

## 유방의 간엽성 종양: 영상의학과 조직학적 연관성

김보미<sup>1,2</sup> · 유재경<sup>2</sup> · 김은경<sup>1</sup>  
김의정<sup>3</sup>

<sup>1</sup>연세대학교 의과대학 영상의학과

<sup>2</sup>국민건강보험공단 일산병원  
영상의학과

<sup>3</sup>국민건강보험공단 일산병원  
병리과

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### Address for reprints :

Eun-Kyung Kim, MD, Department of  
Radiology, Research Institute of  
Radiological Science, Yonsei University  
College of Medicine, 250 Seongsanno,  
Seodaemun-gu, Seoul 120-752, Korea.  
Tel. 82-2-2228-7400  
Fax. 82-2-393-3035  
E-mail: ekkim@yuhs.ac

## Mesenchymal Tumors of the Breast: Imaging and the Histopathologic Correlation

Bo-mi Kim, MD<sup>1,2</sup>, Jae Kyoung You, MD<sup>2</sup>, Eun-Kyung Kim, MD<sup>1</sup>,  
Yee Jeong Kim, MD<sup>3</sup>

<sup>1</sup>Department of Radiology, Yonsei University, College of Medicine,

<sup>2</sup>Department of Radiology, NHIC Ilsan Hospital,

<sup>3</sup>Department of Pathology, NHIC Ilsan Hospital

Various benign and malignant mesenchymal tumors can occur in the breast. Most radiologists are unfamiliar with the imaging features of these tumors and the imaging features have not been described in the radiologic literature. It is important that radiologists should be familiar with the broad spectrum of imaging features of rare mesenchymal breast tumors. In this pictorial review, we demonstrate the sonographic findings and the corresponding pathologic findings of various mesenchymal tumors of the breast as defined by the World Health Organization classification system.

**Key words :** Breast mesenchymal tumor; Mammography; Ultrasonography

## Introduction

The World Health Organization (WHO) classifies breast tumors according to their cellular origin, and these lesions are classified into epithelial tumors, myoepithelial tumors, mesenchymal tumors, fibroepithelial tumors, malignant lymphoma and metastatic tumors (appendix) [1]. The category of mesenchymal tumors contains various kinds of rare benign and malignant tumors. Since these lesions are rare, they are seldom seen in routine mammographic and ultrasonographic practice. Their radiologic features have not been described nor well documented, and so they are unfamiliar to most radiologists. The purpose of this article is to describe the imaging features and

histopathologic characteristics of mesenchymal tumors of the breast.

## Benign Mesenchymal Tumors of the Breast

### 1. Hemangioma

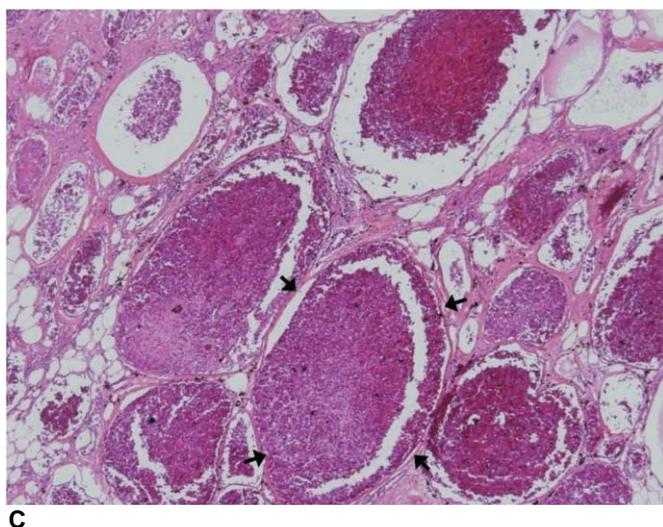
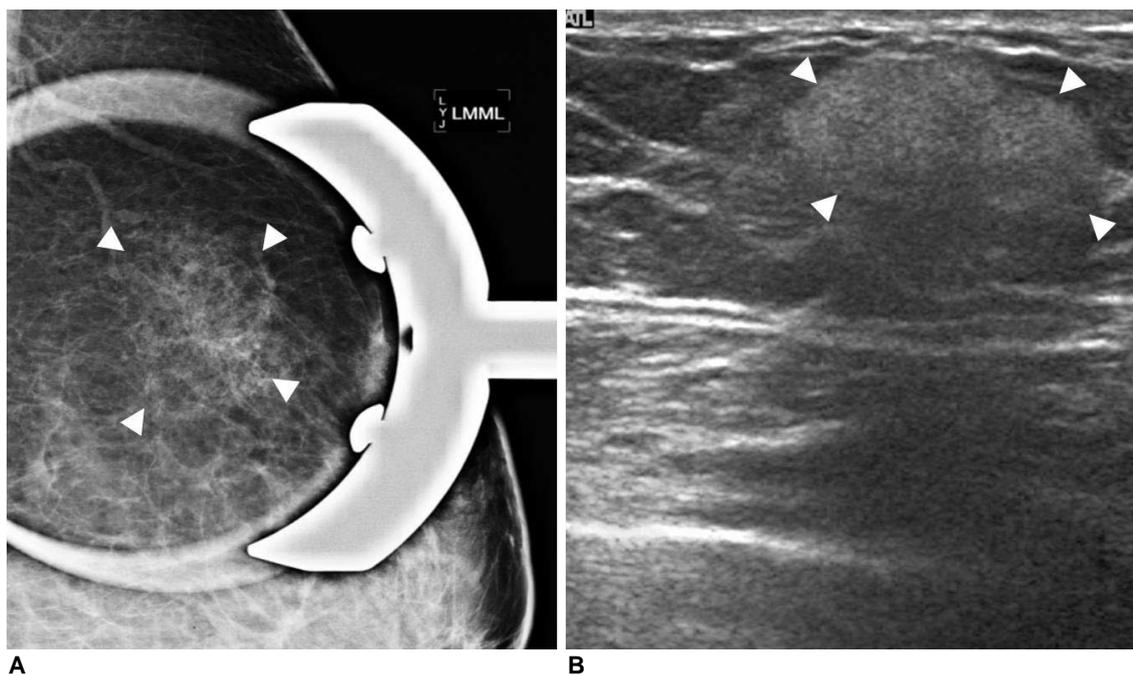
Hemangioma is a benign vascular tumor that is usually incidentally identified during the histological examination of specimens obtained during lumpectomy or mastectomy [2]. Cavernous hemangiomas may present as masses, depending on their size and location, but most of the palpable and symptomatic vascular tumors are angiosarcomas [2].

