Breast sarcomas

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COIs

- Ipsen
- Genesis
- MSD
- BMS
- Merck

Epidemiology

- Less than 1% of breast malignancies
- 5% of sarcomas

What to expect?

- Phyllodes tumor (benign, borderline, malignant)
- Angiosarcomas
- DFSP
- Radiation induced sarcomas
- Any other type

Glory for the surgeons!

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NCCN Guidelines Version 4.2022
Phyllodes Tumor

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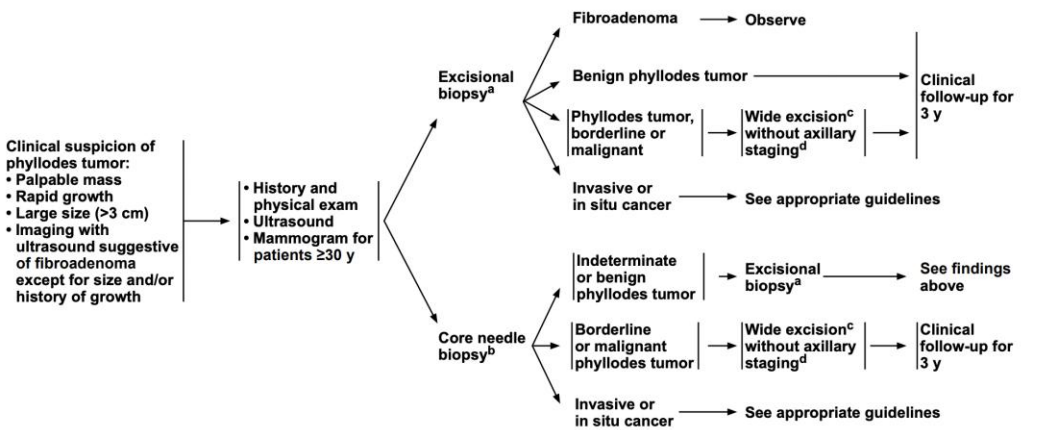

[a] Excisional biopsy includes complete mass removal, but without the intent of obtaining surgical margins.

[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] For malignant or borderline disease, wide excision means excision with the intention of obtaining surgical margins ≥1 cm. Narrow surgical margins are associated with heightened local recurrence risk, but are not an absolute indication for mastectomy when partial mastectomy fails to achieve a margin width ≥1 cm.

[d] There are no prospective randomized data supporting the use of RT for phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (eg, chest wall recurrence following mastectomy), RT may be considered following the same principles that are applied to the treatment of soft tissue sarcoma.

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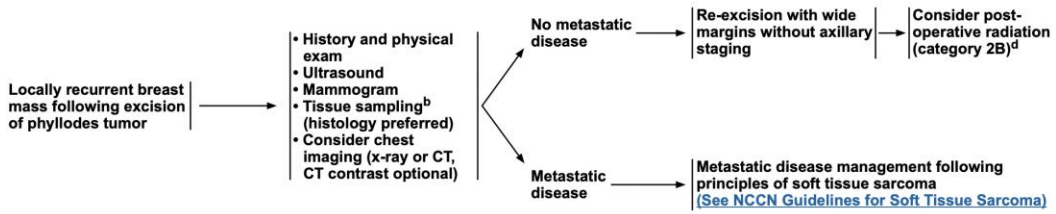
PHYLLODES TUMOR RECURRENCE



[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.

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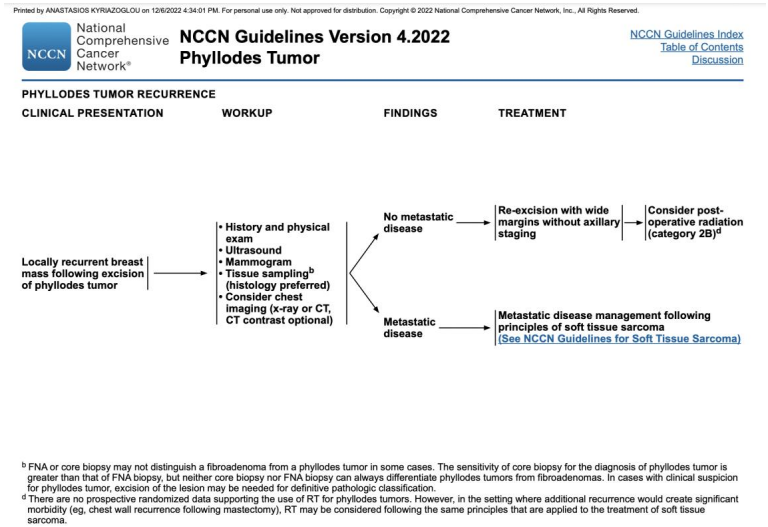
When surgeons are not needed anymore?

