National Comprehensive Cancer Network®

NCCN 2026 Breast Cancer Congress with Updates from the 2025 San Antonio Breast Cancer Symposium

Phyllodes Tumors of the Breast: Challenges in Diagnosis and Treatment

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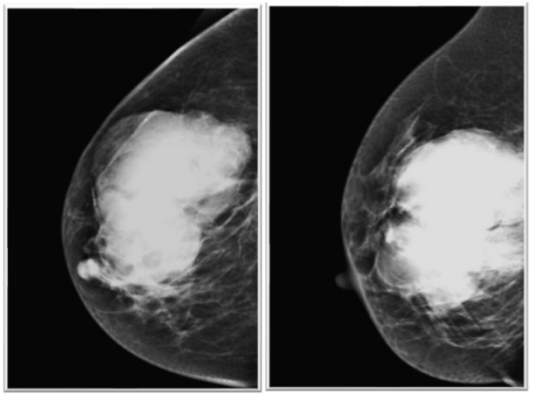
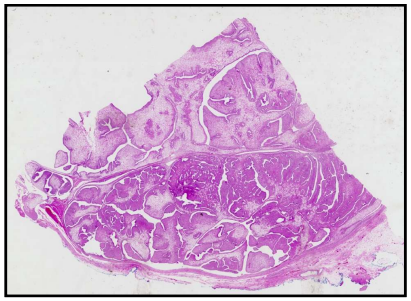
Introduction: Phyllodes Tumors

- First described by Johannes Müller, 1838 – “cystosarcoma phyllodes”
- ***Rare*** *fibroepithelial breast neoplasms*
- Annual incidence: *1-2 cases/100,000**
- Median age is 40-45 years
- Leaf-like architecture, cleft-like epithelial spaces, hypercellular stroma
- *Benign*, *Borderline*, & *Malignant* by scaled histopathologic features

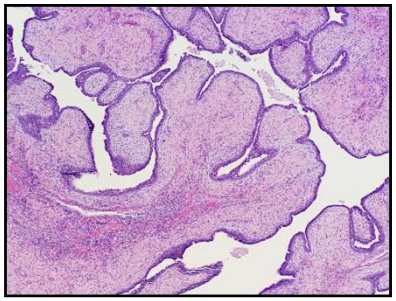


66 F, 10.0cm borderline phyllodes

Case Courtesy of Dr. LH Rosenberger



Whole mount, ultra-low power, **malignant**, micrograph courtesy of Dr. Rex Bentley



40x, **benign** phyllodes, micrograph courtesy of Dr. Rex Bentley

- Reimer G, Berlin, Germany, 1838.
- Rosen PP. Tumors of the Mammary Gland. Washington, DC: AFIP, 1993.
- Rosen PP. Rosen’s Breast Path. Lippincott William Wilkins, NY, USA. 2001. 2nd Ed.

World Health Organization Classification

COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Resection Specimens From Patients with Phyllodes Tumor of the Breast

https://documents.cap.org/protocols/Breast.Phyllodes_1.1.0.1.REL_CAPCP.pdf

	Histologic feature	Benign	Borderline	Malignant
1.	Stromal cellularity	Mild	Moderate	Marked
2.	Stromal atypia	Mild or none	Mild or moderate	Marked
3.	Stromal overgrowth	Absent	Absent or very focal	Present
4.	Mitotic rate	≤4 mitoses per 10 HPFs or <2.5 mitoses per mm^2	5 - 9 mitoses per 10 HPFs or 2.5 - 5 mitoses/mm^2	≥10 mitoses per 10 HPFs or ≥5 mitoses/mm^2
5.	Tumor border	Circumscribed	Usually circumscribed but may be focally infiltrative	Focally or extensively infiltrative (permeative)
+1	Malignant heterologous stromal elements	Absent	Absent	Sometimes present

HPF: High power field (40x objective and 10x eyepiece)

World Health Organization, Classification of Tumours, **5th Ed**, Volume 2: Breast Tumours. Lyon, **2019**, 172-176.

World Health Organization Classification

COLLEGE of AMERICAN PATHOLOGISTS

Important Note

The American Joint Committee on Cancer (AJCC) eighth edition and the World Health Organization (WHO) recommend staging malignant phyllodes tumors according to guidelines established for soft tissue sarcomas – extremity and trunk. T category, N category and stage group assignments do not apply to benign or borderline tumors. An abbreviated stage group table that only applies to malignant phyllodes tumors is included in the Explanatory

Authors

Stuart J. Schnitt, MD*; Laura H. Ros
FCAP; James L. Connolly, MD.
With guidance from the CAP Cancer
* Denotes primary author.

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor 5 cm or less in greatest dimension
___ pT2: Tumor more than 5 cm but not more than 10 cm
___ pT3: Tumor more than 10 cm but not more than 15 cm
___ pT4: Tumor more than 15 cm in greatest dimension

AJCC Prognostic Stage Groups

T	N	M	Stage group
T1	N0	M0	≤ 5cm II
T2	N0	M0	>5cm - ≤10 IIIA ★
T3, T4	N0	M0	>10cm IIIB
Any T	N1	M0	IV
Any T	Any N	M1	IV

World Health Organization, Classification of Tum
5th Ed, Volume 2: Breast Tumours. Lyon, **2019**, 17

Distribution of Phyllodes Subtypes

TABLE 1 Characteristics of the included studies

Study	Year	Time frame	Country	Age (years)[c]	Total patients (*n*)	Grade (*n*)		
						Benign	Borderline	Malignant
Yom et al.	2015	1989–2008	Korea	36.44	285	191	61	33
Narayanakar et al.	2015	2001–2012	India	38	162	95	29	38
Ng et al.	2015	NA	Singapore	43	97	57	29	11
Akrami et al.	2015	1999–2013	Iran	39	129	105	8	16
Xiao et al.	2015	1993–2012	China	NA	127	75	41	11
Ouyang et al.	2016	2005–2013	China	37.3	225	225	0	0
Borhani-Khomani et al.[e]	2016	1999–2014	Denmark	45.6	479	354	89	0
Ruvalcaba-Limon et al.	2016	2005–2015	Mexico	41.7	305	179	43	32
Moutte et al.	2016	2003–2013	France	37.9	76	67	9	0
Bellezza et al.	2016	1988–2009	Italy	42	62	40	13	9
Kim et al.	2016	2000–2010	Korea	40.1	194	153	27	16
Tremblay-LeMay et al.[e]	2017	1998–2010	Canada	44.4	114	81	20	13
Moo et al.	2017	2002–2013	USA	35	216	216	0	0
Matos et al.	2017	1976–2013	Brazil	45.9	52	30	11	11
Varghese et al.	2017	2005–2014	India	43	92	55	21	16
Wang et al.	2018	2014–2015	China	NA	54	33	11	10
Ganesh et al.	2018	1999–2017	Canada	48.9	79	9	17	53
Rodrigues et al.	2018	1999–2014	Canada	48	183	81	49	49
Choi et al.	2018	1981–2014	Korea	43	362	0	127	235
Co et al.	2018	1998–2014	Hong Kong	44	469	281	124	64
Zhou et al.	2018	2002–2013	China	41	404	168	184	52
Chng et al.	2018	2006–2015	Singapore	37.7	240	196	27	17
Slodkowska et al.	2018	1994–2012	Canada	NA	94	45	28	21
Sevinc	2018	1994–2017	Turkey	40.6	122	108	14	0

*Meta-analysis including benign- or malignant-only series

Benign	**64%**
Borderline	**20%**
Malignant	**16%**

Singapore National Series
N=605

- Benign **72.7**%
- Borderline **18.4**%
- Malignant **8.9**%

United States Multi-Center
N=550

- Benign **68.9**%
- Borderline **19.6**%
- Malignant **10.5**%

Benign: 70 %
Borderline: 20 %
Malignant: 10 %

Lu, et al. Ann Surg Oncol. 2019; 26:1263-1275.
Tan, et al. J Clin Pathol. 2012; 65:69-76.
Rosenberger, et al. J Clin Oncol, 2021; 39:178-189.

