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In Vivo Classification of Breast Masses Using Features Derived From Axial-Strain and Axial-Shear Images

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Abstract

Breast cancer is currently the second leading cause of cancer deaths in women. Early detection and accurate classification of suspicious masses as benign or malignant is important for arriving at an appropriate treatment plan. In this article, we present classification results for features extracted from ultrasound-based, axial-strain and axial-shear images of breast masses. The breast-mass stiffness contrast, size ratio, and a normalized axial-shear strain area feature are evaluated for the classification of in vivo breast masses using a leave-one-out classifier. Radiofrequency echo data from 123 patients were acquired using Siemens Antares or Elegra clinical ultrasound systems during freehand palpation. Data from four different institutions were analyzed. Axial displacements and strains were estimated using a multilevel, pyramid-based two-dimensional cross-correlation algorithm, with final processing block dimensions of 0.385 mm × 0.507 mm (three A-lines). Since mass boundaries on B-mode images for 21 patients could not be delineated (isoechoic), the combined feature analysis was only performed for 102 patients. Results from receiver operating characteristic (ROC) demonstrate that the area under the curve was 0.90, 0.84, and 0.52 for the normalized axial-shear strain, size ratio, and stiffness contrast, respectively. When these three features were combined using a leave-one-out classifier and support vector machine approach, the overall area under the curve improved to 0.93.

Keywords

breast cancer; axial-strain; axial-shear; stiffness contrast; size ratio; NASSA

Introduction

Breast cancer is the second leading cause of cancer death in women, with more than 230,000 new cases of invasive breast cancer being diagnosed in the United States in 2011.¹

Mammography, the primary screening modality for breast cancer detection, has a sensitivity of 67.8% and an accuracy of 0.70 as described in Berg et al.² (Table 1). However, its sensitivity drops from 100% in fatty breasts to about 45% for extremely dense breasts.²

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Declaration of Conflicting Interests

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Therefore, additional imaging modalities whose sensitivity is not affected by breast density are necessary for supplemental detection. Magnetic resonance (MR) imaging and ultrasound have been utilized to supplement mammography.² However, due to patient claustrophobia, time, and financial constraints, in one study only 57.9% of the patients with an elevated risk of breast cancer agreed to undergo MR imaging after mammography and ultrasound scanning.³ Thus, ultrasound has emerged as a useful modality in the workup of patients with suspected breast masses. Its traditional role has been to differentiate between solid and cystic masses and to guide biopsy procedures. For women with an elevated risk of breast cancer, the diagnostic accuracy increased from 0.78 using mammography alone or 0.80 using ultrasound alone to 0.91 with the combination.⁴ It has also been suggested that ultrasound strain imaging,^{5–16} which is becoming commercially available on clinical ultrasound systems, may improve the specificity of ultrasound to differentiate benign from malignant masses.^{11,12,17–23}

Because of the need for sensitive, noninvasive methods to differentiate breast masses, emerging ultrasound-based approaches are immensely important.^{11,18–21,24} Very promising results indicate that axial-strain imaging may improve breast-mass classification utilizing the strain stiffness contrast (SSC; defined as ratio of the lesion stiffness to that of normal background tissue estimated from the axial strain image)^{12,18} and size ratio (SR; defined as ratio of the lesion area on the axial strain image to that obtained on the B-mode image) features.^{11,12,19–21} Many benign breast masses such as fibroadenomas and fibrocystic nodules tend to have low SSC values with mechanical testing, while cancers are frequently stiffer than surrounding breast tissue.²⁵ However, some fibroadenomas have similar modulus distributions as, say, infiltrating ductal carcinomas.²⁵ Hence, the SSC feature obtained from axial strain imaging alone likely will not provide sufficient information to assess the malignancy of a detected lesion.¹¹ Another feature first described by Garra et al.¹² utilizes discrepancies between the size of a lesion on a B-mode image and the size on a corresponding axial strain image to distinguish benign from malignant lesions. Malignant lesions tend to appear larger on axial strain images than they do on B-mode, while benign lesions usually appear smaller or of the same size on axial strain images compared with their size on B-mode.^{11,12} This difference in SRs between benign and malignant lesions has been attributed to axial-strain images also depicting regions around the tumor that have undergone desmoplastic reaction and have thereby become stiffer.^{11,12} Unfortunately, this change in the tissue is not captured on B-mode images.

