By Prof Andy Evans

Comparing Histologic Prognostic Features of Invasive Breast Cancer With Mean Stiffness Using ShearWave Elastography

A recently published study [1] was conducted by the author and colleagues comparing the prognostic value of histologic features of invasive breast cancer for the lesion's mean stiffness as measured by ShearWave™ Elastography (SWE™). The quantitative measurement of a lesion's stiffness can be achieved, in kilopascal with SWE, during a routine ultrasound breast examination. Two published studies have already demonstrated SWE to be accurate in helping the differentiation of probably benign and probably malignant solid breast masses, with a very high level of reproducibility. The technology therefore holds promise as a diagnostic tool for women who are recalled because of mass lesions at mammographic screening as well as with symptomatic masses.

In terms of radiologic appearance and behavior, invasive breast cancer is a heterogeneous disease. Both in pathologic prognostic features and radiologic appearance correlations have been found. It can be clinically useful to recognize such findings, such as with the poor correlations between the histologic size [Figure 1] of invasive lobular carcinoma with its mammographic and US size. The appearance of the basal-phenotype cancers seen often in BRCA1 carriers on mammographic and US images [figure 2] is another example of misleadingly benign appearance. Invasive breast cancers are usually stiffer than normal and benign tissues and often display areas of stiffness that are larger than the morphological area [Figure 3]. The study aim was to compare the prognostic value of histologic features of invasive breast cancers for their stiffness. As such SWE™ was an indispensible tool for the visualization of breast masses and their stiffness measurement in this study.

In fact the study showed that invasive cancers with poor prognostic features had higher mean stiffness values than cancers with good prognostic features. There was a statistically significant positive association of mean stiffness with several histologic features, such as the high histological grade, increased size of the cancers, lymph node involvement, and increased vascular invasion.

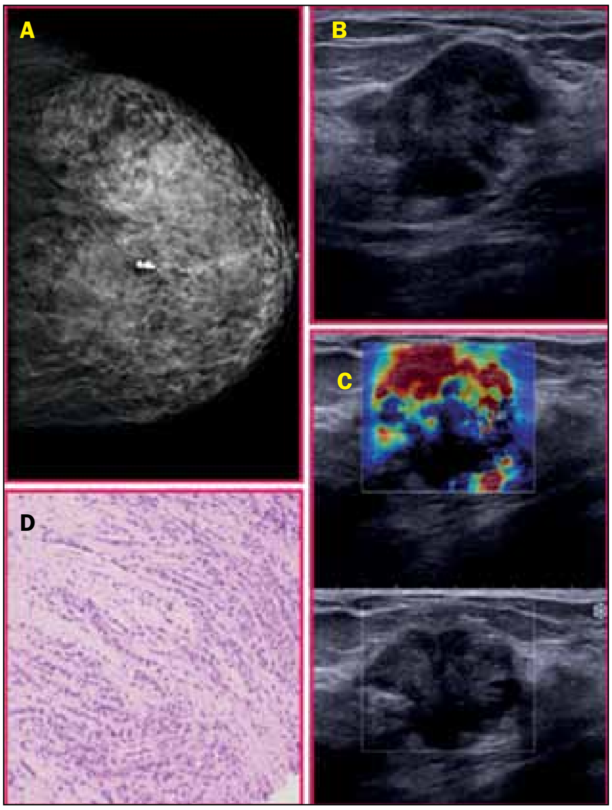

FIGURE 1. Invasive Lobular Carcinoma.
A 66-year old patient presented with a symptomatic clinically indeterminate left breast lump. A. The tumour was mammographically occult in a BIRADS 4 density breast. B. A lobulated mixed echogenic mass was demonstrated on B-mode imaging. C. There was a surrounding stromal stiffness on SWE. D. Histology (x20) showed a typical single file linear streaming, «indian-file» appearance of carcinoma cells within the fibrous tissue.

