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REVIEW

# Refining the classification of breast phyllodes tumours

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**Summary**

Phyllodes tumours of the breast are uncommon fibroepithelial neoplasms that pose recurrent classification challenges, in large part due to the multiple histological parameters of stromal hypercellularity and atypia, stromal mitotic count, stromal overgrowth and tumour borders, that are used for grading. While the World Health Organization (WHO) Classification of Breast Tumours provides recommendations on diagnostic features, defining criteria are not always applied in routine practice. Lack of concordance among pathologists in typing and grading further underscores the classification difficulties, especially in the borderline category. Although there has been significant molecular information on phyllodes tumours in recent years which has been diagnostically helpful, it has not been translated into daily clinical practice.

In order to refine the classification of phyllodes tumours into one that is simple yet comprehensive, reproducible and prognostically precise, a multipronged approach is needed that leverages on global contributions of the International Fibroepithelial Consortium, support by the International Collaboration on Cancer Classification and Research (IC$^3$R) in amalgamating evidence translation, and guidance from the International Collaboration on Cancer Reporting (ICCR) for standardised reporting. It is hoped that the evidence generated can be used towards refining the classification of phyllodes tumours for the future.

*Key words:* Phyllodes tumours; classification; WHO.

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## INTRODUCTION

Disease classification harks back to ancient Egypt, with initial descriptions based on macroscopic appearances and the specific organs affected.[1,2] The advent of the microscope, with wider use in the 19th century, led to the development of cellular pathology as a discipline, fostering microscopic documentation of disease. Histological criteria used in tumour classification allowed for consistent recognition and diagnosis of specific tumour types, forming the basis for prognostication and optimised therapy.

The World Health Organization (WHO) recognised this need in 1956, publishing the first edition of the WHO classification of tumours from 1967–1981,[1] with the current set of WHO tumour books in its fifth series.

Tumour classification today is truly multidimensional, with many facets to how tumours are defined. Histopathology remains the main classification tool of the diagnostic pathologist, aided by adjunctive studies including immunohistochemical and molecular tools. Other factors that influence classification include emerging knowledge and evolving concepts of disease, improved understanding of biological behaviour of diverse tumours, and discovery of novel entities, propelled by advances in molecular pathology. The availability of screening for early disease has also impacted on discussions on disease nomenclature. For example, there has been debate on whether ductal carcinoma *in situ*, which has seen a rising incidence with mammographic screening, should be re-named as ductal intraepithelial neoplasia, in view of the low grade nature of some screen detected lesions and the difficulty in distinguishing atypical ductal hyperplasia from low grade ductal carcinoma *in situ*.[3] Standardisation and international harmonisation of criteria are key to effective use of classification schemes. Biopsy modalities may bring about different approaches to classification, as in lung cancer diagnostic terminology and criteria applied to small biopsy and cytology samples as opposed to resection specimens.[4] Digital pathology and artificial intelligence are potential levers for classification improvement.[5]

This article reviews the current classification of breast phyllodes tumours, including its evolution from historical perspectives, the importance and challenges of the existing classification scheme, interesting insights from 'real world' applications of grading criteria, and how we can bridge evidence gaps to inform future classification approaches.

## BREAST PHYLLODES TUMOURS

The WHO 5th series defines the phyllodes tumour as a fibroepithelial neoplasm with a prominent intracanalicular architectural pattern and leaf-like stromal fronds, capped by luminal epithelial and myoepithelial layers, accompanied by stromal hypercellularity.

The term 'classification' in the context of this manuscript encompasses both tumour type and tumour grade, with greater emphasis on issues with grading. Accurate tumour typing allows correct designation as a phyllodes tumour and separation from histological mimics, while precise grading into low, borderline and malignant categories permits prediction of clinical behaviour. Periductal stromal tumour is listed as a subtype of phyllodes tumour in the WHO blue

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book due to overlapping histological features and shared molecular characteristics.[6]

The phyllodes tumour comprises between 0.3% and 1% of all breast tumours and accounts for 2.5% of all fibroepithelial tumours. It affects older women in the fifth decade with higher incidence and younger age in Asian women. Clinically, it can present as a firm to hard breast mass which may stretch and ulcerate overlying skin. Mammographic screening detects smaller lesions. Although there have been many imaging studies attempting to distinguish phyllodes tumour from its closest mimic the fibroadenoma, current clinicoradiological features are unable to accurately and consistently discriminate them.

## HISTORICAL PERSPECTIVES

Although the term 'phyllodes' was formally attributed to Johannes Müller in 1838, it is likely that the tumour was recognised as far back as 1774 when a huge 4 kg tumour was described in a young woman.[7] Subsequently, there have been sporadic reports of similar tumours variously labelled as cystic and cellular hydatids, before the nomenclature of cystosarcoma phyllodes earned its place in the medical lexicon. There have been contests to this name however, with intracanalicular fibroma, pseudosarcoma, serocystic tumour, and comments about its biological behaviour opined by Virchow in 1867, that the tumour had limited malignancy but possessed the capacity to metastasise.[7] In the 20th century and earlier than 1941, it was cautioned that the prefix of sarcoma may not be appropriate as the biological behaviour did not always pursue an aggressive sarcomatous course. In 1960, tumour phyllodes, dropping the cystosarcoma prefix, was applied, and remains the terminology used today.[7]

Dr Müller's original literary record of this tumour accurately describes the key pathological features which are also observed today: large firm mass, cavities or clefts, excrescences of a foliated form, projecting into fissures, appearances that typify the gross morphology (Fig. 1).

In 1838, Müller decreed that the disease was 'perfectly innocent'. In the early 1900s, there were reports of recurrences as well as metastasis.[8,9] In 1943, it was proposed that benign and malignant categories be assigned, and in 1951, it was acknowledged that there were tumours which could not be neatly separated into either benign and malignant groups, and suggestion of a borderline category was proposed,[10] thus spawning the three tiered scheme of benign, borderline and malignant groups.

