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Review

Rare breast tumors: Review of the literature

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ABSTRACT

Breast cancer tumors have different morphological phenotypes and specific histopathological types with particular prognostic and clinical characteristics. The treatment of rare malignant lesions is frequently controversial due to the absence of trials to determine the optimal managements. This review describes the spectrum of rare breast tumors indicating the clinical, epidemiological and treatment characteristics.

1. Background

Breast cancer is the most common cause of death from cancer in women worldwide. In 2012, an estimated of 100,000 cases of invasive breast cancer were diagnosed in the United States. The histology type is predominantly ductal in 70–80% of all cases followed by invasive lobular carcinoma in 5–15% of patients.[1] These tumors had been studied in randomized trials to determine the optimal treatment approach including surgery, endocrine, and chemo or radiation therapy. In these types of tumors, the therapeutic approach is generally well defined. However, breast tumors exhibit a wide range of morphological phenotypes and rare specific histopathological types (less of 2% of all breast cancer) have particular prognostic or clinical characteristics.[2–4] Because of the rarity of these tumors, there is no consensus regarding optimal treatment and it is difficult to allow large studies to define the optimal adjuvant treatment. Most cases have been treated with standard therapy as there are no data to indicate special protocols. The management of uncommon tumors is often controversial due to the lack of large single-institution studies or randomized trials to define optimal treatment. In this article, we describe the spectrum of rare breast tumors indicating the clinical, epidemiological and treatment characteristics.[2]

Including all the histological types, Ellis et al.[5] compared 10-year survival in 1621 cases of primary breast cancer. Ductal carcinoma *in situ*, cribriform and tubular carcinoma presented excellent prognoses, with 10-year survival rates of 92%, 91% and 90%, respectively, compared to 80% for mucinous carcinoma, 51% for medullary carcinoma, 54% for lobular carcinoma and 47% for invasive ductal carcinoma. Table 1 summarizes the main rare breast cancer classified in epithelial and non-epithelial breast tumors. Additionally, Table 2 shows the main characteristics of rare breast cancers.

2. Rare epithelial breast cancers

2.1. *Pure tubular carcinoma*

Pure tubular carcinoma is a very rare breast cancer that accounts for less than 2% of invasive breast cancers in most

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Table 1 – Rare breast cancer classified in epithelial and non-epithelial breast tumors.

Rare epithelial breast cancer
Tubular carcinoma
Invasive cribriform carcinoma
Mucinous carcinoma
Invasive solid papillary carcinoma
Apocrine carcinoma
Neuroendocrine tumors
Medullary carcinoma
Secretory breast carcinoma
Adenoid cystic carcinoma
Acinic cell carcinoma
Metaplastic carcinoma
Glycogen-rich clear-cell carcinoma
Oncocytic carcinoma (malignant oncocytoma)
Sebaceous carcinoma
Primary squamous cell carcinoma
Pleomorphic variant of lobular carcinoma
Papillary Carcinoma of the Breast
Rare non-epithelial breast cancer
Sarcomas
Phylloides tumor
Lymphomas

clinical series. This specific histological type is more likely to occur in older patients, and it is characterized by small size (the majority are less than 1 cm), and less nodal involvement.[6] This tumor is nearly always estrogen (ER) and progesterone receptor (PR)-positive, well-differentiated, and mostly human epidermal growth factor receptor type 2 (HER2)-negative. Patients with pure tubular carcinoma have an excellent prognosis compared with invasive ductal carcinoma with low ipsilateral recurrence rates. Therapy is based on radiation treatment after breast conserving surgery.[7] The effect of adjuvant radiotherapy reducing local failure following breast conservative surgery has been described in the literature.[6] Due to the excellent survival rate of patients with breast tubular cancer, the need of axillary staging in these patients is questionable.[6] However, the incidence of axillary metastases may range from 4% to 17%.[4,8] Thus, the use of sentinel lymph node biopsy (SLNB) should be considered for patients with tubular carcinoma if the positive biopsy finding will modify adjuvant treatment.[2] However, the survival of patients with tubular carcinoma is similar to that of the general population, and there is no evidence that adjuvant therapy due to positive SLNB influences survival.[6]

