33rd European Study Group with Industry pp. 55 – 61
14 — 18 September 1998

Detection of Metastases in Human Lungs from CT-Scans

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One of the possibilities to assist physicians with their diagnostic work based on CT-scans would be a tool for automatic detection of metastases in human lungs. The present project stems from the 'Dr. Daniel den Hoedkliniek' in Rotterdam. The problem was successfully tackled during the week and resulted in a highly efficient algorithm to detect metastases from CT-data. The algorithm is restricted to metastases that are not attached to each other or to the lung edges. A first attempt to implement it into a Fortran program yielded successful results on artificial data sets. For fine-tuning of parameters the algorithm should be applied to real data from the clinic.

1. Introduction

One of the problems presented during the Study Group in Leiden, September 1998, concerned the automatic detection of possible metastases - i.e. clusters of tumor cells - in human lungs. These metastases are approximately spherical with diameters in the range 0.3-2 cm. A computer assisted diagnostic program should be able to identify these objects efficiently.

The lungs often serve as initial 'target organ' for tumors with venous drainage primarily to this organ. The entire output of the right side of the heart as well as virtually all lymphatic fluids produced by body tissues flows through the pulmonary vascular system. Therefore it is not surprising that metastases to the lungs are quite common. Patients with tumors that initially arise in the lungs are at high risk of developing pulmonary metastases early. If left untreated such metastases may be a primary cause of death.

In the seventies computers were introduced in X-ray diagnostics. They had an enormous impact on the field of röntgenology. New measuring and imaging methods became available, which gave the field a new impetus. One of the main improvements was the possibility of transaxial scanning of patients. Until then tomography produced only longitudinal scans.

Nowadays the spiral volumetric CT technique has introduced truly contiguous scanning which is independent of e.g. breathing. Subsequent serial-section axial images are generated by means of filtered back projection after interpolation.

Earlier research by students of Prof. M. Keane, see [Ber94] and [Sch95], showed that the route starting from random lung shapes, edge/contour detection, in order to come to detection of metastases was not quite feasible. With the Study Group we attempted a direct approach which has the advantage of being very efficient since the grid points of a CT-scan are visited only once.

2. PROBLEM

At the Study Group Dr.M. Oudkerk of the Dr. Daniel den Hoedkliniek, a medical center for cancer treatment in Rotterdam, presented a problem, which - reduced to its essence - reads as:

‘When making a diagnosis by using a CT scan, one looks for spherical shapes amidst bones and lung tissue. Where the bones show a value of 1000 in an appropriate system of units on the CT scan and long tissue are at 0, the spheres distinguish themselves at a value of around 150. For the automatic pattern recognition one can assume that the spheres are unconnected from each other and the lung edges, with unknown diameter and position’.

The present way of scanning the data makes use of the presentation of the grey value pattern in a horizontal slice on a screen. Here `horizontal' is meant with respect to the patient in an upright position. In fact, no 3-D but only 2-D representations are used. The sophisticated interface allows the user to scroll through adjacent horizontal slices in a fast and convenient way. If a suspicious 2-D object is observed in one slice, the inspector may immediately deduce from the pictures of the slices directly above and below the slice under consideration whether the object is part of a 3-D spherical object or that it is connected to, e.g., a vein image. The expert knowledge comprises a lot of experience about the objects that can be expected to be present in specific regions of the lung. Although the lungs of different people may differ considerably, the human eye is highly capable in detecting irregular patterns.

However, the present detection method of visual inspection is not yet perfect. Clinical studies in the use of chest radiographs for the detection of lung metastases have demonstrated that even highly skilled and highly motivated radiologists, task directed to detect any finding of suspicion for metastases, and working with high quality chest radiographs, still fail to detect more than 30% of lung cancers that can be detected retrospectively [LLF98]. So, a computer tool pointing out suspicious cells or giving a clearance could be an enormous help in saving valuable time to the physicians.

In the Dr. Daniel den Hoedkliniek screening of the lungs using computer tomography is conducted on a daily basis. This screening serves for the detection of pulmonary metastases. The head of the radiology section would like to dispose of a mathematical model of the lungs and the process of an optimal scanning protocol.

It was explicitly mentioned to focus the project on spherical metastases that are not attached to the lung boundaries or the heart. The metastases may be easily distinguished from areas filled with air, water, or bones. More problems are to be expected with discriminating metastases from lung and heart tissues and veins.