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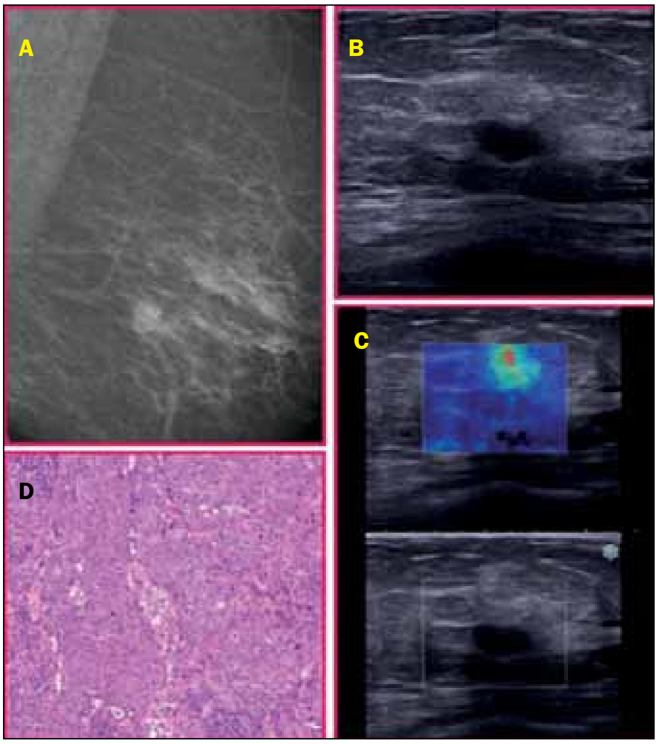


FIGURE 2. Medullary Carcinoma.
A 56-year old patient presented with a small palpable breast lump in her left breast showing tenderness. A. A small well defined mass was visualised on mammograms. B. Ultrasound demonstrated a slightly lobulated hypoechoic lesion with minor posterior attenuation. C. The peritumoural stroma was stiffer than the surrounding tissue and than the lesion itself.
D. Histology (x10) demonstrated a syncytial growth pattern and abundant mononuclear cell infiltrate.

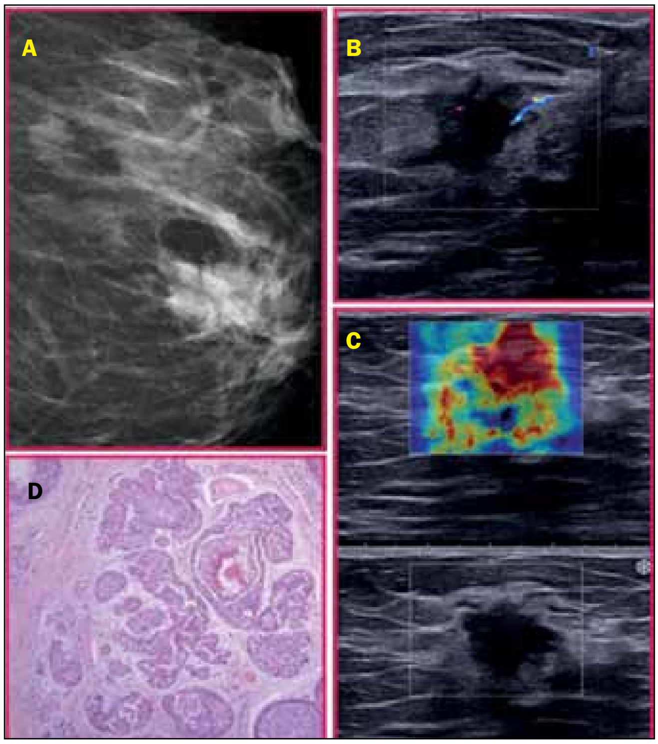


FIGURE 3. Invasive Ductal Carcinoma of no specific type (NST).
This mass was screen-detected in a 71-year old patient. A. On mammography, there was a 2cm spiculate mass deep to the nipple. B. On ultrasound, an irregular hypoechoic lesion was visible, with associated penetrating vascularity. C. SWE demonstrated a ring pattern of increased stiffness, with a superficial focus of marked stiffness. D. Histology (x10) showed a fibrofatty breast tissue, infiltrated by pleomorphic tumour cells with a high mitotic index, and no specific features.

