Dokkyo Journal of Medical Sciences
36(1) : 17～25, 2009

Originals

Computer-aided Diagnosis of Breast Elastography

Etsuo Takada[a], Ruey-Feng Chang[b], Wei-Chih Shen[c], Yu-Chun Ho[b],
Woo Kyung Moon[d], Michiko Nakajima[e], Masayuki Kobayashi[e]

[a]*Center of Medical Ultrasonics Dokkyo Medical University School of Medicine, Mibu, Tochigi, 321-0293, Japan,*
[b]*Department of Computer Science and Information Engineering National Taiwan University, Taiwan,*
[c]*Department of Computer Science and Information Engineering National Chung Cheng University,*
[d]*Department of Diagnostic Radiology, College of Medicine Seoul National University Hospital, Korea,*
[e]*Comprehensive Regional Medical Service, Saitama Medical University, Japan*

SUMMARY

Ultrasonography has been an important imaging technique for detecting breast tumors. As opposed to the conventional B-mode image, the real-time tissue elastography by ultrasound is a new technique for imaging the elasticity and applied to detect the stiffness of tissues. The red region of color elastography indicates the soft tissue and the blue one indicates the hard tissue. The harder tissue usually is classified as malignancy. In this paper, the authors proposed a computer-aided diagnosis (CAD) system on elastography to measure whether this system is effective and accurate to classify the tumor into benign and malignant. According to the features of elasticity, the color elastography was transferred to hue, saturation, and value (HSV) color space and extracted meaningful features from hue images. Then the neural network was utilized in multiple features to distinguish tumors. In this experiment, there are 180 pathology-proven cases including 113 benign and 67 malignant cases used to examine the classification. The results of the proposed system showed an accuracy of 83.89 %, a sensitivity of 82.09 % and a specificity of 84.96 %. Compared with the physician's diagnosis, an accuracy of 78.33 %, a sensitivity of 53.73 % and a specificity of 92.92 %, the proposed CAD system had better performance. Moreover, the agreement of the proposed CAD system and the physician's diagnosis was calculated by kappa statistics, the kappa 0.64 indicated there is a fair agreement of observers.

Key Words : breast ultrasound, elastography, computer-aided diagnosis

INTRODUCTION

Breast cancer is the most frequent cancer in Japanese women and still increasing year by year. Ultrasonic examination could be an effective method for early detection of breast cancer as well as mammography and is thought to reduce breast cancer mortality. The national trial is going on in Japan for confirming the evidence of reducing the mortality rate of breast cancer by screening ultrasonography. Ultrasound elastography[1～6] is a newly developed technique of imaging the tissue elasticity and it has been used clinically to examine a variety of breast lesions in patients. And this technique is also used for other organs[7～9]. In general, the breast cancer tissue is harder than the adjacent normal breast tissue or mostly benign lesions. The principle of elastography is that the tissue compression produces the strain displacement with smaller strain in harder tissue and the larger strain in softer tissue. In the past, the elastograms are grey-level im-

Received November 17, 2008 ; accepted December 4, 2008
Reprint requests to : Etsuo Takada, M.D.
Center of Medical Ultrasonics, Dokkyo Medical University School of Medicine, Tochigi 321-0293 Japan.

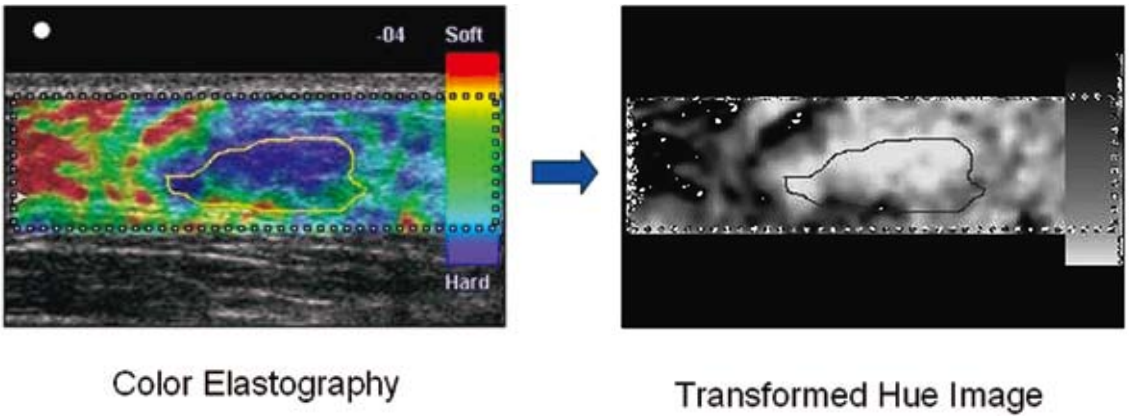

Fig. 1 Color elastography is transformed to hue image
Hue is monochrome, grey image. CAD system acquires the strain magnitude from hue image.

