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# Evaluation of Elastographic Features in Complex Fibroadenomas With Radiologic-Pathologic Correlation

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Fibroadenoma is the most common benign tumor of the breast, and complex fibroadenoma (CFA) is one of its variants. Of the fibroadenomas, 22% are CFAs, and in women with CFAs, the malignancy development is found to be higher than in women with noncomplex fibroadenomas. Although there is an increased risk of malignancy with CFAs, the imaging findings of CFAs are fundamentally similar to those of other variants of fibroadenomas. In the literature, B-mode ultrasound features of CFAs were reported in detail. To our knowledge, there is no study that has specifically described the elastographic findings of CFAs. This article aims to illustrate the elastographic features of CFAs and to correlate radiologic and histopathologic findings of different cases.

***Key Words***—complex fibroadenoma; elastography; shear wave elastography; strain elastography; ultrasound

Complex fibroadenoma (CFA) is a variant of simple fibroadenoma (SFA) including 1 or more specific complex histopathologic features.[1,2] These histopathologic features include epithelial calcifications, papillary apocrine metaplasia, sclerosing adenosis, and cysts larger than 3 mm.[3] CFAs comprise 22% of histopathologically proven fibroadenomas.[4]

It is very well known that the development of malignancy in women with SFAs is higher than in the unaffected population. In addition, in women with CFAs, the malignancy development is found to be higher than in women with noncomplex fibroadenomas. Invasive breast cancers are seen 3.1 times more frequently than in women in the general population and 1.89 times more frequently than in women with noncomplex fibroadenomas.[5] In both the unaffected population and women with SFAs or CFAs, an increased malignancy risk is typically related to perilesional benign proliferative changes and an elevated familial risk of breast cancer. Additionally, this increased malignancy risk is not limited to the lesion site; any site in the same or contralateral breast may be affected by the malignancy.[4] As a result, the treatment of CFA is total surgical excision with large margins and close radiologic follow-up.[6]

Although there is an increased risk of malignancy with CFAs, the imaging findings of CFAs are fundamentally similar to those of SFAs.[2] In the literature, B-mode ultrasound (US) findings and even US texture features of CFAs were reported.[1,2,7] To our knowledge, there is no study that has specifically described the elastographic findings of CFAs. This article aims to illustrate the

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**Abbreviations**

*BI-RADS, Breast Imaging Reporting and Data System; CFA, complex fibroadenoma; MG, mammography; SFA, simple fibroadenoma; US, ultrasound*

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elastographic features in CFAs and correlate radiologic and histopathologic findings of different cases. Institutional Review Board approval was not needed for these cases, and the need for informed consent was waived. All of the B-mode US examinations were performed with ML 6–15-MHz linear transducers, and elastographic examinations were performed with 9 L linear transducers (LOGIQ S8; GE Healthcare, Milwaukee, WI). Several cutoff values were evaluated for shear wave elastography and elasticity scores for our cases. In a study by Barr and Zhang,[8] the cutoff elasticity value in shear wave elastography for the best sensitivity and specificity was 4.5 m/s. In a study by Lee et al,[9] elasticity scores were classified into 3 categories: 72 kPa or lower, soft as negative; 72 to 108 kPa, intermediate as equivocal; and 108 kPa or higher, stiffer.

## Strain and Shear Wave Elastography

Elastography is an emerging imaging method that evaluates the tissue stiffness.[10,11] There are 2 types of elastographic techniques: strain and shear wave elastography. In strain elastography, the tissue displacement by an external source is evaluated, and a qualitative result is obtained.[12]

Basically, in strain elastography, the change in shape due to stress application is evaluated. As the amount of applied strain is not known precisely, it is a qualitative measurement. This qualitative evaluation is developed by using different methods to evaluate strain elastograms. There are 3 different methods in strain elastographic evaluations: a 5-point color scale, the strain ratio, and the elastographic–to–B-mode length ratio.[13,14]

In the 5-point color scale, the color pattern in the lesion is used to classify the lesion. The grading scale according to the color pattern, called Tsukuba scoring, has been described by Itoh et al.[15] The classification in the elastographic images is evaluated according to color patterns in both the lesion and surrounding normal tissue. According to the classification, there are 5 scores. In score 1, the lesion is completely blue or red (the color pattern depends on the setting and calibration of the US device), compatible with a soft and mild tissue structure. Score 2 refers to a mosaic and heterogeneous color pattern, including blue and green or red and yellow, compatible with a semiloose tissue structure. In score 3, the lesion is stiffer and has a color pattern formed by blue or red at the central part of the mass. In this score, the color pattern at the peripheral part includes green or yellow. A score 4 lesion has a diffuse blue or red pattern, which is compatible with a hard tissue structure. In score 5, the lesion and the surrounding tissues have diffused blue and red patterns. This finding refers to a hard tissue structure that is formed by increased mitosis, high cellularity, and a desmoplastic reaction in both the lesion and peripheral tissue. The size of the color is larger than the size of the lesion.[11,15]