PATIENTS AND METHODS

Between April 2010 and March 2011, 101 women of mean age 61 (range of 38-91) with solid breast lesions were imaged with the Aixplorer ultrasound system (SuperSonic Imagine) in gray scale and then in ShearWave™ Elastrography mode.

Lesions were all visible on the scans and a core needle biopsy confirmed invasive cancers. Patients subsequently underwent primary surgical treatment. Sixty-four of the women had presented with breast symptoms and 37 women had screening-detected cancer. Of the cancers in the study group, 54% were smaller than 20 mm in invasive size at pathologic examination, 37% were node positive, 28% had vascular invasion, 11% were grade 1, 45% were grade 2, and 44% were grade 3.

For each lesion, four elastographic images were obtained in two orthogonal planes. This was done by holding the probe still without the application of pressure and allowing the image to build up over approximately 10 seconds. By moving a delineated region of interest (ROI) over the color map, the mean stiffness measurements were obtained. The figures change in real time so the ROI can be moved to the stiffest part of the image as the ROI moves. The ROI was kept as small as possible to allow measurement of the stiffest tissue anywhere within or adjacent to the lesion as many cancers are not uniformly stiff but have a halo of peritumoural stiffness.

The histologic features, on the basis of the surgically resected specimen, were correlated with the mean stiffness measured with SWE™. Histological features were the histologic grade (Elston and Ellis method) tumor type, the invasive size at pathologic examination, the vascular invasion status, and the lymph node invasion status.

By using cut-off points at 50 kPa and 150 kPa, the data were divided into three groups. The cut of point used for benign versus malignant differentiation in a previous preliminary study was, fifty kilopascals, while 150 kPa was close to the average stiffness observed in this series for an invasive breast cancer.

STATISTICAL CORRELATION

The mean coefficient of variation of stiffness readings was 25.8+/-14.2. The intraclass correlation coefficient was 0.64. Higher histologic grade was associated with higher mean stiffness ($P = 0.0001$). The difference in mean stiffness was more marked between invasive cancers grade 1 and 2 than between grade 2 and 3 At univariate analysis, larger invasive size ($P<0.0001$), axillary lymph node involvement ($P<0.0001$), tumor type ($P<0.0001$), and vascular invasion ($P = 0.0077$) all showed significant associations with higher mean stiffness values. Multiple linear regression indicated that the invasive size was the strongest pathologic determinant of mean stiff- ness ($P<0.0001$),