Another significant difference between fibroadenomas and cancers involves a difference in bonding to surrounding tissues,^{26,27} a feature that might be depicted on *shear strain* images.^{28,29} Previous studies^{26,27} have shown that malignant breast tumors typically are stellate or speculated, and are firmly bound to surrounding tissue through infiltration, whereas fibroadenomas (the most common benign solid masses) have smoother margins, are more loosely bound to surrounding tissue, and in some instances may be surrounded by a pseudocapsule.³⁰ Konofagou et al.³¹ studied images based on computed shear strains following unidirectional deformations to the breast. They were one of the first groups to conclude that shear strain estimates may be valuable in diagnosing breast masses. Thitaikumar et al.²⁹ utilized the axial-shear component to differentiate between benign and malignant masses (since lateral shear estimates are noisy) and developed the “normalized area of the axial-shear strain region” concept.²⁹ This was coined into the acronym NASSA to refer to the “normalized axial-shear strain area” feature in Xu et al.,^{28,32} where the normalization to the breast-mass area was derived from the axial-strain image as opposed to the B-mode image in Thitaikumar et al.²⁹ The NASSA feature^{28,29,32} derived from axial-shear and axial-strain images has the potential to depict sliding or slipping of breast masses during deformation, thereby improving differential diagnosis.

The value of SSC, SR, and NASSA as individual features for breast lesion differentiation has been investigated in several clinical studies.^{11,12,18–21,28,29} In this article, our objective is to evaluate the utility of combining these three features for the differentiation of benign breast masses from malignant breast cancers in vivo. The three features are evaluated both as single features as well as in different possible combinations to determine potential improvements in differentiation performance. Performance characteristics for all possible combinations are quantitatively evaluated using the area under the curve (AUC) the receiver operating characteristic (ROC) curve^{33–36} by fitting the ROC curve into a conventional binormal model.^{37–42} The AUC may be interpreted as the average value of the sensitivity over all possible values of the specificity (between 0 and 1) or vice versa. ROC analysis was applied to features computed from axial-strain and axial-shear images derived from data during a previous, multi-institutional study of pathology-proven breast masses.³²

Materials and Methods

In vivo data, acquired during freehand “palpation imaging” done by pressing the ultrasound transducer against the breast, were utilized to evaluate the performance of features derived from axial-strain and axial-shear images for breast-mass differentiation. Radiofrequency (RF) data loops were acquired at the University of Wisconsin (UW) Breast Center (Location A) using a Siemens SONOLINE Antares clinical scanner (Siemens Healthcare, Malvern, Pennsylvania, USA) equipped with a VFX13-5 linear-array transducer pulsed at 10 MHz. This study was performed on patients who were scheduled to undergo a breast biopsy at the UW Hospitals and Clinics Breast Center. Patient consent was obtained before the ultrasound scans. The study was approved by the UW-Madison institutional review board (IRB) for human studies.