2.2. *Invasive cribriform carcinoma*

Breast invasive cribriform carcinoma (ICC) is a rare tumor reported to range from 0.3% to 3.5% of all breast cancers. The new definition of the World Health Organization (WHO) describes pure ICC as a carcinoma with infiltrating components presenting more than 90% of cells of invasive cribriform pattern.[9] The tumor may present as a frequently occult mass, difficult for radiological detecting. For this reason, the lesions are usually large at presentation although they grow slowly. ER and PR expression is common in these tumors. Prognosis of ICC is excellent, approaching that of the general population mainly in pure ICC tumors.[10] At present, distant metastasis of pure ICC has rarely been reported. Treatment guidelines are extrapolated from other breast cancers without clear validation.

2.3. *Mucinous carcinoma*

This rare tumor accounts for 1–4% of breast tumors and is characterized by a better prognosis than infiltrative ductal cancer.[11] This breast type is characterized by production of abundant extracellular and/or intracellular mucin. Pure and mixed variants of mucinous carcinoma have been described. The pure type consists of tumor tissue with extracellular mucin production (90% purity), while the 'mixed' form of mucinous carcinoma (50–90% purity) also contains infiltrating ductal epithelial component without mucin.[12] The pure type shows a better differentiation with low grade and expression of ER (to 94%) and PR (80%) and the majority of cases. Compared to infiltrating ductal carcinoma, mucin tumors are smaller and present less nodal involvement.[2]

The diagnosis age ranges from 25 to 85 years, with a median age at diagnosis of 71 years in a large retrospective review of 11,400 breast cancer cases.[2] Clinically, mucinous carcinoma manifests as a palpable lump, with a mammographic appearance of well-defined and lobulated lesion. Due to the benign course, a late diagnosis does not worsen the clinical outcome.[13] This benign pattern is confirmed in a large retrospective series that shows that 10-year survival is more than 90%.[2] Only 3–15% of the pure variety of mucinous carcinomas show axillary node metastases compared to 33–46% of the mixed type.[8] This involvement is a marker of poor prognosis. However the incidence of nodal involvement is less that 5% in mucinous tumor of $\leq$1 cm of diameter. Thus, some authors recommend that axillary node staging is not beneficial in tumors measuring less of 1 cm.[8] Nevertheless, SLNB should be considered also in these cases because positive nodal status seems to be the most important factor associated with worse prognosis. Patients with pure mucinous carcinomas without skin invasion are candidates for a breast-conserving therapy. Concerning the systemic adjuvant therapy, there are no consensus, thus the treatment is based on classical breast cancer strategies.[2]

2.4. *Solid papillary carcinoma*

Solid papillary carcinomas of the breast are rare tumors (to 1.7% of all breast cancers), characterized by round, well-defined nodules composed of low-grade ductal cells separated by fibrovascular cores. Pathologically, solid papillary carcinomas exhibit low-grade features, and the tumors often display neuroendocrine and mucinous differentiation.[14] ER and PR are generally positives and her2 negative. Clinically, these tumors present as a palpable, centrally located mass or as bloody nipple discharge and affects older women (mean age 66 years). The most common mammographic appearance of a papillary tumor is as a soft-tissue mass, with calcification present in less than half of cases.[15] The treatment for solid papillary carcinomas is based on surgical excision. When invasive carcinoma is not present, the prognosis is excellent.[14] There are limited studies focused solely on treatment strategies for papillary carcinoma. The absence of definitive guidelines for

Table 2 – Main characteristics of rare breast cancers.

