

# Our 20-Year Institutional Experience with Surgical Approach for Breast Hamartomas

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## ABSTRACT

**Objective:** Hamartomas are rare, slowly-growing breast tumours. Clinical, radiological and histopathological examination together increase the diagnostic accuracy. To evaluate the clinicopathologic features of hamartomas and outline our clinical approach to hamartomas in our 20-year experience at our Breast Clinic.

**Materials and Methods:** Between 1995 and 2015, 24 cases were retrospectively analyzed with a diagnosis of breast hamartoma at our Breast Clinic followed by excisional biopsy. Data was obtained on patient demographics, clinical examination, radiological findings and histopathological subtypes.

**Results:** Of 1338 benign breast tumours excised from January 1995 to January 2015, 24 (1.8%) were identified as breast hamartoma. Median age of patients was 42 (range, 13-70), whereas the median tumour size was 5 cm (1-10 cm). On preoperative imaging, hamartoma was most commonly misdiagnosed as fibroadenoma. Pathological examination of the 24 biopsy specimens revealed 3 cases with pseudoangiomatous stromal hyperplasia, and another hamartoma associated with a radial scar within the centre of the lesion. Of those, one patient was diagnosed with malignant phyllodes tumour in the same breast. At a median follow-up 58.4 months, none of the patients recurred or developed malignancy.

**Conclusion:** Hamartomas can often be missed by clinicians, due to its benign nature which is poorly understood. Despite their slow growth, hamartomas can reach large sizes and can cause breast asymmetry. Although it is rare, hamartoma can be seen along with malignancy, as it is formed from similar components of breast tissue. Therefore, careful diagnosis and appropriate management including surgery are required.

**Keywords:** Breast disease, hamartoma, phyllodes tumor

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## Introduction

Hamartomas were first defined as mastomas by Pym (1). Before the term hamartoma came in to use in 1971 by Arrigoni, the lesion was also described as an adenolipoma and fibroadenolipoma. At present, some authors accept adenolipomas, adenohibernoma and myoid hamartomas as variants of hamartoma (2-4). Breast hamartomas are rare benign tumors comprising 0.7-1.2% of benign breast lesions in women. It is most commonly seen in perimenopausal period (5-7).

Hamartomas are slowly-growing lesions with a mean diameter ranging from 2 cm to 5 cm. However, sometimes hamartomas can reach giant dimensions (8). Patients usually present with a painless mass or breast anisomastia (7, 9-12). Hamartomas may be missed by physical examination. Mammographically, these lesions can be seen as mass containing fibrous and fatty tissue (9, 10). Furthermore, an excisional biopsy is generally required to distinguish hamartoma from other benign breast lesions such as fibroadenoma, lipoma and cystosarcoma phyllodes (12). Similar to what the breast epithelial cells do, the stromal cells also express estrogen and progesterone receptors (13). Despite hamartomas are considered as benign disease, it can be uncommonly seen along with a breast malignancy (14-16).

In this report, we aimed to evaluate the clinicopathologic features of hamartomas and outline our clinical approach to hamartomas in our 20-year experience at our Breast Clinic.

### Materials and Methods

Between January 1995 and January 2015, 1338 patients who underwent surgery with a diagnosis of benign breast disease at the Breast Clinic of the Department of Surgery, İstanbul University School of Medicine, were retrospectively analyzed. Of those, 24 cases (1.8%) were identified with a definitive pathology of hamartoma. A database was created for patient demographics, clinical findings including physical examination and radiological findings, surgery, and histopathological characteristics. All patients underwent excisional biopsy. Clinical follow-up data was also obtained. Statistical Packages for the Social Sciences (SPSS) version 17 (SPSS Inc.; Chicago, IL, USA), and Fisher’s exact test was used for categorical analysis. Spearman’s correlation test was used to examine the associations between parameters. Mann Whitney-U test was used for continuous variables. Ethics committee approval was obtained for this retrospective analysis.

### Results

Of the 24 patients, 8 were diagnosed from 1995 to 2005, and 16 patients were diagnosed between the years 2005-2015. Of those, there was only one male patient (4.2%), whereas the remaining were female (95.8 %). The median age of patients was 42 (range, 13 - 70 years), and 17 were premenopausal (74%). Five patients (20.8%) had a family history of breast carcinoma. The majority of the patients (n=15, 62.5%) presented with a soft painless mass, whereas 4 presented with a breast lump and pain (Table 1). Nevertheless, 2 patients were asymptomatic who were diagnosed during routine screening.

