In 1991, Judah Folkman emphasized the 'angiogenic switch' hypothesis for tumor progression. Studies have showed that angiogenesis positively correlates with the degree of metastasis, tumor recurrence and shorter survival rates, thereby demonstrating the value of angiogenesis as a prognostic cancer marker. Tumor angiogenesis is similar to physiological angiogenesis; however, latter proceeds in an uncontrolled and excessive manner giving rise to leaky and tortuous vessels that are in a constant state of inflammation. As the malignant breast mass grows, tumor cells secrete peptide growth factors, which promote angiogenesis. Angiogenesis, in turn, provides the tumor mass with nutrients essential to sustain growth. In theory, the altered hemodynamics that accompany tumor angiogenesis provide the basis for discriminating between malignant and benign masses of the breast by color Doppler sonography. Lack of smooth muscle in the arteriolar wall and absence of a normal capillary bed results in modified end-organ resistance and arteriovenous shunting.

Tumor angiogenesis plays an important role in the growth and extension of malignant neoplasms, including those of the breast. The increase of tumor mass and the formation of metastasis require the formation of new vessels. Malignant tumors secrete angiogenic factors to help the recruitment on new vessels that allow tumoral enlargement. Therefore, it seems reasonable that a technique that allows vascularization assessment, such as Doppler sonography, could be used to differentiate between benign and malignant breast lesions and even to predict the prognosis of the tumors. Until now, various parameters of Doppler sonography have been analyzed to determine their usefulness in the diagnosis of breast lesions. The detection of vascularization in the lesion was the first Doppler feature used to differentiate between benign and malignant tumors, and this sign has shown a significant association with malignancy of lesions. New vessels that originated as the result of tumor angiogenesis have characteristics that differ from those of normal vessels. These vessels are characterized by their lack of muscle layer, atypical branching pattern, and irregularity, and they frequently present stenosis, occlusions, or arteriovenous fistulas. These vascular anomalies produce alterations in the dynamics of the arterial flow that can be evaluated by means of pulsed Doppler sonography. The RI and PI values for malignant and benign lesions overlap significantly, which makes these values show little usefulness as a tool to differentiate between both types of lesions. The disappearance or reversal of vascular flow in the diastole, which indicates the presence of very high resistance flow, appears to be closely connected to malignancy. This disappearance or reversal of vascular flow can be explained as an extreme case of the previously described phenomena of vascular occlusion, encasement, and stenosis, typical of malignant vascularity causing a great increase in the peripheral resistance of the vascular bed of some of these tumors. The detection of vessels in a tumor has been connected with the involvement of axillary lymph nodes and with lymphatic vascular invasion.
The vascular morphology of abnormal masses is proving to be a useful aid in prediction of malignancy. The typical position of normal vessels (along the glandular surface or running with the Cooper’s ligaments) with a straight or gently curved path are helpful in their distinction from pathological vessels which tend to be numerous, tortuous and abnormally positioned. Similarly, vessel branching is a predictor where the greater the branching and the closer the branching, the greater the likelihood of malignancy. Comparison with the contra lateral breast is helpful.

Atler et al. (1990) in a study of 55 breast cancers observed 82 % of them were moderately or markedly vascular. Four percentages of the cancers had no detectable flow. The high, 82%, detection rate of tumour vessels in this study suggested the potential use of colour flow Doppler.

Moon et al. (2000) observed in their study of 50 patients with palpable breast cancers, by using power doppler USG vascularity was detected in 73–84% of cases. The presence of penetrating vessels as a marker for malignancy produced a sensitivity of 68%, specificity of 95%. But this study also showed that Contrast-enhanced power Doppler US was superior to non enhanced power Doppler US in the demonstration and characterization of tumour vascularity.

Sehgal et al. (2000) in their study of 74 patients stated that quantitative Doppler imaging could be used reliably to evaluate patterns of vascularity in the breast masses. Although the malignant masses exhibited a strong gradient in vascularity, core > periphery > surrounding tissue, the benign masses had relatively uniform distribution of vascularity.

Svensson et al. (2002) in a study of 351 fibroadenomas and 117 cancers showed that the vascular morphology of abnormal masses was proving to be a useful aid in prediction of malignancy. The typical position of normal vessels with a straight or gently curved path were helpful in their distinction from pathological vessels which tend to be numerous, tortuous and abnormally positioned. Similarly, vessel branching was found to be a predictor where the greater and closer the branching, the greater the likelihood of malignancy.

Stuhrmann et al. (2000) in a study of 84 tumours suggested that the use of Levovist improved the evaluation of benignity with Doppler sonography. The characteristic pattern of vessel morphology and course were found to be the best parameters. Otherwise difficult distinction between a postoperative scar and a tumour recurrence on sonography and mammography was found to be solvable by this method. However, they opined that a definitive answer could not be achieved based on the Doppler findings.

Del Cura et al. (2005) on a study of 826 breast lesions found that flow visualization on power Doppler sonography indicated a higher possibility of malignancy but it was not useful as the main sign for malignancy. However, any lesion with a vessel that had RI value greater than 0.99 or PI value greater than 4 within it should be considered as probably malignant regardless of any other sonography sign present. They also opined that Doppler findings were not useful in predicting tumour grade or lymph node involvement.

Chao et al (1995) suggested that though high velocity flow pattern was seen in malignant tumors, due to a considerable overlap between values of benign and malignant lesions, a definite cut off could not be suggested. Lee et al (1995) suggested that there was no correlation between velocity
and tumoral angiogenesis, however they suggested that it could be related to axillary lymph nodal metastasis

Thus our review suggests that appropriate usage of Doppler parameters and observation of the vascular pattern and location could be used as an adjunct to regular sonological morphological assessment in determining the probability of lesion being malignant. Though it does not provide us with a pathological diagnosis; it may help in averting inadvertent biopsies/surgeries, and also help in diagnosing apparently benign looking malignant lesions.

REFERENCES


