초음파 유도하 핵생검에서 진단된 유방의 엽상종양 혹은 세포충실성섬유상피병변: 절제생검 결과와 초음파 소견과의 비교

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Phyllodes Tumors and Fibroepithelial Lesions with Cellular Stroma of the Breast and Diagnosed by Sonographically Guided Core Needle Biopsy: A Comparison Between the Results of Excision Biopsy and the Sonographic Findings

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Purpose: The purpose of this study was to analyze the histologic concordance of sonographically guided core needle biopsy for phyllodes tumors or fibroepithelial lesions with cellular stroma of the breast by comparing this with the outcomes of excision biopsy and to identify any sonographic features that are helpful to predict phyllodes tumors.

Materials and Methods: We retrospectively reviewed 60 breast masses that were diagnosed as phyllodes tumors (n = 43) or fibroepithelial lesions with cellular stroma (n = 17) on a sonographically guided core needle biopsy. The tumors were all subsequently excised by surgery. The sonographic features were compared between the phyllodes tumors and the non-phyllodes tumors according to the results of excision biopsy.

Results: By the results on excision biopsy, there were 48 (80%) phyllodes tumors and 12 (20%) non-phyllodes tumors. Phyllodes tumors were diagnosed at a rate of 90.7% (39/43) for the nodules with phyllodes tumors on the sonographically guided core needle biopsy, and at a rate of 52.9% (9/17) for the nodules with fibroepithelial lesions with cellular stroma on the sonographically guided core needle biopsy. On sonography, heterogeneous internal echotexture (58% vs. 17%, respectively, p = 0.0239), clefts (56% vs. 17%, respectively, p = 0.0331) and horizontal linear striations (71% vs. 33%, respectively, p = 0.0221) were significantly more frequent in the phyllodes tumors than that in the non-phyllodes tumors.

Conclusion: Identification of a heterogeneous-internal echotexture, clefts and horizontal linear striations on sonography might help differentiate phyllodes tumors from non-phyllodes tumors.

Key words : Breast; Phyllodes tumors; Ultrasound (US); Core biopsy

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Introduction

Phyllodes tumor of the breast is a rare, aggressive neoplasm with an unpredictable clinical course, and it comprises < 1% of all mammary tumors and 2% to 3% of all fibroepithelial breast tumors [1]. This tumor has a high local recurrence rate after surgical excision,

and this rate has been variably reported as 8.2−42% [2−7]. Many authors have agreed that local recurrence was mainly due to positive resection margins and this was independent of the histologic types, and the authors recommended phyllodes tumor should be treated by wide local excision or mastectomy [2, 3, 8−11]. An inadequate preoperative diagnosis frequently leads to local excision with a positive margin [4].

Jacklin et al. reviewed various methods of clinical examination, imaging, fine needle aspiration biopsy, core needle biopsy and immunohistochemical techniques for the optimal preoperative diagnosis of phyllodes tumor and they concluded core needle biopsy was the most useful tool among them [12]. However, core needle biopsy obtains small samples and sometimes there is a diagnostic dilemma for borderline histology such as fibroepithelial lesion, which has the possibility of being either phyllodes tumor or fibroadenoma [13, 14]. To the best of our knowledge, there are few studies that have focused on the pathologic correlation of the lesions diagnosed as phyllodes tumor or fibroepithelial lesion with cellular stroma (FELCS) on a core needle biopsy [15−21].

This study is aimed to analyze the surgical outcomes of breast masses (phyllodes tumors and FELCS diagnosed by core needle biopsy) and to investigate whether any sonographic features can be helpful to predict a phyllodes tumor.

Materials and Methods

Study Population

The institutional review board approved this retrospective study, and informed consent was not required from the patients. Between October 2002 and October 2008, sonographically guided core needle biopsy was done for 7858 patients at our institution and the pathologic results of phyllodes tumor or FELCS were indentified in a total of 82 patients with 82 lesions. FELCS included biphasic or equivocal fibroepithelial tumor, fibroepithelial tumor favoring phyllodes tumor or fibroepithelial tumor favoring fibroadenoma. So these 82 cases represented 1.04% of all the breast sonographically guided core needle biopsies. From these 82 patients, sixty lesions in 60 patients were surgically excised and these comprised this study's population. The pathologic results of the sonographi-cally guided core needle biopsy were 43 phyllodes tumors and 17 FELCS. There were 41 benign and 2 borderline tumors from 43 phyllodes tumors.

