Parallel Artery and Vein: Sign of Benign Nature of Breast Masses

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OBJECTIVE. The purpose of this study was to assess the parallel artery and vein sign at color Doppler breast ultrasound as a predictor of the benign nature of breast masses.

SUBJECTS AND METHODS. A prospective study was performed to identify evidence of a parallel artery and vein in breast lesions consecutively biopsied with a 14-gauge needle under ultrasound guidance. Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and 95% CIs for the parallel artery and vein sign were calculated.

RESULTS. The parallel artery and vein sign was identified in 142 of the 1074 masses (13.2%). The specificity for benignity was 99.3% (CI 95%, 98.3–100.0%); sensitivity, 17.6% (CI 95%, 15.0–20.3%); positive predictive value, 99.0% (CI 95%, 96.7–100); negative predictive value, 30.0% (CI 95%, 27.0–32.9); positive likelihood ratio, 24.7 (CI 95%, 21.2–28.7); and negative likelihood ratio, 0.83 (CI 95%, 0.80–0.86). Among masses found to have the parallel artery and vein sign, all BI-RADS ultrasound category 3 and 95.1% of BI-RADS 4 lesions were determined to be benign.

CONCLUSION. Although the parallel artery and vein sign is an uncommon finding, it has a significant association with benign pathologic results (96.5%) with a positive likelihood ratio of 24.7. The presence of this color Doppler ultrasound finding in breast masses in BI-RADS ultrasound categories 3 and 4 reinforces the benign nature and may allow follow-up rather than biopsy in the care of some patients.

Ultrasound is a well-known imaging technique for characterization of breast masses. The American College of Radiology has standardized sonographic findings to establish a common language among radiologists. The shape and margin of the lesion, orientation in relation to the skin, lesion boundary, echotexture, posterior acoustic features, relation to the surrounding parenchyma, and additional findings, such as presence of calcification and vascularization, are described in the lexicon [1].

Vascular elements in solid lesions have been examined with various Doppler techniques, such as color, spectral, and power Doppler. Flow patterns and waveforms are analyzed with spectral Doppler technique, and morphologic features are analyzed with color and power Doppler techniques [2–13]. The following elements are described as characteristic of malignancy: more than one vascular pole; abnormal afferent vascularity (tortuous vessels penetrating the tumor); and hypervascularity with irregular, branching, disorganized intratumoral vessels [3]. Benign lesions tend to have weak and peripheral vascularity and no central vessels [4]. Spectral Doppler analysis has been described as less useful than color Doppler imaging in differentiating benign from malignant masses, having considerable overlap of parameters such as pulsatility and resistance index [14]. Because no reliable standard findings exist, a common language for Doppler findings has not been established. Assessment of lesion vascularity is recommended but is not considered mandatory in the BI-RADS ultrasound lexicon.

Normal vascular anatomy in structures such as the kidneys, lymph nodes, and extremities consists of an artery and one or two veins in the same bundle. Because of their characteristic color pattern and waveforms, these vascular structures are easily identifiable during color and pulsed Doppler evaluation. Malignant tumors stimulate growth of new vessels by secretion of angiogenic factors. These new vessels differ from the native vessels, are morphologically distinct,

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and are highly tortuous because of their increased endothelial proliferation, high capillary growth rate, and irregular branching and formation of loops [2, 14–17].

We can infer that the presence of an artery and a vein in parallel distribution in the periphery or inside a lesion is a normal anatomic condition that contrasts to the anomalous neovessels generated by tumoral angiogenesis in malignant lesions. We have observed this finding at Doppler ultrasound examination of some breast masses and have called it the parallel artery and vein sign. In this study, we assessed the usefulness of the parallel artery and vein sign in predicting the benign or malignant nature of a breast lesion. We hypothesized that the parallel artery and vein sign is a predictor of a benign pathologic result.

Subjects and Methods

This study, approved by the institutional review board of our institution, was performed from April 2003 to April 2008. All patients with breast masses undergoing ultrasound-guided biopsy in our department were consecutively enrolled. We used ultrasound systems (ATL HDI5000 SonoCT, IU22 Gemini, Philips Healthcare) with 5–12 and 5–17 MHz transducers and color Doppler mode. Core needle biopsies were performed with an automated gun (Magnum, Bard) and 14-gauge needles.

