Image Processing for Morphological Investigation of the Carcinome Thyroid Gland: Modern Facilities

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Abstract: *This paper describes automation methods for diagnostics of the thyroids gland carcinoma. It based on image processing technology and calculation of characteristics from image. Methods are used for investigation of histological samples.*

Keywords**:** Medical image processing, calculation of characteristics.

1. INTRODUCTION

Digital image processing became one of mainstreams in computer science that bring technical progress in many fields of human activity. An application of methods to be discussed here is intended for efficiency and reliability increasing of accepted decisions since histological diagnostics of oncological diseases is one of urgent problems in medical practice. It can be solved by using of modern computer system of the image analysis [1-5].

Morphological analysis of histological samples is usually carried out by analysis of images made with different optical magnifications (low and high, for instance). In the first case architectonics is investigated under magnification about 50-100X. In the second case cells and endocellular structures are investigated at magnification of 400-1000X in compliance with class of cells.

Simple thresholding methods based on brightness histogram analysis are applied to define patterns of tissue. These patterns are optionally modified then by operations of mathematical morphology. While it should consist of the integral objects with approximately repeating borders of cells, it preserves a hierarchy of objects (nucleus and nucleolus). After morphometrical analysis the formalized characteristics are calculated, that creates a basis for allocations of conclusion.

2. MORPHOLOGICAL CHARACTERISTICS AT LOW OPTICAL MAGNIFICATION

There are fragments of tissue resented on image at low optical magnification of specimen (fig. 1). Cells are to be detected as small contrast objects [2], so after segmentation image contains binary patterns which include both nucleus and noise (fig. 2). Then, full histology functional representation (fig. 3) is brought by distance map transformation [2, 7]. The described method is used for investigation of tumour's morphometric characteristics of thyroid glands.

It is considered that at low magnification any new tumour formation may be investigated by following characteristics:

- blood circulation infringement;
- adjournment of salts of calcium;
- texture of colloids;
- characterization of a fibrous tissue distribution and growth features;
- the architectonic of tumours;
-degree of expressiveness of productive inflammation (mononuclear infiltration);
- size of follicles;
- characteristic of papillae;
- presence of capsule.

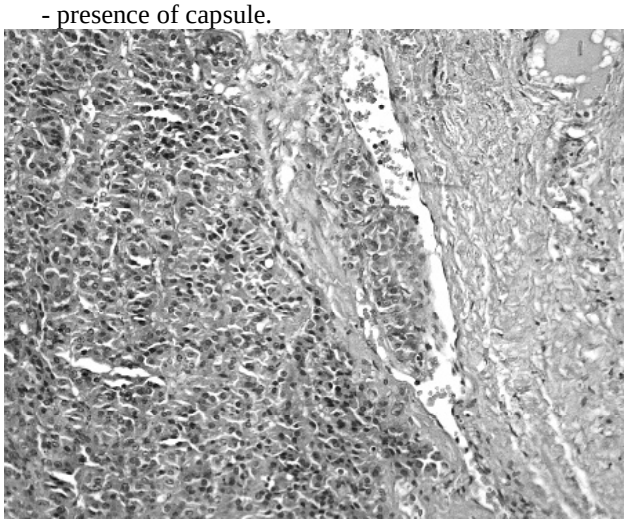


Fig.1 –Initial histological image of carcinoma of the thyroid gland, x100

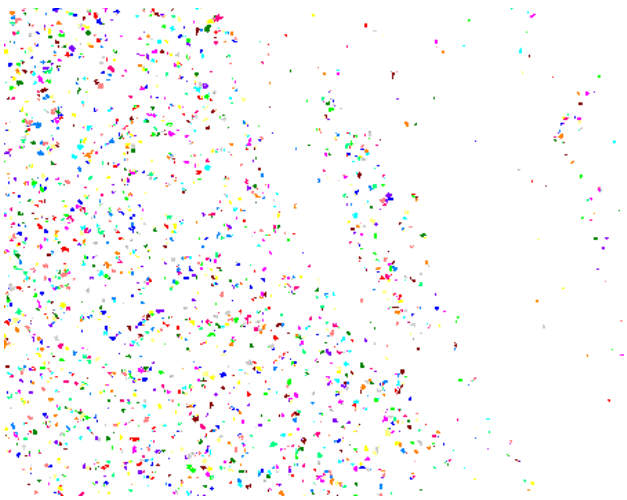


Fig.2 – The binary image of cells, x100

The formalization of these characteristics is carried out in two ways: definition of specific objects and calculation of morphometric characteristics.

