Computer-aided Diagnosis of Breast Tumors with Different US Systems[1]

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Rationale and Objectives. The authors performed this study to determine whether a computer-aided diagnostic (CAD) system was suitable from one ultrasound (US) unit to another after parameters were adjusted by using intelligent selection algorithms.

Materials and Methods. The authors used texture analysis and data mining with a decision tree model to classify breast tumors with different US systems. The databases of training cases from one unit and testing cases from another were collected from different countries. Regions of interest on US scans and co-variance texture parameters were used in the diagnosis system. Proposed adjustment schemes for different US systems were used to transform the information needed for a differential diagnosis.

Results. Comparison of the diagnostic system with and without adjustment, respectively, yielded the following results: accuracy, 89.9% and 82.2%; sensitivity, 94.6% and 92.2%; specificity, 85.4% and 72.3%; positive predictive value, 86.5% and 76.8%; and negative predictive value, 94.1% and 90.4%. The improvement in accuracy, specificity, and positive predictive value was statistically significant. Diagnostic performance was improved after the adjustment.

Conclusion. After parameters were adjusted by using intelligent selection algorithms, the performance of the proposed CAD system was better both with the same and with different systems. Different resolutions, different setting conditions, and different scanner ages are no longer obstacles to the application of such a CAD system.

Key Words. Breast neoplasms, diagnosis; breast neoplasms, US; computers, diagnostic aid.

Technical advances in diagnostic ultrasound (US) have expanded the potential usefulness of this modality in the evaluation of breast lesions. The computing power of sonography has been substantially increased, which has allowed for fully digital systems. Resolution and contrast improvements make it easy to assess breast lesions by using morphologic features. Breast cancer, however, is highly heterogeneous. Malignant tumors are different from each other, and there is often variation from one part of a nodule to another part within the same nodule. Because of this heterogeneity, the use of a single morphologic criterion for sonography does not fulfill the diagnostic demand. Characteristic sonographic features of benign and malignant solid breast masses have been investigated in an attempt to decrease the large number of benign biopsies. Stavros et al (1) evaluated the ability of simple measurement of mass dimensions to help predict the probability of cancer. They indicated that a number of multiple sonographic findings are necessary to evaluate solid breast masses, including shadowing, single nodule, spiculation, angular margins, thick echogenic halo, mi-

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crolobulation, taller-than-wide, hypoechogenicity, calcifications, and duct extension or branch pattern. The sonographic technique described by these authors, however, necessitates extensive real-time evaluation by an experienced interpreter, which may not be practical in most clinical settings.

The use of computer technology in decision support is now widespread and pervasive across a wide range of businesses and industries. The introduction of computer-aided diagnosis (CAD) in mammography (eg, ImageChecker M1000 System, R2 Technology, Los Altos, Calif) has enhanced performance and improved confidence by drawing the radiologist to suspicious microcalcifications and tumors on the mammogram (2,3). To our knowledge, however, the application of a CAD system to sonography has still not been established. A few articles have been published about this topic (4–11). CAD analysis has faced skepticism and numerous criticisms in the past. Its practical utility is controversial. The role of CAD in sonography is not the same as that in screening mammography. It is used to provide the second opinion for the interpretation of a sonographically detected tumor and to improve diagnostic confidence. Image texture analysis plays an important role in the CAD US system (8–10). The potential of sonographic texture analysis to improve breast tumor diagnosis was demonstrated by Goldberg et al (8) in 1992. Garra et al (9) in 1993 and Valckx and Thijssen (10) in 1997 also demonstrated that texture analysis with co-occurrence matrix parameters could help improve the differentiation of benign from malignant breast lesions. Although proposed CAD systems—for example, those proposed by Chen and colleagues in 1999 and 2000 (4–7)—could be readily adapted to US machines, there were no data available to verify whether a designed system was suitable from one US machine to another with or without the adjustment of the parameters by using intelligent selection algorithms. In fact, with the rapid development of US technologies, many different US systems are used for current medical diagnosis. The aim of this study was to clarify this point; we believe that is valuable for future development of a US CAD system.