All ultrasound examinations and Doppler analyses of the breast masses and core needle biopsies were performed by six radiologists with at least 5 years of experience in ultrasound-guided breast procedures. A minimum of six cores per lesion were obtained, as defined by our National Consensus [18]. To ensure uniform performance, before the start of the protocol the radiologists underwent basic training on the pattern of the parallel artery and vein sign. Informed consent was obtained from all patients.

The parallel artery and vein sign was considered present in a mass when two parallel vessels were visualized in the capsule or interior. In this case, one vessel appeared blue and the other red (Fig. 1), indicating the presence of an artery and a vein, which could be confirmed with spectral Doppler imaging. Images of the optimal plane or video captures to confirm the findings were registered and stored in our hospital PACS.

As a standard protocol, all masses were assessed with color Doppler ultrasound before the biopsy procedure. Specific parameters to detect very low blood flow were established on both ultrasound systems with identical settings for every mass (pulse repetition frequency, 700–1000 Hz; wall filter, 50–100 Hz; gain, 85–90%; medium

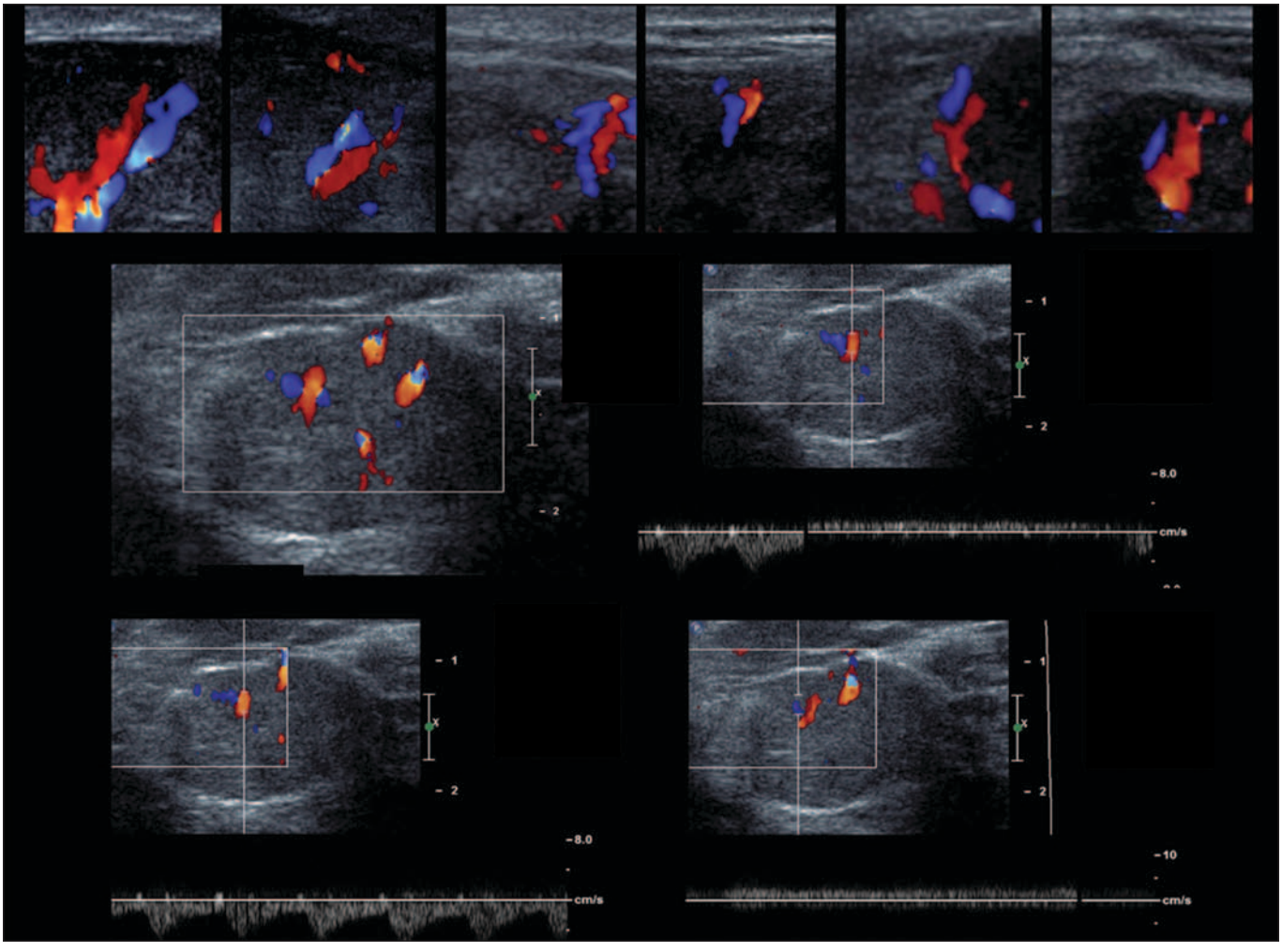

Fig. 1—38-year-old woman with breast mass. Ultrasound images (*top row*) show parallel blood flow in periphery and interior of breast mass corresponding to artery (*red*) and vein (*blue*) and signifying normal anatomic condition. Parallel artery and vein sign is present. Pulsed Doppler ultrasound images confirm venous and arterial characteristics of fluid.

persistence; no window angling). The mass and adjacent breast parenchyma, containing the afferent and efferent vessels, were included in the color box (Fig. 1). The examination was performed with particular care to applying minimal pressure on the masses with the transducer to prevent vessel collapse.

For each biopsied mass, patient demographics, sonographic characteristics, color Doppler imaging findings, presence or absence of the parallel artery and vein sign, size, BI-RADS ultrasound category [1], and histologic results were entered into a specially designed database (FileMaker Pro 8.5, FileMaker). The radiologists performing the examinations were instructed not to use the presence or absence of the parallel artery and vein sign for BI-RADS ultrasound classification. BI-RADS ultrasound category 4 was not subclassified in the initial protocol design. The standards of reference were the definitive histologic result on the masses that were surgically excised and extensive follow-up results for benign and high-risk lesions diagnosed with core needle biopsy and not surgically treated.