Initial histological features to evaluate the tumours included nature of tumour contours, size, mitotic activity and cellular atypia.[11] Stromal overgrowth was suggested as an additional adverse prognostic factor,[12,13] further augmented by semiquantitative evaluation.[14] Eleven years ago, our group devised a nomogram that could predict biological behaviour of individual patients based on stromal atypia, mitotic rate, overgrowth and surgical margins.[15]

## WHO CLASSIFICATION

In 2012, the 4th edition of the WHO breast tumour classification presented a table which listed the histological criteria for phyllodes tumour grades, with benign tumours having well defined borders, mildly increased stromal cellularity, mild or no stromal atypia, few mitoses less than five per 10 high power fields, no stromal overgrowth, or malignant heterologous elements, comprising 60–75% of all phyllodes tumours (Fig. 2). The borderline tumour may have a focally permeative border, with moderate stromal cellularity, mild to moderate stromal atypia, mitoses usually ranging from 5–9 per 10 high power fields (hpf), often devoid of stromal overgrowth though it can be focally present (Fig. 3). No malignant heterologous elements are seen and the borderline category accounts for 15–20% of the tumours. The malignant phyllodes tumour shows permeative tumour borders with marked and diffusely cellular stroma, marked stromal atypia, abundant mitoses with 10 or more per 10 hpf, malignant heterologous elements may be present, and it comprises

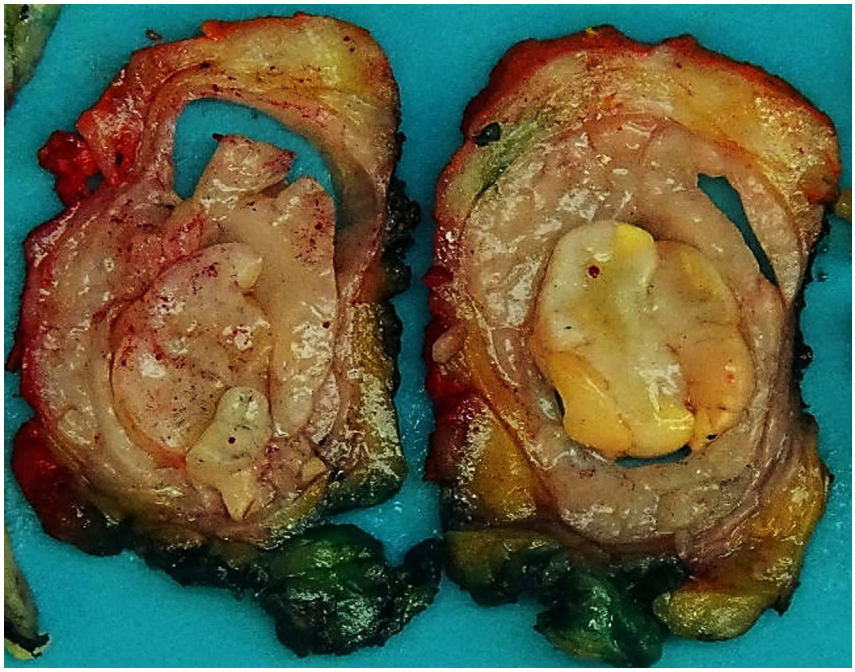

**Fig. 1** Gross appearance of a phyllodes tumour shows a circumscribed myxoid mass with broad fronds projecting into clefted spaces.

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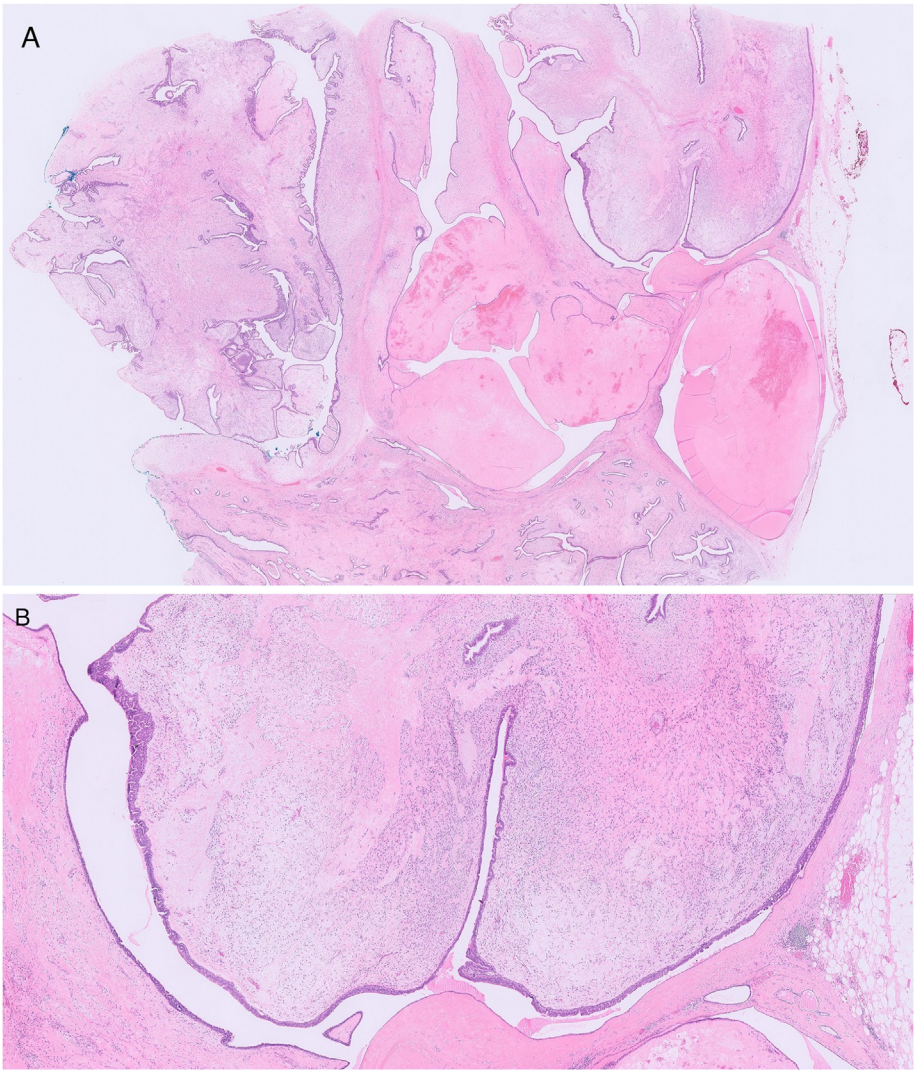


**Fig. 2** (A) Benign phyllodes tumour shows large leafy fronds, irregularly dilated clefted spaces, areas of increased stromal cellularity with haemorrhagic infarction observed in this case. (B) Higher magnification shows variably cellular stroma with interspersed oedema forming the broad frond-like stromal expanses, surmounted by benign epithelium with usual ductal hyperplasia.