All the sonographically guided core needle biopsies were performed using the free-hand technique and a high-resolution sonography unit with 7.5- or 12- MHz linear array transducers (HDI 5000 or 3000, Philips-Advanced Technology Laboratories, Bothell, WA; Logic 9, GE Medical systems, Milwaukee, WI). Each procedure was performed in an outpatient setting under local anesthesia with the patient in the supine position and using an automated gun (Pro-Mag 2.2, Manan Medical Products, Northbrook, IL) and a 14-guage Tru-Cut needle with a 22 mm throw (SACN™ Biopsy Needle, Medical Device Technologies, Gainesville, FL). Four or more core samples per a lesion were routinely obtained.

Imaging Evaluation

Mammography was available for 26 patients, and the remaining 34 patients were not scheduled for mammography because of their young ages (n=18), the surgeon's preference (n=11), tumors that were too big to be properly imaged by mammography (n=2) or because the lesions were detected on sonography follow up (n=3). The sonographic images were available in all 60 cases and the tumors were clearly identified on sonography. The sonographic findings were retrospectively reviewed by 2 radiologists, who were experienced in breast imaging, with using the sonography Breast Imaging Reporting and Data System (BIRADS) lexicon [22]. In addition to the BIRADS lexicon, we added cysts, clefts and horizontal linear striations (HLS), which are well known to be sonographic features of phyllodes tumor [23]. Cyst was defined as a greater than a 3 mm sized anechoic, round area, whereas a cleft, which reflects the slit-like cystic spaces that occur between the leaf-like stromal

proliferations, was defined as a flattened anechoic area. HLS means the observed slit-like spaces that are perpendicular to the direction of the beam, and these were defined as horizontally oriented echogenic lines [23]. During the imaging review, the reviewers were kept 'blind' to the pathologic reports.

Data Analysis

The pathological results of the excisional biopsy were divided into phyllodes tumors and non-phyllodes tumors. The patents' ages and sonographic findings were compared between these two sets of data.