The strain ratio method is the second method of strain elastography. Breast fat tissue is used as a reference standard in this method. Two regions of interests are used: one is placed in fat tissue, and the other is placed in the lesion. The relative stiffness of the lesion compared to the breast fat tissue is measured by the software.[13,16]

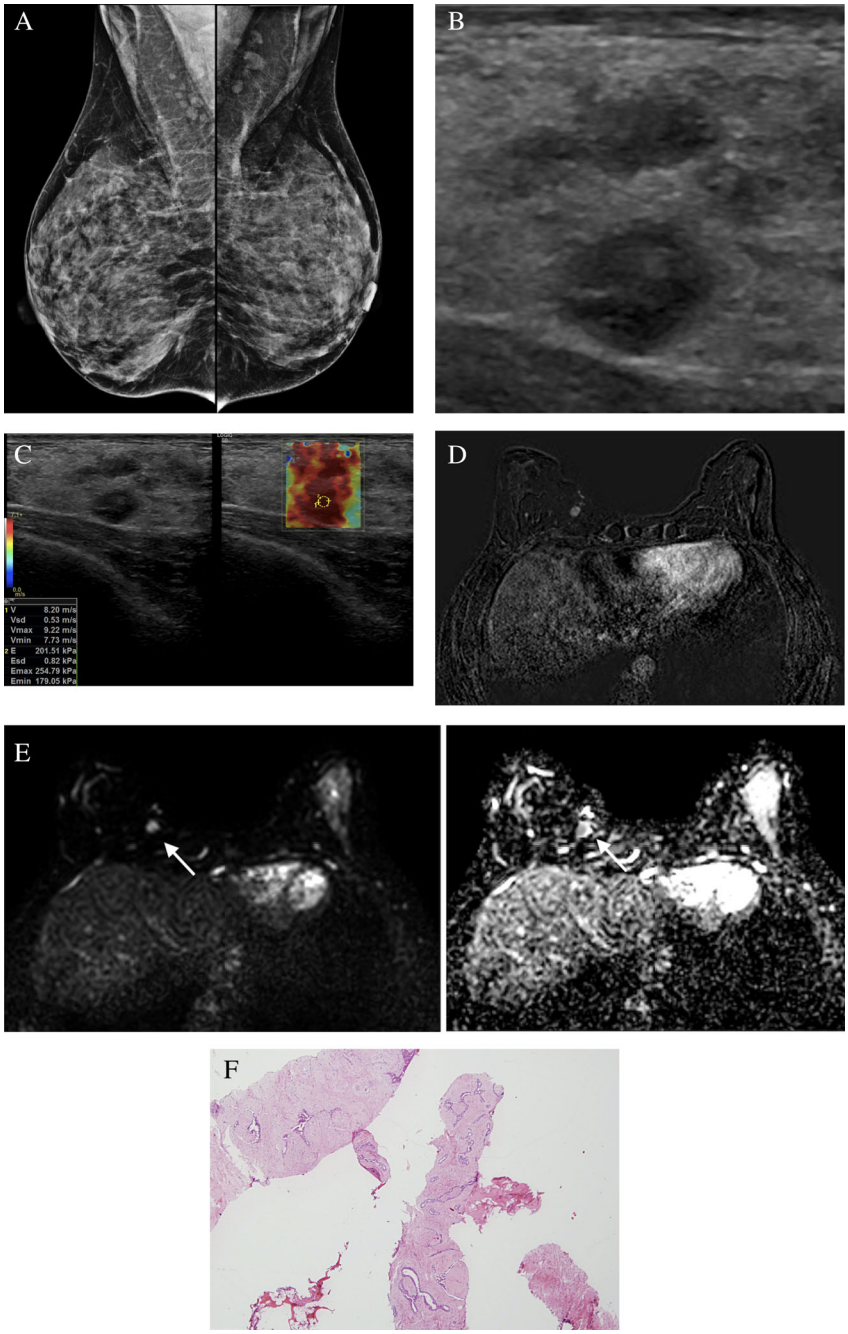
The elastographic–to–B-mode length ratio evaluation depends on the calculation of the ratio of the measurement on the elastographic image to the length measured on B-mode images of benign and malignant breast lesions. Elastographic–to–B-mode length ratios of 1 and greater than 1 are prominently predictive of malignant lesions.[13] The sensitivity of the elastographic–to–B-mode length ratio method has the highest value of 96% among all of the methods.[13] The specificity value of this method was found to be 87% in a study conducted by Barr et al.[13] This value is similar to the specificity value of the 5-point color scale method, which is higher than that of the strain ratio method.[13]

All of these strain elastographic methods have some limitations. In the 5-point color scale method, because of little changes, instantaneous changes occur in the color map of the lesion. As a result, the lesion can be classified as the wrong score. In the elastographic–to–B-mode length ratio method, it is very important to measure the lengths of the lesion accurately with both B-mode US and elastography. Some lesions such as invasive lobular carcinomas and ductal carcinomas in situ may not be visualized and measured with certainty on US images because of their structural natures. In the strain ratio method, similar stresses should be applied in both tissues, and this is a difficult issue because of the shape of the breast.[13]