The mammographic appearance of a cavernous hemangioma is a well-defined, oval lobulated mass

that may have fine, punctuate, bizarre or coarse calcifications [3], but the mammographic appearance can be nonspecific (Fig. 1A). Coarse or egg-shell macrocalcifications indicate phleboliths. On ultrasound, the cavernous hemangioma is seen as a well-defined, lobulated, solid, mainly hypoechoic mass or an ill-defined, hyperechoic mass (Fig. 1B) [4] that contains small, bright echoes, which are consistent with areas of calcifications [5], or cavernous hemangioma is seen as a cystic septated lesion with echogenic areas of calcifications [3]. The echogenicity of hemangiomas is related to the size of the vessels

contained within the mass and the presence or absence of fibrosis, scarring, thrombosis or phleboliths [6]. Color Doppler sonography allows for the analysis of the tumor's neovascularity, and it can help determine the presence of arteriovenous shunting and distortion of internal vessels, as well as assessing the tumor's vascularity relative to the surrounding tissue [7].

Pathologically, most hemangiomas have grossly well-circumscribed borders, but microscopically, the vascular channels may blend with the surrounding breast parenchyma [8]. Microscopic examination



**Fig. 1.** A 44-year-old woman with hemangioma. **A.** The mammogram shows an irregular and ill-defined heterogenous mass-like lesion (arrows). **B.** The ultrasonography shows an indistinct hyperechoic solid mass in the subcutaneous fat layer (arrows). **C.** The tumor shows dilated vascular channels (arrows) with thin walls lined by endothelial cells (H & E, ×40).

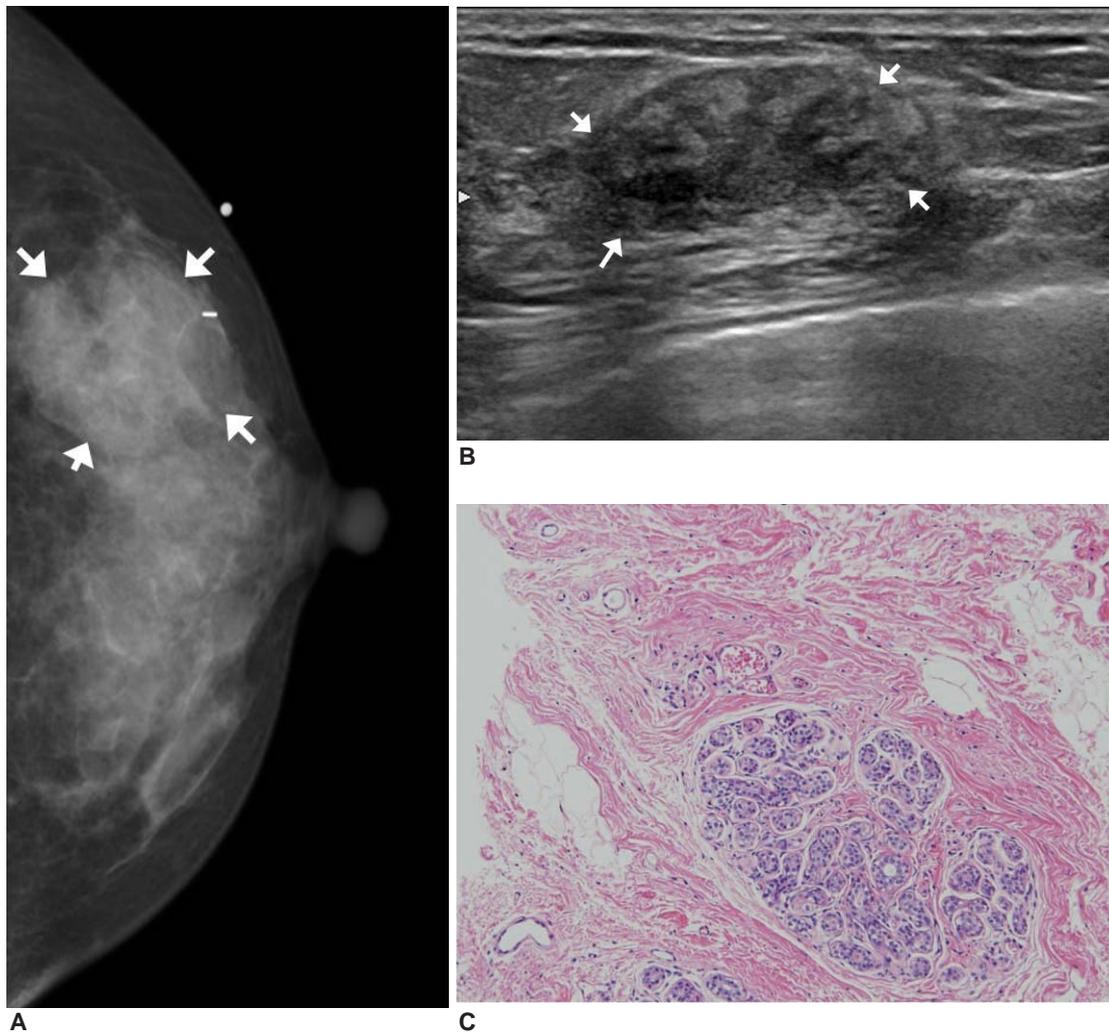
reveals dilated vessels congested with red blood cells and the vessels are separated by fibrous septa, and there can be extensive fibrosis and sometimes phleboliths [3, 8] (Fig. 1C).

