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Guideline

Contemporary management of phyllodes tumours of the breast: recommendations from the UK Association of Breast Surgery

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Introduction

Phyllodes are rare tumours, historically referred to as cystosarcoma or cystosarcoma phyllodes[1], that account for about 0.5% of all breast tumours, most frequently occurring in women in their 40s and 50s[2]. Recent data from National Health Service (NHS) Digital have shown that there are approximately 60 new cases of malignant phyllodes tumours (PT) diagnosed per year in England with an incidence of 2 per 1 000 000 women[3]. PT are biphasic with both stromal and epithelial components and are classified into three groups[2] with the following proportions: benign, 50–70%; borderline, 12–26%; and malignant, 20–30%. Group stratification is important to guide clinical management and inform prognosis and recurrence risk.

Internationally, there is a considerable variation in the management of PT with a tendency for overtreatment of benign lesions, especially in regional hospitals and with clinicians less experienced in the condition[4]. Similarly, within the UK, clinical practice varies widely[5,6] and this is also observed in other parts of Europe[4]. A recent analysis of data from the National Cancer Registration and Analysis Service (NCRAS) in England showed that patients with breast sarcomas, including malignant PT, were more likely to have a preoperative biopsy and less likely to require multiple operations if managed at a centre with specialist sarcoma services compared with non-specialist centres[3].

Recommendations for the management of PT exist but are frequently incorporated into broader guidelines such as the British Sarcoma Group (BSG) UK guidelines for the treatment of soft tissue sarcomas (STS) of all types, which include recommendations for the management of borderline and malignant PT[7]. Similarly, in the USA, there is a section about the management of PT within the National Comprehensive Cancer Network (NCCN) guidelines for breast cancer[8].

Therefore, this document is intended to provide easily accessible evidence and consensus recommendations for multidisciplinary teams (MDT) managing patients with PT to advise best practice and streamline clinical care. The author group believe this document will be of relevance to clinicians and the wider MDT managing PT in the UK and across the world.

These guidelines have been produced with the involvement of the Association of Breast Surgery (ABS). The guidelines have been endorsed by: the Association of Breast Pathology, the British Society of Breast Radiology (BSBR), the Royal College of Radiologists (RCR), the Association of Breast Surgeons of India (ABSI), the Society of Irish Breast Surgeons (SIBS), and the UK National Coordinating Committee for Breast Pathology (NCCBP). Moreover, the patient information has been reviewed with support from Breast Cancer Now and Sarcoma UK.

Methodology

A multidisciplinary panel of experts in radiology, pathology, surgery, and oncology from breast and sarcoma services authored these recommendations. The first stage was a

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Table 1 Definition of 'levels of evidence' and 'grades of recommendation'

Levels of evidence	
I	Evidence from at least one large RCT of good methodological quality (low potential for bias) or meta-analysis of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analysis of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, or expert opinions
Grades of recommendation	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient benefit for efficacy or benefit does not outweigh the risk or the disadvantages, optional
D	Moderate evidence against efficacy or for adverse outcomes, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

literature search of full-text papers performed using PubMed and Cochrane databases, covering the interval from 1990 to July 2023, using the keyword 'phyllodes'. Studies in languages other than English were excluded. The available evidence was reviewed by the author panel. Virtual meetings were conducted between August 2022 and August 2023 to discuss relevant sections of the document and agree on the recommendations. Between August 2023 and July 2024, ongoing literature searches were conducted and further iterations of the manuscript were agreed through ad-hoc virtual meetings, e-mail, and face-to-face discussions at the ABS's Annual Scientific Meeting (Bournemouth, UK) in May 2024. Patient advocate input was provided by Sarcoma UK and Breast Cancer Now leading to the development of patient information sheets (*Appendix S2*).

The writing panel has summarized the current knowledge identified in the literature and derived recommendations based on the best available peer-reviewed evidence for management of PT, supported by expert panel consensus opinion where evidence is lacking. Levels of evidence and grades of recommendation (*Table 1*) have been provided, where appropriate, for all the key recommendations.

The consensus recommendations were independently reviewed and approved by the Clinical Practice and Standards Committee and the Executive Board at the ABS. Feedback from the committees was incorporated. The final draft was reviewed by an independent expert using the Appraisal of Guidelines for Research and Evaluation (AGREE II) Checklist (*supplementary material*).

Economic evaluation was not carried out, as the purpose of these recommendations is to streamline clinical care and there are no available comparators in the literature.

The recommendations are summarized in *Appendix S1*.

Diagnosis of phyllodes tumours

Clinical findings

Patients with PT will often present to a breast clinic with a breast lump, which should undergo standard triple assessment[9] following established local or national protocols. A proportion of PT will be identified after referral from breast screening assessment for surgical diagnostic excision of cellular fibroepithelial lesions or 'benign' lesions which are enlarging[10]. Patients with confirmed PT may be referred from another hospital for tertiary opinion.

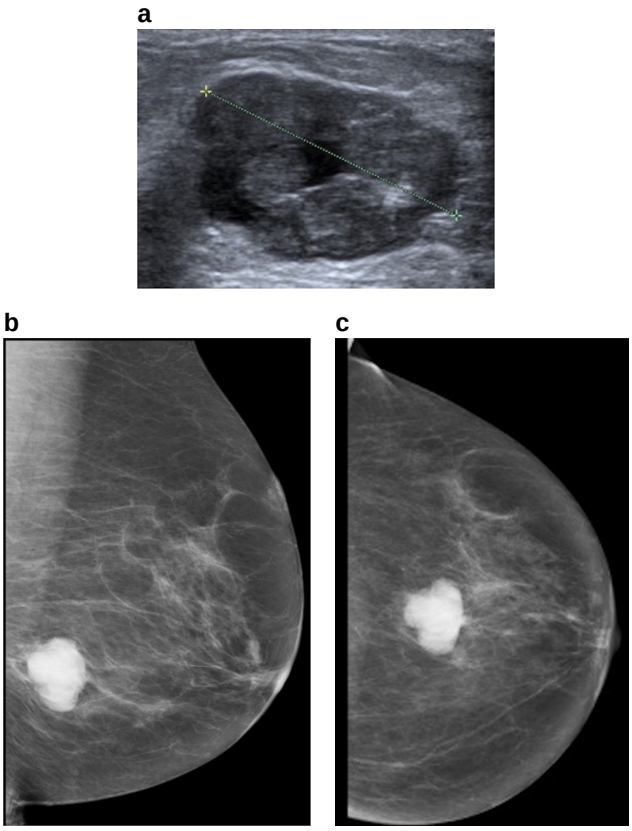

Fig. 1 Radiological images of PT

a Ultrasonographic image of a well-defined, lobulated, oval mass with an internal cystic space suggestive of a PT (core biopsy suggestive of being benign, but malignant according to postoperative histology). **b** and **c** Mammographic images (mediolateral oblique (MLO) projection and craniocaudal (CC) projection respectively); left-sided mammography demonstrates a dense, partially well-defined, lobulated mass in the left lower central breast (from the same patient as the ultrasonographic image). PT, phyllodes tumours.

In some cases, a patient with a previously diagnosed fibroadenoma may return to the breast clinic because the fibroadenoma is increasing in size. Sanders and Sara[11] suggested that a growing fibroadenoma may have a higher relative risk of other pathology, therefore justifying excision or repeat biopsy. In their series of 83 growing fibroadenomas, the incidence of PT as a subsequent histological diagnosis was 2.4%[11]. More recently, Lee *et al.*[12] suggested a growth threshold of >15% change in volume per month in radiologically diagnosed fibroadenomas was suspicious for PT.