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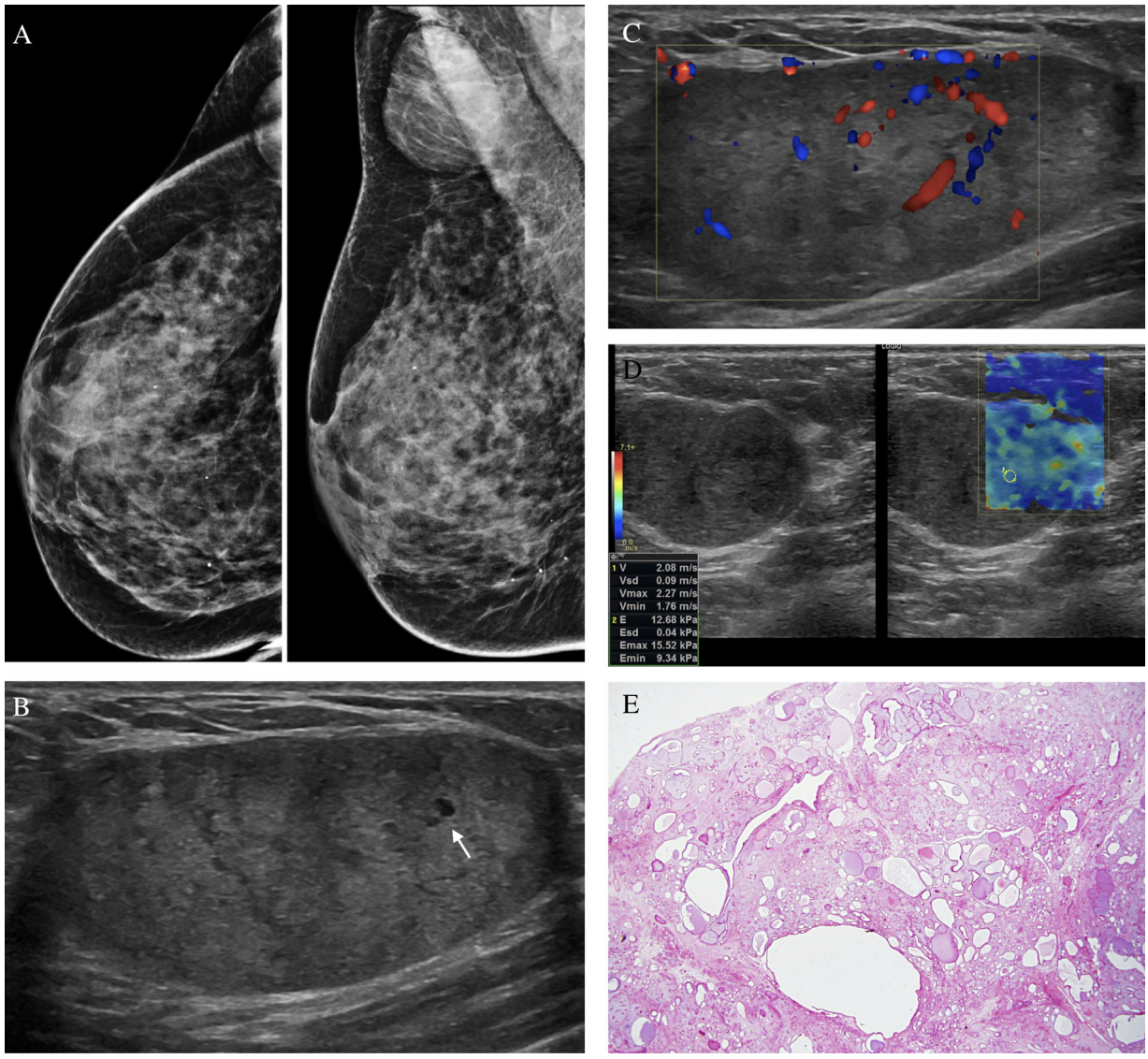
**Figure 1.** A 42-year-old female patient was evaluated for breast pain and a palpable lesion at her right breast. **A**, On MG, the breast was in the type D categorization, and no prominent finding was evaluated. **B**, On a US examination, the lesion was round with indistinct margins. The echogenicity of the lesion was hypoechoic with a heterogeneous echo texture. The size of the lesion was measured as 13 mm. **C**, Ultrasound elastography showed a color pattern, including a diffuse red color pattern compatible with a score of 5. The elasticity score was measured as 8.20 m/s (201.51 kPa). The lesion was classified as BI-RADS 4A from both B-mode and elastographic findings. **D** and **E**, Magnetic resonance imaging showed enhancement (**D**) with diffusion restriction (**E**, arrows). **F**, Core needle biopsy was performed, and the lesion was diagnosed as CFA including sclerosing adenosis with epithelial calcifications. The immunohistochemical evaluation showed that there was a 1% to 2% Ki-67 proliferation index (hematoxylin–eosin, original magnification ×20).