Statistical analyses were conducted using the chi-

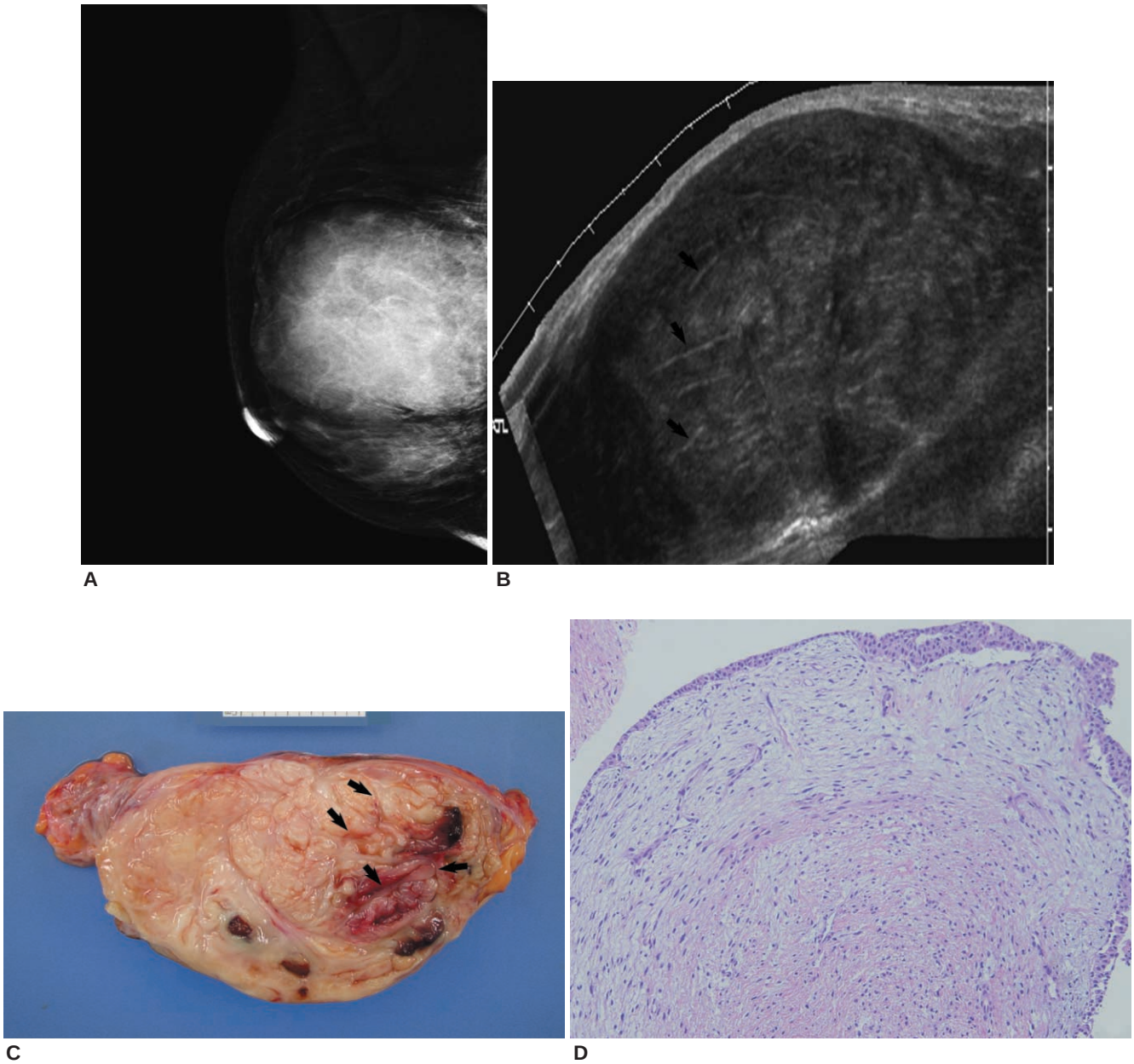
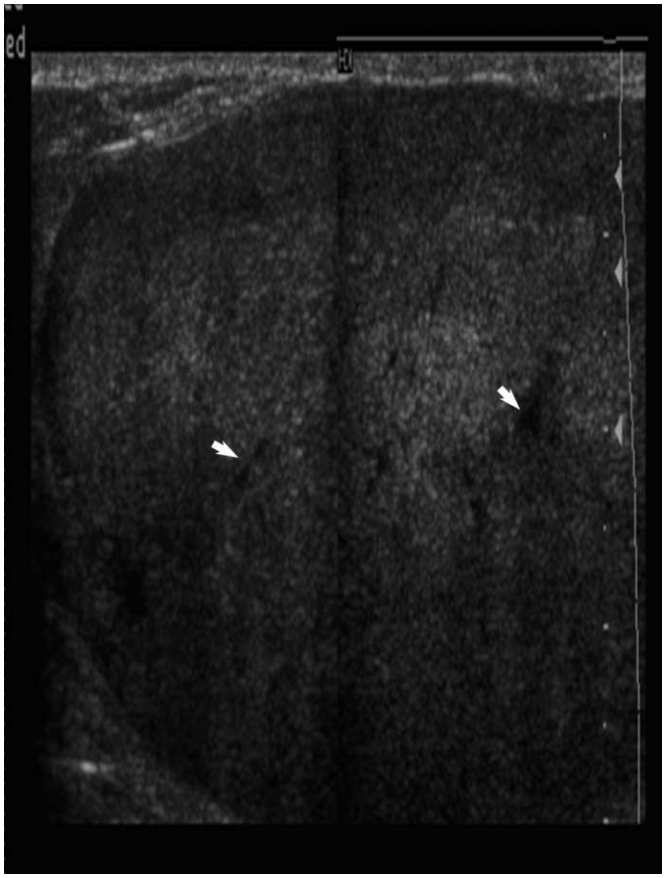