10–20% of all these neoplasms[16] (Fig. 4). It was the recommendation of the WHO Working Group that all histological criteria should be at the malignant end of the spectrum for categorisation as malignant grade.

More recently, the 2019 5th edition of the WHO breast tumour classification incorporated a similar table, without significant changes from that provided in the 2012 volume, apart from the recommendation that mitotic activity ought to be stipulated as per $mm^2$ for standardisation across different microscopes and to accommodate the increasing use of digital pathology, as well as the fact that well differentiated liposarcoma is now not included among malignant heterologous elements that could individually allow malignant categorisation of a phyllodes tumour.[17] The editorial board of the 2019 WHO breast blue book considers liposarcoma in the breast to have no metastatic potential and hence is insufficient as a sole criterion to warrant malignant grading (Fig. 5). This view is also supported by the abnormal adipocytes lacking *MDM2* or *CDK4* amplifications in contrast to extramammary well differentiated liposarcoma.[18–20] For such cases, one needs to evaluate other stromal parameters for grading.

## PHYLLODES TUMOUR GRADING

Grade predicts clinical behaviour with correlation to local recurrences and metastases. Metastasis can occur in malignant and rarely borderline tumours.

The practising pathologist needs to be aware of a few immediate grading pitfalls. Phyllodes tumours are notoriously heterogeneous and adequate sampling of at least one block per centimetre of maximum tumour dimension, with additional sampling of grossly heterogeneous areas, is recommended. Core biopsy changes should not be mistaken for permeative tumour borders (Fig. 6), and stromal multinucleated giant cells are not to be equated with stromal atypia (Fig. 7). For the latter cases, evaluation of adjacent non-multinucleated stromal cells is required. Grading of phyllodes tumours diagnosed on core biopsy is not advocated due to the heterogeneity of the tumour. Unless there are overt malignant features in which case a malignant grade may be concluded, phyllodes tumours showing bland stromal features may disclose more adverse appearances in the subsequent excision, hence final grading is often best achieved on the excised specimen.

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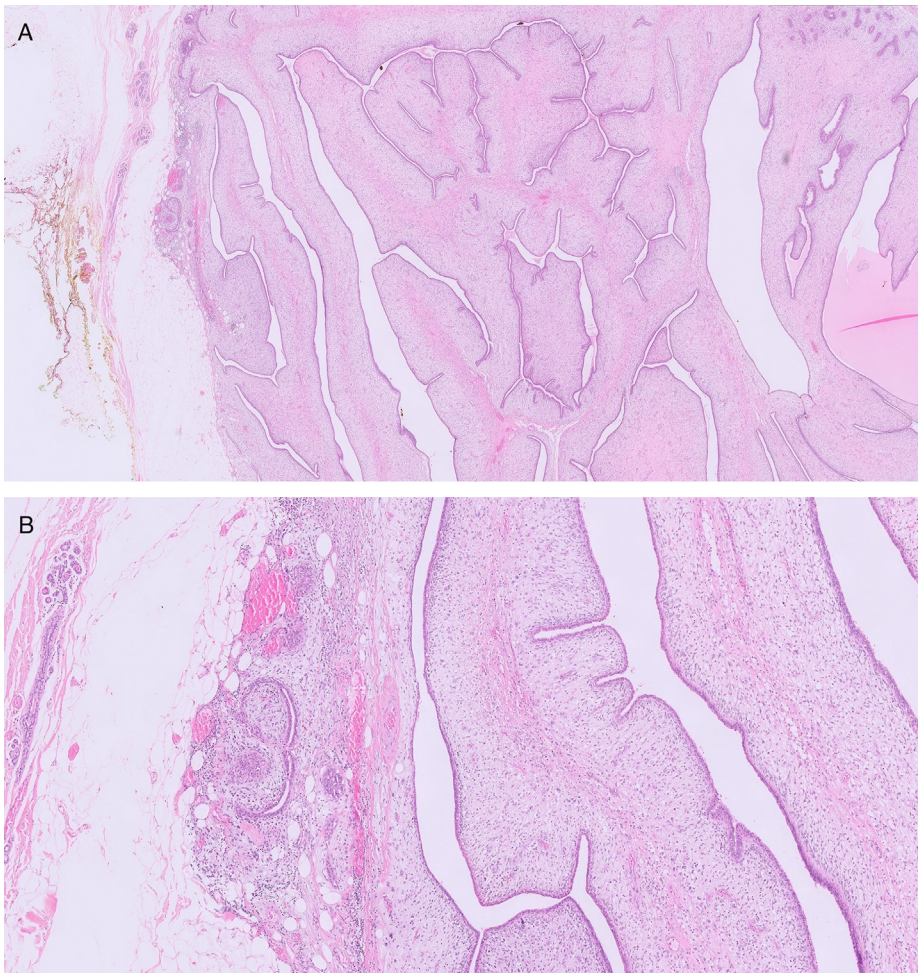


**Fig. 3** (A) A borderline phyllodes tumour shows focally permeative borders with peripheral adipose entrapment. (B) Higher magnification of the irregular tumour border where stromal cells encircle adipocytes. Mild to moderate stromal atypia is noted.

A more deep seated, intrinsic and recurrent challenge is in the assessment of histological parameters used in grading or classifying phyllodes tumours which relates to the use of multiple histological parameters for grading. Tumour borders can be circumscribed in both benign and borderline tumours, permeative margins can be observed in both borderline and malignant lesions. The degree of stromal cellularity overlaps between benign and borderline, borderline and malignant tumours, while stromal atypia can be mild in both benign and borderline tumours. Although the range of mitotic counts appears relatively well defined, tumours do not necessarily possess mitotic frequency strictly according to these values in relation to the corresponding defined grades. Stromal overgrowth can be absent in benign and borderline tumours, and present in both borderline and malignant tumours. While malignant heterologous elements can be definitive for designating a malignant grade, they are rarely encountered in routine practice, and therefore are not useful in the majority of cases. All these multiple permutations confound and complicate the grading process. In reality, this is not altogether unexpected as phyllodes tumours do not occur in dichotomous grades but exist along a biological continuum with overlapping histological features (Fig. 8).

