Automated Assessment System for Pleural Thickenings
Towards an Early Diagnosis of Pleuramesothelioma

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Abstract. Assessment of the growth of pleural thickenings is crucial for an early diagnosis of pleuramesothelioma. The presented automatic system supports the physician in comparing two temporally consecutive CT data-sets to determine this growth. The algorithms perform the determination of the pleural contours. After surface-based smoothing, anisotropic diffusion, a model-oriented probabilistic classification specifies the thickening’s tissue. The volume of each detected thickening is determined. While doctors still have the possibility to supervise the detection results, a full automatic registration carries out the matching of the same thickenings in two consecutive datasets to fulfill the change follow-up, where manual control is still possible thereafter. All algorithms were chosen and designed to meet runtime requirements, which allow an application in the daily routine.

1 Introduction

1.1 Objective

Malignant pleuramesothelioma (MPM) is a high-grade malignant tumor of the pleura, of which 70\%-90\% can be traced back to asbestos exposure [1]. Without any therapy MPM can rapidly lead to death. Thus, an early diagnosis and subsequent therapy are important to extend patients’ life expectancy. To detect MPM in its early stage, physicians have to examine and observe significant changes of pleural thickenings out of consecutive CT scans taken at different points in time from those asbestos-exposed workers (Fig. 1). This diagnosis is not only a time-consuming and tedious task, but underlies both inter- as well as intra-reader variability [2]. An integration of a computer-aided diagnosis system may reduce the expenditure of time by providing the physician with a quantitative and repeatable documentation of the thickenings’ growth rate [3].

1.2 State of the art

A reported semi-automatic computer-assisted system to estimate the dimension of MPM starts with automatic lung detection in combination with an user esti
Observation of thickening’s growth is the key to an early diagnosis of pleuramesothelioma.

Another system for automated detection of pleural thickenings differentiates between diffuse pleural thickenings with its smooth appearance and pleural plaques as local and sharply defined bumps [6]. Pleural plaques are initially detected by subtracting the original segmented lung contour from its convex hull. By applying a radial walk, the lung’s contour is dilated iteratively pixel by pixel. For every pixel of the dilated contours, various features are extracted. These features encode local information for each thickening and are used for later classification. No follow-up study was carried out with this system.

2 Materials and Methods

The implemented system (Fig. 2) consists of the determination of the pleural contours, the detection of the thickening’s tissue, and the volumetry of the detected thickenings. A full automatic registration of two consecutive CT data carries out the matching of the same thickenings to fulfill the change follow-up, while doctors still have the possibility to supervise the assessment results.

Fig. 2. Schematic workflow of the new implemented automated assessment system for pleural thickenings with consecutive CT data as input and the follow-up assessment report as output.
2.1 Automatic segmentation of pleural contour

1. After an initial segmentation using the 3D histogram by supervised range-constrained Otsu thresholding twice, the 3D histogram of connected pulmonary organs is modeled as a finite mixture of \( c \) Gaussian distributions \( p(x, \phi) \) to detect and remove trachea and bronchi. Parameters \( \phi \) are estimated using the Expectation-Maximization algorithm with all \( n \) voxels:

   \[
   L(\phi) = \prod_{i=1}^{n} p(x_i, \phi). \]

   Application of the maximum a posteriori criterion to map all voxels \( i \) to discrete labels \( L_k = \arg\max_{x_k \in \{1, \ldots, c\}} p(i | x_k, \phi) \) leads to the classification of that pulmonary region. After removing trachea and bronchi, left and right lungs are separated.

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

   \[
   P(X) = \frac{1}{Z} \exp \left( -\frac{n_A x_0 + n_B x_1}{2} \right), \quad \text{where} \; Z, T \; \text{are constant}, \; n_A \; \text{is the number of horizontal and vertical, and} \; n_B \; \text{of diagonal inhomogeneous second order cliques}. \]

   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 labeling

   \[
   \hat{X} = \arg\max_{x_k \in \{1, \ldots, c\}} p(X | Y) \propto \arg\max_{x_k \in \{1, \ldots, c\}} p(Y | X) P(X) \quad (1)
   \]

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

   \[
   \frac{N_0 | \hat{x} = 0 \ln \hat{\sigma}^{2}_0 | \hat{x} = 0 + N_1 | \hat{x} = 0 \ln \hat{\sigma}^{1}_0 | \hat{x} = 0 \; \hat{x} = 0 + \sqrt{2} n_B | \hat{x} = 0}{N_0 | \hat{x} = 1 \ln \hat{\sigma}^{2}_0 | \hat{x} = 1 + N_1 | \hat{x} = 1 \ln \hat{\sigma}^{1}_0 | \hat{x} = 1 \; \hat{x} = 1 + \sqrt{2} n_B | \hat{x} = 1} < 1 \quad (2)
   \]

   where \( N_{c|x} \) represents the pixel number in either region \( c = 1 \) for the lung inside, or \( c = 0 \) for the outside, and \( \hat{\sigma}^{2}_c | \hat{x} \) is the estimated variance corresponding to the class of \( \hat{x} \), while \( N \) is the total number of all pixels.