Clinical suspicion of PT should be raised if, in the past, they have had a benign breast lump excised at the same site or previous excision of a PT from either breast. Other features that increase the risk of PT are lesions >4 cm and/or lobulated or with multinodular appearances on imaging[12] (*Fig. 1*). Li–Fraumeni syndrome (TP53 germline mutation) is associated with PT[13] and other germline mutations have been reported in PT patients, including BRCA1, BRCA2, NF1, and RB1. However, their association with PT is not well established[14–17].

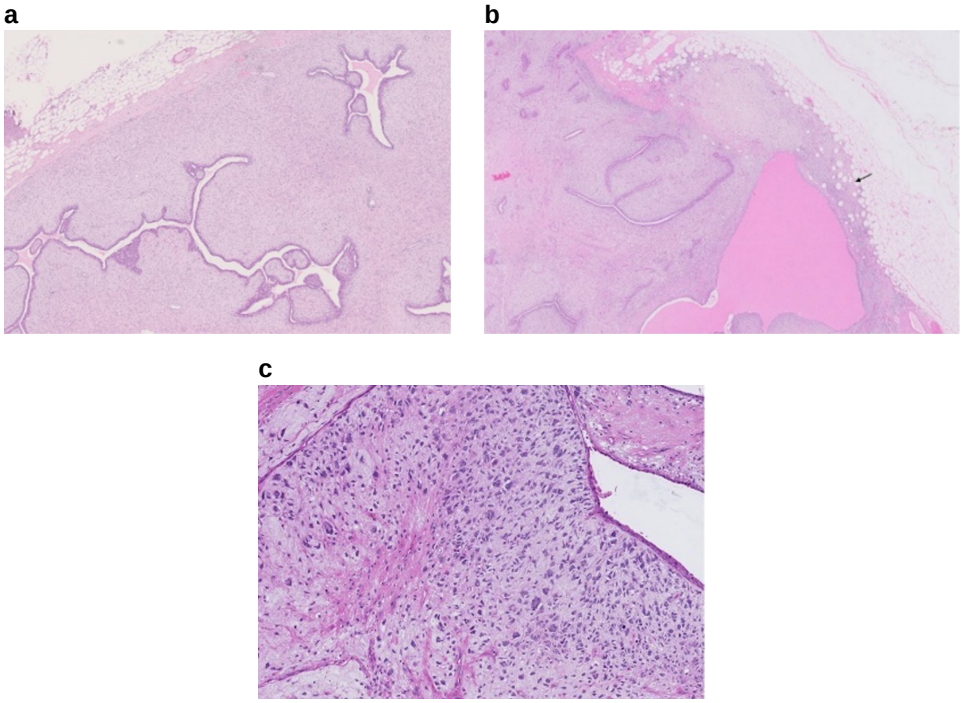

Fig. 2 Microscopy images of benign, borderline, and malignant PT

a Benign PT. Cleft-like epithelial-lined spaces within mildly to moderately cellular stroma. A well-defined edge is seen adjacent to fatty tissue (top left). **b** Borderline PT. Moderately cellular stroma in which epithelial-lined spaces, some cleft-like, are seen. The margin is more infiltrative than in a benign lesion with an area of fat cells surrounded (arrow) by stroma of the tumour. **c** Malignant PT. Markedly atypical stromal cells surround compressed benign cleft-like epithelial spaces. PT, phyllodes tumours.

Pathology

Both fibroadenomas and PT are formed from stroma with interspersed ductal structures. It is likely that they have a common origin as evidenced by the shared MED12 somatic mutations[18]. Distinction between cellular fibroadenoma and PT relies almost solely on assessment of the cellularity of the stroma. This can be challenging on core biopsies[19–21] and is not possible on fine needle aspiration cytology (FNAC). Core needle biopsy may be reported, for example, as a 'cellular fibroepithelial lesion, PT cannot be excluded'. These cases reported as 'cellular fibroepithelial lesion' carry a risk of underlying phyllodes diagnosis (18–38%), but only a small risk of malignant PT subtype(<2%)[22–25]. These are included in the range of entities that pathologists report as being of uncertain malignant potential, termed in the UK and some other European countries as a 'B3' lesion[26], and should be managed expediently.

The classification of PT in surgical excisions can also be difficult, especially when distinguishing borderline from malignant PT (*Fig. 2*)[27]. Features of malignant PT include marked stromal atypia, marked stromal cellularity, stromal overgrowth, mitotic rate ≥10/10 high-power fields, and infiltrative tumour borders[19]. In a small retrospective study of 20 malignant PT, re-classification using these histological parameters downgraded five lesions to borderline, which in turn correlated with clinical outcome with a single locoregional recurrence in this group. The most significant histological parameters identified were stromal overgrowth and a broadly infiltrating tumour border[28].

In a similar fashion, distinguishing malignant PT from spindle cell metaplastic carcinoma and primary breast sarcoma can occasionally be difficult. Stromal overgrowth may mean that the PT architectural hallmark of 'leaf-like' fronds are difficult to find and the malignant PT stroma may show heterologous sarcomatous differentiation[19].

Radiology

Diagnosis

Mammographic features of PT are generally non-specific and may mimic benign lesions such as cysts and fibroadenomas. They often appear as well-defined, lobulated, dense masses that can have a lucent halo. Rarely, they may have coarse calcifications (*Fig. S1*) but almost never finer, small calcifications. Malignant PT may have ill-defined or spiculated margins[29]. Using ultrasonography, PT are hypoechoeic, are oval, and around 50% are lobulated. When compared with the imaging features of fibroadenomas, PT can have increased lobulations, cystic areas, septa, horizontal linear clefts, and a heterogeneous internal texture. In addition, PT can be vascular with irregular margins[29]. Up to half of PT are interpreted as fibroadenomas using ultrasonography[30]. MRI of the breast does not offer any diagnostic advantage over conventional imaging using mammography and ultrasonography[31,32].

Staging

Malignant PT carry the highest risk of distant metastases and the most common site is lung then bone[33]. Other rare, reported sites of metastases are brain, liver, adrenal glands, small intestine, kidneys, pancreas, pelvis, and heart[34]. There are no published studies with large numbers of patients comparing the diagnostic accuracy of standard CT *versus* PET-CT in newly diagnosed cases of malignant PT. In addition, the benefit of abdominal and pelvic scanning to chest CT has not been determined. Similarly, in cases of locally recurrent malignant PT there are no published studies, other than case reports, to offer evidence of the benefit of PET-CT rather than standard CT for staging.

Diagnostic surgery

Excision biopsy with an intact capsule can assist histopathological assessment and allow a definitive diagnosis in cases where it is difficult to differentiate between cellular fibroadenoma and PT on needle core biopsy. Vacuum-assisted excision (VAE) is not recommended for these lesions.

