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● *Original Contribution*

CLASSIFICATION OF THE THYROID NODULES BASED ON CHARACTERISTIC SONOGRAPHIC TEXTURAL FEATURE AND CORRELATED HISTOPATHOLOGY USING HIERARCHICAL SUPPORT VECTOR MACHINES

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Abstract—In this study, the ultrasound images of thyroid nodules were classified to facilitate clinical diagnosis and management. The hierarchical support vector machines (SVM) classification system was used to select the characteristic sonographic textural feature that represents the major histopathologic components of the thyroid nodules. Two ultrasound systems (LA39 and i12L mentioned in the Materials and Methods section) were used for comparison. Seventy-six thyroid nodular lesions and 157 regions-of-interest thyroid ultrasound image from each system were recruited in the study. The parameters affecting image acquisition were kept in the same condition for all lesions. Commonly used texture analysis methods were applied to characterize thyroid ultrasound images. Image features were classified according to the corresponding pathologic findings. To estimate their relevance and performance to classification, SVMs were used as a feature selector and a classifier. The thyroid nodules are first categorized as two main types, *i.e.*, follicle base and fibrosis base nodule, by sum average. The follicle base nodules can be further and completely classified into follicles with few cells, follicles with follicular cells and follicles with papillary cancer cells by run length nonuniformity (RLNU). The fibrosis base nodules are further classified by sum square into fibrosis with few cells and fibrosis with dominant cells. The fibrosis base neoplasm with dominant cells can be separated into fibrosis with follicular cells and fibrosis with papillary cancer cells by entropy. The hierarchical SVM classification system achieves a diagnostic accuracy between 96.34% and 100%. Besides, the best sonographic textural feature can be selected by the system for the differentiation between the follicle and fibrosis base thyroid nodules or the cell types mixed in them. In follicle base thyroid nodules, papillary cancers show higher sonographic textural RLNU but less than follicular cells. In fibrosis base thyroid nodules, papillary cancers show increased sonographic textural variance and entropy. (E-mail: a120930@tzuchi.com.tw) **Crown Copyright © 2010 Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Thyroid nodule, Sonographic image, Textural analysis, Histopathologic components, Tissue characterization, Support vector machine.**

INTRODUCTION

Thyroid nodules contain various sonographic textural features. The echo pattern of nodular goiter, thyroid adenoma or thyroid carcinoma can be isoechoic, hyperechoic or hypoechoic. No ultrasound feature has both a high sensitivity and a high positive predictive value for thyroid cancer (Frates et al. 2005). The nonspecific sonographic findings make the differential diagnosis of thyroid nodules difficult.

Chen et al. (2009) tried to correlate the texture of thyroid nodules in sonographic images with their histopathologic findings. In that study, the thyroid nodules were divided into two main types, *i.e.*, follicle base and fibrosis base nodule. Each main type is further divided into subcategories. The Relief-F method was used to select one out of various feature measurements for the differentiation between follicle and fibrosis. The result shows that the sum average (a feature derived from

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co-occurrence matrix, as shown in Appendix A) is the most effective sonographic textural feature with values in a specific range and significantly different for follicle and fibrosis base nodules. The difference sum average value of a follicle base nodule is significantly higher than that of a fibrosis base nodule. Among follicle base nodules, the follicles subcategory shows the highest difference sum average value. On the other hand, the fibrosis subcategory shows the lowest difference sum average value among fibrosis base nodules. Subcategories such as dominant follicular cells or papillary cancer cells in follicle or fibrosis base nodules have intermediate values. The connection between a thyroid nodule type and its textural representation was thus established, which could be helpful in interpreting thyroid nodules based on their ultrasound textures. However, the values of one main nodule type may overlap with those of the other, and this potential overlap becomes more significant when nodular subcategories are considered. Therefore, a single feature cannot be used as a criterion to divide nodules into different categories, nor to accurately classify nodules.

The aim of the study is to select the significant features towards a complete classification of common thyroid nodules using hierarchical support vector machines (SVMs) (see Appendix B). The accuracy of classification will be assessed rather than statistically different values between the classes, as reported in the previous study (Chen et al. 2009). We will highlight the image-pathology correlation for each classification by the coupling of ultrasound image analysis with histopathology. The selected typical textural features and their related ultrasound images will also be compared between the classes of thyroid nodules.

MATERIALS AND METHODS

We used the same data set as was used in the Chen's article (2009). Sixty-one patients (48 females, 13 males, age range: 23–82 years old) with 76 thyroid nodular lesions were recruited and the study was approved by ethics committee of Buddhist Dalin Tzu Chi General Hospital. All patients consented to the ultrasound evaluation, fine needle aspiration, surgery and pathologic examination due to malignancy, suspicious neoplasm by fine needle aspiration, cosmetic reasons or symptoms of concern. The ultrasound imaging machine used in our clinic is a GE LOGIQ 700 (General Electric Healthcare, Chalfant St. Giles, UK). Two ultrasound probe systems, LA39 and i12L (General Electric Healthcare, Chalfant St. Giles, UK), were used. The first probe (LA39) is a B-mode linear array with an operation frequency range of 5 to 10 MHz (system 1). All the acquisition settings were kept constant (dynamic range, 78 dB; gain, 34; edge enhance, E2; gray map, MC; frame average settings, A2) for all the patients except for the focus number and position. Also, we adjusted the gain to obtain an optimal representation even of deep-located nodules. To evaluate if there were differences for the image acquisition settings of the same thyroid nodule, a second probe of B-mode linear array (i12L) with the operation frequency for 6-11 MHz (system 2) was used for comparison. The parameters used were as follows: dynamic range, 69 dB; gain, 34; edge enhance, E3; gray map, MC; frame average settings, A3 (GE Healthcare 1999).

ROI sonographic images of thyroid nodules

Before surgical removal of the nodules, the sonographic images were obtained during the scan of the longitudinal section of the thyroid nodule. Only nodules with uniform echo pattern were analyzed. Heterogeneous nodules with complex echo texture were not used. For each nodule, only the image with the maximum longitudinal section was analyzed. The location and size of the nodules were recorded. After surgical removal of the nodules, the gross specimen was examined and several pathologic slices were made according to the scan imaging plane. Through routine paraffin embedding and hematoxylin-eosin (H&E) staining, the histopathologic findings corresponding to the sonogram were reviewed *via* light microscopy by an experienced pathologist.

Similar to the uniform echo pattern of the sonography, the histopathologic findings were found to have consistent feature for the slices by the pathologist and were classified as enlarged follicles, follicular cells with follicles, papillary cancer cells with follicles, follicular cells with fibrosis, papillary cancer cells with fibrosis and fibrosis. After correlation of the sonogram and the corresponding pathologic slice, the largest rectangular region-of-interest (ROI) ultrasound image containing the above classified histopathologic feature was selected manually by an experienced radiologist and verified by the pathologist. An ROI example is shown in Figure 1. The cystic area in pathologic specimen is poorly fixed and the sonographic image quality inside and posterior to the calcification and artifacts is substandard, therefore, the cystic areas, calcification and artifacts were excluded in the study. Several ROIs may be used to cover the disconnected interested areas of the same nodule (Fig. 2).

Feature extraction

Methods including statistical feature matrix (Wu and Chen 1992) (Appendix C), co-occurrence matrix (Haralick et al. 1973; Baraldi and Parmiggiani 1995) (Appendix A), Laws' texture (Wu et al. 1992) (Appendix D), neighboring gray level dependence matrix (Wee and Sun 1983) (Appendix E) and gray level run-length matrix (Loh et al. 1988) (Appendix F) were applied in feature extraction of ROI thyroid ultrasound