The nodules with the parallel artery and vein sign were selected for further analysis. Sensitivity, specificity, negative and positive predictive values, and likelihood ratios for benignity were calculated. Qualitative characteristics were compared between groups by chi-square test, and quantitative characteristics were assessed with the Student *t* test. When pertinent, 95% CI was determined; $p < 0.05$ was considered statistically significant.

TABLE 1: Histologic Findings on 137 Benign Masses Exhibiting the Parallel Artery and Vein Sign

Finding	No. of Masses
Fibroadenoma	92
Complex fibroadenoma	6
Fibroadenosis	7
Adenomatoid hyperplasia	8
Pseudoangiomatous hyperplasia	4
Fibrocystic mastopathy	2
Tubular adenoma	2
Adenosis	4
Lactating adenoma	1
Benign papilloma	4
Fat necrosis	1
Lymphoid tissue	4
Other benign	2
Total	137

Results

In a 5-year period, 829 patients underwent 1074 core biopsies, and the parallel artery and vein sign was identified in 142 masses in 137 patients (136 women, one man; mean age, 42.5 [SD, 9.2] years), representing 13.2% (142/1074) of the sample studied. The size of the masses with the parallel artery and vein sign ranged from 5 to 41 mm (median, 12 mm; interquartile range, 10–16 mm). Forty masses were in BI-RADS ultrasound category 3; the other 102 lesions were in category 4.

Core biopsy findings confirmed that 137 of 142 masses (96.5%) were benign. These lesions were therefore not surgically treated. During the follow-up period, which ranged from 30 to 96 months, no malignancy was diagnosed. Table 1 shows the histologic distributions.

At core biopsy, three masses (2.1%) were determined to be high-risk lesions. All were surgically excised, and the definitive histologic diagnosis was benign (Table 2). The other two masses were malignant, and definitive histologic examination of both of these excised masses confirmed malignancy. These two false-negative cases represented 1.4% (2/142) of the masses in which the parallel artery and vein sign was found. The results of evaluation of the presence of the parallel artery and vein sign as an indicator of the benignity of a mass with surgical diagnosis or follow-up findings as the reference standard are shown in Table 3.