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**Figure 2.** A 55-year-old female patient with a palpable mass showed a size increase at her right axillary groove. **A**, Mammography showed an opacity with a round shape and a lobulated contour. **B**, B-mode US revealed an isoechoic-hypoechoic solid mass showing a heterogeneous echo texture with millimetric cysts (arrow). The size of the lesion was measured as 53 mm. **C**, On the Doppler US examination, a vascularity increase was seen. **D**, Ultrasound elastography showed a heterogeneous color pattern including blue-green, compatible with a score of 2. The elasticity score was measured as 2.08 m/s (12.68 kPa). **E**, The lesion was excised at the request of the patient. The histopathologic diagnosis was CFA with sclerosing adenosis (hematoxylin–eosin, original magnification ×40).

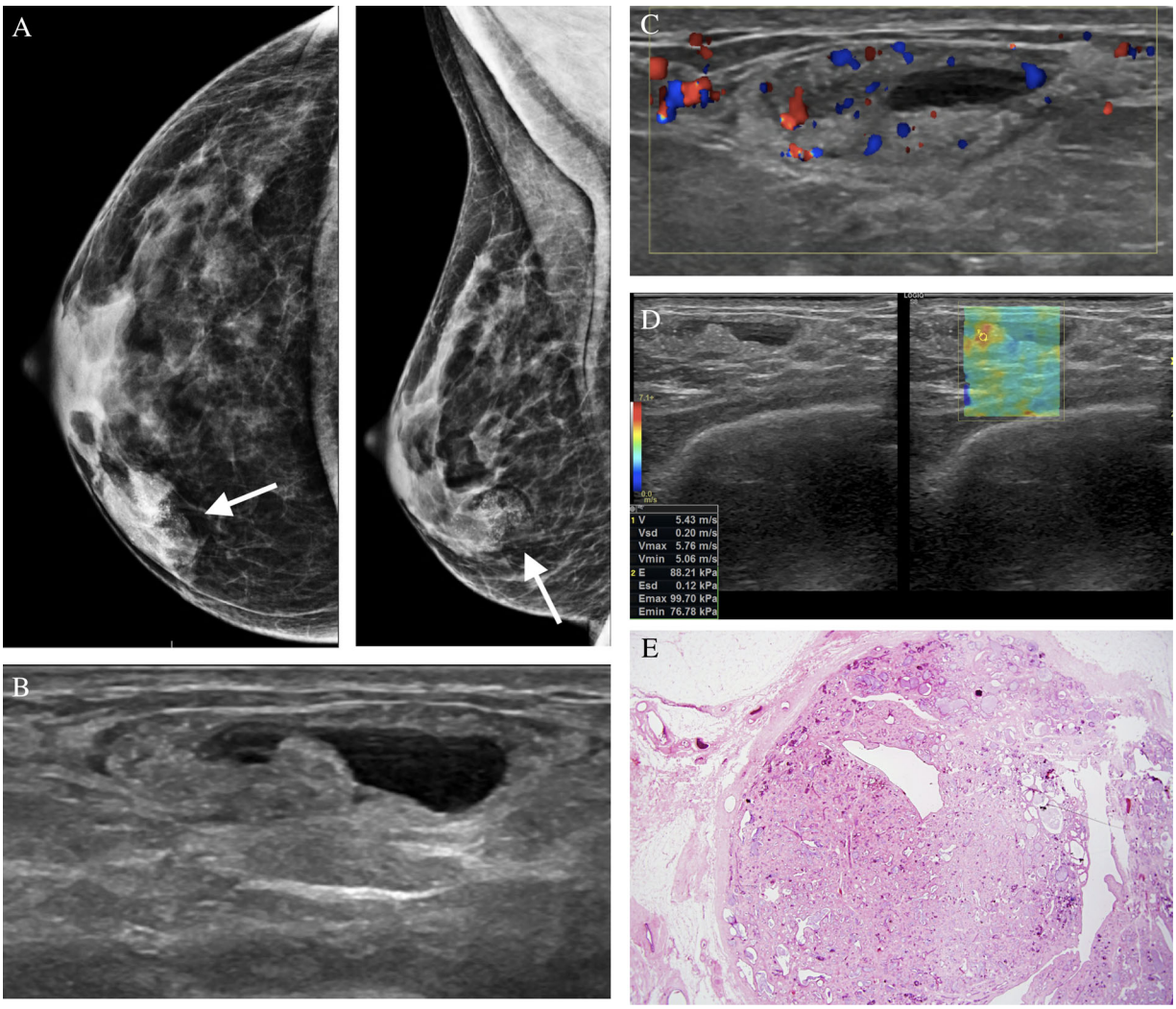



Shear wave elastography results in a quantitative value in terms of velocity by applying a push pulse, forming a shear wave propagation. The quantitative value depends on changes in the speed of the sound as a result of tissue stiffness.[12] Since malignant tissues have stiffer contents and higher velocities than benign tissues, elastography can improve the discrimination of benign and malignant lesions.[3] Shear wave elastography provides quantitative data obtained during a real-time examination. Moreover, these data are repeatable compared to strain elastography.[11] In a previous study, it was found that the results of strain



