Multiscale Nodule Detection in CT Data

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Abstract

In this paper I am describing a computer aided detection (CAD) method, which is able to detect lung nodules in medical data sets. The data sets are obtained by a high resolution computer tomography. The goal of the nodule detection is to gain an early nodule detection which increases the probability of survival. Introduced method is able to detect nodules of variable size and variable shape. It is also rotation-invariant. The detection algorithm is based on the Hessian matrix. This matrix consists of the second-order partial derivatives. The eigenvalues of this matrix are used to determine the probability of a nodule-like shape. This method is well adapted to detect nodules of a size larger than 4 mm diameter. Tests with synthetic nodule data sets and some real data sets provided a high probability of true nodule detection with a very low number of false positives per data set.

1 Introduction

Lung cancer is the leading cause of cancer deaths in the first world. In the European Union (EU) occur 295.000 new cases of lung cancer every year. 270.000 people die on the consequences of lung cancer in the same period. The overall 5-year survival rate is 11% in the EU. This high death rate results from the difficulty to detect lung cancer in an early stage.

There are many different ways for lung cancer detection, but usually by the time nodules are detected, it is too late. The nodules are either too large or too advanced to be effectively cured.

A widely-used technique for lung nodule detection is the analysis of the thoracic computer tomography (CT) data. The computer tomography takes axial images along the thorax. These images are viewed by radiologists. A nodule is spherical, so it slowly appears and disappears over a sequence of axial images. This is the way how a radiologist can detect a nodule.

A conventional computer tomography takes around 30 to 50 images over the lung. Newer high resolution computer tomography takes around 300 to 600 images. With a high resolution image of the lung much smaller nodules can be detected. With this method nodules down to a diameter of 3 mm can be found in the lung area. A detection of nodules in such early stage raises the probability of surviving rapidly.

The problem with large volume data sets is that they are impractical to review in current radiology practice. So Computer Aided Detection (CAD) is needed to simplify and speed up the detection process.

In the ideal case a CAD system should detect all nodules in a data set. So the detection process of the radiologist can be replaced by the CAD system.

Unfortunately the nodule detection is a challenging task in medical imaging. There are many aggravating circumstances which make the detection complex.

The main problem is the varying form of the nodules. They are approximately spherical, but dependent on their position the form can differ drastically. For example nodules on the lung wall look like cut spheres, others can be more elliptical. Another problem is the density distribution of the nodules. Through the data acquisition with a computer tomography the density in the middle of a nodule is higher than the density in the border area.

These problems and many others are the reason why a CAD system will hardly detect all nodules (true positives) without classifying other healthy parts (false positive). So the goal of a CAD system should be to detect all true positives with a low number of false positives. The detected areas can then be observed by a radiologist, who finally classifies them as true or false positives. So the CAD system in combination with a radiologist can be an efficient and fast method for the nodule detection.

In the following an algorithm is shown, which meets requirements of a good nodule detection system.

2 Related Work

In the last few years a number of papers about lung nodule detection have been published. Nodule detection is a challenging task in medical imaging, but it may help a lot of people, when nodules can be detected earlier.

For the detection there are three fundamental differently approaches. One approach is used on slice images to detect the nodules. For this approach the nodules are detected through two-dimensional feature detection. Another approach examines each lung lobe separately. With the knowledge about differences between nodules in different lung lobes, the detection can be improve. The third attempt tries to find nodules using there three-dimensional feature detection.

The first approach is used by Mota [1]. He employed a conventional template matching to detect the nodules on the two-dimensional slice images. After initial detection, he extracted seven feature values and used them to eliminate false-positive findings. A more complex method was developed by Yongbum et al. [11]. This method consists of two template matching approaches, based on simple models that simulate real nodules. A template matching technique based on a genetic algorithm template matching for detecting nodules within the lung area. The other template matching technique was designed for nodule detection on lung wall.

There are also approaches which combine two- and three-dimensional feature detection. For example Xu et al. [10] first process each CT slice separately to extract two-dimensional contours of the nodule which can then be stacked together to get the whole 3D shape. Gurcan et al. [3] designed rule-based classifiers to distinguish nodules and normal structure using 2D and 3D features. After the rule-based classification, linear discriminant analysis have been used to reduce the number of false positive objects.

Knowledge based methods use the knowledge about the lung. Hongshun et al. [8] use a lung model, which contains anatomical knowledge about lung in the form of semantic networks, to guide the interpretation process.

The presented methods are used for nodule detection in normal resolution computer tomography (CT). A newer computer tomography generation can produce data with a higher resolution. In Wiemker et al. [9] the options for nodule detection with this high resolution computer tomography are described.