Fig. 1. A 53-year-old woman with a palpable right breast mass that was surgically confirmed to be phyllodes tumor. The result of sonographically guided core needle biopsy was benign phyllodes tumor.
A. The right mediolateral oblique mammogram shows a large, hyper-dense, circumscribed mass.
B. Sonography shows an oval, circumscribed, heterogeneous echoic mass approximately 5.8 cm in size with internal multiple horizontal echogenic lines (arrows).
C. The gross specimen shows a white to yellow mass with curved clefts (arrows) and hemorrhage.
D. Photomicrographs of the surgically excised specimens show an elongated epithelial lining with stromal proliferation and increased stromal cellularity, and this is compatible with phyllodes tumor (H & E ×100).

square test or Fisher's exact test for the categorical data and t-tests for the continuous data. P values < 0.05 were considered statistically significant. The data was analyzed by using software (MedCalc Software, version 10.2.0.0, Mariakerke, Belgium).

Results

A total of 60 patients were included and their ages ranged from 19 years to 64 years, and the mean age of the patients was 39.6 years. The mean diameter of all 60 lesions measured via sonography was 2.8 cm (range: 0.7−10 cm). There were associated palpable



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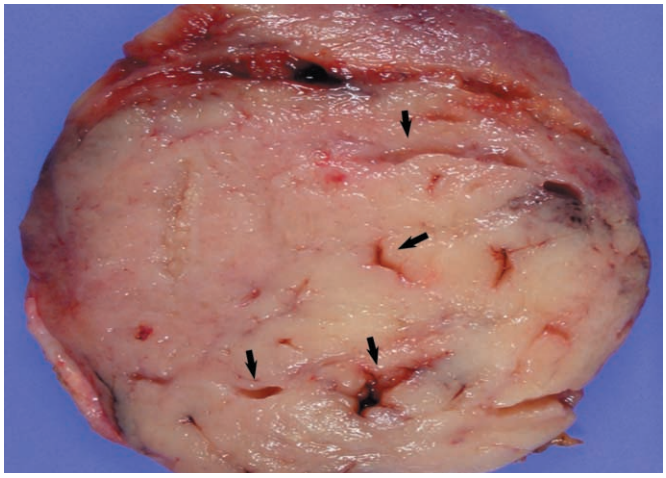

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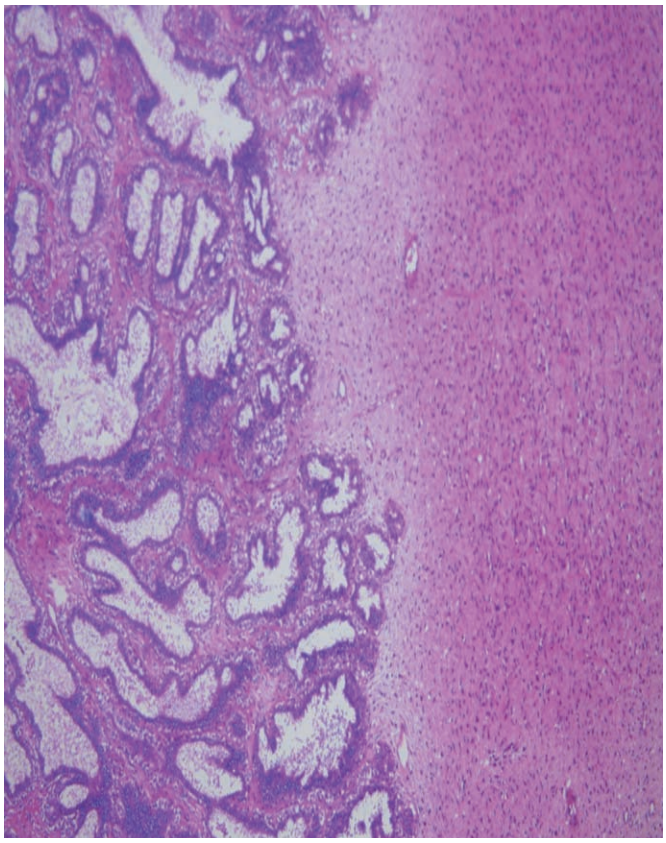


C

Fig. 2. A 24-year-old woman with a palpable right breast mass that was surgically confirmed to be phyllodes tumor. The result of sonographically guided core needle biopsy was fibroepithelial tumor with cellular stroma.
A. Sonography shows an oval, circumscribed, isoechoic mass 10cm in size with clefts (arrows).
B. The gross specimen shows a well-circumscribed, white to pink colored mass with clefts (arrows).
C. The photomicrograph of the surgical specimens shows a well-defined interface with the surrounding breast parenchyma and significant cellular stromal spindle cells (H & E ×100), which is all compatible with a borderline phyllodes tumor.

symptoms in 50 (83.3%) of the 60 lesions.

