Introduction
Phyllodes tumours also known as cystosarcoma phyllodes, cystosarcoma phylloides, serocystic disease of Brodie and phyllodes tumour, are typically large, fast-growing masses that form from the periductal stromal cells of the breast. It accounts for less than 1% of all breast neoplasms.

[Picture Credit: Phyllodes Tumour]

Phyllodes tumours are a fibro-epithelial tumour composed of an epithelial and a cellular stromal component. They may be considered benign, borderline, or also malignant, depending on histologic features including stromal cellularity, infiltration at the tumour's edge, and mitotic activity (having to do with the presence of dividing or proliferating cells). Cancer tissue generally has more mitotic activity than normal tissues. All forms of phyllodes tumours are regarded as having malignant potential. They are also known. Phyllodes tumours rarely spread outside the breast.

Phyllodes Tumour
Although most phyllodes tumours are benign (not cancerous), some are malignant (cancerous) and some are borderline (in between non-cancerous and cancerous with a tendency to probably become cancerous). All three kinds of phyllodes tumours tend to grow quickly, and they require surgery to reduce the risk of a phyllodes tumour coming back in the breast (local recurrence).

Phyllodes tumours can occur at any age, but they tend to develop when a woman is in her 40s. Benign phyllodes tumours are usually diagnosed at a younger age than malignant phyllodes tumours. Phyllodes tumours are extremely rare in men.
The three main types of phyllodes tumour:

- **Non-cancerous (benign) tumours** – these make up about 50–60% of phyllodes tumours.
- **Borderline tumours** – these are not yet malignant (cancerous) but are more likely to turn malignant.
- **Cancerous (malignant) tumours** – these make up about 20–25% of all phyllodes tumours.

**Liew, K.W., Siti ubaidah, S. & Doreen, L. 2018.**

**BACKGROUND:** Malignant phyllodes tumors of the breast are uncommon fibroepithelial breast tumors with diverse biological behavior. Our study aim is to share our experience in treating patients with malignant phyllodes presenting to our center.

**PATIENTS AND METHODS:** A total of 11 cases of malignant phyllodes were retrospectively reviewed between Nov 2014 and Oct 2017.

**RESULTS:** The median age was 45 years old (31-61 years). The median pathological tumor size was 10.5cm (2-28cm). 6 patients (55%) were premenopausal. 7 patients (64%) were treated eventually with mastectomy and 4 (36%) were treated with breast conserving surgery. 4 (36%) patients had Axillary Clearance done while axillary sampling was done in 2 patient. The remainder 5 (45%) required axillary clearance at a later op. 6 (55%) patients received postoperative radiotherapy. After a median follow up period of 11 months (range 4-33 months), 8 developed local recurrence. The overall 2 year survival rate was 18%.

**CONCLUSION:** Malignant Phyllodes tumors are rare tumors that occur in fairly young women, when compared with the adenocarcinoma of the breast. They tend to grow to reach large with absence of nodal metastasis. Ultimately surgery is the mainstay of management but with postoperative radiotherapy it can decrease the local recurrence rates in certain presentations however recurrence rate is high and overall survival rates are poor.

**Incidence of Malignant Phyllodes Tumour in South Africa**

The National Cancer Registry (2014) does not reflect the incidence of Phyllodes Tumour. However, according the National Cancer Registry (2014) the following cases of histologically diagnosed breast cancer cases in South Africa among women was as follows. Histologically diagnosed means that a tissue sample (biopsy) was forwarded to an approved laboratory where a specially trained pathologist confirmed the diagnosis of cancer:

According to the National Cancer Registry (2014) the following number of breast cancer cases in women was histologically diagnosed during 2014:

<table>
<thead>
<tr>
<th>Group</th>
<th>Actual Number of Cases</th>
<th>Estimated Lifetime Risk</th>
<th>Percentage of All Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All females</td>
<td>8 230</td>
<td>1 : 27</td>
<td>21,78%</td>
</tr>
<tr>
<td>Asian females</td>
<td>456</td>
<td>1 : 15</td>
<td>39,30%</td>
</tr>
<tr>
<td>Black females</td>
<td>3 226</td>
<td>1 : 53</td>
<td>20,05%</td>
</tr>
<tr>
<td>Coloured females</td>
<td>1 169</td>
<td>1 : 19</td>
<td>28,57%</td>
</tr>
<tr>
<td>White females</td>
<td>3 370</td>
<td>1 : 11</td>
<td>20,51%</td>
</tr>
</tbody>
</table>
**Frequency of Histologically Diagnosed Cases of Breast Cancer**

