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Management of Phyllodes Breast Tumors

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■ **Abstract:** Phyllodes tumors are a rare distinctive fibroepithelial tumors of the breast and their management continues to be questioned. The aim of our study was to examine the treatment and outcome of 165 patients with phyllodes tumors and to review the options for surgical management. This is a retrospective study of 165 patients who presented to the Institut Curie between January 1994 and November 2008 for benign, borderline or malignant phyllodes tumors. The median follow-up was 12.65 months [range 0–149.8]. The median age at diagnosis was 44 years [range 17–79]. One hundred and sixty patients (97%) had breast-conserving treatment, of whom 3 patients (1.8%) had oncoplastic breast surgery. Younger women had a significantly higher chance of having a benign phyllodes tumor ($p = 0.0001$) or a tumor of small size ($p < 0.0001$). Histologic examination showed 114 benign (69%), 37 borderline (22%) and 14 malignant tumors (9%). The median tumor size was 30 mm [range 5–150]. The tumor margins were considered incomplete (<10 mm) in 46 out of 165 cases (28%) with 52% revision surgery. Only the tumor grade was a significant risk factor for incomplete tumor margins ($p = 0.005$). Fifteen patients developed local recurrence (10%) and two, metastases. In univariate analysis, the histologic grade ($p = 0.008$), and tumor size ($p = 0.02$) were significative risk factors for local recurrence with an accentuated risk for "borderline" tumors and tumors of large size.).Similar results were obtained using multivariate analysis ($p = 0.07$). The mainstay of treatment for phyllodes tumors remains excision with a safe surgical margin, taking advantage breast conserving surgery where amenable. For borderline or malignant phyllodes tumors or in cases of local tumor recurrence, mastectomy, and immediate breast reconstruction may become the preferred option. Genetic analysis will potentially supplement classical histologic examination in order to improve our management of these tumors. The role of adjuvant treatments is unproven and must be considered on a case-by-case basis. ■

Key Words: breast cancer, oncoplastic surgery, phyllode

INTRODUCTION

Phyllodes tumors are fibroepithelial tumors of the breast, which represent 2–3% of all fibroepithelial breast tumors (1) and less than 1% of all breast tumors (2). They most commonly affect women from 35 to 55 years of age, and very few cases have been reported in men (3–6).

Phyllodes tumors are classified as benign, borderline, or malignant based on the presence of cellular atypia, mitotic activity, and overgrowth in the stroma (7).

Irrespective of tumor grade, the standard treatment of phyllodes tumors is surgical excision with a clear margin, preferably more than 1 cm, to achieve definitive local control (2,8–10). Provided a safe margin is maintained both tumourectomy and mastectomy provide good control with low recurrence rates. But, because phyllodes tumors look like fibroadenomas both on clinical presentation, imaging, and in tissue sampling, most phyllodes tumors are still not diagnosed preoperatively. As a result, most phyllodes tumors are surgically enucleated at initial intervention, resulting in inadequate surgical margins.

In general, surgical treatment alone is adequate (11,12). Some units have proposed adjuvant chemo and radiotherapy in certain cases (recurrent phyllodes after mastectomy, stromal overgrowth) but the role of adjuvant treatments is not yet clear (11–13). The aim of our study is to examine the management and outcome of 165 patients with phyllodes tumors, and to determine factors that correlate with local control (type of surgical excision and margins). Also, we will

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show the absence of benefits of adjuvant therapy in the management of any phyllode tumors.

PATIENTS AND METHODS

Medical records of 165 patients who presented at the Institut Curie with phyllodes tumors between January 1994 and November 2008 were reviewed. All patients had their initial surgical management at the Institut Curie and none had prior chemo or radiotherapy.

Pathologic analysis of hematoxylin eosin safran (HES) stained slides was performed according to the WHO classification of breast tumors (7). Phyllodes tumors are biphasic (combined epithelial and stromal elements) and histologic analysis commented specifically on the stromal component of the tumors, the degree of stromal hyperplasia, stromal cellularity, nuclear pleomorphism, the number of mitoses per 10 high power fields, and the state of the tumor margins (whether microscopically involved or uninvolved). As per WHO criteria (7) the tumors were classified into benign, borderline, or malignant. In our unit the excision margins are considered sound when they are greater than 10 mm.

For each patient we recorded the age at diagnosis, preoperative cytology, or biopsy, the type of surgery – either breast conservation surgery (with or without oncoplastic techniques), or mastectomy (with or without reconstruction), histologic characteristics (size, grade, margins), adjuvant treatments, and outcome (local recurrence, metastasis). The results were then compared to those in the literature.

When delivered, adjuvant chemotherapy consisted of ifosfamide (4300 mg) and Adriamycin (100 mg) in combination for six cycles.

When delivered, adjuvant radiotherapy consisted of parietal irradiation alone after mastectomy (45–50 gy) and whole breast irradiation with a boost to the tumor bed after breast conservation therapy.