In this study, we used data mining with a decision tree model to classify breast tumors seen with different US systems as benign and malignant. The databases of training cases and testing cases were collected from different countries (Taiwan and South Korea). Regions of interest (ROIs) on US scans and co-variance texture parameters were used in our diagnosis system. Meanwhile, proposed adjustment schemes for different US systems were used to transform information needed for the differential diagnosis.

MATERIALS AND METHODS

A physician extracted the subimage of the ROI, and then the computer analyzed the subimage by using the intensity variation and texture information. Then, adjustment of the parameters by using intelligent selection algorithms according to the different rules achieved by retraining data obtained from different machines was performed to achieve better diagnostic results.

Data Acquisition

The images used in this study were obtained with two different US systems: an SDD 1200 scanner (ALOKA, Tokyo, Japan) with a 7.5-MHz linear real-time transducer and an HDI 3000 system (Advanced Technology Laboratories, Bothell, Wash) with an L10-5 38-mm linear-array transducer. The images obtained with the SDD 1200 system were used as the training set, and the images obtained with the HDI 3000 system were used as the testing set.

SDD 1200 system (analog signals).—Two hundred forty-three digital US scans of the breast were obtained with the SDD 1200 system. There were 161 benign breast tumors and 82 carcinomas. Tumors were pathologically proved by means of cytology, core-needle biopsy, or surgical biopsy. One breast surgeon (D.R.C.) who was also familiar with the interpretation of breast US scans captured all these breast images and selected the ROI before tissue proof. The data were consecutively collected from 1997 to 1998. Patients ranged in age from 17 to 64 years, and tumor diameter ranged from 0.8 to 4.2 cm.

Acoustic standoff pads were not used. The following steps were performed to obtain digital US images. First, the analog signals from the VCR output of the scanner were transmitted to a frame grabber (Video CATcher; Top Solution Technology, Taipei, Taiwan). The digitized data were underplayed with a resolution of 736×566 pixels for a National Television Systems Committee, or NTSC, video screen. The digital image was quantized into 8 bits (ie, 256 gray levels) by using a software package (ProImage; Prolab, Taipei, Taiwan) with the frame grabber.

The rectangular ROI, which extended beyond the lesion margins by 1–2 mm in all directions, was made and saved as a file with an impression before tissue proof was obtained for further analysis and diagnosis. These ROI images were used in our breast image database to investi-

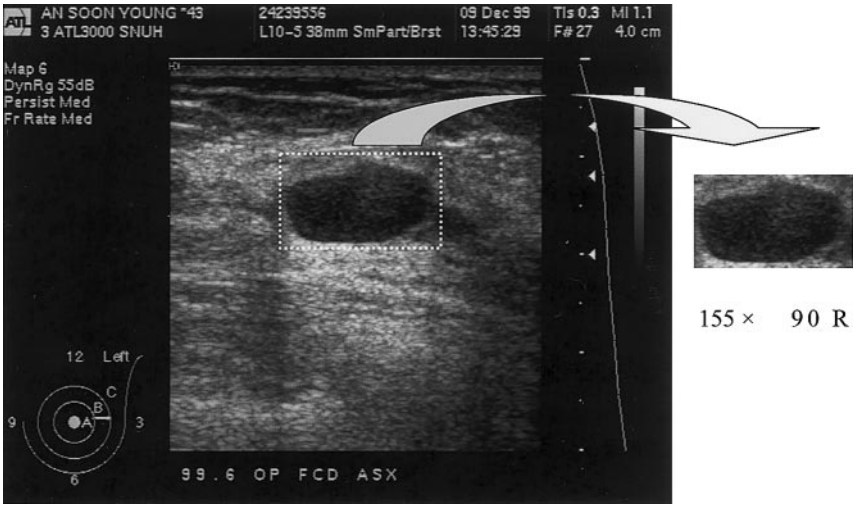

Figure 1. Digital image (640 × 480 pixels) captured from the US scanner. In a 1 × 1-cm rectangle, there are 94 × 94 = 8,836 pixels. The ROI rectangle (arrow) is 1.65 × 0.96 cm and 155 × 90 pixels.

gate further the texture characteristics of benign and malignant tumors.