Local & Distant Recurrence Rates

Pooled **local** recurrence rates:

TABLE 2 Local recurrence (LR) rat

Grade of PTs	ES	95% CI
Overall PTs	0.12	0.10–0.14
Benign PTs	0.08	0.06–0.09
Border PTs	0.13	0.11–0.16
Malignant PTs	0.18	0.14–0.21

ES effect size, *CI* confidence interval

Benign: **8%**
Borderline: **13%**
Malignant: **18%**

Overall *pooled* recurrence = **14.9%**

★ **20%** *upgrade* with LR

- World J Surg. 2006; 30:1414-1421
- J Clin Oncol. 2021; 39:178-189
- J Clin Pathol. 2012; 65:69-76

Local & Distant Recurrence Rates

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- World J Surg. 2006; 30:1414-1421
- J Clin Oncol. 2021; 39:178-189
- J Clin Pathol. 2012; 65:69-76

Pooled **distant** metastatic rates:

Benign	0.1%
Borderline	1.6%
Malignant	16.7%

~75% of metastases to the **lungs**
Other sites: **bone, brain, *unusual***
Prognosis: median OS = *7-15 months* ★

Reason, Rosenberger, BMJ Case Rep. 2024; 17(7): e258640.

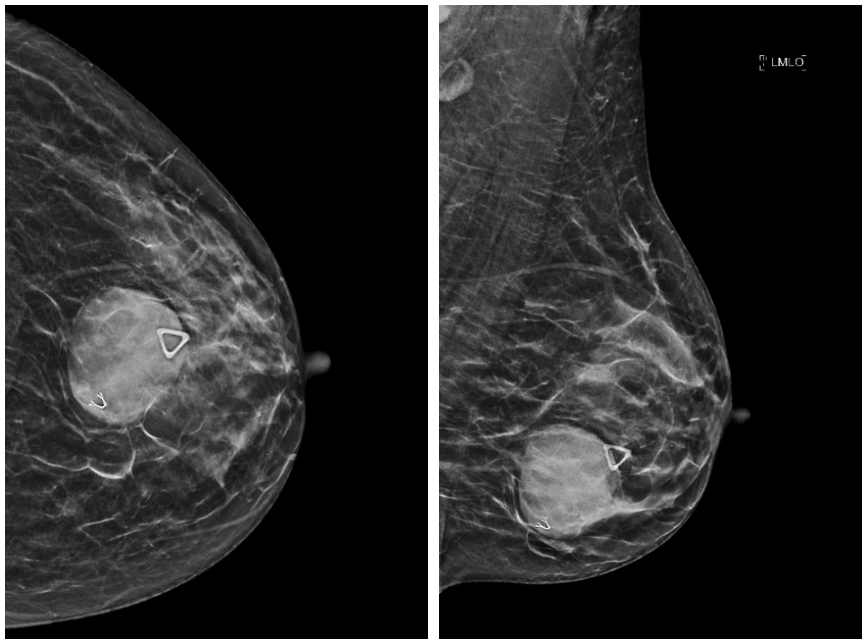
- Tan, et al. Histopathology. 2016; 66(1):5-21
- Palassini, et al. Breast Ca Res Treat. Epub, Feb 2022.
- Mitus, et al. World J Surg. 2016; 40:323-328

Case #1: Unusual Scar-Based Recurrence & *Upgrade*

41 year old
Surgery: "benign" excisional biopsy –
(grew *rapidly* before excision)

- fibroadenoma? benign phyllodes?

3 years later: enlarging mass, 4.0cm oval
Rapid growth, x2 mo –> Surgical excision



Surgery: BCS **9.0cm borderline phyllodes**

- **Stromal cellularity:** *not reported*
- **Stromal atypia:** Moderate
- **Stromal overgrowth:** Present
- **Histologic tumor border:** Infiltrative, focal
- **Mitoses:** 6 /10 hpf
- **Malignant heterologous elements:** *not reported*
- **Margins:** negative, *widths not reported*

- ***No adjuvant radiation***

Case #1: Unusual Scar-Based Recurrence & *Upgrade*

18 months later – new rapidly enlarging scar-based lesion

PATHOLOGY: **3.5cm malignant phyllodes**

- **Stromal cellularity:** marked
- **Stromal atypia:** marked
- **Stromal overgrowth:** present
- **Histologic tumor border:** infiltrative, extensive
- **Mitoses:** **23** /10 hpf
- **Malignant heterologous elements:** not identified

Histologic upgrade, Completion TM, No RT

Case Courtesy of LH Rosenberger

Factors Associated w/ Local Recurrence

Phyllodes ***grade***, tumor ***size***, surgical ***margin status***
Pathologic features: stromal **atypia**, **stromal overgrowth**, **mitoses**, **necrosis**

Positive Margins *Matter*

Significantly *increased* local recurrences:

- Chen (N=172)
- Cheng (N=182)
- Spitaleri (N=172)
- Jang (N=164)
- Co (N=465)
- Ben Hassouna (N=106)
- Belkacemi (N=443)
- Spanheimer (N=125)
- Tan (N=605)
- Jang (N=164)

Positive Margins are *OK*

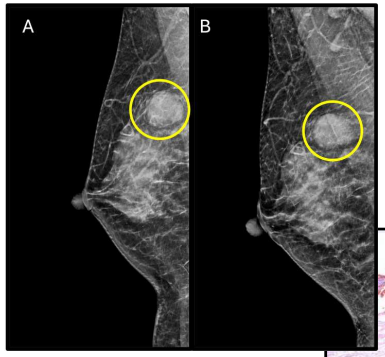
A negative margin *may not* be necessary

- Yom (N=285)
- Kim (N=193)
- Moo (N=246, *Benign only*)
- Lu (2019 Meta-analysis *Benign/BL only*)

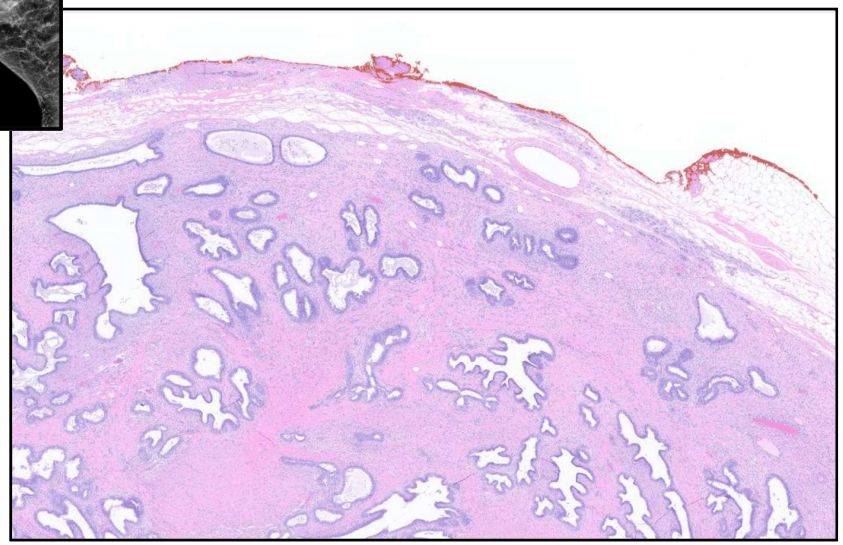
Significant limitations

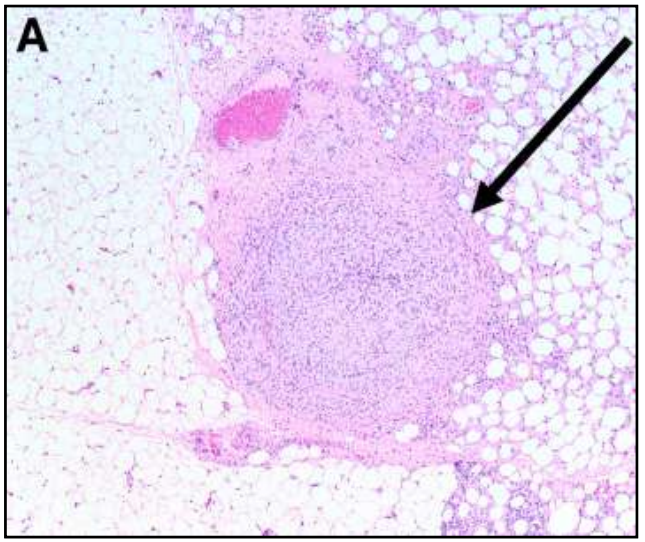
- Retrospective and small series
- Short follow up
- Few recurrence events
- Combined analyses (BPT, BLPT, MPT)

Negative Margin *may not* be Negative



- Well-circumscribed borderline phyllodes tumor
- Returned to OR for wider margins
- Distinct ***satellite nodule*** identified in re-excision specimen





**Case series of N=10 forthcoming*

BLPT, well-circumscribed histologic tumor border

Reason, Rosenberger. Cureus, 2025; 17(3):e79890.