Type tumor	%[a]	Main histological characteristics	ER	EP	HER2	Clinical features	Nodal invasion	Prognosis
Pure tubular carcinoma	2	Haphazardly arranged, infiltrative ducts well formed, uniform in size, and separated by abundant desmoplastic fibrous stroma	+	+	–	Small size mass	Low (4–17%)	Excellent
Invasive cribriform carcinoma	0.3–3	Infiltrating components presenting more of 90% of predominantly arranged in a sieve-like or cribriform growth pattern	+ (96%)	+ (86%)	– (98%)	Frequently clinically occult	Low	Excellent
Mucinous	1–4	Abundant production of extracellular and/or intracellular mucin	+ (96%)	+ (80%)	–	A palpable lump, with a mammographic appearance of well-defined and lobulated lesion	Low (3–15%)	Benign pattern, 10-year survival > 90%
Solid papillary	1.7	Round, well-defined nodules composed of low-grade ductal cells separated by fibrovascular cores. It presents low-grade features, with neuroendocrine and mucinous differentiation	+	NA	NA	Palpable, centrally located mass or as bloody nipple discharge and affects older women	Low (13%)	Excellent
Apocrine	0.3–4	Apocrine cells show large round nuclei and plump, eosinophilic, granular and sharp-bordered cytoplasm.	–	–	+	Small size mass	Low	Favorable
Neuroendocrine	0.1	Neuroendocrine markers (mainly chromogranin or synaptophysine) in more than 50% of cells.	+	+	–	Undistinguished from other breast cancer types	Low	Uncertain
Medullary	5	Solid sheets within an indistinct cell border (syncytial growth pattern), large vesicular nuclei and prominent nucleoli, a broad pushing margin, and an important lymphocytic infiltrate both at the periphery and within the tumor	–	–	–	Well delineated and soft on palpation	Low (16–21%)	Favorable
Secretory	Rare	Histologically, it belongs to the phenotypic spectrum of basal-like breast carcinomas, with intracellular and extracellular secretory material	–	–	–	Painless and firm mass	Low	Indolent course
Adenoid cystic	0.1	Cribriform, tubular or solid cells	–	–	–	Unilateral, small breast lump	Low (2%)	Favorable

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; NA, not available.
[a] Percentage of all breast cancers.

management underscores the need for further treatment and outcome-related studies related to papillary carcinoma.

2.5. *Apocrine carcinoma*

Reported frequency of apocrine carcinoma in breast cancer ranges from 0.3% to 4% of all breast cancer patients,[16] due probably to pathologist observations. Apocrine breast carcinoma is a microscopically defined type of invasive ductal carcinoma.[16,17] Clinically, apocrine carcinomas usually present with palpable mass, tend to be unilateral but are frequently multifocal/multicentric. Histologically, the apocrine cells show large round nuclei and plump, eosinophilic, granular and sharp-bordered cytoplasm. The tumor expresses mainly androgen receptor (AR), while ER and PR are absent.[17] On the other hand, over-expression of HER2 is frequently seen.[16] This type of tumor shows a favorable prognosis.[18] Also for the apocrine HER2 negative cancer, a better outcome is suggested compared with triple negative non apocrine cancer due to a lower proliferation rate. There are not treatment recommendations. Hormone therapy targeted against AR may be applicable. For the triple negative apocrine, chemotherapy should be chosen.[16]

2.6. *Neuroendocrine tumors*

Breast localization of neuroendocrine tumors is rare. It represents less than 0.1% of all breast cancers and less than 1% of all neuroendocrine tumors.[19] They are characterized by neuroendocrine markers (mainly chromogranin or synaptophysine) in more than 50% of cells according to the OMS classification.[20,21] Clinical presentation is undistinguished from other breast cancer types, with a palpable mass, well-defined by imaging studies.[22] HER2 expression is generally negative, while hormone-receptors are positive. Treatment is based on surgery, with the same indications for chemotherapy and radiotherapy as for other breast cancers. Prognosis is uncertain due to the reduced number of tumors.