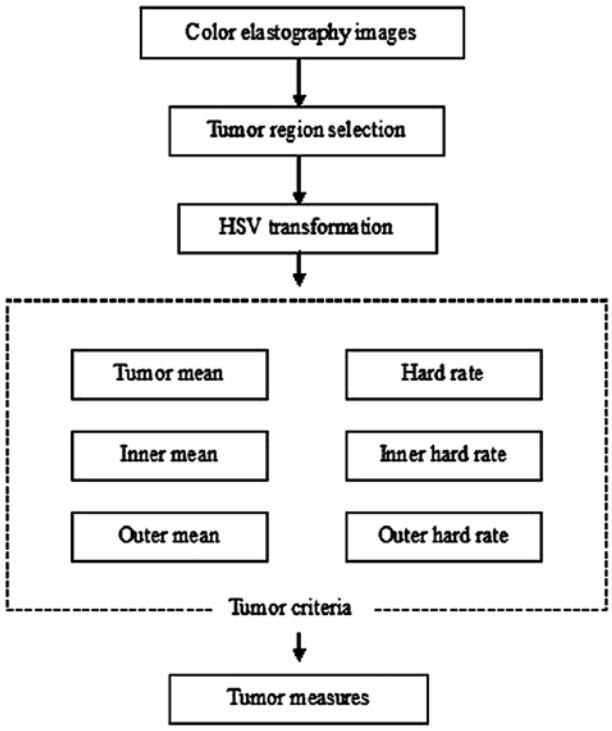

Fig. 2 The flow chart of elastography analysis for computer-aided diagnosis
Tumor region is determined on color elastograhpy. 2) Transform color image to HSV. 3) Calculate on six features 4) Make diagnosis

ages with dark region for the hard tissue and the bright one for the soft tissue [10,11]. The color elastograms, in which the strain information is superimposed on B-mode images with a translucent color scale, are proposed recently by Shiina et al.[12,13] In the color elastograms, the color scale is distributed from red, green to blue which presents soft, moderate, and hard tissue, respectively. Moreover, Ueno [14] classified the elastographic images into five categories by the hardness distribution of inner and outer tumor. The best cutoff point between the elastographic scores for differentiating the benign and malignant tumors was between 3 and 4 with sensitivity 86.5 % and specificity 89.8 %.

The CAD is an effective tool to assist the physicians in diagnoses and it can automatically detect certain diseases from medical images. The radiologists can get the second option to reduce incautious mistakes especially in suspicious cases. Sahiner [15] indicated that physicians can obtain rapid and accurate diagnosis with the aid of the CAD. In this paper, we propose a computer-aided diagnosis using color elastography features for classifying breast lesions in ultrasound images. The elastography is firstly transformed to the hue image to obtain the elasticity information as Fig. 1, and the inner and outer tissue distribution is analyzed to get six features. Then, we utilize the neural network to train the feature information and classify tumors into benign or malignant. The flow chart of elastography analysis is illustrated in Fig. 2. The aim of this study was to evaluate whether the new computer-aided method of color elastography could perform the effective and objective differentiation of benign and malignant breast lesions. Therefore, the proposed CAD is also compared with the physician's diagnosis. Furthermore, the agreement of our CAD system and the physician's diagnosis is calculated by kappa statistics [16].

