Computerized Detection of Pulmonary Nodules on CT Scans

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Helical computed tomography (CT) is the most sensitive imaging modality for detection of pulmonary nodules. However, a single CT examination produces a large quantity of image data. Therefore, a computerized scheme has been developed to automatically detect pulmonary nodules on CT images. This scheme includes both two- and three-dimensional analyses. Within each section, gray-level thresholding methods are used to segment the thorax from the background and then the lungs from the thorax. A rolling ball algorithm is applied to the lung segmentation contours to avoid the loss of juxtapleural nodules. Multiple gray-level thresholds are applied to the volumetric lung regions to identify nodule candidates. These candidates represent both nodules and normal pulmonary structures. For each candidate, two- and three-dimensional geometric and gray-level features are computed. These features are merged with linear discriminant analysis to reduce the number of candidates that correspond to normal structures. This method was applied to a 17-case database. Receiver operating characteristic (ROC) analysis was used to evaluate the automated classifier. Results yielded an area under the ROC curve of 0.93 in the task of classifying candidates detected during thresholding as nodules or nonnodules.

INTRODUCTION

Computed tomography (CT) is the most sensitive imaging modality for detection of pulmonary nodules (1). However, a single thoracic CT examination may result in acquisition of more than 30 separate images for 10-mm reconstruction intervals; recent changes in CT acquisition protocols have increased the number of images in a single examination to more than 60. Each image contains information that must be evaluated by a radiologist and assimilated into the larger context of the volumetric data acquired during the examination.

The vast amount of image data that must be interpreted to detect pulmonary nodules on CT scans has prompted investigators to develop computer-aided diagnostic techniques to detect nodules automatically (2–7). Kanazawa et al (3) and Armato et al (5) performed analyses on individual two-dimensional section images, as did Giger et al.
However, the latter two groups used information from immediately adjacent sections under certain circumstances to complement the analysis of each section. Few three-dimensional approaches to detection of pulmonary nodules on CT scans have been reported. Ryan et al (2) used three-dimensional geometry to model nodules and vessels, and Okumura et al (7) incorporated a three-dimensional morphologic filter into their detection scheme.

We are developing a computerized scheme that uses both two-dimensional and three-dimensional analysis methods to automatically detect pulmonary nodules within the image data that make up a CT study of the thorax. The intent of such a method is to complement the radiologist’s interpretation of CT scans by directing attention to those regions identified as most suspicious. The final diagnostic decision will be based on the expertise of the radiologist, who will incorporate the additional information provided by the computer (8). In this article, we describe our method of nodule detection and its application in selected cases.

**METHOD OF NODULE DETECTION**

Our method of nodule detection is outlined in Figure 1. First, a diagonal gray-level profile is constructed for each CT section to determine a threshold for segmentation of the thorax. A gray-level histogram is then constructed from pixels within the thorax, and the gray level that maximizes the separation between the two main peaks of the histogram is used to segment the lungs. A rolling ball algorithm is applied to the lung segmentation contours to avoid the loss of juxtapleural nodules. Multiple gray-level thresholding is then used to extract three-dimensional nodule candidates from the segmented lung volume. These candidates represent both nodules and normal pulmonary structures. For each candidate, two- and three-dimensional features such as volume, sphericity, maximum compactness, and mean gray level are calculated. To distinguish between nodule candidates that correspond to actual nodules and candidates that correspond to normal anatomy, these features are merged with linear discriminant analysis. Linear discriminant analysis effectively projects the parameter space defined by a set of features to optimize the separation between distributions of two populations (9), which represent nodules and nonnodules in this instance. The ability of linear discriminant analysis to distinguish nodules from nonnodules can be evaluated with a leave-one-out method and receiver operating characteristic (ROC) analysis (10).
Two-dimensional Analysis: Segmentation

Initial analysis of each CT scan is performed on individual sections. For each section, a cumulative gray-level profile is constructed from pixels along a diagonal that extends from the upper corner of the image to the image center (Figs 2, 3). The slope along this cumulative gray-level profile is analyzed to determine a single gray-level threshold for thoracic segmentation (4) (Fig 3). A binary image is then constructed such that all pixels with a corresponding gray level greater than the selected threshold are turned “on” (ie, are assigned a value of 1) and all other pixels are turned “off” (ie, are assigned a value of 0) (Fig 4). The thoracic contour is constructed by delineating the outermost border of the large “on” region in this binary image (Fig 4). All pixels in the original section image that lie within this contour make up the thoracic region, whereas pixels outside this contour are suppressed (Fig 5).

