Clinical plus Color Doppler Assessment of Benign and Malignant Breast Diseases

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Abstract:

Background: Tumor growth and metastases require the development of new vessels (angiogenesis), and the extent of angiogenesis predicts metastases and correlate with early death. Recently developed color Doppler mapping can detect the tumor flow signals in breast cancer and help to distinguish it from benign lesions.

Objective: Evaluation of differences between the blood supply in benign and malignant breast lesions by the use of color Doppler image assessment of the lesions vascularity.

Method: Clinical assessment, ultrasound examination and color Doppler mapping were done for 83 female patients with breast lesions. The following flow data analyses were undertaken; presence or absence of color Doppler signal, number of blood vessels, architectural arrangement and the maximum systolic velocity of blood vessels in the lesions and around it.

Results: Histopathological reveals that 21 cases had carcinoma of the breast and 62 had benign lesions. 27 patients provisionally diagnosed as having malignant lesions; of them 15 cases were truly malignant (sensitivity: 71.5%) and 56 benign one; of them 50 lesions were truly benign (specificity: 80.6%).

An increasing number of blood vessels found in malignant lesions; (85.7%) showed more than 3 vessels in a given lesion, while this figure found only in (8%) of benign lesions. For a cutoff of more than 3 vessels sensitivity and specificity are (85.7%), (91.9%) subsequently.

Architectural differences in the form of penetrating central neoplastic vessels were present in 18 (85.7%) of the malignant lesions with sensitivity (90.4%), while only in 3 (6.1%) of the benign lesions with specificity (93.8%).

The maximum systolic velocity of tumor vessels showed an increasing velocity in malignant lesions, for a cutoff more than 15 cm/s the sensitivity was (90.4%) and specificity was (91.8%).

Combination of the three parameters gave (90.4%) sensitivity and (96.7%) specificity.

Conclusion: Color Doppler imaging considered as an adjuvant primary investigation tool in addition to the ultrasound examination in improving differential diagnosis of breast lesion.

Keywords: Color Doppler, Breast diseases, Benign, Malignant.

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Introduction:

Although an accurate history and clinical examination are important methods of detecting breast diseases, imaging procedure such as mammography and ultrasound which play an established role in the investigation of breast masses [(1)], these methods are limited by their inability to answer questions about the likely growth potential of suspicious breast masses [(2)].

Since advent of color Doppler sonography, however, the visualization of blood flow deep within the breast becomes practicable [(3)].

By demonstrating blood vessel architecture and measuring blood flow parameters, the color Doppler technique has the potential to determine the tumor's tendency towards malignancy [(4)].

Doppler flow in malignant breast lesions is enhanced, so Doppler flow signal can be used to detect increased flow and may further distinguish benign from malignant lesions. Malignant lesions produce signals of high frequency and amplitude with continuous flow through diastole [(5)].

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Vasculature of neoplasm (Tumor angiogenesis) is one of the most important factors other than cell kinetics modifies the rate of tumor growth. Tumor cannot enlarge beyond 1-2 mm in diameter unless they are vascularized, presumably the 1-2 mm zone represent maximal distance across which oxygen and nutrient can diffuse from blood vessel. Neovascularization has dual effect on tumor growth; perfusion supplies nutrients and oxygen, and newly formed endothelial cell stimulate the growth of adjacent cells by secreting polypeptides such as insulin like growth factor, PDGF (Platelet Derived Growth Factor), IL-1 [(6)].

Angiogenesis is a request not only for continued tumor growth; the tumor cells cannot metastasis with out access to vasculature. Several studies have revealed a correlation between the extent of angiogenesis (micro-vessel density) and probability of metastasis in melanomas, lung, colon, prostate, and specifically breast cancers, so vessel density has proven to be significant prognostic indicator [(6)].

In addition the architecture of tumor's vascular supply is a reflection of it's propensity towards malignancy, and is a marker of tumor aggressiveness and correlated with an over all poor prognosis [(7)].