HDI 3000 system (digital images).—The HDI 3000 database contained US scans of the breast obtained in 259 patients. There were 130 benign tumors and 129 carcinomas. Tumors were pathologically proved by means of fine-needle cytology, core-needle biopsy, or surgical biopsy. The tumor was larger than 0.8 cm in diameter in all cases (benign and malignant). The database contained only one image from each patient. The US scans were captured at the largest diameter of the tumor. The images were collected from August 1, 1999, to May 31, 2000; the patients ranged in age from 18 to 64 years. Dynamic range was set at 55 dB. Acoustic standoff pads were not used. Except for changes made to obtain the best view, the sonographic gain setting remained unchanged throughout the entire study period.

The monochrome US scan was digitized into 8 bits (ie, 256 gray levels), and the features were stored on magneto-optical disks. The entire database was supplied by an author (W.K.M.). Data were collected consecutively, and all cases were used for analysis. A breast surgeon (D.R.C.) who was familiar with breast US interpretations but unfamiliar with the tissue diagnosis and cell type manually selected the subimage of an ROI by using a software package (ProImage). The ROI subimage was then saved as a file for later analysis. ROI images were used in our breast image database to investigate further the texture characteristics of benign and malignant tumors. Figure 1 shows an example of a 640 × 480-pixel digital image captured from the US scanner. In a 1 × 1-cm rectangle, there are 94 × 94 = 8,836 pixels. The ROI rectangle is 1.65 × 0.96 cm and 155 × 90 pixels.

Image Analysis

Co-occurrence matrix is the most adopted scheme for analyzing the texture variations in a region in various directions and distances (10,12). The main power of the co-occurrence matrix approach is that it characterizes the spatial interrelationships of the gray levels in a texture pattern and is invariant under monotonic gray-level transformations. In general, a minimum set of co-occurrence matrixes is four (0°, 45°, 90°, and 135° with distance equal to 1) for a texture that there is no prior knowledge about (10,12). It is obvious, however, that the size of the matrix is a function of the number of gray levels in the image and that it would be prohibitively computationally expensive to evaluate a matrix for each pixel in a general 8-bit image (256 × 256 elements in a co-occurrence matrix). Thus, we use the statistical parameter matrixes (12) with the same texture preservation properties instead of the co-occurrence matrix.

The statistical method including contrast, co-variance, and dissimilarity was used to evaluate the texture parameters for several distances between pixels and directly from the image without using co-occurrence matrixes. The main advantage of this method resides in its calculation cost, which depends only on the size of the image treated and not on the number of gray levels. Moreover, it enables the extraction of visually perceptible physical pa-

rameters from the image (eg, contrast, granularity, regularity, periodicity, fineness or coarseness of the texture) (1,8–10,12–14). We will briefly describe the evaluation of texture parameters.

Let S be a region of an image, $g(i,j)$ the intensity value at the position (i,j) of S, $\delta = (\Delta i, \Delta j)$ the distance between 2 pixels, and η the gray level average of region S. For a value of δ, the contrast, co-variance, and dissimilarity are calculated as follows: contrast $= E\,[g(i,j) \cdot g(i + \Delta i, j + \Delta j)]$, co-variance $= E\,\{[g(i,j) - \eta] \cdot [g(i + \Delta i, j + \Delta j) - \eta]\}$, and dissimilarity $= E\,[g(i,j) - g(i + \Delta i, j + \Delta j)]$, where $E =$ expectation. The accuracies of the three texture parameters were as follows: contrast, 86.9%; co-variance, 88.9%; and dissimilarity, 54.7%. We find that the co-variance performs better than other texture parameters. Thus, we adopted the co-variance as our texture feature.