Approaches for high resolution CT data mostly use only 3D feature detection to detect nodules. Paik et al. [5] uses a surface normal overlap method. The relation between the normals of a nodule candidate and the normals of a reference model classifies the feature as healthy lung tissue or lung nodule. A method of Lu et al. [4] base on a concept of machine learning. A rotation-invariant feature is proposed to extract the volume intensity distribution along the radial directions of the 3D volume sample. The volume intensity is utilized and the 3D characteristics of the volume are incorporated to extract features of more discriminating power.

In some papers the Hessian matrix is used to extract some features of the data. Sato et al. [6] use it for enhancement of curvilinear structures such as vessels in three-dimensional medical images. For the enhancement a combination of the 3D Hessian matrix is used. In the paper of Frangi et al. [2] the Hessian matrix is also used to enhance vessel-like structures. A vesselness measure is obtained on the basis of all eigenvalues of the Hessian matrix. Sato et al. [7] design a 3D transfer function with

the eigenvalues of the Hessian matrix. The transfer function is used to highlight line, sheet or blob-like structures.

Proposed approach also uses the eigenvalues of the Hessian matrix. In the next chapter a detailed description of the algorithm is given.

3   Multiscale Nodule Detection

For the detection an algorithm is needed, which enables a size- and rotation-invariant detection. This helps to detect nodules with different diameter and arbitrary orientation. The algorithm should also be invariant from the density of a nodule. The density at the middle point of a nodule is between -500 and 300 Hounsfield Unit (HU).
The nodule size, which will be detected, is going to vary from 4 to 20 mm diameter. The described algorithm focuses mainly on the detection of small nodules (4 - 10 mm), as it is important to detect nodules in an early growth stage. For larger nodules the technique focuses radiologist's attention and makes the diagnosis process faster.
The algorithm should be able to detect nodules without a perfect spherical shape. For example lung nodules on the lung wall look like cut spheres. This and other nodules have to be detected as well.
It is also important to reduce the number of false positives, because a too large number of false positives is impractical for the further observation through a radiologist. False positives for example show up at bifurcations of vessels. These and other false positives on healthy lung tissue should be classified as true negatives by the algorithm.
In general the algorithm should be able to detect all nodules with a low number of false positives. In the next sections an algorithm is introduced, which achieves this goal. In the following a description of the synthetic nodule generation is given. Then the calculation of the Hessian matrix is described. Finally a discussion on the use of the Hessian matrix for the nodule detection concludes the report.

3.1   Generation of synthetic nodules

Without a profound knowledge about nodule locations in real data sets, it was impossible to test the algorithm. So first it was necessary to generate synthetic nodule data sets for an efficient testing of the detection algorithm.

The synthetic nodules should simulate real nodules in shape and density distribution. Real nodules are blob-like. They can be a little elliptical and can also be cut spheres, when they are on the lung wall. For this reason the generation of the synthetic lung nodules must be able to generate nodules with these different shapes. For testing different data sets, nodules with different shapes were produced.
Real nodules have a stable density over the whole area. Through the physical properties of the computer tomography, the density of a nodule in a produced data set decreases from the middle point to the border of the nodule area. The function of this decrement can be simulated by the Gaussian function.

$$g(x, y, z) = m * e^{\frac{-(x^2 + y^2 + z^2)}{r}} \qquad (1)$$

The equation describe the density distribution of a nodule g in dependency of the distance to the middle point. The variable m express the maximum density of the nodule in the middle point. r is the radius of the nodule. For points, which are farther away from the middle point than distance r, the density is set to 0. The variables x, y and z are the distances to the middle point in the three cardinal headings.
This equation was used to produce the synthetic nodules for testing. The maximum density m was chosen between -700 and 200 HU.

3.2   Calculation of the Hessian matrix

The Hessian matrix is a square matrix of second partial derivates of a scalar-valued function. In the case of nodule detection the function is three-dimensional.

$$F = F[x, y, z] \qquad (2)$$

This function expresses the density distribution of the CT data over the three-dimensional space.
A second partial derivation of F is for example given through:

$$\frac{\partial}{\partial y}\left[\frac{\partial}{\partial x}F[x, y, z]\right] = F_{xy} \qquad (3)$$

With this notation the Hessian matrix has the following conformation:

$$H = \begin{bmatrix} F_{xx} & F_{xy} & F_{xz} \\ F_{yx} & F_{yy} & F_{yz} \\ F_{zx} & F_{zy} & F_{zz} \end{bmatrix} \qquad (4)$$

The Hessian matrix is symmetric, because the second partial derivation F_{zx} is the same as F_{zx}. This also apply for the function F_{xy} and F_{yz}. This property simplifies the calculation of the Hessian matrix, since not every value of the matrix must be calculated separately.