Despite the challenges, there is correlation of grade as it is currently determined, with clinical behaviour. Benign tumours recur in 10–17% of cases, borderline 14–25% and malignant ones 23–30%.[17] Metastases occur almost exclusively in malignant tumours, occurring in 16.7% of cases, with rare borderline tumours capable of metastasising as well, estimated at 1.6%. Isolated cases of benign phyllodes tumours that are reported to metastasise account for 0.1%, though it is uncertain if these tumours were well sampled and appropriately categorised. Metastases usually comprise malignant stromal or heterologous elements devoid of epithelium (Fig. 9).

When considered as an entire group, phyllodal metastases are rare, seen in up to 2% of all tumours. Several authors have studied if there are predictors of metastasis, with age >50 years, stromal overgrowth, diffuse marked atypia, necrosis, mitoses $\geq$10/10 hpf discovered to be of predictive importance;[21] large tumours (>9 cm) with heterologous elements[22] and marked stromal cellularity, stromal overgrowth, infiltrative borders, mitoses $\geq$10/10 hpf are also reported to be useful.[23]

## SINGAPORE NOMOGRAM

Because of the imperfection and imprecision in grading, we conducted a large study of 605 patients to determine the relative impact of individual histological parameters on outcome, leading to a nomogram based on stromal atypia, mitoses, overgrowth and surgical margins (AMOS criteria)

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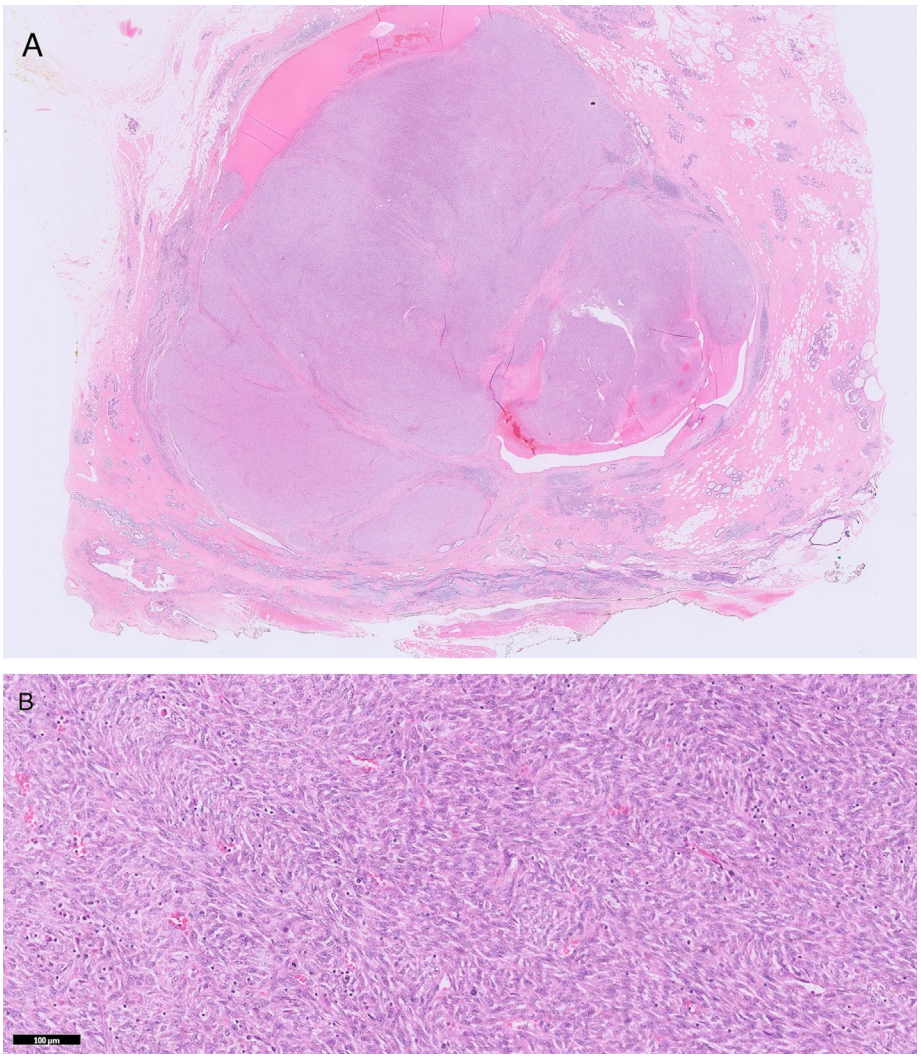


**Fig. 4** (A) Malignant phyllodes tumour shows extensive stromal overgrowth with areas of haemorrhage. (B) Moderate to marked stromal hypercellularity, atypia and readily discerned mitoses are present.

that could predict recurrence risk (https://jcp.bmj.com/content/65/1/69).[15] This nomogram has been validated in several studies in different geographic populations.[24–28] The nomogram was previously available as a web calculator, with the risk assessment tool being able to provide estimates of recurrence-free probability at 1, 3, 5 and 10 years calculated from a score generated from the assessment of stromal atypia, mitotic count, stromal overgrowth and whether the surgical margins are involved. Unfortunately, this tool is no longer accessible at the original online site and is in the process of being established at an alternative location.

Limitations of the nomogram include its inability to distinguish between local and distant recurrences, with the vast majority of recurrences in the original study being of local rather than distant nature.[15] There also remain interobserver reproducibility issues in assessing the AMOS criteria. The nomogram was developed based on excision specimens, and requires validation on larger cohorts with more recurrent events. Recent emerging and novel biological data are not integrated, and the nomogram's emphasis on surgical margin status is not borne out in recent studies, where recurrence rates of benign tumours are low despite positive margins.[29–34]

A recent study from Pittsburg compared the WHO classification of phyllodes tumours with the Singapore nomogram scores, finding that there was correlation for tumours with negative margins. The authors reiterated that the nomogram features of stromal atypia, mitoses and overgrowth are also integral to the WHO classification.[35]

## PHYLLODES TUMOUR TYPING

Accurate classification allows precise typing of a neoplasm as a phyllodes tumour, separating it from histological mimics, with the main differential diagnosis of benign phyllodes tumour being the cellular fibroadenoma (Fig. 10). Fibromatosis and low grade fibromatosis-like metaplastic carcinoma can resemble stromal predominant borderline phyllodes tumour. High grade metaplastic carcinoma and primary breast sarcoma are mimics of the malignant phyllodes tumour (Fig. 11), though there is a belief that breast sarcoma could represent malignant phyllodes tumours whereby the malignant stromal elements efface the underlying phyllodal architecture.[36,37]