All patients were examined by ultrasound imaging, whereas 16 (66.7%) had a mammogram. Ultrasonography frequently showed an oval-shaped, well-defined, heterogeneous mass containing cystic areas defining a diagnosis of hamartoma in 9 cases (37.5 %). Other common findings were associated with a diagnosis of fibroadenoma in 7 patients (29%), and cystosarcoma phyllodes in 2 patients (8.3 %). Mammography mostly revealed a nodular opacity (n=11, 68.8%) or an asymmetric density (n=2, 12.5%), or BIRADS IV microcalcifications (n=2, 12.5%).

Seven cases (29.1 %) were diagnosed as likely fibroadenoma on imaging. For masses of large size on radiological examination, a misleading preliminary diagnosis of phyllodes tumour was established. The mammography and ultrasonography findings of the cases are given in Table 2. For 11 patients with radiological less than 5 cm and 13 patients with a radiological mass greater than 5 cm, hamartoma was identified as a possible diagnosis in 18.2% and 46.2% respectively (p=0.21). Mammographic image of hamartoma was shown in Figure 1.

For preoperative diagnosis, fine needle aspiration (FNA) was performed in 10 patients (41.7%), whereas 4 patients had only core biopsy (16.7%). Furthermore, 5 patients had both FNA and core biopsy, whereas the remaining underwent excisional biopsy for diagnosis. None of the FNA finding predicted the final pathology of hamartoma. Of patients with a core biopsy (n=9), the core biopsy revealed fibrolipomatous cell fragments in 3 patients (33.3%) that was concordant with a diagnosis of hamartoma. However, hamartoma diagnosis could not be confirmed in 6 patients where the pathological finding was stromal fibrosis in 3 patients, fibrosis/adenosis in 1 patient, myxoid tumor in 1 patient and fibrocystic changes in 1 patient.

On pathological examination of the excisional biopsy specimens of hamartoma cases, pseudoangiomatic stromal hyperplasia was pres-

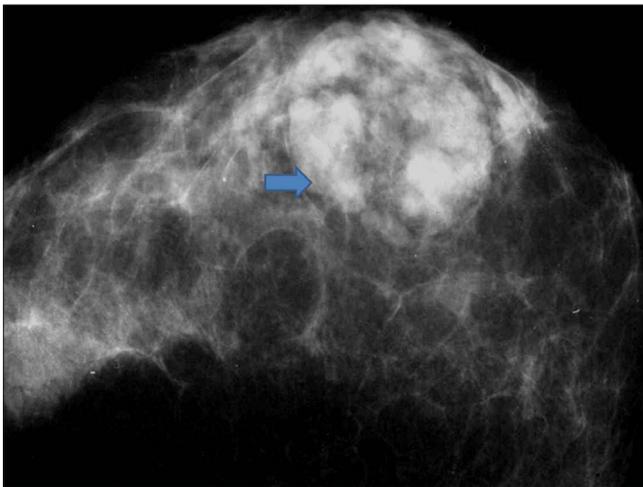
Table 1. Demographic and Clinical and Tumor Characteristics of Patients

Patient and Tumor Characteristics	N	%
Median age	42 (range, 13-70)	
Age groups		
≤20	2	8.3
20-30	3	12.5
30-40	6	25
40-50	5	20.8
50-60	4	16.7
60-70	4	16.7
Premenopausal	17	74
Postmenopausal	6	26
Family history	5	20.8
Gender		
Female	23	95.8
Male	1	4.2
Presenting symptoms		
Pain	2	8.3
Pain & palpable mass	4	16.6
Palpable mass	15	62.5
Palpable mass & anisomastia	1	4.2
Screening	2	8.3
Imaging techniques		
Ultrasound	24	100
Mammogram	16	66.7
Magnetic Resonance Imaging	6	25
Preoperative Diagnosis		
Fine Needle Aspiration (FNA)	10	41.7
Core Biopsy	4	16.7
FNA & core biopsy	5	20.8
Excisional biopsy	5	20.8
Median tumor size	5 cm (range, 1-10 cm)	
Associated lesions with hamartoma		
Pseudoangiomatosis hyperplasia	3	12.5
Radial scar	1	4.2
Malignancy	1	4.2
Unknown data were excluded from the analysis		