3. DATA

In a CT scan a 6 – 8 mm spiral slice of the patient is made. This raw data is first translated into about 60 – 100 horizontal slices, flat and equidistant. The available data are 512x512 grid points per horizontal slice ($\Delta x = \Delta y \geq 0.5$mm), 60 – 100 times ($\Delta z \geq 1.5$mm). Values, called Hounsfield Units (grey value), range from –1000 (air) over 0 (water) to 1000 (bone). Lung and heart tissues, veins, and metastases have values in the range of about 40 – 150.

4. APPROACH

There are many possible approaches to detect discs represented by grid points in two dimensions. The important issue is to do this as accurate and as fast as possible. In view of the enormous number of points to be considered it is important to visit each point preferably only once.

As a first step we simplify the problem such that to each grid point the value 1 is assigned if the Hounsfield filter value of the CT scan is between 40 and 150 (the range in which metastases data are known to fall), and the value 0 otherwise. Suspicious objects thus correspond to connected areas of neighboring grid points labeled with a one. Positions are considered to be neighbors if they are in contact horizontally or vertically; diagonal neighbors are not included, although this definition could be relaxed easily. The second step is looking for discs in 2-D, and eventually for spheres in 3-D. The Study Group only discussed the application of sieves for detection of discs in 2-D slices, realizing that extension to 3-D sieves will be relatively straightforward.

In 2-D the problem is to determine whether a set of identified neighboring pixels in a rectangular grid is more or less 'disc-like'. The following ideas were proposed and discussed:

1. Spotlight approach.

Construct predefined discs, $B_1, ..., B_M$, of sets of grid points which are considered to represent discs on a rectangular grid. The object S is compared to the predefined discs that have nearly the same number of pixels as the still unidentified object. As a measure of similarity between the objects the number of grid points that both objects have in common, could be taken. This measure could be referred to as the 'Hamming distance'. A selection criterion then could be

$$\frac{d(S,B_i)}{N} \leq \varepsilon_i \quad , \qquad i = 1, \ldots, M$$

with *d(S1,S2)* the 'Hamming'-distance and N the number of pixels of S. Reliable values for the parameters ε_i should be fitted from analyzing real data sets.

2. Borderline search.
From computer graphics it is known that efficient techniques are available to determine the borderline of the 2-D object once one point of the object is indicated. This borderline should be compared to a circle. An appropriate measure for this comparison could be found following the previous idea in 1 .

3. *Paint filling approach.*
From computer graphics efficient techniques are available to find an object indicated by neighboring 'ones' in a data file if only one point of the object is indicated. The painted area should be compared to a disc. It should be simple to find an appropriate measure for this comparison, in the same spirit as for methods 1 and 2.

4. *Hemker approach.*
We eventually decided to use a method suggested by Hemker. The idea is as follows. The data points (containing zeros and ones) are visited in a systematic way: the matrix is searched by columns, top down, starting left. The first position containing a one is assigned the label 'a'. The next position containing a one is initially assigned the label 'b'. However, if this position is neighboring to a position with label 'a', the position under consideration gets the label 'a' instead of 'b'. The next position containing a one and not being a neighbor of a position with label 'a' or 'b' gets the label 'c'. Etcetera. If at some moment in the labeling process it turns out that two positions with different labels are neighboring, it is administrated that these objects, which until that time have been considered as being separated, are part of one and the same object. This is done by identifying the labels accordingly. From then on both objects are treated as one object. An example of the labeling and identification procedure is as follows:

labeling of 'ones'			
0	1 ***b***	0	0
1 ***a***	1 ***a=b***	1 ***a=b***	0
1 ***a***	0	0	0
0	1 ***c***	1 ***c***	0

Identification label		
a ***b*** ***c*** ***d*** . .	$\Rightarrow$	***a*** ***a*** ***c*** ***d*** . .

Per object (or label) the following properties are calculated: the total number of grid points N and the quantities $\sum_i x_i$, $\sum_i y_i$, $\sum_i x_i^2$, $\sum_i y_i^2$, where x_i and y_i are the 2-D coordinates of the grid points. The method has the advantage that each point in the data matrix is visited only once. That is because these quantities, being simple sums over the members of an object, can be updated as soon as a new point is assigned to a label.