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**Figure 3.** A 43-year-old female patient had a palpable breast mass at her right breast. **A**, There was an isodense-hyperdense nodular lesion with multiple calcifications showing a cluster on MG (arrows). **B**, B-mode US revealed an oval, well-defined complex cystic lesion with asymmetric wall thickening and an isoechoic solid component including multiple calcifications. The lesion size was 26 mm. **C**, On the Doppler US examination, a vascularity increase was seen in the solid component. **D**, Ultrasound elastography showed a minimal heterogeneous color pattern at the asymmetric solid component, generally including yellow with mineral red, compatible with score 3. The elasticity score was measured as 5.43 m/s (88.21 kPa). The thickened walls had a low elasticity score with blue-green, compatible with score 2. **E**, The lesion, classified as BI-RADS 4B, was excised by needle-guided biopsy and diagnosed as CFA with sclerosing adenosis and epithelial calcifications (hematoxylin–eosin, original magnification ×20).



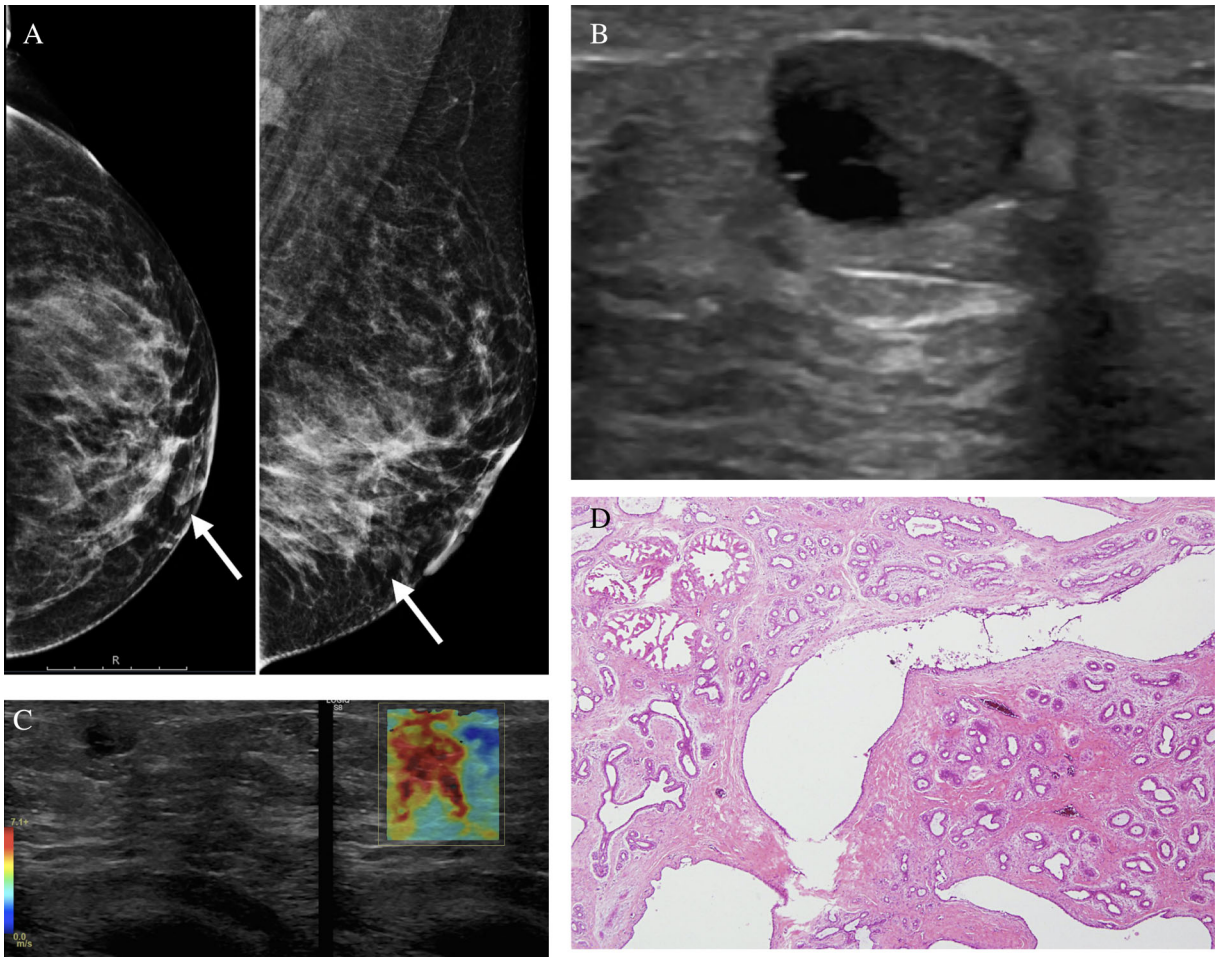

elastography had more accurate rates for characterization of benign or malignant breast lesions than shear wave elastography.[8]