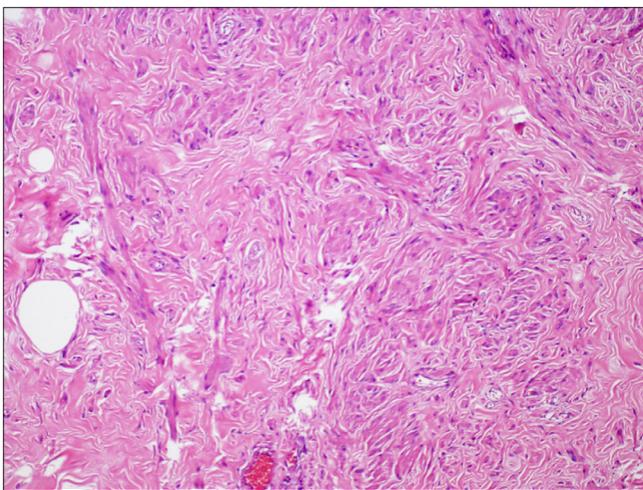
ent in 3 specimens. In one case, fatty necrosis was identified, whereas fibro-hyaline stroma were present in another case (Figure 2). Furthermore, histopathological examination established multiple foci of microcalcification in 4 cases (16.6%). Both foci of adenosis and sclerosing adenosis were present in 2 cases. Interestingly, hamartoma was associated with a radial scar in one case.

Table 2. Mammography and ultrasonography findings

Ultrasonography Sign	n:24	100%
Heterogenous mass containing cystic areas	9	37.5
Fibroadenoma	7	29
Cystosarcoma phloides	2	8.5
Non-descriptive findings	6	25
Mammography sign	n:16	100
Nodular opacity	11	68.8
Asymmetrical density	2	12.5
Microcalcifications	2	12.5
Non-descriptive findings	1	6.2

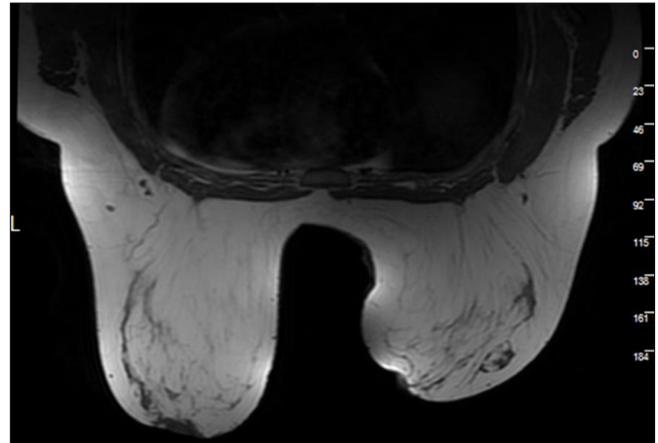


**Figure 1.** Mammographic appearance of a hamartoma who underwent surgery for diagnostic purposes

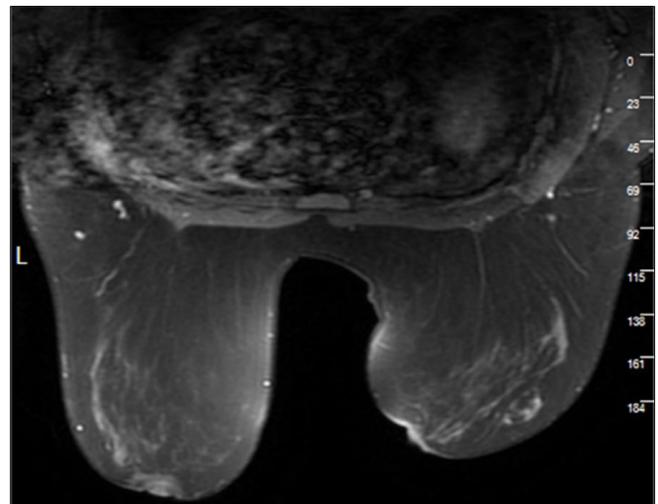


**Figure 2.** Microscopic findings of hamartoma in a patient who underwent excisional biopsy for diagnosis and therapy (hematoxylin & eosin staining, 4X)

The median tumour size was 5 cm (1-10 cm). The patient's age and tumour size were negatively correlated ( $r=-0.414$ ;  $p=0.045$ ). However, no significant difference could be found in the mean tumour size be-



**Figure 3.** Pre-contrast fat-suppressed T1-weighted images in Magnetic Resonance imaging (MRI) of hamartoma showing a hyperintense fatty signal



**Figure 4.** Postcontrast MRI images of ovoid shaped-hamartoma in the lower upper quadrant of the right breast as a lesion having both a fatty density fat-suppressed and contrast-enhanced glandular component inside

tween premenopausal and postmenopausal patients (premenopausal,  $5.58 \pm 2.82$ , vs postmenopausal,  $4.31 \pm 2.92$ ;  $p=0.309$ ).

