Original Article

Real-world efficacy of postoperative radiotherapy with a moderate dose-escalation for phyllodes tumors of the breast

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Background: Phyllodes tumors are rare breast tumors comprising less than 1% of cases, categorized as benign, borderline, or malignant. Treatment typically involves complete surgical excision with wide margins. Adjuvant radiotherapy may be recommended for borderline or malignant tumors, or when clear margins cannot be achieved through surgery alone.

Methods: We conducted a retrospective review of 14 women diagnosed with phyllodes tumors between 2015 and 2023. Among them, 36% had benign tumors and 64% had borderline/malignant tumors. The majority (86%) underwent breast-conserving surgery. Postoperative radiation therapy was delivered to the whole breast/chest wall, with a median biologically effective dose (BED) of 92.7 Gy (90.0–102.6 Gy), representing a moderate dose-escalation over conventional breast cancer schedules

Results: After a median follow-up of 48.5 months, no local or distant recurrence were observed. Mild to moderate skin toxicity occurred in all patients: 36% reported grade 1, 43% grade 2, and 21% grade 3 toxicity. One patient developed grade 2 fibrosis during follow-up. No significant correlations were found between the severity of acute/late toxicity and tumor size, surgical approach, or the radiation field's planning target volume (PTV).

Conclusions: Adjuvant radiation therapy appears to be well tolerated and feasible for high-risk phyllodes tumors. However, the decision to utilize radiotherapy should be personalized, considering tumor characteristics and the risks and benefits associated with treatment.

Keywords: Phyllodes breast tumor; radiation therapy; moderate dose-escalation

Received: 01 June 2023; Accepted: 26 July 2023; Published online: 30 July 2023.
doi: 10.21037/tbcr-23-37
View this article at: https://dx.doi.org/10.21037/tbcr-23-37

Introduction

Phyllodes tumors (PTs) are rare breast neoplasms, accounting for less than 1% of all breast tumors. The term "Phyllodes" is derived from the Greek word *phullon*, meaning leaf, because of the leaf-like appearance of its papillary projections observed during histopathological study, which gives it a cracked appearance. The tumor was initially described in 1838 by Johannes Müller, who named it cystosarcoma phyllodes due to its neoplastic appearance with a prominent cystic component (1). In 1982, the World Health Organization renamed it as PT and classified it into three variants: benign, borderline, and malignant, based on the presence of stromal overgrowth with atypia, brisk

mitotic activity, and permeative margins (2).

PTs primarily affect individuals aged 35–55 years, and the benign variant is the most commonly encountered. In their less aggressive forms, these tumors exhibit a similar behavior to fibroadenomas. Malignant PTs comprise approximately 25% of all cases and are characterized by a higher propensity for local recurrence and distant metastasis, with rates ranging from 10% to 65% and 5% to 40%, respectively (3-6). The recommended approach for treating PTs involves complete surgical excision, which can be achieved through mastectomy or conservative surgery with wide margins. However, in cases where the tumor is borderline or malignant, or when it is not feasible to obtain clear margins through surgery alone, adjuvant radiotherapy has been proposed to diminish the risk of recurrence (7-10). Nevertheless, due to the lack of randomized studies with enough patients, the efficacy of radiotherapy as an adjuvant treatment for PTs remains inconclusive.

In this paper, we present the results of our analysis of a series of PTs considered to be at risk for recurrence undergoing postoperative radiotherapy. We also review the existing evidence regarding the use of radiotherapy in the management of these neoplasms. We present this article in accordance with the STROBE reporting checklist (available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-23-37/rc).

Highlight box

Key findings

- Adjuvant radiation therapy is effective and well tolerated in patients with high-risk phyllodes tumors (PTs).
- A moderate dose-escalation over traditional breast dosing is feasible and it is an option worth considering.

What is known and what is new?

- PTs are rare breast tumors with an indolent behavior similar to fibroadenomas in the less aggressive types. However, high-risk borderline/malignant PTs exhibit a propensity for local recurrence and distant metastases.
- We retrospectively analyzed our experience by using postoperative radiotherapy with moderate dose-escalation for PTs with high-risk features, including borderline/malignant histologies and benign PTs with narrow or positive margins after surgery.

What is the implication, and what should change now?

- Although postoperative radiotherapy seems to be useful with a low toxicity profile, further studies with higher number of patients and longer follow-up is desirable to confirm these observations.