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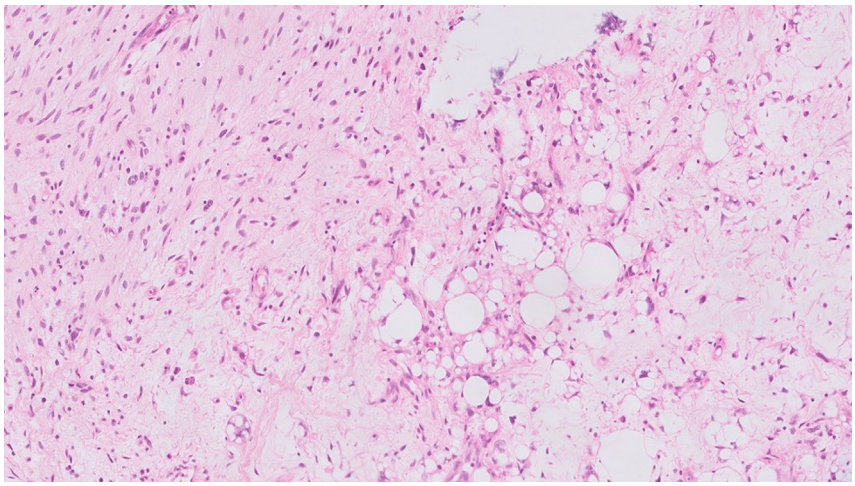

**Fig. 5** Well differentiated liposarcoma comprising univacuolated cells with peripherally compressed hyperchromatic nuclei, as well as a few multivacuolated cells, within a phyllodes tumour.

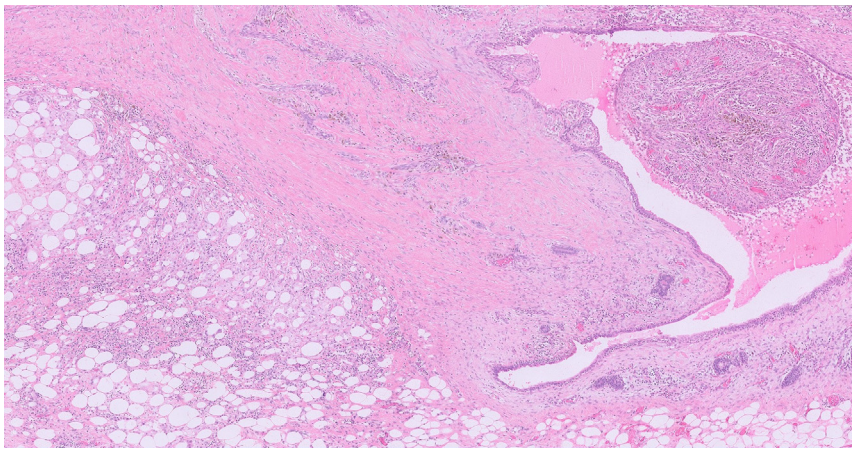

**Fig. 6** Phyllodes tumour shows biopsy site changes with fibrosis, fat necrosis, granulation, haemosiderin deposits and chronic inflammation – this should not be misinterpreted as a permeative tumour border.

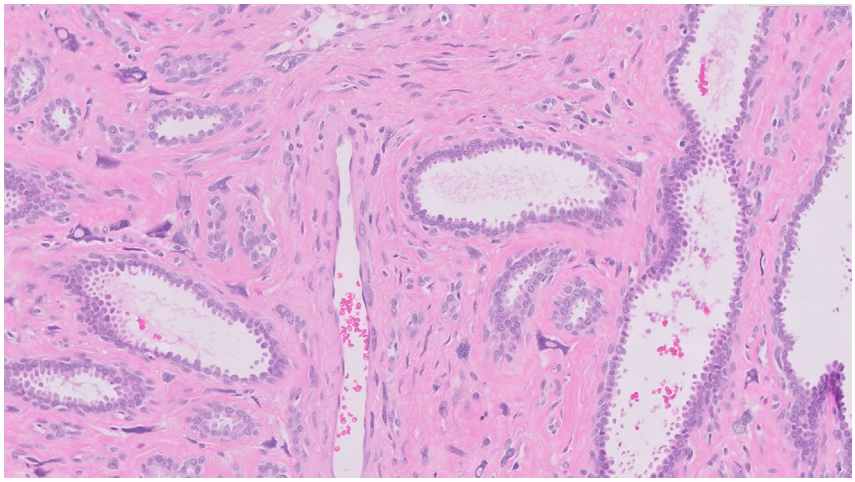

**Fig. 7** Stromal multinucleated cells with degenerative nuclear atypia are seen among stromal cells and epithelial elements.

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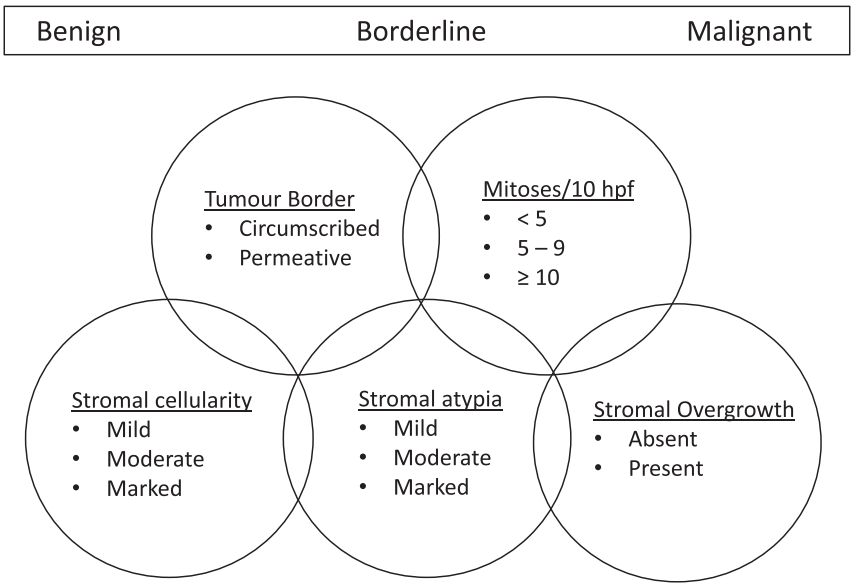


**Fig. 8** Phyllodes tumours, while divided into three distinct grades, in reality exist along a biological continuum with overlapping histological features.