The data acquisition was similar to RF data acquired in a multi-institutional study of “palpation imaging” using the Siemens SONOLINE Elegra system with a VFX13-5 linear-array transducer pulsed at 10 MHz or the 7.5L40 linear-array transducer pulsed at 7.2 MHz (Siemens Healthcare, Malvern, Pennsylvania, USA). RF echo data from the three hospitals contributing to that study (Mayo Clinic, Rochester, Minnesota, Location B; Charing Cross Hospitals, London, UK, Location CC; and University of Kansas Medical Center, Location KU) were also analyzed. The study at the Mayo Clinic was approved by the Mayo Foundation IRB and was compliant with the Health Insurance Portability and Accountability Act (HIPPA). Data acquisitions at Charing Cross Hospital were approved by the Riverside research ethics committee, Chelsea and Westminster Hospital (National Health Service Trust, for Charing Cross Hospital). Data acquired at Kansas University Medical Center were approved by the appropriate IRB. Patient consent was obtained prior to any studies being performed. Details of the patients scanned are presented in Burnside et al.,¹⁹ where the same database was utilized in a multiobserver study on the SR feature along with ROC analysis.

The number of patient RF data sets utilized from the different hospitals is shown in Table 1. In the combined data set, we report on 65 benign cases and 58 malignant ones. The ratio B/M denotes the number of Benign to Malignant cases in each institution for the analysis reported in this article. B/M = 6/17 for Location B; for Location CC, B/M = 23/26; for Location KU, B/M = 7/7; and for UW, Antares data, Location A, B/M = 29/8.

RF echo data loops were used to derive the underlying tissue displacements while the transducer was used to deform the breast. Local displacement and strain were estimated from the pre- and postdeformation RF data frames using a multilevel, pyramid-based, two-dimensional cross-correlation displacement tracking algorithm.⁴³ Coarse displacement estimates computed utilizing subsampled B-mode or envelope signals guide subsequent

processing stages with improving spatial resolution. The final processing stage utilizes pre- and postdeformation RF echo signals. The motion tracking kernel in the final processing step was $0.385 \text{ mm} \times 0.507 \text{ mm}$ (three A-lines), with a 75% overlap. An axial displacement image with an approximate background strain of 1% and the highest normalized cross-correlation value for the pre- and postdeformation RF data frame pair was selected from the RF data loop to compute an axial-strain and an axial-shear strain image.

The SSC was calculated as the ratio of the mean strain estimated within a region of interest (ROI) in the breast mass to the average strain in background ROIs on either side of the mass.²⁸ A region within the mass was selected, and two rectangular shaped ROIs at the same depth were used for the background ROIs. The applied strain was determined from the average strain in the background ROIs.

The SR is the ratio of the largest area of the mass on the axial-strain image to that on the B-mode image. An axial-strain image with the maximum cross-correlation map and with the most obvious boundary was selected for this analysis. Lesion areas were segmented manually by the authors (Xu and Varghese) on these B-mode and corresponding strain images using MAT-LAB software. The area was also computed automatically using MATLAB. Fibroadenomas generally appear as lesions with similar areas on B-mode and strain images such that $SR \approx 1$ or lower. However, carcinomas typically appear larger on the strain image when compared with the B-mode depiction and, thus, would have a SR greater than 1.

NASSA^{28,32} was determined by first computing the shear strain over the entire image. Then, a ROI was outlined that extended beyond the region of the mass as depicted on the strain image (green box in Figure 1 below). The area of the region within this box where the axial-shear estimate exceeded a threshold of 20% of the applied deformation,^{28,32} and where the frame-to-frame normalized cross-correlation coefficient value was greater than 0.75 (to ensure high signal-to-noise ratios for the NASSA feature values^{28,32}) was determined. This area was normalized to the lesion area segmented on the strain image for computing the SR feature in our approach.^{28,32} Normalization of the axial-shear strain area has also been previously described,²⁹ where mass area estimates were obtained from the B-mode image.²⁹ On composite shear strain images, areas depicted in red represent positive values of the axial-shear, while those in blue depict negative or opposite shearing strains as also shown in Figure 1.