Table 4 compares the characteristics of the total study sample with the groups with and without the parallel artery and vein sign. There were no significant differences in the sizes of the masses ($p = 0.84$). A greater proportion of suspicious lesions (BI-RADS ultrasound categories 4 and 5) was found in the group without the parallel artery and vein sign (612 and 188) than in the group with the sign (102 and zero).

TABLE 2: Surgical Results

Core Biopsy Histologic Finding	No. of Lesions	Definitive Histologic Finding
Malignant lesions		
Malignant phyllodes tumor	1	Malignant phyllodes tumor
Papilloma plus ductal carcinoma in situ	1	Papilloma plus ductal carcinoma in situ
High-risk lesions		
Fibroepithelial tumor suggestive of phyllodes tumor	1	Benign phyllodes tumor
Papilloma plus atypical ductal hyperplasia	1	Papilloma without atypia
Complex fibroadenoma plus atypical ductal hyperplasia	1	Fibroadenoma without atypia
Total	5	

Note— All high-risk lesions detected at core biopsy were classified as benign at definitive histologic examination.

TABLE 3: Value of the Parallel Artery and Vein Sign in Diagnosis of Benign and Malignant Lesions Based on Definitive Histologic or Follow-Up Findings

Characteristic	Benign	Malignant	Total
Parallel artery and vein present (no.)	140	2	142
Parallel artery and vein absent (no.)	654	278	932
Total no. of masses	794	280	1074
Sensitivity (%)	17.6 (15.0–20.3)		
Specificity (%)	99.3 (98.3–100)		
Positive predictive value (%)	99.0 (96.7–100)		
Negative predictive value (%)	30.0 (27.0–32.9)		
Positive likelihood ratio	24.7 (21.2–28.7)		
Negative likelihood ratio	0.83 (0.80–0.86)		

Note—Values in parentheses are 95% CI.

TABLE 4: Characteristic of Masses

Characteristic	All Masses	Parallel Artery and Vein Sign		*p*
		Present	Absent	
Size (mm)				0.84
Average	13.74	13.64 (6.26)	13.76 (8.94)	
Range	3–70	5–41	3–70	
Patient age (y)				< 0.001
Average	48.77	42.5 (9.26)	49.8 (12.17)	
Range	14–98	20–74	14–98	
BI-RADS ultrasound category				< 0.001
3	172	40	132	
4	714	102	612	
5	188	0	188	
Nature of lesion				< 0.001
Benign	758	137	621	
High risk	38	3[a]	35[b]	
Malignant	278	2	276	
Total	1074	142	932	

Note—Values in parentheses are SD.
[a]At definitive histologic examination, all were benign.
[b]At definitive histologic examination, two were malignant.

TABLE 5: Distribution of Lesions by BI-RADS Category and Parallel Artery and Vein Status at Core Biopsy

BI-RADS Category	Parallel Artery and Vein Sign		Total
	Present	Absent	
3			
Benign	40	124	164
High-risk lesion	0	6[a]	6
Malignant	0	2	2
4			
Benign	97	485	582
High-risk lesion	3[a]	26[b]	29
Malignant	2	101	103
5			
Benign	0	12	12
High-risk lesion	0	3[a]	3
Malignant	0	173	173
Total	142	932	1074

[a]At definitive histologic examination, all were benign.
[b]At definitive histologic examination, two were malignant.

The parallel artery and vein sign was present in 23.2% (40/172) of the masses considered BI-RADS ultrasound category 3, and all of these masses had benign histologic results. We found that 14.3% (102/714) of the masses confirmed to exhibit the parallel artery and vein sign were BI-RADS 4 and that 98% (100/102) of them were benign (Table 5).

Discussion

For a long time, color Doppler ultrasound was not considered a useful tool in the diagnosis of breast disease because it could not be used to accurately differentiate benign from malignant lesions. Along with improvement in the technology, color Doppler ultrasound and power Doppler angiography have become important complements to bidimensional gray-scale breast ultrasound. Although consensus has not been reached on usefulness, these techniques have been proposed as ways to analyze afferent vessels and the internal vascularization of breast masses to improve characterization [5]. We use these techniques systematically as an integral part of our breast ultrasound protocol; all solid masses are studied with color Doppler ultrasound.