Methods

Patients

We conducted a retrospective review of medical records from adult patients who received adjuvant radiation treatment for histologically confirmed primary PTs of the breast at our institution. The analysis included patients with borderline and malignant PTs as well as those with benign PTs characterized by narrow (≤10 mm) or affected margins that prevented further excision. We analyzed the rates of local-relapse free survival, distant-metastasis free survival, and overall survival (OS), along with the acute and late tolerance of radiation treatment. All procedures were conducted in strict accordance with the ethical standards outlined in the Declaration of Helsinki of 1975, revised in 2008, and each patient provided informed consent before their treatment. Due to the retrospective nature of the analysis and the anonymization of patient data in the database, formal approval from the local ethics committee was deemed unnecessary.

Radiation treatment

The standard radiation treatment schedules for breast cancer involve the use of conventional fractionation at 1.8–2.0 Gy, reaching a total dose of 50.4–50.0 Gy in 28.0–25.0 fractions, or moderate hypofractionation with 15 fractions of 2.7 Gy, resulting in a total dose of 40.5 Gy. The linear-quadratic (L-Q) formalism allows for different radiotherapy regimens comparison by calculating the biologically effective dose [$BED = n \times d \times (1 + d(\alpha/\beta)$], where n is the number of fractions, d is the fraction size of the applied regimen, and α/β is the ratio of radiation fractionation sensitivity [which has been assumed to be equal to 4 Gy for soft-tissue sarcomas and for PTs (11)]. Corresponding BED values would be e of 73.1–75.0 Gy and 67.8 Gy for the conventional and moderate hypofractionated schedules used for breast cancer, respectively. The patients with PTs attended in our institution underwent whole breast/chest wall irradiation with different schedules at physician discretion but always trying to reach a BED value above 90 Gy, representing a slight increase over the dose usually used in the postoperative setting for breast cancer and is closer to the dose used for soft tissue sarcomas. Regional lymph nodes were not irradiated in any of the included patients.

Patients were immobilized in the supine position

using a breast wing or T-board with the ipsilateral arm rose above the head. Axial images with a thickness of 5 mm were obtained from the level of the mandible and extended below the inframammary fold. Volumes of interest were defined by using the RayStation® planning system (RaySearch Laboratories, Stockholm, Sweden) and in accordance with European SocieTy for Radiotherapy and Oncology (ESTRO) consensus guidelines (12). The whole breast/chest wall was identified on simulation computed tomography (CT) from the skin edge and up to the ventral side of the pectoralis major muscle. The ipsilateral and contralateral lungs, heart, and contralateral breast were outlined as organs at risk.

Follow-up and evaluation

All patients were evaluated before treatment, weekly during radiotherapy, every 3 months during the first 2 years and every 6 months thereafter by physical examination and image tests including mammography, ultrasound or breast magnetic resonance imaging (MRI), and body CT scan. Acute toxicity was defined as the occurrence of complications during treatment or up to 90 days after completion of treatment. Late toxicities were considered when developing 3 months after the end of treatment. Toxicities were graded according to the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer (EORTC) toxicity scale (13) and were reported by physicians and nurse practitioners.

Follow-up was considered from the date of diagnosis to the date of the last evaluation. Local relapse-free survival (LRFS) and distant metastases-free survival (DMFS) were estimated at the time of first event. Patients dying from intercurrent disease without evidence of tumor were censored at the date of death. OS was defined as the time interval between diagnosis and the date of death, whatever the cause, or to the date of last follow-up. Statistics was performed using SYSTAT, version 20.0 (SPSS, Chicago, IL, USA). Spearman's rank correlation coefficient was used to measure the strength and direction of association between ranked variables. The Spearman correlation coefficient (Rho) can take values from +1 to −1. A Rho of +1 indicates a perfect association of ranks, a Rho of zero indicates no association between ranks and a Rho of −1 indicates a perfect negative association of ranks. The closer Rho is to zero, the weaker the association between the ranks.

Results

From 2015 to 2023, our department attended to a total of 14 patients with histological proven PTs of the breast. All these patients were women, with a median age of 40 (range, 19–57) years old. According to institutional criteria, the clinical indication for adjuvant radiation therapy included 5 cases (36%) classified as benign PTs with close or affected surgical margins and no candidates for re-excision, along with 9 patients (64%) classified as borderline/malignant tumors. Most of patients (86%) underwent breast-conserving surgery. For a comprehensive overview of the patients' characteristics, please refer to *Table 1*.