Recommendations for diagnosis

- The diagnosis of PT should involve triple assessment with needle core biopsy of the lesion and indeterminate/abnormal axillary lymph nodes if present (evidence/grade IV/A).
- Core biopsy is recommended rather than FNAC (evidence/grade IV/A).
- All PT cases should be reviewed in a breast MDT meeting (evidence/grade V/A).
- Given the challenges with histological classification of these lesions, referral for second pathological opinion should be considered in difficult cases (evidence/grade V/B).
- Breast MRI is not routinely recommended for the diagnostic workup of PT (evidence/grade IV/C).
- Preoperative CT staging is not recommended for benign or borderline PT (evidence/grade IV/D).
- Preoperative chest CT staging is recommended for malignant PT (evidence/grade IV/A).
- MDT should have a low threshold for diagnostic surgical excision biopsy when phyllodes cannot be excluded on needle biopsy (evidence/grade V/A).
- Tertiary referrals for suspected or confirmed phyllodes should be directed towards the breast MDT for review and triage (evidence/grade V/A).
- Management of biopsy-confirmed borderline and malignant PT should be referred and discussed at a sarcoma MDT with expert pathology review and shared care between breast and sarcoma MDT is recommended (evidence/grade V/A).
- MDT should consider that surgical management of malignant PT is time sensitive and pathway delays should be avoided (evidence/grade V/A).

Surgical management for phyllodes tumors

Surgery is the primary treatment for PT. Surgical planning should be based on the subtype of PT and the desired surgical margin.

Breast-conserving surgery (BCS) *versus* mastectomy

Based on the available but limited evidence, it is likely that there is no difference in distant disease-free survival (DFS) or overall survival (OS) between BCS and mastectomy for the surgical treatment of PT[35,36]. BCS is oncologically safe in all subtypes of PT, if adequate margins can be achieved[37–39]. A recently published study from an Italian group of 131 malignant PT patients showed no difference in local and distant recurrence in patients treated with mastectomy or BCS, even after controlling for adverse pathological factors[40].

Published data on breast reconstruction with either implant or autologous techniques after mastectomy for PT are scarce. There are recognized surgical challenges with reconstruction, but it is not associated with a higher recurrence rate compared with simple mastectomy[36,41–44]. Surgical planning should consider whether skin and chest wall resection is required to achieve adequate margins. Complex cases may need combined planning with specialized plastic techniques.

Recommendations for breast surgery

- For all PT, BCS can be offered if adequate surgical excision margins can be achieved (evidence/grade IV/B).
- If complex oncoplastic BCS techniques are required, or, a mastectomy is required to achieve clear margins, this should be discussed at a local oncoplastic MDT meeting with plastic and breast surgeons where available (evidence/grade V/B).
  - Consideration should be given to individual patient risk factors including smoking, BMI, and receipt of previous radiotherapy.
- Breast reconstruction should be offered to all patients undergoing mastectomy for PT, but, for patients with malignant PT, careful consideration should be given to the timing of reconstruction including the likelihood of early progression (local and distant), operative recovery time, and potential effects on timing of adjuvant therapy (evidence/grade V/B).
- Consideration should be given as to whether significant skin excision or chest wall musculature is required to achieve oncological margins (evidence/grade V/B).

Management of the axilla

In a similar fashion to other sarcomas, malignant PT metastasize mostly by haematogenous spread. Lymphatic spread to ipsilateral axillary lymph nodes is very rare[45].

Recommendations for axillary management

- Given the extreme rarity of axillary nodal involvement and the possibility of reactive lymph nodes, histopathological (for example by core biopsy) examination of suspicious nodes is recommended to guide the need for axillary lymph node dissection (evidence/grade IV/A).
- Axillary staging surgery, for example sentinel lymph node excision biopsy, is not recommended for any of the PT subgroups (evidence/grade V/E).
- In the case of biopsy-proven axillary nodal involvement, axillary lymph node dissection is indicated. Cases with locoregional spread should be discussed in a sarcoma MDT meeting (evidence/grade V/A).

Margin assessment and management

The optimum margin width has remained controversial with regards to the surgical management of PT. Published evidence suggests that surgical margins are a prognostic risk factor for local recurrence (*Table 2*). However, most studies do not apply consistent differentiation between ‘negative’, ‘wide’, ‘close’, and ‘positive’ margins[46]. Historically, this has resulted in varied interpretation in individual institutions[47]. It is becoming more widely accepted that a generic 10 mm margin for surgical therapy for all PT is overtreatment[48]; however, the target margin width for the three different groups of PT (benign, borderline, and malignant) is more nuanced.

Benign PT and surgical excision margins

Most benign PT recurrences occur when the margin is involved[49] or <1 mm[50], but re-excising positive margins for benign PT has uncertain benefit[49,51]. A literature review by Shaaban and Barthelmes[52] on benign PT surgical margin management was published in 2017. In total, 1702 patients were included and the results indicated that the recurrence rate was low (11%) even with a high rate of margin involvement[52]. Belkacemi *et al.*[53]

Table 2 Literature review of studies addressing the impact of surgical margins in PT

Study, year	Study type	PT subtype (*n*)	Median follow-up (months)	Surgical margin cut-off	Pertinent findings
Barth[60], 1999	Literature review	Benign: 752 Borderline: 107 Malignant: 85 Total: 944	Variable	WLE defined as achieving margins of at least 10–20 mm	LR rates with local excision *versus* WLE: Benign: 21% ($n = 111$ of 540) *versus* 8% ($n = 17$ of 212). Borderline: 46% ($n = 18$ of 39) *versus* 29% ($n = 20$ of 68). Malignant: 65% ($n = 26$ of 40) *versus* 36% ($n = 16$ of 45).
Chaney *et al.*[61], 2000	Single-centre retrospective study	Benign: 59 Borderline: 12 Malignant: 30 Total: 101	47	10 mm	Benign/borderline: actuarial 10-year local failure rate was 7%. Malignant: actuarial 10-year local failure rate was 9%. Three of four instances of LR occurred in patients with tumours >5 cm in greatest dimension, despite adequate margins.
Cheng *et al.*[62], 2006	Single-centre retrospective study	Benign: 138 Borderline: 13 Malignant: 31 Total: 182	30	>10 mm	On multivariable analysis, positive resection margins were significantly associated with LR risk (HR 8.0 (95% c.i. 2.8,23.0); $P < 0.001$). Histological upgrading at recurrence was noted in 20% of cases ($n = 4$ of 20). Two originally benign PT recurred locally as borderline PT and another two benign PT recurred locally as malignant.
Spitaleri *et al.*[63], 2013	Single-centre retrospective study	Benign: 68 Borderline: 42 Malignant: 62 Total: 172	85	>1 mm Positive margin defined as ≤1 mm	On multivariable analysis, the independent predictors of phyllodes-related events were positive margins (HR 3.9 (95% c.i. 1.1,14.3)), age <35 years (HR 5.4 (95% c.i. 1.5,19.6)), and tumour necrosis (HR 3.9 (95% c.i. 1.1,14.1)).
Mituś *et al.*[64], 2014	Single-centre retrospective study	Malignant: 70	82	10 mm Close margin defined as <10 mm	All patients had clear surgical margins. Six patients had close margins (range 3–8 mm) and received adjuvant radiotherapy. No LR occurred. The 5-year survival without evidence of disease was the same (83%) in patients treated with BCS with adequate margins (≥10 mm) and those treated with BCS with close margins (<10 mm) plus subsequent radiotherapy.
Yom *et al.*[65], 2015	Single-centre retrospective study	Benign: 191 Borderline: 61 Malignant: 33 Total: 285	81	10 mm Positive margin defined as tumour at or within 0.1 mm of inked margin	Positive resection margins were noted in 45 patients (16%), more commonly in benign PT (17% positivity rate; $P = 0.005$). Among those patients, only three with benign PT developed LR and one with malignant PT developed distant metastasis. LR rates: benign, 4% ($n = 8$ of 191); borderline, 11% ($n = 7$ of 61); and malignant, 15% ($n = 5$ of 33). Neither margin status nor type of surgery was a significant predictor of LR risk. The highest LR risk (56%) was noted for tumours measuring ≤5 cm with ≥10 mitoses/10 HPF ($P < 0.001$).
Tremblay-LeMay *et al.*[20], 2017	Single-centre retrospective study	Benign: 81 Borderline: 20 Malignant: 13 Total: 114	Benign: 15 Borderline: 60 Malignant: 65	1 mm	The LR rate was 4.4% ($n = 5$; 3 benign and 2 borderline cases); four of those occurred in patients with margins <1 mm. No recurrences occurred in patients with malignant PT despite all having margins ≤1 mm (5 received adjuvant radiotherapy).