## 2. Pseudoangiomatous stromal hyperplasia (PASH)

Pseudoangiomatous stromal hyperplasia (PASH) is a benign tumor that is likely related to the levels of hormones since it is most commonly seen in premenopausal women or women receiving hormonal therapy [9]. The clinical spectrum varies from insignificant incidental microscopic changes in the breast to focal palpable or nonpalpable mass-like nodules (nodular PASH) [10].

Mammographically, these lesions are usually well defined with a smooth border [11] and they do not contain calcifications. However, their margins may occasionally be ill defined or partially defined (Fig. 2A) [12]. On US, the lesions are usually seen as well-defined, hypoechoic or heterogeneously echogenic solid masses with sound attenuation characteristics that vary from posterior enhancement to mild posterior shadowing (Fig. 2B) [11–13]. Some large lesions contain numerous lacelike reticular areas with scattered cystic changes [14].

Pathologically, PASH consists of complex anastomosing slit-like pseudovascular spaces that are either acellular or they are lined by spindle-shaped



**Fig. 2.** A 45-year-old woman with pseudoangiomatous stromal hyperplasia (PASH).  
**A.** The mammography shows an isodense mass with a partially defined margin (arrowheads).  
**B.** The ultrasonography shows a heterogenous, ovoid mass with mild posterior enhancement (arrowheads).  
**C.** The tumor shows complex, anastomosing, empty slitlike spaces within a dense collagenous stroma (H & E,  $\times 100$ ).