Figures 2–4. (2) Original section image shows the diagonal along which a gray-level profile is constructed for segmentation of the thorax. (3) Cumulative gray-level profile constructed from pixels along the diagonal shown in Figure 2. Pixel location 0 represents the upper left corner of the image. Arrow = selected threshold for segmentation of the thorax. (4) Binary image that results after gray-level thresholding is performed in the original section. The thoracic segmentation contour is also shown.

Figure 5. Segmented thoracic region used to construct a gray-level histogram for lung thresholding.
To segment the lung regions, a gray-level histogram is constructed from the pixels in the thoracic region (Fig 6), and the gray level that maximizes the separation between the two major peaks in this histogram is selected as the gray-level threshold for lung segmentation (4) (Fig 6). A binary image is constructed such that all pixels with a corresponding thoracic region gray level less than the selected threshold are turned on and all other pixels remain off (Fig 7). Analogous to the method for thoracic contour construction, construction of lung contours is performed by delineating the on regions in this binary image (Fig 7). All pixels in the original section image that lie within these contours make up the segmented lung regions, whereas pixels outside these contours are suppressed.

Figure 8 shows the initial lung segmentation contours superimposed on the original section. The gray level selected for lung segmentation has erroneously resulted in the exclusion of a prominent juxtapleural nodule in the right lung.

To compensate for this type of segmentation error, a rolling ball algorithm (5,11) is implemented along the lung segmentation contours. A two-dimensional ball filter is successively placed tangential to each contour point (Fig 9). An indentation is identified when the ball filter contacts the contour at more than one location (Fig 9 [inset]). A new contour segment that linearly connects the endpoints of the indentation is constructed to bridge the indentation, and the image pixels that are newly encompassed by the contours are included within the lung segmentation regions (Fig 10). The final lung segmentation regions are shown in Figure 11.

- **Multiple Gray-Level Thresholding**

The set of segmented lung regions from each section in a CT scan constitutes a lung volume within which multiple gray-level thresholding is performed. At each of 36 equally spaced gray-level thresholds that range in value from 50 to 225, a thresholded lung volume is created. A pixel in the lung regions of each CT section is turned off if its gray level is less than the current gray-level threshold; the values of pixels with gray levels greater than the threshold remain unchanged. As the gray-level threshold increases, the number of remaining pixels in the lung regions of any one section decreases (Fig 12). The result of gray-level thresholding is
Figures 9–11. (9) Initial placement of the rolling ball filter for each lung segmentation contour. The inset shows the filter spanning a contour indentation. (10) Lung segmentation contours after interpolation is used to bridge indentations. White areas indicate regions that have been included within the new lung segmentation regions. (11) Segmented lung regions after implementation of the rolling ball algorithm. These regions are subjected to multiple gray-level thresholding for initial nodule identification.

Figure 12. Pixels that remain on in the section from Figure 11 after thresholding at two of the 36 gray-level thresholds. The threshold used to create a was lower than the threshold used to create b.
demonstrated in a volumetric sense by means of maximum intensity projection (MIP) images (Fig 13).

Three-dimensional Analysis: Identification of Nodule Candidates
At each threshold level, all pixels that remain on are grouped by means of a three-dimensional 10-point connectivity scheme. (The term grouped means that the pixels are identified as belonging to the same three-dimensional structure.) In this scheme, an on pixel (the pixel of interest) within a thresholded lung volume is grouped with all on pixels that exist within a 10-pixel neighborhood composed of (a) the eight pixels that border the pixel of interest in the present section, (b) the pixel spatially corresponding to the pixel of interest in the section immediately above the present section, and (c) the pixel spatially corresponding to the pixel of interest in the section immediately below the present section (Fig 14). This method is applied to all on pixels in each thresholded lung volume. In this manner, individual structures within all 36 thresholded volumes are identified. The geometric volume of each structure is computed by multiplying the number of pixels in the structure by the known voxel dimensions. Structures with a volume less than that of a 3-cm-diameter sphere (ie, 14.1 cm³) make up the set of nodule candidates (Fig 15). The basis for this upper volume bound is the generally accepted maximum size of pathologic structures that may be referred to as a “nodule” when seen on radiographs (12).