Tumor vessels grow to produce a disorderly tangle and random orientations [(4)]. However, because of focal area of narrowing and dilatation within tumor vessels, focal area of high systolic velocity results [(8)].

Tumor cells in lymph node also stimulate angiogenesis in the surrounded tissue to invade enlarged lymph node resulting in an extrahilar vessel leading to abnormal architectural vasculature that can be assessed by color Doppler for accurate staging of lymph nodes [(9)].

Color flow mapping; two dimensional color flow mapping system which none invasively maps intra organ blood flow in that previously could only be done with angiography

Positive Doppler shift (flow toward the transducer) displays in shades of red through orange to yellow where as negative shifts (flow away from the transducer) are displayed in blue to blue green [(10)].

Materials and Methods:

Eighty-three female patients with breast lesions included in this prospective study were presented to the consultant unit. After a detailed history and thorough physical examination, patients were assessed by imaging and laboratory investigations.

All patients were examined sonographically, then color Doppler image studies were performed using available KRETZ Techink voluson 530 OD machine versa pro utilizing 7.5 MHz linear array prop.

After full examination of breast and axilla, the mass identified and kept with field of color Doppler flow mapping,

The following parameters were assessed

1.Presence or absence of color Doppler signal and counting the total number of blood vessels in and adjacent to the lesion (mass).

2.Vascular architecture in relation to the lesion (mass), vessels were classified as either peripheral as in (Fig. 1) or central penetrating (neoplastic vessel) as in (Fig. 2).

3.Maximal systolic velocity (of that lesion or mass) measured from the time velocity diagram, (Fig.3), (Fig.4).

Color Doppler flow mapping of axillary Lymph Nodes were done for patients with palpable enlarged axillary Lymph Nodes, any abnormal signals were recorded as in (Fig. 5).

Biopsy examinations were done for the lesions after appropriate surgical management depending on clinical, imaging, and cytological examinations.

Statistical Analysis:

Sensitivity measures fraction of patients with malignant breast disease detected by the test under study.

Specificity measures the fraction of patients correctly identified as having

benign breast lesions and proved by histopathology.

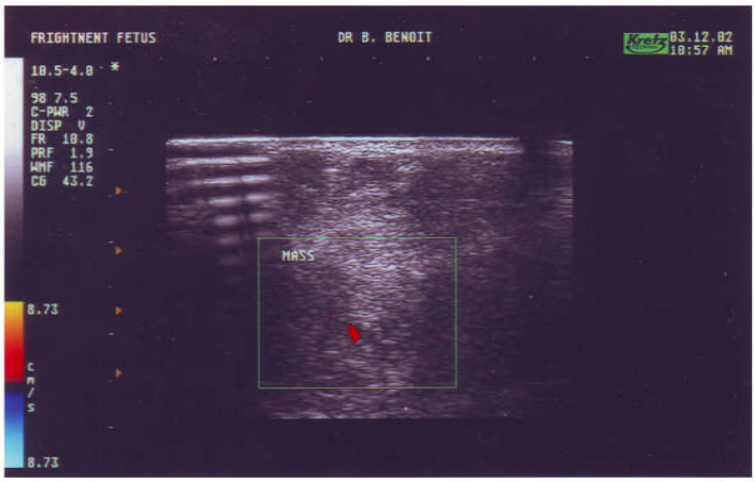

Figure 1: Peripheral feeding vessel (red spot) out side the tumor.