- Same dilemma: to treat or not to treat with ADJUVANT?
- And what type of adjuvant? RT or chemo?
- Which chemo regimen?



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PHYLLODES TUMOR RECURRENCE

CLINICAL PRESENTATION	WORKUP	FINDINGS	TREATMENT	
Locally recurrent breast mass following excision of phyllodes tumor	• History and physical exam • Ultrasound • Mammogram • Tissue sampling[b] (histology preferred) • Consider chest imaging (x-ray or CT, CT contrast optional)	No metastatic disease	Re-excision with wide margins without axillary staging	Consider post-operative radiation (category 2B)[d]
		Metastatic disease	Metastatic disease management following principles of soft tissue sarcoma (See NCCN Guidelines for Soft Tissue Sarcoma)	

[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.
[d] There are no prospective randomized data supporting the use of RT for phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (eg, chest wall recurrence following mastectomy), RT may be considered following the same principles that are applied to the treatment of soft tissue sarcoma.

As far as adjuvant/neoadjuvant ChT is concerned, there is a higher degree of uncertainty, although one may use the same principles of STS at other sites. Considering the high risk of angiosarcoma to develop local and systemic relapses, preoperative treatments including ChT and RT may be used. Re-irradiation can be considered in radiation-associated angiosarcomas.

ESMO and NCCN Guidelines in this case pinpoint Pubmed!!!!

- 36 relevant articles out of the first 1000 results, search: breast sarcomas treatment

- 9 meta-analyses or reviews
- 1 Scottish guidelines
- 26 retrospective studies

Adjuvant RT?

Original article

Phyllodes tumors of the breast: Adjuvant radiation therapy revisited

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ABSTRACT

Background: Phyllodes tumors (PT) are rare entity and surgical resection is the cornerstone of treatment. No standard of care exists regarding adjuvant treatment especially radiation therapy (RT).
Patients and methods: We analyzed all patients with non-metastatic, resected phyllodes tumors who presented to our institution from January 2005 through December 2019. Primary study endpoints included local recurrence free survival (LRFS) and overall survival (OS).
Results: One hundred and eight patients were analyzed (patients with incomplete treatment and follow up data were excluded). Fifty patients had benign phyllodes, 26 patients had borderline and 32 patients had malignant phyllodes. In the benign group, no significant difference in LRFS was observed between patients who received adjuvant RT (n = 3) and those who did not (5-year LRFS 100% vs. 85% respectively, p = 0.49). The 5 year OS for patients who received RT was 60% vs. 89% for those who did not (p 0.40). In the borderline/malignant group, adjuvant RT significantly improved five year LRFS (90% in the RT group vs. 42% in the no RT group, p = 0.005). The 5 year LRFS in patients treated with margin negative breast conserving surgery and RT was 100% vs. 34.3% in patients who did not receive RT (p 0.022). Patients treated with mastectomy and RT had a 5 year LRFS of 100% vs. 83% for patients who did not receive RT (p 0.24). On multivariate analysis, radiation therapy was independently associated with decreased hazard of local failure (HR 0.21, CI 0.05–0.89, p = 0.03). No difference in OS was found between the RT and no RT groups (5-year OS was 52% vs. 45% respectively, p 0.54).
Conclusion: The results of the current study confirm the excellent prognosis of benign phyllodes tumors; warranting no further adjuvant treatment after margin-negative surgical resection. For patients with borderline/malignant phyllodes tumors, adjuvant radiation therapy significantly improved LRFS after margin negative wide local excision; however, patients treated with mastectomy did not attain the same benefit from adjuvant irradiation.

Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis

Xue Chao[1,2†], Kai Chen[1,2†], Jiayi Zeng[3], Zhuofei Bi[1,4], Mingyan Guo[1,5], Yi Chen[1,2], Yandan Yao[1,2], Wei Wu[1,2], Shi Liang[1,2] and Yan Nie[1,2*]

Abstract

Background: As the efficacy of radiotherapy and chemotherapy for treatment of phyllodes tumors (PTs) remains unclear, this study aimed to review all available data and evaluate the roles of radiotherapy and chemotherapy in PT treatment.

Methods: We performed a comprehensive search of databases, including PubMed, Web of Science and the Cochrane Library. The outcomes of interest included the local recurrence (LR) rate, metastasis rate, disease-free survival rate and overall survival rate.

Results: Seventeen studies enrolling 696 patients were included in this random effect meta-analysis. Subgroup analysis and meta-regression were also conducted to determine study heterogeneity. A pooled local recurrence rate of 8% (95% CI: 1–22%) was observed with a statistical heterogeneity of $I^2 = 86.6\%$ ($p < 0.01$) for radiotherapy. This was lower than the recurrence rate of 12% for simple surgical treatment (95% CI: 7–18%). Meta-regression analysis found that surgical margin status was the main source of heterogeneity ($p = 0.04$). The metastasis rate of 4% (95% CI: 0–11%) for patients receiving radiotherapy without significant heterogeneity was also lower than the rate for the simple surgery group (8, 95% CI: 3–15%). The available data for chemotherapy were too limited to support meta-analysis. Accordingly, we offer a pure review of these data.

Conclusion: Our findings suggest that radiotherapy is effective in achieving local disease control and preventing metastasis.

Keywords: Phyllodes tumors, Radiotherapy, Chemotherapy, Meta-analysis

Breast Cancer (2021) 28:110–118
https://doi.org/10.1007/s12282-020-01135-7

ORIGINAL ARTICLE

The role of adjuvant radiotherapy in patients with malignant phyllodes tumor of the breast: a propensity-score matching analysis

Wen Zhao[1] · Qi Tian[1] · Andi Zhao[1] · Biyuan Wang[1] · Jiao Yang[1] · Le Wang[1] · Lingxiao Zhang[1] · Danfeng Dong[1] · Ling Chen[1] · Jin Yang[1]

Received: 3 November 2019 / Accepted: 16 July 2020 / Published online: 3 August 2020

Abstract

Background and objectives Malignant phyllodes tumor of the breast (MPTB) is a kind of rare tumor. Our objective was to investigate the role of adjuvant radiotherapy (RT) in MPTB patients.

Methods MPTB patients were identified in the Surveillance, Epidemiology and End Results (SEER) database. Kaplan–Meier curves and multivariable Cox proportional hazards analyses were conducted to determine the effect of adjuvant RT on MPTB patients. Propensity-score matching (PSM) method was used to balance the clinicopathological characteristics.

Results A total of 1353 MPTB patients were included in our study and the median follow-up time was 99 months (range: 0–331 months). 16.7% (226) MPTB patients received adjuvant RT, of which 49.1% (111) received mastectomy and 50.9% (115) underwent breast conservation surgery (BCS). Patients receiving adjuvant RT were more likely to be white, with better differentiation and larger tumors ($p < 0.05$). Multivariate analysis showed that poorer tumor differentiation grade, larger tumor size, and lymph node metastasis were associated with reduced survival while BCS was a protective factor of disease-specific survival (DSS) (HR 0.297; 95% CI 0.184–0.480) and overall survival (OS) (HR 0.445; 95% CI 0.321–0.616). After PSM, survival curves showed patients did not achieve an improved OS or DSS from adjuvant RT ($p > 0.05$). In subgroup analysis, no subgroup benefited from adjuvant RT. Exploratory analysis showed a survival benefit trend from adjuvant RT in patients with tumor larger than 50 mm and undergoing BCS.