2.7. *Medullary carcinoma*

The medullary cancer is a relatively infrequent histological form of invasive breast cancer representing approximately 5% of all types.[6] These tumor may be defined as classical (present in the entire lesion),[23] or atypical tumor if a less lymphocytic infiltrate is present.[24,25] In this type of mutation-associated tumors, the presence of medullary or atypical medullary carcinoma is associated with favorable prognosis in this specific setting. Patients with medullary carcinoma are generally younger at the time of diagnosis than patients with infiltrating ductal carcinoma. The mean age of the women ranges from 45 to 52 years.[2] Clinically, the tumor is well delineated and soft on palpation. ER and HER2 are generally negative, and p53 mutations are positive.[2] Prognosis in medullary carcinomas is more favorable compared with infiltrating ductal carcinoma.[26] The incidence of lymph node compromise is low (from 16% to 21%) compared to other breast cancers.[2] BCRA 1 tumors with high tumor grade, hormone receptor negativity and somatic p53 mutation are characterized by a worse prognosis.[25] Axillary nodal staging and adjuvant radiotherapy following breast conserving surgery are indicated in these patients.

2.8. *Secretory breast carcinoma*

Secretory carcinoma of the breast is a rare breast cancer accounting for less than 0.15% of all breast cancers; it is associated with incidence at a young age and an indolent course. Histologically, secretory breast carcinoma belongs to the phenotypic spectrum of basal-like breast carcinomas, characterized by the presence of intracellular and extracellular secretory material. A painless and firm mass is the predominant form of clinical presentation. Most cases are negative for ER, PR and HER2. A basal-like marker (epidermal growth factor receptor is found in around 90% of cases. The reported incidence rate of axillary lymph node metastasis of secretory breast carcinoma is 15–30%. Studies have shown that lymph node metastasis is rare in children and teenagers.[27] Sentinel lymph node biopsy has proven to be a useful evaluation method for the lymph node status of secretory breast carcinoma. There is no consensus on this tumor. Most children and adults have been treated by surgical excision techniques ranging from local resection to radical mastectomy. The real value of postoperative radiotherapy and chemotherapy has not been examined. This tumor is associated with good long-term survival.

2.9. *Adenoid cystic carcinoma*

Adenoid cystic carcinoma (ACC) of the breast is a very rare tumor that is responsible for less than 0.1% of all breast cancers.[28] ACC of the breast may be histologically classified as cribriform, tubular or solid. The cribriform type is the most symptomatic and most frequently presented. ACC affects women with mean age of 50–65 years.[29] This tumor presents as unilateral, small breast lump of 2 to 3 cm in diameter. ER, PR and HER2 expression are mostly negative.[28] The prognosis of ACC is favorable, with uncommon lymph nodes invasion of distant metastases. Axillary nodal involvement is reported in between 0.8% and 2% of ACC cases and distant metastases (mainly pulmonary metastases) are present in up to 9% of cases.[28,30,31] A better prognosis is observed in patients with negative hormone receptor expression. The treatment is based on surgical and adjuvant radiotherapy. The surgical treatment ranges from local excision to radical mastectomy.[28,30] The role of radiotherapy has been evaluated after surgery. The series by Khanfir et al.[28] shows the results of radiotherapy in 40 ACC patients treated surgically (35 after lumpectomy, 5 after mastectomy). In the conservative group, radiotherapy improved 5-year loco-regional control from 83% to 95% ($p = 0.03$) to warrant a conclusion that breast-conserving surgery followed by adjuvant radiotherapy is the treatment of choice for patients with ACC breast cancer.[28]

According to the pathological grading from I to III (defined by the proportion of solid growth elements), the proposed treatment is lumpectomy for grade I, simple mastectomy for grade II tumors and mastectomy with axillary clearance for grade III tumors.[29] Radical mastectomy is not advised due to the low incidence of nodal metastasis. Concerning

adjuvant chemotherapy, endocrine or biological therapies for ACC, there are few studies, and their use is not recommended.

