# Anisotropy of Solid Breast Lesions in 2D Shear Wave Elastography is an Indicator of Malignancy

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**Abbreviations and Acronyms**

**AD**
anisotropic difference (difference of the measurements in each plane)

**AF**
anisotropy factor (square of AD)

**AUC**
area under the curve (statistic measurement to evaluate the diagnostic performance of a method)

**E**
Young's modulus (measurement unit of tissue elasticity)

**$E_{max}$**
maximum elasticity

**$E_{mean}$**
mean elasticity

**ROC**
receiver operator characteristics (statistical tool to evaluate the diagnostic performance of a method)

**ROI**
region of interest

**SD**
standard deviation

**SWE**
shear wave elastography (elastography technique used in the paper)

**Rationale and Objectives:** To investigate if anisotropy at two-dimensional shear wave elastography (SWE) suggests malignancy and whether it correlates with prognostic and predictive factors in breast cancer.

**Materials and Methods:** Study group A of 244 solid breast lesions was imaged with SWE between April 2013 and May 2014. Each lesion was imaged in radial and in antiradial planes, and the maximum elasticity, mean elasticity, and standard deviation were recorded and correlated with benign/malignant status, and if malignant, correlated with conventional predictive and prognostic factors. The results were compared to a study group B of 968 solid breast lesions, which were imaged in sagittal and in axial planes between 2010 and 2013.

**Results:** Neither benign nor malignant lesion anisotropy is plane dependent. However, malignant lesions are more anisotropic than benign lesions ($P \leq 0.001$). Anisotropy correlates with increasing elasticity parameters, breast imaging-reporting and data system categories, core biopsy result, and tumor grade. Large cancers are significantly more anisotropic than small cancers ($P \leq 0.001$). The optimal anisotropy cutoff threshold for benign/malignant differentiation of 150 $kPa^2$ achieves the best sensitivity (74%) with a reasonable specificity (63%).

**Conclusions:** Anisotropy may be useful during benign/malignant differentiation of solid breast masses using SWE. Anisotropy also correlates with some prognostic factors in breast cancer.

**Key Words:** Elastography; Breast; Breast cancer; Ultrasound; Shear wave elastography.



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## INTRODUCTION

Supersonic shear wave elastography (SWE) is an ultrasound imaging modality that visualizes the elasticity of tissue. It was introduced by Bercoff et al. in 2004 (1) and has been in clinical use since 2009 (2). During examinations, the propagation speed of the shear wave is measured and the elasticity, represented as Young's modulus E, is calculated as

$$E = 3\varrho c^2 \quad (1)$$

where c is the propagation speed of the shear wave and ϱ is the density of the tissue. Thus. SWE is a quantitative measurement method. The elasticity is visualized as a color map overlaying the grayscale B-mode ultrasound image of the lesion. As the shear wave is induced by applying an acoustic radiation force, there is no need to move the transducer. A good interobserver reproducibility can be achieved (2). Furthermore, Berg et al. have shown that analyzing the quantitative elasticity of a lesion with SWE is useful for the differentiation of benign and malignant lesions (2) as malignant tissue is generally stiffer than benign tissue (3). Berg et al. recommended the use of a cutoff threshold for the maximum elasticity ($E_{max}$) of 80 kPa for the optimal benign/malignant differentiation (2). Evans et al. recommended a cutoff threshold for the mean elasticity ($E_{mean}$) of 50 kPa (4).

Evans et al. obtained four SWE images per lesion; two each in two orthogonal planes (5). Observation of anisotropy during routine SWE evaluation of breast lesions prompted the present study. Although Ciurea et al. observed anisotropy in solid breast lesions in 2011 (6), to our knowledge, there have been no publications on the evaluation of the anisotropy of solid breast lesions on SWE to date.

Anisotropy is found in normal breast tissue and breast lesions. Ductal carcinoma in situ is known to grow faster in the radial than in the antiradial plane (7). Furthermore, collagen alignment is prognostic in invasive breast cancer (8). This suggests that detection of anisotropy in SWE could potentially help characterize lesions with ultrasound.

The aim of this study is to observe the frequency and the directional characteristics of anisotropy at SWE in benign and in malignant lesions and correlate anisotropy with prognostic and predictive factors in breast cancer.

## MATERIALS AND METHODS

### Study Groups

Study group A comprised 244 solid lesions visible on ultrasound (78 benign, 166 malignant) in 243 patients (age range 17–92, mean 58) scanned in our clinic at Ninewells Hospital between April 2013 and May 2014. For each lesion, four images were obtained; two in the radial plane and then two in the antiradial plane. As preliminary data from a subgroup of the study group A (174 of the 244 lesions in study group A) suggested that anisotropy in solid breast lesions is not plane dependent (9), a study group B of 968 solid breast lesions (306 benign, 662 malignant) in 949 patients (age 17–95, mean 57) was also evaluated. For this group, images had been obtained in two orthogonal planes unrelated to the radial plane. The lesions of the study group B were evaluated between January 2010 and April 2013. Some of the 968 lesions in study group B were evaluated in previous studies investigating the diagnostic performance of SWE (53 lesions (5), 165 lesions (4)), its correlation with prognostic factors (101 lesions (10)), lymph node involvement (396 lesions (11)) and tissue subtypes (302 lesions (12)), and whether SWE stiffness suggests response to neoadjuvant chemotherapy (40 lesions (13)). However, anisotropy was not measured on any of the SWE examinations in any of the previous studies.

Only patients who underwent core biopsy or surgical excision were included. Women younger than 25 years old with breast imaging-reporting and data system (BIRADS) 3 lesions did not undergo biopsy or short-term follow-up in our institution. Further exclusion criteria did not apply. Ethical approval by the National Research Ethics Service guidance was not necessary for this retrospective study (14). Written informed consent for research purposes was available according to standard procedure in our clinic.

### Ultrasound Device

All examinations were performed using the ultrasound device Aixplorer (SuperSonic Imagine, Aix en Provence, France). The probe that was used to acquire the grayscale and the SWE images had a frequency range of 4–15 MHz, which at −6 dB gives an axial resolution of 0.3–0.5 mm and a lateral resolution of 0.3–0.6 mm.

### Image Evaluation

All images were obtained by observers with 5–20 years' experience in breast ultrasound and at least 3 months' experience in the performance of SWE. All four images in the two orthogonal planes were evaluated using a region of interest size of 2 mm positioned at the stiffest point of $E_{mean}$ in or adjacent to the lesion. Artifacts and areas without measured elasticity (black on the color map) were excluded. Each image plane was centered at the approximated center of the lesion. The elasticity parameters $E_{max}$, $E_{mean}$, and standard deviation (SD) were measured. To evaluate the anisotropic behavior of the lesions, the two measurements of $E_{mean}$ for each plane were averaged. To estimate the plane dependence, the anisotropic difference (AD) of the estimations per plane in study group A was calculated as

$$AD = antiradial - radial \quad (2)$$

The AD values comprised positive and negative numbers accordingly to the stiffer plane. Hence, the anisotropy factor (AF) was calculated as the squared AD to evaluate the general plane independent anisotropy of the lesion:

$$AF = (antiradial - radial)^2 \quad (3)$$