



## Fibroepithelial breast lesions diagnosed by core needle biopsy demonstrate a moderate rate of upstaging to phyllodes tumors



Gabriel Marcil <sup>a, b, \*, 1</sup>, Stephanie Wong <sup>a, b</sup>, Nora Trabulsi <sup>a, b</sup>, Alexandra Allard-Coutu <sup>a, b</sup>, Armen Parsyan <sup>a, b</sup>, Atilla Omeroglu <sup>b, c</sup>, Gulbeyaz Atinel <sup>c</sup>, Benoit Mesurrolle <sup>b, d</sup>, Sarkis Meterissian <sup>a, b</sup>

<sup>a</sup> Department of Surgery, McGill University Health Centre, Montreal, QC, Canada

<sup>b</sup> Cedars Breast Clinic, McGill University Health Centre, Montreal, QC, Canada

<sup>c</sup> Department of Pathology, McGill University Health Centre, Montreal, QC, Canada

<sup>d</sup> Department of Radiology, McGill University Health Centre, Montreal, QC, Canada

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### ABSTRACT

**Background:** Fibroepithelial lesions of the breast (FEL) are atypical lesions diagnosed on core-needle biopsy. The purpose of this study was to determine the rate at which FELs are upstaged to phyllodes tumor on excision, and to examine the clinical and radiological factors that may be predictive of upstaging.

**Methods:** A retrospective review from the medical records of patients diagnosed with FEL on CNB at a single institution between 2010 and 2015 was performed. Patients diagnosed with benign or borderline phyllodes tumors were compared to those diagnosed with fibroadenoma.

**Results:** Of 74 patients diagnosed with FEL, 48 underwent excision (64.9%). Of the 48 lesions excised, pathology revealed 30 fibroadenomas (62.5%), 14 benign phyllodes tumors (29.2%), and 4 borderline phyllodes tumor (8.3%). No malignant phyllodes tumors were identified. On preoperative ultrasound, heterogeneous echotexture ( $p = 0.03$ ) and lack of internal vascularity ( $p = 0.03$ ) were significantly associated with upstaging to phyllodes tumor.

**Conclusions:** Surgical excision of FELs yield a pathological diagnosis of benign and borderline phyllodes tumor in 37.5% of cases. A high BIRADs score ( $\geq 4b$ ), heterogeneous echotexture and lack of internal vascularity on ultrasound may help predict upstaging to phyllodes tumor.

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### 1. Background and objectives

Fibroepithelial lesions (FEL) of the breast represent a heterogeneous group of biphasic neoplasms composed of a proliferation of both epithelial and stromal components. These lesions include the more common fibroadenoma and phyllodes tumor, both of which present as round or lobulated, mobile, well-circumscribed masses.<sup>1</sup> Phyllodes tumors are sub-classified into benign, borderline and malignant categories on the basis of mitotic activity, degree of stromal overgrowth, stromal cellularity and

atypia, and margin characteristics.<sup>2</sup> Borderline and malignant phyllodes tumors, if inadequately treated, have a propensity for rapid growth, recurrence, and metastatic spread, whereas benign phyllodes tumors are often indistinguishable from fibroadenomas on clinical, radiological and cytological grounds, and can be cured by local surgery alone, which remains the widely adopted practice.<sup>3–5</sup>

The management of fibroepithelial lesions diagnosed on core needle biopsy remains a challenge for breast surgeons, as selective excision has been associated with upstaging to phyllodes tumor in 18%–42% of reported series.<sup>6–9</sup> Several radiological and histological factors have been studied in an attempt to differentiate phyllodes tumor from fibroadenoma following a diagnosis of fibroepithelial lesion, but these factors often overlap and are seldom predictive enough to guide clinical management.<sup>7–11</sup> When there is

\* Corresponding author. Department of Surgery, Glen Site Hospital, MUHC, 1001 Decarie Boulevard, Montreal, QC, H4A 3J1, Canada.

E-mail address: [gabriel.marcil@mail.mcgill.ca](mailto:gabriel.marcil@mail.mcgill.ca) (G. Marcil).

<sup>1</sup> Present address: (August 2016) 735 36st NW, Calgary, Alberta, T2N 3A7, Canada.

histological ambiguity, the WHO recommends favouring a diagnosis of fibroadenoma over a benign phyllodes tumor in order to avoid overtreatment.<sup>12</sup> However, with current clinical guidelines favoring surgical excision for phyllodes tumors and clinical surveillance for fibroadenoma, the treating surgeon faces a dilemma when deciding on therapy for fibroepithelial lesion. At present, National Comprehensive Cancer Network (NCCN) guidelines suggest that palpable masses suspicious for phyllodes tumor that exhibit rapid growth and size greater than 3 cm on imaging be assessed for surgical excision, regardless of whether core needle biopsy yields fibroadenoma or an indeterminate result.<sup>13</sup> Yet the optimal management strategy of these lesions is yet to be determined and could consist of close clinical and radiological follow-up in selected patients in order to avoid the cost and morbidity associated with a surgical procedure.<sup>6,7</sup>

The purpose of this study was to determine the rate at which FELs managed surgically are upstaged to phyllodes tumor on final excision pathology, and to identify clinical and radiological factors predictive of such upstaging.