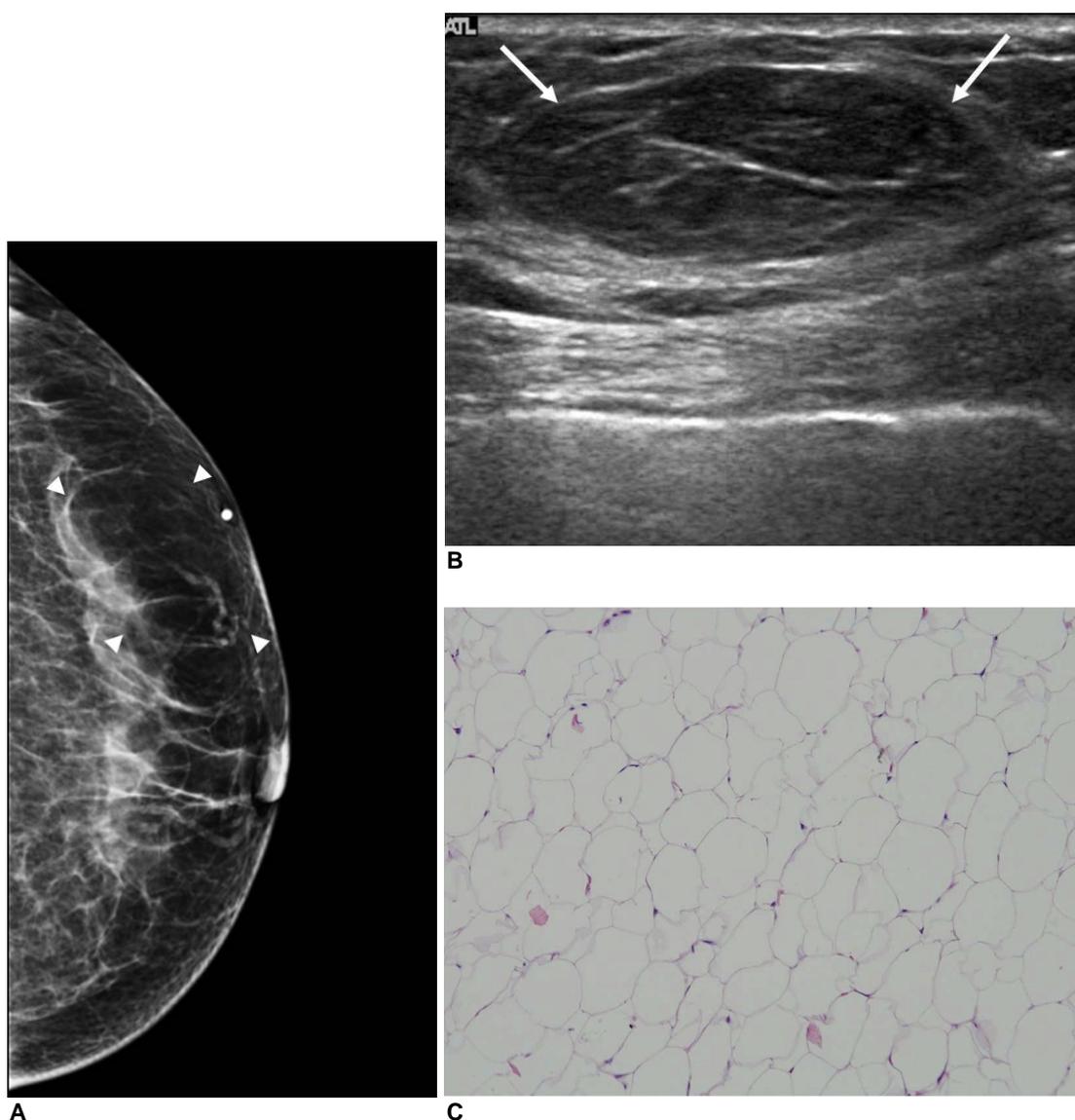
stromal cells. These slit-like spaces resemble the vascular spaces in lesions such as low-grade angiosarcoma (hence the name pseudoangiomatous) and from which PASH must be histologically differentiated. PASH lesions also show a benign myofibroblastic proliferation of the mammary stroma that separates into lobules and ducts (Fig. 2C) [9].

### 3. Lipoma

Lipoma of the breast is a slow growing benign neoplasm of mature fat cells. Lipoma of the breast is a

benign condition that has drawn little interest in the literature and it is hardly mentioned in standard medical texts [15].

Both mammographic scanning and ultrasound scanning for lipoma are often negative [16]. The mammographic finding is a well defined, encapsulated radiolucent mass (Fig. 3A) and there is often compression of the adjacent breast tissue. On ultrasound, lipoma appears as an oval, lobulated, homogeneous, solid mass with an echogenicity similar to that of normal fat (Fig. 3B) [17].



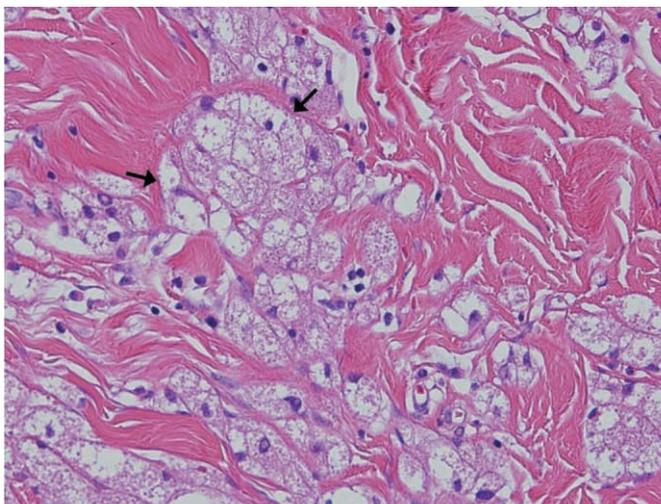
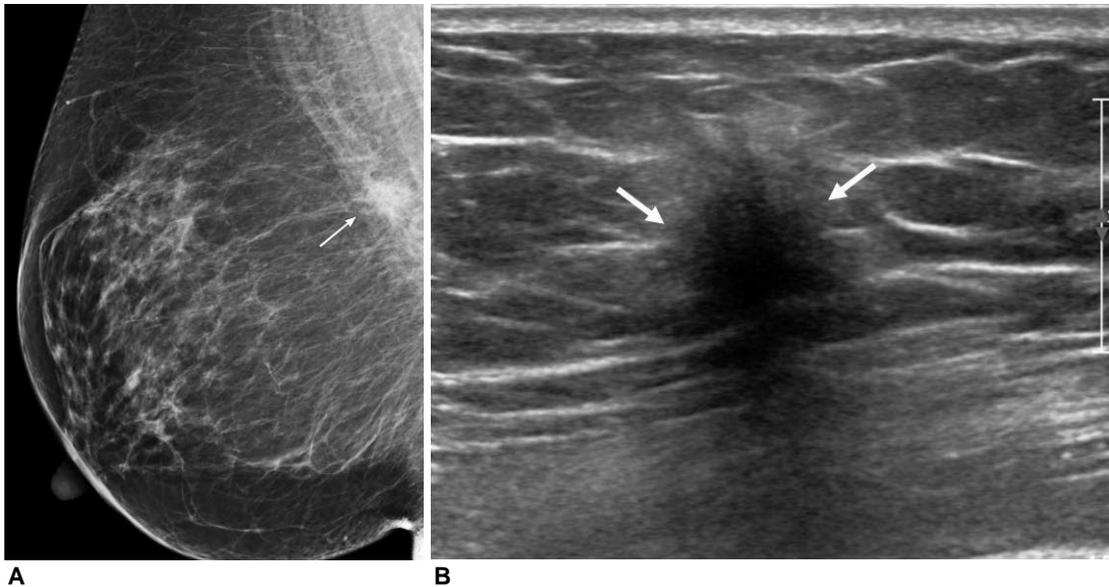
**Fig. 3.** A 55-year-old woman with lipoma.  
**A.** The mammography shows a well-defined, encapsulated radiolucent mass (arrowheads).  
**B.** The ultrasonography shows an oval shaped homogenous solid mass with echogenicity that is similar to that of normal fat (arrows).  
**C.** The tumor shows fat cells without any component that would indicate the presence of a capsule status (H & E,  $\times 100$ )