Elastography Imaging

For elastography, two frames of ultrasound data are

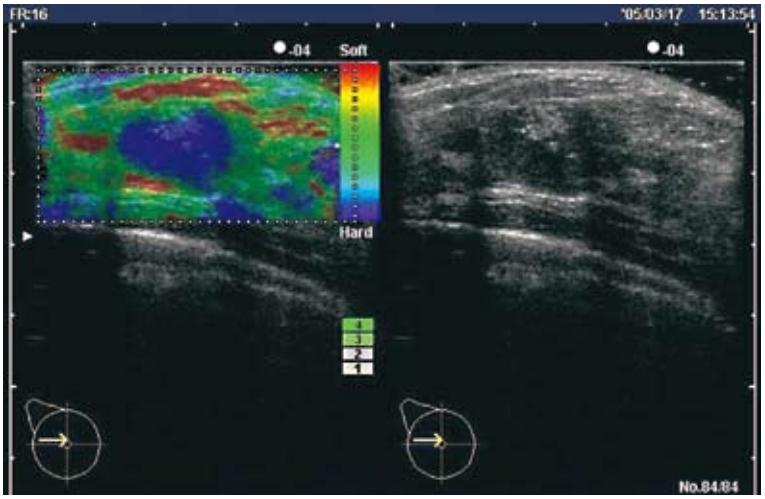

Fig. 3 Left : Color elastography of malignant case, Right : B-mode image

recorded, one before and one after the tissue is compressed. The tissue shifts can be estimated by windowing data in the pre- and post-compression signals, and identifying the displacement that produces the closest match between the windows. The local gradient of the displacement estimates could be used to estimate the strain.

The cross-correlation analysis and phase-shift estimation are used for tracking of small displacements with ultrasound and could be applied for elastography and Doppler flow. The cross-correlation analysis [17,18] is commonly used to track larger tissue displacements for elastography. The maximum of cross-correlation function between two signals, one obtained before and the other obtained after compression, indicates the point at which two signals are most similar to each other. However, due to the high computational cost, the cross-correlation analysis is not practical for real-time assessment. On the other hand, the phase-shift estimation or Doppler methods can be used to rapidly track the tissue motion and commonly used to determine the blood flow velocity. However, the phase-shift tracking method fails to measure large displacements due to aliasing errors. In order to provide the real-time elastography, Shiina et al.[12,13] proposed the combined autocorrelation method (CAM) to produce an elasticity image with high-speed processing and accuracy by combining envelope correlation and phase shift. The envelope correlation is used to solve the problem of phase aliasing in the phase-shift tracking method. In this paper, the used elastography machine is based on the CAM technique.

Color Elastography and Scoring System

In general, the elasticity information is displayed in the form of a gray image [11,12]. The dark region of elastogram indicates the hard tissue and the bright one indicates the soft tissue. However, Shiina et al.[12,13] display the strain image that is superimposed on B-mode images with a translucent color scale. Using a translucent strain image, it is easy to recognize the strain information of each region in a tumor. In the color scale strain image, red indicates that tissue is soft and blue that it is hard. Fig. 3 is a malignant case of breast tissue. The left image is an elastographic image and the right image is a conventional B-mode image. The middle blue regions of elastographic images expand as the pressure increases, whereas the conventional B-mode images have only less change. The scale at the lower-right corner of the elastographic image indicates the pressure. In the B-mode images, the breast imaging reporting and data system (BI-RADS) [19] is used to assess breast tumors. In elastography, Ueno [14] proposed a scoring system based on the strain distribution of a tumor and the elastographic score is defined as

- Score 1 : elasticity tissue extended the entire lesion (e.g. cyst)
- Score 2 : elasticity tissue over the most part with individual solid structures (e.g. fibroadenoma)
- Score 3 : elasticity tissue in the periphery region and solid in the center of the lesion

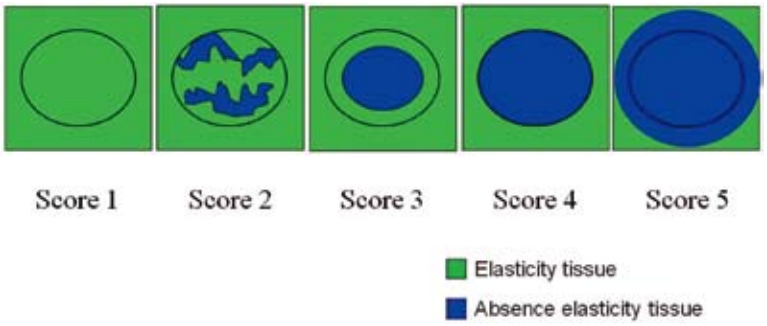

Fig. 4-1 Elastography scoring system (Tsukuba Score)
Ueno proposed physician's elastography score according to the strain distribution
Score 1-3 benign, Score 4-5 malignant