Continuous variables were tested using a *t*-test. Discrete variables were compared using a chi-squared test or using Fisher's exact test. Survival analysis was generated using Cox's proportional hazards model. Survival curves were compared using a logrank test. The variables were initially tested using a univariate analysis model. Only significant variables ($p < 0.05$) or variables of particular clinical or pathologic interest were analyzed using multivariate analysis. All statistical analyses were performed using the R: 7.0 package.

RESULTS

Initial State (Table 1)

The median age at diagnosis was 44 years [range 17–79]. Fifty-nine percent of patients (97/165) had fine-needle aspiration cytology (FNAC), but in 9% of FNACs (9/97) was phyllodes tumor diagnosed. Thirty-three percent (54/165) of patients underwent core biopsy which showed phyllodes tumor in 44% of biopsies (24/54).

Table 1. Summary of Patient Characteristics and Initial Management

Age (years)	44 [17–79]	
Type of surgery		
Breast conserving	157	95%
Breast conserving using oncoplasty	3	1.8%
Mastectomy	2	1.2%
Mastectomy and axillary clearance	3	1.8%
Cytology		
No	65	39%
Yes	97	59%
Adenofibroma/benign	64/97	66%
Cellular atypia requiring surgery	24/97	25%
Phyllodes tumor	9/97	9%
No information	3	2%
Core needle biopsy		
No	108	65%
Yes	54	33%
Adenofibroma/benign	16/54	30%
Cellular atypia requiring surgery	14/54	26%
Phyllodes tumor	24/54	44%
No information	3	5%
Histologic size (mm)	30 [5–150]	
Histologic type		
Benign (I)	114	69%
Borderline (II)	37	22%
Malignant(III)	14	9%
Surgical margin		
Negative (>10 mm)	119	72%
Close or positive (>10 mm)	46	28%
Revision surgery (for positive margins, $n = 46$)		
No	21	46%
Yes	24	52%
Refused	1	2%
Type of revision surgery ($n = 24$)		
Breast conserving surgery	16	66%
Oncoplastic breast conserving surgery	2	8.3%
Mastectomy	3	12.5%
Mastectomy and axillary clearance	1	4.15%
Mastectomy and immediate reconstruction	2	8.3%
Residual tumor after revision surgery ($n = 24$)		
No	20	84%
Yes	4	16%
Adjuvant treatment		
Chemotherapy	4	2.4%
Radiotherapy	1	0.6%
Chemotherapy and radiotherapy	4	2.4%
Follow-up (months)		
Average follow-up	12.65 [0–148.8]	
Average follow-up (recurrence group)	9.06 [0.29–149.8]	
Average follow-up (no recurrence group)	23.58 [0–84.65]	

There was no significant difference between the follow-up for the "recurrence" and the "no recurrence" groups, $p = 0.08$.

Breast-conserving treatment (BCT) was possible in 160 patients (97%), of whom three (1.8%) had oncoplastic surgery. Five patients (3%) had a mastectomy, of whom three had axillary clearance as well. The three patients who had axillary clearance had either malignant (2 cases) or borderline (1 case) tumors, and two of the three patients had very large tumors of 100 and 120 mm respectively. Of the five mastectomy patients, two had immediate breast reconstruction either with a free Transverse Rectus Abdominis Myocutaneous flap (free TRAM) or a Pedicled Latissimus Dorsi Musculocutaneous flap (LD). The remaining three had secondary reconstruction (2 TRAMs and 1 LD) at intervals of 1, 3, and 4 years respectively from their original surgery.

Histologic results were benign for 114 tumors (69%), borderline for 37 tumors (22%), and malignant for 14 patients (9%). The median tumor size was 30 mm [range 5–150]. The malignant tumors tended to be significantly larger ($p = 7.4^{e}–8$) (Fig. 1). The three axillary clearances performed were uninvolved by tumor. The surgical excision margin was considered incomplete (<10 mm) in 46 cases out of 165 (28%). Only the tumor grade appeared to be a risk factor for incomplete surgical margins ($p = 0.004$). On the other hand neither tumor size, nor the age of the patient was related to positive surgical margins (Table 2). Wider excision of the tumor bed was performed in 24 patients out of 46 (52%), usually with breast conserving surgery (75%). Wider excision demonstrated residual tumor in four patients (16%). The 21 patients who did not have wider excision in spite of the involved margins underwent biannual outpatient follow-up. The recurrence rate was no higher in this group.

The eleven patients who had a mastectomy during their initial management (either as primary surgery or as treatment for incomplete margins) had malignant (7/11, 64%), or borderline tumors (4/11, 36%).

Nine patients (5.4%) had an adjuvant treatment composed by chemotherapy, radiotherapy or both (Table 1). All the patient had malignant tumors with a median tumor size measured 66.6 mm [range 30–150]. Nine of 14 women with malignant phyllode tumors (64%) had adjuvant treatment.