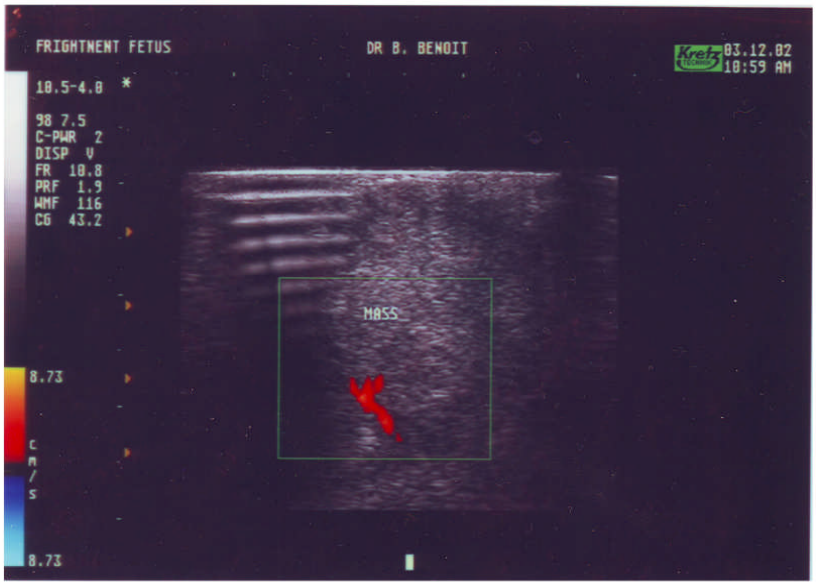

Figure 2: Central penetrating neoplastic vessel (red line) within the nidus of tumor.

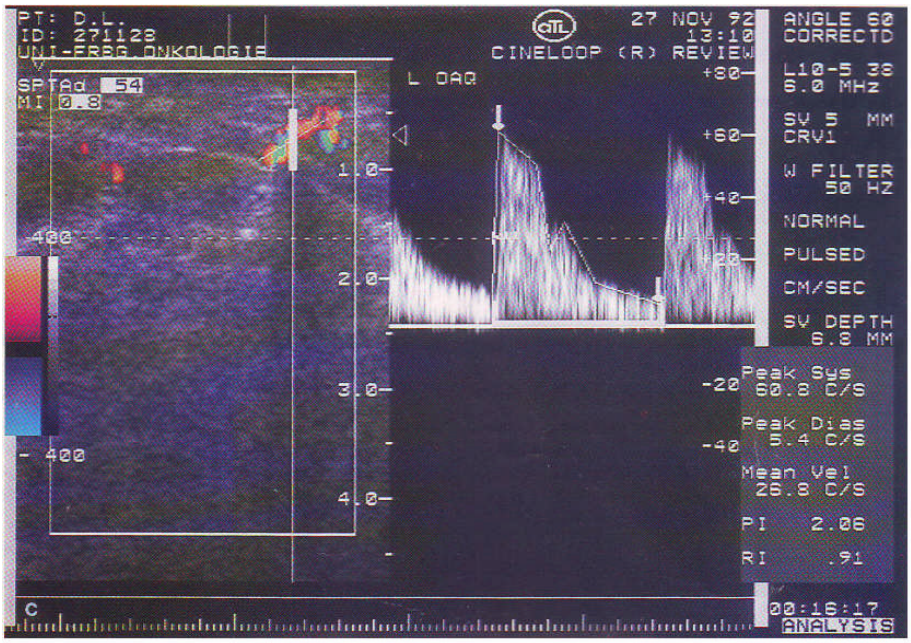

Figure 3: Maximal systolic velocity in malignant breast lesion.

