LESION SIZE RATIO FOR DIFFERENTIATING BREAST MASSES

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Abstract— We are developing a clinical ultrasonic imaging system for real-time estimation and display of tissue elastic properties. We have demonstrated that real-time feedback of elasticity images is essential for obtaining high-quality data (consecutive images with high spatial coherence). The key element to successful scanning is real-time visual feedback which guides the patient positioning and compression direction. One of our findings, consistent with previous reports, is that benign breast masses are typically about the same size in B-mode and mechanical strain images. However, invasive cancers tend to be significantly larger in strain images than in B-mode images. In this work we continue testing that hypothesis with an increasingly large data set with greater diversity of breast mass types. Results from a single-observer ROC study demonstrate that the lesion size ratio is a useful criterion for classifying benign versus malignant breast masses.

I. INTRODUCTION

We are implementing and testing real-time mechanical strain imaging integrated into a clinical ultrasound imaging system (SONOLINE Elegra, Siemens Medical Solutions) [1]. Our work was motivated by promising *in vivo* results first reported in the peer-reviewed literature by Garra et al. [2]. In that report they described data acquisition based on a modified mammography system. The use of that system limited the areas of the breast from which they could acquire data and typically only acquired a few frames of echo fields per patient.

Freehand scanning has been the dominant method of clinical sonography for many years. So, freehand scanning will likely more quickly gain clinical acceptance of elasticity imaging if it can be performed efficiently. We have argued that real-time feedback to the hand-eye coordination system allows constant manipulation of the boundary conditions of deformation and allows the observer to know when high quality strain image data are acquired. The small delay between acquiring successive frames (tens of milliseconds) and the relatively slow deformation rate (cyclic freehand deformation at about 1 Hz) likely results in a mostly elastic response in tissue (minimal viscous effect) [3]. *In vivo* elasticity images of breast lesions obtained with our system have high contrast-to-noise ratios. In fact, relatively long sequences (30 sequential frames or more) of high quality strain images are normally obtained in clinical trials.

Our preliminary tests of this imaging system [1] included a relatively small subject population and scanning was performed by only one sonographer. Results of measurements with five observers making lesion size measurements on that data were very encouraging and suggested nearly perfect separation of benign and malignant lesions. Those results are overly optimistic because of correlation among the data (multiple lesions in the same patients were included), the limited variety of lesion types included (only invasive ductal carcinoma, fibroadenoma and cyst), and the small patient population.

The focus of this study is to further test the hypothesis that the ratio of lesion sizes (strain measurement divided by B-mode measurement) can accurately classify breast masses as benign or malignant. This study includes only uncorrelated data from the previous study (one lesion, and one image sequence, per patient). It also includes data acquired at an additional institution with multiple people performing the ultra-

sound scanning. The subject population is considerably larger and there is a wider variety of lesion types included. It is more limited that the previous study in that only one observer performed the measurements.

Results demonstrate that the lesion size ratio is a sensitive criterion for classifying breast masses. This study also demonstrates that these measurements can be repeated at other institutions, suggesting that the technique and measurements are robust.

II. Materials and Methods

Strain Image Formation

Data were acquired with the Siemens SONOLINE Elegra using either the 7.5L40 or VFX13-5 linear arrays. A 2-D block matching algorithm is used for motion tracking in our implementation [4]. The algorithm displays streaming B-mode and strain images side-by-side at about seven frames per second to ensure acquisition of high-quality data for strain image formation. Data were processed off-line using a more computationally intensive algorithm than currently programmed on the Elegra.

Patient Scanning

Patients were referred to sonography with either a palpable breast lump or indeterminate mammogram, or as follow-up from a previous sonogram. All patients provided informed consent consistent with the protocol approved by the Institutional Review Board at Kansas University Medical Center or the Charing Cross Hospital. Patient scans were performed in a manner consistent with a normal breast ultrasound exam; the breast was scanned with the patient (typically) in the supine position with her arm behind her head. When the breast lesion was located, the transducer was pressed toward the chest wall at a steady rate in an effort to achieve about 0.5–1.2% compression frame-to-frame while repeating the compress/release cycle for relatively large ($>$10%) compression. The compression technique was adjusted, by changing the compression direction or patient position, until there was nearly uniaxial compression with minimal elevation motion. Real-time B-mode and strain image display allowed visualization of the data quality. Using this scanning technique, no patient has experienced any discomfort in our procedures.