Conclusions Among MPTB patients, adjuvant RT did not improve OS or DSS. In patients with tumor larger than 50 mm and receiving BCS, a survival benefit trend from adjuvant RT existed.

Patterns of care and predictors of adjuvant radiation therapy in phyllodes tumor of the breast

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Abstract

Patterns of care, utilization, and predictors of adjuvant radiation therapy (RT) for phyllodes tumors of the breast were retrospectively analyzed using the National Cancer Database. We identified 3080 patients; 53.4% received lumpectomy and 35.9% mastectomy. 25.9% of patients had lymph node sampling or dissection. 23.2% received adjuvant RT, which doubled in utilization over a decade. Predictors of RT were younger age, fewer comorbidities, less favorable pathologic features, and treatment at academic centers. There was no association between RT and overall survival (AHR 1.21, 95% CI 0.97-1.53, $P = .097$). Despite national guidelines recommending against nodal sampling or RT, it remains prevalent. Further research on indications for adjuvant radiation for phyllodes is needed.

KEYWORDS
adjuvant radiation, lymph node sampling, phyllodes of the breast

1 prospective trial supporting adj RT

Published in final edited form as:
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A Prospective, Multi-Institutional Study of Adjuvant Radiotherapy After Resection of Malignant Phyllodes Tumors

Richard J. Barth Jr., MD[1], **Wendy A. Wells, MD**[2], **Sandra E. Mitchell, MD**[3], and **Bernard F. Cole, PhD**[4]

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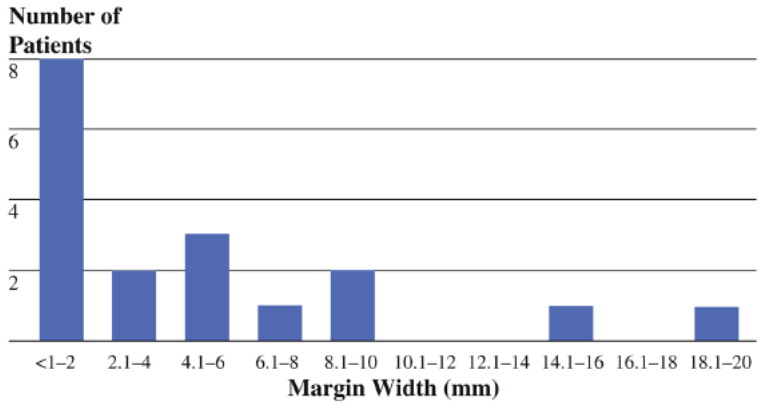
Abstract

Background—Malignant phyllodes tumors of the breast are unusual neoplasms, with an incidence of approximately 500 cases annually in the United States. Published local recurrence rates after margin-negative breast-conserving resections of borderline malignant and malignant phyllodes tumors are unacceptably high, at 24 and 20%, respectively. It is uncertain whether radiotherapy after resection of phyllodes tumors is beneficial.

Methods—We prospectively enrolled patients who were treated with a margin-negative breast-conserving resection of borderline malignant or malignant phyllodes tumors to adjuvant radiotherapy. The primary endpoint was local recurrence.

Results—Forty-six women were treated at 30 different institutions. The mean patient age was 49 years (range, 18–76 years). Thirty patients (65%) had malignant phyllodes tumors; the rest were borderline malignant. The mean tumor diameter was 3.7 cm (range, .8–11 cm). Eighteen patients had a negative margin on the first excision. The median size of the negative margin was .35 cm (range, <.1–2 cm). Twenty-eight patients underwent a re-excision because of positive margins in the initial resection. Two patients died of metastatic phyllodes tumor. During a median follow-up of 56 months (range, 12–129 months), none of the 46 patients developed a local recurrence (local recurrence rate, 0%; 95% confidence interval, 0–8).

Conclusions—Margin-negative resection combined with adjuvant radiotherapy is very effective therapy for local control of borderline and malignant phyllodes tumors. The local recurrence rate with adjuvant radiotherapy was significantly less than that observed in reported patients treated with margin-negative resection alone.