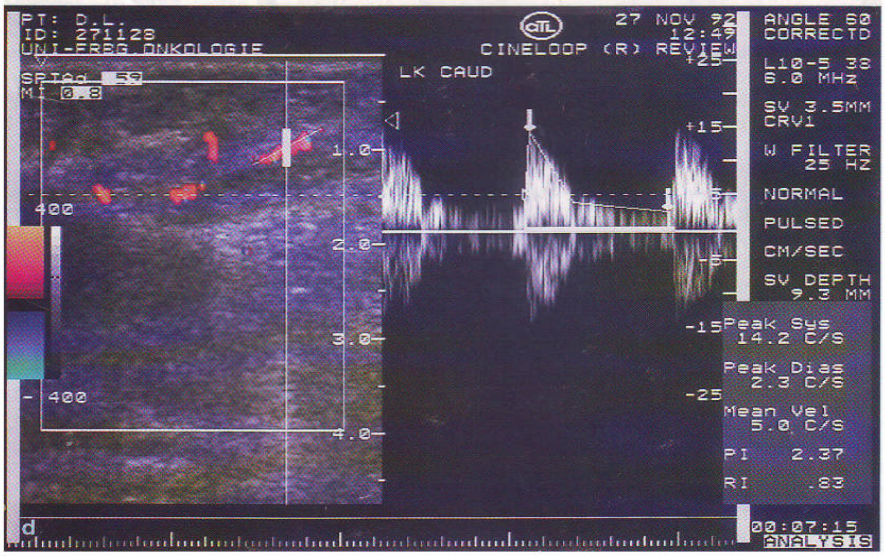

Figure 4: Maximal systolic velocity in benign breast lesion.

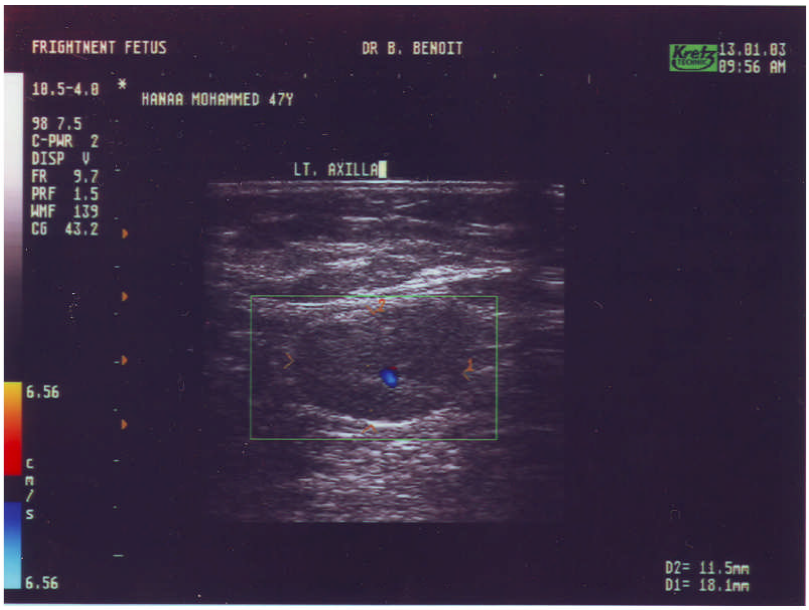

Figure 5: Color Doppler imaging of an enlarged left axillary LN in patient with CA breast showed a central vessel (blue spot).

RESULTS

Three female patients included in this study, histopathological findings showed that 62 samples were benign lesions and 21 were malignant

Based on the clinical findings; 56 patients provisionally diagnosed as having benign lesions, of them 50 patients were truly benign by histopathological examination, whereas 27 patients provisionally diagnosed as having malignant lesions; 15 patients of them proved malignant by histopathology, **Sensitivity** 71.5%, **Specificity** 80.6%

malignant lesions it was central (neoplastic) vessel in 19 lesions & Lesions

; (1 was scrrihous carcinoma & 1well differentiated ductal carcinoma).

The 49 vascular benign lesions detected by color Doppler image showed central neoplastic vessels in only 3 lesions (1 hyperplasia, 1 giant fibroadenoma & 1chronic abscess).

Sensitivity was (**90.4%**), while specificity was (**93.8%**).

3. Maximal systolic velocity; of the lesions blood flow measured by time

Of the eighty

Color Doppler image:

1. Number of blood vessels; in all malignant lesions color Doppler signals were detected, in 18 cases the number of blood vessels were >3, other cases showed <3 vessels, while in benign group; signals were detected in 49 cases, only 5 of them have >3 vessels (Figure. 6).

For a cut off of more than 3 vessels, the sensitivity for detecting cases with carcinoma was (**85.7%**) while specificity was (**91.9%**).

2. Vascular architecture; in peripheral (curvilinear) in the remaining 2

velocity scale in centimeters per second (Figure. 7).

For a cutoff more than 15 cm/s; sensitivity was (**90.4 %**), while specificity was (**91.8 %**).