The only male case was 65-year old patient with a diagnosis of prostate cancer who presented with a mass in the right upper quadrant of his breast. Even though a metastatic lesion to the breast was suspected, ultrasonographic findings revealed a solid mass with a size "47x20 mm" with a preoperative diagnosis of fibroadenoma. Interestingly, the definitive pathology of the excisional biopsy showed pseudoangiomatic stromal hamartoma.

In another case, a 21-year old female presented with mass following an excision for a malignant phyllodes tumour at another institute. There was suspicion of residual disease on imaging and re-excision was therefore completed at our institution. No residual tumour could be detected in the surgical specimen. However, the pathological examination of the 6x9 cm mass unexpectedly revealed a diagnosis of hamartoma.

The median follow-up of these patients was 58.4 months (1-186 months). There was no recurrence of hamartoma or no malignancy was detected during the follow-up period.

## Discussion and Conclusion

Hamartomas are very rare benign tumours. Breast cancer screening programs and breast cancer awareness activities in Turkey have gained momentum in recent years. This situation increased the number of women undergoing examinations, breast ultrasonography, and mammography. As a result, the detection of benign diseases as well as those of breast malignancies has increased. Our 20-year clinical experience have also shown only 2% of patients with benign lesions underwent surgery for hamartomas. Of 24 patients revealed in the 20-year study, 8 of them were diagnosed between 1995 and 2005, whereas 16 of them were detected between 2005 and 2015. In a study conducted in 1978, 10000 mammograms were recorded in a 9-year period and there were only 16 diagnoses of breast hamartoma identified (17). In another study, the authors stated they found 41 hamartomas in 5834 patients undergoing breast biopsy (5). The present study included 1338 patients operated for benign breast disease, of which 24 (1.8 %) were breast hamartoma. One of our patients was male which is relatively rare. The male patient firstly presented with concerns that the breast mass was metastasis of his prostate cancer. However, an ultrasound finding indicated that the mass present in the breast was a fibroadenoma. The patient then underwent excisional biopsy with a final pathology of hamartoma. There are very few published cases of male hamartoma. In a study by Gupta et al. (18), there were only three reported cases of male breast hamartoma. Ravakhah et al. (19) identified a hamartoma in a 36-year-old male patient with a complaint of slow-growing mass in the left breast.

Hamartomas are seen in middle-aged women as a painless mass of soft consistency or present as a complaint of breast asymmetry. Hamartomas are most commonly seen between the ages 40 to 45 (9, 10, 18). In our case series, the median age was 42 years. Of those, 15 (62.5%) presented with a painless palpable breast mass. The average diameter of a hamartoma is reported at 2 to 5 cm (20). In the literature, breast hamartomas have been detected in very large sizes (21, 22). Weinzweig et al. (22) described a young female patient in the post-lactational period who was diagnosed with a giant size hamartoma followed by an excisional biopsy and required mastopexy. The median size was 5 cm ranged from 1 cm to 10 cm in our study.

Histopathologic features of hamartoma are not characteristic. Breast hamartomas consist of breast ducts and lobules, fibrous stroma, adipose tissue and smooth muscle in varying quantities (23). Clinically, fibroadenomas and phyllodes tumours are often indistinguishable from hamartomas. Especially breast hamartomas are mostly diagnosed as fibroadenomas (12, 20, 24). In our study, the ultrasound findings have shown that hamartoma was most commonly misdiagnosed as fibroadenoma in 7 cases, and secondly phyllodes tumour in 2 cases.