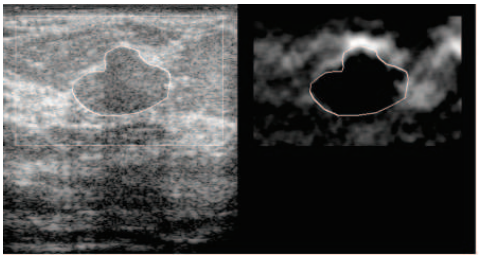

Fig. 1. A B-mode and strain image pair obtained by freehand scanning of an in vivo breast fibroadenoma.

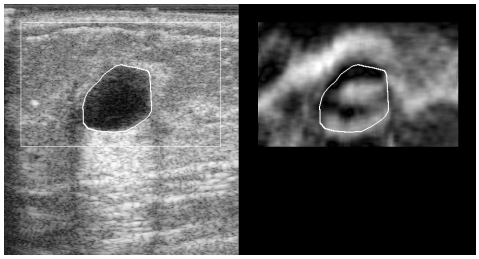

Fig. 2. Freehand strain imaging of an in vivo breast cyst.

To date over 250 lesions have been scanned. The average patient age in this group is about 43yrs old. All lesions included in this study were either biopsied or surgically excised for identification. Example images from in vivo breast masses are shown in Figs. 1, 2 and 3. In those figures the lesion is traced in the B-mode image and that tracing is also displayed in the strain image.

The relatively large lesion size displayed in strain images of invasive ductal carcinomas, compared to the size displayed in the corresponding B-mode image, suggests that a comparison of these sizes is most effective when the breast mass is relatively small in both image modalities. This difficulty is illustrated in Fig. 4.

Other significant difficulties with in vivo elasticity

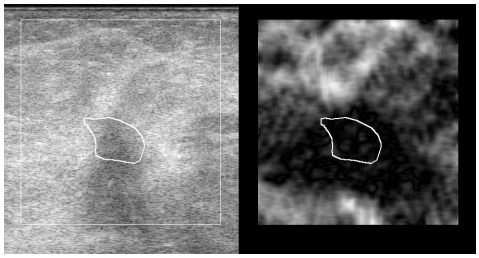

Fig. 3. Freehand strain imaging of an in vivo invasive ductal carcinoma.

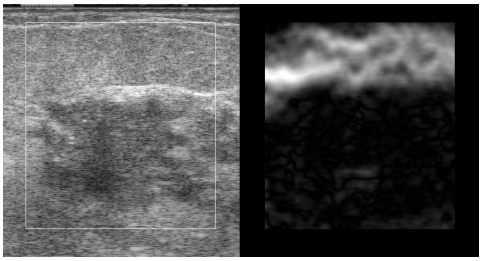

Fig. 4. Freehand strain imaging of a relatively large invasive ductal carcinoma.

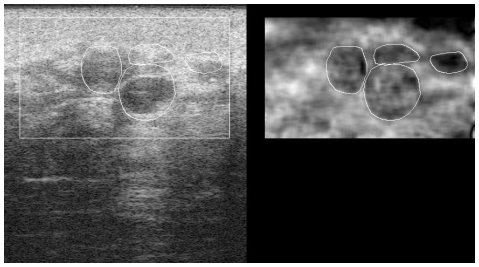

Fig. 5. Freehand strain imaging of an in vivo breast cyst cluster.

imaging occur when multiple closely spaced lesion are imaged, as shown in Fig. 5. In these situations, the boundary conditions for motion of the individual lesions is affected by the motion of the other neighboring lesions. Motion can be quite complex, or the cluster of lesions can behave as a single large object. In either case, the strain image can be more difficult to interpret. In early clinical trials we are avoiding these cases to focus effort on lesions that are separated by at least twice their major dimension from any other nearby lesion.