Mammography in 26 patients showed nonspecific features; well circumscribed and hyper-dense masses in 21 (80.8%) patients (Figs. 1 and 2), negative findings in 4 (15.4%) and findings suspicious for malignancy in 1 (3.8%) patient.

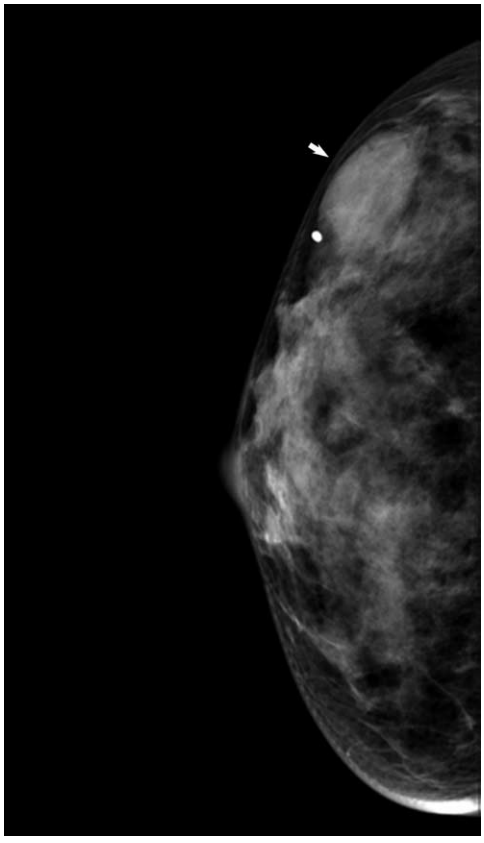
The final pathologic results of the surgical excision revealed 48 (80%) phyllodes tumors (29 benign, 14 borderline and 5 malignancy) and 12 (20%) non-phyllodes tumors (fibroadenoma (n = 9), stromal fibrosis (n = 1), fibrocystic change (n = 1) and adenosis (n = 1)). Of the 43 lesions that were phyllodes tumors and that were diagnosed by sonographically guided core needle biopsy, the excision biopsy revealed 39 (90.7%) phyllodes tumors, whereas of the 17 FELCS lesions, 9 (52.9%) were phyllodes tumors (Table 1). Phyllodes tumors were surgically/pathologically diagnosed at a rate of 90.7% (39/43) for the nodules of phyllodes tumors on the sonographically guided core needle biopsy, and phyllodes tumors were surgically/pathologically diagnosed at a rate of 52.9% (9/17) for the nodules of fibroepithelial lesions with a cellular stroma on the sonographically guided core needle biopsy.

Table 1. Summary of the Core Needle Biopsy Results and the Excision Biopsy Results

Results of the Core-Needle Biopsy	Results of the Excision Biopsy
Phyllodes tumor (n = 43)	Phyllodes tumor (n = 39)
	Fibroadenoma (n = 3)
	Adenosis (n = 1)
FELCS* (n = 17)	Phyllodes tumor (n = 9)
	Fibroadenoma (n = 6)
	Fibrocystic change (n = 1)
	Stromal fibrosis (n = 1)

* FELCS: fibroepithelial lesion with cellular stroma

The sonographic features were analyzed according to the pathologic results of excision biopsy (Table 2). The patients' mean age and the mean tumor size were not statistically different in these two groups (p = 0.5081, p = 0.1066). However, heterogeneous-internal