Data Mining with the Decision Tree Model

Data mining gradually becomes an important issue in many applications. The term "data mining" refers to the use of a variety of techniques to identify numeric information or decision-making knowledge in large bodies of data. It is possible to develop predictive applications with an accurate learning method. Classification and regression are the main crucial types of prediction problems. The classification approach is developed when the goal of prediction has discrete valued, and the regression solution is developed when the goal of prediction is discrete or continuous. Predictive modeling methods have been developed that draw on techniques from statistics, pattern recognition, and machine learning. This type of data analysis has been an active area of research in many scientific areas for a considerable period of time (15–19).

Decision tree models are commonly used in data mining to examine the data and to induce the tree and its rules, which will be used to help make predictions. The decision tree contains the decision node, branches, and leaves. Each branch will lead either to another decision node or to the bottom of the tree, called a leaf node. Decision trees used to predict categoric variables are called *classification trees*. As a consequence, models can be built very quickly, which makes decision trees suitable for large sets.

Decision trees are most commonly used for classification to predict what group a case belongs to. As a result, the decision tree has become a very popular data mining technique in many current applications. In this study, the decision tree model was used as a technique for mining the information we needed for the diagnosis.

The decision tree model encompasses a number of specific algorithms such as Classification and Regression Trees, χ^2 Automatic Interaction Detection, C4.5 (20), and C5.0 (from work by J. Ross Quinlan, Rulequest Research Pty Ltd, St Ives, Australia). In the artificial intelligence field, C4.5 is one of the most popular inductive learning algorithms and was originally proposed by J. R. Quinlan (20). In our study, the C5.0 algorithm, in which the speed and quality of rule generation are improved over its predecessor C4.5, was adopted to construct the decision tree model. The co-variance texture parameters were used as the inputs to construct the decision tree model and for further diagnosis.

Adjustment Schemes for Different US Systems

The general disadvantage of CAD systems is that they usually perform well only in one specific US system. With the rapid development of US technologies, many different US systems are used to make medical diagnoses. It becomes an important issue to develop a CAD system that is suitable for different US systems. The main concerns of this problem are the different resolution and contrast with each US system, and, as a consequence, a designed CAD system cannot be used for each US unit. Thus, how to transform the information needed for diagnosis between two different systems is important.

Resolution adjustment.—Image resolution plays an important role in the analysis of image properties. The situation becomes more obvious when one needs to perform some comparison between two images obtained from two different systems. In this study, texture parameters evaluated with the ROI image helped characterize the interrelationship among pixels. Thus, it is important to carefully adjust the relationship of resolution between two different images coming from different systems for further feature extraction.

The resolution adjustment should be carried out before the evaluation of texture parameters. The interrelationship considered in the texture parameters is between a pixel at position (i,j) and a pixel at position $(i + \Delta i, j + \Delta j)$. Consider that the resolutions of two images are M pixels per centimeter and N pixels per centimeter, where M is larger than N. Then, the pixel at position $(i + \Delta i, j + \Delta j)$ is adjusted to $(i + \Delta i \cdot M/N, j + \Delta j \cdot M/N)$. For example, the adjusted co-variance texture feature is $E\,\{[g(i,j) - \eta] \cdot [g(i + \Delta i \cdot M/N, j + \Delta j \cdot M/N) - \eta]\}$. This adjustment is better than directly resampling the image resolution be-

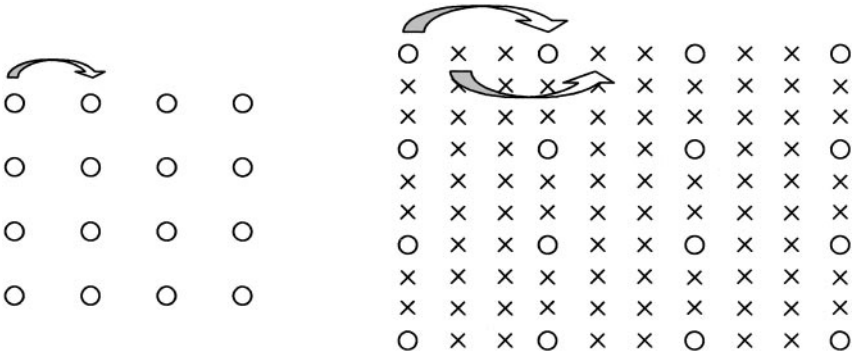

Figure 2. Diagram illustrates the resolution adjustment relationship between two images with different resolutions.

cause it enables evaluation of more numbers of pixels in their original resolution while reserving the relationship of resolution correlate to the other image. Figure 2 shows the resolution adjustment relationship between two images with different resolutions.