Eliminating lesion clusters, as shown in Fig. 5, multiple views of the same lesion, multiple lesions in the same patient, lesions that were not biopsied, etc. we have 169 unique data sets. Among these are 43 cancers (38 invasive ductal carcinoma, 1 ductal carcinoma in situ, 2 mucinous carcinoma, 1 invasive lobular carcinoma, 1 invasive apocine carcinoma) and 126 benign lesions (69 fibroadenoma, 40 cyst, 5 lymph nodes, 4 inflammation, 2 ductal ectasia, 6 other benign conditions).

Using our system we have demonstrated that fibroadenomas often have a surface pressure-dependent strain image contrast [1]. The strain image contrast for a fibroadenoma is generally highest with the least surface pressure and contrast decreases as the pressure is increased. Fibroadenomas tend to be imaged at their largest size when data are acquired with minimal surface pressure. The nonlinear stress-strain relationship of many fibroadenomas, compared to their surrounding tissue, results in the apparent size of those lesion getting smaller as the surface pressure is increased. Therefore, lesion size measurements are generally made with the lowest pre-compression (largest lesion size) for which consistent strain images are obtained.

III. Results

Plots of lesion size ratio (strain/B-mode) versus lesion area measured in the corresponding B-mode image are shown in Figs. 6 and 7. The red line in those figures represents the lowest possible linear threshold to separate all cancers in this data set from most benign lesions. Lesions with an area ratio larger than the threshold value are likely cancer; those below the threshold are very likely benign and could potentially avoid being biopsied. ROC analysis for the continuous lesion area ratio data results in $A_z = 0.930 \pm 0.019$.

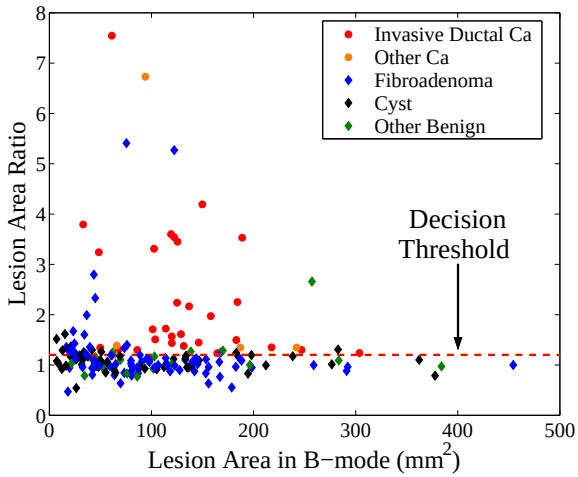

Fig. 6. A comparison of lesion area for breast carcinomas and benign breast masses.

IV. Discussion

The ability to accurately and reproducibly determine the boundary of breast masses is greatly increased when the observer is provided with a movie clip of the ultrasound scan instead of a single frame B-mode image. Viewing that relative motion is also very helpful in interpreting strain images of in vivo breast masses.

The performance of this single criterion for classifying breast masses is impressive when compared to the set of criteria proposed by Stavros et al. [5]. Given the relatively young average age of this patient group,

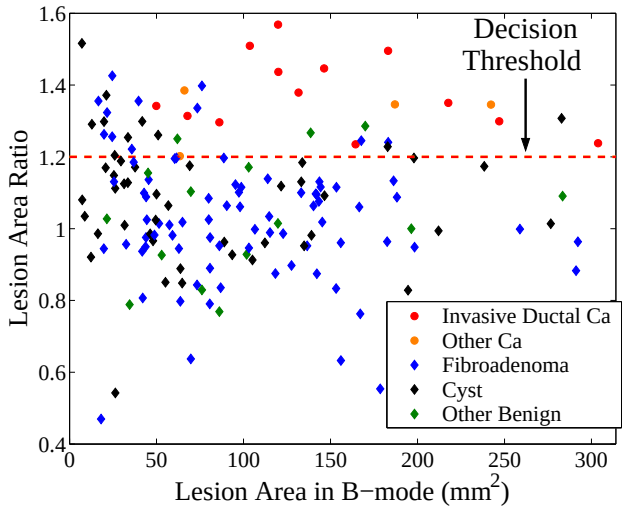

Fig. 7. A comparison of lesion area for a variety of in vivo breast masses. This is a subset of the data shown in Fig. 6 with the axes scaled to highlight lesions below 1cm in effective diameter.