2.10. *Acinic cell carcinoma*

Acinic cell carcinoma of the breast with features of acinar-type differentiation was first described by Roncaroli et al.[32] in 1996 as the breast counterpart of identical tumors of the parotid gland. It is a very rare tumor. After this first description, approximately eighteen cases of acinar cell-like breast carcinoma have been reported.[33,34] In image, a well-defined mass is observed and mean-age at presentation reported in the literature is 56 years.[35,36] Pathological findings are diffuse infiltrative growth patterns of small glandular structures composed of cells with a coarse granular or clear cytoplasm resembling acinar cells of the salivary glands. ER, RP and HER2 are regularly negative. Although considered as a tumor of good prognosis, systemic and local recurrence are described.[1,35,36] In view of the small number of cases and short follow-up period, there is no treatment consensus.

2.11. *Metaplastic carcinoma*

Metaplastic breast carcinoma (MBC) is a rare malignancy characterized by histologic presence of two or more cellular types, commonly a mixture of malignant epithelial and mesenchymal components (sarcoma type).[37,38] MBC represents 0.25–1% of breast cancers diagnosed annually.[37] In comparison to classical breast adenocarcinomas, tumor size is usually greater. Median size of the tumor was reported to be in the range of 3.4–5.0 cm in some series.[39–42] The incidence of axillary lymph node involvement is less in MBC cases.[40,43] The median age of MBC patients was over 50 years of age in the literature.[39,41,44] Hormone and HER2 receptor positivity rates are also lower (0–26% for hormone receptors).[37] These tumors have a poor prognosis due to the high metastatic and recurrence potential. Concerning the treatment options, classical surgery techniques such as radical mastectomy and modified radical mastectomy, including axillary dissection, are the preferred surgery choices in the literature.[1,37,41] In routine clinical practice, there is no standard treatment regimen specific for MBC or its subgroups, so clinical practice guidelines for invasive breast adenocarcinoma is mostly used instead.[37]

2.12. *Pleomorphic variant of lobular carcinoma (PLC)*

This tumor represents a rare variant of invasive lobular carcinoma, accounting only for 0.97% of all breast carcinomas and less than 5% of lobular carcinomas.[45] Histology is characterized by eosinophilic cytoplasma and large pleomorphic hypercromatin nuclei. The mean age at presentation is 58.9 years (range from 24 to 94 years) with multifocal and bilateral localization.[45,46] The tumor presents higher Ki67 index, low ER and PR expression and high HER2 amplification. This tumor has an aggressive clinical course and poor prognosis. The treatment strategy is similar to that in other invasive lobular carcinomas.

2.13. *Papillary carcinoma of the breast*

Papillary breast cancer accounts for 0.5% of all invasive breast cancers. The tumor is characterized by proliferative cells arranged around fibrovascular cores, forming a circumscribed mass.[47] Papillary breast cancer includes different histological types: ductal carcinoma *in situ* arising in an intraductal papilloma, papillary ductal carcinoma *in situ*, encapsulated papillary carcinoma, solid and invasive papillary carcinoma. The benign intraductal papillomas present a myoepithelial cell layer within the papillae, which is different from malignant papillary proliferation that lacks this layer. Clinically, papillary breast tumors are manifested with bloody nipple discharge, abnormal mass or mammographic abnormalities.[48] The ER and PR are usually positive and HER2 negative. The tumor has a good prognosis. A new treatment approach is not described in the literature at this moment.

3. Rare non-epithelial breast cancer

3.1. *Sarcomas*

Sarcomas of the breast are a rare group of diverse mesenchymal tumors accounting for less than 1% of all breast tumors. Several histological types including fibrosarcoma, malignant fibrous histiocytoma, liposarcoma, rhabdomyosarcoma, leiomyosarcoma, hemangiosarcoma, malignant schwannoma, osteogenic sarcoma and chondrosarcoma have been described.[49] The tumor occurs in the fifth and sixth decades of life and clinically presents as a painless breast lump.[50] The size of tumor may range from less than 1 cm to more than 40 cm. The prognosis of primary breast sarcomas depends on the size and the histological grade. The tumors may spread by direct of hematogenous invasion.[51,52] However, axillary nodal involvement is rare.[50,53]