Pathologically, the tumor shows fat cells without any component that would indicate the presence of a capsule (Fig. 3C) [18]. Fine needle aspiration cytology may create diagnostic confusion in cases of pleomorphic lipoma or spindle cell lipoma [19].

#### 4. Granular Cell Tumor

Granular cell tumor (GCT) is a relatively rare neoplasm that is occasionally located in the breast. It is most often encountered in middle-aged, premenopausal women and it more frequently occurs in the upper inner quadrant of the breast, which is in contrast to breast carcinoma as the latter is more commonly found in the upper outer quadrant [20].

The mammographic presentation of GCT is variable. These lesions may present as round circumscribed masses, as indistinct densities or as spiculated masses that are indistinguishable from carcinomas (Fig. 4A). Microcalcifications are usually not present. The ultrasound appearance is also variable, including solid, uncircumscribed masses with marked posterior shadowing (Fig. 4B), as well as more benign appearing circumscribed masses [21]. This tumor may clinically and radiologically simulate breast cancers and particularly scirrhous carcinoma due to its infiltrative growth pattern that is associated with fibrosis, and this fibrosis results in fixation to the pectoral muscle and skin retraction [22].



**Fig. 4.** A 54-year-old woman with a granular cell tumor.

**A.** The mammogram shows a high density mass with an irregular shape and a spiculated margin (arrow). There are no calcifications.

**B.** The ultrasonography shows a hypoechoic, spiculated mass with posterior shadowing (arrows).

**C.** This tumor is composed of small irregular islands or solid nests of uniform rounded or polygonal cells with granular eosinophilic cytoplasm and small dark nuclei (arrows) (H & E,  $\times 200$ ).

C

Pathologically, GCT apparently originates from Schwann cells because the tumor shows positivity for S-100 protein [23] and the similarities of the ultrastructural features of the tumor cells and those of a Schwann cell [24]. Macroscopically, the tumor is usually infiltrative at its margins and an appearance that correlates with the US and mammographic characteristics. The tumor is composed of compact nests or sheets of uniformly-rounded or polygonal cells that have coarsely granular cytoplasm and small centrally located round nuclei [25] (Fig. 4C).

### 5. Schwannoma

Schwannoma is a benign tumor of a nerve sheath origin and this type of tumor is commonly found in the neck, head and flexor surface of the extremities. Its occurrence in the breast is very unusual [26]. These benign tumors arise from the neuroectodermal nerve sheath and they are usually solitary.

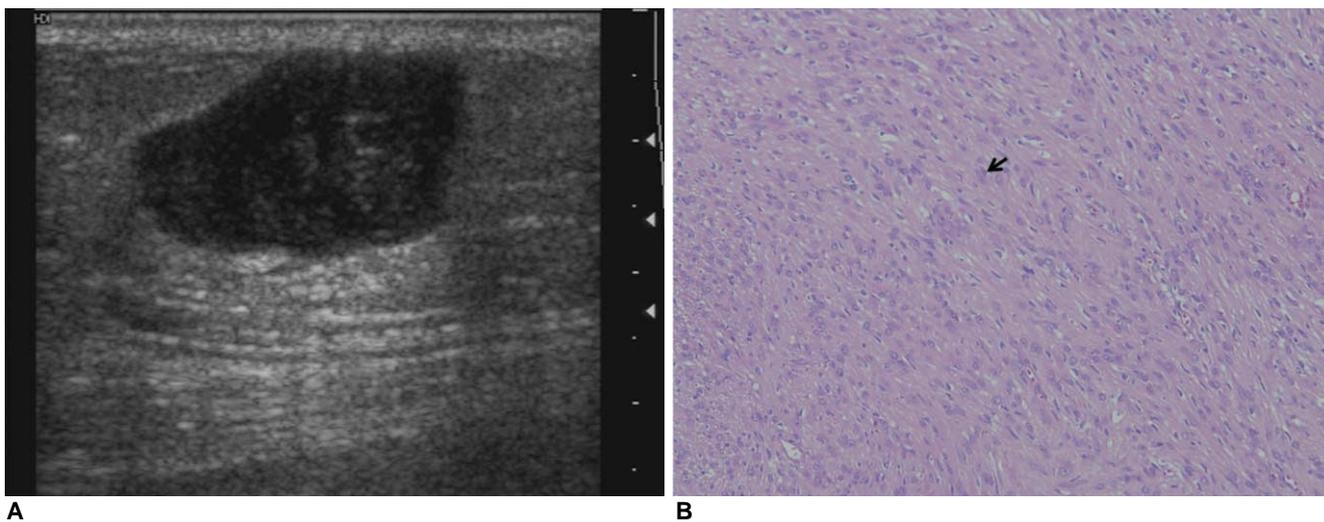
The imaging findings of schwannoma have not been extensively described since only a few cases have been reported. According to Bellezza et al.[27], ultrasound examination revealed a well-circumscribed hypoechoic mass with a benign appearance and no cystic degeneration (Fig. 5A). On mammography, the lesion appeared as a circumscribed, round-oval, equally dense nodule without microcalcifications.