ROC analysis was used in this study to evaluate the accuracy, sensitivity, and specificity of the SSC, SR, and the NASSA features to differentiate benign from malignant breast masses. A classifier that utilizes the leave-one-out approach was first utilized^{31,35} to estimate the potential of these features both individually and in combination for breast-mass differentiation. For ROC analysis, the reference metric for differentiation was the pathology report from core needle biopsy obtained on the patient. ROC analysis was performed using both LIBSVM⁴⁴ and ROCKIT software (Version 1.0.3 beta, Kurt Rossmann Laboratories, University of Chicago, Chicago, Illinois). The LIBSVM library⁴⁴ was used for the implementation of a linear support vector machine (SVM) using MATLAB (The Mathworks, Natick, Rhode Island). In vivo data together with feature values and the class or biopsy label (± 1) were organized into N (equal to the total number of patient data sets) data sets using a leave-one-out approach; that is, we sequentially chose a patient data set as the validation data set, and all the remaining $N - 1$ data sets as the training set. Since only a small number of biopsy-proven malignant cases were available, the data set was not separated into training and testing groups. A linear SVM⁴⁵ classifier using a C value of 1 was used to train the training set. The validation data set was tested based on the training set to obtain a decision value and the predicted label (± 1). Finally, the decision value and class

label for all of the validated data sets are sorted and used to plot the ROC curve and to calculate the AUC. Since each patient data set was only tested once, the accuracy is estimated from the percentage of cases that were correctly classified from the entire testing data set (N). ROC analysis for a single feature (SSC, SR, NASSA) or that using combined features (SR and SSC, SR and NASSA, NASSA and SSC, NASSA and SR and SSC) was performed using leave-one-out independently. In addition, specificity at 100% sensitivity was also computed out from each trapezoidal ROC curve.

For single features, ROCKIT software was also used to estimate the upper and lower boundary of classification at a 95% confidence interval (CI), along with the sensitivity and specificity. The two sides of the 95% CI for each AUC were estimated using the nonparametric bootstrap method.

Results

Figure 1 presents imaging results for a benign breast mass. Shown from left to right are the B-mode image, the axial-strain image, and the axial-shear image superimposed on the corresponding axial-strain image. The red dashed lines indicate the inclusion boundary generated by manual segmentation in both B-mode and axial-strain images. The blue dashed line shows the ROIs utilized to estimate the mean strain of the background region. The green line in Figure 1c indicates the selected region over which a normalized axial-shear strain is computed. The SSC estimated from the axial-strain image was 6.77, and the SR was 0.87. The NASSA value computed for this patient was 0.152, a relatively low value as will be shown by additional results.

Figure 2 presents analogous images for a patient diagnosed with invasive ductal carcinoma. For this patient, the SSC value was 4.58, the SR value was 1.08, and the NASSA feature value was 2.89. Note that the SSC for this mass is lower than the value for the benign mass in Figure 1. Importantly, the SR is greater than 1, and the axial-shear strain region is significantly larger for this mass than for the benign mass in Figure 1.

Calculation of the SR is complicated by the fact that identification of the breast-mass extent from B-mode images is quite difficult in many cases, such as the one shown in Figure 3 for a patient diagnosed with a carcinoma. The breast mass is almost indistinguishable in B-mode with a very small region being identified. However, the mass is clearly seen on the axial-strain image, and the NASSA feature value of 1.41 suggests that this mass is malignant. The SSC was 2.19. Diagnosis based on the SR feature in Figure 3 fails to provide accurate differentiation results. The SR estimate is biased by the poor boundary delineation on the B-mode image. The NASSA feature on the other hand accurately classifies the breast mass as malignant. Since no obvious breast-mass boundaries were visualized on 21 of the B-mode images that were isoechoic or similar to that of the background tissue, SR estimates could be obtained on only 102 data sets. Visualization and segmentation of the mass were performed by an ultrasound scientist, and improved delineation might be obtained with a radiologist reading the same scans.