(continued)

Table 2 (continued)

Study, year	Study type	PT subtype (*n*)	Median follow-up (months)	Surgical margin cut-off	Pertinent findings
					Histological upgrading at recurrence occurred in one benign and one borderline PT, both recurring locally as malignant PT.
Shaaban and Barthelmes[52], 2017	Literature review of 12 studies	Benign: 1052 Borderline: 400 Malignant: 250 Total: 1702	Variable	Variable	In benign PT, the relapse rate was low (11% ($n = 112$ of 1052)) despite a high rate of margin positivity (8–43%). This was significantly lower than relapse rates in borderline (18%) and malignant (28%) subtypes ($P = 0.00001$). Overall, no significant difference was noted in recurrence rates between the 10 mm margin group and the 1 mm group (8% *versus* 6% respectively; $P = 0.13$). Overall, the recurrence rate was doubled in the group with margin involvement compared with the group with a margin of 1 mm (13% *versus* 6% respectively; $P = 0.006$).
Park *et al.*[35], 2019	Single-centre retrospective study	Malignant: 70	76	>2 mm Close margin defined as ≤2 mm	Involved resection margins were associated with inferior 7-year local control and DFS on univariable, but not multivariable, analysis. Six patients had involved margins, four of whom developed LR (67%).
Lu *et al.*[51], 2019	Meta-analysis of 6 studies	Benign: 606 Borderline: 145 Malignant: 135 Total: 886	Variable	10 mm	In malignant PT, a significantly higher LR rate was noted with positive margins <10 mm compared with ≥10 mm (OR 6.9 (95% c.i. 1.6,29.6)). No significant difference was noted in benign or borderline subtypes.
Thind *et al.*[46], 2020	Meta-analysis of 10 studies	Borderline: 345 Malignant: 565 Total: 910	Variable	10 mm	No statistically significant difference was observed between margins <10 and ≥10 mm in terms of local control, distant relapse, or mortality.
Neron *et al.*[66], 2020	Multicentre retrospective study	Malignant: 212	49	3 mm	Performing a pre-surgical biopsy was associated with subsequent negative surgical margins ($P = 0.044$) and improved LRFS ($P = 0.012$), despite a low detection rate of malignant PT on biopsy (39%). On multivariable analysis, the only prognostic factor for improved LRFS was mastectomy (as first or subsequent surgery) ($P < 0.001$). Margin width 0–2 mm, but not ≥3 mm, was associated with improved OS ($P = 0.005$). Margin width >8 mm was not associated with better outcomes compared with 3–7 mm ($P = 0.7$).
Wen *et al.*[48], 2020	Single-centre retrospective study	Benign: 75 Borderline: 10 Malignant: 11 Total: 96	47 (mean)	>2 mm Close margin defined as ≤2 mm	LR rate: 6% ($n = 6$ of 96), with histological upgrading in one borderline PT to malignant PT upon recurrence. The 5-year DFS was significantly better in the benign group (96%) compared with the borderline (80%) and malignant (82%) groups ($P = 0.016$). On univariable analysis, predictors of relapse were positive margins ($P = 0.025$) (but not margin width ≤2 mm or >2 mm), tumour size ($P = 0.018$), mitotic count ($P = 0.001$), and necrosis ($P = 0.03$).

(continued)

Table 2 (continued)

Study, year	Study type	PT subtype (*n*)	Median follow-up (months)	Surgical margin cut-off	Pertinent findings
Ibreaheem *et al.*[67], 2020	Single-centre retrospective study	Benign: 60 Borderline: 34 Malignant: 33 Total: 127	36	Not specified	The LR rate was significantly lower in the group with negative margins (16%) compared with positive (64%) or close (61%) margins ($P < 0.001$). With regards to OS, negative surgical margins predicted for improved outcomes only in the malignant subtype ($P = 0.012$). After initial diagnosis of benign PT, histological upgrading was reported to borderline and malignant PT. After initial diagnosis of borderline PT, histological upgrading to malignant PT and carcinosarcoma was reported.
Genco *et al.*[68], 2021	Single-centre retrospective study	Benign: 191 Borderline: 14 Total: 205	27	>1 mm Close margin defined as ≤1 mm	The final margin status was positive in 23% ($n = 46$) and close in 7% ($n = 14$). Among 131 patients with follow-up, LR occurred in 3 patients (2.3%), all of whom had benign PT and only 1 had a positive margin. There was no significant difference in LR rate by margin status.
Toussaint *et al.*[69], 2021	Meta-analysis of 13 studies	Benign: 1313 Borderline: 289 Malignant: 279 Total: 1881	Variable	10 mm	Surgical margins ≥10 mm reduced the LR incidence rate by 30% in benign PT and 24% for both borderline and malignant subtypes. No significant difference was noted for the incidence rate of distant relapse.
Yu *et al.*[47], 2022	Meta-analysis of 16 studies	Total: 3022	Variable	Variable	In nine studies ($n = 1763$ patients) analysing a margin cut-off of 10 mm, there was a significant reduction in recurrence risk in the group with margins ≥10 mm compared with <10 mm (OR 0.4 (95% c.i. 0.2,0.8)). In three studies ($n = 537$ patients) analysing a margin cut-off of 5 mm, there was no significant difference in recurrence risk between margin groups of ≥5 and <5 mm. In eight studies ($n = 1611$ patients) analysing a margin cut-off of 1 mm, there was a significant reduction in recurrence risk in the group with margins ≥1 mm compared with <1 mm (OR 0.4 (95% c.i. 0.3,0.6)).
van Olmen *et al.*[70], 2023	Population-based registry	Benign: 1908	31	No tumour on ink Positive margin defined as tumour on ink	The risk of LR was associated with positive margins (OR 2.5 (95% c.i. 1.4,4.6)) and bilateral tumours (OR 4.9 (95% c.i. 3.0,28.3)). Histological upgrading to malignant PT occurred in 6% of LR.
Kim *et al.*[71], 2023	Single-centre retrospective study	Benign: 87	31	10 mm	In practice, a high proportion of patients had margins ≤10 mm (57% ($n = 50$ of 87)). The overall LR rate was 9% ($n = 8$ of 87) with non-significant differences between the margin groups of ≤10 and >10 mm.
Moldoveanu *et al.*[72], 2023	Single-centre retrospective study	Benign: 155 Borderline: 32 Total: 187	35	2 mm Positive margin defined as tumour on ink Close margin defined as <2 mm	The LR rate was 3.7% ($n = 7$ of 187). LR was significantly associated with positive margins at initial surgery (HR 9.5 (95% c.i. 1.9,49.2)), but not margin width. After initial positive margins, margin revision was not associated with local control benefit compared with observation.

