DEVELOPING A COMPUTER-AIDED DIAGNOSIS SYSTEM FOR CLASSIFICATION OF MALIGNANT BREAST TUMOR GRADE IN ULTRASOUND IMAGING

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Abstract: This work developed a computer-aided diagnosis (CAD) system for discriminating malignant grades of breast tumors in three-dimensional (3D) ultrasound (US) imaging. US imaging is a widely used noninvasive detection approach for breast cancer. The grades of breast cancer masses are standard prognostic indicators in patients. Knowing the tumor grades allows doctors to be more selective in their diagnosis and to appropriately determine the treatment to the patients. In this study, a total of 148 3D US images of malignant breast tumors were obtained. The tumor masses were segmented. The patient's age, texture, morphological, ellipsoid fitting features, and were quantified to describe the characteristics of the tumor masses. A support vector machine (SVM) model was then developed using machine learning algorithms to classify breast tumor grades. Performance of the proposed approach was evaluated using ten-fold cross-validation. It is demonstrated that the developed CAD system can effectively classify between low and high grades of breast tumors.

Key Words: Breast tumor, Three-dimensional ultrasound image, Machine learning, Image processing.

INTRODUCTION

Breast cancer is a leading cause of death for women throughout the world (Jemal et al., 2006). Early detection is essential for improving the patient survival rate. In previous decades, ultrasound (US) imaging has been reported as an effective method for screening breast cancer because of its low cost, high efficacy, real-time results, and lack of radiation. Grade of a malignant tumor is a measure of the tumor abnormality. According to the Nottingham's grading system, breast cancers can be categorized into 3 grades (Elston and Ellis, 1991; Genestie et al., 1998; Elston, 2005). Tumor grading has been regarded as the important...
prognostic indicator (Rakha et al., 2010). The tumor grade information is essential for helping the doctors to decide appropriate treatments for the patients.

Analysis of sonographic characteristics can assist in differentiating breast tumor grades by using BI-RADS (American College of Radiology, 2003) criteria (Kim et al., 2008; Aho et al., 2013; Wojcinski et al., 2013). The BI-RADS®-US lexicon classification for breast tumors provides a variety of categories, such as morphological and textural features. Experienced physicians evaluate breast tumor according to BI-RADS. However, US images are usually speckled and include tissue-related textures. The image interpretation is operator-dependent (Huang et al., 2008). Hence, computer-aided diagnosis (CAD) system is developed to enhance the diagnostic accuracy.

In this study, a CAD (Huang et al., 2008; Chen et al., 2009; Chen et al., 2011; Moon et al., 2011) system was proposed for discriminating tumor grade with 3D US imaging. The specific objectives were as follows: (1) to quantify the features of the breast cancer on US image; (2) to develop a model for distinguishing between high grade and low grade tumors by using the feature sets; and (3) to evaluate the performance levels of developed model. In the process, volumetric US breast images were collected, and the tumor lesions were segmented based on the images. The textural, morphological, and ellipsoid fitting features of these tumor masses were then quantified. A support vector machine (SVM) classifier was then developed to distinguish tumor grades with the different features. The performance of developed models was assessed by receiver operating characteristic (ROC) analysis.

MATERIALS AND METHODS

IMAGE ACQUISITION

The breast US images used in this study were samples of diagnostic cases obtained during routine clinical care at Changhua Christian Hospital (Changhua, Taiwan). The images were acquired using a US scanner (Voluson 730; GE Healthcare, Zipf, Austria) equipped with a 5.6-18 MHz volume transducer (RSP6-16; GE Healthcare, Zipf, Austria). All images were collected from patients diagnosed between June 2007 and August 2009. The ages of the patients ranged from 24 to 87 years (mean 51.3 years). Regarding patients that exhibited multiple tumor masses, only images of the largest lesion were collected from the database. The grades of the tumors were identified based on a pathological diagnosis, involving biopsy methods and the Nottingham’s grading system. The numbers of grade 1, 2, and 3 tumors were 25, 94, and 29. In this study, grade 1 and 2 were defined as low grade, whereas grade 3 was considered as high grade. The US images were converted into 3D grey-level images in a Cartesian coordinate system by using 4D View software (Chang et al., 2012). The mean voxel resolution was 0.2 mm. The ethics committee of the hospital approved the study. No patient identification was disclosed in an effort to avoid diagnosis bias and ensure patient privacy.

TUMOR SEGMENTATION

Tumor segmentation was performed to extract the region of the tumor before quantifying the lesion features. The tumor masses were semiautomatically segmented using ITK-SNAP software (Yushkevich et al., 2006), which performed active contouring based on level set.
algorithm (Osher and Sethian, 1988; Sethian, 1999). The operators identified the lesions in the US images, then placed seeds (i.e., starting points) at appropriate locations inside the tumor masses. The seeds expanded until they reached the tumor boundaries. Appropriate control parameters were set to ensure optimal segmentation results were attained (Yushkevich et al., 2006). Compared with manual methods, semiautomatic segmentation is more consistent and less laborious when sketching precise contours and is particularly suitable for use with 3D US images. Figure 1 shows a segmented volumetric tumor mass.

![Figure 1. The sonographic A-, B-, and C-view and segmented volumetric tumor mass using ITK-SNAP.](image)

**FEATURE QUANTIFICATION**

Features were used to describe the characteristics of tumors for classification. They could be categorized into three sets – textural, morphological and ellipsoid fitting features. The age of the patient was an important attribute and was also considered as a feature.