2.2 Detection and volumetry of pleural thickenings

A topology-oriented and tissue-specific detection algorithm was applied which allows the separation of pleural thickenings from the surrounding thoracic tissue. The 3D detection of pleural thickenings is accomplished by the so-called adaptive surface-based smoothing (ASBS) algorithm [7].

1. 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 roughness of the pleural surface by the local adaptation of smoothing degree. Differences between the healthy model and the original data are considered as potential pleural thickenings.
2. For a model-based tissue-specific segmentation, a probabilistic Hounsfield Unit (HU) model for pleural plaques was created. A pre-processing step performs an orientation-based 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.

3. In order to determine the volume of a pleural thickening, all voxels of each thickening are counted, its volume can be calculated according to the voxel dimensions.

2.3 Registration and spatiotemporal matching

Several registration techniques were explored regarding their precision and especially their runtime. Comprising the extracted lung mask from sec. 2.1, a Markov-Gibbs random field based approach yields robust results in a short runtime [8]. Due to the following matching process and the typically size and distribution of the findings, registration accuracy does not have a significant influence on the matching. 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 mean values over all voxels’ Hounsfield units $\mu$.

Difference of each feature $\nu \in \{x, y, z, \mu\}$ can be calculated as $\Delta\nu(i, j) = \nu_j - \nu_i$, with $i = 1 \ldots I$, $j = 1 \ldots J$, 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 [9], 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.

$$\hat{\Delta}\nu(i, j) = \frac{\Delta\nu(i, j) - \min_{j=1\ldots J} (\Delta\nu(i, j))}{\max_{j=1\ldots J} (\Delta\nu(i, j)) - \min_{j=1\ldots J} (\Delta\nu(i, j))} \in [0, 1]$$  (3)

To match two corresponding thickenings, a decision rule $i \mapsto r(i)$ is set up to assign a thickening $i$ to the thickening $j$ by minimizing the cost function

$$r(i) = \arg\min_j \left\{ \sqrt{\hat{\Delta}_x^2(i, j) + \hat{\Delta}_y^2(i, j) + \hat{\Delta}_z^2(i, j)} + w \|\hat{\Delta}\mu(i, j)\| \right\}$$  (4)

consisting of the normalized Euclidean distance between two centroids $c_i$, $c_j$ and the weighted absolute value of the normalized HU mean difference $\hat{\Delta}\mu(i, j)$. Since the HU mean is the feature, which describes the tissue’s character of the thickening, and in order to avoid a decision, only based on a topological neighborhood, difference of HU mean value $\hat{\Delta}\mu(i, j)$ should have more influence on the cost function than the topological feature $\hat{d}(i, j)$. This can be done by assigning a high value to the weight $w$. 
3 Results

In order to realize such a system, different components were implemented, including the handling of DICOM data, the analysis algorithms, and the visualization of the results, based on the software framework MITK [10] (Fig. 3). Physicians’ requirements were taken into account during the development. In order to verify the whole automated system, 20 CT data sets have been applied in two steps. For the reliability of the detection of pleural thickenings, three occupational physicians marked and the machine detected, respectively. This primary analysis was carried out on each CT-slice of two CT data sets, containing 397 and 348 slices. All marked results were overlapped to determine the total number of considered areas. Gold standard has been set up as consensus between human and machine results. Altogether, 4537 thickening areas are processed. 30 working hours have been spent on the verification. The evaluation showed that 71.4% of the thickenings found to be correctly detected. The system showed high sensitivity, but low specificity of 35.2% as expected. The sensitivity of the computer-aided detection together with doctors was 89.0% which demonstrated an improvement of the total detection rate in comparison to human reader only of 86.5%.

To validate the automatic matching of thickenings from the machine, physicians have evaluated the matching results using further 18 CT data from 9 patients. After the evaluation, the matching revealed to be correct in 95% of all cases, which reflected high sensitivity as well.

Fig. 3. GUI of the implemented automated assessment system for pleural thickenings displays CT data of the same patient from different point in time. The matching results are displayed in the middle and can be manually supervised. Doctors have the possibility to comment each case individually, while report output as well as documentation are provided.
4 Discussion

With the improvement of the total detection rate in comparison to human reader only, the system demonstrated the ability to increase the reliability of diagnosis. This system, which has never existed elsewhere before, comprises fully automatic algorithms for the detection and assessment. Also the spatiotemporal matching of the detected pleural thickening from consecutive 3D CT data at different points in time was carried out automatically.

A comparison to previous works is difficult since purpose and usage of each system vary. The only similarity among them was the detection of pleural anomalies. All algorithms were implemented to meet runtime requirements (i.e. the processing of all steps for a pair of each 700 slices takes ca. 8 min on an Intel® Core™ i7 2600k Quad-Core with 16 GB RAM), therefore promise to reduce physicians’ workload, while they still have access to modify the results at every step.

However, to improve the specificity of the detection, error due to anatomic condition such as spinal cord indentations might be reduced by enhancement the algorithm with the anatomic information. This will be the future task.

References