastases
- The World Health Organization (WHO) recommends classification of phyllodes into three subtypes as follows:
- 1) benign phyllodes,
- 2) borderline phyllodes (also known as “low grade malignant”) 3)malignant phyllodes (also known as “high grade malignant”)

- Nonmalignant phyllodes tumors typically have a gross appearance similar to fibroadenomas, presenting as a circumscribed, round or oval mass that lacks a true histologic capsule but which generally can be easily shelled out from surrounding tissues.

- Most phyllodes tumors are detected in the 1 to 2 cm range but there are reports in the literature of lesions ranging from less than 1 cm up to 40 cm .



Differential Diagnosis :

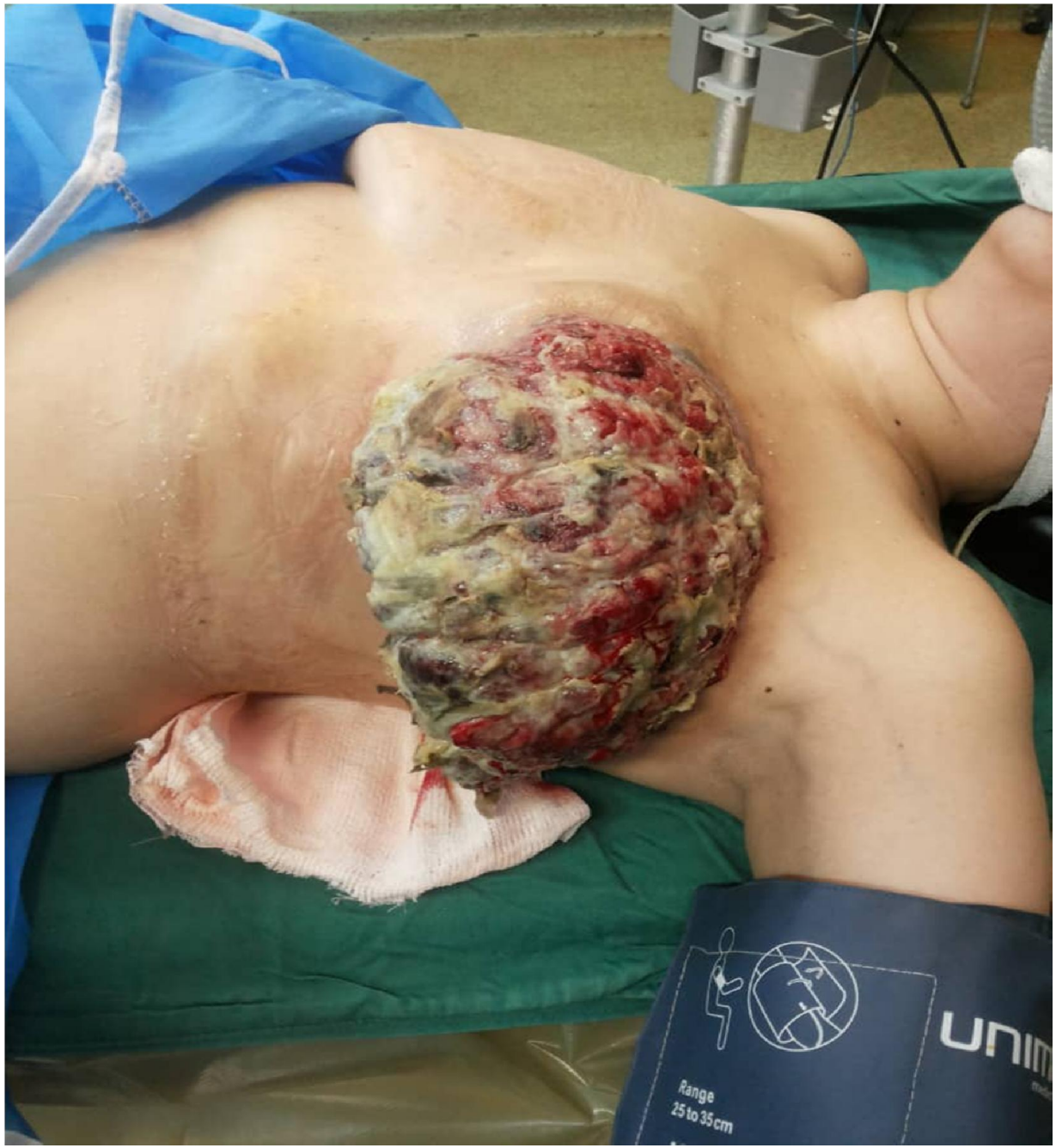
- The differential diagnosis for benign phyllodes tumors includes cellular fibroadenoma and juvenile fibroadenoma.
- Distinction of benign phyllodes tumors from fibroadenoma variants can be challenging.

CLINICAL CHARACTERISTICS :

- Typically, phyllodes tumors present as ***painless, palpable masses in the breast*** that demonstrate continuous growth.