BENIGN Phyllodes Tumors

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NCCN Guidelines Version 1.2026
Phyllodes Tumor

NCCN Guidelines Inde
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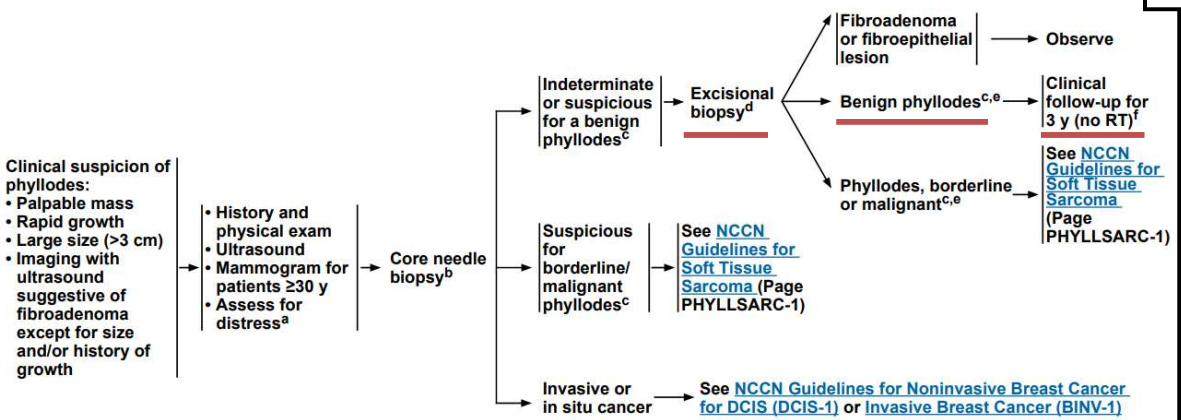

[a] Refer to the NCCN Guidelines for Distress Management (DIS-A) for the NCCN Distress Thermometer and Problem List, which includes social determinants of health.
[b] FNA or core biopsy may not distinguish a fibroadenoma from a phyllodes tumor in some cases. The sensitivity of core biopsy for the diagnosis of phyllodes tumor is greater than that of FNA biopsy, but neither core biopsy nor FNA biopsy can always differentiate phyllodes tumors from fibroadenomas. In cases with clinical suspicion for phyllodes tumor, excision of the lesion may be needed for definitive pathologic classification.
[c] Genetic counseling and testing if patient is at risk for hereditary cancer syndromes, particularly breast, ovarian, and pancreatic cancer.
[d] Excisional biopsy includes complete mass removal, but without the intent of obtaining surgical margins.
[e] The Panel endorses the College of American Pathologists Protocol for standardized pathology reporting for all phyllodes tumors (https://documents.cap.org/protocols/Breast.Phyllodes_1.1.0.1.REL_CAPCP.pdf).
[f] Adjuvant RT is not indicated for positive margins.

Note: All recommendations are category 2A unless otherwise indicated.

PHYLL-1

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer

Version 1.2026 — January 16, 2026

- **Excisional biopsy includes complete removal, *without* an intent for surgical margins**
  - Complete excision
  - Capsule intact
  - No morcellation
- **Fully excised BPT**
  - Consider genetics
  - No routine re-excision
  - No radiation
- **Surveillance**
  - Variable recommendations*
  - Consider tumor factors & shared decision-making

2023: Management of Benign Phyllodes Tumors: A Dutch Population-Based Retrospective Cohort Between 1989-2022.

- **Intent**: margin controversy, benign phyllodes
- **Source:** Netherlands, **Dutch nationwide pathology databank** (Palga)
  - **National coverage** since 1991
  - All reports are digitally archived here
- **Years:** 1989 – 2022
- **N = 1908 benign phyllodes**

RESULTS

- Median age, **43 years** (IQR, 34 - 52)
- Median tumor size, **30 mm** (IQR, 19-40)
- 95% breast-conservation (25%, ≥2 operations)
- Median time to LR, **31 months** (IQR, 15-61)
- Local recurrence rate, **6.2%** (N=119)
  - LR w/ *negative* margins, **4.0%**
  - LR w/ *positive* margins, **8.9%**
- **Multi-variable analysis**
  - No assoc w/ age, year, size, re-excisions
  - LR assoc w/ B/L status, ***positive margin*** (**+** vs. **-**, ***OR 2.4*** (1.3 – 4.5, p = 0.006)

Conclusions:

- The LR rate for benign PT remains low (6.2%), even in cases of *positive* surgical margins (8.9%), *obviating* the need for re-excision in these patients.

(positive margin okay) – supports the NCCN, UK, & Canadian national guidelines

Van Olmen, Ann Surg Oncol. 2023; 30:8344-8352.

Borderline & Malignant PT

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Soft Tissue Sarcoma

Version 1.2026 — January 16, 2026

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NCCN Guidelines Version 1.2026
Borderline Phyllodes Tumor of the Breast

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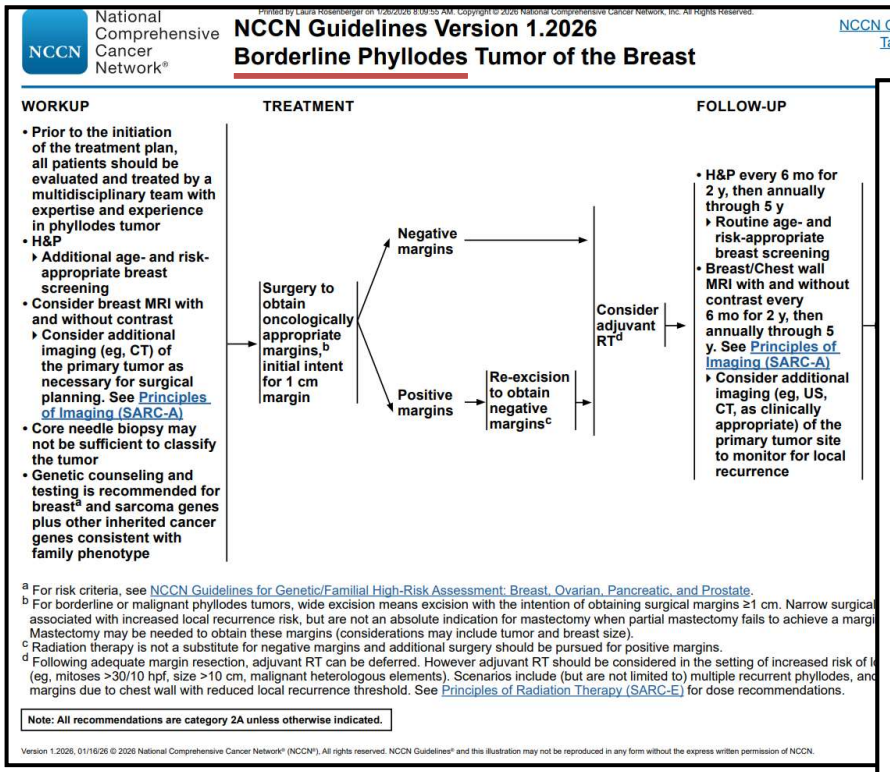

[a] For risk criteria, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate.
[b] For borderline or malignant phyllodes tumors, wide excision means excision with the intention of obtaining surgical margins ≥1 cm. Narrow surgical
associated with increased local recurrence risk, but are not an absolute indication for mastectomy when partial mastectomy fails to achieve a margi
Mastectomy may be needed to obtain these margins (considerations may include tumor and breast size).
[c] Radiation therapy is not a substitute for negative margins and additional surgery should be pursued for positive margins.
[d] Following adequate margin resection, adjuvant RT can be deferred. However adjuvant RT should be considered in the setting of increased risk of l
(eg, mitoses >30/10 hpf, size >10 cm, malignant heterologous elements). Scenarios include (but are not limited to) multiple recurrent phyllodes, and
margins due to chest wall with reduced local recurrence threshold. See Principles of Radiation Therapy (SARC-E) for dose recommendations.

Note: All recommendations are category 2A unless otherwise indicated.