Four different radiotherapy schedules were used to treat the 14 patients (*Table 1*), with a number of fractions between 15 and 33 and a dose per fraction between 2.0 and 3.6 Gy. The median radiation BED delivered to the patients was 92.7 Gy, with a range of 90.0–102.6 Gy. Except for one patient who received volumetric-modulated arc therapy (VMAT) planning treatment, all others were treated with three-dimensional (3D) conformal radiation therapy. It is worth noting that respiratory control was utilized in only one left-sided patient. In terms of image-guided radiotherapy, two different systems were employed: digitally reconstructed radiograph (DRR) was used in 80% of the cases, while kV-cone-beam was utilized in the remaining cases.

With a median follow-up period of 48.5 (range, 3.0–95.0) months, and a minimum follow-up of 12 months in all but one patient, all patients are alive without evidence of local or distant recurrence. It is important to note that acute skin toxicity was observed in all patients; however, the majority experienced mild to moderate symptoms. Specifically, 5 patients (36%) reported grade 1, 6 patients (43%) reported grade 2, and 3 patients (21%) reported grade 3 acute skin toxicity. Only one patient developed breast grade 2 fibrosis during the follow-up period.

We conducted an analysis using the Spearman correlation coefficient (Rho) to investigate any potential relationship between the severity of acute/late toxicity and various factors, including age, the dose delivered, tumor size, type of surgery, and the planning target volume (PTV) encompassed in the radiation field. However, our findings indicate that there is no significant correlation between these factors and the observed toxicity levels (*Table 2*).

Discussion

PTs are classified based on nuclear pleomorphism, mitotic

Table 1 Patients' characteristics

Characteristics	N [%]
Breast side	
Right	4 [29]
Left	10 [71]
Surgery	
Mastectomy	2 [14]
Conservatory	12 [86]
Tumor size	
T1	4 [29]
T2	4 [29]
T3	5 [36]
T4	1 [7]
Histology	
Benign	5 [36]
Borderline	5 [36]
Malignant	4 [29]
Surgical margins	
Negative	9 [64]
Close/positive	5 [36]
Radiation treatment (n°fx/dfx) (BED)	
30.0/2.0 Gy (90.0 Gy)	3 [21]
20.0/2.7 Gy (90.5 Gy)	3 [21]
32.0/2.0 Gy (96.0 Gy)	4 [29]
15.0/3.6 Gy (102.6 Gy)	4 [29]

T1: tumor ≤5 cm in greatest dimension; T2: tumor >5 and ≤10 cm in greatest dimension; T3: tumor >10 and ≤15 cm in greatest dimension; T4: tumor >15 cm in greatest dimension. N°fx, number of fractions; dfx, dose per fraction; BED, biologically effective dose.

index, presence of infiltrative borders, and stromal growth into three categories: benign, borderline, and malignant tumors. Benign PTs are more common than borderline or malignant ones, with a ratio of 2:1. They share similarities with fibroadenomas but have a higher tendency for local relapse after excision. In the 1960s, Norris and Taylor observed that tumors with a diameter above 4 cm, infiltrated margins, and high levels of nuclear atypia and mitosis (≥3 mitoses per 10 high magnification fields) exhibited a greater risk of recurrence and metastasis (14). PTs, particularly malignant and borderline tumors, but also occasionally benign tumors, can transform into sarcomatous lesions and give rise to distant metastases, primarily in the lungs and less frequently in other organs such as bone, central nervous system (CNS), liver, or muscle tissue (15).

The primary treatment for PTs is surgical intervention, aiming to achieve complete excision with adequate free margins of at least 1–2 cm. The decision between mastectomy and conservative surgery depends on factors such as the breast-to-tumor ratio and the feasibility of obtaining clear margins while considering the desired cosmetic outcome. Although extremely rare, locoregional lymph node involvement has been occasionally described in PT cases (16-18). However, due to its exceptional occurrence, routine axillary lymph node dissection or sentinel lymph node biopsy is not indicated. The majority of patients with PTs can achieve a cure through surgical intervention, and their prognosis is excellent when complete excision is achieved. Five-year OS for patients with nonmalignant (benign or borderline) and malignant phyllodes cystosarcoma were 91% and 82%, respectively. Ten-year OS rates were 79% for nonmalignant PTs and 42% for malignant PTs (19).