(continued)

Table 2 (continued)

Study, year	Study type	PT subtype (*n*)	Median follow-up (months)	Surgical margin cut-off	Pertinent findings
Valenza *et al.*[40], 2024	Single-centre retrospective study	Malignant: 131	77	10 mm Positive margin defined as <10 mm	After initial surgery, 72 cases (55%) had positive margins. After re-excision/ mastectomy, the final margin was positive in two cases (2%). The rate of mastectomy was higher in patients with tumour size ≥5 cm compared with <5 cm (79% *versus* 41% respectively; $P < 0.001$). The type of surgery (local excision *versus* mastectomy) was not associated with local or distant relapse. The cumulative 5-year incidence of LR was 16.0% (95% c.i. 10.0%,24.0%) and that of distant relapse was 10.0% (95% c.i. 5.3%,16.0%).
Su *et al.*[73], 2024	Single-centre retrospective study	Borderline: 85 Malignant: 65 Total: 150	66	10 mm Close margin defined as <10 mm	There was a significant improvement in 5-year LRFS and DFS in patients with margins ≥10 mm compared with <10 mm. Among patients with initial close margins, there was a significant improvement in 5-year LRFS and DFS in those who underwent re-surgery to achieve clear margins ≥10 mm. Independent risk factors for LRFS were age <45 years (HR 2.1 (95% c.i. 1.0,4.2); $P = 0.04$) and margins <10 mm (HR 2.6 (95% c.i. 1.1,5.8); $P = 0.023$). Independent risk factors for DFS were tumour size >5 cm (HR 2.7 (95% c.i. 1.3,5.7); $P = 0.007$) and margins <10 mm (HR 3.1 (95% c.i. 1.6,5.8); $P = 0.001$).
Ranjbar *et al.*[54], 2024	Single-centre retrospective study	Benign: 267 Borderline: 24 Malignant: 27 Total: 318	115 (mean)	No tumour on ink Positive margin defined as tumour on ink	LR rates: 7.5% in benign, 8.3% in borderline, and 22.2% in malignant PT. There was no statistically significant difference in LR rates by margin status across all subtypes. On multivariable analysis, predictors of recurrence were stromal overgrowth ($P = 0.017$), stromal cell atypia ($P = 0.026$), tumour size >4 cm ($P = 0.005$), smoking ($P = 0.027$), and oral contraceptive use ($P = 0.002$).
Bartels *et al.*[74], 2024	Population-based registry	Borderline: 452 Malignant: 469 Total: 921	115	No tumour on ink Positive margin defined as tumour on ink	Re-excision rates after BCS were significantly higher in malignant PT compared with borderline subtype (53% *versus* 35% respectively; $P < 0.001$). Estimated cumulative 5-year LR incidence: 8.7% (95% c.i. 6.0%,11.4%) in borderline PT and 11.7% (95% c.i. 8.6%,14.8%) in malignant PT. Histological upgrading at recurrence from borderline to malignant histology occurred in 24% ($n = 10$ of 42). On multivariable analysis, a positive margin was predictive of a higher LR rate (HR 3.0 (95% c.i. 1.6,5.6); $P < 0.001$). Margin width (0–1 mm *versus* >1 mm) had no statistically significant impact on LR risk. Additional predictors of increased LR risk were malignant histology ($P = 0.01$), tumour size ≥2 cm ($P < 0.001$), and BCS ($P < 0.001$).

Studies included in meta-analyses and literature reviews are not listed separately. Studies varied in their clarity when defining positive, close, and negative margins; when provided, clear definitions are included in the table. PT, phyllodes tumours; WLE, wide local excision; LR, local recurrence; BCS, breast-conserving surgery; HPF, high-power fields; DFS, disease-free survival; LRFS, local recurrence-free survival; OS, overall survival.

reported a 10-year local recurrence rate of 13% for benign PT treated with wide local excision with negative margins (>10 mm). In those studies where a 1 mm surgical margin was specified, the local recurrence rate was 5.7%[53].

In a recent retrospective study of 319 PT cases treated over a 19-year interval, Ranjbar *et al.*[54] found a recurrence rate for benign PT of 10.2% for positive margins and 4.6% for negative margins ('no tumour on ink'), but the difference was not statistically significant. Chen *et al.*[38] published a single-institution retrospective review of 172 PT cases and defined the surgical procedures as local excision with a margin <5 mm (described as excision, enucleation, lumpectomy, or simple excision), wide local excision with 10 mm resection margins, and mastectomy. Most cases were benign PT (131 cases), with 12 borderline PT and 29 malignant PT. For benign PT, the overall local recurrence rate was 14.5% and none of the 13 patients treated with mastectomy had a recurrence. Sixty-nine patients were treated with local excision and 11 (16%) had a recurrence. A further 49 were treated with wide local excision and 8 (16%) had a recurrence[38]. In a small series of patients with benign PT who were treated with breast conservation, 13 patients with disease at the surgical margins with a median follow-up of 35 months did not have a local recurrence[55]. Another study compared local recurrence rates in three groups of patients with benign PT who were treated with ultrasound-guided VAE, lesion excision with an intact capsule, or lesion excision with a planned 10 mm surgical margin. At a median follow-up of 39 months, of the 193 patients, there were no statistical differences in the rate of local recurrence between the groups (6 of 89, 8 of 57, and 3 of 47 respectively)[56].

Borderline and malignant PT and surgical excision margins

Compared to benign PT, recurrence rates are higher in the borderline subtype with a rate of 26% histological upgrade to malignant phyllodes at time of recurrence[57]. However, there is no reported correlation between a specific margin width and local recurrence[36]. For patients with malignant PT, in small individual series, OS and local recurrence were reported to be worse for malignant PT resected with margins <10 mm[58,59]. Conversely, Thind *et al.*[46] published a systematic review in 2020 suggesting that, for malignant PT, margins <10 mm may provide adequate tumour excision. Their meta-analysis with pooling of ten studies showed no statistically significant difference between <10 and ≥10 mm for either local recurrence rates or OS. Tan *et al.*[19] included 14 studies documenting the surgical margin width in malignant PT; however, only 2 studies described margins <10 mm. The most recent systematic review, published in 2022 by Yu *et al.*[47], specifically included studies that had reported individual subtypes and margin width. Meta-analysis of pooled data (some of which was for patients who had received adjuvant therapy) revealed a higher recurrence rate with a <10 mm margin than with a ≥10 mm margin for malignant PT[47].

There is no level I evidence supporting an optimum margin width; therefore, the recommendations listed below and in *Table 3* reflect the consensus opinion of the panel of experts informed by the available literature. Because borderline PT behave more aggressively than benign types, and because distinction between borderline and malignant PT can be difficult, a pragmatic approach is to accept a wider margin for borderline PT resection than for benign PT resection. For malignant PT, a reasonable and safe approach is to be cautious and to recommend a wide surgical margin until further prospective data are available, recognizing the aggressive behaviour of malignant PT. For malignant PT surgical teams should consider tumour position within the breast, including proximity to skin, fascia, and muscle, which may also need resection to achieve a clear margin. When reviewing pathological margins and the potential need for further surgery, MDTs should consider pathological features (for example proliferation/mitotic frequency and infiltrative margin) that can inform whether borderline PT are more likely to behave as malignant or benign lesions.