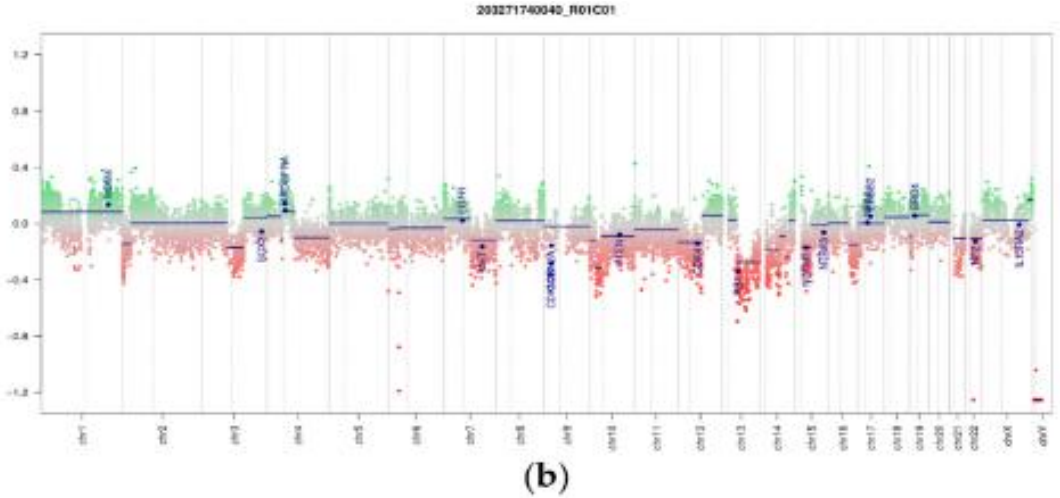
0% of local recurrence with adjuvant RT!!!

2 pts with malignant phyllodes recurred with metastatic disease

Systemic treatment

- No benefit of adjuvant chemo!
- Doxo-Ifo/ Doxo monotherapy → best responses (PFS 5-9months)
- Other regimens show worse outcomes (PFS less than 3 months)

Genetics: p53, TERT, MED12, NF1, BCOR



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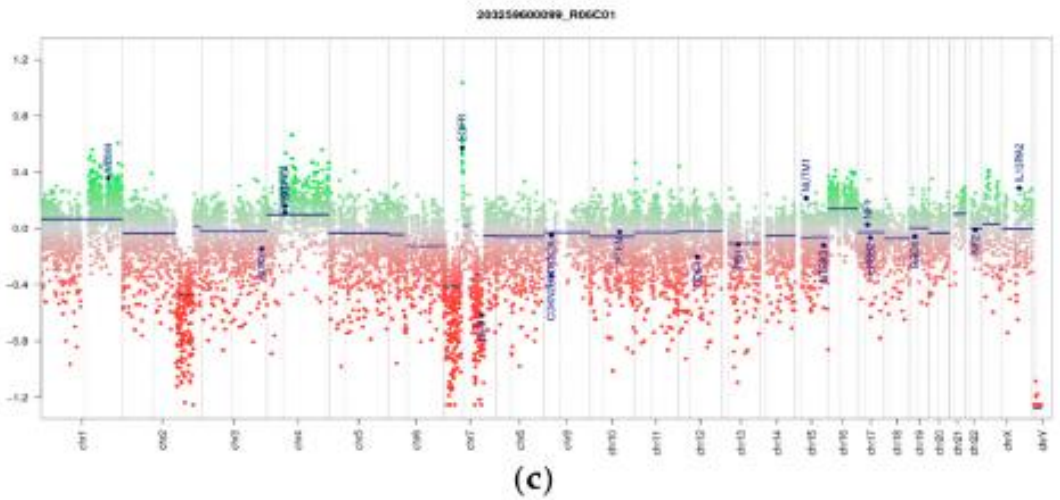


(c)

Genomic profile of breast sarcomas: a comparison with malignant phyllodes tumours

Sue Zann Lim[1] · Cedric Chuan Young Ng[2,3] · Vikneswari Rajasegaran[2,3] · Peiyong Guan[4] · Sathiyamoorthy Selvarajan[5] · Aye Aye Thike[5] · Nur Diyana Binte Md Nasir[5] · Valerie Cui Yun Koh[5] · Benita Kiat Tee Tan[1] · Kong Wee Ong[1] · Bin Tean Teh[2,3,6,7] · Puay Hoon Tan[8]