However, it is important to note that all PTs tend to recur after surgery, particularly if the excision is incomplete, margins are positive, or the surgical treatment is less aggressive. A meta-analysis conducted by Lu *et al.*, which included 54 studies involving a total of 9,234 PT patients, reported global rates of local relapse after surgery as 8%, 13%, and 18% for benign, borderline, and malignant PTs, respectively (20). Regular follow-up and close monitoring are essential to detect and manage potential recurrences in PT patients. Previous studies have provided significant insights into local recurrences in low or indeterminate grade PTs. Histologic grades higher than those of the primary tumor occur in 28% to 44% of local recurrences in benign and in 14% to 25% of borderline PTs, and approximately 12% to 54% of recurrences can transform into malignant PTs (21). Several risk factors contribute to the occurrence of local recurrence after surgery. These include the presence of mitoses, infiltrative margins, stromal cellularity with atypia and overgrowth, as well as the presence of associated tumor necrosis (19,20).

The aim of adjuvant radiotherapy is to reduce disease recurrence and improve the quality of life for patients with PTs. However, the clinical data supporting the use of adjuvant radiotherapy are limited and sometimes anecdotal. Previous studies have shown significant heterogeneity in various series, including different patient characteristics,

Table 2 Results of the Spearman correlation between analyzed variables with respect to acute and late toxicity

	Age (years)	Size (mm)	PTV	Surgery	Total BED	Acute toxicity	Late toxicity
Age (years)							
Correlation coefficient	1.000	–0.379	–0.178	0.051	–0.535*	0.124	0.103
Sig. (bilateral)	–	0.181	0.542	0.863	0.049	0.673	0.725
N	14	14	14	14	14	14	14
Size (mm)							
Correlation coefficient	–0.379	1.000	–0.163	0.153	0.526	0.127	0.311
Sig. (bilateral)	0.181	–	0.577	0.602	0.053	0.666	0.279
N	14	14	14	14	14	14	14
PTV							
Correlation coefficient	–0.178	–0.163	1.000	0.357	0.437	–0.156	–0.202
Sig. (bilateral)	0.542	0.577	–	0.211	0.118	0.594	0.489
N	14	14	14	14	14	14	14
Surgery							
Correlation coefficient	0.051	0.153	0.357	1.000	–0.154	0.353	–0.113
Sig. (bilateral)	0.863	0.602	0.211	–	0.599	0.216	0.700
N	14	14	14	14	14	14	14
Total BED							
Correlation coefficient	–0.535*	0.526	0.437	–0.154	1.000	–0.129	0.175
Sig. (bilateral)	0.049	0.053	0.118	0.599	–	0.660	0.551
N	14	14	14	14	14	14	14
Acute toxicity							
Correlation coefficient	0.124	0.127	–0.156	0.353	–0.129	1.000	0.074
Sig. (bilateral)	0.673	0.666	0.594	0.216	0.660	–	0.802
N	14	14	14	14	14	14	14
Late toxicity							
Correlation coefficient	0.103	0.311	–0.202	–0.113	0.175	0.074	1.000
Sig. (bilateral)	0.725	0.279	0.489	0.700	0.551	0.802	–
N	14	14	14	14	14	14	14

*, P<0.05. PTV, planning target volume; BED, biologically effective dose; Sig., significance.

surgical treatments, and criteria for adjuvant radiotherapy, what makes the analysis even more complicated. Nonetheless, the use of radiotherapy in the multidisciplinary treatment of PTs has increased in recent decades. A study by Oladeru *et al.*, analyzing the National Cancer Database (NCDB), found an increase in radiotherapy utilization among younger patients with fewer comorbidities and less favorable pathologic features, particularly at academic centers. However, the results did not demonstrate a survival benefit for these patients, and the authors acknowledged limitations such as the lack of local recurrence data and a possible selection bias in offering radiotherapy to patients with poorer prognosis tumors (22). In our series, adjuvant radiotherapy was offered to patients with narrow or affected

margins, including 5 patients with benign tumors treated by breast conserving surgery, and to patients with moderate or high-grade tumors.

