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Computer-Aided Grading of Lymphangioleiomyomatosis (LAM) using HRCT

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Abstract

Lymphangioleiomyomatosis (LAM) is a multisystem disorder associated with proliferation of smooth muscle-like cells, which leads to destruction of lung parenchyma. Subjective grading of LAM on HRCT is imprecise and can be arduous especially in cases with severe involvement. We propose a computer-aided evaluation system that grades LAM involvement based on analysis of lung texture patterns. A committee of support vector machines is employed for classification. The system was tested on 36 patients. The computer grade demonstrates good correlation with subjective radiologist grade ($R=0.91$, $p<0.0001$) and pulmonary functional tests ($R=0.85$, $p<0.0001$). The grade also provides precise progression assessment of disease over time.

1. Introduction

Lymphangioleiomyomatosis (LAM), a multisystem disorder affecting primarily women of childbearing age, is associated with proliferation of smooth muscle-like cells, “LAM cells”, leading to destruction of lung parenchyma, with cyst formation, lymphatic abnormalities, and abdominal tumors [1]. The most common pulmonary function abnormalities in patients with LAM are impairment of gas exchange, with a decrease in the diffusing capacity of the lung for carbon monoxide (DLCO), and airflow obstruction.

High resolution CT (HRCT) of the chest is currently the most definitive imaging technique for diagnosing LAM. It also provides the capability to assess the degree of pulmonary involvement. On a CT scan, the presence of thin-walled cysts uniformly spread throughout the lung is a notable characteristic of LAM.

Radiologists normally grade lung LAM disease by its severity (minimal, moderate and severe). Typical examples of LAM are shown in Figure 1. This method of grading is subjective, imprecise and can be arduous. Therefore, we conducted an investigation to develop a computer-aided evaluation system to grade the severity of lung disease in LAM.

2. Background

Computed-aided diagnosis (CAD) of lung disease is still an open research area. Different types of tissues and pathologies manifest different texture patterns on lung CT images. Hence, textures are one of the most important image attributes to identify, characterize, compare and distinguish objects and regions. Several texture-based recognition systems have been developed to detect and classify pulmonary tissue patterns. [2] was a survey article on computer analysis of lung CT. [3] introduced a technique called Adaptive Multiple Feature Method for the classification of pulmonary tissue patterns into six groups. [4]

proposed a 3D texture analysis method based on morphological analysis. [5] investigated the texture block selection, data reduction, and texture smoothing in CAD system for lung fibrosis. [6] compared three classification techniques in lung CAD systems and concluded that support vector machines achieved the best performance.

None of the previous detection systems explicitly targeted LAM. In this paper, we propose a texture-based detection and classification method that by using statistical texture analysis, advanced texture correlation, and a committee of support vector machines (SVM), that can find, distinguish, and diagnose areas where LAM exists, and grade its severity.

3. Methods

The proposed CAD system extensively analyzes 2D texture patterns to classify and distinguish between regions affected by LAM and normal lung regions. Our CAD system consists of five stages: *Segmentation*, *Texture Analysis*, *Training*, *Classification*, and *Grading*. Figure 2 presents a diagram of the proposed system.

3.1 Lung Segmentation

Human lungs are composed of several anatomical entities that have to be segmented before any analysis and classification can be performed. Lung segmentation relies on the grayscale contrast between the lungs and surrounding tissues and the texture patterns of different lung tissues.

We have developed a segmentation technique based on region-growing and dynamic programming that accurately segments the left and right lungs. First, the trachea is located and segmented out. By using the segmented position of the trachea, two seed points are located in the right and left lungs. Then, by using a 2D/3D region-growing algorithm, the seeds are expanded to segment the entire area of the lungs. After the lungs are segmented, a histogram-based threshold technique is used to remove blood vessels and refine the segmentation step. Finally, a rolling ball algorithm is applied to smooth the lung boundary.

Figure 3 shows the results of our lung segmentation technique. As part of the segmentation process, we distinguish between the left and right lung and compute the actual volume in each lung.

3.2 Texture analysis

Once a segmented lung is obtained, the image is subdivided into blocks. For each block, a characteristic multi-dimensional feature vector is computed. By default, an 8×8 kernel with a 4-pixel margin on each side is used as the texture block (16×16 in sizes) to compute the characteristic texture features; however the software provides the flexibility to change the texture block size as needed. Figure 4 shows a set of texture kernels for normal lung and LAM regions. A multi-dimensional feature vector is computed and used to differentiate and group each texture block.

The multi-dimensional feature vector is composed of 25 different texture features, including mean and variance features from histogram statistics, energy and entropy features from co-occurrence matrix, and short-run and long-run emphasis features from run-length matrix. Table 1 lists the 25 texture features computed for each texture block.

The proposed CAD system relies heavily on co-occurrence and run-length matrices for texture analysis and therefore, classification. Run-length matrices are based on the assumption that long gray-level runs would occur more often in an image than short runs, which represent fine textures. Most of the run-length matrices used in our system were

proved in [7] to be excellent in preserving texture information. Co-occurrence matrices are used to measure the frequency that a grayscale value appears in relation to another grayscale value on the image. [8] presented 14 texture features that can be obtained automatically from a co-occurrence matrix including contrast, correlation, variance, and entropy.