- The mass may produce visible bulging when tumors expand quickly.

- In neglected cases, skin ulceration may develop from ischemia secondary to stretching and pressure.
- Such skin changes can occur with all types of lesions, so while ulceration associated with carcinoma is an indication of malignant behavior (T4 lesion), it is not necessarily an indication of a malignant phyllodes tumors.
- The nipple may be effaced, but invasion and/or retraction is unusual , as is bloody nipple discharge.


Range
25 to 35 cm

- Most phyllodes tumors, therefore, are surgically “shelled out” (enucleated) at initial intervention, resulting in the inadequate surgical margins associated with an increased risk of local recurrence in the absence of additional surgery.

- Although large size (>3 cm) and presence of intramural cystic regions or clefts make the diagnosis of phyllodes tumor more likely, these features can also be present in fibroadenomas.
- Thus, any circumscribed mass presenting on imaging with large initial size or significant interval growth warrants excision to rule out phyllodes tumor.

- Although MRI may more accurately delineate the true extent of disease prior to surgery, there is little data to support the routine use of MRI for imaging phyllodes tumors.
- MRI may be most helpful when mastectomy is being considered and the full extent of the tumor is difficult to determine from standard imaging.

Treatment

- Surgery:

- Most studies advocate at least a 1-cm margin, which has traditionally been accepted as an adequate resection.
- Some authors actually argue that 2-cm should be considered the standard of care for desired surgical margin for excision of phyllodes tumors, with a goal of a 2–3-cm margin if a phyllodes tumor locally recurs .