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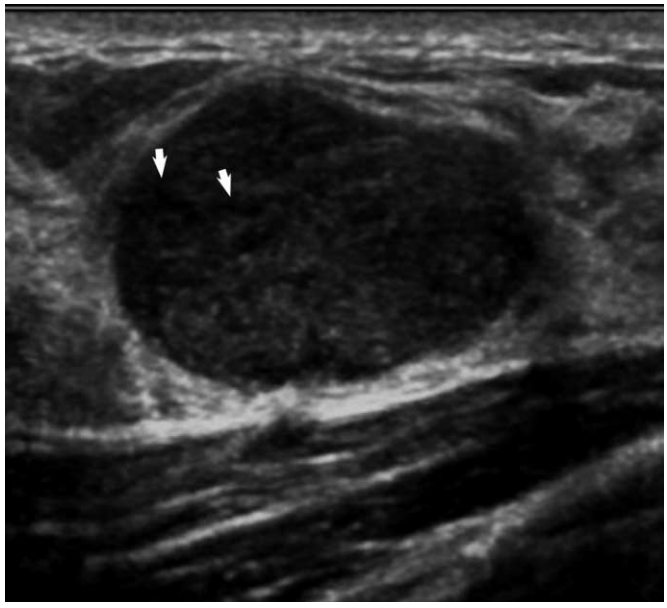

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Fig. 3. A 33-year-old woman with a palpable right breast mass that was surgically confirmed as fibroadenoma. The result of sonographically guided core needle biopsy was benign fibroepithelial tumor.
A. The right craniocaudal mammogram shows a well-defined, round, hyper-dense mass (arrow) at the palpable site.
B. Sonography reveals an oval, circumscribed, isoechoic mass approximately 2.8 cm in size with clefts (arrows).

Table 2. Sonographic Findings of the Surgically Confirmed Phyllodes Tumors and the Non-phyllodes Tumor

	Phyllodes Tumor (n= 48)	Non-phyllodes Tumor (n=12)	P value
Lesion diameter			0.1066
> = 3 cm	21 (44)	2 (17)	
< 3 cm	27 (56)	10 (83)	
Shape			0.5265
Oval	24 (50)	4 (33)	
Round	16 (33)	5 (42)	
Irregular	8 (17)	3 (25)	
Margin			0.1066
Circumscribed	27 (56)	3 (25)	
Not Circumscribed	21 (44)	9 (75)	
Internal Echogenicity			0.7555
Isoechoic	6 (12.5)	3 (25)	
Hypoechoic	31 (65)	7 (58.4)	
Marked Hypoechoic	6 (12.5)	1 (8.3)	
Complex	5 (10)	1 (8.3)	
Internal echotexture			0.0239
Homogenous	20 (42)	10 (83)	
Heterogenous	28 (58)	2 (17)	
Posterior Acoustic Enhancement			0.5593
Yes	45 (94)	10 (83)	
No	3 (6)	2 (17)	
Cyst			1.0000
Yes	5 (10)	1 (8)	
No	43 (90)	11 (92)	
Cleft			0.0331
Yes	27 (56)	2 (17)	
No	21 (44)	10 (83)	
Horizontal Linear Striations			0.0221
Yes	34 (71)	4 (33)	
No	14 (29)	8 (67)	

The data is the number of nodules. The numbers in the parentheses are percentages.

echotexture, clefts and HLS (p = 0.0239, p = 0.0331, p = 0.0221, respectively) were more common in the patients with phyllodes tumors than in the patients with non-phyllodes tumors (Figs. 1, 2 and 3).

Discussion

Percutaneous imaging-guided core needle biopsy for breast lesions is increasingly being used as a fast, safe, accurate, cost-saving and non-operative sampling method [24−26]. Although this technique is regarded as a reliable method for making the preoperative diagnosis of phyllodes tumor of the breast [12], there are only a few studies about the diagnostic accuracy of core needle biopsy for predicting phyllodes tumor [12, 15−21]. Dillon et al. insisted that core needle biopsy rarely produced the definite diagnosis of phyllodes neoplasm [21] whereas other authors concluded that core needle biopsy was useful for making the diagnosis of phyllodes tumor, and especially for the differentiation of phyllodes tumor from fibroadenoma [12, 16−18]. However, the sample size of several of these studies was too small to reach a definite diagnosis (size range: 7−57 lesions) [12, 15−20]. Two previous studies retrospectively reviewed the core needle biopsies of surgically confirmed phyllodes tumors and the core needle biopsy correctly diagnosed 11 of 17 (64.7%) and 10 of 12 (83.3%), respectively [16, 17]. In a study by Komenaka et al., of the 23 lesions that the core needle biopsy favored the diagnosis of phyllodes tumor, 19 (82.6%) were confirmed as phyllodes tumor by the surgical excision [18]. Dillon et al. reported that of 35 core needle biopsies that were suggestive of the possibility of