In color Doppler ultrasound imaging, blue and red indicate the direction of blood flow with respect to the position of the transducer. When two vessels are found to flow in parallel, blue and red generally indicate a vein and an artery, the presence of which can be confirmed with spectral Doppler imaging (Fig. 1). However, tortuous vessel curling can mimic a similar color Doppler pattern, and aliasing can cause confusion, although the colors in the aliased vessel (most likely an artery, where flow is faster) would appear as a mosaic. Therefore, the parallel artery and vein sign is valid when the color-encoded signal shows a clear blue and red pattern during a Doppler examination. In case of doubt, spectral Doppler technique can be used to confirm the arterial and venous flow patterns. We believe that this limitation does not affect our results; special care was taken in this respect, and spectral Doppler ultrasound was performed in most cases.

The detection of vessels in breast masses depends on the sensitivity of the ultrasound system, the frequency of the transducer used, and the appropriate selection of technical parameters for the study of the breast. To accurately capture very low blood flow and to obtain optimal images of all vessels examined, all necessary technical parameters have to be adjusted (pulse repetition frequency, wall filter, gain, persistence, window), and care has to be taken to avoid compressing the breast with the transducer; excess pressure can collapse the vessel and lead to the interpretation that the lesion is avascular.

Precise semiologic criteria for benign and malignant lesions according to location and morphologic features of the vessels detected have been established [6–13]. The following criteria have 73–98% sensitivity for malignancy and 16–90% specificity [13]: intratumoral vessels without capsular vessels, vascularization of a large percentage of the