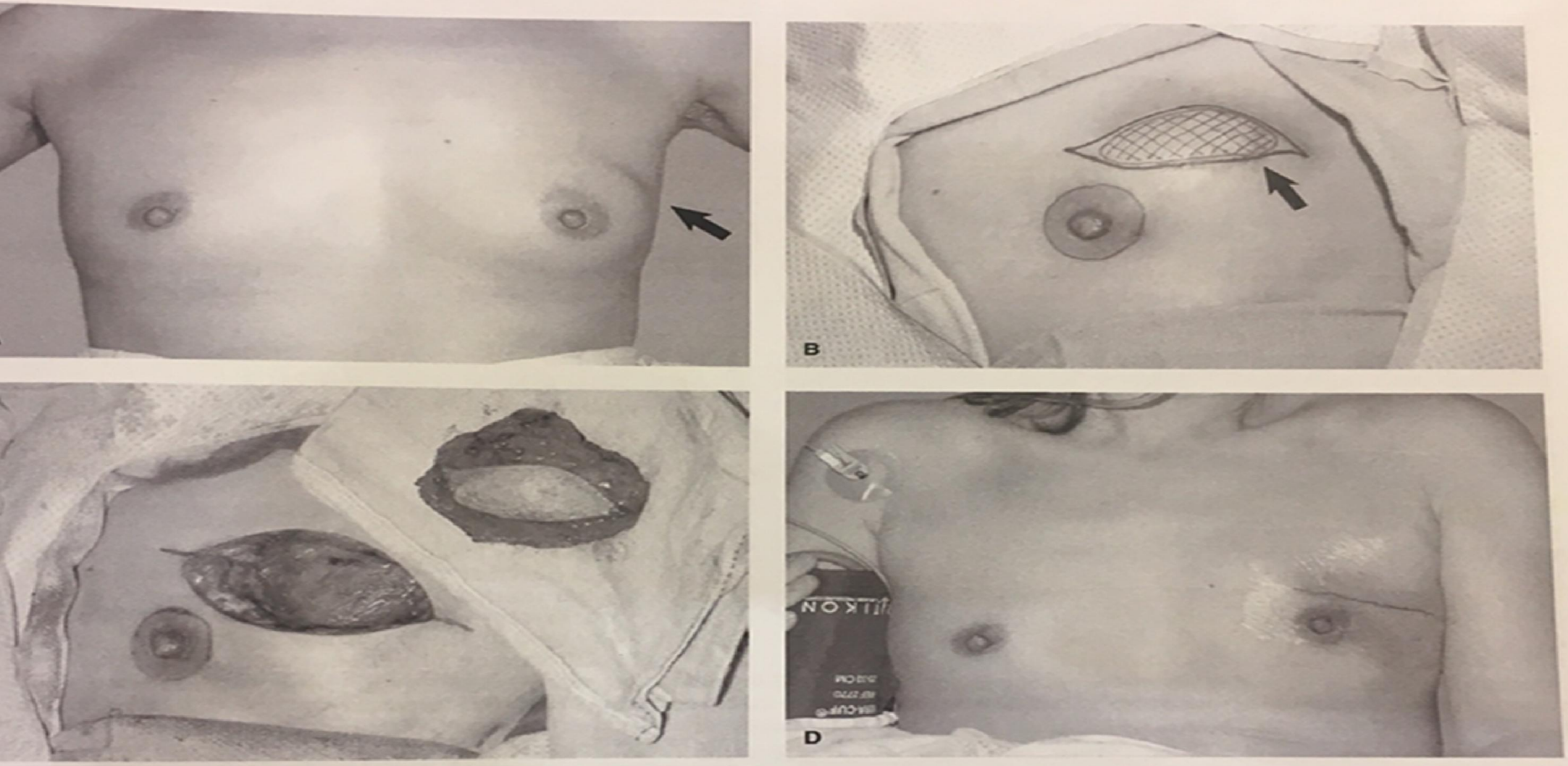


FIGURE 62-5 Presentation and excision of a primary phyllodes tumor. A 44-year-old female presented with a palpable mass in the left upper outer quadrant, which had grown from 2.4 to 5.2 cm over 6 months. Imaging and core needle sampling at first presentation were interpreted as "fibroadenoma." The final pathology on excision was a borderline phyllodes tumor. **(A)** Preoperative presentation with bulging mass apparent on inspection. The mass is located in the upper outer quadrant (*arrow*). **(B)** Operative preparation showing the borders of palpable tumor (*hatch marks*) and planned skin excision (*outer line*), which is located immediately superficial to the mass. **(C)** Operative excision down to level of pectoral fascia. **(D)** Postoperative closure with flap advancement mastopexy closure.

Reexcision Following Narrow Margin excision:

- Approximately 20% of phyllodes tumors recur locally if excised with inadequate margins.
- The proportion of recurrences appears to be somewhat higher with borderline or malignant varieties and lower with benign phyllodes tumors .

- with lumpectomy, special approaches may be necessary, particularly when a phyllodes tumor develops in a smaller breast. Tunneling through the fibroglandular tissue from a periareolar incision is contraindicated with phyllodes tumor excisions because of the potential for tumor seeding.

- Full thickness excisions from skin to chest wall muscle can be very helpful in achieving the 1 cm desired surgical margins.

- This approach allows en bloc removal of skin, tumor, and surrounding fibroglandular tissue in an oncoplastic fashion .

- Routine axillary dissection is unnecessary in patients with phyllodes tumors .

- While axillary nodes are palpable in 20% of cases, fewer than 5% will actually have histological nodal involvement .
- If suspicious lymph nodes are identified clinically or on imaging studies, directed axillary ultrasound with fine needle aspiration or, preferably, core needle sampling can be performed.

- If this work-up is nevgatie, sentinel lymph node biopsy can be considered if there is still reason to believe that the axillary nodes are involved.

- In the absence of such suspicion, neither sentinel node biopsy nor axillary node dissection are considered standard care in the surgical management of the clinically node-negative patient with phyllodes tumors.

Adjuvant Radiation Therapy :

- the role of radiation therapy for phyllodes tumors remains unclear, with the majority of data derived from single-institution retrospective studies .
- For benign phyllodes tumors managed conservatively with surgery alone, adjuvant radiotherapy appears unnecessary when adequate margins are achieved.
- Similarly, most authors show that treatment of borderline and malignant phyllodes tumors with mastectomy alone yields excellent local control rates .

- with lumpectomy alone, local control rates appear worse for borderline and malignant phyllodes patients
- One study endorsed the use of adjuvant radiotherapy after breast conserving surgery for borderline or malignant phyllodes tumors larger than 3 cm : with local recurrence rates of 45% with conservative surgery alone , while another demonstrated the benefits of post lumpectomy radiotherapy in the treatment of malignant phyllodes tumors with a local failure rate as low as 12% .

- Adjuvant radiation therapy may be considered appropriate treatment for selected locally recurrent phyllodes tumors, such as following mastectomy.

Adjuvant endocrine Therapy :

- Phyllodes tumors variably express steroid receptors, but there is no known value to adjuvant endocrine therapy with tamoxifen or aromatase inhibitor.

RECURRENCE AND PROGNOSIS :

- Recurrence of phyllodes tumors is possible for all lesions with recurrence rates as high as 46%.
- surgical margins remain the best predictor of local recurrence.

- full thickness soft tissue excision from skin to rib cage may be necessary to achieve 1 cm margins .
- Soft tissue advancement flap closure is typically necessary to close the defect and, in some cases, skin grafting or more complex reconstructive approaches are needed.

- MANAGEMENT SUMMARY:
- • Suspicion of phyllodes tumor is typically based upon clinical criteria including older patient age, rapid growth, or large tumor size.
- Mammogram and ultrasound evaluation are advised.
- core needle sampling is the preferred modality.
- Surgical management consists of excision to achieve widely negative surgical margins to decrease the likelihood of local breast recurrence.
- The majority of studies indicate a margin of more than 1 cm is preferable, with some actually advocating for more than 2 cm.

- When phyllodes tumors are excised with positive or close margins, reexcision should be performed.
- • The role of adjuvant radiation is controversial, with some studies indicating improved local control but no increased survival when used in patients with borderline or malignant tumors.
- • Locally recurrent tumors may warrant adjuvant chest wall radiation following reexcision.