Treatment is based on a multidisciplinary approach including surgery, radiation and chemotherapy. In a small retrospective series of the National Cancer Institute, the role of the adjuvant radiotherapy to treat patients with high-grade non-metastastatic primary sarcoma was evaluated. In this study, the prognosis of breast sarcoma was similar to that of extremity, after 99 months of follow-up. When radiotherapy was added, excellent control was achieved. In the next section, some of the histological types of primary breast sarcomas are described.

a. **Primary breast fibrosarcoma** is a rare neoplasm with not established incidence. Clinically, this tumor presents as a lump that may be painful in one-third of cases.
b. **Primary leiomyosarcoma of the breast:** This tumor is a rare neoplasm, with less than 20 reported cases in the medical literature.[52] This tumor resembles clinically a malignant phyllodes tumor, with a firm lobulated mass. Surgery is the main approach to treatment. Because leiomyosarcoma often invades peripheral tissues, such as the skin and fascia, curative surgery requires a wide resection. The axillary block dissection is usually not recommended, since none of the reported cases have shown nodal metastases.[52] Metastatic spreading usually occurs *via* the hematogenous

Table 3 – Adjuvant therapy for rare breast tumors.

Histologic type	Radiotherapy	Chemotherapy	Endocrine therapy[b]
Tubular carcinoma	Useful	Useful[a]	Useful
Invasive cribriform carcinoma	Useful	Useful[a]	Useful
Mucinous carcinoma	Useful	Useful[a]	Useful
Invasive solid papillary	Useful	Useful[a]	Useful
Apocrine carcinoma	Useful	Useful	Useful[c]
Neuroendocrine tumors	Useful	Useful[a]	Useful
Medullary carcinoma[d]	Useful	Useful[a]	Useful
Secretory breast carcinoma[d]	Useful	Useful[a]	Useful
Adenoid cystic carcinoma[d]	Useful	Useful[a]	Useful
Acinic cell carcinoma[d]	Useful	Useful[a]	Useful
Metaplastic carcinoma[d]	Useful	Useful	Useful
Pleomorphic variant of lobular carcinoma[d]	Useful	Useful	Useful
Papillary carcinoma	Useful	Useful[a]	Useful
Sarcoma	Useful	Useful	Not applicable
Phylloides tumor	Useful	Useful	Not applicable
Lymphoma	Useful	Useful	Not applicable

[a] Chemotherapy may not be needed.
[b] For hormone-receptor-positive breast cancers.
[c] Androgen receptor as a targeted therapy.
[d] Mostly hormone receptor negative.

route. The benefits of chemotherapy and radiotherapy have not been confirmed yet.[53] Compared to other breast sarcomas, the prognosis of leiomyosarcoma is better. However, long-term follow-up is recommended because local recurrence and distant metastases may appear up to 20 years.[52]

3.1.1. *Primary breast lymphoma*

The primary breast lymphoma (PBL) is a malignant lymphoma primarily occurring in the breast in the absence of previously detected lymphoma in other localizations. It accounts for less than 0.5% of all malignant lymphomas.[54] B-cell lymphoma is more frequently observed than T-cell lymphoma in the breast. Histologies like, follicular non-Hodgkin's lymphoma or extranodal marginal zone (MALT) lymphoma occur less commonly.[55] The usual clinical feature of breast lymphoma is a rapidly expanding, painless mass.[54] The differentiation between primary and secondary lymphoma is difficult, and some criteria are used to determine the primary localization of breast lymphoma:

1. The availability of adequate pathology material.
2. Both mammary tissue and lymphomatous infiltrate are present.
3. No widespread disease or preceding extramammary lymphoma.
4. Ipsilateral axillary node involvement is considered acceptable.[56]