3.3 Training

In the training stage the computer learns the properties and texture patterns of normal lung and LAM regions. Since the training process is critical to the overall results of the system, four steps were followed to achieve an accurate training process:

1. A radiologist expert in lung diseases manually selected portions of the HRCT images and classified them into two classes: normal or LAM.
2. The areas manually selected by the radiologist were divided in kernel blocks. As explained in section 3.2, the default kernel size was 8×8 with 4 pixels of margin in each side.
3. The 25 statistical texture features were computed for each texture block.
4. The set of feature vectors and texture kernels were input to a support vector machine that dynamically selected the committee of features that best distinguished normal lung and LAM regions.

3.4 Classification process

The fourth step of the pipeline is classification. During the classification stage, the computer automatically groups the segmented lung as normal or as a LAM region. This is based on the information provided and learned from the expert's selection.

The underlying classification algorithm used in our CAD system is a committee of support vector machines (SVM). SVM is a supervised learning method that uses hyperplanes in a high dimensional space to classify and geometrically divide features among classes [9]. It has been shown that an SVM committee configuration can improve the overall accuracy by taking a very high dimensional feature vector and breaking it down to subsets of lower dimension [10]. The members of the committee work collaboratively to reach the classification decision.

In this paper we introduce the use of such a technique to evaluate lung LAM disease. A forward stepwise feature selection method is first conducted to obtain a set of top performing 3-feature vectors. Then a committee optimization process is performed to form a seven member SVM committee [10].

After the initial classification, the classification result inside each texture block is further refined. The histogram of the lung region is first computed and the threshold value for the normal lung tissue is calculated using a K-means clustering algorithm [11]. Then this threshold value is used to further classify the actual pixels inside the already classified texture block. The system presents the results by overlaying a color mask on top of the HRCT image, as shown in figure 5.

3.5 Grading

Finally the severity of LAM is graded as the percentage of classified LAM regions over the entire segmented lung regions,

$$CG = V_{\text{LAM}} / V_{\text{Lung}}$$

here CG is the computer grade, V_{LAM} is the volume of classified LAM region, and V_{Lung} is the volume of segmented lung.

4. Results and discussion

Our evaluation system was tested on 36 patients. Each patient had a baseline HRCT study and yearly follow-up studies for 5 years. The HRCT contains 9–13 slices and the slice thickness ranges from 1mm–1.25mm. For each study, an experienced radiologist visually examined the HRCT and subjectively graded the severity of lung LAM disease as follows: the lungs were divided into three sections (upper, mid, and lower); the extent of involvement in each section group was classified into one of three grades based on the fraction of the lungs judged as abnormal (grade 1 if $< 1/3$ of the lungs were involved; grade 2 of $1/3$ to $2/3$; grade 3 if $> 2/3$); the grades of the three sections were added to provide an overall severity grade for each study. Lung diffusion capacity for carbon monoxide (DLCO) was also measured at the time of each patient's visit.

We separated the baseline and 5th-year follow-up data and conducted the regression analysis on each data separately (Figure 6). The correlations between computer grade (CG) and radiologist grade (RG) are $R=0.91$ ($p<0.001$) and 0.86 ($p<0.001$) for baseline and follow-up studies. The correlations between CG and DLCO are $R=0.85$ ($p<0.001$) and 0.81 ($p<0.001$). The results indicate that CG can be reliably used to replace the subjective RG. Furthermore, the regression lines of CGs of baseline and follow-up studies are parallel and well separated (Figure 6.1 and 6.2) while those of RGs are collapsed together (Figure 6.3). The results imply that CG is more precise in evaluating the changes of LAM than RG when the DLCO test is used as reference.

For five patients in our cohort, we retrieved all six years data from baseline to 5th year follow-up and analyzed the trend of LAM progression. The trend was validated against the trend in DLCO test. The results are plotted in Figure 7. This result further indicates that our computer grade is precise in evaluating the disease progression since similar trend is demonstrated in both tests.

In conclusion, the computer grading of the severity of lung LAM disease based on texture patterns provides an objective quantitative index that correlates with subjective assessment, pulmonary functions and progression of disease over time. This CAD system allows for quantification of LAM of baseline and follow-up studies without the direct supervision of a radiologist.

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Figure 1. Examples of LAM in HRCT
Left: minimal, Middle: moderate, Right: severe

Figure 2. System diagram

Figure 3. Lung segmentation results
Left: input image, Right: segmented image

Figure 4. Texture examples
First row: normal, Second row: LAM

Figure 5. LAM evaluation results
Red: normal lung, Green: LAM

Figure 6. Regression analysis

Figure 7. Progression analysis over 5 years

Table 1

List of texture features

Histogram Statistics	Co-occurrence Matrix	Run-Length Matrix
Mean	Energy	Long run emphasis
Skewness	Inertia difference	Run length non-uniformity
Deviation	Correlation	Low gray-level run emphasis
Variance	Average difference	Short run low gray-level emphasis
Kurtosis	Entropy difference	Long run low gray-level emphasis
	Inertia	Short run high gray-level emphasis
	Entropy	Long run high gray-level emphasis
	Average sum	Short run emphasis
	Entropy sum	Run gray-level non-uniformity
		Run percentage
		High gray-level run emphasis