After the matrix has been searched through, the information gathered per object allows for the calculation of the inertia tensor ***I*** of the 2-D object with *N* points:

$$I = \begin{bmatrix} I_{xx} & I_{xy} \\ I_{yx} & I_{yy} \end{bmatrix},$$

with

$$I_{xx} = (\tfrac{1}{N}\sum_1^N y_i^2) - \bar{y}^2, \quad \bar{y} = \tfrac{1}{N}\sum_1^N y_i, \quad I_{xy} = I_{yx} = \bar{x}\bar{y} - \tfrac{1}{N}\sum_1^N x_i y_i,$$

and I_{yy} defined in an analogous manner. The eigenvalues I_1 and I_2 of $\boldsymbol{I}$ are the principal moments of inertia of the object. For a uniform disc the inertia tensor is diagonal and $I_1 = I_2$.

These moments are to be compared to the principal moments of inertia of a disc of nearly the same size. The radius of such a disc can be deduced from the number N of grid points per object, since the area per grid point is known.

Although these ideas are quite simple, inaccuracy comes in via the discretization: even a perfect disc is represented in the data by a finite number of points and the shape of this collection depends on the relative positions of disc and grid points. The smaller the disc, the fewer the number of representing points and thus the bigger the inaccuracy will be. This inaccuracy has been estimated as a function of disc size. To that end some simulations have been performed. The procedure used was as follows:

- Position a disc of prescribed radius R randomly in the plane.
- Compute its pixel discretization.
- Compute N, the number of pixels covered by the disc.
- Compute I_1 and I_2 of the discretized disc; they depend on R, N, and the geometry.
- Compare these moments with the moments of inertia $I_1 = I_2 = I_d$ of the original disc by calculating

$$\varepsilon(R,N) = \frac{(I_1(R,N) - I_d(R)) + (I_2(R,N) - I_d(R)}{I_d(R)}.$$

The results of the simulations are used as follows. Given a 'disc-like' set of N pixels, a family of discs exists which all have this set as discretized representation. Of this family the smallest and the biggest discs are found with radii $R_{\min}$ and $R_{\max}$. For these the deviations $\varepsilon^- = \varepsilon(R_{\min}, N)$ and $\varepsilon^+ = \varepsilon(R_{\max}, N)$ are calculated. For the biggest disc the difference is positive, whereas for the smallest disc it is negative. In the table below the averages of ε^- and ε^+ are given as functions of the number N of pixels in a number of classes.

N	$\varepsilon^-(N)$	$\varepsilon^+(N)$
1–2	–1	+1.5
3–12	–0.4	+0.7
13–28	–0.2	+0.35
29–50	–0.15	+0.25
51–82	–0.12	+0.15
83–108	–0.06	+0.10

This table can be used as a sieve to decide whether a detected discretized object of N points is likely to represent a disc.

5. RESULTS AND CONCLUSIONS

During the week we developed a computer program for the analysis of 2-D data via the Hemker approach. In these data files artificial disc-like objects were added at random. The results showed that disc-like objects could be detected without any problem. The chance to detect an object depends on its shape. Using ranges in the table given above, we could only detect ‘nearly-discs’. In CT-Scan practice the objects may be quite far from disc-shaped (or spheres in 3-D), so that fine-tuning of the parameters in the sieve is necessary. Reliable values of the parameters to be used in analyzing real data should be obtained with use of expert experience and from analysis of a great number of scans.

Later the method was extended to 3-D but this is straightforward, since the present approach does not contain any element specific for 2-D. Computing times appeared to be very short. The search procedures could be implemented even in a more efficient way than sketched above. Extension to 3-D data did not cause any trouble in this respect, even for real data sets that contain as much as 10 million data points per scan.

It should be emphasised that the approach outlined above is only applicable in case of metastases that are not attached to each other, the lung edges or the heart. In those cases more sophisticated methods of pattern recognition are necessary.

ACKNOWLEDGEMENT

The first author wishes to thank Drs. J.G. Heeres, radiodiagnost of the Enschede hospital MST, for his explanations of the medical aspects of the problem.
During the workshop contributions were obtained from Pieter Roos (Universiteit Twente), Erik Fledderus (KPN Research), Piet Hemker (Cenbtrum voor Wiskunde en Informatica), Bob Planque (Universiteit Leiden), Damien White (Universiteit Utrecht).

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