Outcome

Of the 154 patients who did not have mastectomy, ninety percent were free of local recurrence at last follow-up, median follow-up being 12.65 months [range 0–149, SD 8]. Fifteen patients (10%) did have a local recurrence (Table 3). There was no significant difference found in duration of follow-up between those who had local recurrence and those who did not (Table 4). The fifteen patient had a surgical treatment of the local recurrence and two (13%) received an adjuvant treatment (radiotherapy and association radiochemotherapy) because of the histologic results (malignant phyllodes tumors).

Forty-seven percent of the local recurrences were benign tumor and 53% borderline tumor. There were significant differences with respect to histologic grade ($p = 0.008$) and to tumor size ($p = 0.02$) when comparing the group of patients who had local recurrence to the group who did not. Six percent of patients with benign tumors in this series developed local recurrence, compared to 25% for borderline. There were no recurrence for malignant tumors, however they had all been treated with mastectomy (Table 4).

Univariate survival analysis showed that tumor size and histologic grade were variables close to reaching significance ($p = 0.07$ and $p = 0.08$ respectively). Similar results were obtained using multivariate analysis ($p = 0.07$) (Table 5). These two factors seem likely therefore to be associated with local recurrence. A second local recurrence was diagnosed in three patients (20%) who were treated by surgery alone.

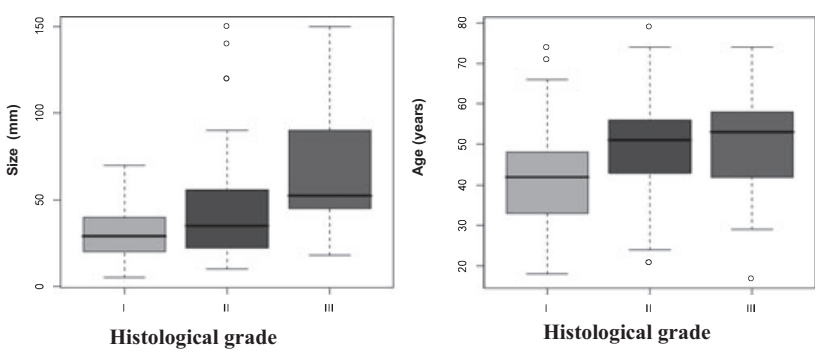


Figure 1. Tumor size and age distribution when grouped according to histologic grade. (Grade I for begnin, grade II for borderline and grade III for malignant phyllode tumor).

Only two patients in the study population developed metastases with pulmonary and bony involvement, and who died of the same. Both had malignant phyllode tumors treated by surgery, chemotherapy, and radiotherapy.

Table 2. Risk Factors Associated With Unsafe Margins

	Safe margins >10 mm		Unsafe margins <10 mm		p-value
Histologic grade					
Grade I	88	74%	26	56%	0.00463
Grade II	26	22%	11	24%	
Grade III	5	4%	9	19%	
Age					
Median age (years)	44 [17–74]		46.5 [22–79]		0.1161
Tumor size					
Median size (mm)	30 [5–150]		35 [10–140]		0.3248

Table 3. Management of Recurrence

Number of patients developing recurrence (n = 154)	15	10%
Surgical management		
Breast conservation treatment	8	53%
Oncoplastic breast conservation	1	6.6%
Mastectomy and immediate reconstruction	4	26.6%
Refused	2	13.3%
Adjuvant treatment		
Radiotherapy	1	6.6%
Radiotherapy and chemotherapy	1	6.6%
Number of patients developing further recurrence (n = 15)	3	20%
Surgical management		
Local excision	1	
Mastectomy and latissimus dorsi reconstruction	1	
Mastectomy and transverse rectus abdominis myocutaneous flap reconstruction	1	

DISCUSSION

Phyllodes tumors of the breast are uncommon tumors, which even more rarely affect men (8,11,14–17). The peak incidence is between 35 and 55 years which is approximately 10 years later than the peak for adenofibroma (11,16,18–28). In our study all the patients were female, the median age at diagnosis was 44 and one-fifth of women were diagnosed under the age of 30. These results are consistent with those in the literature (29–31), and Table 6 summarizes the patient clinical characteristics. One 37 years old woman was pregnant at diagnosis of a malignant phyllode tumor, and only one case of phyllodes tumors during pregnancy is described in the literature (32).