Figure 4 presents scatter plots of the SSC, SR, NASSA, and combined feature values for the patients in this study. Cases are separated according to the different institutions over which the data were collected. In Figure 4a–c, the x-axes of the scatter plots represent the patient ID from the four institutions, while the y axes represent the computed feature values. The SSC and the NASSA feature values are shown over all the 123 subjects in Figure 4a,c. The SR feature value, however, is shown for only 102 patients in Figure 4b. Note that the SSC feature values do not provide effective classification between benign and malignant masses alone as shown in Figure 4a. In contrast, both the SR feature values from 102 patients and

NASSA feature values from 123 patients appear to provide good differentiation between benign and malignant disease. Observe in Figure 4b that the values of the SR feature from subjects diagnosed with malignant masses are larger than those from subjects diagnosed with benign masses. Finally, data in Figure 4c show that most of the malignant masses exhibit a NASSA value larger than 1.4, while benign masses tend to have a NASSA value lower than 1.4. Figure 4d presents a three-dimensional scatter plot of the three features obtained from 102 patients, where the x-axis represents SSC, the y-axis represents SR, and the z-axis represents NASSA. Note that most malignant masses exhibit larger NASSA and SR feature values.

For the ROC analysis, we choose malignant masses as the “True” category for the classification based on the core needle biopsy results. As previously mentioned, the leave-one-out approach was utilized for the ROC analysis. The ROC results presented in Figure 5 demonstrate the enhanced discrimination capability of the NASSA feature when compared with either the SSC or the SR feature. Note that the SSC feature provides an AUC value of only 0.52 compared with an AUC for the SR feature of 0.84, while that for the NASSA feature was 0.90 for the combined data set (Benign/Malignant[B/N] = 55/47).

ROCKIT software was also utilized to evaluate single-feature performance, including AUC at both sides of the 95% CI and the sensitivity and specificity values from the ROC curve. As shown in Table 2, AUC values estimated from ROCKIT software were consistent with the AUC values estimated using LIBSVM; however, the AUC values were somewhat lower for the LIB-SVM classifier. This is due to the conservative, leave-one-out classifier used with LIBSVM. The AUC of SSC was 0.52 using SVM and 0.53 using ROCKIT software. SR provided an AUC value of 0.84 using LIBSVM and 0.85 using ROCKIT software. Finally, for the NASSA feature, the AUC values were 0.90 using LIBSVM and 0.91 using ROCKIT software.

The diagnostic accuracy of SSC alone was 57.73% (95% CI, 0.6355-0.4260). The accuracy improved to 77.45% for the SR feature (95% CI, 0.9285-0.7651) and to 82.93% (95% CI, 0.9631-.8582) for the NASSA feature alone. Note that only 102 data sets were available for SR feature analysis due to the remainder of the breast masses being isoechoic with the background. Keep in mind that the AUC for the SR feature is subjective since it will vary with the observer and their visualization of the mass on the B-mode image. However, trained observers (i.e., radiologists) with sufficient time allocated to segment images have achieved a ROC area of about 0.93 when applying the SR.^{11,19,20} The sensitivity and specificity of each classifier were also obtained from each binormal fitting curve. Observe that the sensitivity and specificity improve greatly from SSC to SR to the NASSA feature.

Combined performance levels of these three features were also evaluated. The linear SVM was utilized to combine two or three of the features, producing a combined discriminant for each patient and evaluating whether combined features improve performance. The ROC results obtained using a linear classifier and the leave-one-out method for a combination of two and three of the features are illustrated in Figure 6, while Table 3 presents values for the AUC as well as other performance criteria. The ROC curve for the combined SR and SSC for the 102 patients shown in Figure 6 has an AUC of 0.833. Note the significant improvement in the AUC values with the incorporation of the NASSA with SSC (0.90) and NASSA with SR (0.93) also shown in Table 3. Although the AUC value with the incorporation of the NASSA feature with SR is slightly greater than the classifier with all the three features, one more data set (fibroadenoma) was discriminated when SSC was added to the classifier. Observe that 90 out of 102 data sets, for an accuracy rate 88.24%, were accurately classified by NASSA and SR; this improved to 89.22% (91 out of 102) with NASSA, SR, and SSC. Also note that 102 of the 123 cases were accurately classified with

the NASSA feature alone, for an accuracy rate 82.93%. This improves to 89.22% with all three features (NASSA, SSC, and SR). In addition, the p values of the SSC, SR, and NASSA features using a regression model for each of these variables were 1.88×10^{-3} , 1.37×10^{-7} , and 1.78×10^{-5} , respectively.