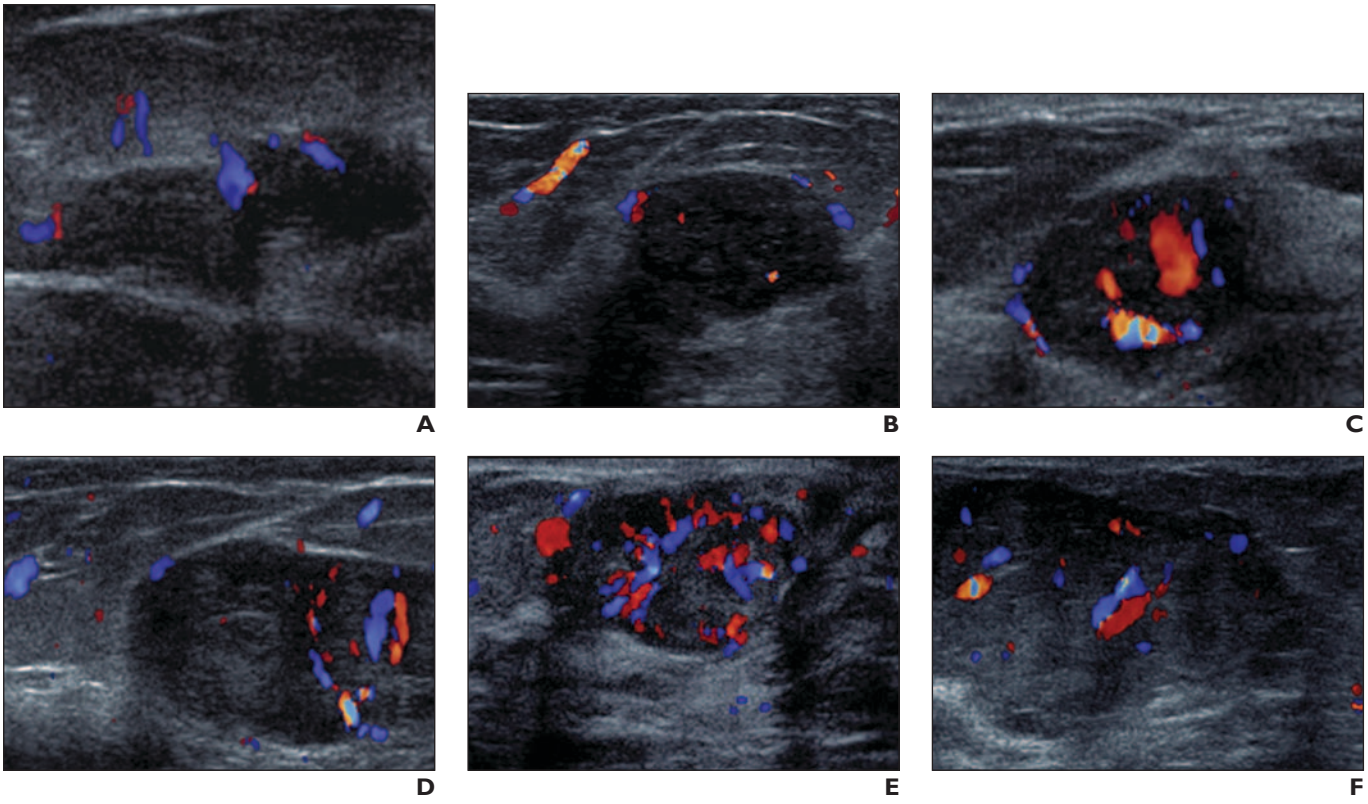

Fig. 2—Ultrasound images of benign masses exhibiting parallel artery and vein sign.
A, 42-year-old woman with fibroadenoma.
B, 50-year-old woman with fibroadenoma.
C, 54-year-old woman with fibroadenoma.
D, 32-year-old woman with fibroadenoma.
E, 50-year-old woman with benign papilloma.
F, 35-year-old woman with lactating adenoma.

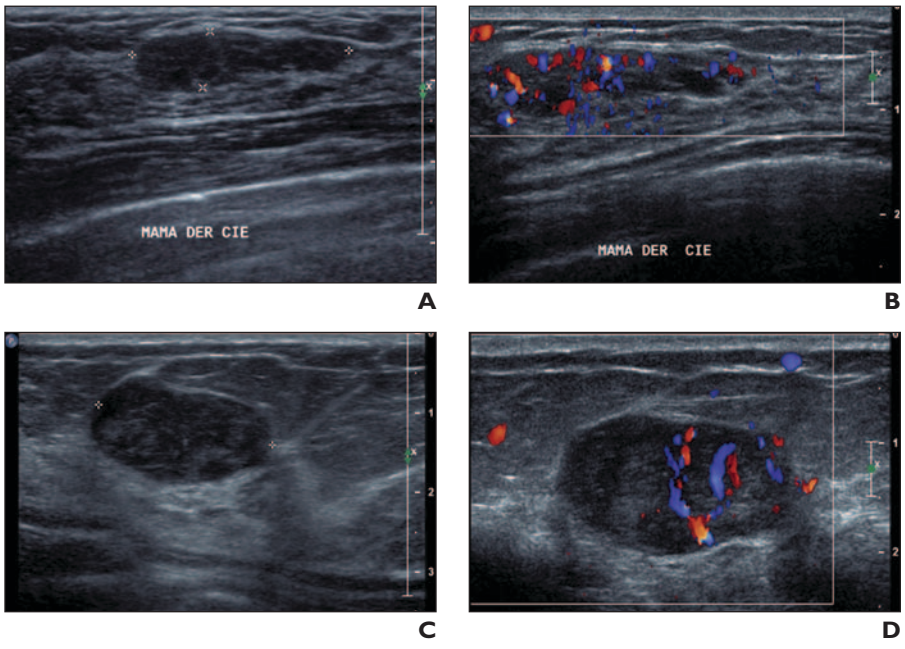

Fig. 3—Malignant tumors exhibiting parallel artery and vein sign. Ultrasound images show papilloma associated with ductal carcinoma in situ in 38-year-old woman (**A** and **B**) and borderline phyllodes tumor in 47-year-old woman (**C** and **D**). Findings were confirmed at histologic examination of surgical specimen.