Color Doppler imaging of axillary lymph nodes; in 16 patients had palpable axillary lymph nodes, signals were positive in 9 cases, all of them were malignant on histological

examination, in the other 7 cases; signals were negative, of them 4 benign and 3 malignant cases, so; Sensitivity **75%,** Specificity **100%.**

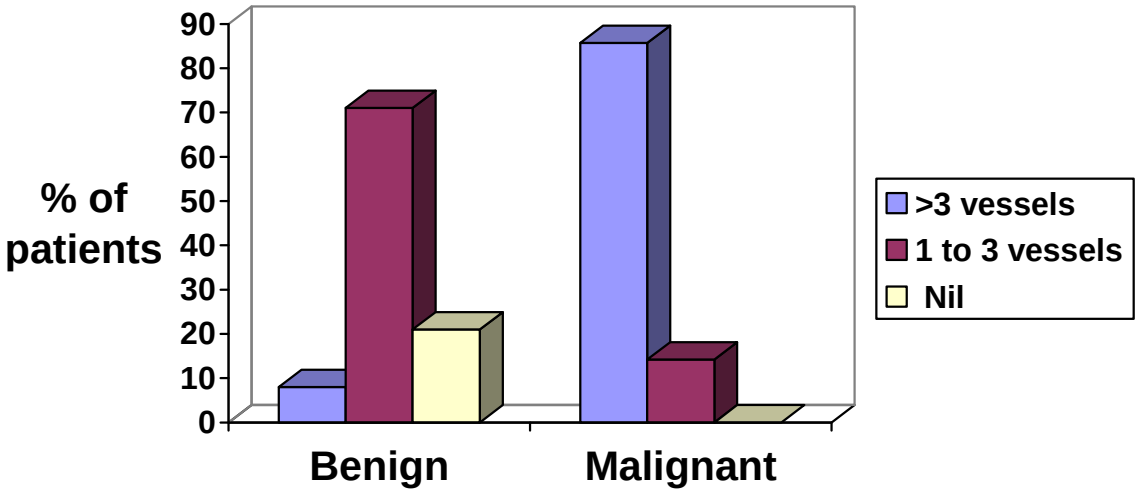

Figure 6: Distribution of the lesions according to the number of blood vessels.