The introduced calculation of the Hessian matrix is essential for a continuous function F, however the function of the density distribution in the data set is represented by a discrete set of samples. For this case the data is convolved with a Gaussian smoothing kernel. The function for the kernel is expressed through:

$$G = \frac{1}{\sqrt{2\pi} * \sigma_f} * e^{\frac{-(x^2+y^2+z^2)}{2\sigma_f}} \qquad (5)$$

The standard deviation of the Gaussian function σ_f controls the smoothing effect. For the nodule detection this value should be fitted to the nodule density distribution. A good choice for this case is:

$$\sigma_f = \sqrt{\frac{K_{size} - 1}{6}} \qquad (6)$$

The K_{size} expresses the kernel size of the convolution kernel. The σ_f was found through experiments. Several tests with this σ_f lead to the best results.

The connection between the convolution and the second-order partial derivatives is given through:

$$\frac{\partial}{\partial y}\left[\frac{\partial}{\partial x}\left[F * G\right]\right] = F * G_{xy} \qquad (7)$$

F is the discrete density distribution function and G is the Gaussian smoothing function from Equation 5. This means that the second partial derivation must only be applied on the Gaussian function. For the calculation of the derivatives a pre-calculation of kernels for the second-order partial derivatives of the Gaussian function is used. To get the values of the Hessian matrix, the discrete function F is convoluted with the appropiate second-order partial derivative kernel of the Gaussian smoothing function. For example the value of F_{xx} can be calculated through the convolution $F * G_{xx}$.

The graphs in Figure 1 show the second-order partial derivative kernels for the two-dimensional case.

As described before the Hessian matrix is symmetric, so only 6 different kernels are needed to get the whole Hessian matrix. Needed filter kernels are G_{xx}, G_{yy}, G_{zz}, G_{xy}, G_{xz} and G_{yz}.
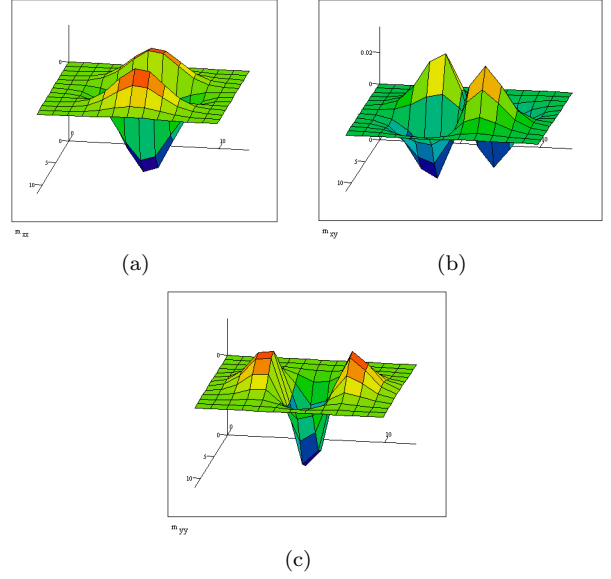

(a) (b)

(c)

Figure 1: *This image shows the 2D convolution kernel for G_{xx} (a), G_{xy} (b) and G_{yy} (c).*

In the following a description of the nodule detection with the Hessian matrix is given.

3.3 Nodule detection with Hessian matrix

The eigenvalues of the Hessian matrix are the important values for the nodule detection. The values of the three eigenvalues provide information about the shape of the considered area in the data set. The eigenvalues can be calculated through the equation:

$$det(H - E * \lambda) = 0 \qquad (8)$$

In this equation H is the Hessian matrix, E is the identity matrix and λ is the eigenvalue. The equation leads to a polynomial of third degree. To find the root of λ a root-finding algorithm is needed. The Newton's method is a good procedure to find an approximation of the roots. In the three-dimensional case there exist exactly three values for λ, which resolve the equation.

The three solutions of λ (λ_1, λ_2 and λ_3) give information about the shape of the considered area. If the shape is blob-like then all three values are smaller than 0 and they have approximately the same value. For the further calculations and classification it is reasonable to normalize the eigenvalues. This could be gain if every eigenvalue is divided through the density value of the discrete function F

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in the middle point of the convolution. After this standardisation the absolute value of the eigenvalues is independent of the density and size of the nodule and leads, for a blob-like shape, to values of approximately -1 for all three eigenvalues.

With this knowledge a pre-selection of the eigenvalues can be made. If one eigenvalue is too small (smaller than -1.3) or too high (higher than -0.5) then no nodule is located at this position with a very high probability. This pre-selection speeds up the algorithm with no measured loss of accuracy.

For the automated detection a classifier is needed, which express the blobness of the shape in the considered area. This classifier is given through the equation:

$$C = -1 * \lambda_3 * (\frac{\lambda_2}{\lambda_1})^{2\gamma} * (\frac{\lambda_3}{\lambda_1})^{\gamma} * (\frac{\lambda_3}{\lambda_2})^{\gamma} \qquad (9)$$

The γ value control the selectivity of the classifier. A value of 6 is a good choice for this variable. For a perfect nodule the value of C should be 1. If a nodule does not have a perfect blob-like shape, then the value is smaller. The boundary value for the classifier to detect the considered area as a nodule is approximately 10^{-5}.