There are published data suggesting a decrease in overall and cause-specific survival rates when radiotherapy is added to surgical treatment for PTs. Most of these data are derived from analyses performed in the Surveillance, Epidemiology, and End Results (SEER) database, which has limitations, such as a lack of data on local or distant relapses and can yield conflicting results depending on the specific analyses conducted (10,23,24). It is worth-noting that a recent analysis of the same SEER database revealed that patients treated with mastectomy for PTs smaller than 10 cm had worse cancer-specific survival (CSS) compared to those treated with breast-conserving surgery. However, patients undergoing radiotherapy were not inferior to those not undergoing radiotherapy when stratified by tumor size, suggesting that radiotherapy may have a potential role in CSS for certain patient subgroups (6). Other institutional series have addressed the efficacy of adjuvant radiotherapy for breast PTs. Varghese *et al.* retrospectively analyzed the outcomes of patients with benign PTs and borderline/malignant PTs who underwent conservative surgery or mastectomy. Adjuvant radiotherapy was administered to all non-metastatic malignant PTs and 7 out of 21 patients with borderline PTs. The authors found that for patients with borderline tumors, local radiotherapy is beneficial when margins are close or positive after surgical resection, while there was a trend towards improved local control with adjuvant radiotherapy for malignant PTs (25). Yogi *et al.* reviewed the outcomes of patients with borderline/malignant PTs who received adjuvant radiotherapy after primary tumor surgery. They observed that patients who received early postoperative radiotherapy had no local recurrence, whereas those who received radiotherapy after one month experienced local recurrence (26). Park *et al.* analyzed patients with malignant PTs who underwent conservative surgery or mastectomy with adjuvant radiotherapy. They found that patients who received adjuvant radiotherapy did not experience local relapse, regardless of the type of surgery performed. The presence of tumor necrosis and infiltrative tumor border were identified as risk factors for disease-free survival and cause-specific survival. Having two of these risk factors significantly reduced the rates of both outcomes, indicating that high-risk patients might require more intensified treatment (27). Wong *et al.* investigated the impact of adjuvant radiotherapy on outcomes in patients diagnosed with malignant PTs. The authors observed a beneficial effect of radiotherapy in terms of decreased risk of locoregional failure and improved locoregional recurrence-free survival (28). Boutrus *et al.* conducted a single institutional retrospective review of patients diagnosed with phyllodes breast tumors demonstrating a significant benefit of adjuvant radiotherapy on local control in the borderline/malignant group, both in univariate and multivariate analyses. Although the difference was not statistically significant, patients with benign tumors who received radiotherapy also showed better local control rates (8). Ananthi *et al.* analyzed patients with malignant PTs who underwent conservative surgery or mastectomy with free margins. They found no significant differences in local control, metastasis-free survival, and cause-specific survival with the addition of adjuvant radiotherapy after surgery (7). Barth *et al.* conducted the only prospective study available, which included 46 patients with borderline/malignant PTs. The patients underwent conservative surgery with free margins followed by adjuvant radiotherapy. With a median follow-up of 56 months, none of the 46 patients developed local recurrence (9). Zeng *et al.* performed a meta-analysis of eight studies published between 2001 and 2014, involving a total of 2,708 patients with borderline/malignant PTs. The analysis showed that patients who received radiotherapy after conservative surgery had a lower risk of local relapse. However, no significant differences were found with the addition of radiotherapy after mastectomy, and no significant differences were observed in terms of disease-free survival or OS (29). The authors noted that caution should be exercised when interpreting these data, as only 5-year results were analyzed, whereas other authors who did not observe differences at 5 years with adjuvant radiotherapy after mastectomy did observe them at 10 years. Therefore, the indication for adjuvant radiotherapy after mastectomy should be individualized and discussed with the patient, taking into consideration factors such as age, tumor size, surgery, and histological criteria of aggressiveness (30). Chao *et al.* recently published the findings of a meta-analysis encompassing 17 studies conducted between 1998 and 2019, involving a cohort of 696 women diagnosed with benign, borderline, and malignant breast PTs. Within their analysis, the authors observed a local relapse rate of 12% for patients undergoing simple surgical treatment, whereas the addition of radiotherapy resulted in an 8% local relapse rate. Furthermore, the metastasis rate was 4% for patients receiving radiotherapy, contrasting with an 8% metastasis rate in patients solely treated with surgery (31). However,

