Ground-Glass-Opacity Nodule Detection and Segmentation Based on Dot Filter and Gaussian Mixture Model Hidden Markov Random Field

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Aiming at solving the problem that ground-glass-opacity (GGO) nodules cannot be detected directly by “dot” filter, a method based on vessel elimination and “dot” filter was used to detect them. Because of spatial properties consideration, it is proposed to use hidden Markov random field based on Gaussian Mixture Model (GMM-HMRF) and Expectation-Maximization (EM) algorithm to segment GGO nodule in this paper. Experiments were performed at 87 scans of CT images of lung alveoli (containing 36 GGO nodule). The sensitivity of the detection method was 83.3%. The time cost was 1.2 minutes per scan. The accuracy of the segmentation method was 80.9%. This new methods are superior to the existing methods on the required time and sensitivity.

Keywords: GGO Nodule, Detection, Segmentation, Dot Filter, GMM-HMRF.

1. INTRODUCTION

Lung cancer is the highest mortality in all kinds of cancers. Pulmonary nodule is the presentation of lung cancer in CT image. Early detection of pulmonary nodule plays a major role in improving the cure rate. Small pulmonary nodules, whose diameter are only about 3 mm to 3 cm, are always missed when the doctor uses CT to detect it, due to the fatigue of visualizing. Nodules can be classified in solid and ground glass opacity (GGO). The type of solid pulmonary nodule is a spherical object whose CT value is similar with vascular CT value. This type nodule can be observed in the mediastinal window by doctors. The GGO nodule is a fuzzy object whose CT value is smaller than vascular CT value and thus cannot be observed in the mediastinal window by doctors. The presentation of the GGO nodule determines that it is difficult to be detected. Generally speaking, nodules with GGO characteristics are either part solid (consisting of solid components and GGO components) or nonsolid (pure GGO). GGO is the largest probability malignant nodule. Studies on lung solid nodule detection are reported frequently by other authors. However, few studies worked on GGO nodule detection and segmentation. This paper proposes a new low dose CT (LDCT) lung GGO nodule detection and segmentation method. The detection method is based on the vascular rejection and Hessian matrix.

The segmentation method employs a Hidden Markov random field based on Gaussian Mixture Model (GMM-HMRF).

1.1. Previous Work on GGO Detection and Segmentation

For detection of GGO nodules, Kim et al. used texture features and a three-layered neural network to detect GGOs. They tested on 14 scans with tube dose from 200 to 400 MA and achieved a sensitivity of 94.3%. Zhou et al. developed a boosting K-Nearest Neighbour (KNN) classifier for automatic detection of GGO. The detected GGO region was then automatically segmented by analyzing the texture likelihood map. They applied their method to chest CT with 10 GGOs. The method detected all of the ten nodules with only 1FP. Ye et al. used dot filter and anti-geometric diffusion to get GGO candidates, then rule-based filtering is applied to reduce false positive objects. The experimental results indicate an average detection rate of 90.2% for 35 GGOs, with approximately 8.2 FP/scans. Tao et al. propose a novel multi-level learning based framework that seamlessly integrates segmentation and detection to improve the overall accuracy for GGO detection. Zhu et al. combine adaptive models of maximum a posteriori (AMAP) with the simulated annealing algorithm to segment GGO. They achieved segmentation results of 86.94%, 94.33%, and 94.06% for 41 GGOs in average sensitivity, specificity and accuracy.
1.2. Our Approach

Because the CT value of GGO nodule is less than that of the vessel but greater than the CT value of lung parenchyma region, dot filter cannot be used in GGO nodule detection directly. Figure 1 is a pulmonary image contained GGO using green arrow to point the GGO nodules and indicates candidate points in red detected by dot filter. The numbers of slices in one GGO nodule are very small, even only one slice for the GGO nodule. Therefore, the 3D Hessian matrix or so-called dot filter cannot detect the candidate GGO nodules, but if we use 2D Hessian matrix, vessels that look like circle objects cannot be distinguished from nodules. These vessels are even easier detected by 2D Hessian matrix because of their higher CT values than GGO nodules. It is shown as Figure 1 that dot filter can only enhance vessels which look like circle objects rather than the GGO nodule. In this paper, we use the following steps to detect GGO nodules. First, extract the lung vessel through the 3D regional growing method; next, filtrate the lung vessels; next, enhance the GGO candidate points in the rest of the highlighted region by the 2D dot filter based on Hessian matrix; then obtain the candidate nodule regions by the 3D regional growing method, analysis the correlation between two adjacent layers of a candidate nodule, and calculate its features (such as area, mean, variance, skewness and kurtosis); finally, remove False Positives (FPs) by SVM classifier.