Our study showed that of the 59% patients who underwent FNAC, diagnostic information was provided in only 9%. Thus, the cytologic analysis is in general not reliable, largely as a result of tumor heterogeneity (33,34). Similarly one-third of patients had a core biopsy preoperatively but this provided a positive diagnosis in only 44% of cases (Table 1). The study of Komenaka et al. (35) looking at core needle biopsy as a way of differentiating between adenofibroma and phyllodes tumor showed a strong negative predictive power (93%) as well as a strong positive predictive power (83%) for the technique. The histologic diagnosis of phyllodes tumor relies on a specific cytologic architecture (predominantly cellular contingent to the stroma with a heterogeneous distribution, a large intraluminal component and an unequal distribution of epithelial structure), which explains the difficulty in

Table 4. Risk Factor for Local Recurrence

	No recurrence		Recurrence		
	n	%	n	%	p-value
Tumor grade					
Grade I (n = 114)	107	77	7	47	0.008
Grade II (n = 34)	26	19	8	53	
Grade III (n = 6)	6	4	0	–	
Follow-up					
Median (m) [range]	9.06 [0.29–149.8]		23.58 [0–84,65]		0.08
Age					
Median age (years) [range]	43 [17–79]		48 [24–66]		0.3
Tumor size					
Median size (mm) [range]	30 [5–120]		35 [10–120]		0.02

Table 5. Univariate and Multivariate Survival Analysis Comparing Age, Tumor Size, and Grade

	Univariate analysis	p	Multivariate analysis	p-value
Age	RR = 1 (0.97–1.05)	0.56		
Size	RR = 1.02 (0.99–1.04)	0.07	RR = 1.01 (0.99–1.03)	0.07
Grade	RR = 2.4 (3.36–6.64)	0.08	RR = 2.1 (0.73–6.04)	

RR = relative risk.

obtaining diagnostic tissue by cytology or core biopsy. Only histopathologic examination of the entirety of the excised specimen allows an accurate diagnosis to be made including an evaluation of tumor grade, especially important due to the heterogeneity of these tumors (co-existance of benign, intermediate, and malignant areas within the same tumor).

The treatment of phyllodes tumors (11,18–28) (Table 7) depends fundamentally on surgery to the breast of which the various techniques will be discussed further. Numerous clinical studies recommend wide excision of the tumor with a 10 mm clear margin (8,11,20,28,30,36–38), or mastectomy if breast conservation surgery is not possible. Shelling out of tumors is not adequate, but frequently done because of the similitude with fibroadenomas and the difficulties of preoperative histologic diagnosis (39).

There is however no clear consensus concerning the type of surgery to be performed (conservative or radical), particularly for recurrent, malignant, or borderline tumors. Certain authors have demonstrated better locoregional control (23,26), or improvement in disease free survival (21,26) when comparing mastectomy with BCT. It is generally agreed that benign phyllodes tumors are treated with breast conserving surgery which may or may not involve oncoplastic surgery depending on the breast to tumor ratio (26).

As far as our study was concerned, breast conserving surgery was performed whenever possible. This policy was also demonstrated in the SEER data (Surveillance, Epidemiology, and End Results) by MacDonald (22) involving 821 patients: The specific 5 years survival for mastectomy or breast conserving surgery is comparable, and the factors predictive of improved specific survival were young age and limited surgery.

In our study, the majority of patients initially had breast conserving surgery (97%) and more than a quarter of these had margins less than or equal to 10 mm (46 patients, 28.7%). Additionally the risk of having excision margins that were narrow or unsound was significantly elevated for benign tumors ($p = 0.00463$) (Table 2). This might be explained by the fact that the majority of benign tumors were diagnosed preoperatively as adenofibromas and enucleation of the tumor had therefore been performed. Only half of the patients with unsafe surgical margins had re-excision performed (24 patients, 52%) and only four patients (16%) demonstrated residual tumor at histology. In our study the condition of the excision margins and the decision to perform wider excision did not appear to be significant factors for local recurrence, this fact may be confounded by the lack of sufficient patient numbers. In the literature there is a lot of evidence to suggest that narrow excision margins are associated with local recurrence (26,30). Some studies (11,18–28) (Table 9) shows that in the group of patients with involved excision margins, the percentage of local recurrences is greater than in the group with uninvolved excision margins. Breast conservation surgery is acceptable only when the margins are safe, however the scope of BCS is considerable while using

Table 6. Literature Review, Descriptive Data

Authors	Study period	Patients (*n*)	Age	Size (mm)	Grade I	Grade II	Grade III
A.W Chaney (11)	1944–1998	101	41 (13–76)	60 (15–300)	58% (59)	12% (12)	30% (30)
O. Asoglu (18)	1971–2000	50	46 (14–77)	35 (15–180)	32% (16)	6% (3)	62% (31)
W.H. Chen (19)	1985–2003	172	37 (11–73)	58 (10–300)	76% (131)	7% (12)	17% (29)
F. Sabban (20)	1996–2002	8	33.4 (17–60)	37.5 (2–8)	75% (6)	12.5% (1)	12.5% (1)
J.B. Hassouna (21)	1986–2001	106	39.6 (14–71)	83 (15–250)	58.5% (62)	15% (16)	26.5% (28)
O.K. Macdonald (22)	1983–2002	821	50 (12–92)				100% (821)
A. Fou (23)	1995–2004	27		60 (2–14)			100% (27)
N. Taira (24)	1980–2005	45	45 (28–75)	35 (10–170)	69% (31)	11% (5)	20% (9)
M.S. Lenhard (25)	1984–2005	33	47 (18–77)	96 (14–300)	40% (12)	33% (10)	27% (8)
Y. Belkacemi (26)	1971–2003	443	40 (12–87)		64% (284)	18% (80)	18% (79)
R.D. Pezner (2008) (27)	1964–2005	478	53 (14–100)				100% (478)
T. Bouhafa (28)	1998–2006	53	37.2 (15–67)	102 (10–300)	13% (7)	17% (9)	30% (16)
Current series Guillot et al.	1994–2008	165	44 (17–79)	30 (5–150)	69% (114)	22% (37)	9% (14)