Table 3 Consensus recommendations for surgical margins in phyllodes tumours

	Clinical considerations for decision-making	Minimum pathological margins
Benign phyllodes	Aim for complete excision with the capsule intact.	Complete excision. Discuss risks and benefits of re-excision *versus* risk of recurrence when margins are involved.
Borderline phyllodes	Consider pathological features (for example proliferation/mitotic frequency and infiltrative margin) to guide likelihood for upgrade to malignant PT and consider whether it should be managed as a malignant subtype. Aim for 5 mm margin.	Recommend re-excision for margin <3 mm. Consider risks and benefits of re-excision when tumour margin 3–5 mm (depending on pathological features).
Malignant phyllodes	Consideration should be given to surgical planning with regards to proximity to the skin and position within the breast. Consider including fascia and muscle if the deep margin is close. Aim for 10 mm margin.	Recommend re-excision for margin <5 mm. Consider risks and benefits of re-excision when tumour margin 5–10 mm (and consider plan for radiotherapy).

Recommendations for surgical excision margins

- For benign PT, aim for complete excision with the capsule intact (evidence/grade IV/A).
- For benign PT, discuss with the patient the risks and benefits of re-excision *versus* risk of local recurrence if the margins are involved after BCS (evidence/grade V/A).
- For borderline PT, aim for a clear surgical excision margin of 5 mm (evidence/grade V/A).
- For borderline PT, if the surgical excision margins are <3 mm after BCS, re-excision is recommended (evidence/grade V/A).
- For borderline PT, if the surgical excision margins are 3 to <5 mm after BCS, consider re-excision *versus* clinical and imaging surveillance alone after discussion with the patient about the risks and benefits of each option (evidence/grade V/A).
- For malignant PT, aim for a clear surgical margin of 10 mm (evidence/grade II/A).
- For malignant PT, if the surgical excision margins are <5 mm after BCS, re-excision is recommended (evidence/grade II/A).
- For malignant PT, if the surgical excision margins are 5 to <10 mm after BCS, whilst the recommendation is to re-excise, consideration of clinical and imaging surveillance alone may be appropriate after discussion with the patient about the risks and benefits of each option (evidence/grade V/A).
- Discuss with the patient the uncertainty around optimal margin width for borderline and malignant PT (evidence/grade V/A).

Adjuvant therapy

Adjuvant radiotherapy

To date, no studies have demonstrated survival benefit for adjuvant radiotherapy in PT[47,49,75] with significant heterogeneity in reported local control outcomes[47,49,75–77]. Nevertheless, two systematic reviews reported local control benefit for adjuvant radiotherapy, mainly in malignant PT[78,79]. In a systematic review by Chao *et al.*[78], involving 696 patients with all PT subtypes, adjuvant radiotherapy was found to be more effective in young patients (<45 years of age), patients with tumours >5 cm, and patients with malignant PT, with a recommendation for adjuvant radiotherapy in high-risk malignant cases (including tumours >5 cm or close margins), without consideration of the surgery type (BCS *versus* mastectomy). Zeng *et al.*[79] conducted a meta-analysis on 2708 patients with borderline and malignant PT revealing that those who received adjuvant radiation treatment had a lower relative risk of local recurrence (HR 0.4 (95% c.i. 0.2 to 0.6)), with an absolute risk difference of 10%. Similarly, a meta-analysis of 922 malignant PT patients demonstrated a lower recurrence rate in patients receiving adjuvant radiotherapy (OR 0.05 (95% c.i. 0.01 to 0.09)) compared with those only treated surgically (OR 0.21 (95% c.i. 0.14 to 0.28)) ($P = 0.017$)[47]. However, a recently published retrospective observational study of 583 patients with T3/4 malignant PT identified from the Surveillance, Epidemiology, and End Results (SEER) database (time interval 2000–2018) did not find a statistically significant benefit in terms of breast cancer-specific survival or OS with radiotherapy[80].

The only prospective study evaluating the role of adjuvant radiotherapy in PT examined its benefit after BCS for PT with borderline or malignant histology[75]. A total of 46 patients were recruited over 10 years, highlighting the challenges of prospective studies in such a rare disease. None of the patients developed disease recurrence after a median follow-up of 4.7 years[75]. The authors recommended adjuvant radiotherapy for all malignant PT cases after BCS; however, 6.5% of the patients were included after re-excision of local recurrence, 35% had tumours ≥4 cm, and 35% had surgical margins <10 mm with no information about the percentage of patients with margins <5 mm[75]. This indicates that a large proportion of patients in this study had high-risk features that would justify adjuvant radiotherapy, rather than it being a blanket recommendation with clear benefit for all patients undergoing BCS.

PT are recognized to exhibit histological similarities to STS, rather than breast carcinomas, providing the basis for adopting similar radiotherapy dose and fractionation to STS (α/β ratio 4 Gy)[81,82]. The standard adjuvant radiotherapy dose for STS is 60–66 Gy in 1.8–2 Gy/fraction[81] and a similar fractionation is often used for adjuvant treatment in PT. When irradiating the breast, to minimize long-term cosmetic changes, radiotherapy is generally delivered as 50 Gy in 25 fractions to the whole breast followed by 16 Gy in 8 fractions to the tumour bed. In the prospective study by Barth *et al.*[75] the following technique was used: 50.40 Gy in 28 fractions to the whole breast using a standard tangential technique, followed by a boost to the tumour bed area, including the resection site plus a 2 cm margin, of a further 10 Gy in 5 fractions. Other schedules are also reported, including hypofractionated regimens, such as 54 Gy in 20 fractions over 4 weeks, 54 Gy in 15 fractions over 3 weeks, and 50 Gy in 20 fractions over 4 weeks, with no significant increase in toxicity, although only in small retrospective studies[53,75,81,83]. The most commonly used fractionation regimens for breast cancer in the UK are 40 Gy in 15 fractions over 3 weeks[84] and an ultrahypofractionation regimen of 26 Gy in 5 fractions over 1 week[85]. These regimens have been shown to give equivalent control to 50 Gy in 25 fractions in invasive breast cancer, which has an α/β ratio of 3.7. However, currently, there are no data on their effectiveness in PT.

Recommendations for radiotherapy

- Adjuvant radiotherapy is not recommended in benign PT (evidence/grade III/A).
- In the majority of borderline PT, radiotherapy is not recommended. It may be considered in high-risk cases such as large tumours and/or infiltrative borders and/or positive/close margins when further surgery is not possible (evidence/grade III/A).
- In malignant PT, adjuvant radiotherapy should be considered in large tumours (>5 cm) and in multifocal disease (evidence/grade II/A).
- In solitary smaller malignant PT, radiotherapy may be considered if a surgical margin of 5 mm was not achieved and further surgery is not possible. Repeat surgery to achieve clear margins is preferable to adjuvant radiotherapy (evidence/grade V/B).
- In recurrent malignant PT, adjuvant radiotherapy should be considered, after surgical excision, if not previously received (evidence/grade V/B).
- The consensus recommendation for adjuvant radiotherapy dose is 50–66 Gy (evidence/grade II/B) and hypofractionated regimens to an equivalent dose could be considered (evidence/grade IV/B).
- TP53 testing eligibility should be considered before offering radiotherapy to evaluate the risk of development of radiation-induced secondary malignancies (evidence/grade III/B).

Adjuvant chemotherapy

There is no evidence for a survival benefit with adjuvant chemotherapy in primary PT[66,78,86]. A single prospective study in 28 patients demonstrated no difference in recurrence-free survival between patients who received adjuvant doxorubicin/dacarbazine compared with no adjuvant chemotherapy[86]. In a retrospective study from the French Sarcoma Group including 212 patients, only 23 patients (11%) received adjuvant chemotherapy with no impact on local control or OS in multivariable analysis[66].