TABLE I

RESULTS OF SETTING A LINEAR DECISION THRESHOLD TO SEPARATE ALL CANCERS FROM MOST BENIGN BREAST MASSES, AS SHOWN IN FIGS. 6 AND7. B-MODE SONOGRAPHY DATA ARE FROM [5], AND FIRST-SCREEN MAMMOGRAPHY DATA ARE FROM [6].

Criterion	Area Ratio	B-mode Sono	1st-Screen Mammo
Sensitivity	100%	98.4%	69%
Specificity	75.4%	67.8%	94%
PPV	56.9%	38%	8.6%
NPV	100%	100%	99.7%

this approach holds great promise for diagnosing breast masses in young women. Women under 50 years of age often have mammographically-dense breasts that significantly reduce the ability to confidently identify small breast abnormalities.

The performance of the lesion area ratio as a diagnostic criterion in broad range of breast mass types is encouraging. This study was sufficiently large to include less common types of cancers such as mucinous and apocine carcinomas. All cancer types, including ductal carcinoma in situ, were found to have increased stiffness in the area outside that seen in the corresponding B-mode image. This phenomenon was expected for invasive ductal carcinoma where collagen, fibrin and elastin infiltrate the normal tissue surrounding the lesion. The source of this increased area of stiffness in these other types of cancers is not yet understood.

V. CONCLUSIONS

The ratio of the lesion area seen in strain images to that seen in the corresponding B-mode images appears to be a very useful criterion for separating malignant from benign breast masses. This parameter integrated into a broader set of criteria, such as that proposed by Stavros, et al. [5] would likely further improve the diagnostic accuracy of breast sonography.

VI. ACKNOWLEDGEMENTS

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REFERENCES

[1] T. J. Hall, Y. Zhu, and C. S. Spalding, "In vivo real-time freehand palpation imaging," *Ultrasound Med Biol*, vol. 29, no. 3, pp. 427–435, 2002.

[2] B. S. Garra, I. Céspedes, J. Ophir, S. R. Spratt, R. A. Zuurbier, C. M. Magnant, and M. F. Pennanen, "Elastography of the breast: Initial clinical results," *Radiology*, vol. 202, pp. 79–86, 1997.

[3] T. A. Kroukop, W. TM, F. Kallel, B. S. Garra, and T. J. Hall, "The elastic moduli of breast and prostate tissues under compression," *Ultrasonic Imaging*, vol. 20, pp. 260–274, 1998.

[4] Y. Zhu, M. F. Insana, P. Chaturvedi, T. J. Hall, L. T. Cook, J. M. Gauch, and H. A. Khant, "Deformable mesh algorithm for strain imaging with complex tissue deformation," in *IEEE Ultrason. Symp. Proc.*, vol. 24, pp. 100–108, 2002.

[5] A. T. Stavros, D. Thickman, C. L. Rapp, M. A. Dennis, S. H. Parker, and G. A. Sisney, "Solid breast nodules: Use of sonography to distinguish between benign and malignant lesions," vol. 196, pp. 123–134, 1995.

[6] C. J. Baines, A. B. Miller, C. Wall, D. V. McFarlane, I. S. Simor, R. Jong, B. J. Shapiro, , L. Audet, M. Petitclerc, D. Ouimet-Olvia, J. Ladouceur, G. Herbert, T. Minuk, G. Hardy, and H. K. Standing, "Sensitivity and specificity of first screen mammography in the Canadian National Breast Screening Study: A preliminary report from five centers," *Radiology*, vol. 160, pp. 295–298, 1986.