Automated Classifier
Nine features are computed for each nodule candidate. These consist of six geometric features (volume, sphericity, radius of the equivalent sphere, maximum compactness, maximum circularity, and maximum eccentricity) and three gray-level features (mean gray level within the structure, standard deviation of the gray level, and the gray-level threshold at which the volume of the structure first decreases below the upper volume bound). Maximum compactness, maximum circularity, and maximum eccentricity are the maximum values of the respective two-dimensional features computed for all sections in which a particular structure exists. The distributions of four of these features are shown in Figures 16 and 17. The values of these features for all nodule candidates are analyzed by a linear discriminant analysis classifier. In this manner, the number of nodule candidates is substantially reduced (Fig 18).

Figure 13. MIP images show the structures that remain on within the complete lung volume at the two gray-level thresholds depicted in Figure 12. These images represent the thresholded volumes as viewed from below with the patient’s left on the right side of the images. The threshold used to create the volume shown in a was lower than the threshold used to create the volume shown in b.
Figure 14. Ten-point connectivity scheme for grouping pixels in three dimensions. The pixel of interest (shown in gray) is identified as belonging to the same structure as all other on pixels within the 10-pixel neighborhood indicated.

Figure 15. MIP image shows the structures that satisfy the maximum volume criterion at any of the 36 threshold levels. These structures form the set of nodule candidates. (A base section that contained a false-positive finding caused by a portion of the left hemidiaphragm was manually eliminated to improve visualization.)

16. Figures 16, 17. (16) Relationship between sphericity and maximum circularity for nodule candidates that correspond to actual nodules (o) and nodule candidates that correspond to nonnodules (stippling). (17) Relationship between maximum eccentricity and maximum compactness for nodule candidates that correspond to actual nodules (o) and nodule candidates that correspond to nonnodules (stippling).
APPLICATION IN SELECTED CASES

The database we collected consisted of 17 clinical helical thoracic CT cases that comprised a total of 493 sections with 187 pulmonary nodules. Cases were selected on the basis of radiology reports that indicated the presence of pulmonary nodules. The clinical CT films for the selected cases were then reviewed by an independent attending chest radiologist (H.M.), who concurred that nodules were present in each case. The specific locations of individual nodules were identified on the films by an experienced chest radiologist, who was asked to make a binary decision regarding the presence of each identified nodule. The effective diameter of the nodules ranged from 3.1 to 27.8 mm. The CT scans were acquired with a HiSpeed Advantage scanner (GE Medical Systems, Milwaukee, Wis) by using our clinical protocol of 1:1 helical pitch, 10-mm collimation, and 10-mm reconstruction intervals. The image matrix size was 512 × 512 pixels, and the field of view had been optimized for each patient during the examination so that the pixel sizes in the database ranged from 0.566 to 0.781 mm.

The gray-level thresholding method combined with the volume criterion yielded a set of nodule candidates that included 82% of the 187 actual nodules. At this initial stage, an average of 796 structures that corresponded to normal anatomy (ie, false-positive findings) were also included per case. A leave-one-out method was used to evaluate the performance of linear discriminant analysis in distinguishing between nodule candidates that corresponded to actual nodules and nodule candidates that corre-
responded to nonnodule structures. In this method, the linear discriminant analysis classifier was trained by using all but one nodule candidate, and the omitted candidate was subsequently used to test the trained classifier. The process of training and testing the classifier was independently repeated until all nodule candidates had been used as the “left out” candidate for testing. Results yielded an area under the ROC curve of 0.93 (Fig 19). An operating point of 85% sensitivity and 89% specificity along this ROC curve indicated an overall sensitivity for nodule detection of 70% with an average of three false-positive findings per section. This outcome corresponded to an 89% reduction in the number of false-positive findings after the application of linear discriminant analysis.

**SUMMARY**

We are developing a computerized method for automated detection of pulmonary nodules on helical thoracic CT scans. The method makes use of gray-level thresholding techniques to segment the lung volume within the image data. Multiple gray-level thresholds are then applied in conjunction with a volume criterion to identify a set of three-dimensional nodule candidates. The number of candidates that correspond to nonnodule structures is reduced by using linear discriminant analysis as an automated classifier. This method demonstrates promising performance in its ability to accurately detect pulmonary nodules on CT scans.

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**REFERENCES**