Location and scale families.—In general, the histogram distributions of images usually have similar properties when they belong to the same family. On US scans, most of the benign or malignant cases have a similar distribution within the same family. Thus, according to the following definition, we can modify the distribution into a similar mean and variance. Let $f(x)$ be any probability density function. Then, for any μ, $-\infty < \mu < \infty$ and any $\sigma > 0$, the family of probability density functions $(1/\sigma) f[(x - \mu)/\sigma]$, indexed by the parameter (μ,σ), is called the location-scale family with standard probability density function $f(x)$; μ is the location parameter and σ is the scale parameter. Consider two images with μ_1,σ_1 and μ_2,σ_2, respectively. Then, the new intensity value $g'(i, j)$ of pixel (i, j) is defined as $(\sigma_1/\sigma_2)[g(i, j) - \mu_2 + \mu_1]$.

To reduce the factors that differ when different physicians operate the US system (eg, contrast, brightness), we used the above properties to adjust the US images into the family with almost the same mean and variance.

Quantization step.—Quantization is the process of representing a set of continuous-valued samples with a finite number of states. If each sample is quantized independently, then the process is known as scalar quantization. A scalar quantizer Q is a function that is defined in terms of a finite set of decision levels d_i and reconstruction levels r_i, as follows: $Q(s) = r_i$, if $s \in (d_{i-1}, d_i)$, $i = 1, \ldots, L$, where L is the number of output states. That is, the output of the quantizer is the reconstruction level r_i if s, the value of the sample, is within the range (d_{i-1}, d_i).

The values for the texture parameters were directly evaluated according to the gray level of the pixel. The texture parameters, however, differ with the gray levels. Thus, we used quantization to reduce this situation because we were concerned about the levels of the comparative relationship of parameters. The cumulative number of the pixels is divided into K intervals, as determined with the quantization step. That is, each interval will have the same number of cumulations. For an image with $M \times N$ pixels, the number of pixels in each interval is $(M \times N)/K$. That is, the number of pixels in the intensity range (d_{i-1}, d_i) for interval i is $(M \times N)/K$, and those pixels in this range are quantized into i. For an image, the histogram is computed first; then, each d_i can be computed with the histogram.

The image resolutions of the two US systems we used (SDD 1200 and HDI 3000) were 94 and 58 pixels per centimeter, respectively. Information about intensity variation and texture of subimages extracted from an ROI selected by a physician was used to make a differential diagnosis. Co-variance was used as the features representing the texture properties of the ROI image to be evaluated. The size of the region used to evaluate the texture parameters was $5 \times 5 = 25$ pixels. The simulations were made with a single CPU 400-MHz personal computer (Pentium-II; Intel, Dallas, Tex) with a Windows 98 (Microsoft, Seattle, Wash) operating system.

RESULTS

Accuracy, sensitivity, specificity, positive predictive value, and negative predictive value are the five most generally used objective indexes to estimate the performance of diagnosis results. The accuracy of using a re-

Table 1
Classification of Breast Nodules with and without Adjustment

Sonographic Classification	Proposed Method		Without Adjustment	
	Benign*	Malignant*	Benign*	Malignant*
Benign	111	7	94	10
Malignant	19	122	36	119
Total	130	129	130	129

*Histologic finding.