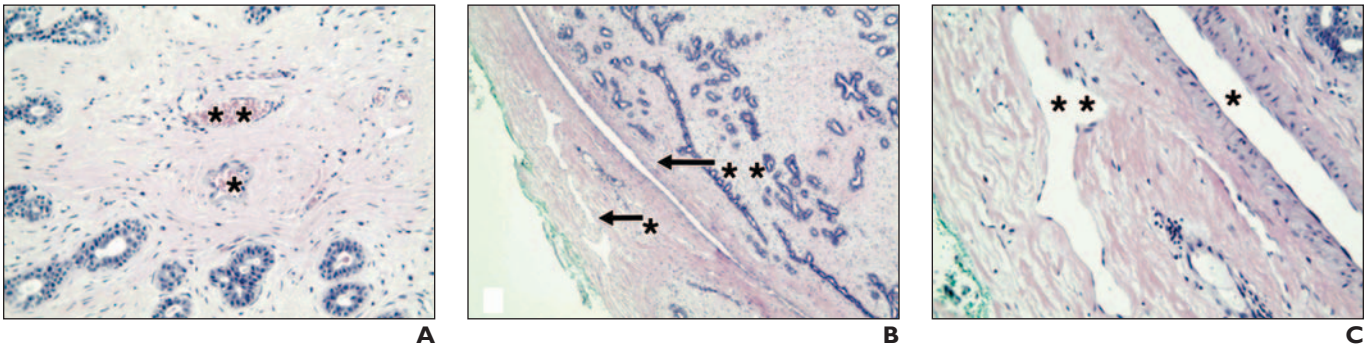

Fig. 4—Fibroadenomas in which arteriole (*single asterisk*) and vein (*double asterisks*) are present together. (Courtesy of Espinoza A, Santiago, Chile)
A, 40-year-old woman. Photomicrograph (H and E, ×200) shows transverse section.
B, 32-year-old woman. Photomicrograph (H and E, ×40) shows longitudinal section. Arrows indicate arteriole and vein.
C, 32-year-old woman. Photomicrograph (H and E, ×100) shows longitudinal section.

mass, tortuous neovessels with irregular caliber, penetrating vessels, and a large number of afferent pedicles. This range in sensitivity and specificity is due to the broad variability of equipment and techniques used for analysis, such as color Doppler, power angiography, and contrast administration.

Among the color Doppler signs suggestive of benignity, we found that capsular vessels with straight or curved lines had a regular caliber and even distribution. The parallel artery and vein sign applies to this type of capsular vessel, which divides into intralesional branches that continue with a parallel flow. This finding is valid only for capsular vessels and their intralesional branches, which should not be confused with other normal vessels in proximity to the mass.

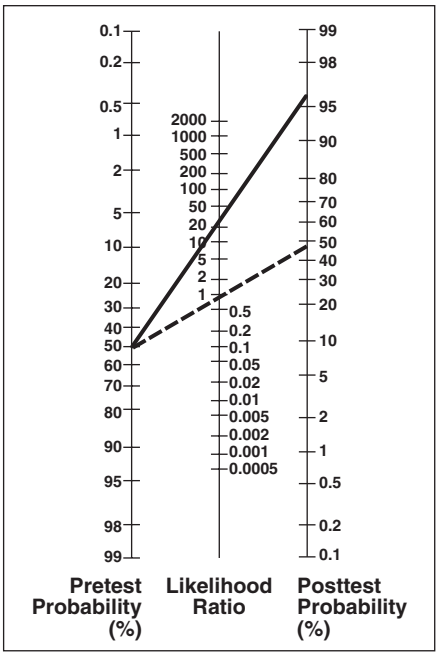

Fig. 5—Fagan nomogram [19] shows clinical application of positive and negative likelihood ratios of parallel artery and vein sign. For 50% clinical pretest estimate of benignity, posttest probability is modified to 96% when sign is present (*solid line*). When sign is absent (*dashed line*), posttest probability has minimal (and clinically insignificant) shift, requiring further study such as biopsy.

In our study, the frequency of masses with the parallel artery and vein sign was a low 13.2%. Considering that 17.5% of this series of core needle specimens were masses in BI-RADS ultrasound category 5, the incidence of the parallel artery and vein sign may be underestimated. Therefore, in the general population, where most benign-appearing lesions are not biopsied, the parallel artery and vein sign may be present in a greater relative proportion. This finding may be due to technical limitations that arise from using color Doppler ultrasound with the amount of signal flow variation that must be detected with current technology. Smaller vessels may exhibit this pattern but are visible only with higher-frequency transducers than those commercially available.

Analysis of the masses in which the parallel artery and vein sign was present showed that most of these lesions were fibroepithelial tumors and papillomas: 71.5% (98/137) of the benign masses in this series that exhibited the parallel artery and vein sign were fibroadenomas (Table 1 and Fig. 2).

