Semi-Automatic Assessment of Pleural Thickenings: Towards an Early Diagnosis of Pleuramesothelioma

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Abstract. The presented semi-automatic method supports the physician in comparing two temporally consecutive CT data-sets to assess the growth of pleural thickenings, which is crucial for an early diagnosis of pleuramesothelioma. The algorithm performs a supervised range-constraint Otsu thresholding and probabilistic contour relaxation to detect the pleural contours. After surface-based smoothing, an anisotropic diffusion in combination with a model-oriented probabilistic classification specifies then the thickening’s tissue. Quantitative assessment of the detected thickening uses the thin-plate-spline interpolation. Based only on a single user interaction to define anatomic landmarks, a global non-rigid registration of the thickenings’ centroids carries out the matching to fulfill the change follow-up task.

Keywords
Computer-aided diagnosis, statistical estimation and decision, pleuramesothelioma, lung segmentation, lung registration, spatiotemporal matching.

1. Introduction

Pleuramesothelioma is a high-grade malignant tumor on the pleura, i.e., the lung enveloping membrane. It is statistically documented that 70%-90% of malignant pleuramesothelioma can be traced back to asbestos exposure [1]. Without any therapy, a malignant pleuramesothelioma can rapidly lead to death. Thus, an early diagnosis and subsequent therapy are important to extend patients’ life expectation. To detect pleuramesothelioma in its early stage, the diagnostic physician has to examine and observe significant changes in pleural thickenings in consecutive CT scans taken at different points in time (Fig. 1). This diagnosis is a time-consuming and tedious task. A computer-aided diagnosis system should reduce the expenditure of time by providing the physician with a quantitative documentation.

Fig. 1. An original CT image of a patient with pleural thickenings.

2. Materials and Methods

As test data, two temporally consecutive low dose thoracic spiral CT data, which contain each 85 slices of 5 mm thickness with a 4 mm spacing and calculated with a sharp B80s kernel, have been used. The first data-set was acquired in 2006 and the second one in 2007.
2.1 Automatic Pleural Segmentation

An initial segmentation is done using the histogram from the volume data by supervised range-constrained Otsu thresholding twice, combined with 3D connected component labelling, to extract first the thorax from the whole CT data and then the pulmonary organs out of the thorax.

In order to detect and remove trachea and bronchi, the volume-based histogram of connected pulmonary organs is modelled as a finite mixture of Gaussian distributions with all voxels to the Likelihood function:

$$L(\theta) = \prod_{i=1}^{n} p(y_i | \theta)$$

$$= \prod_{i=1}^{n} \sum_{k=1}^{c} \omega_k p_k(y_i | \theta_k)$$

Application of the maximum a posteriori criterion to map all voxels $i$ to discrete labels $x_i \in \{1, \ldots, c\}$:

$$X_k = \arg \max_{x_i \in \{1, \ldots, c\}} p_i(y_i | x_i, \theta)$$

leads to the classification of that pulmonary region (Fig. 2). After removing trachea and bronchi as well as pixels related to partial volume effects and motion artifacts (Fig. 3), left and right lungs are separated.

A Gibbs-Markov random field describes the prior probability $P(X)$ of the Markov random field $X$ that contains the class $x_k \in \{1, \ldots, c\}$ in each CT slice:

$$P(X) = \frac{1}{Z} e^{\frac{-\sum A|x_i| + \sum B|x_i|}{T}},$$

with $Z = \text{const}$, where $n_A$ is the number of horizontal and vertical, and $n_B$ of diagonal inhomogeneous second order cliques. The diagonal potential $B$ is set to $1/\sqrt{2}$, the horizontal and vertical potential $A$ to 1. The maximum a posteriori rule is applied to estimate the optimal final labelling

$$\hat{X} = \arg \max_{x_i \in \{1, \ldots, c\}} p(X | Y)$$

$$= \arg \max_{x_i \in \{1, \ldots, c\}} p(Y | X) P(X).$$

By assuming that $p(Y | X)$ takes a Gaussian distribution, the contour relaxation can be done for all pixels lying along the contour of the current lung region according to:

$$\frac{N_{0|x_0} \ln \sigma_{0|x_0}^2 + N_{0|x_0} \ln \sigma_{1|x_0}^2}{2} + n_{0|x_0} + \frac{n_{0|x_0}}{\sqrt{2}} z_{0|x_0} \leq 1$$

where $N_{0|x_0}$ represents the pixel number in either region $c=1$ for lung, or 0 for outside lung, and $\sigma_{c|x_0}$ is the estimated variance corresponding to the class of $x$, $n_{0|x_0}$ the number of all horizontal and vertical pixels, and $n_{0|x_0}$ the number of diagonal inhomogeneous second order cliques both with the given label $x$, while $N$ is the total number of all pixels (Fig. 4).
2.2 Detection of pleural thickenings

A topology-oriented and tissue-specific detection algorithm was developed which allows the segmentation of pleural thickenings from the surrounding thoracic tissue. The 3D detection of pleural thickenings is accomplished by the new developed adaptive surface-based smoothing (ASBS) algorithm [3].

Since pleural thickenings can be understood as fine-scale occurrences on the rather large-scale lung surface, the applied algorithm creates a “healthy” volume model of the pleura by smoothing the roughliness of the pleural surface by the local adaptation of smoothing degree. This occurred by using an adaptive \( h \times h \) 2D Gaussian smoothing kernel, where the window size \( h \) of the kernel will be changed adaptively according to the degree of local roughliness (Fig. 5). Differences between the healthy model and the original data are considered as initial pleural thickenings.

For a model-based tissue-specific segmentation of pleural thickening, a probabilistic Hounsfield Unit (HU) model for pleural plaques was created. A pre-processing step performs an anisotropic diffusion filtering on the region-of-interest around the initially detected thickenings. For the first estimation, a significance test was carried out to initially label each voxel to be either a member of pleural thickenings tissue or of other residual thoracic tissue. The final determination was carried out with the application of posterior probability in combination with Gibbs-Markov random field (Fig. 6).

2.3 Thin plate spline interpolation

In order to determine the volume of a pleural thickening, a local model of each pleural thickening has to be constructed. Based on the segmented pleura contour on each layer, an interpolation of pleura contour will take place to reconstruct the missing lung wall. The interpolation uses the Thin Plate Spline method, which is reported as suitable for the deformation of biological tissues [4]. Thin plate spline is a physically based 2D interpolation scheme for arbitrarily spaced tabulated data. This technique is used for surface interpolation over scatter data. The spline surface represents a thin metal sheet that is constrained to pass through those grid points.

In order to find the minimizing thin plate spline function, a set of input constraint data, called here as landmark points, is needed to obtain the linear system approximation form of the minimizing function of the thin plate spline. In consideration of calculation time, the number of 4 points turned out to be good enough (Fig. 7).
After the interpolation, numerical integration technique was applied to calculate the detected area lying between the fitted curve by thin plate spline and the pleural contour. With the thickness of each CT slice, the volume of each thickening can be calculated (Fig. 8).

![3D visualization of an interpolated thickening.](image)

**Fig. 8.** 3D visualization of an interpolated thickening.

### 2.4 Semi-automatic registration

Based on the performed volume calculations of the thickenings, two features are used to match pleural thickenings of two temporally consecutive CT data-sets, i.e. 3D centroids of the thickenings \(c=(x,y,z)^T\) and their 3D mean values over all voxels’ Hounsfield units \(\mu\).

Due to differences in patient’s position and respiration phase, a registration of the two thoracic CT scans is done based on a non-rigid transformation with eight degrees of freedom, i.e. translation in \(x\) (transversal), \(y\) (sagittal), \(z\) (vertical), rotation around \(y,z\) and linear scaling in \(x,y,z\). The rotation around \(x\) can be omitted because the CT table prevents the body from moving around the transversal axis. The transformation parameters are obtained from a manual definition of significant anatomic landmarks such as the position of Carina Trachea and the centre of Processus Spinosus.