## INTEROBSERVER REPRODUCIBILITY AND CONCORDANCE

Whether pathologists agree with one another on classifying phyllodes tumours was evaluated in a publication applying the WHO 2012 criteria, where 21 fibroepithelial lesions that were challenging to classify between fibroadenoma and phyllodes were reviewed by 10 breast pathologists. Only two cases showed complete consensus between fibroadenoma and phyllodes tumour. For the remaining 19 cases, separating fibroadenoma and benign phyllodes tumour as a group, from borderline and malignant phyllodes tumours as a separate group, yielded full agreement in 53% of cases, and 90% agreement in 79% of cases.[38]

In a more recent study from Nottingham,[39] returns from an average of 607 participating pathologists were evaluated to determine the diagnostic concordance of 26 phyllodes tumours from the United Kingdom External Quality Assurance (EQA) scheme, circulated over 17 years, comprising 14 benign, six borderline and six malignant phyllodes tumours. There was 86% agreement when broadly grouped into benign lesions, borderline phyllodes tumours and malignant lesions, which decreased to 63% when they were specifically separately categorised into benign, borderline and malignant grades. The highest agreement was achieved for malignant phyllodes tumour (86%) while the lowest agreement was seen for borderline phyllodes tumour (42%).

These two studies underscore the challenges of classifying phyllodes tumours based on current criteria, and the generally suboptimal agreement among pathologists.

## PHYLLODES TUMOUR SURVEY

In order to gain insights and better understand how pathologists diagnose phyllodes tumours in routine practice, an online survey was conducted, to which 213 pathologists from 29 countries responded. Over half of the pathologists reported diagnosing 10–50 phyllodes tumours per year. A majority of 84% considering increased stromal cellularity to be key for the diagnosis of the tumour, and despite stromal fronds being part of the WHO definition, only 59% thought they were of prime importance.[40]

With regard to grading, many pathologists were ambivalent about the relative importance of histological parameters, with mitoses, stromal overgrowth and atypia being the top three features used to determine grade, though the proportions of pathologists ranking these microscopic features as most important were 55.5%, 54% and 51.9%, respectively.

Additional significant findings included the discovery that close to half of respondents stated that they would diagnose malignant phyllodes tumour without a full array of adverse features, deviating from the WHO recommendation that full-fledged malignant features be seen in all the histological parameters for a diagnosis of malignant grade. Close to 70% considered age an important factor in separating fibroadenoma from phyllodes tumour though age is not a specific criterion for classification as phyllodes tumour. Over half found particular challenge in the diagnosis of the borderline grade, in line with the lowest interobserver concordance for this tumour grade in the Nottingham study alluded to above.[39]

The survey results disclose that there is a divergence between recommended criteria and real practice, with 84.3% of pathologists prioritising stromal cellularity in the diagnosis of phyllodes tumour rather than a fronded architecture. A significant proportion of pathologists ranked the multiple histological parameters differently for grading purposes. Malignant phyllodes tumour is diagnosed even when not all microscopic features are adverse. These findings reinforce the challenges in classification and consistent grading of phyllodes tumours.

## MOLECULAR GENETICS

Information on the molecular genetics of fibroepithelial tumours, including phyllodes tumours, has burgeoned significantly in the last few years. A genomic study published in 2015 showed *MED12* mutations as the underpinning abnormality for both fibroadenomas and phyllodes tumours, with additional aberrations in other genes observed for borderline and malignant tumours.[41,42] This prompted the proposal for the progression model for fibroepithelial tumourigenesis, where initial mutations in the *MED12* and *RARA* genes

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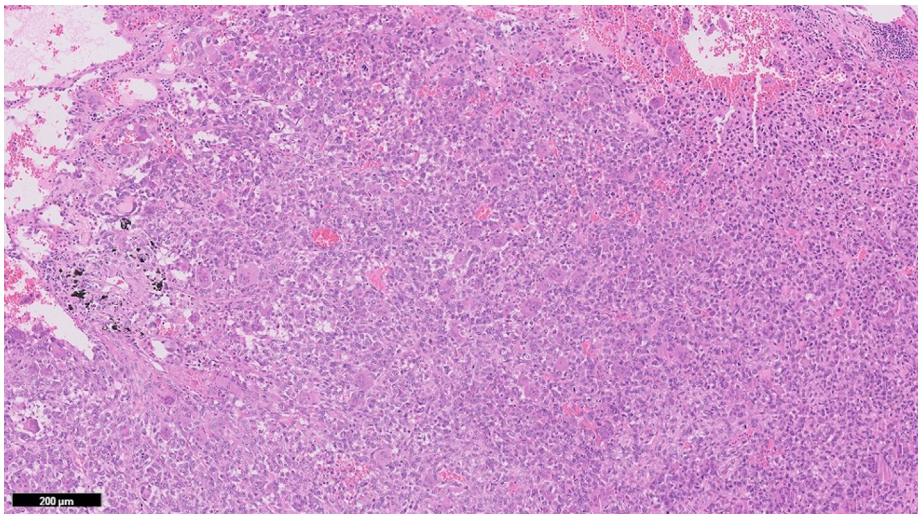


**Fig. 9** Metastatic phyllodes tumour to the lung shows only the malignant stromal component with malignant epithelioid and spindle cells, accompanied by osteoclastic type multinucleated giant cells. A few lung alveoli are seen in the left upper field.