According to the National Cancer Registry (2014), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>0 to 19 Years</th>
<th>20 to 29 Years</th>
<th>30 to 39 Years</th>
<th>40 to 49 Years</th>
<th>50 to 59 Years</th>
<th>60 to 69 Years</th>
<th>70 to 79 Years</th>
<th>80 + Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>All females</td>
<td>8</td>
<td>121</td>
<td>805</td>
<td>1 763</td>
<td>1 937</td>
<td>1 799</td>
<td>1 129</td>
<td>525</td>
</tr>
<tr>
<td>Asian females</td>
<td>1</td>
<td>5</td>
<td>33</td>
<td>89</td>
<td>109</td>
<td>118</td>
<td>67</td>
<td>19</td>
</tr>
<tr>
<td>Black females</td>
<td>6</td>
<td>84</td>
<td>469</td>
<td>789</td>
<td>722</td>
<td>526</td>
<td>287</td>
<td>174</td>
</tr>
<tr>
<td>Coloured females</td>
<td>0</td>
<td>11</td>
<td>90</td>
<td>266</td>
<td>300</td>
<td>237</td>
<td>166</td>
<td>72</td>
</tr>
<tr>
<td>White females</td>
<td>1</td>
<td>17</td>
<td>187</td>
<td>586</td>
<td>769</td>
<td>889</td>
<td>589</td>
<td>250</td>
</tr>
</tbody>
</table>

**Signs and Symptoms of Phyllodes Tumour**

These tumours will usually present as a smooth lump felt beneath the skin. The breast may become red or warm to the touch. These tumours can grow very fast, so it is important to have them evaluated as soon as possible. Symptoms can also mimic those of other types of breast cancer.

**Differential Diagnosis of Phyllodes Tumour**

The differential diagnosis of Phyllodes Tumour include:

<table>
<thead>
<tr>
<th>Juvenile Fibroadenoma</th>
<th>Low Grade Phyllodes Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>No leaf-like architecture</td>
<td>Prominent leaf-like architecture</td>
</tr>
<tr>
<td>No condensation around ducts</td>
<td>Stromal condensation around ducts</td>
</tr>
<tr>
<td>Does not infiltrate</td>
<td>May infiltrate surrounding breast</td>
</tr>
</tbody>
</table>

The histologic border between these two is not always sharp.

<table>
<thead>
<tr>
<th>Juvenile Fibroadenoma</th>
<th>High Grade Phyllodes Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stromal atypia</td>
<td>Atypical stroma</td>
</tr>
<tr>
<td>Stromal mitotic rate &lt; 3/10 hpf</td>
<td>Elevated stromal mitotic rate</td>
</tr>
<tr>
<td>No stromal overgrowth</td>
<td>Stromal overgrowth</td>
</tr>
<tr>
<td>Does not infiltrate</td>
<td>May infiltrate surrounding breast</td>
</tr>
</tbody>
</table>

Stromal overgrowth defined as at least one low power field (40x total magnification) composed entirely of stroma.

<table>
<thead>
<tr>
<th>Fibroadenoma</th>
<th>Low Grade Phyllodes Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacks significant stromal hypercellularity</td>
<td>Hypercellular stroma is prominent</td>
</tr>
<tr>
<td>No stromal overgrowth</td>
<td>May have stromal overgrowth</td>
</tr>
<tr>
<td>No leaf-like architecture</td>
<td>Prominent leaf-like architecture</td>
</tr>
<tr>
<td>No condensation around ducts</td>
<td>Stromal condensation around ducts</td>
</tr>
<tr>
<td>Does not infiltrate</td>
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</tr>
</tbody>
</table>