it should be noted that both meta-analyses lack specific information regarding the type of radiotherapy employed, as well as the total dose and fractionation utilized. In the meta-analysis conducted by Zeng *et al.*, which included 8 studies, only 4 studies provided details regarding the total dose, while the data concerning dose and fractionation remain unknown in the meta-analysis by Chao *et al.* Due to the resemblances that PTs may bear to certain soft-tissue sarcomas, our study opted for administering slightly higher doses than those typically used in breast cancer treatment, more closely with that employed in the former condition. Overall, these studies provide insights into the use of adjuvant radiotherapy in the management of breast PTs. However, further research is needed to determine the optimal role of radiotherapy in the treatment of this condition. We did not observe any local or distant recurrence in our patients, although longer follow-up of the complete series is mandatory to address these results.

We acknowledge several limitations and weaknesses of our analysis. Firstly, the retrospective nature of the study introduces inherent biases and may affect the reliability of the results. Additionally, the small number of patients included in our analysis limits the generalizability of our findings. The low number of observed events further restricts the statistical power of our study, making it challenging to draw definitive conclusions. Furthermore, the relatively short follow-up period for the entire series may not capture long-term outcomes and potential late effects of adjuvant radiotherapy. Moreover, we recognize that the decision to offer adjuvant radiotherapy for benign PTs can be debatable, even in cases with narrow margins. The existing evidence regarding the use of adjuvant radiotherapy in these cases is complex and does not provide clear-cut guidelines.

Conclusions

The decision to use adjuvant radiotherapy for PTs should be individualized and based on a comprehensive assessment of the patient's specific characteristics, tumor features, and the risks and benefits associated with radiotherapy, such as malignant subtype, borderline, or close margins. In order to make robust treatment decisions, multidisciplinary discussions involving oncologists, surgeons, and radiation oncologists are essential. This collaborative approach ensures that all relevant perspectives are considered and facilitates the development of the most appropriate treatment strategy for each patient. Further research and well-designed studies are necessary to gain a better understanding of the role of adjuvant radiotherapy in the management of PTs and its impact on long-term outcomes. These future studies should aim to address the limitations of previous research and provide more robust evidence to guide clinical practice effectively.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-23-37/rc

Data Sharing Statement: Available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-23-37/dss

Peer Review File: Available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-23-37/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-23-37/coif). AM serves as an unpaid editorial board member of *Translational Breast Cancer Research* from March 2023 to February 2025. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and informed consent was taken from all the patients. Due to the retrospective nature of the analysis and the anonymization of patient data in the database, formal approval from the local ethics committee was deemed unnecessary.