Since the consequences of missing a cancer are significantly worse than those for a benign biopsy finding, we also present specificity values for 100% sensitivity in the last column in Table 3, obtained from the ROC curves. The specificity using a linear SVM for the three features (NASSA, SSC, and SR) was 0.33, while the specificity for NASSA and SR was 0.31, for NASSA and SSC was 0.29, and for SR and SSC was only 0.09. As shown in the scatter plot in Figure 4, the presence of outliers greatly reduces the specificity values for a 100% sensitivity.

The improved detection performance of both single and combined features is also presented in Table 4. For the 102 (B/M = 55/47) in vivo data sets, 52 (B/M = 28/24) data sets were classified using SSC alone, 79 (B/M = 40/39) were discriminated by SR alone, and 86 (B/M = 47/39) sets were accurately classified using NASSA alone. Compared with the single feature, that is, SSC, we obtained an improvement in the classification of 12 benign cases and 15 malignant cases with SR. NASSA further improves the benign mass discrimination performance by 5 cases and malignant mass discrimination performance by 2 cases. Observe that adding the SSC feature to either the SR or NASSA feature improves the discrimination of the malignant at the expense of reducing benign mass discrimination. As a result, the combined SSC and SR feature does not improve the overall performance of SR alone, and the combined NASSA and SSC features improved the discrimination by only 1 case compared with using only the NASSA feature. Note that the combined NASSA and SR feature greatly improves the performance over the use of only the SR feature by 7 benign and 4 malignant masses, and this can be further improved by adding the SSC feature.

Discussion and Conclusions

In this article, we present a conservative leave-one-out classifier utilizing the SSC, B-mode to strain image SR, and the NASSA features for breast-mass differentiation. Although some of these features have been independently evaluated by several investigators,^{11,12,18–21,46} improvements in the differentiation obtained using a multifeature analysis has not been evaluated thus far. These features, extracted from both the axial-strain and axial-shear strain images, demonstrate the potential for accurate classification of breast masses scanned in vivo as being benign or malignant. Utilization of features such as the SSC and NASSA, a feature that can be derived from the axial-strain and axial-shear images, may also enable automated breast-mass classification. In particular, the normalization of the NASSA feature using features derived from the axial-strain image as described in this article and Xu et al.^{28,32} can reduce the subjectivity associated with mass delineation on B-mode images reported by Thitaikumar et al.²⁹ Breast-mass delineation from B-mode images may require a radiologist or commercial segmentation software, while the breast mass can be easily segmented on the axial-strain images using automated approaches because of the large SSC as shown in Figure 4a where all masses have SSC values greater than 1.5.

In our analysis, we had to discard 21 scans since we were unable to determine the SR feature for these patients because the breast mass could not be accurately demarcated on the B-mode image. The SR and combined feature analysis were performed on 102 data sets (B/M = 55/47). Deriving a SR value can be a limitation since some breast masses are not clearly visualized in B-mode, and drawing the mass boundary is subjective and varies with the observer.¹⁹ Stavros⁴⁷ describes that a large percentage of fibroadenomas and around a third of the malignant masses are depicted on ultrasound B-mode images as isoechoic, which

contributes to the difficulty of delineation on conventional ultrasound images. This uncertainty with mass delineation on B-mode images can also lead to errors in the normalization of the NASSA feature value as proposed by Thitaikumar et al.,²⁹ but this is not the case when the mass boundary from the axial-strain image is utilized to compute NASSA as in Xu et al.^{28,32}