Difference of each feature \(\nu\in\{x,y,z,\mu\}\) can be calculated as \(\Delta\nu(i,j) = \nu_i - \nu_j\), with \(i=1...I, j=1...J\), where \(I\) is the number of thickenings detected in the first data-set and \(J\) the number of thickenings detected in the second temporally successive CT data-set. Every difference component \(\Delta\nu(i,j)\) is separately normalized on its extreme value in order to obtain a finite and unique feature space, since the range of \(z\) values, representing the number of slices, is different to the range of \(x\) and \(y\) values representing width and height of the slice image [5]:

\[
\hat{\Delta}\nu(i,j) = \frac{\Delta\nu(i,j) - \min_{i,j} \Delta\nu(i,j)}{\min_{i,j} \left(\Delta\nu(i,j) - \min_{i,j} \Delta\nu(i,j)\right)}
\]

To come to a matching of two corresponding thickenings, a decision rule \(i \rightarrow r(i)\) is set up to assign a thickening \(i\) to the thickening \(j\):

\[
r(i) = \arg\min_j \left\{ L(i,j) \right\},
\]

by minimizing the cost function \(L(i,j)\):

\[
L(i,j) = \hat{a}(i,j) + w \|\hat{\Delta}\nu(i,j)\|
\]

consisting of the normalized Euclidian distance \(\hat{a}(i,j)\) between two centroids \(c_i, c_j\)

\[
\hat{a}(i,j) = \sqrt{\hat{\Delta}x^2(i,j) + \hat{\Delta}y^2(i,j) + \hat{\Delta}z^2(i,j)},
\]

and the \(w\) weighted absolute value of the normalized HU mean difference \(\Delta\mu(i,j)\).

Since the HU mean is the feature, which describes the tissue’s character of the thickening, and in order to avoid a decision based only on a topological neighborhood, the difference of HU mean value \(\Delta\mu(i,j)\) should have more influence on the cost function than the topological feature \(\hat{a}(i,j)\). This can be done by assigning a high value to the weight \(w\).

### 3. Results

To evaluate the results of the implemented method, an expert radiologist had to select true thickenings from the list of thickenings, automatically detected in the first step of the system, in both data sets. Then, to be used as gold standard, the thickenings from 2006 were assigned manually to the thickenings found one year later in 2007. After the manual determination of strategic anatomic landmarks through a physician user, the automatic matching was executed.

In the first step of the process, the system found altogether 125 pleural thickenings, i.e. 61 thickenings in 2006 and 64 thickenings in 2007. 56 of 125 were then identified by medical expert as genuine pleural thickenings, 28 in each data set. Among these findings, the radiologist linked 18 pairs of corresponding thickenings, which were taken as reference to be compared with the semi-automatic matches.

Examples of correct computerized matches between thickenings are also illustrated (Fig. 9). Finally, the system reported for each matched result a quantitative measurement of changes of thickening’s characteristics such as volume (Fig. 10). Moreover, accurate location and dimension of each thickening were also given. Each thickening was also traceable since each of them was identified with a unique number.

### 4. Conclusion and Discussion

In order to cope with a time consuming and tedious task of manual investigation of the pleural thickening in the spiral 3D CT data, a system has been developed for automatic detection, manual measurement and visualization...
of pleural thickenings. In this work, a new detection of pleural thickening technique which considers the tissue-similarity, was implemented. The measurement of the detected pleural thickening was then carried out by an automatic interpolation technique, using the 3D Thin Plate Spline interpolation. Moreover, a semi-automatic method which compares thickenings detected on two temporally consecutive CT scans to create a quantitative documentation is now implemented in this system.

![Fig. 9. Examples of computerized matched thickenings. Upper, thickenings found in 2006, lower, in 2007.](image)

![Fig. 10. Semi-automatic spatiotemporal matching shows changes of each matched thickening.](image)

In comparison to the fully manual investigation, the new automatic pre-matching expedites the finding process and allows the physician to diagnose more data-sets on the same expense of time.

The influence of the deviation through manual definition of anatomic landmarks is not critical to the matching results. This conclusion is underlined by a robustness test which was manually repeated ten times and the matching results after each new registration remained the same.

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**References**


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