phyllodes tumor, 12 (35%) were phyllodes tumor [21]. Our results showed that phyllodes tumors were confirmed for 39 (90.7%) of the 43 phyllodes tumors diagnosed at core needle biopsy and this is higher than the rate in the previous studies, which may be the result of the differences of biopsy methods. The previous reports used various biopsy methods such as stereotactic or sonographically guided core biopsy with various needle sizes [15, 17, 18, 21] or fine needle aspiration cytology [16], whereas only sonographically guided 14-gauge core needle biopsy was employed as a biopsy method in our study. Therefore, our study is unique in dealing with only sonographically guided 14-guage core needle biopsy for making the diagnosis of phyllodes tumor.

Core needle biopsy could produce dilemmas with regard to the most appropriate clinical management subsequent to the results of FELCS. FELCS was first mentioned by Jacobs et al. in 2005 [15]. It was presented as a diagnostic term ranging from cellular fibroadenoma, fibroadenoma with cellular stroma, fibroepithelial lesions with cellular stroma to phyllodes tumor or cystosarcoma phyllodes. When biopsy specimens show equivocal findings between cellular fibroadenoma and phyllodes tumor, FELCS could be used for the diagnosis. Therefore, the presence of FELCS in core needle biopsy specimens needs subsequent surgical excision due to the possibility of phyllodes tumor [13, 14]. However, few studies have reviewed the surgical outcomes of FELCS encountered at core needle biopsy [15, 18−20]. Table 3 shows a summary of the published studies and the pathologic results of the surgically excised FELCSs that were diagnosed by core needle biopsy. According to this data, when the core specimens showed the features of FELCS, 22−44% of them were diagnosed as phyllodes tumor. In our study, 52.9% [9] of 17 FELCSs diagnosed by core needle biopsy were confirmed as phyllodes tumor and this is also higher than that in the previous studies.

The imaging findings have been not regarded as helpful for differentiating phyllodes tumors from fibroadenoma. A few articles have reported that there is substantial overlap in the imaging characteristics of phyllodes tumor and fibroadenoma [27−30, 32]. Particularly on sonography, most phyllodes tumors present as non-specific, lobulated, hypoechoic masses with heterogeneous internal echoes [27, 28].

However, in a large series that retrospectively analyzed the sonographic features of 110 phyllodes tumors and 2204 fibroadenomas, lobulation, heterogeneous internal echoes and the absence of calcifications were the independent sonographic features to distinguish phyllodes tumor from fibroadenoma [29]. Stavros stated that clefts or HLS, which represented the slit-like nature of the cystic

Table 3. Summary of the Surgical Excision Results of the Phyllodes Tumor or FELCS* Diagnosed by Core Needle Biopsy

Authors	Biopsy Guidance and Technique	Results of the Core Needle Biopsy	Results of the Excision
Jacob et al (2005)	US* 14G* auto* (n = 21) Stereotactic 11 or 14G vacuum* (n = 4) Palpation-14G auto (n = 4)	FELCS (n = 29)	Fibroadenoma (n = 16, 55%) Phyllodes tumor (n = 12, 41%) Benign fibromatosis-like lesion (n = 1, 4%)
Komenaka et al (2003)	US-14G auto (n = 44) Stereotactic 11G vacuum (n = 13)	Possibility of phyllodes tumor (n = 57)	Fibroadenoma (n = 32, 56%) Phyllodes tumor (n = 25, 44%)
Dershaw et al (1996)	Stereotactic 14G auto (n = 7)	Fibroadenoma vs phyllodes tumor (n = 7)	Fibroadenoma (n = 4, 57%) Phyllodes tumor (n = 3, 43%)
Meyer et al (1998)	US or Stereotactic 14G auto (n = 9)	Probable fibroadenoma with cellular stroma or phyllodes tumor (n = 9)	Fibroadenoma (n = 7, 78%) Phyllodes tumor (n = 2, 22%)
This study	US-14G auto (n = 60)	FELCS (n = 17)	Fibroadenoma (n = 6, 35.3%) Phyllodes tumor (n = 9, 52.9%) Fibrocystic change (n = 1, 5.9%) Stromal fibrosis (n = 1, 5.9%)