Other reports have claimed that absence of a mass [28] and/or the presence of an ill-defined area of dense soft tissue [29] were common findings. The pathologic definitive diagnosis of nerve sheath tumors requires visualization of nerves in relation to the mass. Pathologically, the tumor contains both Antoni type A and type B tissue patterns. The cellular areas (Antoni type A) consist of spindle cells with oval or elongated nuclei that have a palisade and wavy appearance. The hypocellular areas (Antoni type B) contain spindle shaped cells, small cells with hyperchromatic nuclei and lipid-laden histiocytes [27] (Fig. 5B).

## Malignant Mesenchymal Tumor of the Breast

### 1. Angiosarcoma

Angiosarcoma of the breast is an unusual malignant tumor. Beside the head, thigh and arm, the breast is one of the most common sites for angiosarcoma. However, this tumor is very rare and only 0.04% of malignant breast tumors have been reported to be an angiosarcoma. Angiosarcoma of the breast usually occurs in patients during their late thirties or early forties. Clinically, this tumor is a rapid growing palpable mass and bluish discoloration of the skin is sometimes present.



**Fig. 5.** A 70-year-old woman with a schwannoma.  
**A.** The ultrasonography shows a well-circumscribed hypoechoic mass without cystic degeneration.  
**B.** The tumor shows spindle cells arranged in a palisading pattern in the cellular area (arrow) (H & E, ×100).

The mammographic appearance of angiosarcoma is not pathognomonic, and the diagnosis cannot be made on the basis of mammography [30]. The tumor shows an ill defined margin without spiculation. Calcifications within angiosarcomas are very unusual [31]. Angiosarcomas are usually larger than carcinomas on mammography and the mean size of angiosarcomas has been reported to be 4.6 cm [30]. On a sonogram, angiosarcomas are usually noted to be poorly marginated and the echogenicity is variable (Fig. 6A).

Pathologically, making a definitive diagnosis is extremely difficult when relying exclusively on the cytologic features. A predominance of epithelioid cells may suggest an epithelial tumor, whereas a predominance of spindle cells can be misinterpreted as phyllodes tumors or other type of sarcomas (Fig. 6B) [32]. Immunohistochemistry for assessing positivity for factor VIII-related antigen, CD31 and CD 34 is helpful in making the diagnosis of angiosarcoma of the breast [31].

## 2. Leiomyosarcoma

Leiomyosarcomas originate from smooth muscle and they are exceedingly rare. The size of this tumor ranges from 1.0 to 23.0 cm. These tumors are usually painless, firm, lobulated and mobile [33].

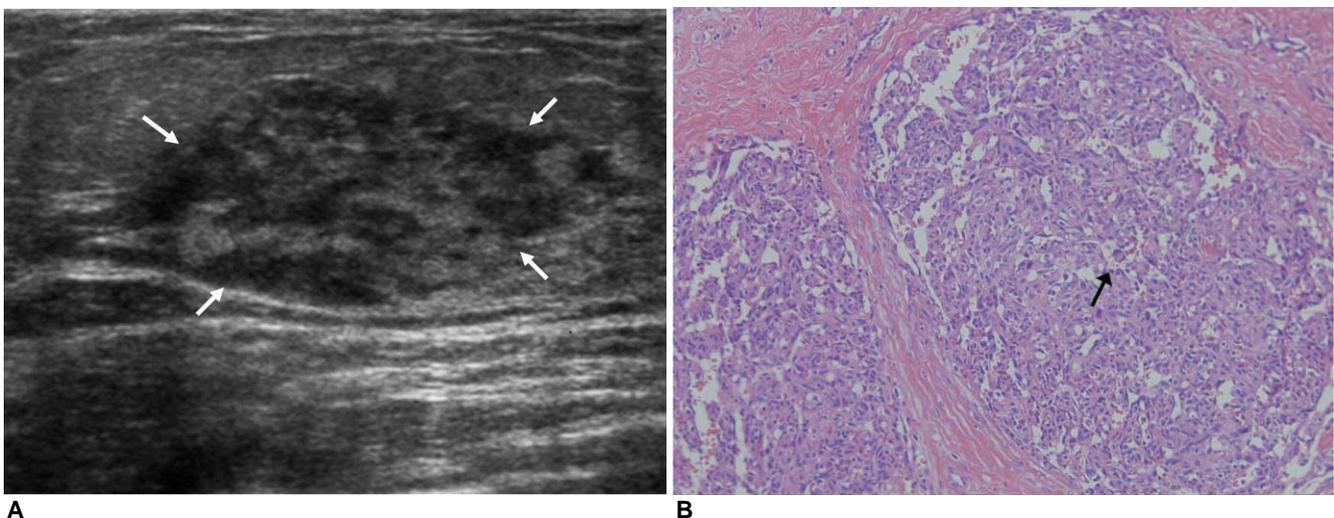
The mammographic findings typically show a dense, well-circumscribed phyllod-like mass and microcalcifications are very rare (Fig. 7A). Ultrasonography reveals a lobulated, hypoechoic tumor with heterogenous internal echogenicity [34] (Fig. 7B).