The histologic border between these two is not always sharp.
Metaplastic Carcinoma | Phyllodes Tumour
---|---
Spindled component may be positive for high molecular weight keratin or p63 | Stromal component negative for high molecular weight keratin and p63
Epithelial component is malignant | Epithelial component is benign
Squamous differentiation may be present | No squamous differentiation

Pure Sarcoma of the Breast
- Very rare
- The presence of an epithelial component defines phyllodes tumour

Fibromatosis
- Bland spindle cells
- Stellate configuration
- Absence of intrinsic epithelial component
  - May entrap normal breast lobules

Myofibroblastoma
- Resembles solitary fibrous tumour
- Lacks intrinsic epithelial component


**CONTEXT:** Phyllodes tumor (PT) of the breast is a rare fibroepithelial neoplasm with risks of local recurrence and uncommon metastases. The classification proposed by the World Health Organization for PTs into benign, borderline, and malignant is based on a combination of several histologic features. The differential diagnosis between PT and fibroadenoma and the histologic grading of PT remain challenging. In addition, the molecular pathogenesis of PT is largely unknown.

**OBJECTIVE:** To provide an updated overview of pathologic features, diagnostic terminology, and molecular alterations of PT.

**DATA SOURCES:** Current English literature related to PT of the breast.

**CONCLUSIONS:** Phyllodes tumor shows a wide spectrum of morphology. There are no clearly distinct boundaries between PT and fibroadenoma. Strict histologic assessment of a combination of histologic features with classification can help to achieve the correct diagnosis and provide useful clinical information. The genomic landscapes of PT generated from genomic sequencing provide insights into the molecular pathogenesis of PT and help to improve diagnostic accuracy and identify potential drug targets in malignant PT.

**Diagnosis of Phyllodes Tumour**
Phyllodes Tumour is diagnosed as follows:

Like other less common types of breast tumours, phyllodes tumours can be difficult to diagnose because doctors do not encounter them all that often. A phyllodes tumour also can look like a more...
common type of benign breast growth called a fibroadenoma. A fibroadenoma is a solid, growing lump of normal breast cells that is the most common kind of breast mass, especially in younger women.

Diagnosing phyllodes tumours usually involves a combination of steps:

• A physical (clinical) examination of the breasts. The doctor may be able to feel the lump in the breast, or a patient may feel it herself during a breast self-examination
• A mammogram to obtain X-ray images of the breast and locate the tumour. On a mammogram, a phyllodes tumour appears as a large round or oval mass with well-defined edges. Sometimes the tumour might look like it has rounded lobes inside it. Calcifications can show up as well. Calcifications are tiny flecks of calcium - like grains of salt - in the soft tissue of the breast. The doctor likely will need to do additional testing to confirm that the lump is a phyllodes tumour
• Ultrasound to obtain sound-wave images of the breast. The images form as the sound waves are ‘echoed back’ by the tissue. On ultrasound, phyllodes tumours look like well-defined masses with some cysts inside of them
• MRI to obtain additional images of the tumour and help in planning surgery
• Biopsy to take samples of the tumour for examination under a microscope. Although imaging tests are useful, biopsy is the only way to tell if the growth is a phyllodes tumour. The doctor can perform one of two procedures:
  ▪ core needle biopsy, which uses a special hollow needle to take samples of the tumour through the skin
  ▪ excisional biopsy, which removes the entire tumour

Some experts believe it is better to use excisional biopsy if a phyllodes tumour is suspected. Examining the whole tumour is often necessary to make the right diagnosis. The smaller tissue samples taken during core needle biopsy may not be enough to confirm that a lump is a phyllodes tumour. A pathologist then examines the tumour tissue under a microscope to make the diagnosis. He or she also classifies the phyllodes tumour as benign, borderline, or malignant. In a benign tumour:

• the edges are well-defined
• the cells are not dividing rapidly
• the stromal cells (connective tissue cells) still look somewhat like normal cells
• there is not an ‘overgrowth’ of stromal cells - there are epithelial cells (the types of cells that line the ducts and lobules) as well

In a malignant tumour:

• the edges are not well-defined
• the cells are dividing rapidly
• the stromal cells have an abnormal appearance
• there is an overgrowth of stromal cells, sometimes with no epithelial cells present at all
Treatment of Benign Phyllodes Tumour
Phyllodes tumours are always treated with surgery. This may be a wide local excision, or a
mastectomy, depending on the size. The specialist will discuss with the patient the type of surgery
she needs.
The aim of the surgery is to remove all of the tumour and an area of healthy tissue around it, known
as clear margin (border). This is because it is important to have a clear margin of healthy tissue when
the lump is removed to reduce the risk of it coming back. If a clear margin was not achieved by the
initial surgery further surgery is usually recommended.