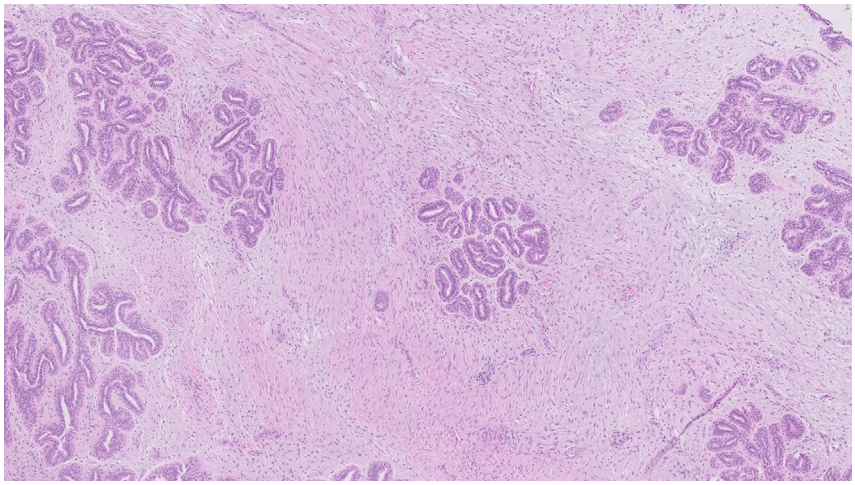

**Fig. 10** Cellular fibroadenoma shows mild increase in stromal cellularity noted among the epithelial elements.

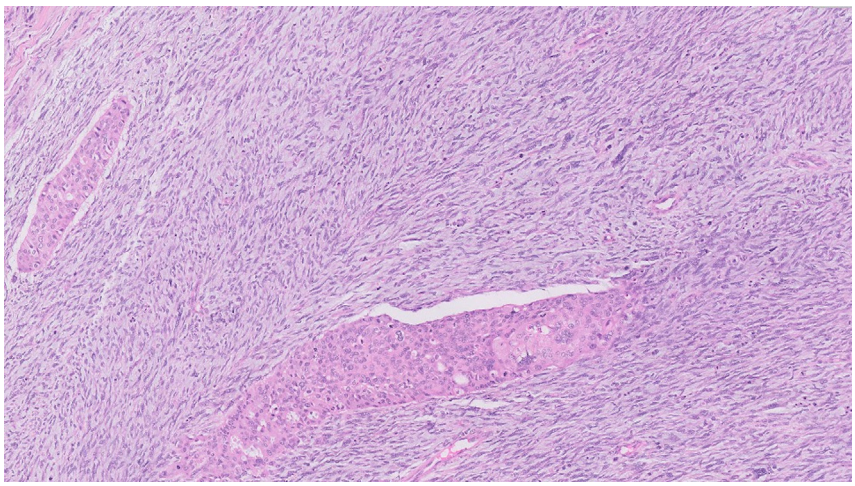

**Fig. 11** High grade spindle cell metaplastic carcinoma shows malignant spindle cell fascicles with scattered abnormal spindle cells containing pleomorphic hyperchromatic nuclei, together with several cohesive islands of malignant epithelial cells, the latter supporting the diagnosis of a metaplastic carcinoma.

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trigger fibroadenoma formation, acquisition of abnormalities in the *TERT*, *FLNA*, *SETD2* and *MLL2* genes leads to phyllodes tumour development, and derangements in cancer driver genes push progression into borderline and malignant forms.

It is important to note that the transition from fibroadenoma to phyllodes tumour is exceedingly infrequent, acknowledging the huge numbers of fibroadenomas diagnosed annually in comparison with the few phyllodes tumours.

The *MED12* gene is located on the X chromosome, encoding mediator complex subunit 12, which associates with transcription factors to recruit the mediator complex and influence target gene expression.[43] Frequent *MED12* exon 2 somatic mutations have been found previously only in the uterine leiomyoma, with a near identical mutation spectrum in fibroadenomas. It was postulated that *MED12* exon 2 mutations could be associated with hormonal expression. There is a proposed *MED12* independent pathway for the formation of borderline and malignant phyllodes tumours which arise *de novo* through genetic alterations of *TERT*, *EGFR* and other oncogenes, as described in a review paper by the Memorial Sloan Kettering Cancer Centre group.[44]

The clinical relevance of molecular discoveries informs the potential utility of a genomics-based classification of breast fibroepithelial lesions that can enhance diagnostic accuracy, such as differentiating fibroadenoma from phyllodes tumour,[45] separating phyllodes tumour from other spindle cell tumours,[46] and distinguishing malignant phyllodes tumour from metaplastic carcinoma.[47]

Discovery of candidate therapeutic targets in borderline/malignant phyllodes tumours like *PIK3CA* activating mutations and *EGFR* amplifications can provide druggable options.[48]

*MED12* mutations may predict improved disease-free survival in patients afflicted with this disease,[49,50] and the linkage of *MED12* and *RARA* mutations to hormone receptor signalling can open alternative treatment avenues.[41]

Past molecular studies have supported both the two-tiered and three-tiered classification schemes of phyllodes tumours using karyotyping,[51] loss of heterozygosity analysis,[52] comparative genomic hybridisation (CGH),[53] array CGH,[54] gene expression profiling[55] and next generation sequencing.[56]

Molecular work by our group on typing and grading of fibroepithelial tumours during recent years has also been published.[41,47,57–60] Preliminary findings on paired primary phyllodes tumours and their recurrences using whole exome sequencing, reveal a few recurrent tumours that harbour *EGFR* mutations that are potential drug targets (unpublished data).

## INTERNATIONAL COLLABORATION ON CANCER CLASSIFICATION AND RESEARCH (IC$^3$R)

In order to systematically amalgamate the growing body of scientific information to plug existing gaps in phyllodes tumour classification that can be globally impactful, leveraging the collaborative networks of international bodies is important.

The IC$^3$R, formed under the auspices of the International Agency for Research on Cancer (IARC), aims to address challenges related to tumour classification, such as its increasingly multidimensional nature, the vast amount of scientific information, as well as the impediments in translating research findings into tumour classification and cancer diagnosis by individual groups (https://ic3r.iarc.who.int/).[61]

The IC$^3$R provides a platform for coordinating evidence generation, synthesis, evaluation, and standard-setting for tumour classifications worldwide.

There is an endorsed study within the IC$^3$R on refining the classification of phylldes tumours using a multipronged approach of evidence gap mapping, molecular profiling of phyllodes tumour recurrences, surveying international practices with key findings mentioned above, and a systematic review, in collaboration with radiation oncology colleagues, on the role of radiation treatment in borderline phyllodes tumours. This project proposes to build a robust, international, living library of the rare phyllodes tumours, with a focus on borderline and malignant grades, as well as phyllodes tumours with malignant heterologous elements. It is believed that genomic and histological analyses will inform and refine future classifications.