Table 7. Literature Review, Management

Authors	BCT	AC	LN + (*n*)	CT(*n*)	RT(*n*)	Threshold M	M +
A.W Chaney (11)	47% (47)	0	0	7	6		
O. Asoglu (18)	44% (22)	10% (5)	1	2	2	<10 mm	
W.H. Chen (19)	73% (126)	25.5% (44)	0			<5–10 mm	7.5% (13)
F. Sabban (20)	87.5% (7)	0		1	1		
J.B. Hassouna (21)	77% (82)	19% (20)	1				4% (4)
O.K. Macdonald (22)	48% (393)				76		
A. Fou (23)	65% (17)						66.5% (18)
N. Taira (24)	93% (42)						33.5% (15)
M.S.Lenhard (25)	59% (19)	30% (10)	0		1	≤20 mm	75% (25)
Y. Belkacemi (26)	85% (377)	10% (46)	1	13	38	<10 mm	15% (67)
R.D. Pezner (27)	35% (19)						
T. Bouhafa (28)	32%	18%	0	1	16	<1 mm	7.5% (4)
Current series Guillot et al.	97% (160)	2% (3)	0	5	5	<10 mm	28% (46)

BCT, breast-conserving treatment; AC, axillary clearance; LN+, positive lymph nodes; CT, chemotherapy; RT, radiotherapy; threshold M, threshold for inadequate margins; M+, positive margins.

Table 8. Literature Review, Distribution of Local Recurrences When Grouped According to Various Criteria

Authors	LR (*n*)	Age <40 years	T <50 mm	Grade I	Grade II	Grade III	M+	BCT
A.W Chaney (11)	4	50% (2)	25% (1)	75% (3)	0	25% (1)	0	50% (2)
O. Asoglu (18)	16		25% (4)	12.5% (2)	12.5% (2)	75%(12)		50% (8)
W.H. Chen (19)	19	68.5% (13)	68.5% (13)	100% (19)	0	0	30% (6)	100% (19)
F. Sabban (20)	3							
J.B. Hassouna (21)	13			23% (3)	38.5% (5)	38.5% (5)		
O.K. Macdonald (22)								
A. Fou (23)	5						80% (4)	100% (5)
N. Taira (24)	6	33% (2)	67% (4)	50% (3)	0	50% (3)	83% (5)	100% (6)
M.S. Lenhard (25)	8	25% (2)	25% (2)	12.5% (1)	25% (2)	50% (4)	87.5% (7)	75% (6)
Y. Belkacemi (2008) (26)	76			41% (31)	30% (23)	29% (22)		
R.D. Pezner (27)								
T. Bouhafa (28)	10							
Current series Guillot et al.	15			46.5% (7)	53.5% (8)	0		100% (15)

LR, local recurrence; T, tumor size; M+, positive margins; BCT, breast-conserving treatment.

oncoplastic techniques to permit wide tumourectomy while preserving the shape of the breast.

As far as axillary dissection is concerned it is now generally accepted that this is not indicated for phyllode tumors, due to the very low incidence of lymph node involvement (16,26,30,31,40). In a recent multicentred study which included 1035 patients axillary clearance was carried out in 9% of patients, and axillary node involvement was demonstrated in only nine cases (41). In our study none of the three patients who underwent axillary dissection demonstrated axillary lymph node involvement. Selective lymph node dissection may be feasible in cases with macroscopic evidence of lymph node involvement (clinically or radiographically).

The histologic results in our series showed 114 benign tumors (69%), 37 borderline tumors (22%), and 14 malignant tumors (9%). This distribution is comparable to other series in the literature (Table 6) (11,18–28,30,31). Belkacémi et al. (26) demonstrated that histologic grade was a major prognostic factor for local disease control with diminishing risk of local recurrence with begnin grade. Evidence from other authors supports this trend for better disease control with begnin tumors (39,42). We have demonstrated that patients with borderline phyllodes tumors have a much greater risk of local recurrence than patients with benign phyllodes tumors. Paradoxically there were no local recurrences associated with malignant phyllodes tumors. This is explained by the small number of patients, and by the fact that most malignant phyllodes tumors had mastectomy rather than breast conservation.