Recommendations for chemotherapy

- Adjuvant chemotherapy is not recommended in the management of non-metastatic PT (evidence/grade IV/A).

Surveillance

Local surveillance

Local recurrence tends to occur early, with the mean(s.d.) time to relapse for benign, borderline, and malignant PT reported to be 20.2(±12.1), 16.9(±10.8), and 20.3(±19.0) months respectively after initial treatment[49]. A systematic review assessed PT subtypes and local recurrence rates and described that the time to local recurrence was comparable between all three subtypes, with a median time of 14.7–22.5 months[51]. Consequently, the first 2–3 years of post-surgical follow-up are the most relevant for the detection of local recurrence.

Follow-up practice is very variable and no consensus for the optimum time interval exists[5]. A European Organisation for Research and Treatment of Cancer (EORTC) international survey

showed that the preferred duration of follow-up for all PT subtypes was 5 years[4]. In the UK, a practice survey identified that for borderline and malignant lesions, most MDT would recommend follow-up for 5 years[5].

Benign PT have a low recurrence rate and, if they do recur, they rarely progress to more aggressive subtypes[87,88]. Clinical and radiological follow-up has been suggested but only two protocols have been published and both advocate patient-directed follow-up without formal clinical or radiological surveillance[29,89]. This seems reasonable as it is well recognized that many local tumour recurrences are detected by patients themselves. It is imperative that patients are counselled on the importance of self-monitoring and how to access clinical services when required[90].

For borderline and malignant PT, both published follow-up protocols agree that early surveillance is important[29,89]. They suggest 6 monthly ultrasonographic scans of the index quadrant of the ipsilateral breast for those patients who have had BCS[89]. The protocols differed on the length of follow-up, but a considered approach would be for 36 months to capture most recurrences. Mammography has also been recommended for follow-up of malignant PT; annually for 5 years as a pragmatic approach in line with current breast cancer follow-up protocols. The increased intensity surveillance compared with breast cancer surveillance is recommended in light of local recurrence rates being higher than those observed with breast cancer, often presenting earlier and with aggressive local invasion.

In subgroups not recommended regular mammographic surveillance, the role of a single postoperative mammogram as a baseline for future comparison should be considered.

Systemic surveillance

Malignant PT also carry a risk of distant metastasis of approximately 20%, mostly to the lungs, which tends to occur within 2 years of primary treatment[35,38,91–93]. Therefore, chest imaging is recommended with the aim of identifying potentially resectable metastatic disease early. Plain chest X-rays are recommended as routine imaging during follow-up, in line with guidelines for STS surveillance[7]. Low-dose thorax CT is an alternative option in line with the NCCN guidelines and the Canadian consensus group suggestions[8,94]. There is no evidence of optimal surveillance for malignant PT and these are pragmatic recommendations. Teams should have a low threshold for dedicated three-dimensional imaging for new symptoms.

Recommendations for surveillance

- Patient-initiated follow-up without imaging surveillance is recommended for benign PT (evidence/grade IV/B).
- For borderline PT, clinical surveillance every 6 months for 3 years, ultrasonography of the index quadrant (after BCS) every 6 months for 3 years, and annual mammography for 5 years is recommended (evidence/grade IV/A).
- For malignant PT, clinical surveillance every 6months for 3 years and then annually for years 4 and 5 is recommended (evidence/grade IV/A).
- For malignant PT, ultrasonography of the index quadrant (after BCS) every 6 months for 3 years and annual mammography for 5 years is recommended (evidence/grade IV/A).
- For PT, breast imaging is not routinely recommended after mastectomy (evidence/grade IV/A).
- For malignant PT, chest imaging (chest X-ray or low-dose thorax CT) every 6 months for 2 years and then annually for years 3 to 5 is recommended (evidence/grade IV/A).

Flow charts regarding follow-up are included as *supplementary material*.

Management of disease recurrence

Local recurrence

Local recurrence constitutes a challenge in all PT subtypes; however, most patients with isolated relapse can undergo salvage surgery with curative intent. In a systematic review and meta-analysis of 54 studies including 9234 PT cases, the local recurrence rates were 8%, 13%, and 18% for benign, borderline, and malignant PT respectively[51]. In a study of 362 patients with borderline and malignant PT, the local recurrence rate was 17% after a median of 2 years, with no significant difference between both subtypes[57]. Of those with malignant PT at the time of local recurrence, 30% were of borderline or benign histology at primary diagnosis and 26% of borderline PT that recurred were upgraded to malignant subtype on recurrence[57]. This phenomenon could be attributed to multiple factors including inadequate histological sampling of heterogeneous tumour components in the initial excision specimen, dedifferentiation, and/or the acquisition of genetic changes at relapse[95].

Patients with malignant PT who develop local recurrence have a six-fold higher risk of developing distant metastases compared with those without local relapse, highlighting the importance of local tumour control in defining the prognostic course[57]. A systematic literature review involving 66 patients with recurrent/metastatic malignant PT demonstrated long-term disease control in a subset of patients who underwent salvage surgery for their isolated local recurrences[96]. The median survival in this cohort of patients was 72 months compared with 24 months in those with distant disease relapse, indicating that a subset of patients with local recurrence can be cured by salvage surgery[96]. In this setting, adjuvant radiotherapy is often delivered after surgical resection, if not previously received, to reduce the risk of further recurrence[75,96].

Distant metastasis

In malignant PT, the majority of metastatic disease develops within the first 2 years[49,91,93] and confers a poor prognosis, with an estimated median survival of 12 months[42,91,97]. Around 2–3% of patients with malignant PT present with metastatic disease at initial diagnosis[67,98] and the rate of metachronous metastatic spread has been reported to range between 5% and 28%, most commonly to the lungs[35,50,57,59,66,67,91,98]. A few studies also reported metastatic relapse, with rates up to 17%, after initial treatment of borderline PT, but it remains unclear whether these cases were associated with histological transformation at relapse[67,91]. A population-based study of 921 borderline and malignant cases in the Netherlands revealed a 5-year cumulative incidence of distant metastasis of 5% in malignant PT only[74].

In small-volume oligometastatic disease, surgical resection of metastatic sites, referred to as metastasectomy hereafter, may play an important role in achieving durable disease control. A multicentre retrospective study by the French Sarcoma Group identified 51 patients with metastatic malignant PT, of whom 31% (16 patients) underwent metastasectomy with improved clinical outcomes[99]. On multivariable analysis, metastasectomy was an independent predictor of improved OS (median 26 months) compared with patients who were managed non-surgically (median 10 months) ($P = 0.01$)[99]. Additionally, the number of metastatic sites was an independent predictor of OS

(median 31 months for one metastatic site *versus* 7.5 months for two or more sites; $P = 0.01$)[99]. These findings recapitulate the improved survival outcomes reported with metastasectomy in STS in general[100]. Due to paucity of data, it remains uncertain whether stereotactic body radiation treatment (SBRT) may represent an alternative to metastasectomy in the oligometastatic setting in PT. A phase 2 study of SBRT in STS patients with oligometastatic disease showed excellent local control outcomes with negligible toxicity, demonstrating this approach to be a valid alternative treatment modality[101]. As metastatic PT patients are managed along the general principles of STS, SBRT could be considered in such cases. Careful selection of patients for this approach is of paramount importance and needs to consider patient performance status, co-morbidities, disease-free interval, site of metastasis, disease burden, number of involved organs, and patient wishes.