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NCCN Guidelines Version 1.2026
Malignant Phyllodes Tumor of the Breast

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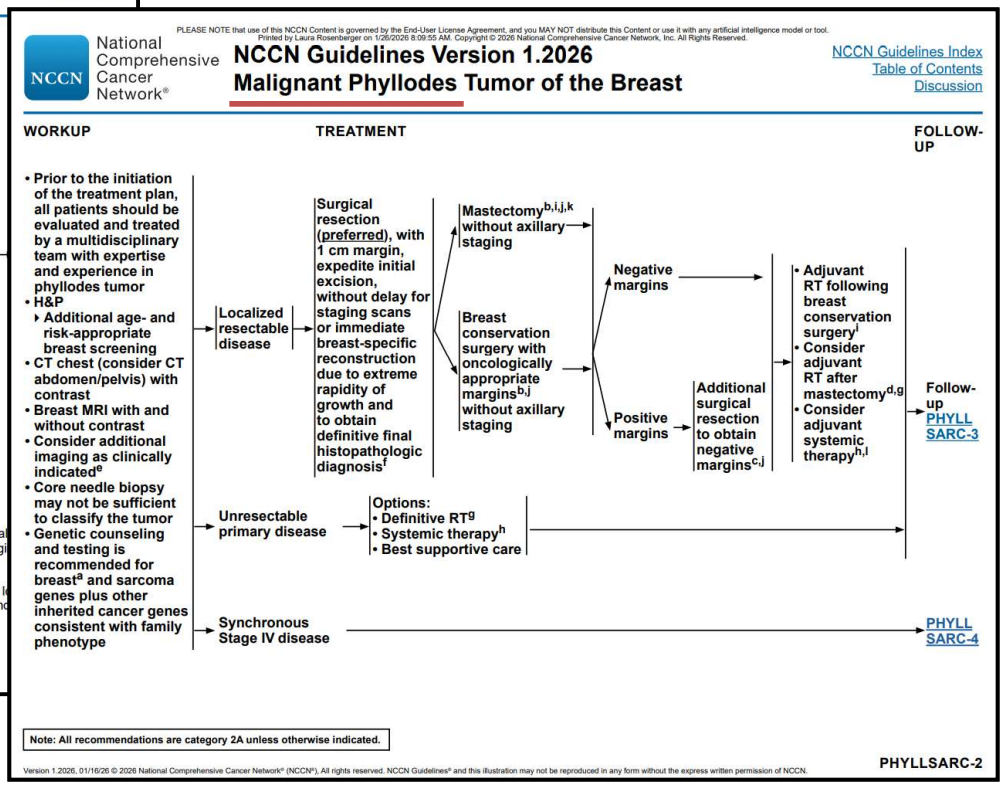

Note: All recommendations are category 2A unless otherwise indicated.

PHYLLSARC-2

2007: Malignant Phyllodes Tumor of the Breast: Local Control Rates with *Surgery Alone*.

- Pezner, 2007, USA
- IMPAC National Oncology Database:
  - N=**478 Malignant PT**, surgery *alone*
  - Median follow up = 64 months
- 5-year Local Recurrence:
  - **20.6%** for lumpectomy
  - **8.8%** for mastectomy

Tumor Size	Lumpectomy (N=169)	Mastectomy (N=207)
0 – 2 cm	9%	0
2 – 5 cm	15%	5%
5 – 10 cm	41%	12%
10 – 20 cm	No cases	15%

A 15% risk of LR is an appropriate threshold to consider adjuvant XRT

Pezner. Int J Rad Oncol Biol Phys. 2007; 71:710-713.

2020: Surgical Margins & Adjuvant Therapies in Malignant Phyllodes: A Multicenter Retrospective Study

- Pezner, 2007, USA
- IMPAC National Oncology Database:
  - N=**478 Malignant PT**, surgery *alone*
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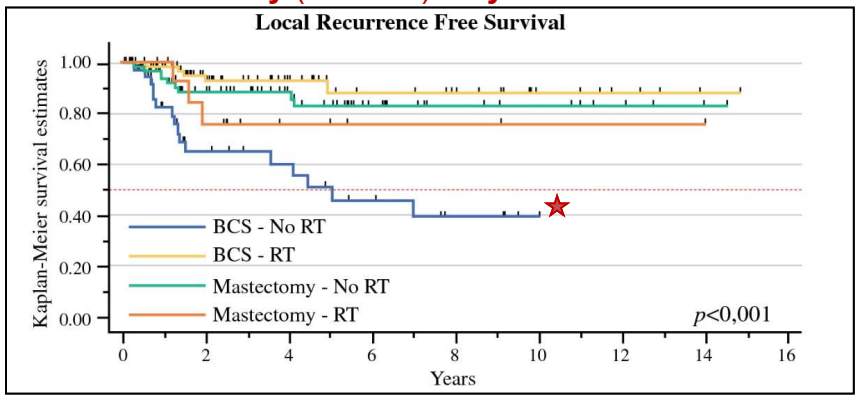
Pezner. Int J Rad Oncol Biol Phys. 2007; 71:710-713.

- Neron, 2020, France
- French Sarcoma Group (13 sites)
  - Malignant phyllodes: N=212, **size**: **5.8cm**
- Surgery type: **73.3%** Mastectomy
- Adjuvant RT: 43.3% (more freq. w/ mast)
- Local Recurrence: **16.6%** @ 50 months

BCS w/out RT, assoc. w/ **lowest LRFS** (p<0.001)
MVA: **Mastectomy** (vs. BCS) ***only factor*** **assoc. w/ LRFS**



Neron. Ann Surg Oncol. 2020; 27:1818-1827.

2024: Real-World Data on Malignant & Borderline Phyllodes: A Population-Based Study of *921 Cases* in the Netherlands

- **Source:** Netherlands, Dutch nationwide pathology databank (Palga)
  - National coverage since 1991
  - All reports are digitally archived here
- **Years:** 1989 – 2020
- **N = 921 (N = 452 BLPT, N = 469 MPT)**

RESULTS

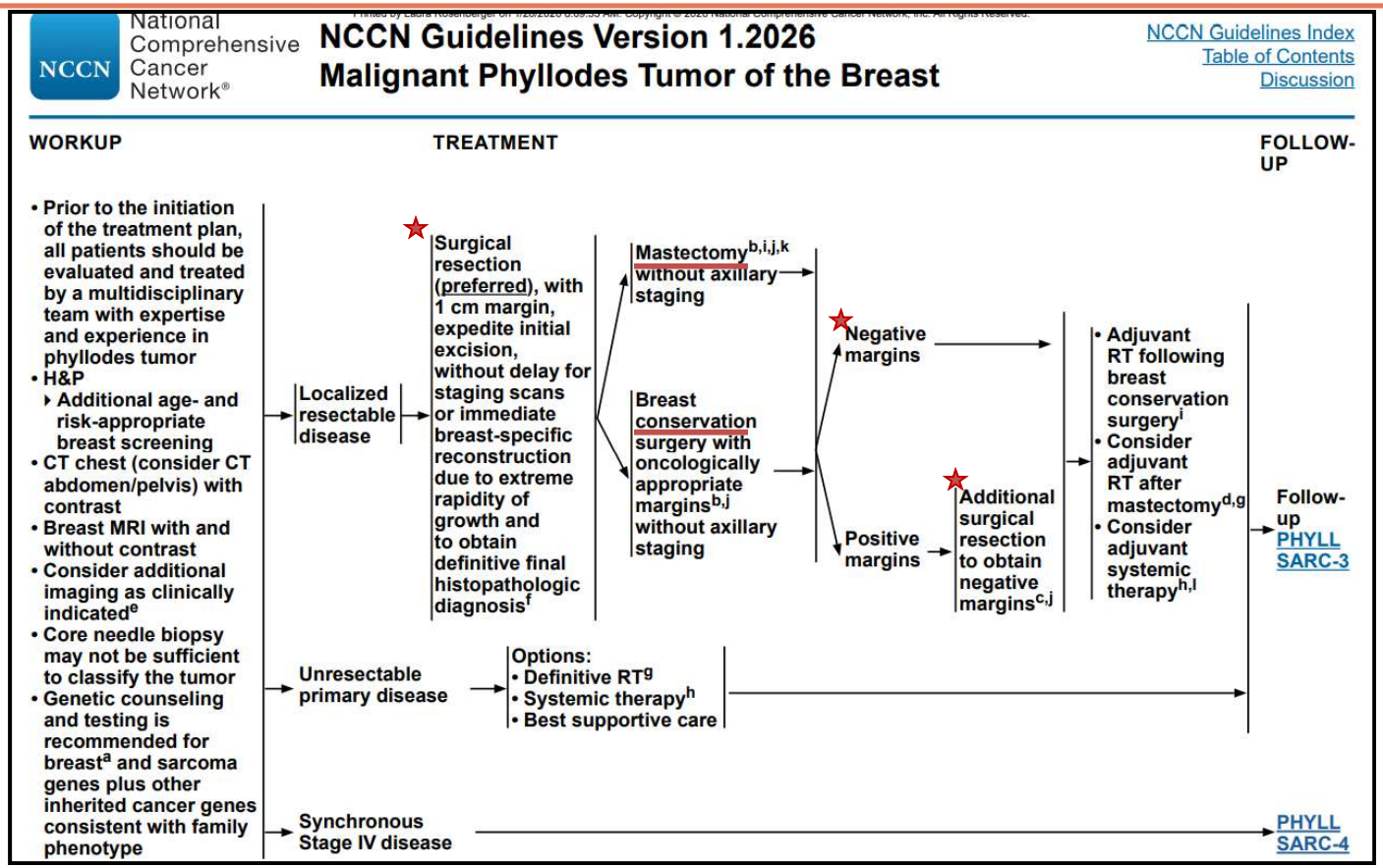
- Median age, **50** years (**BLPT**), **55** years (**MPT**)
- Median tumor size, **3.8cm** (**BLPT**), **4.7cm*** (**MPT**)
- **Surgery**:
  - BLPT **18.6%** mastectomy
  - MPT **53.5%** mastectomy
- **Adjuvant RT**: 2.9% BLPT, **14.7% MPT**
- **Median follow-up**: *9.6 years*
- Local recurrence: BLPT: **9.3%**, MPT: **8.7%**
- Metastases: BLPT: **0%**, MPT: **10.4%**
- **MVA: risk factors assoc. w/ LR**
  - **Malignant** (vs. BLPT): *p=0.01*
  - **Positive margin** (vs. 0-1, >1mm) *p=<0.001*
  - **Breast conservation** (vs. TM): *p=<0.001*
  - **Tumor Size** (>20 vs. 0-19mm): *p=<0.001*
  - Radiation (vs. no RT): ***p=0.46***
- *No difference* in 5-year LR w/ 0-1mm vs. >1mm
  - **analyzed borderline/malignant together*