In the literature the average size of phyllodes tumors is around 4–8 cm varying from 1 to over 40 cm at the extremes(8,11,14,18–28,43) (Table 6). In

Table 9. Literature Review, Percentage of Local Recurrences When Grouped According to Various Criteria

Authors	T <50 mm	T >50 mm	Grade 1	Grade 2	Grade 3	M+	M–	BCT	MR
A.W Chaney (11)	2% (1)	53.5% (3)	5% (3)	0	3.5% (1)	0	4% (4)	4% (2)	3.5% (2)
O. Asoglu (18)	15% (4)	45% (9)	12.5% (2)	66.5% (2)	35.5%(12)			36% (8)	28.5% (8)
W.H. Chen (19)	63.5% (13)	10.5% (6)	14% (19)	0	0	46% (6)	8% (13)	15% (19)	0
F. Sabban (20)									
J.B. Hassouna (21)			5% (3)	31% (5)	18% (5)				
O.K. Macdonald (22)									
A. Fou (23)						22% (4)	12.5% (1)	29.5% (5)	0
N. Taira (24)	14% (4)	12% (2)	9.5% (3)	0	33.5% (3)	33% (5)	3.5% (1)	14.5% (6)	0
M.S.Lenhard (25)	15.5% (2)	40% (6)	8.5% (1)	20% (2)	50% (4/8)	28% (7)	12.5% (1)	31.5% (6)	15.5% (2)
Y. Belkacemi (26)			11% (31)	28% (23)	28% (22)				
R.D. Pezner (27)									
T. Bouhafa (28)									
Current series Guillot et al.			47% (7)	53% (8)	0			100% (15)	0

LR, local recurrence; T, tumor size; M+, positive margin; M–, negative margin; BCT, breast-conserving treatment; MR, mastectomy rate.

our study the average size was 3 cm with a range of 0.5–15 cm, the largest tumors were of the highest grade (Figure 1). In our series, univariate analysis showed tumor size to be a significant prognostic indicator for local control ($p = 0.02$), which is consistent with other authors (26,29).

Nine patients in our study (5.4%) had received adjuvant treatment after the initial diagnosis of malignant phyllode tumors (Table 1). Two patients had radiotherapy after recurrence of disease, one of whom also had chemotherapy. All these patients had high-grade phyllodes tumors. The role of radiotherapy in borderline to malignant grade tumors has not been clearly established in the literature (11–13,44,45). According to Belkacémi et al. (26) adjuvant radiotherapy improves local disease control without any impact on overall survival. Pezner et al. recommend adjuvant radiotherapy after breast conservation treatment for tumor sizes greater than 2 cm, or after mastectomy for a large volume tumor (>10 cm) (27). Recommendations for adjuvant radiotherapy are not consistent however and may vary from study-to-study (11,18–28) (Table 7). Similarly there is a paucity of information in the literature to confirm that adjuvant chemotherapy improves overall or disease free survival (20,26,46,47). In our study, the benefit of chemotherapy or radiotherapy is unproven and must be considered on a case-by-case basis. The management of phyllodes tumors remains controversial. Where surgical management is concerned clear surgical margins is the only agreed predictive factor for local recurrence (usually understood to be margins >1 cm) (Tables 7, 8, and 9) (8,11,18–28,30,36–38). Provided clear margins are maintained then breast conservation is preferable. Oncoplastic reconstruction permits the largest tumor resections while guaranteeing good esthetic results (48–51). On conclusion, the surgical management needs to be tailored to the clinical situation, with more aggressive management reserved for higher grade or recurrent tumors. In the latter case if wide local excision is still possible while allowing satisfactory cosmesis then breast conservation surgery should still be considered. If satisfactory cosmesis cannot be obtained then mastectomy is unavoidable, but the possibility of simultaneous breast reconstruction should also be anticipated. In a few instances more radical surgery will be required for optimal control. In our experience, there is no benefit of chemotherapy or radiotherapy.

Further study is needed to elucidate the biologic and histologic factors associated with local recurrence in order to refine and improve the initial surgical management. As has become commonplace in breast cancer management gene microarrays have allowed us to differentiate benign phyllodes tumors from borderline and malignant tumors (52). Genetic analysis will potentially supplement classical histologic examination in order to improve our management of these tumors.

REFERENCES

1. Liberman L, Bonaccio E, Hamele-Bena D, Abramson AF, Cohen MA, Dershaw DD. Benign and malignant phyllodes tumors: mammographic and sonographic findings. *Radiology* 1996;198: 121–4.

2. Rowell MD, Perry RR, Hsiu JG, Barranco SC. Phyllodes tumors. *Am J Surg* 1993;165:376–9.

3. Bapat K, Oropeza R, Sahoo S. Benign phyllodes tumor of the male breast. *Breast J* 2002;8:115–6.

4. Bartoli C, Zurrida SM, Clemente C. Phyllodes tumor in a male patient with bilateral gynaecomastia induced by oestrogen therapy for prostatic carcinoma. *Eur J Surg Oncol* 1991;17:215–7.