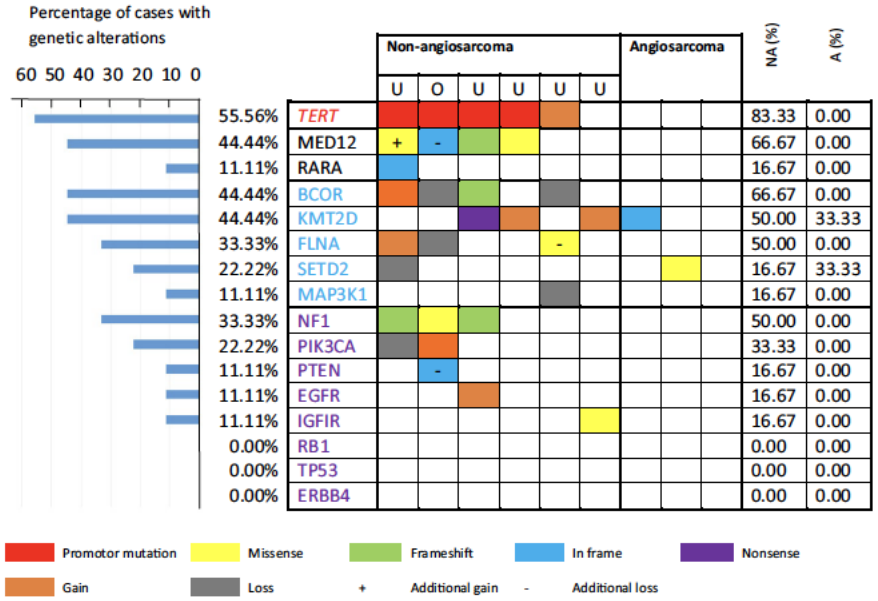
Received: 8 October 2018 / Accepted: 20 November 2018

Abstract

Purpose We aimed to investigate the genomic profile of breast sarcomas (BS) and compare with that of malignant phyllodes tumours (MPT).

Methods DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) specimens from 17 cases of BS diagnosed at Singapore General Hospital from January 1991 to December 2014. Targeted deep sequencing and copy number variation (CNV) analysis on 16 genes, which included recurrently mutated genes in phyllodes tumours and genes associated with breast cancer, were performed on these samples. Genetic alterations (GA) observed were summarised and analysed.