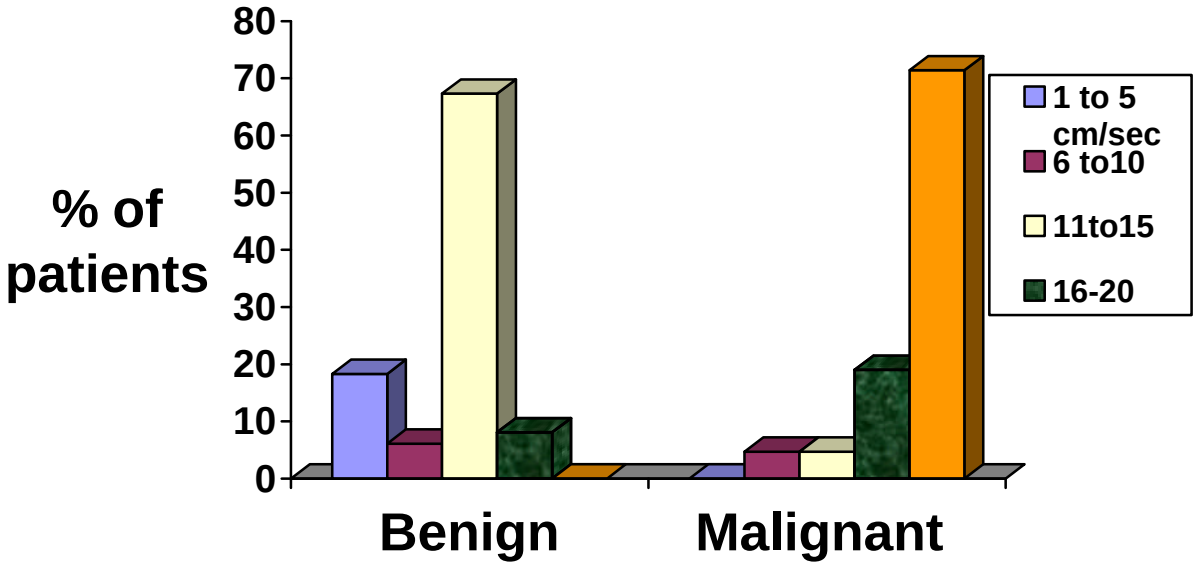

Figure 7:Distribution of lesions according to the maximum systolic velocity cm/s.

Discussion

According to the clinical evaluation, our provisional diagnosis revealed a sensitivity (71.6%) and specificity (80.5%), which is comparable to the results of a study done in Baghdad Teaching Hospital in 2001; sensitivity (73.68%) and specificity (89.4%) [(11)].

Color Doppler examination is diagnostically useful in identifying solid nature of markedly hypo-echoic malignant lesion, however the vascularity is highly increased in cases of mastitis where patient management should not be based on Doppler findings, in addition Doppler artifact can cause false positive results and this must be taken into consideration;

movement of the transducer or the patient, breathing, heart motion and fluid movement in a cyst, microcalcification must be differentiated from true signals caused by blood cells movement [12].

In our study the detected signals were demonstrated in all malignant masses (100%), and majority (79%) of benign lesions, in a study done by Wei-Jei Lee et al, in National Taiwan Hospital (department of surgery) showed that signals were detected in (92%) of malignant one and (54%) of benign lesions [13]. Other study showed absence of vascularity only in (4%) of malignant lesions [12].

In this study more than three blood vessels were found in (85.7%) of malignant lesions and only (8%) of benign cases, in comparison with a study [12]; (89%) of malignant tumor showed more than three vessels.

McNicholas et al, evaluate the number of blood vessels; they found that three and more blood vessels present in (83%), (46%) of malignant and benign lesions subsequently [14].

We found that a cut off more than three tumor vessels, the sensitivity, specificity were (85.7%) and (91.9%) subsequently, compared with literature; they were (89%) and (92%) subsequently [12].

Regarding the vascular architecture, a centrally penetrating vessel (neoplastic vessel) is a character of malignancy, it was found in (90.5%), (6.1%) of malignant and benign lesions subsequently. Wei-Jei Lee found that signal was central in 83% of malignant lesions, while all benign lesions show only peripheral signals [13].

The maximal systolic velocity is recommended as the best parameter in the differentiation of benign from malignant tumor by Dock [14], they suggest that systolic peak flow more than 20 cm/s is the best cut off value. In our study; a peak flow of more than 15 cm/s found in 19 of 21 malignant lesions (sensitivity 90.4%, specificity 91.8). Wei-Jei lee found that for a systolic peak of more than 15 cm/s 26 of 28 (93%) patients had malignant lesion [13]. Other study done by Madjar et al, they found that a cut off value more than 15 cm/s has (86%), (91%) sensitivity and specificity respectively [15].

The number of blood vessels detected by color flow mapping has been identified as the easiest parameter for describing tumor vascularity, but diagnostically it is not entirely reliable as the flow velocity [16].

In cases with positive signals axillary lymph nodes; the original primary lesions had a maximal systolic velocity > 20cm/sec; including 3 cases with tumor size about 3 cm. indicating that high velocity is associated with early metastatic potential rather than the size of primary [12].

Conclusion:

Color Doppler examination is a complementary tools to the clinical evaluation and other investigations especially the ultrasound.

Based on vascular architecture, number of blood vessels, systolic velocity within the lesions, a provisional diagnoses whether a lesion is benign or malignant, could be suggested with high accuracy.

The presence of high flow tumor signal in early breast carcinoma is significantly associated with the presence of axillary lymph nodes metastases.

Recommendation :

Standardization of the color Doppler examination technique and equipment parameter is essential for vascularity assessment of tumors.

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