References

1. Müller J. Ueber den feinern Bau und die Formen der krankhaften Geschwülste. Berlin: G. Reimer; 1838.
2. The world Health Organization Histological Typing of Breast Tumors--Second Edition. The World Organization. Am J Clin Pathol 1982;78:806-16.
3. Spitaleri G, Toesca A, Botteri E, et al. Breast phyllodes tumor: a review of literature and a single center retrospective series analysis. Crit Rev Oncol Hematol 2013;88:427-36.
4. Strode M, Khoury T, Mangieri C, et al. Update on the diagnosis and management of malignant phyllodes tumors of the breast. Breast 2017;33:91-6.
5. Guillot E, Couturaud B, Reyal F, et al. Management of phyllodes breast tumors. Breast J 2011;17:129-37.
6. Chen C, Huang X, Xu Y, et al. Rethinking on the management strategy of malignant phyllodes tumor of the breast: An analysis based on the SEER database. Medicine (Baltimore) 2023;102:e33326.
7. Ananthi B, Rama R, Priya I, et al. Is there a survival benefit with adjuvant radiotherapy in margin negative malignant phyllodes tumor of the breast after mastectomy? A single institutional study. Revista de Senología y Patología Mamaria 2021;34:214-9.
8. Boutrus RR, Khair S, Abdelazim Y, et al. Phyllodes tumors of the breast: Adjuvant radiation therapy revisited. Breast 2021;58:1-5.
9. Barth RJ Jr, Wells WA, Mitchell SE, et al. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. Ann Surg Oncol 2009;16:2288-94.
10. Zhao W, Tian Q, Zhao A, et al. The role of adjuvant radiotherapy in patients with malignant phyllodes tumor of the breast: a propensity-score matching analysis. Breast Cancer 2021;28:110-8.
11. Koukourakis IM, Zygogianni A, Kouloulias V, et al. Successful Treatment of a Locally Recurrent and Metastatic Malignant Phyllodes Tumor with Accelerated Radiotherapy and Nab-Paclitaxel, Cisplatin, and Liposomal Doxorubicin Chemotherapy. Chemotherapy 2021;66:82-6.
12. Offersen BV, Boersma LJ, Kirkove C, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. Radiother Oncol 2015;114:3-10.
13. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995;31:1341-6.
14. Norris HJ, Taylor HB. Relationship of histologic features to behavior of cystosarcoma phyllodes. Analysis of ninety-four cases. Cancer 1967;20:2090-9.
15. Mituś JW, Blecharz P, Walasek T, et al. Treatment of Patients with Distant Metastases from Phyllodes Tumor of the Breast. World J Surg 2016;40:323-8.
16. Koh VCY, Thike AA, Tan PH. Distant metastases in phyllodes tumours of the breast: an overview. Applied Cancer Research 2017;37:15.
17. Le QH, Mai VT. Malignant phyllodes tumor with synchronous metastases to axillary lymph nodes, lung at the presentation: a case report and literature review. J Surg Case Rep 2021;2021:rjab302.
18. Johnson ED, Gulbahce E, McNally J, et al. Malignant Phyllodes Tumor Presenting in Bone, Brain, Lungs, and Lymph Nodes. Case Rep Oncol 2016;9:861-8.
19. Chaney AW, Pollack A, McNeese MD, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer 2000;89:1502-11.
20. Lu Y, Chen Y, Zhu L, et al. Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. Ann Surg Oncol 2019;26:1263-75.
21. Jabeen D, Vohra LM Sr, Siddiqui T, et al. Recurrent Phyllodes Tumour of the Breast Transforming to a Fibrosarcoma. Cureus 2020;12:e7457.
22. Oladeru OT, Yang DD, Ma SJ, et al. Patterns of care and predictors of adjuvant radiation therapy in phyllodes tumor of the breast. Breast J 2020;26:1352-7.
23. Zhang H, Tang S, Biskup E, et al. Long-term Survival After Diverse Therapeutic Modalities in Malignant Phyllodes Tumors of the Breast. Technol Cancer Res Treat 2022;21:15330338221121086.
24. Chen CY, Ya-Chen. Better survival was found in patients treated with breast-conserving surgery compared with mastectomy in malignant phyllodes tumor of the breast. Updates Surg 2023. [Epub ahead of print]. doi: 10.1007/s13304-023-01547-y.
25. Varghese SS, Sasidharan B, Manipadam MT, et al. Radiotherapy in Phyllodes Tumour. J Clin Diagn Res 2017;11:XC01-3.

26. Yogi V, Singh OP, Malviya A, et al. Effect of postoperative time for adjuvant radiotherapy in malignant phyllodes tumor: An institutional experience. J Cancer Res Ther 2018;14:1054-8.
27. Park HJ, Ryu HS, Kim K, et al. Risk Factors for Recurrence of Malignant Phyllodes Tumors of the Breast. In Vivo 2019;33:263-9.
28. Wong RX, Koh YS, Wong FY, et al. The Impact of Radiotherapy and Histological Risk Factors on Outcomes in Malignant Phyllodes Tumors. Clin Breast Cancer 2020;20:e695-700.
29. Zeng S, Zhang X, Yang D, et al. Effects of adjuvant radiotherapy on borderline and malignant phyllodes tumors: A systematic review and meta-analysis. Mol Clin Oncol 2015;3:663-71.
30. Belkacémi Y, Bousquet G, Marsiglia H, et al. Phyllodes tumor of the breast. Int J Radiat Oncol Biol Phys 2008;70:492-500.
31. Chao X, Chen K, Zeng J, et al. Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer 2019;19:372.

doi: 10.21037/tbcr-23-37
Cite this article as: Álvarez B, Montero A, Ciérvide R, García-Aranda M, Valero J, Chen-Zhao X, López M, Alonso R, García J, Hernando O, Sánchez E, de la Casa MA, Fernandez-Letón P, Rubio C. Real-world efficacy of postoperative radiotherapy with a moderate dose-escalation for phyllodes tumors of the breast. Transl Breast Cancer Res 2023;4:19.