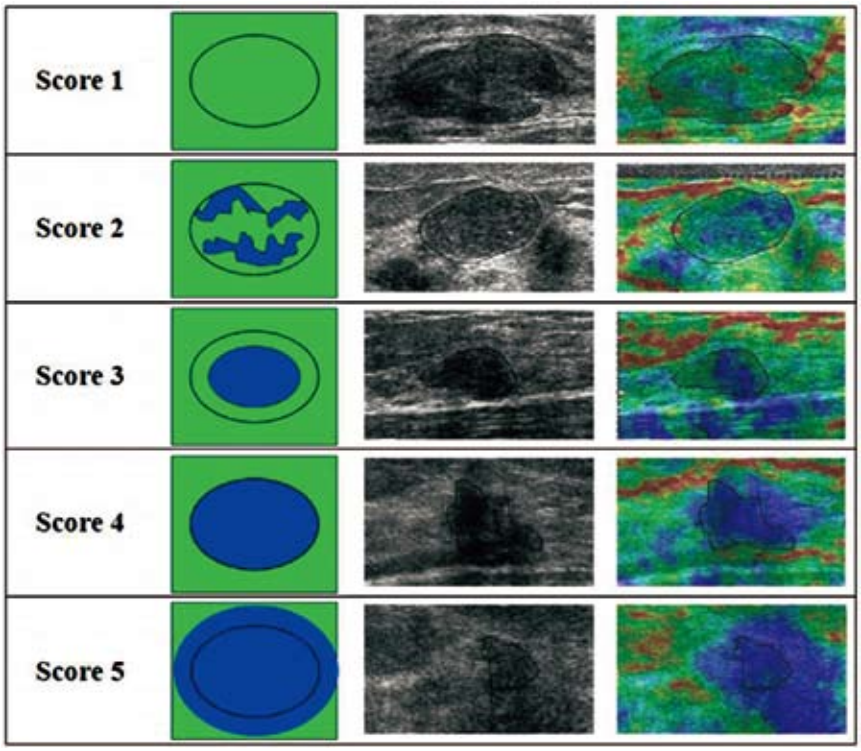

Fig. 4-2 Elastography Score and corresponding images

● Score 4 : absence of elasticity over the entire lesion (e.g. suspicion of carcinoma)

● Score 5 : absence of elasticity over the entire lesion and surrounding area (e.g. infiltrating carcinoma)

The corresponding images are illustrated in Fig. 4-1 and 4-2.

METHODS

In the proposed analysis, the physicians need to manually draw the tumor contour for each case on the B-mode image and the tumor contour on the B-mode image is mapped to the color elastographic image. From our experiments, the elasticity information could be separated from the color images by using the hue information. Hence, the color elastographic images will be transferred in order to extract the hue information. In order to acquire the strain magnitude, the original color image in the RGB color space will be transformed to the image in the HSV color space firstly, and then the hue values could represent the strain magnitude from our experiments. The RGB color space is a three-dimensional color space with the Red, Green, and Blue components and this model is used to display the colors on a monitor screen. The HSV color space stands

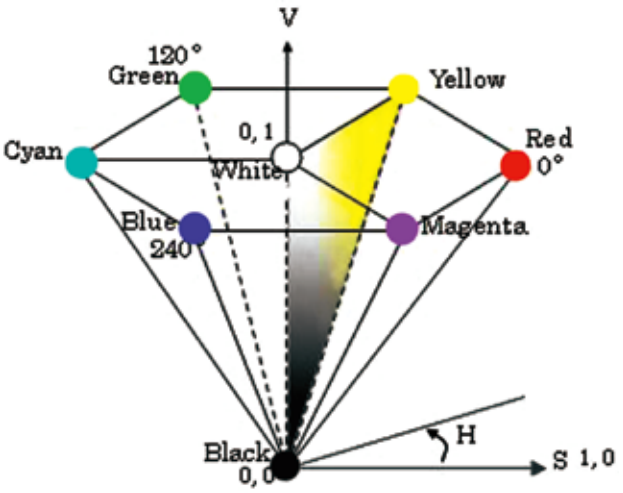

Fig. 5 The color elastography is transferred to HSV color space.
HSV：hue, saturation and value