Histologic examination of the malignant masses (two false-negative findings of the parallel artery and vein sign) showed two noninvasive breast tumors: a papilloma associated with ductal carcinoma in situ (Figs. 3A and 3B) and a malignant phyllodes tumor (Figs. 3C and 3D), both confirmed at examination of the surgical specimen. In general, multiple intratumoral vessels are frequently observed in papillomas as the parallel artery and vein sign (Fig. 2E). The foci of ductal carcinoma in situ (low grade in this case) did not alter the typical vascular architecture of the mass, and thus the parallel artery and vein sign was present.

The parallel artery and vein sign can be found in a vessel during histologic analysis of sections. Figure 4 shows fibroadenomas in histologic sections in which an arteriole and vein are present together inside the mass (Fig. 4A) and in its periphery (Figs. 4B and 4C). Three high-risk lesions were found at core needle biopsy: a fibroepithelial tumor suggestive of a phyllodes tumor, an intracystic papilloma associated with atypical ductal hyperplasia, and a complex fibroadenoma associated with atypical ductal hyperplasia. However, as Table 2 shows, these three lesions had benign diagnoses at definitive histologic analysis of the excised specimen (benign phyllodes tumor, intracystic papilloma, and fibroadenoma without atypia). In spite of the absence of confirmed malignancy as determined at the surgical procedure, both masses were considered atypical because foci of atypical ductal hyperplasia were evident in the core needle biopsy sample.

Our results suggest that the presence of the parallel artery and vein sign is a strong predictor of benignity, having a positive likelihood ratio of 24.7. Therefore, if the pretest probability is intermediate, for example, 50%, the posttest probability of benignity is close to 96% (Fig. 5). If the parallel artery and vein sign is not present, the posttest probability is not significantly different.

As Table 4 shows, a significant percentage of the total biopsy series (16.0%, 172/1074) was BI-RADS ultrasound category 3 masses. Biopsy had clinical indications in various cir-

cumstances (e.g., cancer phobia, family history of breast cancer, patient preferring biopsy over follow-up observation, initiation of hormone replacement therapy, treatment of precancerous lesions or cancer already administered, presence of contralateral cancer, geographic isolation). Of these lesions, 164 (95.3%) were histologically benign, six (3.5%) were high-risk lesions, and two (1.2%) were malignant.

The parallel artery and vein sign was present in 23.2% (40/172) of the BI-RADS ultrasound category 3 masses in the total biopsy series, and all had benign histologic findings. The sign was present in 14.3% (102/714) of all BI-RADS ultrasound category 4 masses, and 95% (97/102) of these lesions were confirmed benign (Table 5). Therefore, the importance of this sign is that it can be used to identify potentially benign lesions for which biopsy may not be necessary, requiring only follow-up observation. Because BI-RADS ultrasound subclassification into 4A, 4B, and 4C lesions was not in complete clinical use at the design and beginning of our study (late 2002 and early 2003), we decided to keep BI-RADS 4 a single category for the entire study.

The rate of malignancy of masses in which the parallel artery and vein sign was present in this series was very low (1.4%) and should be compared with the accepted 2% rate of malignancy of BI-RADS ultrasound category 3 lesions. We argue that the results should be considered specifically for BI-RADS ultrasound category 4 lesions because these are the only ones that may make a difference in the decision whether to perform a biopsy. Because two of 102 BI-RADS 4 malignant lesions exhibited the parallel artery and vein sign, our rate is similar to the accepted rate for positivity in BI-RADS 3 cases and therefore have a behavior closer to category 3. It may be possible to use the parallel artery and vein sign for follow-up rather than to biopsy selected BI-RADS ultrasound category 4 masses.

One of the limitations of our study was that we evaluated our results on the basis of core needle biopsy findings but did not obtain definitive histologic results on all of the masses because the benign masses were not excised. However, we conducted prolonged follow-up during which no new malignant lesions were detected. In addition, for color Doppler ultrasound to be useful for evaluation of breast masses, the technique ought to be standardized. However, even with standardization, results depend on the equipment used and the experience of the operator.

Conclusion

The parallel artery and vein sign is infrequent, but it is predominantly associated with benign breast lesions and has a low association with malignancy, giving it excellent positive predictive value for benignity and a high positive likelihood ratio. The presence of this Doppler finding in BI-RADS ultrasound category 3 and 4 breast masses reinforces their benignity, potentially allowing the use of clinical and sonographic follow-up procedures and avoiding unnecessary biopsy in the care of some patients.

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