Pathologically, leiomyosarcoma is yellowish-grayish white, well defined and multinodular. Microscopically, it reveals bundles of pleomorphic spindle cells with smooth muscle differentiation (Fig. 7C). The mitotic activity of these tumors varies from 0 to 24 mitoses/10 high power field (HPF) with a mean of 11 mitoses/HPF [33].

Malignant phyllodes tumors represent a specific subset of breast sarcomas that are composed of epithelial elements with a connective tissue stroma. Malignant phyllodes tumors encompass a wide variety of tumors with mixed epithelial and benign or malignant mesenchymal proliferation.

## Conclusion

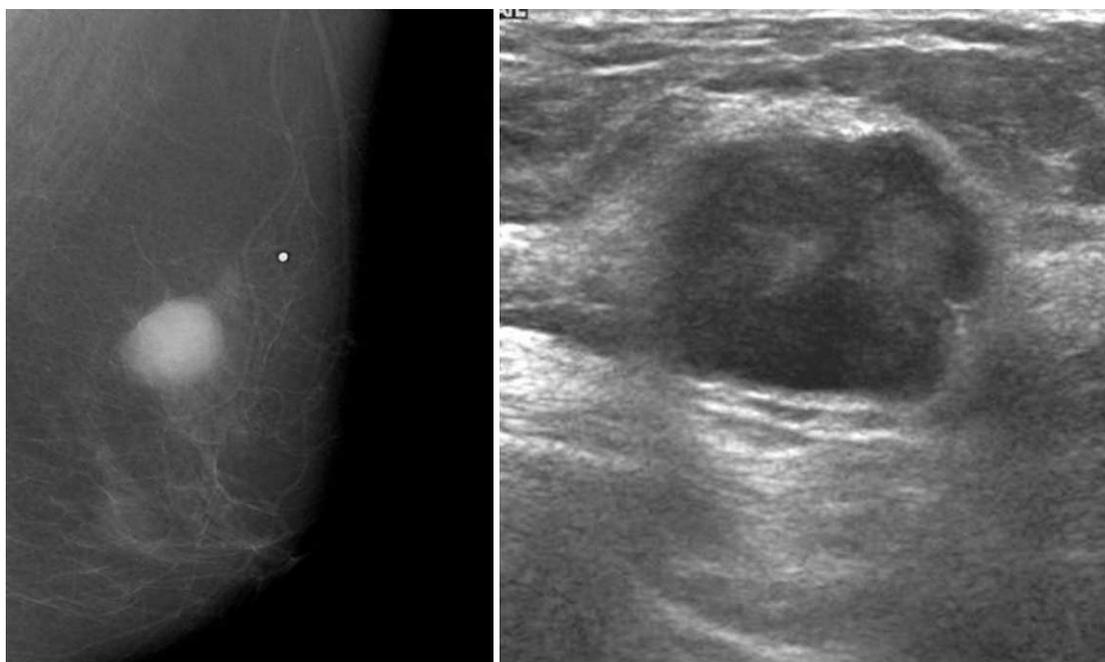
Various rare mesenchymal tumors have mammographic and US features that are similar to those of breast carcinomas. Although some lesions may have a classic imaging appearance, there is considerable



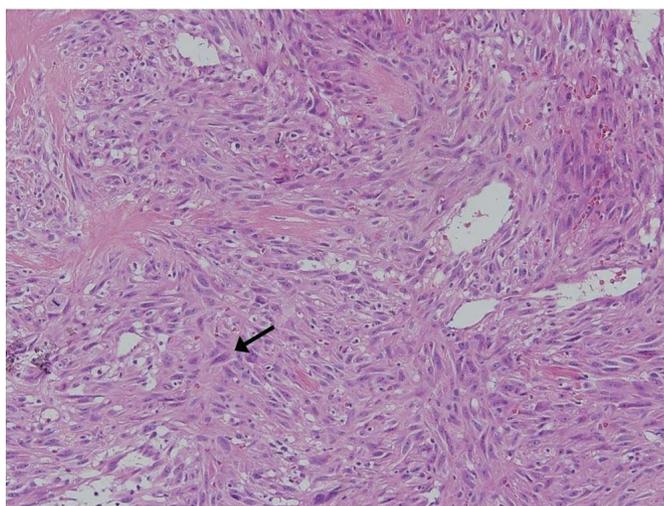
**Fig. 6.** A 49-year-old woman with an angiosarcoma.