5. Nielsen VT, Andreasen C. Phyllodes tumour of the male breast. *Histopathology* 1987;11:761–2.

6. Ansah-Boateng Y, Tavassoli FA. Fibroadenoma and cystosarcoma phyllodes of the male breast. *Mod Pathol* 1992;5:114–6.

7. Tavassoli FA, Devilee P (eds). *World Health Organization Classification of Tumors. Pathology & Genetics of Tumors of the Breast and Female Genital Organs*. Lyon: International Agency for research on Cancer Press, 2003:99–103.

8. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: an analysis of 170 cases. *Cancer* 1996;77:910–6.

9. Mangi AA, Smith BL, Gadd MA, Tanabe KK, Ott MJ, Souba WW. Surgical management of phyllodes tumors. *Arch Surg* 1999;134:487–92; discussion 492–3.

10. de Roos WK, Kaye P, Dent DM. Factors leading to local recurrence or death after surgical resection of phyllodes tumours of the breast. *Br J Surg* 1999;86:396–399.

11. Chaney AW, Pollack A, McNeese MD, *et al.* Primary treatment of cystosarcoma phyllodes of the breast. *Cancer* 2000; 89:1502–11.

12. August DA, Kearney T. Cystosarcoma phyllodes: mastectomy, lumpectomy, or lumpectomy plus irradiation. *Surg Oncol* 2000;9:49–52.

13. Haberer S, Lae M, Seegers V, *et al.* Management of malignant phyllodes tumors of the breast: the experience of the Institut Curie. *Cancer Radiother*. 2009;13:305–12.

14. Grimes MM. Cystosarcoma phyllodes of the breast: histologic features, flow cytometric analysis, and clinical correlations. *Mod Pathol* 1992;5:232–9.

15. Pietruszka M, Barnes L. Cystosarcoma phyllodes: a clinicopathologic analysis of 42 cases. *Cancer* 1978;41:1974–83.

16. Keelan PA, Myers JL, Wold LE, Katzmann JA, Gibney DJ. Phyllodes tumor: clinicopathologic review of 60 patients and flow cytometric analysis in 30 patients. *Hum Pathol* 1992;23:1048–54.

17. Cohn-Cedermark G, Rutqvist LE, Rosendahl I, Silfversward C. Prognostic factors in cystosarcoma phyllodes. A clinicopathologic study of 77 patients. *Cancer* 1991;68:2017–22.

18. Asoglu O, Ugurlu MM, Blanchard K, *et al.* Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. *Ann Surg Oncol* 2004;11:1011–7.

19. Chen WH, Cheng SP, Tzen CY, *et al.* Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. *J Surg Oncol* 2005;91:185–94.

20. Sabban F, Collinet P, Lucot JP, Boman F, Leroy JL, Vinatier D. Phyllodes tumor of the breast: analysis of 8 patients. *J Gynecol Obstet Biol Reprod (Paris)* 2005;34(3 Pt 1):252–6.

21. Ben Hassouna J, Damak T, Gamoudi A, *et al.* Phyllodes tumors of the breast: a case series of 106 patients. *Am J Surg* 2006;192:141–7.

22. Macdonald OK, Lee CM, Tward JD, Chappel CD, Gaffney DK. Malignant phyllodes tumor of the female breast: association of primary therapy with cause-specific survival from the Surveillance, Epidemiology, and End Results (SEER) program. *Cancer* 2006;107:2127–33.

23. Fou A, Schnabel FR, Hamele-Bena D, *et al.* Long-term outcomes of malignant phyllodes tumors patients: an institutional experience. *Am J Surg* 2006;192:492–5.

24. Taira N, Takabatake D, Aogi K, *et al.* Phyllodes tumor of the breast: stromal overgrowth and histological classification are useful prognosis-predictive factors for local recurrence in patients with a positive surgical margin. *Jpn J Clin Oncol* 2007;37:730–6.

25. Lenhard MS, Kahlert S, Himsl I, Ditsch N, Untch M, Bauerfeind I. Phyllodes tumour of the breast: clinical follow-up of 33 cases of this rare disease. *Eur J Obstet Gynecol Reprod Biol* 2008;138:217–21.

26. Belkacemi Y, Bousquet G, Marsiglia H, *et al.* Phyllodes tumor of the breast. *Int J Radiat Oncol Biol Phys* 2008;70: 492–500.

27. Pezner RD, Schultheiss TE, Paz IB. Malignant phyllodes tumor of the breast: local control rates with surgery alone. *Int J Radiat Oncol Biol Phys* 2008;71:710–3.

28. Bouhafa T, Masbah O, Bekkouch I, *et al.* Phyllodes tumors of the breast: analysis of 53 patients. *Cancer Radiother*. 2009: 85–91.

29. Tse GM, Lui PC, Lee CS, *et al.* Stromal expression of vascular endothelial growth factor correlates with tumor grade and microvessel density in mammary phyllodes tumors: a multicenter study of 185 cases. *Hum Pathol* 2004;35:1053–7.