Although elastography is a useful method in discrimination of malignant and benign lesions, there may be false-negative and false-positive results. These results depend on the lesion size, histologic features of the lesion, composition of the surrounding tissue, thickness of the tissue, and application techniques.[17,18] Malignant lesions such as lymphomas yield false-negative results and have less stiffness with lower scores than the other malignant lesions.[8] In benign lesions with sclerosing components, fibrous parenchyma, mastitis, and fat necrosis, elastography may cause false-positive results.[8,11]



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**Figure 4.** A 43-year-old female patient with a history of familial breast cancer anamnesis was evaluated for a palpable lesion at her left retroareolar region. **A**, On MG, there was a retroareolar round, well-defined, isodense-hyperdense nodular opacity (arrows). **B**, On a US examination, the complex cystic lesion was round with well-defined margins. The echogenicity of the lesion was hypoechoic. The size of the lesion was measured as 11 mm. **C**, Ultrasound elastography showed a color pattern including heterogeneous red and yellow, compatible with score 3. The lesion was classified as BI-RADS 4A from both B-mode and elastographic findings. **D**, Excisional biopsy was performed, and the lesion was diagnosed as CFA including apocrine metaplasia and cysts (hematoxylin–eosin, original magnification ×40).




## B-Mode Ultrasound Features of CFAs

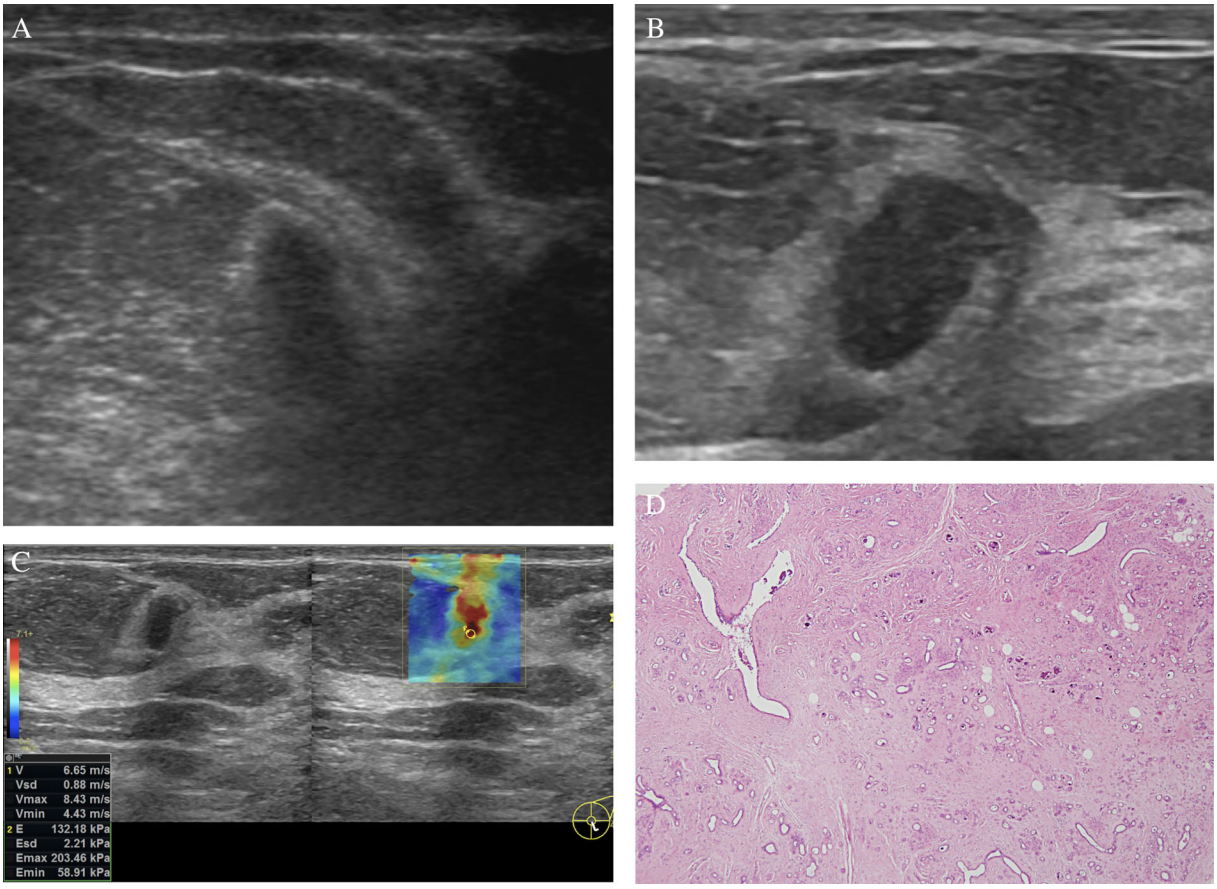
The US findings of CFAs do not have distinctive features from SFAs.[19] Pinto et al[1] reported that most CFAs were oval, circumscribed, and in a parallel orientation with no posterior acoustic enhancement or calcification content. Additionally, they showed that epithelial calcification and cysts larger than 3 mm were more common among CFAs.[1] In another study, a complex-cystic echo pattern was also reported in most CFAs.[7]