Conclusions:

- Consider mastectomy for MPT
- Positive margins impact LR
- However narrow negative margins were not associated with higher risk of LR*.

Bartels. Eur J Cancer. Apr:201:113924, Epub 2024 Feb

What are the *SURGICAL* options?



Should we deliver adjuvant radiation therapy?

Gnerlich, 2014, USA

- NCDB, 1998-2009
- Malignant PT only
- **N=3,120** (57% BCS, 42% mastectomy)
- 14% received RT, assoc. 50+ years, >10cm size
- Overall LR; 14%
- In adjusted models: **RT reduced risk of LR (HR 0.53, p=0.037)**

Gnerlich. Ann Surg Oncol. 2014; 21:1222-1230.

Bartels, 2024, Netherlands

- Dutch national study
- **N=921** (452 BLPT + 469 MPT)
- 9% received RT (15% MPT)
- In subgroup analysis, **RT after BCS for MPT had improved LRR of 5% vs. 19% w/out RT**
- *RT did not hold statistical significance in MVA

Bartels. Eur J Cancer. Apr:201:113924, Epub 2024, Feb.

Chao, 2019, China

- Systematic review & meta-analysis
- 17 studies (8 BLPT+MPT, 9 MPT)
- **N=696**
- Pooled LR rates:
  - **Surgery +RT = 8%**
  - Surgery alone = 19%

Chao. BMC Cancer. 2019; 19:372-378.

Should we deliver adjuvant radiation therapy?

Belkacemi, 2008, France

- Rare Cancer Network, 1971-2003
- Retrospective, N=80 BLPT, N=79 MPT
- Mastectomy **15%**, Adjuvant RT **9%**
- LR **28%*** for MPT

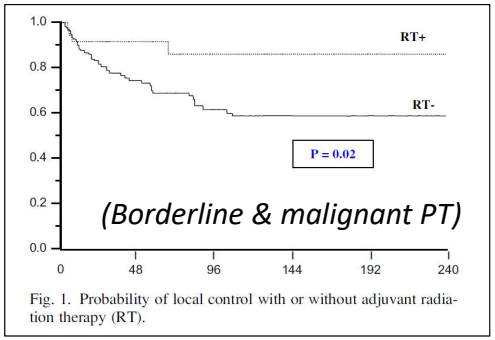


Fig. 1. Probability of local control with or without adjuvant radiation therapy (RT).

- **Adjuvant RT improved LC** (**14%** **vs.** **41%**), RT **held** in MVA

Belkacemi, et al. Int J Rad Onc Bio Phys. 2008; 70:492.

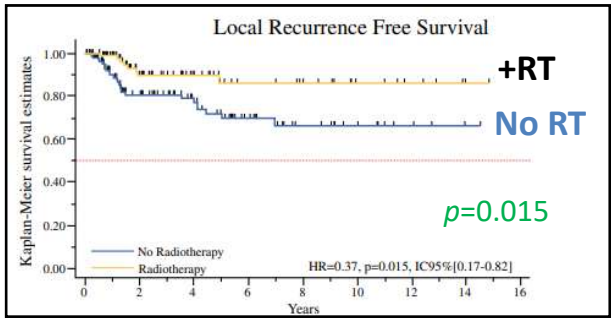
Barth, 2009, USA

- *Prospective,* multicenter, adjuvant RT
- **N=46**, all BCS, all neg margins, *no tumor on ink*
  - BLPT, n=16
  - MPT, n=30
- Age = 49 years, **size = 3.8cm***
- Margin width, most 1-4mm
- **RT**: 5040 cGy + 1000 cGy boost
- Results: @ 56 months follow up, ***No cases developed LR***

Barth, et al. Ann Surg Oncol. 2009; 16:2288-2294.

Neron, 2020, France

- French Sarcoma Group (13 sites)
  - N=**212** MPT, **size**: **5.8cm**
- Surgery: BCS: 26.7%, **Mast: 73.3**%
- Adjuvant RT: 43.3% (more w/ mast)
- Recurrence: **16.6**% (local) @50 mo.



Adjuvant RT improved LRFS
*RT did not hold in MVA

Neron. Ann Surg Oncol. 2020; 27:1818-1827.

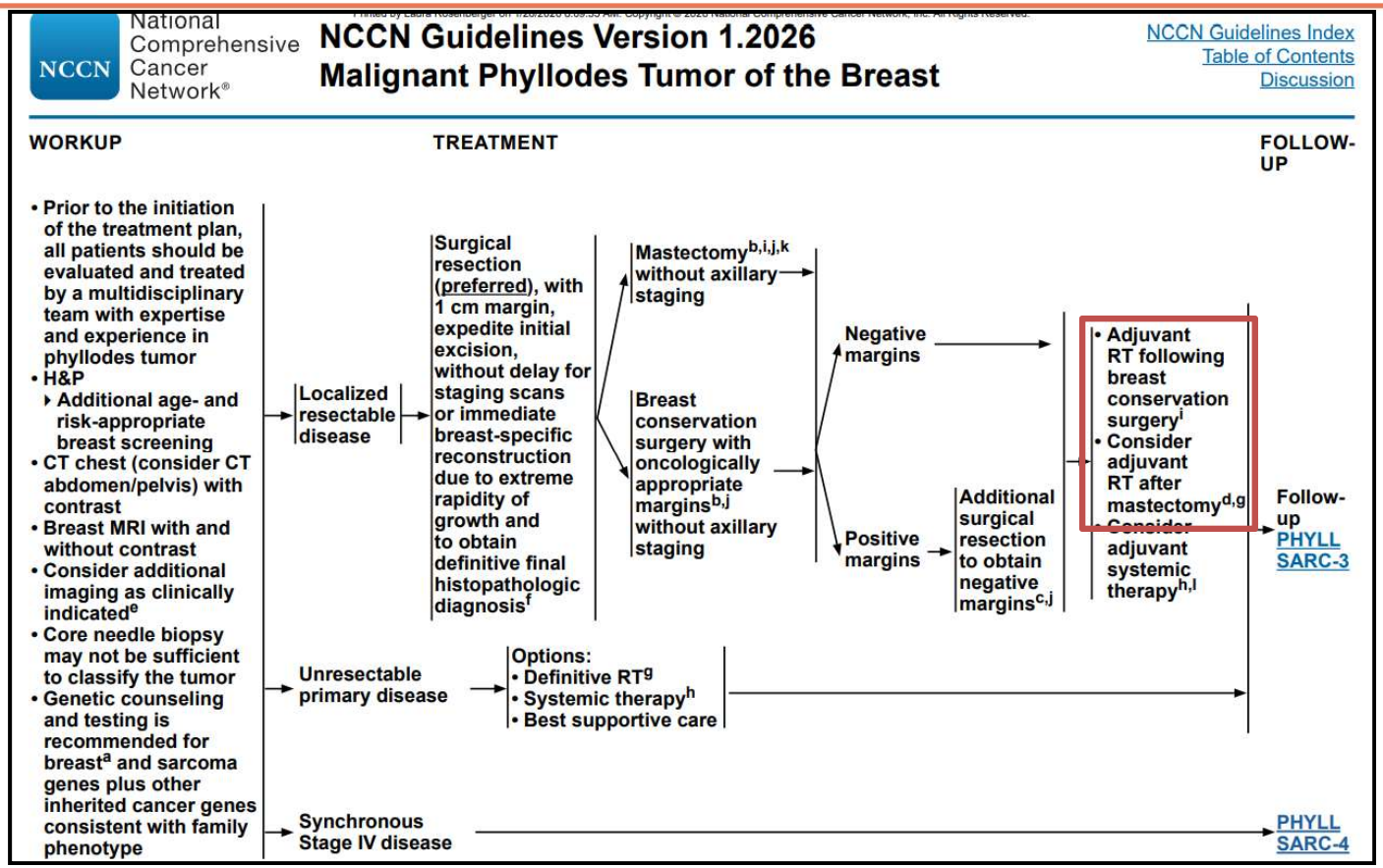
Should we deliver adjuvant radiation therapy?