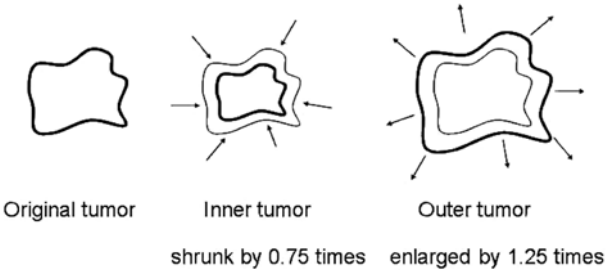

Fig. 6 Original tumor border and "Inner tumor", "Outer tumor".
The inner and outer tumor regions are decided by tumor size

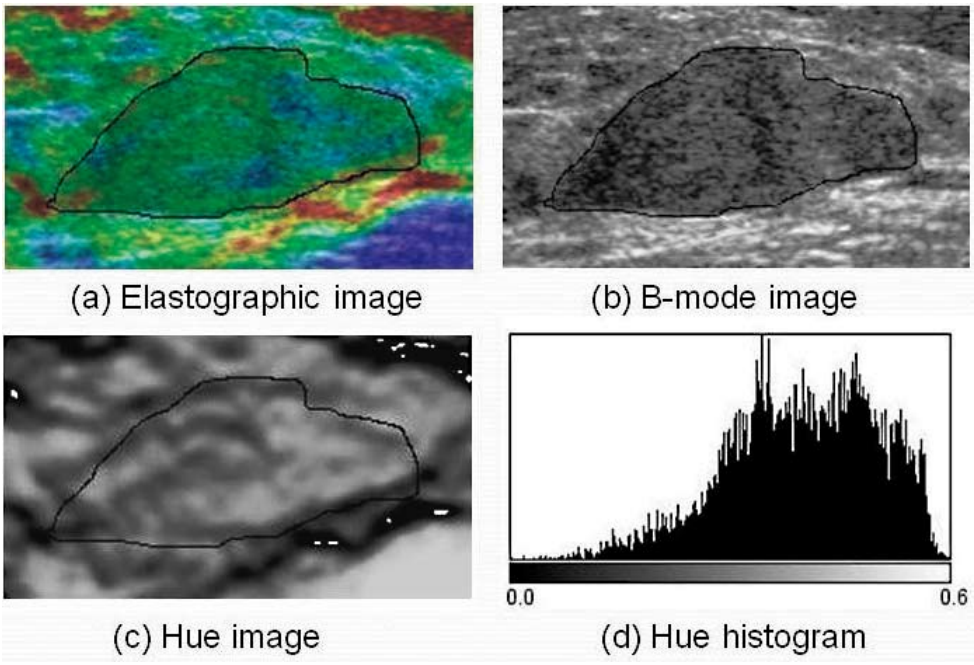

Fig. 7 A benign case
A true negative example of physician's elastography score 1

for Hue, Saturation, and Value illustrated in Fig. 5. The Hue component refers to a specific wavelength of color, and in the form of an angle between [0, 360] degrees. The black line in the Fig. 5 at the lower right shows the Hue angle. The second component Saturation describes the purity of the color and displays by the length of the S vector with ranges [0, 1]. The final component Value of the color determines its brightness along the V axis from 1 to 0.

Then meaningful features are extracted from hue images. The neural network was utilized in multiple features to distinguish tumors. Six proposed features including tumor mean, inner tumor mean, outer tumor mean, hard rate, inner hard rate, and outer hard rate will be calculated from the inner and outer of tumor as Fig. 6 to distinguish benign and malignant tumors. These features could be depicted by two categories, mean measures and hard rate measures as Fig. 7 and 8.