Core needle biopsies are the standard for breast-mass diagnosis with an approximate accuracy of 96%.⁴⁸ A majority of the core needle biopsies performed has been reported to fall into three categories, that is, normal (BI-RADS 1 or B1), benign/negative (B2), or malignant (B6) cases.⁴⁹ Variations with excision histology results⁵⁰ have been reported for borderline categories, that is, masses that are suspicious for malignancy (B4 and B5) and lesions of uncertain malignant potential (B3).^{51–53} Interobserver variability between pathologists for B3 and B4 masses has also been documented.⁵⁴ Studies have reported that only one-fifth⁵¹ to one-sixth⁵³ of B3 core needle biopsies proved to be malignant on excision histological analysis. In addition, as expected, the likelihood of malignancy varied significantly for different malignancy subtypes.^{51,52}

Improvements in the signal-to-noise ratios^{55–57} in the axial-strain and axial-shear images can also significantly improve the classification performance. Note that for the ROC analysis reported with the RF data acquired using the Siemens Antares system in Xu et al.,^{28,32} we obtained an AUC value of 0.996 with a smaller data set. The RF data obtained with the Antares have slightly improved electronic SNR when compared with data acquired with the Siemens Elegra system. For axial-strain and axial-shear images generated for in vivo breast masses, the mass definition and shear strain patterns below the mass are not as clearly defined; in some instances, significant noise artifacts are observed below the mass. Approaches such as angular compounding^{58–61} that can improve the elastographic signal-to-noise may therefore significantly improve mass delineation and reduce noise artifacts in the discriminant features, leading to improved differentiation and classification of breast masses.

When using freehand palpation during data acquisition for elasticity imaging, axial-shear strain images are susceptible to out-of-plane deformations. Out-of-plane deformations can be considered to apply deformations to the lesion in an asymmetric manner. Previous work has demonstrated that asymmetrical deformation of a lesion will introduce “fill-in”⁶² artifacts within loosely bound masses, while firmly bound masses do not appear to be affected in this manner.³² However, the overall classification feasibility of using the NASSA feature is not compromised if only shear strains outside the mass are utilized for classification.³² In addition, our previous study³² shows that NASSA features estimated from full-shear strain images provide a robust and improved classification result compared with that obtained from axial-shear strain images alone. Approaches such as beam steering^{58–61} can be utilized to estimate full-shear strain images. However, trade-offs involving data acquisition, computational time, and complexity versus the improved signal-to-noise, contrast-to-noise,⁶³ and spatial resolution obtained have to be balanced.

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Figure 1.

(a) B-mode, (b) axial-strain, and (c) composite image obtained by superimposing the axial-shear on the axial strain for a patient diagnosed with a fibroadenoma. Note that the NJASSA value for this patient was 0.15, the SR was 0.87, and the SSC value was 6.77.

NASSA = normalized axial-shear strain area; SR = size ratio; SSC = strain stiffness contrast.

Figure 2.

(a) B-mode, (b) axial-strain, and (c) composite image obtained by superimposing the axial-shear on the axial strain for a patient diagnosed with invasive ductal carcinoma. Note that the NASSA value for this patient was 2.89, the SR was 1.08, and the SSC value was 4.58. NASSA = normalized axial-shear strain area; SR = size ratio; SSC = strain stiffness contrast.

Figure 3.

(a) B-mode, (b) axial-strain, and (c) composite image obtained by superimposing the axial-shear on the axial strain for a patient diagnosed with carcinoma. Note the difficulty in visualizing the size or contour of the breast mass on the B-mode (a), but clearly seen on the strain image (b). However, the NASSA value of 1.41 identifies this mass as malignant. The SSC is 2.19.

NASSA = normalized axial-shear strain area; SSC = strain stiffness contrast.