Such features as fibrosis and/or capsules, infringement of blood circulation, suspension of salts of calcium can be defined by specialized segmentation operations. For example, fibrosis is characterized by tissue that is optically homogeneous. For its definition it is possible to use threshold segmentation and morphological filtration. This allows to modify borders and remove geometrical noise.

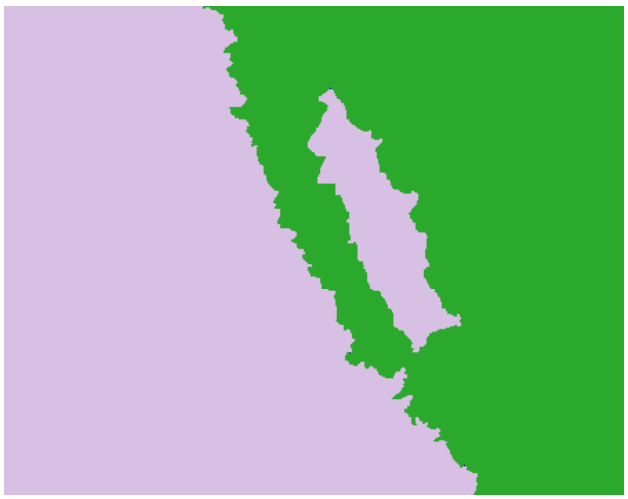


Fig.3 – Segmented binary image of tumour tissue

There are three kinds of fibrosis (fig. 3) and each of them is characterized by certain geometrical complexity.

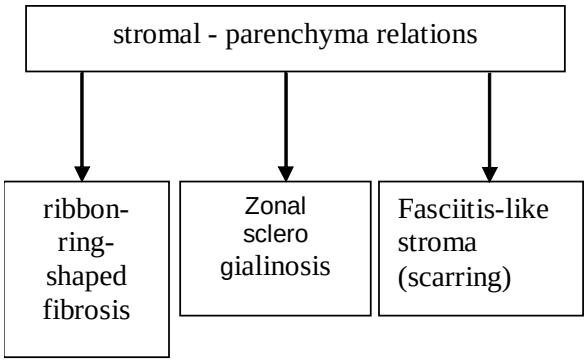


Fig.4 – Character of tumour fibrosis.

The character of tumour growth depends on regions of fibrosis (fig. 5). It is characterized by properties of a capsule. In such a case the capsule should have fibrosis-like optical properties, since in the ideal case the capsule's border is narrow and closed.. Therefore image processing by the morphological filtration demands satisfaction of additional conditions to control over geometrical characteristics of the defined objects.

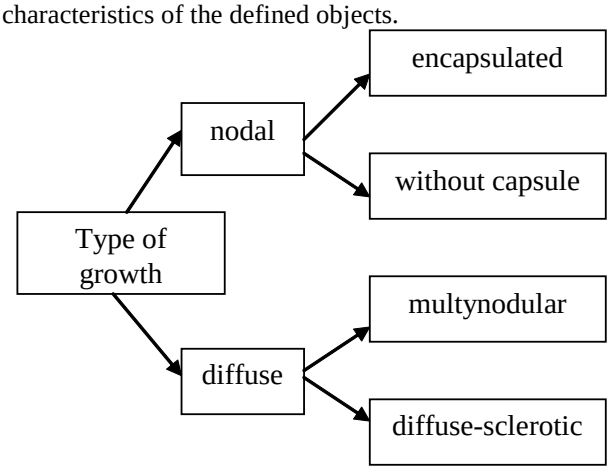


Fig.5 –Features of tumour growing

The colloid is described as "liquid", "dense", "pseudo-calcification". So, optical density is used for it characterization and can be calculated as follows:

$$OD_{x,y} = -1 \cdot \log\left(\frac{I_{x,y} - I_{min}}{I_{max} - I_{min}}\right), \quad (1)$$

where OD_{xy} -- optical density; I_{xy} - brightness of a point; I_{min} and I_{max} - minimal and maximal brightness correspondingly.

A tumor's architectonics is presented by follicular, solid and papillary structures (fig. 6).