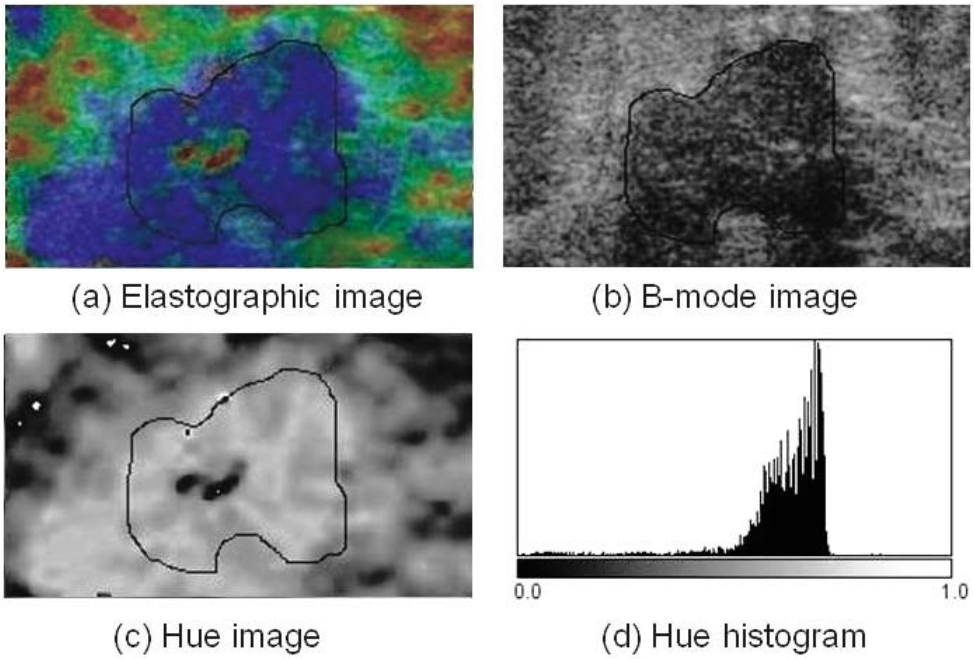

Fig. 8 A malignant case
A true positive example of physician's elastography score 5

1) Mean features

Suppose that h_i is the hue value of pixel i in the tumor region, the mean of ROI could be expressed as

$$mean = \frac{\sum_{i=0}^{n-1} h_i}{n}$$

Where i is the pixel index and n is the total pixels in the tumor region.

The inner mean ***meani***

The outer mean ***meano***

2) Hard rate features

The rate of the hard pixels ***hard_rate*** in a tumor is defined as

$$hard\_rate = \frac{hard\_pixel}{n}$$

Where ***hard_pixel*** is the number of hard pixels and ***n*** is the number pixels in the region

Furthermore, a neural network is used to combine these features and then to classify tumors into benign or malignant. Fig. 7 is a case of benign and Fig. 8 is a case of malignant tumor.

RESULTS

In this experiment, there are 180 pathology-proven cases including 113 benign and 67 malignant cases used to examine the classification of elastography. Table 1 are results of mean values of six proposed features. The Kolmogorov-Smirnov test was applied to test for data distribution and all the features were normal distribution. All those features are statistically significant between benign and malignant tumors by Student's t test ($p < 0.05$). Table 2 shows the results of physician's diagnosis and CAD analyses of six features. The results of the proposed system showed "Tumor Mean" is the best among six features, an accuracy of 82.78 %, a sensitivity of 85.07 % and a specificity of 81.42 %. After adapting neural network, results of CAD system are an accuracy of 83.89 %, a sensitivity of 82.09 % and a specificity of 84.96 %, while the results of physician's diagnosis are an accuracy of 78.33 %, a sensitivity of 53.73 % and a specificity of 92.92 % as shown in Table 3. The Chi-square test is used to calculate p-value.

DISCUSSION

Elastography is a recently introduced technique to ultrasonography. CAD is already applied for diagnostic images such as mammography, B-mode ultrasonography and so on. The authors developed CAD system for breast color elastography and studied its diagnostic accuracy. For physician's diagnosis, Ueno et al proposed

Table 1 Mean values of six proposed features for benign and malignant cases and Student's **t** est.

Features	Type	Mean ± Standard Deviation	*p*-value
Tumor Mean	Benign	116.7 ± 23.15	< 0.05
	Malignant	145.2 ± 13.53	
Inner Mean	Benign	121.3 ± 25.43	< 0.05
	Malignant	152.6 ± 14.16	
Outer Mean	Benign	113.2 ± 20.79	< 0.05
	Malignant	136.3 ± 13.00	
Hard Rate	Benign	43.76 ± 27.98	< 0.05
	Malignant	77.57 ± 17.82	
Inner Hard Rate	Benign	47.79 ± 32.97	< 0.05
	Malignant	85.78 ± 17.57	
Outer Hard Rate	Benign	40.91 ± 24.06	< 0.05
	Malignant	68.21 ± 16.31	

All those features are statistically significant between benign and malignant tumors ($p < 0.05$).
All the features are confirmed as normal distribution by Kolmogorov-Smirnov test.