## 2. Methods

### 2.1. Patient selection and data acquisition

Following institutional review board approval, patients diagnosed with a FEL on core needle biopsy at the McGill University Health Centre Cedars Breast Clinic between 2010 and 2015 were identified from a prospectively maintained, comprehensive breast biopsy database. Patients with a personal history of phyllodes tumor were excluded. Pertinent clinical, radiologic, surgical, and pathologic information obtained from electronic medical records were then used to supplement database information. Variables examined included demographic and clinical information (age, medical comorbidities, clinical presentation) as well as mammographic findings including the presence of a mass, mammographic density, shape, size in greatest diameter, margins, and the presence of calcifications. Sonographic findings included mass size, shape, margin characteristics, vascularity, and echotexture. The Breast Imaging Reporting and Data system (BI-RADS) assessment categories were also obtained.

Core needle biopsies were performed under sonographic guidance by one of four dedicated breast radiologists at our centre. All biopsies were performed with 14-gauge core biopsy needles under local anesthesia. Pathological evaluations of all core-needle and excisional biopsy specimens were performed at our centre by two experienced breast pathologists (AO, GA). Management decisions regarding excisional biopsy versus close clinical surveillance were based on surgeon and patient preference.

### 2.2. Statistical analysis

Patient demographic and clinical characteristics were compared between those who received excision and those undergoing surveillance to assess for any potential differences in selecting patients for surgery. For those that underwent excision, final pathology results were analyzed. Because no malignant phyllodes tumors were diagnosed on final pathology, post-excision patients were categorized into “fibroadenoma” or “benign/borderline phyllodes” groups. Preoperative clinical, mammographic, and sonographic findings were then compared between the two groups. Statistical analyses were performed using Fisher's exact test for all categorical variables, and Student's T-test for continuous variables. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) with p-values of <0.05 considered statistically significant.

## 3. Results

### 3.1. Patient characteristics and management

In our centre, we identified 75 FELs diagnosed on core needle biopsy from 2010 to 2015 that could not be further classified as fibroadenoma or phyllodes tumor. One patient was excluded in the context of a previous phyllodes tumor. The final analytic cohort included 74 patients, 48 (64.9%) of whom underwent excision for definitive diagnosis, and 26 (35.1%) underwent clinical and radiological surveillance. Table 1 summarizes patient demographic characteristics and echographic findings with regards to management strategy.

The median age of the patients who underwent surgical excision was 41 years (interquartile range, IQR 30–47) and was not significantly different from the median age of patients who underwent surveillance (38 years, IQR 31–45;  $p = 0.75$ ). While a greater proportion of women with a personal history of breast cancer (20.8 vs. 7.7%,  $p = 0.19$ ) or positive family history (27.1 vs. 19.2%,  $p = 0.15$ ) opted to undergo excision, these differences did not reach statistical significance. In addition, the excisional group was comprised of patients with higher BI-RADS classification (97.8% vs. 61.6% BI-RADS 4a or greater,  $p < 0.001$ ) and slightly larger lesions (median size 2.4 cm vs. 1.9 cm,  $p = 0.06$ ) compared to lesions of women who chose active surveillance. All patients who underwent surgery underwent wide local excision, with one patient with borderline phyllodes requiring re-excision for positive margins.

### 3.2. Pathologic outcomes following excisional biopsy

Out of the 48 fibroepithelial lesions excised, final pathology results revealed 30 (62.5%) fibroadenomas, 14 (29.2%) benign phyllodes tumors, and 4 (8.3%) borderline phyllodes tumors, yielding an overall upstage rate of 37.5%. No malignant phyllodes tumor was identified on final excision pathology. Pathologic outcomes following excision are demonstrated in Table 2.

Table 3 summarizes preoperative patient's characteristics as well as radiological findings according to final pathology. Regarding patient age, patients diagnosed with benign/borderline phyllodes tumor were slightly older than patients diagnosed with fibroadenoma (median 42 years [IQR 31–48] vs 39 years [IQR 29–47]), although this difference was not statistically significant ( $p = 0.29$ ). Tumor size on imaging and clinical presentation of a palpable or rapidly enlarging mass were also similar between excised fibroadenoma and phyllodes groups, likely owing to these factors being common indications for excision.

Both groups demonstrated sonographic features of a lobulated appearance (66.7% phyllodes vs. 60% fibroadenoma,  $p = 0.76$ ), although phyllodes tumors were more likely to exhibit heterogeneous echotexture (38.9% vs. 10.0%,  $p = 0.03$ ) and less likely to demonstrate internal vascularity (22.2% phyllodes vs. 56.7% fibroadenoma,  $p = 0.03$ ). BI-RADS classification was also more likely to be higher in the phyllodes group (50% vs. 10% BI-RADS 4b or greater,  $p = 0.004$ ).

Phyllodes tumors demonstrated a median size of 2.75 cm (IQR 2.2–3.6 cm) on pathology. Borderline phyllodes were more likely to be larger (median 5.5 cm [IQR 4.0–9.8 cm]) than benign phyllodes (median 2.3 cm [IQR 2.0–3.1 cm],  $p = 0.006$ ), and present as rapidly expanding masses (75% vs. 0%,  $p = 0.005$ ). There were no other significant distinguishing radiologic features between the benign and borderline phyllodes groups.

## 4. Discussion

The majority of fibroepithelial lesions diagnosed on core needle

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