2. METHODS FOR DETECTION

2.1. Lung Vessels Elimination

First of all, segment lung parenchyma by the method of Ref. [2] as shown in Figure 2. Then extract lung vessel by 3D regional growing. In the 3D regional growing method regards any a highlighted point which belongs to the lung parenchyma as the seed point. The vascular results are shown in Figure 3. At last, obtain the remained region such as Figure 4 of lung parenchyma except the lung vessel.

2.2. Candidate GGO Points Enhancement by Dot Filter

If detect GGO in Figure 4 using dot filter directly, the cost of time will spend a lot. The reason is that so many pixels in Figure 4 need to compute. It is necessary to get the highlighted region using adaptive threshold in this method. Then detect GGO using dot filter in the highlighted region.

For the sphere object detection, the enhanced method based on local shape feature should be used. Model the object of nodule as 2D normal distribution. The function of modeling is as following:

\[ d(x, y) = \exp(\frac{-(x^2 + y^2)}{2\sigma^2}) \]

Let \( \lambda_1, \lambda_2 \) denote the Eigenvalues of 2D Hessian matrix. If \( \lambda_1, \lambda_2 < 0 \) and \( \lambda_1 \approx \lambda_2 \), the pixel is regarded as belonging to a candidate nodule. If \( \lambda_1 \ll \lambda_2 < 0 \), the pixel is considered as belonging to vessel. The function of enhancement is following:

\[
Z_{\text{dot}}(\lambda_1, \lambda_2) = \begin{cases} 
\frac{|\lambda_2|^2}{\lambda_1}, & \lambda_1, \lambda_2 < 0 \\
0, & \text{otherwise}
\end{cases}
\]

Detect GGO candidate points by dot filter of Figure 4, then the result is shown as Figure 5 in red.

2.3. Removing FPs by SVM Classification

Extract the features of candidate nodule regions, such as area, average mean, average variance, average skewness and average kurtosis. Then remove FPs by SVM classification.

SVM (support vector machine) classifier can map nonlinear detachable samples into high dimensional space through kernel function and construct an optimal separating hyper-plane.
The separating hyper-plane is not only able to separate the two types of samples properly, but also make the maximum interval between the two types of samples. The classifier used in this paper is C-SVM, and the kernel function is Radial Basic Function (RBF):

\[ K(xi, xj) = \exp(-\gamma \| xi - xj \|^2) \quad \gamma > 0 \]

where \( \gamma \) is the reciprocal of the number of trained samples in the classifier. When the numbers of the two sides trained sample sets do not balance, the classification results always bias the side which own large number samples. To avoid this phenomenon, in this article the same number trained samples of two sides are used. The adopted classification program is LIBSVM. The result of removing FPs is shown as Figure 6.

### 3. METHODS FOR SEGMENTATION

#### 3.1. GMM-Based HMRF-EM Framework for 3D Segmentation

To properly segment GGO, in this paper, the HMRF-EM framework taking into consideration spatial properties is proposed. According to the result of GGO nodule detection, a VOI (volume of interesting) contained a GGO nodule is obtained adaptively.

For simplicity, we first assume that the intensity distribution of background and foreground to be segmented follows a Gaussian distribution. Given an image \( Y = (y_1, \ldots, y_N) \) where \( N \) is the number of pixels, and each \( y_i \) is the gray-level intensity of a pixel, we want to infer a configuration of labels \( X = (x_1, x_2) \) where \( x_i \in L = \{0, 1\} \). According to the MAP (Maximum a posteriori probability) criterion, we seek the labeling \( X^* \) which satisfies

\[ X^* = \arg \max P(Y | X, \theta)P(X). \]

The prior probability \( P(X) \) is a Gibbs distribution, and the joint likelihood probability is

\[ P(Y | X, \theta) = \prod_i P(y_i | x_i, \theta_i) \]

where \( P(y_i | x_i, \theta_i) \) is a Gaussian distribution with parameters \( \theta_i = (\mu_i, \sigma_i) \).