In mammography, presence of peripheral lucent halo, and normal breast pattern are indicators of hamartoma. Therefore, it's described as "breast within a breast". The mammographic findings of hamartoma are the presence of fat and soft tissue density, a mass with a well-defined border, and the presence of a thin radiopaque border (pseudocapsule). Hamartoma contains fatty, glandular or fibrous tissue in varying quantities seen as a mammographic opacity. Although not often, microcalcifications can be seen with hamartoma (10, 13, 17, 25, 26). The ultrasonographic findings revealed that hamartomas were seen as oval, well-defined mass with heterogeneous echogenicity. Furthermore, in general, echogenic or echolucent halo and posterior strengthening was seen in hamartoma (27). Fibroadenoma appears to

be encapsulated and well-defined lesion in USG. It is usually homogeneous and hypoechoic as compared to the normal breast parenchyma, and sometimes there may be low-level internal echoes. Characteristically, the transverse diameter is greater than the anteroposterior diameter. Calcifications may occur and uncommonly, the mass may appear complex, isoechoic, or hyperechoic. Cystosarcoma phyllodes are a mass with well-defined boundaries that have a non-homogeneous echogenic structure with generally cystic areas. (28)

In 9 of our 24 hamartoma cases, ultrasonography indicated a diagnosis of hamartoma, that might be helpful in differential diagnosis. Although not statistically significant, ultrasonography was found to be more diagnostically useful in patients with a mass greater than 5 cm compared to those other smaller lesions. In 5 cases (20.8%), mammography results correlated with USG findings, and both USG&MMG were found to be useful in diagnosis of breast hamartomas. In our current practice, breast MRI has been commonly used as a diagnostic imaging tool to confirm hamartomas in addition to ultrasound and mammogram as reported before (29). MRI has been especially helpful to determine whether excisional biopsy is required for diagnostic and therapeutic purposes. Patients with a radiological diagnosis of hamartomas can be conservatively followed without surgery with 6-month intervals without performing surgery for at least 2 years. The appearance of the breast hamartoma with MRI is shown in Figure 3 and 4.

There is no specific histological findings in the diagnosis of hamartoma and the pathological diagnosis is often difficult. Many studies have pointed out that there is a limited role in the diagnosis of fine needle aspiration cytology and core biopsy. Core or fine needle biopsy usually provides an inadequate or nonspecific biopsy result. Core biopsy seems to be more important to exclude malignancy (4, 9, 11). Our results suggest that, fine needle and core biopsy have been useful to confirm a benign lesion, however they may not be adequate for diagnostic purposes.

Tse and colleagues reported 25 cases of hamartoma. On histopathological examination of these cases, all contained the fatty tissue, whereas interlobular fibrosis was seen in 21 patients and pseudoangiomatous stromal hyperplasia was detected in 8 patients (11). In a further study, of 27 cases analyzed, pseudoangiomatous stromal hyperplasia was identified in 25.9% (10). In this study, 3 cases contained pseudoangiomatous stromal hyperplasia (12.5%), and two cases (8.3%) were found to have both sclerosing adenosis and adenosis. Foci of microcalcification were detected in 4 of our cases (16.6 %). A radial scar was identified in one case of hamartoma. Papillomas, fibrocystic disease, epithelial changes, ductal ectasia and atypical lobular hyperplasia frequently accompany hamartomas (10, 11).

Uncommonly, hamartomas are reported with invasive ductal and invasive lobular breast carcinoma (14, 15, 24). Albawardi et al. (23) reported mammary hamartomas to be associated with columnar cell changes including flat epithelial atypia. In our study, invasive ductal or lobular carcinoma was not detected with hamartoma. In addition, there were no cases diagnosed with ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) within hamartoma. However, one of our cases in this series was interestingly diagnosed with malignant phyllodes tumour that was found in the same breast as hamartoma, which has not been described in the literature before.

Daya et al. (3) noted in 25 patients, there were 2 cases of recurrence at 7 and 18 months postoperatively. In many studies, an emphasis

has been given to the need to complete a total excision to avoid recurrence. In this study, at a median follow-up period of 58.4 months postoperatively, no recurrence was detected or none of them developed malignancy.

In conclusion, due to the development of radiological methods in recent years, the diagnosis of hamartoma can easily be made. This could be more valid and reliable if confirmed by core-needle biopsy. For those patients in this situation, surgical excision is unnecessary, and follow-up is appropriate as the hamartoma is benign. However, surgical excision is required in patients with suspected malignancy who cannot be determined hamartoma on radiographically.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the Ethics Committee of İstanbul University School of Medicine.

**Informed Consent:** Informed consent was not received due to the retrospective nature of the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - N.C., Z.T.; Design - N.C., A.İ.; Supervision - M.M., A.D.; Resources - A.İ., G.A.; Materials - M.M., M.T.; Data Collection and/or Processing - T.A., E.Ö.; Analysis and/or Interpretation - S.Ö., G.A.; Literature Search - T.A., R.Y.; Writing Manuscript - Z.T., E.Ö.; Critical Review - V.Ö., A.D.; Other - S.Ö., R.Y.

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