## EVIDENCE GAP MAPPING OF THE PHYLLODES TUMOUR CHAPTER IN THE WHO BLUE BOOK 2019

The use of evidence gap mapping methodology in assessing the available evidence for a particular tumour provides an accurate summary of information gaps which can spur future research. It can also help inform and update content for future WHO blue books.[62]

We have evaluated the cited references in the phyllodes tumour chapter of the 5th edition of the WHO breast book,[63] with studies represented in spheres and colours corresponding to the levels of evidence, where red, blue and green indicate low, moderate and high evidence levels, respectively (Fig. 12). Briefly, of 78 studies referenced in the chapter, the majority of papers were of low evidence level (82%), while the rest were moderate level (17%) or unclassifiable (1%). There were no high evidence level papers. This should improve in the next classification update, with several systematic reviews that are now available in the literature since the 2019 publication of the breast blue book that should improve the evidence level distribution.

## ARTIFICIAL INTELLIGENCE

The availability of digital whole slide images has propelled studies using artificial intelligence (AI) to augment pathological diagnosis. Our recently published study utilised AI to distinguish fibroadenoma from phyllodes tumour on core biopsy based on whole slide images of 187 fibroadenoma and 100 phyllodes tumour core biopsies.[64]

The AI model achieved an overall slide level accuracy of 87.5%, with accuracies of 80% and 95% for fibroadenoma from phyllodes tumour slides, respectively, suggesting that there is a potential role of AI in diagnostic discrimination between these lesions on core biopsies which may be further refined for use in routine practice. AI may also be tapped to assist in grading accuracy and objectivity.

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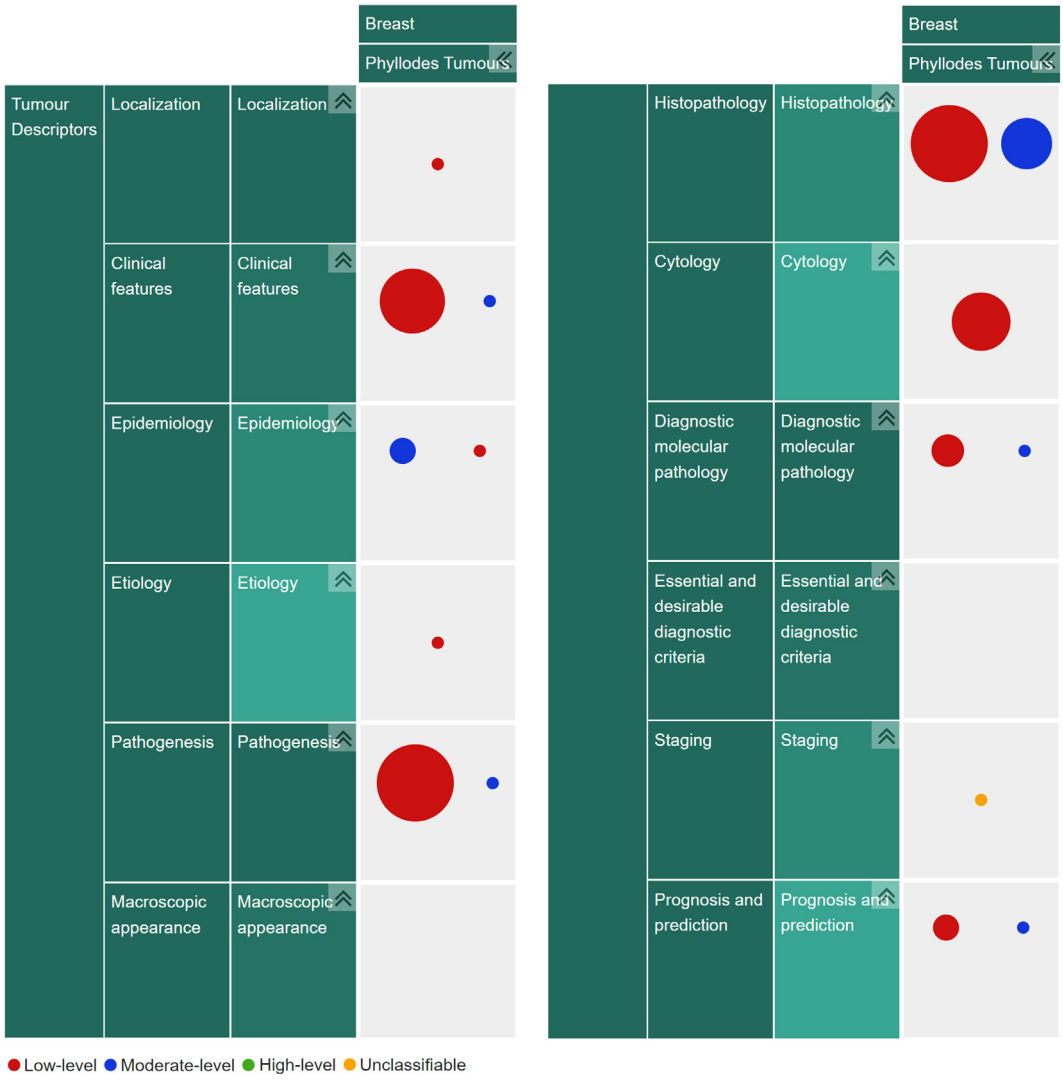


**Fig. 12** Evidence gap map of cited references in the phyllodes tumour chapter of the WHO Classification of Tumours of the Breast (5th edition). The colours of the bubbles correspond to the level of evidence of a publication: red (low level), blue (moderate level), green (high level), and orange (unclassifiable).

## CONCLUSION

It is believed that pathologists would hope for, and appreciate, a refined phyllodes tumour classification that is simple to apply, comprehensive, reproducible, concordant and prognostically relevant, which can bring the recommended histological criteria to real practice. Evidence gaps should be plugged through scientific research. Integration of molecular and digital tools, and engagement of collaborative networks like the International Fibroepithelial Consortium, can improve consistency in diagnosis. Standardised reporting supported by international pathology reporting bodies like the International Collaboration on Cancer Reporting can help improve application of recommended criteria.[65] It is noted that the College of American Pathologists has recently launched a reporting guide for breast excision specimens containing phyllodes tumours.[66]

In summary, phyllodes tumours are uncommon breast neoplasms with continued challenges in classification and grading. Combined international efforts are needed to devise a unified practical system that informs and optimises treatment for individual patients.

Additional concerted research is needed to improve the classification of phyllodes tumours that can be pathologically accurate, readily applicable, and clinically meaningful, translating to refinements of a future WHO classification of breast tumours that reflects the latest understanding of the field, embraced by both experts and practising pathologists.

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