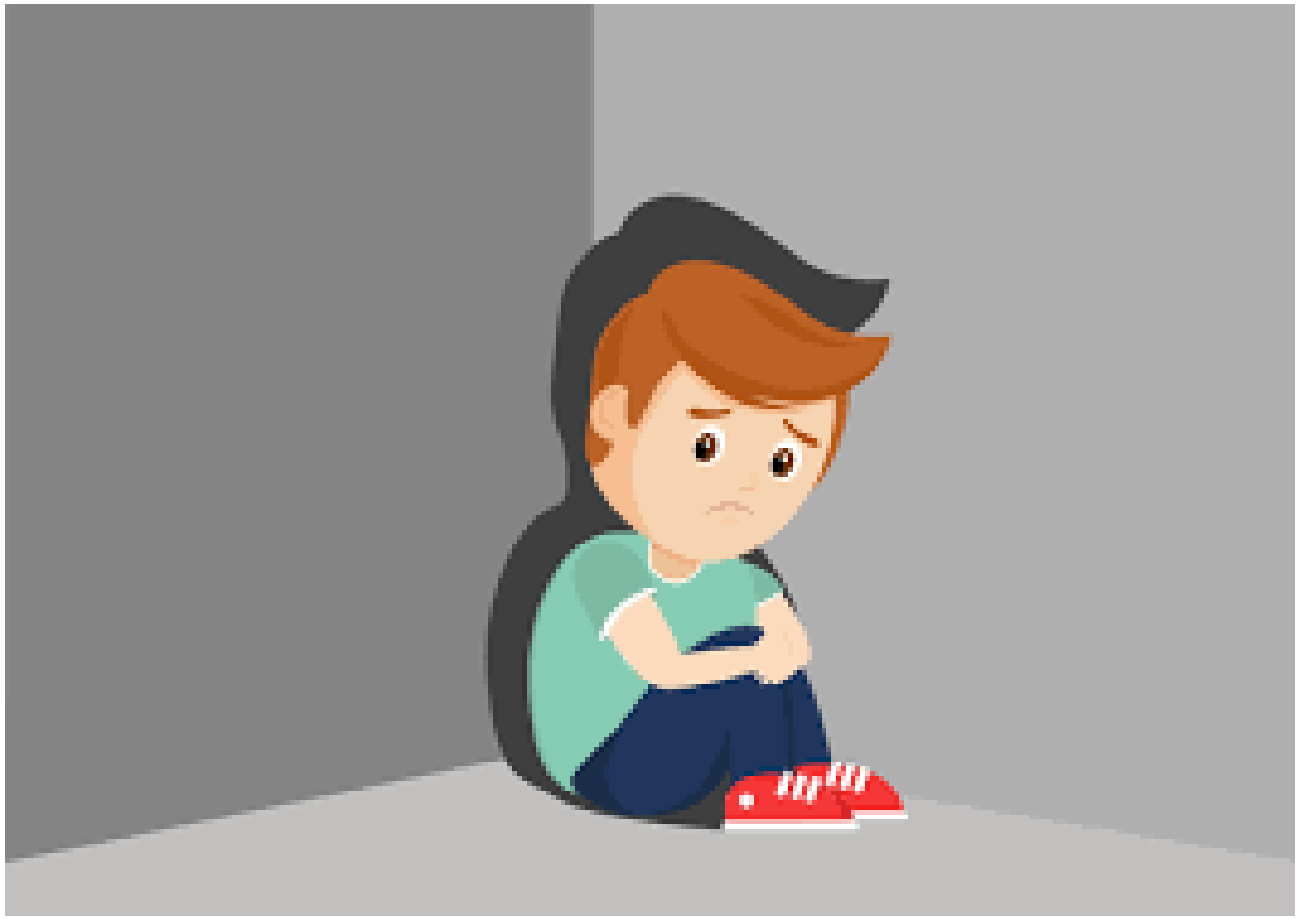
Results Nine cases met the quality control requirements for both targeted deep sequencing and CNV analysis. Three (33.33%) were angiosarcomas and 6 (66.67%) were non-angiosarcomas. In the non-angiosarcoma group, 83.33% ($n=5$) of the patients had GA in the *TERT* gene. The other commonly mutated genes in this group of tumours were *MED12* ($n=4$, 66.67%), *BCOR* ($n=4$, 66.67%), *KMT2D* ($n=3$, 50%), *FLNA* ($n=3$, 50%) and *NF1* ($n=3$, 50%). In contrast, none of the angiosarcomas had mutations or copy number alterations in *TERT*, *MED12*, *BCOR*, *FLNA* or *NF1*. Eighty percent of patients with GA in *TERT* ($n=5$) had concurrent mutations in *MED12*. Sixty percent ($n=3$) of these cases also demonstrated GA in *NF1*, *PIK3CA* or *EGFR* which are known cancer driver genes.



Clinical trials

- 1 trial recruiting in Singapore with cryotherapy

Neglected patients



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Thank you!!!

Σ Sarcomas in two words:

- They are malignant tumors and can appear anywhere on the body.
- They are divided into two main groups, bone and soft tissue
- They have names depending on the tissue they look like, such as liposarcoma (fat), leiomyosarcoma (smooth muscle fibers), osteosarcoma (bone), chondrosarcoma (cartilage), etc.
- They are rare tumors and make up **1% of all malignancies** .
- It is more common in children and young adults.
- About **13,000 people** will be diagnosed with sarcoma worldwide this year.
- Basic treatment is surgical resection, sometimes in combination with chemotherapy and radiotherapy.
- People can survive a sarcoma if it is diagnosed early. It is vital that patients are referred to a special sarcoma group as soon as possible.

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