Surgery Type	Margin Size	BENIGN	BORDERLINE	MALIGNANT
BCS	*Any*	**No RT**	*Maybe* RT*	**YES RT**
Mastectomy	Wide Margin Small Tumor	**No RT**	**No RT**	*Probably* RT*
	Less Wide Margin Large Tumor			**YES RT**

*Table modified from **Dr. Andrew Bishop**, MDACC

*High-risk features (mitoses >30/10hpf, size >8-10.0cm, presence of malignant heterology elements), locally recurrent, chest wall proximity, morbid surgical salvage

Should we deliver adjuvant radiation therapy?



Should we deliver adjuvant radiation therapy?

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Malignant Phyllodes Tumor of the Breast

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Discussion

FOOTNOTES

[a] For risk criteria, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate.

[b] For borderline or malignant phyllodes tumors, wide excision means excision with the intention of obtaining surgical margins ≥1 cm. Narrow surgical margins are associated with increased local recurrence risk, but are not an absolute indication for mastectomy when partial mastectomy fails to achieve a margin width ≥1 cm. Mastectomy may be needed to obtain these margins (considerations may include tumor and breast size).

[c] Radiation therapy is not a substitute for negative margins and additional surgery should be pursued for positive margins.

[d] Following adequate margin resection, adjuvant RT can be deferred. However adjuvant RT should be considered in the setting of increased risk of local recurrence (eg, mitoses >30/10 hpf, size >10 cm, malignant heterologous elements). Scenarios include (but are not limited to) multiple recurrent phyllodes, and surgically narrow margins due to chest wall with reduced local recurrence threshold. See Principles of Radiation Therapy (SARC-E) for dose recommendations.

[e] Given propensity for lung/bone/visceral metastases, consider additional imaging with whole body FDG-PET/CT to evaluate metastatic disease, bone scan, or brain MRI as clinically indicated (Parkes A, et al. Breast Cancer Res Treat 2021;186:871-882; Mituś JW, et al. World J Surg 2016;40:323-328). See Principles of Imaging (SARC-A).

[f] Consider preoperative RT in marginally unresectable disease or when anticipated narrow margins despite radical resection. Effort should be made to expedite the initiation of preoperative RT when recommended by the multidisciplinary team as delays may impact outcomes in this rapidly growing tumor. Surgical re-evaluation should occur during and immediately after preoperative RT to reassess resectability.

[g] Principles of Radiation Therapy (SARC-E).

[h] Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma Subtypes and Aggressive Soft Tissue Neoplasms (SARC-G).

[i] Data indicate that local recurrence is less likely to occur with mastectomy than breast conservation surgery. If patient has undergone breast conservation surgery, adjuvant RT is recommended regardless of margin status. Neron M, et al. Ann Surg Oncol 2020;27:1818-1827; Bartles SAL, et al. Eur J Cancer 2024;201:113924.

[j] Principles of Surgery (SARC-D).

[k] Due to high rates of local recurrence with narrow or positive margins, attempts at nipple or skin sparing approach in close proximity to the tumor to facilitate reconstruction is discouraged. The goal should be to obtain widely negative margins even if that requires resection of extensive amounts of skin.

[l] Consider systemic therapy if high risk for occult metastatic disease or high-risk features (eg, mitoses >30/10 hpf, size >10 cm, malignant heterologous elements). Use of systemic therapy should be discussed with a multidisciplinary team with expertise and experience in phyllodes tumor and considered after careful discussion with surgeon.

Case #2: Marginal Failure s/p Resection and Radiation

56 year old

- 6 mo enlarging breast mass, filled breast
- **SURGERY:** MRM

  Malignant phyllodes, 27.3cm
  - **Stromal Cellularity:** Marked
  - **Stromal Atypia:** Marked
  - **Stromal Overgrowth:** Present
  - **Mitoses:** **39** / 10 hpf
  - **Histologic border:** Infiltrative
  - **Malignant heterologous features**: no
  - 0/10 axillary LNs, margins
  - Margins: negative, >5mm
- **RADIATION**:
  - 16-wk *delay – wound break down*
  - **50 +10 Gy** (scar boost), 30 Fx

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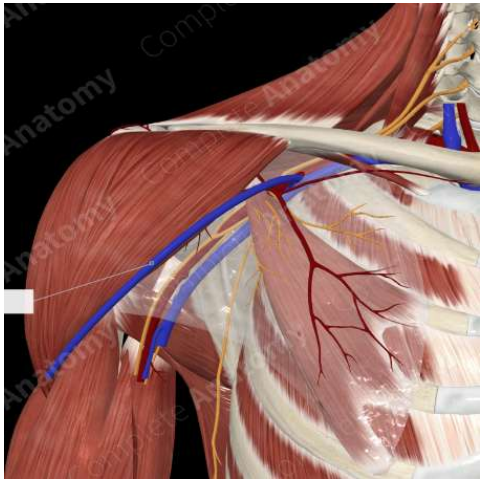
- 9-month interval – **recurrent chest wall mass**
- Split-thickness skin graft
- Latissimus myocutaneous flap
- Abdominal advancement flap

- No evidence of metastases
- ***Challenging locoregional problem**

Case #2: Marginal Failure s/p Resection and Radiation

Radiation: IMRT: 5200 cGy in 40 Fx (BID)

Surgery: Right radical resection of tumor



www.elsevier.com/resources/anatomy

Case #2: Marginal Failure s/p Resection and Radiation

Radiation: IMRT: 5200 cGy in 40 Fx (BID)

Surgery: Right radical resection of tumor

Pre-treatment

Post-operative

Final Pathology:

- Minimal residual malignant phyllodes tumor
- Margins are negative
- **Rare foci of spindle cell proliferation**
- **Treatment effect is extensive (>98%)**

6-month follow-up

Should we give adjuvant systemic therapy?

- Morales-Vasquez, 2007, Mexico
- Single institution, *non-randomized*, prospective
- N=27, non-metastatic*, all had surgery
- 4 cycles *doxorubicin & dacarbazine*

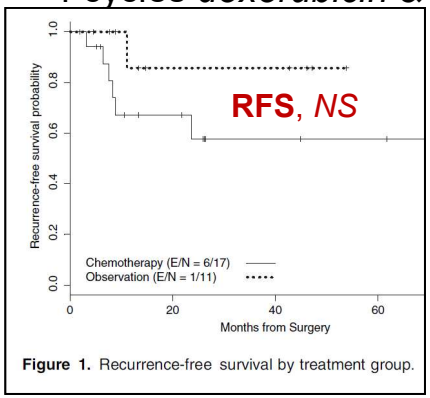


Figure 1. Recurrence-free survival by treatment group.