#### 3.2. EM Algorithm for Parameters Estimation

The major difference between MRF and HMRF is that, in HMRF, the parameter set is learned in an unsupervised manner. In this paper, a natural proposal for solving a HMRF problem is to use the EM algorithm.

EM algorithm needs initial parameter. Use \( k \)-means cluster method \((K = 2)\) to segment VOI of a GGO nodule, firstly. Calculate mean and variant values of the background and foreground and regard them as initial parameters.

The HMRF-EM algorithm is given below:

1. Start with initial parameter set \( \theta^{(0)} \).
2. Calculate the likelihood distribution \( P^{(i)}(y_i | x_i, \theta^{(i)}) \).
3. Using current parameter set \( \theta^{(i)} \) to estimate the labels by MAP estimation:

\[ X^{(i)} = \arg \max P(Y | X, \theta^{(i)})P(X) \]

\[ = \arg \max U(Y | X, \theta^{(i)}) + U(X) \]

(4) Calculate the posterior distribution for all \( k \in K \) and all pixels using the Bayesian rule:

\[ P^{(i)}(k | y_j) = \frac{G(y_j; \theta_k)P(k | x^{(i)}_y)}{P^{(i)}(y_j)} \]

where \( x^{(i)}_y \) is the neighborhood configuration \( x^{(i)} \) of and

\[ P^{(i)}(y_j) = \sum_{k=1}^{K} G(y_j; \theta_k)P(k | x^{(i)}_y) \]

Note here we have

\[ G(y_j; \theta_k) = \frac{1}{\sqrt{2\pi \sigma^2_j}} \exp \left(-\frac{(y_j - \mu_k)^2}{2\sigma^2_j} \right) \]

(5) Use \( P^{(i)}(k | y_j) \) to update the parameters

\[ \mu^{(i+1)}_k = \frac{\sum P^{(i)}(k | y_j)y_j}{\sum P^{(i)}(k | y_j)} \]

\[ (\sigma^{(i+1)}_k)^2 = \frac{\sum P^{(i)}(k | y_j)(y_j - \mu^{(i+1)}_k)^2}{\sum P^{(i)}(k | y_j)} \]

#### 3.3. MAP Estimation for Labels

The only difference between 2D image segmentation and 3D image segmentation is the neighborhood system. In 2D images, we usually use the 4-neighborhood system, while in 3D images, we usually use the 6-neighborhood system, such as shown in Figure 7. Then the clique potential is defined on pairs of neighboring pixels:

\[ V_c(x_i, x_j) = \frac{1}{2} (1 - I_{x_i, x_j}) \]

where

\[ I_{x_i, x_j} = \begin{cases} 
0 & x_i \neq x_j \\
1 & x_i = x_j
\end{cases} \]
We developed an iterative algorithm to solve
(1) To start with, we have an initial estimate \( X^{(0)} \), which can be from the previous look of the EM algorithm.
(2) Provided \( X^{(k)} \), for all \( 1 \leq i \leq N \), we find
\[
x_i^{(k+1)} = \arg\min_{x_i} \left\{ U(y_i | k) + \sum_{j \in N_i} V_c(x_i, x_j^{(k)}) \right\}
\]
where \( U(Y | X, \theta) = \sum_i [(y_i - \mu_i)/(2\sigma_i^2) + \ln\sigma_i] \) and \( U(X) = \sum_{c \in C} V_c(X) \), \( V_c(X) \) is the clique potential and \( C \) is the set of all possible cliques.
(4) Repeat step 2 until \( U(Y | X, \theta) + U(X) \) stops changing significantly or a maximum \( (k) \) is achieved.

The segmentation result of the GGO nodule is shown in the form of 3D visualization, as shown in Figure 8. In Figure 8, the GGO nodule is described by green color and vessels are described by red color.