Despite these, an irregular shape, a non-circumscribed contour, microcalcification content, and posterior acoustic enhancement are more common in CFAs than SFAs. In some cases, the imaging findings are challenging. Although most fibroadenomas and even CFAs are classified as American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) category 3, lesions with suspicious findings are classified as BI-RADS 4A according to the imaging findings. Breast Imaging Reporting and Data System 4A lesions have a rate of malignant transformation of 3% to 10%.[20] All fibroadenoma variants may be classified as BI-RADS 4A, but this is particularly true for CFAs and cellular fibroadenomas with suspicious imaging findings.



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**Figure 5.** Routine US evaluation of a 32-year-old female patient. **A**, On a US examination performed 1 year previously, an oval, well-defined, hypoechoic lesion was in a vertical orientation. The size of the lesion was measured as 7 mm. The lesion was classified as BI-RADS 4A. However, the patient refused any interventional procedure. **B**, On a subsequent US examination, the size of the lesion was measured as 13 mm. As a result of the size increase, the location of the lesion had become nearer to skin. **C**, Ultrasound elastography showed a color pattern including predominantly red, compatible with score 4. The elasticity score was measured as 6.65 m/s (132.18 kPa). **D**, Core needle biopsy was performed, and the lesion was diagnosed as CFA including sclerosing adenosis with epithelial calcifications (hematoxylin–eosin, original magnification ×40).




Irregular shapes, noncircumscribed margins, nonparallel orientations, heterogeneous echogenicity, and posterior acoustic shadowing are suspicious imaging findings compatible with BI-RADS 4A.[20]

## Elastographic Features of CFAs

Complex fibroadenoma is a mixture of complex histopathologic features, including sclerosing adenosis and epithelial calcifications.[3] As a result of this complex structure, the lesion becomes stiffer than the normal breast tissue. However, because of cysts in the CFA, combined fibrocystic changes occur, and as a result, the lesion structure becomes softer than malignant breast lesions.[3,21] The nature of the breast tissue in which fibroadenoma develops is also important in the evaluation of the stiffness. Fibroadenomas that are located very close to skin are stiffer,[22] but during an elastographic examination, compression can be applied directly to the lesion easily. Additionally, fibroadenomas growing in fatty breast tissue have less stiffness than those growing in dense fibroglandular tissue.[22]

The mean size of SFAs is smaller than that of CFAs.[1,7,23] In the literature, there is a hypothesis that larger fibroadenomas have stiffer structures than smaller ones because of prominent compression of



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adjacent breast tissue.[24,25] Patients with CFAs are older than patients with SFAs. As the patient gets older, fibroadenomas regress; hyaline degenerations occur; and the structures develop complex histopathologic features.[7,23] In fibroadenomas in elderly women and those including calcification, the stiffness increases.[26,27]

B-mode US images of SFAs and CFAs may show an overlap, and as a result, the lesions might be classified as BI-RADS 3 and 4A.[28] As the treatment approach and follow-up procedures have different characteristics, the exact decision about the lesions is very important. Especially, correct diagnosis in preoperative or preinterventional processes can eliminate unnecessary procedures or provide the most appropriate approach to the lesions. Elastography is an easily applicable examination in the evaluation of the lesions. The combination of B-mode US and even Doppler US features with elastography provides a prominent contribution in the diagnosis of solid lesions. In 73% of fibroadenomas, including CFAs, the combination of both B-mode US and elastographic findings can be used to differentiate them from malignant lesions.[29]

Finally, taking all of the factors influencing the stiffness features above into consideration, CFAs have different elastographic findings. The histopathologic structure, the patient's age, and the size of the lesion are very important factors, which are determinative of the elastographic features of CFAs. These factors can cause false-positive elastographic results (Figure 1). As a result, there is a spectrum of different strain elastographic categories and quantitative data from shear wave elastography in these lesions.