The textural features quantify the spatial correlation of voxel gray levels of the tumor mass. The textural features were calculated based on the gray level co-occurrence matrix (GLCM; (Haralick et al., 1973) $P_d$ of volumetric images (Chen et al., 2007). In the process, the US images were quantized to 16 gray levels. The frequencies of gray level differences between 2 adjacent voxels in the images then were cumulated to form the $P_d$ (Chen et al., 2007). In this study, a displacement vector $d$ was defined to represent the geometric relationship between the 2 adjacent voxels. The vector $d$ was set to be (1,1,1), (1,0,0), (0,1,0), and (0,0,1) in this study. Afterward, 6 textural feature were calculated based on the GLCM, including the angular second moment $T_{ASM}$, contrast $T_{Con}$, inverse different moment $T_{I}$, entropy $T_{E}$, dissimilarity $T_{D}$, and correlation $T_{Cor}$ (Haralick et al., 1973; Jobanputra and Clausi, 2004). For instance, the $T_{Con(0,1,0)}$ feature represent the contrast feature evaluated by GLCM $P_{(0,1,0)}$ in vector (0,1,0). A total of 24 textural features were included in this study.

The morphological features (Huang et al., 2008) describe the superficial and boundary regularity of the tumor masses. There were 6 morphological features included in this study.
Tumor volume $M_v$ (unit: mm$^3$) and tumor surface area $M_A$ (unit: mm$^2$) assess basic structural characteristics of the tumor mass. Classical compactness $M_{Cc}$ describes the degree of similarity between a tumor mass and its optimally fitted sphere, and discrete compactness $M_{Cd}$ describes the degree of similarity between a tumor mass and its optimally fitted cube (Bribiesca, 2008; Moon et al., 2011). The mean radius $M_{Rm}$ and standard deviation of radius $M_{Rstd}$ were used as indices to represent the characteristics of irregular tumor surface.

The ellipsoid fitting features (Moon et al., 2011) describe the degree of similarity between a tumor mass and its optimally fitted ellipsoid. The optimally fitted ellipse can be regarded as the baseline for measuring the degree of shape irregularity of the tumor mass. Nine ellipsoid fitting features were applied in this study. Three of them were related to the properties with the ellipsoid and the tumor, including axis ratio $E_A$, surface ratio $E_S$, and volume covering ratio $E_V$. The outside region $E_{RO}$ and inside region $E_{RI}$ quantified the numbers of regions of a tumor outside and inside, respectively, its best-fitted ellipsoid. The sum of regions $E_R$ is the sum of outside and inside regions $E_{RO}$ and $E_{RI}$. The angularity is used to evaluate the protruding level in the outside region and indenting level in inside region. The feature $E_{ROa}$ is the number of regions whose angularity is larger than a threshold for outside region. Similarly, the feature $E_{RIa}$ is the number of regions whose angularity is smaller than a threshold for inside region. The feature $E_{Ra}$ is the sum of $E_{ROa}$ and $E_{RIa}$.

**TUMOR GRADE CLASSIFICATION**

SVM classifiers were developed to differentiate high and low grade tumors. The patient’s age, textural, morphological, and ellipsoid fitting features were model inputs. In this study, a soft margin SVM classifier with radial basis function kernel was developed using LIBSVM (Chang and Lin, 2011). The margin and parameters were determined using grid search. The dataset used in this study was unbalanced (119 and 29 of the low-grade and high-grade tumors). In the model development, the soft margin parameter ratio was set to be the inverse of the tumor number ratio between the two grades (Ben-Hur and Weston, 2010). The details of model parameter selection can be referred to LIBSVM (Chang and Lin, 2011).

**PERFORMANCE EVALUATION**

ROC analysis was applied to measure the performance levels of the developed CAD systems with ten-fold cross-validation (CV). Six indices were calculated: the area under the curve ($A_Z$), accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (Hanley and McNeil, 1982). The sensitivity and specificity were defined as the percentages of actual high-grade and low-grade tumors, respectively, that were correctly classified. The PPV was defined as the percentage of predicted high-grade tumors which were correctly classified, and NPV was defined as the percentage of predicted low-grade tumors correctly classified. $A_Z$ is a measure of the overall performance of a model. The calculation of the ROC indices was performed using MATLAB (MathWorks, Inc.).

**RESULTS & DISCUSSION**

A SVM model was developed to discriminate the low-grade and high-grade tumors using 24 textural, 6 morphological, 9 ellipsoid fitting features, and patient's age as the inputs. Table 1 shows the classifier performance in terms of the 6 ROC indices. Accurate diagnosis of
high-grade tumor is crucial for a CAD system. High-grade tumors are more threatening. Misdiagnosing a high-grade tumor may increase risk of harm to life and should be avoided. Therefore, the sensitivity and NPV are 2 critical indices for evaluating the performance of the CAD system. Although the current model achieved a reasonable accuracy (75.0%), the sensitivity (55.17%) given by the proposed approach needed to be improved.

Table 1. ROC indices of the classifier

<table>
<thead>
<tr>
<th>Index</th>
<th>Value</th>
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<tbody>
<tr>
<td>Accuracy</td>
<td>75.00%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>55.17%</td>
</tr>
<tr>
<td>Specificity</td>
<td>79.83%</td>
</tr>
<tr>
<td>PPV</td>
<td>40.00%</td>
</tr>
<tr>
<td>NPV</td>
<td>87.96%</td>
</tr>
<tr>
<td>$A_Z$</td>
<td>0.6620</td>
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</tbody>
</table>

CONCLUSIONS

This study proposed a CAD system to be used with 3D US imaging for discriminating grades of breast cancer lesions. The textural, morphological, and ellipsoid fitting features were quantified from US images and were used to present the characteristics of the tumors. Then a SVM classifier was applied to distinguish low-grade and high-grade tumors using these features as input. The future works include improvement of the model sensitivity.

REFERENCES