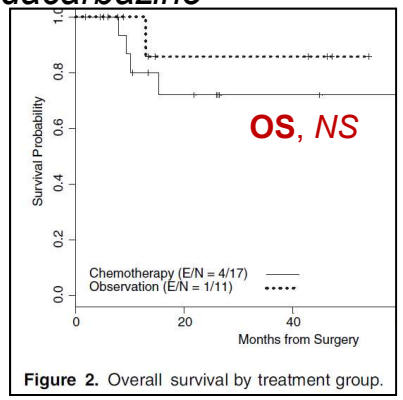


Figure 2. Overall survival by treatment group.

- Adjuvant chemotherapy ***did not*** impact RFS or OS
  - Median follow up, *15 months*
  - Median tumor size; ***13.0cm*** (130mm), CXR to r/o mets

Morales-Vasquez, et al. Breast J. 2007;13(6):551-6.

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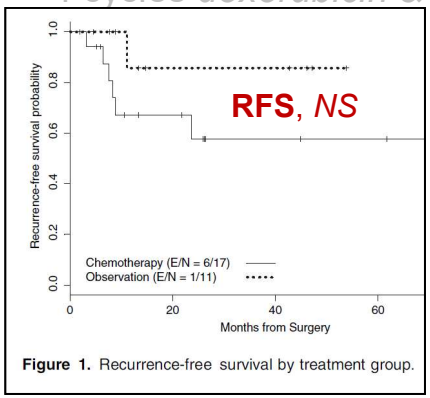

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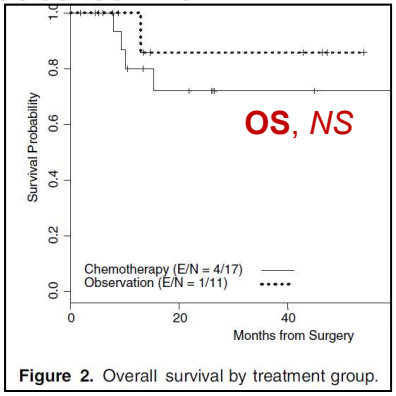

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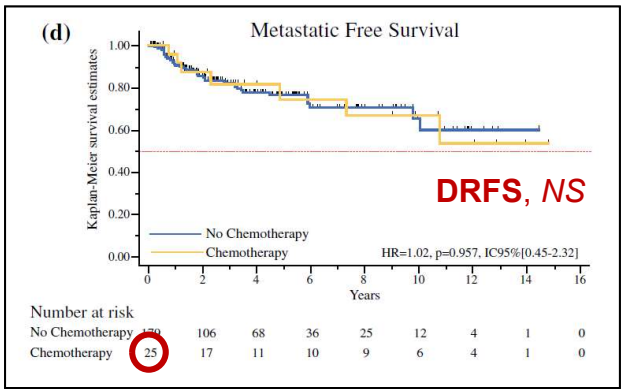
- Neron, 2020, France
- French sarcoma group – retrospective
- Non-metastatic, all underwent surgery
- **11% had adjuvant chemo**, most 6 cycles doxorubicin/ifosfamide

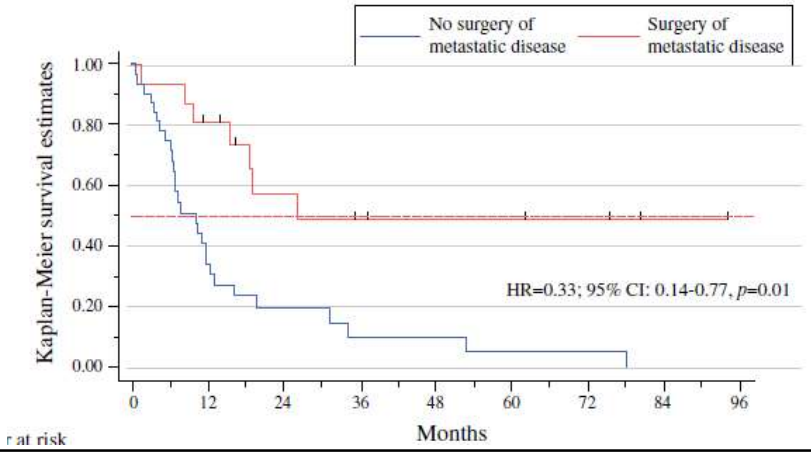


- Adjuvant chemotherapy ***did not*** improve metastatic free survival. *significant selection bias

Neron, et al. Ann Surg Oncol. 2020; 27:1818-1827.

Systemic therapy in *metastatic* disease

- Neron, 2020, France
- 10 centers, retrospective, 2000-2016
- Time-to-mets = 10.3 mo, OS = 11.5 mo
- **N=51**, alkylating agents ↑OS vs. anthracycline
- **Surgery for Mets ↑OS in MVA,** HR=0.33, *p*=0.01



- Palassini, 2022, Italy
- 15 centers, retrospective, 1999-2019
- Systemic therapy in advanced MPT
- **N=56**, 96% were metastatic
- Median # of regimens per patient = 2

Regimen	ORR	mPFS
Anthracycline/Ifosfamide (n=27)	**44.4%**	**5.7 mo**
High-dose Ifos* (n=16)	18.8%	3.4 mo
Tyrosine-kinase inh (n=6)	16.7%	3.4 mo
Anthracycline-single (n=12)	16.7%	3.2 mo
Gemcitabine-based (n=17)	0%	2.1 mo
Trabectedin (n=13)	8.3%	1.8 mo

Palassini. Breast Cancer Res Treat. 2022; 192:603-610.

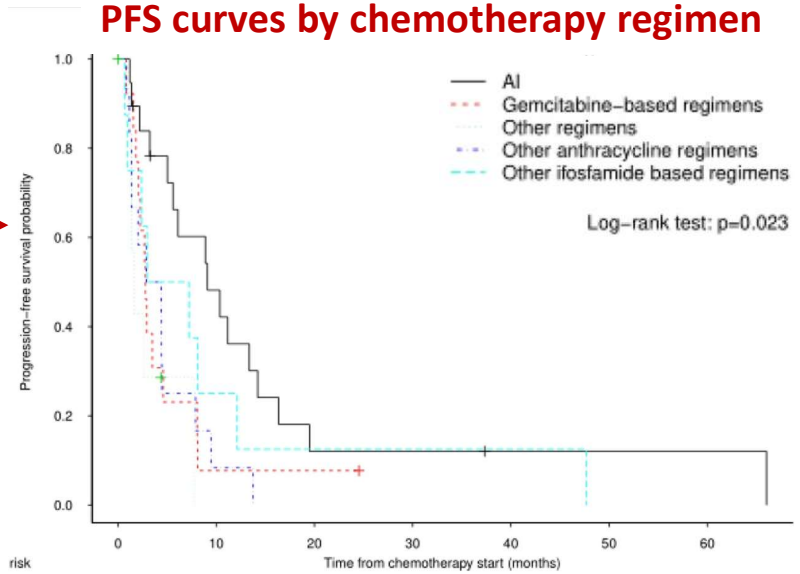
Systemic therapy in *metastatic* disease

- Parkes, 2021, USA, MDACC
- **N=50** *metastatic* MPT (all prior MPT, no BLPT)
- **Adjuvant* chemo for index tumor, n=4/50
  - Time to mets w/ Adj Tx: **41.0** months
  - Time to mets w/out Adj: **17.1** months
- Median # of regimens per patient = 2

Regimen	ORR	mPFS
AI (n=18)	**56%**	**9.1 mo**
I-based (n=4)	50%	5.1 mo
A-based (n=12)	42%	3.65 mo
G-based (n=9)	33%	2.8 mo
Other (n=8)	17%	1.67 mo