4. EXPERIMENTAL DETAILS
4.1. Synthetic Dataset
To validate the proposed algorithms for 3D volume segmentation, we generate a synthetic 3D image of size 50 \( \times \) 50 \( \times \) 50 with a foreground sphere of radius 20 at the center. The intensity of background is 0, and the foreground is 100. Random noise uniformly distributed with [0, 120] is added to the entire image, at all positions. With 10 EM iterations and 10 MAP iterations, the 3D segmentation takes about 14 seconds on a 2.53 GHz Intel(R) Core(TM) i5 CPU. The segmentation result is shown as Figure 9.

4.2. True Dataset
Describe data source and attribute of this paper in Table I. One of the image datasets for the experiment is Lung Image Database Consortium (LIDC)\(^{10}\), the other comes from the first hospital of Guangzhou Medical College. Every nodule is tagged by the doctor can be considered the gold standard. The LIDC data set is composed of CT examinations with 23 nodules from screening and diagnostic studies. All CT images have a matrix of 512 \( \times \) 512 pixels and spacing between 0.605 mm and 0.742 mm. All nodule phantoms were scanned with a 16 rows of detector CT scanner (Somatom Plus 4; Siemens Medical System, Erlangen, Germany). The two parameters of the detector are 120 kVp and 130 mAs. In this paper, we select 4 GGO nodules and 4 FPs randomly to make up of the trained sets for the classifier.

4.3. Experiment Environment
The proposed procedures were implemented using VC++6.0 language in Windows XP environment by using the Insight Segmentation and Registration Toolkit (ITK)\(^{11}\) library for the image processing algorithms. The development and test platform was a PC with 2.53 GHz Intel(R) Core(TM) i5 CPU and 4 GB of RAM memory.

4.4. Evaluation Segmentation Methods
To evaluate the segmentation performance, we calculate overlapping rate to measure error segmentation result including over-segmentation and under-segmentation. All GGO nodules were compared with the reference standard which determined by a radiologist or the gold standard file. The overlapping rate is calculated through the following formula
\[
\text{Overlap} = \frac{|R_{\text{gold}} \cap R_{\text{new}}|}{|R_{\text{gold}} \cup R_{\text{new}}|} \times 100\%
\]

<table>
<thead>
<tr>
<th>Table I. The database for testing the performance in this paper.</th>
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<tbody>
<tr>
<td>LIDC</td>
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<tr>
<td>------</td>
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<tr>
<td>Set of CT Images</td>
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<tr>
<td>Volume of Pixel</td>
</tr>
<tr>
<td>Average number of slice</td>
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<tr>
<td>Number of GGO</td>
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where $R_{\text{gold}}$ and $R_{\text{new}}$ are sets of pixels in the GGO nodule in the proposed segmentation and the reference standard, respectively. Overlap rate is a number between 0 and 1.

4.5. Results and Discussion

The segmentation result of GGO nodule in Figure 1 is shown as Figure 10 by a red outline. According the above evaluation segmentation methods, the accuracy of the segmentation method was 80.9%.

In 30 out of 32 GGO nodules, the proposed method provided successful detection for the dataset of the first hospital in Guangzhou Medical College. All of the GGO nodules in LIDC can be detected in our method. The methods of Refs. [12 and 13] are also re-implemented in the same PC environment as the proposed method. Use correlation analysis between slices to differentiate GGO nodule from a vessel in Ref. [12]. If a GGO nodule only owns one slice, the correlation is small, and the GGO nodule cannot be detected. Only use a threshold value cannot differentiate GGO nodule from the vessel in Ref. [13]. Reference [13] uses high-pass filter based on FFT transform to stretch the histogram, and it wastes so much time. Missing rate and costing time are compared among the three methods shown in Table II.

<table>
<thead>
<tr>
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<th>Miss rate (%)</th>
<th>Cost time (minute)</th>
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<tbody>
<tr>
<td>Paper12</td>
<td>42.5</td>
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</tr>
<tr>
<td>Paper13</td>
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<tr>
<td>The proposed method</td>
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</tbody>
</table>

5. CONCLUSION

Aiming at solving the problem that the 3D dot filter cannot detect GGO nodules, a method based on vessel removing and 2D dot filter was used to detect them. Comparing this proposed method and the existing methods for detecting GGO, the cost time and missing rate are all decreased. The proposed method can be used to detect GGO effectively. In this paper, use GMM-HMRF model and EM algorithm to segment GGO nodule.

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References and Notes


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