Treatment options include surgery, chemotherapy and radiation therapy. There is no agreement on the appropriate treatment. Recommendation of chemotherapy for bulky or stage II disease are founded in the literature. Radiotherapy can be used to provide local control or may be adjuvant to chemotherapy.[54] Clinical series show that overall 5-year survival of 53%. Factors influencing a better prognosis are: early stage, conservative surgery, radiotherapy, and combined modality.[57]

3.1.2. *Phyllodes tumor*

Phyllodes tumors account for less than 1% of all primary breast neoplasms. These tumors are biphasic neoplasms, basically analogous to fibroadenomas, composed of stromal and epithelial elements. Phyllodes tumors exist in benign (35–64%), borderline, and malignant subtypes, although there is no uniform agreement on the criteria for assigning a subtype or for predicting biological behavior.[4] A subtype of phyllodes tumors appears to be less important for the risk of recurrence than does the margin of tumor-free resection achieved by surgical treatment. Phyllodes tumors are usually benign, but recurrences are not uncommon, and a relatively small number of patients will develop hamatogenous metastases.

Generally, phyllodes tumor presents as a rapidly growing and clinically benign breast lump in females within the 4th or 5th decade of life.[57] Diagnosis of phyllodes tumor prior to excisional biopsy/lumpectomy is uncommon. Phyllodes tumors often appear on ultrasound and mammography as fibroadenomas, and core needle biopsy seems inadequate to reliably distinguish phyllodes tumor from fibroadenoma.[4] Local recurrences of phyllodes tumors are the most common site of recurrence. Positive margins, fibroproliferation in the surrounding breast tissue, and necrosis are associated with a marked increase in local recurrence rates. Most distant recurrences occur in the lung, and may be solid nodules or thin-walled cavities. Patients with stromal overgrowth, particularly with tumor size >5 cm, have shown a high rate of distant failure. Death from phyllodes tumor is rare (2%), and only phyllodes tumors that demonstrate uniformly aggressive pathologic features seem to be associated with mortality. Wide local excision with tumor-free margins of 1 cm or greater is the preferred surgical therapy for patients with phyllodes tumors regardless of the histological subtype. Total mastectomy is necessary only if negative margins cannot be obtained by breast conserving surgery.[58,59] Since phyllodes tumors rarely metastasize to the axillary lymph nodes (10–15%), surgical axillary staging is not necessary unless the lymph nodes are

pathologic on clinical examination.[59] The role of adjuvant radiotherapy is uncertain and requires further investigation.[57] There are only few reported successful treatments with post-operative irradiation in malignant phyllodes tumors,[4] its role remaining undefined because of the rarity of the condition. A prospective clinical trial, 'Phase II study of adjuvant radiotherapy after resection in patients with borderline or malignant phyllodes tumors of the breast', was initiated by the American National Cancer Institute in 1998.[2] A total of 50 patients should have been accrued for this study within 6–7 years; however, the study is still active for recruitment. While the epithelial component of most phyllodes tumors contains ER (58%) and/or PR (75%), endocrine therapy has no proven role in the treatment of phyllodes tumors. Similarly, there is no evidence that adjuvant cytotoxic chemotherapy provides a benefit in reducing recurrences or death. In those patients who experience a local recurrence, resection of the recurrence with wide tumor-free surgical margins should be performed. Some members of the NCCN Panel recommend local radiation therapy following resection of a local recurrence, but this recommendation is controversial. The German panel discussed chemotherapy and radiotherapy as an option after R1 resection for local recurrence but gave no general recommendation for these therapies.

In summary, despite a less aggressive treatment, the survival for the described favorable histological subtypes appears to be very high, even comparable with that of women without breast cancer. After adjustment for age, stage, and grade, patients with tubular, mucinous, and medullary carcinoma, or malignant phyllodes tumors exhibited such a low risk of death that in some cases even less aggressive treatment should be considered. Because of the rarity of these tumors, the treatment recommendations have been extrapolated from common breast tumors (Table 3). Patients with these specific histological types should be informed of this relatively favorable prognosis.[2]

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