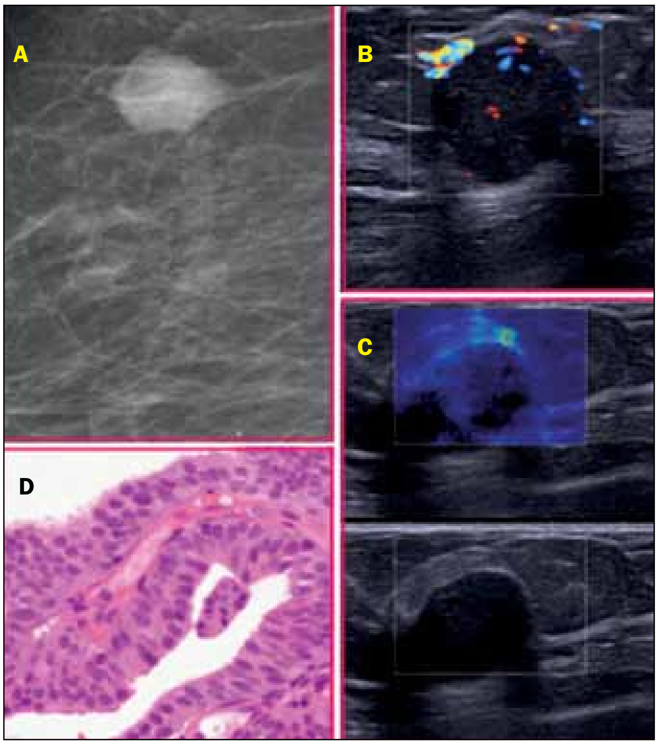


FIGURE 4. Invasive Papillary Carcinoma.
This palpable breast lump was found in the right breast of a 63-year old patient. A. Mammogram demonstrated a well circumscribed breast mass.
B. Ultrasound with Doppler flow showed peripheral vascularity around a homogeneously hypoechoic well defined mass. C. Subtle peritumoural stromal stiffness was visible on SWE. D. Histology (high power) demonstrated the presence of monotonous epithelial cells with poorly formed cytoplasmic cores.

with histologic grade also having a significant influence (P = 0.022)

Particularly among young women, it is common practice for a benign diagnosis to be made on the basis of clinical and US findings without immediate biopsy. The accuracy of modern gray-scale US in differentiating malignant from benign masses has made this possible. ShearWave Elastography is likely to lead to an expansion in the number of lesions that can be accepted as benign without percutaneous biopsy (figure 4) when added to gray-scale US clinical findings. Since tumors might be confused with benign disease, it is important to explore which sub-groups of breast cancer are associated with low stiffness at ShearWave Elastography. This can help radiologists to understand the technique's potential pitfalls. A 50-kPa cutoff was derived from the initial 10 patients and prospectively applied to 53 further patients in a previous preliminary study. A sensitivity of 97% and specificity of 83% resulted from use of this cut off. Different cut-off values could be chosen, however, since stiffness is a continuous variable. If improved specificity was desired, for instance, a higher cut-off could be used but the sensitivity would be reduced.

CONCLUSION

High histological grade, large invasive size, lymph node involvement, and vascular invasion all show, on the basis of univariate analysis statistically significant associations with increased mean stiffness values, as measured by ShearWave™ Elastography. A larger invasive size and a higher histological grade, were found to be significantly associated with increased SWE™ stiffness of invasive breast cancer at multivariate analysis.

REFERENCES

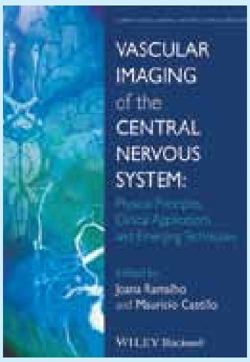
1. Evans A, Whelehan P, Thomson K, McLean D, Brauer K, Purdie C, Baker L, Jordan L, Rauchhaus P, & Thompson A. Radiology. Invasive breast cancer: relationship between shear-wave elastographic findings and histologic prognostic factors. 2012 Jun; 263(3): 673-7. doi: 10.1148/radiol.12111317. Epub 2012 Apr 20.

Book review

Vascular Imaging of the Central Nervous System:

Physical Principles, Clinical Applications and Emerging Techniques
Ed by Joana Ramalho & Mauricio Castillo

Pub by Wiley-Blackwell, March 2014, 432 pages. Hardcover € 133; E-book € 109.99



The last ten years has seen vascular imaging of the central nervous system (CNS) evolve from fairly crude, invasive procedures to more advanced imaging methods that are safer, faster, and more precise—with computed tomographic (CT) and magnetic resonance (MR) imaging methods playing a special role in these advances.

Vascular Imaging of the Central Nervous System is the first full-length reference text that shows radiologists—especially neuroradiologists—how to optimize the use of the many techniques available in order to increase the sensitivity and specificity of vascular imaging, thereby improving the diagnosis and treatment of individual patients. Each chapter is formatted carefully and divided into two essential parts: The first part describes the physical principles underlying each imaging technique, along potential associated artifacts and pitfalls; the second part addresses clinical applications and novel applications of each method.