Table 2
Performance Summary for the Proposed Adjustment Method

Parameter	Proposed Method	Without Adjustment	*P* Value*
Accuracy (%)	89.9	82.2	<.025
Sensitivity (%)	94.6	92.2	NS
Specificity (%)	85.4	72.3	<.01
Positive predictive value (%)	86.5	76.8	<.05
Negative predictive value (%)	94.1	90.4	NS

*P values were obtained with the χ^2 test. NS = not significant.

trieval technique to classify malignancies with the proposed CAD system was 89.96%, the sensitivity was 94.6%, the specificity was 85.4%, the positive predictive value was 86.5%, and the negative predictive value was 94.1%. Table 1 lists the classification of breast nodules with the proposed scheme and without any adjustment. Comparisons of the proposed diagnostic system with and without adjustment, including the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value, are listed in Table 2. The improvements in accuracy, specificity, and positive predictive value with the adjustment were statistically significant ($P < .025$, $P < .01$, $P < .05$, respectively; χ^2 test). Our results showed that the diagnostic performance was improved after the adjustment.

DISCUSSION

Detection and diagnosis are the most important steps in the evaluation of breast lesions. Breast US is routinely used as an adjunct to mammography to help differentiate benign from malignant lesions. The accuracy of US diagnostic methods is controversial because there is a considerable overlap of benign and malignant characteristics on US images and interpretation is subjective, dependant on the operator. The role of CAD in sonography is to provide a second opinion for the interpretation of a sonographically detected tumor and to improve diagnostic confidence. CAD in sonography differs from CAD in commercialized mammography in that it is used more for diagnosis than detection. Early detection, diagnosis, and treatment have an effect on the survival rate in patients with breast cancer. The 5-year survival rate for patients with breast cancer decreases from approximately 96% for cancers treated at an early stage to 77% for mid-stage cancers to just 21% for late-stage cancers that have spread to distant organs. According to the American Cancer Society, early detection of breast cancer is important for a positive outcome; however, breast cancer is difficult to identify because of the complex anatomy of the breast.

It would be of great clinical value if the CAD system could perform immediately or at least act within minutes of US. The key to shortening the computing process is to decrease the actions of data input to the computer by the user. Clinically, multiple US morphologic features as described by Stavros et al (1) are valuable in the gross classification of breast lesions. Nevertheless, from a computational point of view, taking much time to input morphologic information (ie, shape, size) is impractical and time consuming. The same problem was seen in other studies that used neural networks for CAD systems (21,22). Texture analysis—that is, textural information extracted from the image—is one possible way to resolve this problem. The extracted information could be fed into a decision algorithm designed to perform the diagnostic task. This two-step approach was successfully described by Chen and colleagues (4–7). Texture is known to be a rich source of visual information and is a key component in image analysis and understanding in humans (23). The human visual system, however, has difficulty discriminating texture information that is related to higher-order statistics on an image. Texture analysis can be classified into three main groups: the models, the mathematic morphology, and the statistical method. The natural textures usually have a highly stochastic characterization whether they are structured or not. It would seem advisable to use statistical measurements to characterize those signals that are insufficiently described with most other approaches. Statistical parameters are evaluated at one order or higher. Texture analysis, however, is not a panacea; its effectiveness is bound by the type of algorithm used to extract meaningful features (24). In this study, we proposed a novel diagnosis system for different US systems in which interpixel correlation on the US images was used to dif-

ferentiate benign from malignant tumors. Co-variance texture features and data mining with a decision tree model were adopted to achieve better results. Nonetheless, each type of US scanner has a different resolution; the information needed for diagnosis between two different US systems can be achieved by using the proposed adjustment technique. The image resolutions of the two different US systems used (SDD 1200 and HDI 3000) were 94 and 58 pixels per centimeter, respectively. The SDD 1200 unit is older than the HDI unit. The reason for its better resolution is owing to different artificial setting of magnification power of each machine, not the quality of the machine. Our promising results indicate that, after parameters were adjusted with intelligent selection algorithms, the proposed CAD system performed well both with the same and with different systems. Different resolutions, different settings, and different scanner ages are no longer obstacles in the application of such a CAD system.

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