For finding the right diameter of a nodule, the algorithm starts at every voxel with the smallest kernel for the convolution. Then the kernel is incrementally extended. For every kernel size the eigenvalues are calculated. For the best fitting kernel size the classifier has the highest value. This means that the detection can be stopped if the value of the classifier begins to decrease. The diameter of the detected nodule is equal to the kernel size with the highest classifier value.

4   Results

For testing purposes a lot of data sets with nodules were generated. The data sets had the size of $100 \times 100 \times 100$ voxels. The number of nodules was varying for the different data sets. One data set consisted of approximately 5 to 50 nodules. The size of the nodules was varying between 4 and 15 mm in diameter.

To create a realistic test situation, nodules with different shapes were produced. For the testing three different shapes of nodules were used. The three different shapes were perfect blob-like nodules, elliptical nodules and cut nodules. For the creation of one test data set one of these three shape types were used.

The last variable parameter for the creation of the test data sets was the voxel spacing. It was varying between $0.35 \times 0.35 \times 1$ to $1.5 \times 1.5 \times 1$. With a smaller spacing like $0.35 \times 0.35 \times 1$ a nodule is spread over more voxels.

The tests were made on a standard PC with an Intel Pentium 3 processor (1.6 GHz frequency) and 512 MB RAM. For a spacing of $1 \times 1 \times 1$ or higher the detection only took some seconds. For a spacing of $0.35 \times 0.35 \times 1$ larger kernels for the convolution are needed, so the detection was a little bit slower. It then took around 25 seconds.

As a result of the tests nodules with perfect blob-like shape have always been detected. Elliptical nodules were detected, if their shape was not too elliptical. If they were too elliptical, than the shape was more similar to a vessel structure than to a nodule. The cut nodules were detected with a cut quote up to 35%. For a small voxel spacing cut nodules with a cut quote of up to 50% have been detected as well.

The algorithm was also tested on a real data set. The size of the data set was $512 \times 512 \times 140$. The detection part has been made on a PC with a Pentium 4 processor (3.2 GHz frequency) and 1024 MB RAM. The detection process took around 10 minutes.

The result of the nodule detection, on this data set, was 6 detected nodules. Two of the detected nodules seem to be real nodules. The other four are probably false positives.

The Figure 2 shows a three-dimensional view of the lung with the detected nodule candidates.

5   Discussion

For a perfect adaptation of the algorithm, a large number of real data sets with pre-detected nodules is needed. The pre-detection should be done by an experienced radiologist. With only a small number of real data sets with no pre-classified nodules, it is hard to say something about the effectiveness of the method.

It was impossible to get a large number of data sets from a high resolution CT. This is because of radiologists do not work with this high resolution data sets. They detect the nodules on two-dimensional slide images with a large slab.

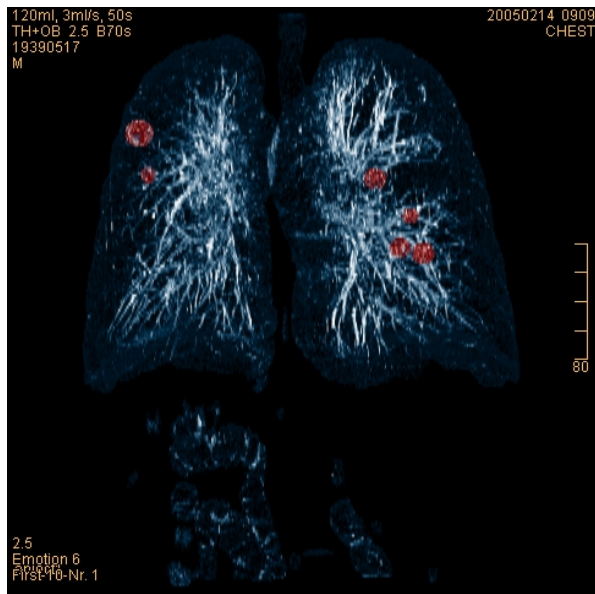A problem of the algorithm is the low speed, because the convolution with different kernels for ev-

Figure 2: *Detected nodules (red spheres) in CT data set.*

ery considered point is very time intensive. There are many possibilties to speed up the algorithm. The goal should be to discard none nodule-like points before the detection algorithm is started. With an appropriate filter the number of points on which the detection is passed can be significantly reduced.

The overall conclusion is that the method can be a very helpful assistance for a radiologist in practical use. But before the appropriation in practice more tests with real data sets must be made.

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