Table 3 Physician's elastography score vs. proposed CAD system after adapting neural network.
The CAD system has better results on sensitivity and NPV. Chi-square test was used to calculate p-value.

	Physician's elastography score	Proposed CAD system	*p*-value
Accuracy	78.33 %	83.89 %	0.1781
Sensitivity	53.73 %	82.09 %	0.0004
Specificity	92.92 %	84.96 %	0.0563
PPV	81.82 %	76.39 %	0.4902
NPV	77.21 %	88.89 %	0.0174

PPV positive predictive value, NPV : negative predictive value

Table 2 The results of physician's elastography score and six elasticity features by CAD (Computer-aided diagnosis)
The results of the CAD system showed "Tumor Mean" is the best among six features. After adapting neural network, results are improved (Table 3).

	Physician's elastography score	Tumor mean	Inner mean	Outer mean	Hard rate	Inner hard rate	Outer hard rate
Threshold	3.5	135	147.5	133.5	0.7	0.843	0.651
TP	36	57	54	42	54	49	46
FN	31	10	13	25	13	18	21
FP	8	21	19	14	22	20	17
TN	105	92	94	99	91	93	96
Accuracy (%)	78.33	82.78	82.22	78.33	80.56	78.89	78.89
Sensitivity (%)	53.73	85.07	80.6	62.69	80.6	73.13	68.66
Specificity (%)	92.92	81.42	83.19	87.61	80.53	82.3	84.96
PPV (%)	81.82	73.08	73.97	75	71.05	71.01	73.02
NPV (%)	77.21	90.2	87.85	79.84	87.5	83.78	82.05

TP : true positive, FN : false negative, FP : false positive, FP : false positive, TN : true negative, PPV positive predictive value, NPV : negative predictive value

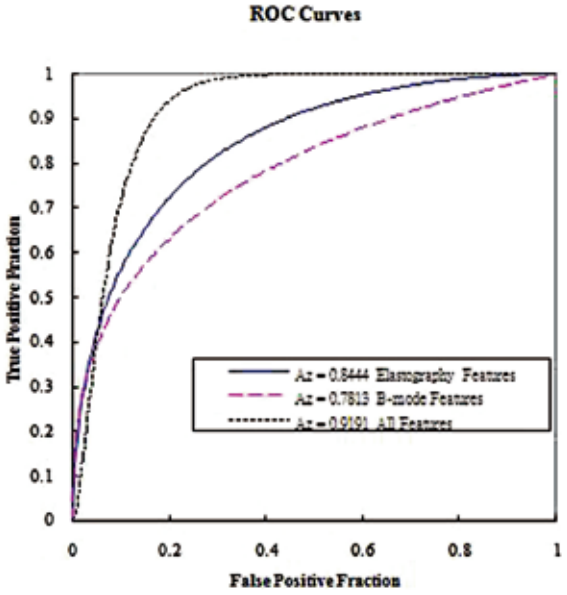

Fig. 9 Elastography and B-mode ultrasonography.
In primitive results, elastography features are better than B-mode features.
Elastography and B-mode features could be combied to improve the diagnostic results.

a scoring system for color elastography as "Tsukuba score"[14]. This scoring system is widely used clinically. In this study, the proposed CAD system was compared with physician's diagnosis by Tsukuba score. From the results, the proposed CAD system had better performance than physician's diagnosis. Moreover, the agreement of the proposed CAD system and the physician's diagnosis was calculated by kappa statistics, the kappa value 0.64 indicated a fair agreement. ROC curve shows combined elastography and B-mode ultrasonogrgaphy has better performance as shown in Fig. 9. Elastography is thought to help physician's diagnosis for breast tumor and the CAD system is considered to assist physician's diagnostic procedure. The radiologists can take the second option by the CAD system to reduce incautious misdiagnoses especially in suspicious cases.

CONCLUSION

The proposed CAD system of breast elastography has better performance than the physician's diagnosis as shown in Table 3.

The agreement of the CAD system and the physician's diagnosis has kappa 0.64 indicated there is a substantial agreement of observers.

The CAD system correctly classified the tumor as benign or malignant with high probability.