The data is the number of nodules. The numbers in the parentheses are percentages.
*FELCS: fibroepithelial lesion with cellular stroma, US: ultrasound, G: gauge, auto: automatic gun biopsy, vacuum: vacuum assisted biopsy

spaces that occur between the leaf-like stromal proliferations, or the slit-like spaces that were seen perpendicular to the direction of the beam were the useful sonographic findings of benign phyllodes tumors, although intracanalicular fibroadenomas can also demonstrate HLS because their fibroblastic stroma encloses the glandular elements and compresses them into slit-like spaces [23]. Those findings are concordant with our results [23, 29].

One study investigated HLS as a sonographic feature of phyllodes tumors, and they found that 22 (28.2%) of 78 phyllodes tumors showed that feature [16].

According to our results, 27 (56%) of the 48 phyllodes tumors showed clefts and 34 (71%) exhibited HLS. Clefts and HLS were significantly visualized more in the phyllodes tumors than in non-phyllodes tumors (56%/17%, p=0.0331, 71%/33%, p=0.0221, respectively). The other statistically significant sonographic finding was the internal echotexture as phyllodes tumors had a more heterogenous echotexture than did the non-phyllodes tumors (58% vs. 17%, respectively, p=0.0239). Heterogenous echotexture may be associated with "clefts or HLS" and it was also a significant sonographic feature that could distinguish phyllodes tumor from fibroadenoma in a previous study [29].

This current study has some limitations. First, this retrospective analysis was limited by the small sample size. A larger study would be helpful for evaluating the diagnostic accuracy of core needle biopsy and the characteristic sonographic features of phyllodes tumor. Second, there could have been inter-observer variability when interpreting the sonographic features, although we used the BIRADS lexicon and the accurately defined sonographic features.

In conclusion, sonographically guided core needle biopsy had high accuracy to diagnose phyllodes tumor. A heterogeneous echotexture, clefts and HLS seen on sonography were significantly more frequent in phyllodes tumors than in non-phyllodes tumors. If we consider both the core needle biopsy results and the sonographic features, then these results can be quite helpful to predict phyllodes tumors.

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요 약

목적: 유방의 초음파유도하핵생검에서 진단된 엽상종양 혹은 세포충실성섬유상피병변 (fibroepithelial lesion with cellular stroma)의 수술 후의 진단 결과를 비교하고 엽상종양을 예측하는데 도움이 되는 초음파 소견이 있는지 알아보고자 하였다.

대상과 방법: 초음파유도하핵생검에서 엽상종양의 가능성이 있다고 진단되고 수술을 시행하여 최종병리가 확인된 60명을 대상으로 하였다. 병변의 수술 결과에 따라 엽상종양과 엽상종양이 아닌 병변의 두 부류로 나눈 후 각각의 초음파 소견을 후향적으로 비교, 분석하였다.

결과: 수술로 확진된 60예의 병변 중 엽상 종양은 48예 (80%), 엽상종양이 아닌 예가 12예 (20%)였다. 초음파유도하핵생검에서 엽상종양으로 진단된 43예 중 39예 (90.7%), 세포충실성섬유상피병변으로 진단된 17예 중 9예 (52.9%)가 엽상종양이었다. 초음파 소견 중에서는 비균일한 내부 에코 (heterogeneous internal echotexture) (58% vs. 17%, p = 0.0239), 틈새 (clefts) (56% vs. 17%, p = 0.0331), 수평방향의 고에코성 줄들 (horizontal linear striations) (71% vs. 33%, p = 0.0221)이 통계적으로 유의하게 엽상종양에서 더 흔하게 관찰되었다.

결론: 유방의 초음파유도하핵생검에서 엽상종양으로 진단될 때 진단적 정확도는 높았으며 비균일한 내부 에코, 틈새, 수평방향의 고에코성 줄들의 초음파 소견을 함께 고려하면 엽상종양을 예측하는데 도움이 된다.

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