## Cases

### *Case 1*

A 42-year-old female patient was evaluated for breast pain and a palpable lesion at her right breast. Routine breast examinations including both mammography (MG) and US were performed. On MG, the patient had dense breast tissue, which was compatible with a type D breast structure. The US examination showed a lesion with indistinct margins and a round shape. Additional elastographic findings were suspicious for malignancy, and the lesion was classified as BI-RADS 4A. Additional magnetic resonance imaging was performed, and prominent enhancement was seen in the lesion. The patient was redirected to core biopsy, and the histopathologic diagnosis was CFA including sclerosing adenosis with epithelial calcifications. The immunohistochemical evaluation also showed the Ki-67 proliferation index (Figure 1). The patient was redirected to surgical excision as a result of these findings. We strongly think that the dense breast parenchyma, sclerosing adenosis components with epithelial calcifications, and Ki-67 proliferation index caused the high strain elastographic category and elasticity scores.

### *Case 2*

A 52-year-old female patient who perceived a palpable mass with an increase in size was redirected for MG and US evaluations. On MG, there was an oval opacity showing contour lobulation at the upper outer quadrant of her right breast. On the US examination, the lesion was isoechoic-hypoechoic with a heterogeneous echo patten including millimetric cysts. An additional Doppler examination showed increased vascularity, whereas elastographic findings were compatible with benign findings. As the size of the lesion showed an increase, it was classified as BI-RADS 4A. According to the patient's request, the lesion was excised instead of undergoing core biopsy in the general surgery operating theater. The pathologic results revealed CFA with sclerosing adenosis according to the histopathologic evaluation (Figure 2). In light of all of these finding, although the patient was older, and the lesion included a sclerosing adenosis component, the low elastographic score was dependent on cyst contents and surrounding fatty accessory breast tissue.

### *Case 3*

A 43-year-old female patient was evaluated for a palpable mass at her right breast. Mammography showed an oval, well-defined nodular opacity including multiple calcifications. On a US examination, the lesion was a complex cystic lesion with diffuse wall thickening and an asymmetric isoechoic solid component. In addition, there were multiple millimetric echogenic areas belonging to the calcifications. A Doppler examination revealed increased vascularity at the asymmetric solid component. The color pattern on



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elastography was compatible with score 3. Thick walls were blue-green, compatible with score 2, whereas the solid asymmetric component had a red-yellow pattern, compatible with score 3. The lesion was classified as BI-RADS 4B from all of the imaging findings. Needle-guided excisional biopsy was performed. In the histopathologic evaluation, it was diagnosed as CFA with sclerosing adenosis including epithelial calcifications (Figure 3). We think that the difference in the elastographic color patterns in the lesion was dependent on different components in the lesion. The lower score was a result of the cystic structure of the lesion, and the higher score was dependent on the asymmetric solid part including increased cellular density and sclerosing adenosis with more epithelial calcifications.

***Case 4***

A 43-year-old female patient was admitted to our breast-imaging department for her first routine breast evaluation. In her family history, her sister had a diagnosis of breast carcinoma at the age of 38 years. Mammographic and US examinations were performed. On MG, the breast density was evaluated as type C. There was a round, well-defined, isodense nodular lesion at her left retroareolar region. The US examination showed a round, well-defined, solid nodular lesion. There was posterior acoustic enhancement, and the lesion included cysts. On elastography, there was a heterogeneous color pattern generally including generally red and yellow. The score was evaluated as 4. Although the lesion's MG and B-mode US findings were compatible with a BI-RADS 3 categorization, excision of the lesion was recommended to the patient according to the elastographic findings and her family history. The lesion was diagnosed as CFA including apocrine metaplasia and cysts (Figure 4). We concluded that the high elastographic score of the lesion was dependent on surrounding dense breast parenchyma, the location of the lesion near the breast skin, and the presence of apocrine metaplasia.

***Case 5***

A 32-year-old female patient was in follow-up for a left breast lesion. Her lesion had been diagnosed 1 year previously. An US examination of the lesion had shown that it had been hypoechoic, oval, and in a vertical orientation. The lesion had been evaluated as BI-RADS 4A. Although biopsy had been recommended to the patient, she had refused all interventional procedures. In her recent breast evaluation, a size increase and occurrence of microlobulation at the anterior part of the lesion were determined. The size was measured as 7 mm 1 year previously, and the recent size was 13 mm. The elasticity score of the lesion was 3 in the elastographic examination, with a yellow and red pattern. As a result of the size increase, change in the contour, and B-mode and elastographic findings, the lesion was evaluated as BI-RADS 4A again. She was convinced to undergo core biopsy. In the histopathologic evaluation, the lesion was diagnosed as CFA including sclerosing adenosis with epithelial calcifications (Figure 5). We think the dense breast parenchyma, location near the breast skin, and histopathologic contents caused these elastographic findings.

## Conclusions

Fibroadenoma is the most common benign tumor of the breast. As CFA is a suspicious variant of fibroadenoma, it is very important to make a differential diagnosis. B-mode US, Doppler US, and other radiologic findings show intersections, and there are no discriminative features. Elastographic features of CFAs show a heterogeneous spectrum depending on different factors. These findings do not have a prominent contribution in the exact diagnosis. The combination of all of the imaging findings can help in the diagnosis and prevent unnecessary interventional applications.

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