**A.** The ultrasonography reveals a heterogenous hypoechoic mass with ill defined margins (arrows).

**B.** This tumor shows poorly differentiated cells resembling solid carcinoma with some capillary-sized vascular channels (arrow) (H & E,  $\times 100$ ).



**A** **B**



**C**

**Fig. 7.** A 66-year-old woman with leiomyosarcoma.  
**A.** The mammography shows a dense, well-circumscribed mass without microcalcifications.  
**B.** The ultrasonography shows a lobulated, hypoechoic tumor with heterogenous internal echogenicity.  
**C.** The tumor shows spindle cells with encapsulated nuclei (arrow) (H & E, ×100).

overlap between them with regard to their imaging features. It is important that those physicians who interpret breast images be familiar with these rare entities so that these tumors can be appropriately managed after the initial biopsy.

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## 요 약

유방에는 다양한 종류의 양성, 악성의 간엽종양이 생길 수 있다. 이는 흔하지 않은 질환으로 특징적인 영상소견이 부족하고 이에 관해 보고된 문헌도 적다. 따라서, 흔하지 않은 유방의 간엽종양의 다양한 영상의학적 소견에 좀 더 익숙해질 필요가 있다. 본 연구에서는 유방의 다양한 간엽종양의 영상 소견과 조직 특징을 World Health Organization (WHO) 분류체계에 따라 접근하고자 한다.

**Appendix.** WHO Histologic Classification of Tumors of the Breast

## Epithelial tumors

Invasive ductal carcinoma, not otherwise specified: mixed type carcinoma, pleomorphic carcinoma, carcinoma with osteoclastic giant cells, carcinoma with choriocarcinomatous features, carcinoma with melanotic features

Invasive lobular carcinoma

Tubular carcinoma

Invasive cribriform carcinoma

Medullary carcinoma

Mucinous carcinoma and other tumors with abundant mucin: mucinous carcinoma, cystadenocarcinoma and columnar cell mucinous carcinoma, signet ring cell carcinoma

Neuroendocrine tumors: solid neuroendocrine carcinoma, atypical carcinoid tumor, small cell (oat cell) carcinoma, large cell neuroendocrine carcinoma

Invasive papillary carcinoma

Invasive micropapillary carcinoma

Apocrine carcinoma

Metaplastic carcinoma: pure epithelial metaplastic carcinomas (squamous cell carcinoma, adenocarcinoma with spindle cell metaplasia, adenosquamous carcinoma, mucoepidermoid carcinoma) and mixed epithelial-mesenchymal metaplastic carcinomas

Lipid-rich carcinoma

Secretory carcinoma

Oncocytic carcinoma

Glycogen-rich clear cell carcinoma

Sebaceous carcinoma

Inflammatory carcinoma

Lobular neoplasia: lobular carcinoma in situ

Intraductal proliferative lesions: usual ductal hyperplasia, flat epithelial atypia, atypical ductal hyperplasia, ductal carcinoma in situ

Microinvasive carcinoma

Intraductal papillary neoplasms: central papilloma, peripheral papilloma, atypical papilloma, intraductal papillary carcinoma, intracystic papillary carcinoma

Benign epithelial proliferations: adenosis-including variants (sclerosing adenosis, apocrine adenosis, blunt duct adenosis, microglandular adenosis, adenomyoepithelial adenosis), radial scar-complex sclerosing lesion, adenomas (tubular adenoma, lactational adenoma, apocrine adenoma, pleomorphic adenoma, ductal adenoma)

Myoepithelial lesions: myoepitheliosis, adenomyoepithelial adenosis, adenomyoepithelioma, malignant myoepithelioma

Mesenchymal tumors: hemangioma, angiomatosis, hemangiopericytoma, pseudoangiomatous stromal hyperplasia, myofibroblastoma, fibromatosis (aggressive), inflammatory myofibroblastic tumor, lipoma (angioliipoma), granular cell tumor, neurofibroma, Schwannoma, angiosarcoma, liposarcoma, rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, leiomyoma

Fibroepithelial tumors: fibroadenoma, phyllodes tumor (benign, borderline, malignant), periductal stromal sarcoma (low grade), mammary hamartoma

Tumors of the nipple : nipple adenoma, syringomatous adenoma, Paget disease of the nipple

Malignant lymphoma: diffuse large B-cell lymphoma, Burkitt lymphoma, extranodal marginal-zone B-cell lymphoma of MALT\* type, follicular lymphoma

Metastatic tumors

Tumors of the male breast: gynecomastia, carcinoma (invasive, in situ)

Source.-Adapted from Reference 1.

\*mucosa-associated lymphoid tissue

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