In the setting of metastatic disease not suitable for local treatment, chemotherapy (doxorubicin and/or ifosfamide) is often used with palliative intent. In the study by the French Sarcoma Group, combination chemotherapy was not superior to single-agent treatment in terms of clinical benefit and alkylating agents (with or without anthracyclines) were associated with better clinical benefit compared with anthracyclines alone ($P = 0.049$)[99]. In the second-line setting, partial responses were observed with cisplatin, doxorubicin, and regorafenib, and the response rates with first- and second-line chemotherapy were 31.4% and 16.7% respectively[99]. Recent molecular profiling studies of malignant PT have identified several targetable mutations, including NRAS, PIK3CA, BRAF V600E, and EGFR exon 19/20 insertions[102,103], representing therapeutic targeting opportunities beyond the conventional chemotherapies currently used in clinics. Hence, somatic mutation testing and enrolment in clinical trials are highly encouraged.

Recommendations for recurrent tumour management

- Locally recurrent PT should be treated with further surgical excision and with appropriate excision margins for benign, borderline, and malignant types (evidence/grade V/A).
- Management of biopsy-confirmed recurrent phyllodes should be referred to a unit with shared care from breast and sarcoma MDT (evidence/grade V/A).
- In recurrent malignant PT, adjuvant radiotherapy should be considered, after surgical excision, if not previously received (evidence/grade V/A).
- In small-volume oligometastatic disease, metastasectomy should be considered if appropriate, after sarcoma MDT discussion (evidence/grade V/A).
- In small-volume oligometastatic disease where metastasectomy is not feasible/acceptable, SBRT could be considered (evidence/grade V/A).
- Metastatic malignant PT should be managed as per local guidelines for STS (evidence/grade V/A).
- Enrolment in clinical trials is highly encouraged (evidence/grade V/A).

Germline genetic testing

The genomic landscape of PT continues to be an evolving area where further research is required. To date, the most recognized germline mutation in PT patients is in TP53. One of the largest studies, involving 28 families with germline TP53 mutations, revealed that the overall frequency of malignant PT relative to the general population was 78.1-fold higher, with a large variation by age (55-fold higher for those 30–44 years of age and 149-fold higher for those 45–59 years of age)[13]. A multicentre study of 550 PT patients in the Netherlands showed that the majority (60%) had at least one close relative with a history of cancer and 20% had three or more family members affected by cancer; however, germline genetic testing was underutilized despite patients meeting the testing criteria[17].

In line with the recent update of the NHS England National Genomic Test Directory[104], the panel recommends that germline TP53 testing is considered for:

- Women with malignant PT under 46 years of age and at least one first- or second-degree relative with breast cancer, STS, osteosarcoma, central nervous system tumour, or adrenocortical carcinoma before 56 years of age.
- Women with malignant PT and a previous history of breast cancer, STS, osteosarcoma, central nervous system tumour, or adrenocortical carcinoma, with first cancer occurring before 46 years of age.
- Women with malignant PT before 31 years of age, irrespective of family history.

A PT registry and prospective data collection are necessary to inform whether wider recommendations for germline genetic testing would be more appropriate in the future.

Clinical considerations for MDTs managing PT

Patients should be managed by an MDT including, as a minimum:

- A surgeon with experience in the full range of oncoplastic surgical procedures.
- A pathologist.
- A radiologist.
- An oncologist.
- A specialist nurse (key worker) with appropriate knowledge regarding surgical treatments and adjuvant therapies and provision of level 2 support.

Management of biopsy-confirmed borderline and malignant PT should be referred and discussed at a sarcoma MDT with expert pathology review. Shared care between breast and sarcoma MDT is recommended to guide surgical decisions and the need for adjuvant treatment. There should be clear local pathways are recommended between local breast units and tertiary breast and sarcoma centres.

Patients should have knowledge that PT are rare tumours. Specific points for discussion should include local experience with management of PT and the published evidence including uncertainty regarding long-term clinical and patient-reported outcomes. There should be an opportunity to meet other patients where practical. Written patients information should be available (see *Appendix S2* for suggested contents).

The panel recommends that MDT and Cancer Alliance give consideration to review of national Cancer Outcomes and Services Data set (COSD) coding for PT based on subtypes to facilitate national audit, long-term follow-up, and service provision.

Quality criteria and audit

There is a need for national prospective audit of management and outcomes for PT. Audit and quality considerations are as follows:

- All MDT should participate in comprehensive prospective audit including outcomes[105].
- All clinicians should contribute to future national audits related to PT.
- All MDT should ensure accuracy and consistency in the ICD coding and data collection within national data sets, for example COSD, to facilitate national audit.
- MDT should ensure patients have access to a key worker with expertise in breast surgery and PT.
- Surgical techniques should be optimized to minimize reoperation rates.
- Patient satisfaction with experience, written information, and outcomes should be reviewed.
- Eligible patients should be invited to take part in local and national clinical trials.

Research

The panel has identified gaps in research relating to the management of PT, including: evaluation of imaging evidence of growth of fibroepithelial lesions (including appropriate interval timing and defined growth parameters that should raise suspicion of PT), optimum circumferential margin widths, benefits of adjuvant therapies, and optimal cost-effective clinical and radiological follow-up schedules. A real unmet need is research relating to tumour genome sequencing for metastatic PT to identify novel targets for treatment. Additional research areas include epidemiology, risk factors, and prevention of PT.

Implementation of consensus recommendations

Based on the above discussion, the panel have summarized the recommendations in *Appendix S1* and developed algorithms for management of patients with PT (*supplementary material*), which can be referred to in MDT meetings.

The authors have considered the possible barriers to implementing these recommendations and it was believed that they can be integrated in current clinical practice without significant challenges or cost implications. The wide variation observed in published reviews of practice has identified several units that provide more intensive pathways than those recommended in this document[4,5]. The authors acknowledge that some sections of this document are specific to UK practice. Nevertheless, the consensus recommendations could be generalizable on an international scale.

After publication, dissemination of this document is planned through the ABS, Breast Cancer Now, and Sarcoma UK networks, webinars, bulletins, newsletters, social media, presentations at national and international meetings, and professional connections within the surgical and oncology communities.

As a standard procedure, these recommendations will be reviewed every 3 years by the ABS Clinical Practice and Standards Committee to determine the need for updates.

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Mai K. Bishr (Resources, Visualization, Writing—original draft, Writing—review & editing), Alex Humphreys (Resources, Visualization, Writing—original draft, Writing—review & editing), Mahbubl Ahmed (Methodology, Project administration, Writing—review & editing), Karina Cox (Conceptualization, Methodology, Project administration, Validation, Writing—original draft, Writing—review & editing), Adam Hughes (Resources, Writing—review & editing), Jen Isherwood (Writing—review & editing), Sarah E. Pinder (Project administration, Resources, Writing—original draft, Writing—review & editing), Dionysios D. Remoundos (Methodology, Project administration, Writing—review & editing), Elinor Sawyer (Methodology, Project administration, Writing—review & editing), Muhammed S. Tamimy (Writing—review & editing), and Lisa Whisker (Conceptualization, Methodology, Project administration, Resources, Supervision, Validation, Writing—original draft, Writing—review & editing)

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Not applicable for a consensus recommendation document. There are no new data presented.

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