Treatment of Malignant (Cancerous) Phyllodes Tumour
Malignant phyllodes tumours are treated by removing them along with a wider margin of normal
tissue, or by mastectomy (removing the entire breast) if needed. Malignant phyllodes tumours are
different from the more common types of breast cancer. They do not respond to hormone therapy
and are less likely than most breast cancers to respond to radiation therapy or the
chemotherapy drugs normally used for breast cancer. Phyllodes tumours that have spread to distant
areas are often treated more like sarcomas (soft-tissue cancers) than breast cancers.

PURPOSE: Malignant phyllodes tumor of the breast (MPTB) accounts for less than 1% of
whole breast neoplasm. Surgery is regarded as the primary treatment of choice in patients with
MPTB, but the necessity of postoperative radiation therapy (RT) has been a subject of debate. Our
aim was to evaluate effects of postoperative RT for MPTB using a large population database.
METHODS: Using the Surveillance, Epidemiology, and End Results Program (SEER) database (1983-
2013), clinico-pathologic prognostic factors were evaluated. Postoperative RT, tumor extent, grade,
and lymph node (LN) metastasis were included in the analysis. Univariate and multivariate Cox
proportional hazards regressions were performed to evaluate prognostic power of variables on
cancer specific survival (CSS).
RESULTS: A total of 1974 patients with MPTB were reviewed. Of these, 825 (42%) and 1149 (58%)
patients underwent mastectomy and breast conserving surgery (BCS), respectively. In each group,
130 (16%) and 122 (11%) patients received postoperative RT. For patients with adverse risk factors
including high grade and large tumor size, postoperative RT was more likely to be performed. In
multivariate analysis, age, ethnicity, tumor size, tumor extension and LN status were correlated with
prognosis in mastectomy group, while postoperative RT did not affect CSS. In BCS group, age and
grade were significant prognostic factors on CSS, meanwhile postoperative RT did not impact CSS in
multivariate analysis.
CONCLUSION: Although patients with more adverse prognostic factors underwent postoperative RT,
RT groups were not inferior to non-RT group on CSS regardless of surgery (mastectomy or BCS).

PURPOSE: The primary treatment of choice for patients with phyllodes tumor of the breast (PTB) is
surgery. Two major problems regarding the treatment of such patients remain unclear: what is the
appropriate surgical margin and what role is played by adjuvant radiotherapy (ART).
METHODS: The study provides a retrospective review of all patients with PTB treated between 1952
and 2013 at a single institute. The histology slides were re-examined based on WHO criteria. The
clinical characteristics and therapy outcomes were obtained. The five-year survival with no evidence of disease (NED) was used as the end point.

**RESULTS:** The study population comprised 340 women with PTB. Fifty-five percent of the patients were diagnosed with the benign, 11.8% with borderline and 33.2% with malignant PTB. All the patients received primary treatment with surgery (mastectomy-27.1%, and BCS- 72.9%). Local recurrence (LR) was found in 28 (9.1%) of these patients. Four patients with borderline and 8 with malignant PTB who were treated with BCS and had tumor-free margins < 1 cm received ART. None of these patients had LR and all survived 5 years NED. Of the 340 patients from our group, 294 (86.4%) survived five-years NED.

**CONCLUSION:** The prognosis for benign PTB is excellent and can be cured with surgery alone. A sufficient margin would be 0.1 cm (data from the literature) or 0.2-0.4 cm (our study). We recommend application of ART for such patients but the role of ART in patients with borderline and malignant PTB treated with BCS and with surgical margin < 1 cm remains uncertain.

**About Clinical Trials**
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:
- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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