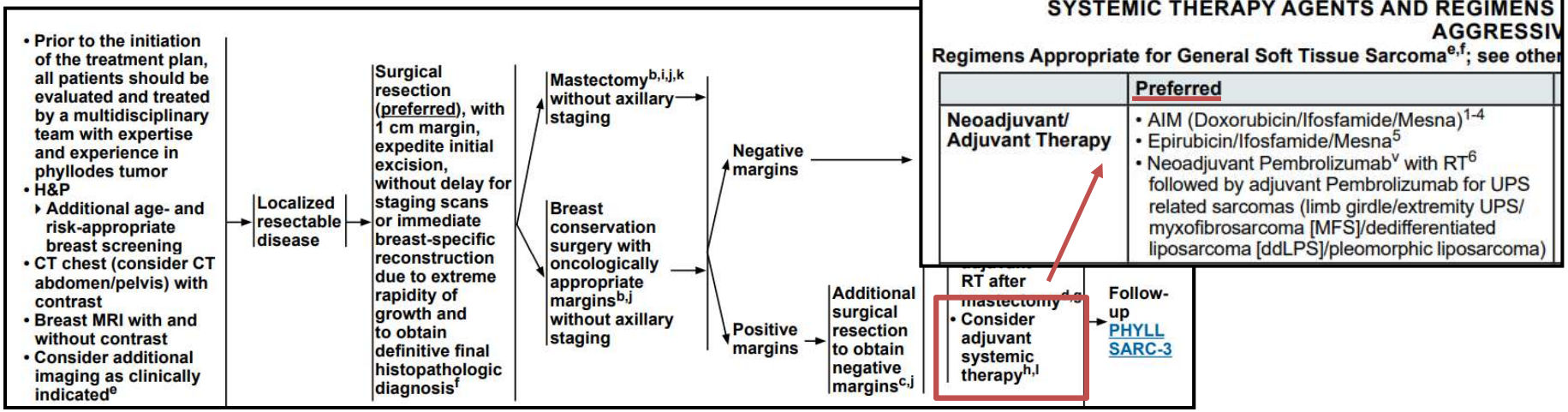
- Median OS for all 50 mMPT = 10.7 mo
- Median OS for 31 w/ chemo = 15.3 mo
- Median OS for 1st line Adria/Ifos = 22.4 mo

PFS curves by chemotherapy regimen



Parkes. Breast Cancer Res Treat. 2021; 186:871-882.

Should we give adjuvant systemic therapy?



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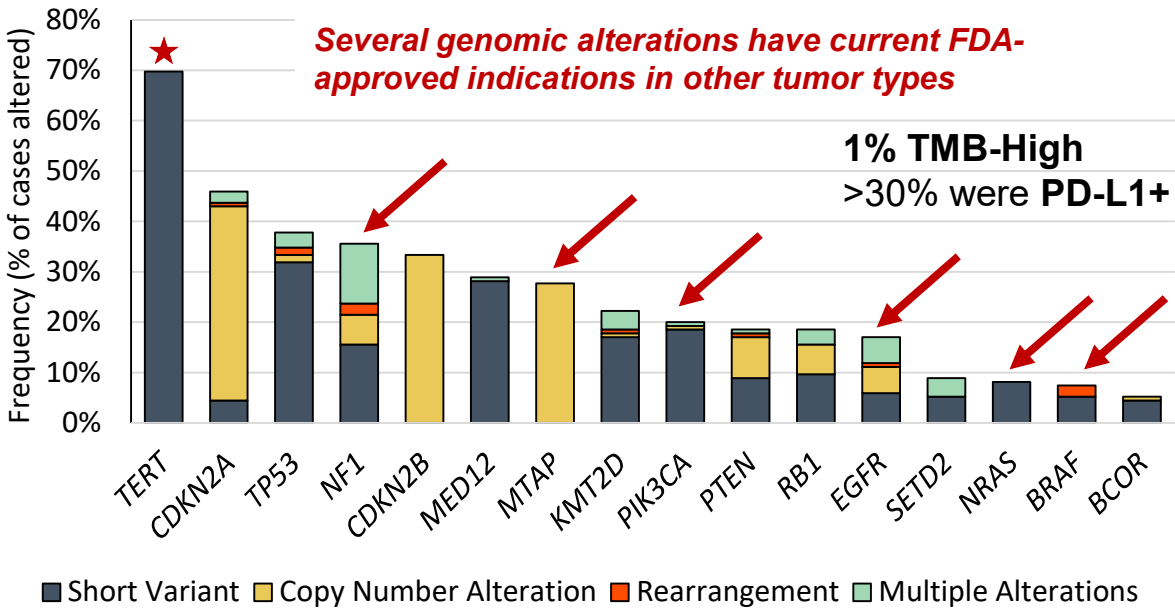
Genomic Landscape of Malignant PT

- Rosenberger, 2024, USA, collaborative data share

Frequency of *Genomic Alterations* identified in 135 cases

Gene	Mutations in Phyllodes Cohort (N=135)	Mutations in Phyllodes Cohort (%)
*TERT**	76	69.7%
CDKN2A	62	45.9%
TP53	51	37.8%
NF1	48	35.6%
CDKN2B	45	33.3%
MED12	39	28.9%
*MTAP***	18	27.7%
KMT2D	30	22.2%
PIK3CA	27	20.0%
PTEN	25	18.5%
RB1	25	18.5%
EGFR	23	17.0%



* N=109 in Phyllodes Cohort
** N=65 in Phyllodes Cohort

Rosenberger. Oncologist. 2024; 29:1024-1031.

Genomic Landscape of Malignant PT

- Bansal, 2024, USA, collaborative data share

Frequency of *Genomic Alterations* identified in 57 cases

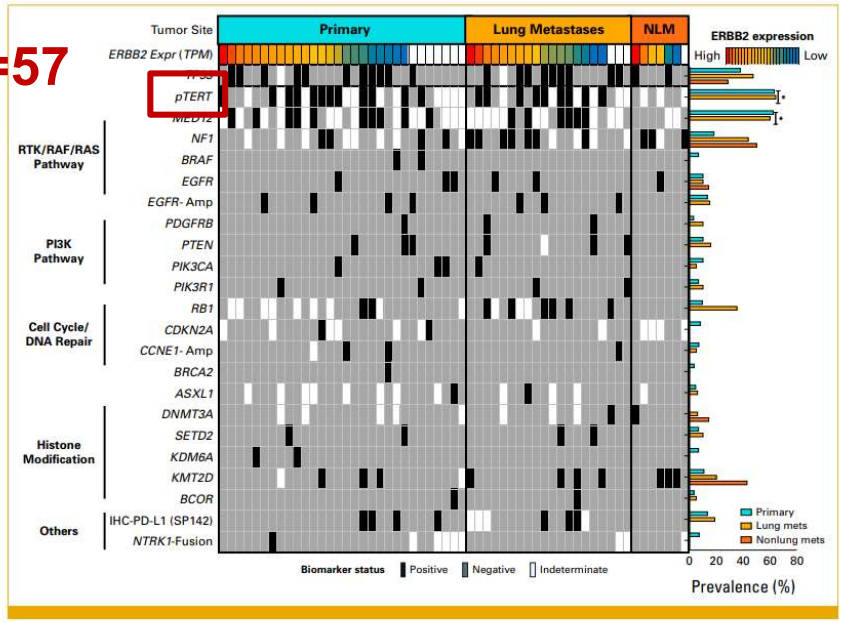
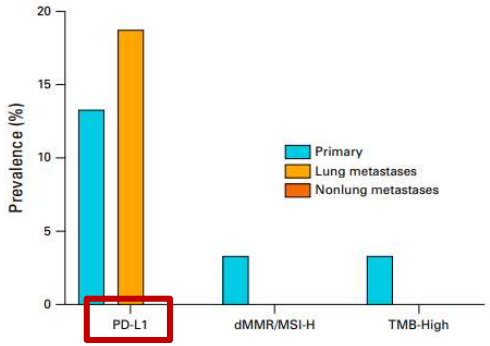


FIG 2. Genomic landscape of phyllodes tumors. Oncoplot shows prevalence of pathogenic gene aberrations in primary MPT, MPT lung metastases, and MPT NLM. *ERBB2* expression (log_2 TPM) is shown at the top for each tumor. Bars at the right indicate the total percentage per group. *P < .05 (Fisher's exact test). Amp, copy number amplification; IHC, immunohistochemistry; mets, metastases; MPT, malignant phyllodes tumor; NLM, nonlung metastases; TPM, transcripts per million.



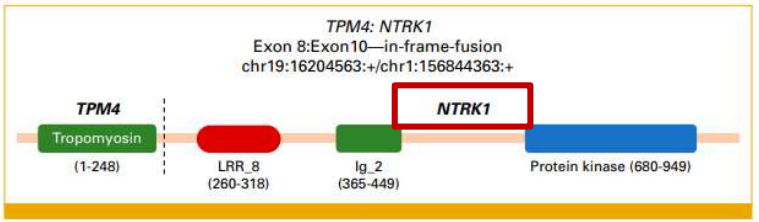


FIG 4. TPM4:NTRK1 fusion event in phyllodes tumor. One patient presented with an *NTRK1* pathogenic fusion and was treated for 16 months with larotrectinib. The diagram shows the representative structure of *TPM4:NTRK1* fusion with amino acid residues noted. Ig_2, immunoglobulin-like domain; LRR_8, leucine-rich repeat.

Bansal, Rosenberger. JCO Precis Oncol. 2024, Dec;8:e2400289

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