REFERENCES

1) R. J. Dickinson and C. R. Hill, "Measurement of soft tissue motion using correlation between A-scans," Ultrasound Med Biol **8**, 263-271, 1982.
2) L. S. Wilson and D. E. Robinson, "Ultrasonic measurement of small displacements and deformations of tissue," Ultrason Imaging **4**, 71-82, 1982.
3) L. Gao, K. J. Parker, R. M. Lerner and S. F. Levinson, "Imaging of the elastic properties of tissue--a review," Ultrasound Med Biol **22**, 959-977, 1996.
4) J. Ophir, S. K. Alam, B. Garra, F. Kallel, E. Konofagou, T. Krouskop and T. Varghese, "Elastography : ultrasonic estimation and imaging of the elastic properties of tissues," Proc Inst Mech Eng [H] **213**, 203-233, 1999.
5) B. S. Garra, E. I. Cespedes, J. Ophir, S. R. Spratt, R. A. Zuurbier, C. M. Magnant and M. F. Pennanen, "Elastography of breast lesions : initial clinical results," Radiology **202**, 79-86, 1997.
6) H. T. Liu, L. Z. Sun, G. Wang and M. W. Vannier, "Analytic modeling of breast elastography," Med Phys **30**, 2340-2349, 2003.
7) A. Lyshchik, T. Higashi, R. Asato, S. Tanaka, J. Ito, J. J. Mai, C. Pellot-Barakat, M. F. Insana, A. B. Brill, T. Saga, M. Hiraoka and K. Togashi, "Thyroid gland tumor diagnosis at US elastography," Radiology **237**, 202-211, 2005.
8) L. Curiel, R. Souchon, O. Rouviere, A. Gelet and J. Y. Chapelon, "Elastography for the follow-up of high-intensity focused ultrasound prostate cancer treatment : initial comparison with MRI," Ultrasound Med Biol **31**, 1461-1468, 2005.
9) N. Miyanaga, H. Akaza, M. Yamakawa, T. Oikawa, N. Sekido, S. Hinotsu, K. Kawai, T. Shimazui and T. Shiina, "Tissue elasticity imaging for diagnosis of prostate cancer : a preliminary report," Int J Urol **13**, 1514-1518, 2006.
10) K. M. Hiltawsky, M. Kruger, C. Starke, L. Heuser, H. Ermert and A. Jensen, "Freehand ultrasound elastography of breast lesions : clinical results," Ultrasound Med Biol **27**, 1461-1469, 2001.
11) T. J. Hall, Y. Zhu and C. S. Spalding, "In vivo real-time freehand palpation imaging," Ultrasound Med

Biol **29**, 427-435, 2003.

12) T. Shiina, M. Yamakawa, N. Nitta, E. Ueno, T. Matsumura, S. Tamano and T. Mitake, "Clinical assessment of real-time, freehand elasticity imaging system based on the combined autocorrelation method," IEEE Ultrasonics Symposium **1**, 664-667, 2003.

13) N. Nitta, M. Yamakawa, T. Shiina, E. Ueno, M. M. Doyley and J. C. Bamber, "Tissue elasticity imaging based on combined autocorrelation method and 3-D tissue model," IEEE Ultrasonics Symposium **2**, 1447-1450, 1998.

14) A. Itoh, E. Ueno, E. Tohno, H. Kamma, H. Takahashi, T. Shiina, M. Yamakawa and T. Matsumura, "Breast disease : clinical application of US elastography for diagnosis," Radiology **239**, 341-350, 2006.

15) B. Sahiner, H. P. Chan, M. A. Roubidoux, M. A. Helvie, L. M. Hadjiiski, A. Ramachandran, C. Paramagul, G. L. LeCarpentier, A. Nees and C. Blane, "Computerized characterization of breast masses on three-dimensional ultrasound volumes," Med Phys **31**, 744-754, 2004.

16) G. Hripcsak and D. F. Heitjan, "Measuring agreement in medical informatics reliability studies," J Biomed Inform **35**, 99-110, 2002.

17) G. F. Pinton, J. J. Dahl and G. E. Trahey, "Rapid tracking of small displacements with ultrasound," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control **53**, 1103-1116, 2006.

18) J. Ophir, I. Cespedes, H. Ponnekanti, Y. Yazdi and X. Li, "Elastography : a quantitative method for imaging the elasticity of biological tissues," Ultrason Imaging **13**, 111-134, 1991.

19) L. Levy, M. Suissa, J. F. Chiche, G. Teman and B. Martin, "BIRADS ultrasonography," Eur J Radiol **61**, 202-211, 2007.