30. Kapiris I, Nasiri N, A'Hern R, Healy V, Gui GP. Outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high-grade malignant phyllodes tumours of the breast. *Eur J Surg Oncol* 2001;27:723–30.

31. Niezabitowski A, Lackowska B, Rys J, *et al.* Prognostic evaluation of proliferative activity and DNA content in the phyllodes tumor of the breast: immunohistochemical and flow cytometric study of 118 cases. *Breast Cancer Res Treat* 2001;65:77–85.

32. Mrad K, Driss M, Maalej M, Romdhane KB. Bilateral cystosarcoma phyllodes of the breast: a case report of malignant form with contralateral benign form. *Ann Diagn Pathol* 2000;4:370–2.

33. Alam I, Awad ZT, Given HF. Cystosarcoma phyllodes of the breast: a clinicopathological study of 11 cases. *Ir Med J* 2003;96:179–80.

34. Foxcroft LM, Evans EB, Porter AJ. Difficulties in the preoperative diagnosis of phyllodes tumours of the breast: a study of 84 cases. *Breast* 2007;16:27–37.

35. Komenaka IK, El-Tamer M, Pile-Spellman E, Hibshoosh H. Core needle biopsy as a diagnostic tool to differentiate phyllodes tumor from fibroadenoma. *Arch Surg* 2003;138:987–90.

36. Abdalla HM, Sakr MA. Predictive factors of local recurrence and survival following primary surgical treatment of phyllodes tumors of the breast. *J Egypt Natl. Canc Inst* 2006;18:125–33.

37. Barrio AV, Clark BD, Goldberg JI, *et al.* Clinicopathologic features and long-term outcomes of 293 phyllodes tumors of the breast. *Ann Surg Oncol* 2007;14:2961–70.

38. Belkacémi Y, Zouhair A, Ozsahin M, Azria D, Mirimanoff R. -O pour le réseau des cancers rares (Rare Cancer Network). Facteurs pronostiques et prise en charge des tumeurs rares. *Cancer/Radiothérapie* 2006;10:323–9.

39. Zurrida S, Bartoli C, Galimberti V, *et al.* Which therapy for unexpected phyllode tumour of the breast? *Eur J Cancer* 1992;28:654–7.

40. Geisler JP, Foster RS, Sutton GP. Chyloperitoneum following treatment for advanced gynecologic malignancies. *Obstet Gynecol* 1994;83(5 Pt 2):883–5.

41. Gullett NP, Rizzo M, Johnstone PA. National surgical patterns of care for primary surgery and axillary staging of phyllodes tumors. *Breast J* 2009;15:41–4.

42. Treves N, Sunderland DA. Cystosarcoma phyllodes of the breast: a malignant and a benign tumor; a clinicopathological study of seventy-seven cases. *Cancer* 1951;4:1286–332.

43. Guerrero MA, Ballard BR, Grau AM. Malignant phyllodes tumor of the breast: review of the literature and case report of stromal overgrowth. *Surg Oncol* 2003;12:27–37.

44. Pandey M, Mathew A, Kattoor J, *et al.* Malignant phyllodes tumor. *Breast J* 2001;7:411–6.

45. Hajdu SI, Espinosa MH, Robbins GF. Recurrent cystosarcoma phyllodes: a clinicopathologic study of 32 cases. *Cancer* 1976;38:1402–6.

46. Morales-Vasquez F, Gonzalez-Angulo AM, Broglio K, *et al.* Adjuvant chemotherapy with doxorubicin and dacarbazine has no effect in recurrence-free survival of malignant phyllodes tumors of the breast. *Breast J* 2007;13:551–6.

47. Hawkins RE, Schofield JB, Fisher C, Wiltshaw E, McKinna JA. The clinical and histologic criteria that predict metastases from cystosarcoma phyllodes. *Cancer* 1992;69:141–7.

48. Clough KB, Nos C, Fitoussi A, Couturaud B, Inguenault C, Sarfati I. Partial reconstruction after conservative treatment for breast cancer: classification of sequelae and treatment options. *Ann Chir Plast Esthet* 2008;53:88–101.

49. Mustonen P, Harma M. Viewpoints on oncoplastic surgery in invasive breast cancer. *Scand J Surg* 2002;91:255, 258–62.

50. Franceschini G, Magno S, Fabbri C, *et al.* Conservative and radical oncoplastic approches in the surgical treatment of breast cancer. *Eur Rev Med Pharmacol Sci* 2008;12:387–96.

51. Hamdi M, Sinove Y, DePypere H, *et al.* The role of oncoplastic surgery in breast cancer. *Acta Chir Belg* 2008;108:666–72.

52. Lae M, Vincent-Salomon A, Savignoni A, *et al.* Phyllodes tumors of the breast segregate in two groups according to genetic criteria. *Mod Pathol* 2007;20:435–44.