Figure 4. Scatter plots illustrating in vivo differentiation between patients with cancers and fibroadenomas using the (a) SSC, (b) SR, and (c) NASSA feature on a combined data set (where B, CC, and KU denote Elegra data obtained from three different clinical hospitals, and A denotes Antares data). A three-dimensional scatter plot of the three features plotted against each other is shown in (d).
SSC = strain stiffness contrast; SR = size ratio; NASSA = normalized axial-shear strain area.

Figure 5.

ROC curves for the NASSA (black curve), SR (red) and contrast (blue) feature from the in vivo data acquired on the combined data set (Locations A, B, CC, and KU) for 102 patients (B/N = 55/47).

ROC = receiver operating characteristic; NASSA = normalized axial-shear strain area; SR = size ratio.

Figure 6.
ROC curves for the combined features for the 102 patients (B/N = 55/47).
ROC = receiver operating characteristic.

Table 1

Number of Patients Diagnosed with Benign and Malignant Breast Masses Based on Needle Core Biopsy Results

Hospitals	Ultrasound system	Benign	Malignant
UW-Madison Hospitals and Clinics	Siemens Antares, VFX 13-5	29	8
Mayo Clinic	Siemens Elegra, VFX 13-5	6	17
Charing Cross Hospitals	Siemens Elegra, VFX 13-5	23	26
Kansas University Medical Center	Siemens Elegra, VFX 13-5	7	7

UW = University of Wisconsin.

AUC of Single Feature Using both SVM-Based Linear Analysis with the Conservative Leave-One-Out Method and ROCKIT Software

Table 2

Strain and shear features	AUC (LIBSVM)	AUC (ROCKIT)	95% (CI _{upper} -CI _{lower})	Sensitivity	Specificity
SSC	0.5239	0.5308	0.6355-0.4260	0.597	0.500
SR	0.8398	0.8468	0.9285-0.7651	0.804	0.715
NASSA	0.9042	0.9106	0.9631-0.8582	0.862	0.800

AUC = area under the curve; SVM = support vector machine; CI = confidence interval; SSC = strain stiffness contrast; SR = size ratio; NASSA = normalized axial-shear strain area.

AUC, Accuracy, Sensitivity, Specificity, and Specificity for a 100% Sensitivity for Different Combined Features Using SVM-Based Linear Analysis Using the Conservative Leave-One-Out Classifier

Table 3

Strain and shear features	AUC (LIBSVM)	Accuracy (LIBSVM)	Sensitivity (LIBSVM)	Specificity (LIBSVM)	Specificity at 100% sensitivity
SR and SSC	0.8333	77.45% (79/102)	0.6383	0.8909	0.091
NASSA and SR	0.9342	88.24% (90/102)	0.8298	0.9273	0.309
NASSA and SSC	0.906	85.29% (87/102)	0.7872	0.9091	0.291
NASSA and SR and SSC	0.9315	89.22% (91/102)	0.8511	0.9273	0.328

AUC = area under the curve; SVM = support vector machine; SR = size ratio; SSC = strain stiffness contrast; NASSA = normalized axial-shear strain area.

Table 4

Improved Performance with the Combined Features over a Single Feature for Both Benign and Malignant Masses for the 102^a In Vivo Data Sets

102 data sets (B/M: 55/47)	<u>Improvement over SSC</u>		<u>Improvement over SR</u>	
	Benign	Malignant	Benign	Malignant
SR	12	15	0	0
NASSA	17	17	5	2
SSC and SR	8	19	−4	4
NASSA and SSC	17	18	5	3
NASSA and SR	19	19	7	4
NASSA and SR and SSC	20	19	8	4

SSC = strain stiffness contrast; SR = size ratio; NASSA = normalized axial-shear strain area.

^a21 data sets could not be utilized to determine the SR feature, thus the performance results over only 102 data sets were compared in this article.