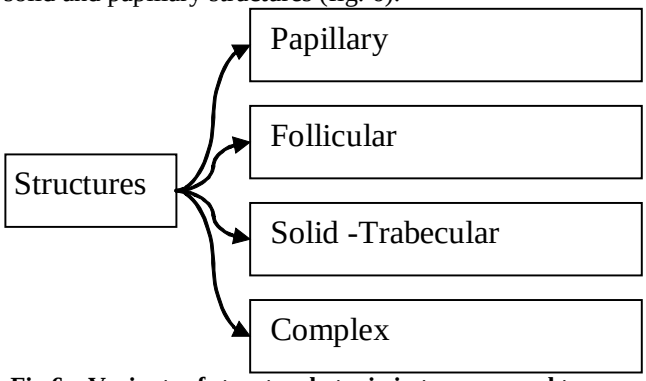


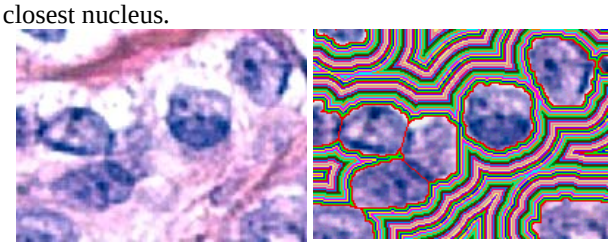
Fig.6 – Variants of structural atypia in tumours and tumor-like diseases of the thyroid.

The expressiveness degree of immune inflammation is formalized by the area of particles and distance distribution between nucleuses.

For the description of follicles (small, large and average) the area of objects is used, but characterization of papillary structures is more difficult. For papillary thyroid cancer "true" papillae (with fibrosis and prominent vasculature in stalk), papillae's hyperplasia (with follicles in similar pouching – in goiter) are usually under consideration. Formalization of these characteristics requires additional investigation, but it is possible to use the characteristic of convex for the simplified case, which must not exceed the value of 0,64 for papillary hyperplasia.

3. MORPHOLOGICAL CHARACTERISTICS AT HIGH OPTICAL MAGNIFICATION

Internuclear distance plays a leading role in the complex analysis. It may be found from pixel value on distance map (fig. 7). Value of each point from the distance map corresponds to the nearest distance to closest nucleus.



a) b)

Fig.7 –Analysis of internuclear characteristics a) the tissue image, b) a distance map of internuclear region.

Internuclear distances between cells and shapes of regions have to be defined for each type tumours. For example, describe the shape of papillary thyroid cancer the convexity feature is used (fig. 8):

$$c \quad o \quad n = \frac{c \; v \quad o \; e \quad pn \; x \quad ev \; i \quad r \; t}{p \quad e \quad r \quad i}, \qquad (2)$$

If object is convex, this value is equal to 1while less then1 if hollows are exist.

The similar description is used for density investigation. It is called “solidity” and defined as relation of the common and convex areas [2]:

$$solidity = \frac{AREA}{convex\ area}., \qquad (3)$$

If the object has no holes and hollows, this size is equal to 1, if else it has less value.

Fig.8 – Objects of different convexity and solidity: convexity and solidity are equal 1; convexity is equal 0,483, solidity - 0,782; convexity is equal 0,349, solidity - 0,592.

At high optical magnification characteristics of cells and their structures become basics for description. Therefore nucleus and cytoplasm are objects of interest in this case. For example, cytoplasm is described as amphophilic or weak-basophilic, eosinophilic and water-clear. Formalization of dimension (fig. 9) is simple and corresponds to the description of optical density.

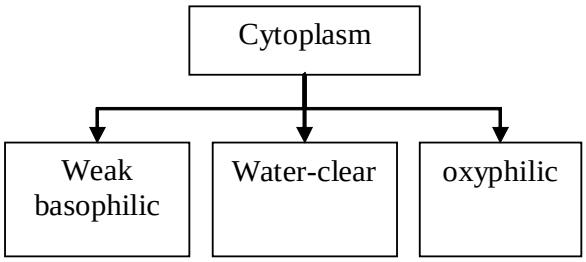


Fig.9 – The cytoplasm features.

Changes of nucleus at various diseases of a thyroid gland are devidedon three groups (fig. 10):

1) intranuclear changes:
   a) an inclusion;
   b) a groove;
   c) presence of a large nucleolus;
   d) a mitosis;
2) chromatin:
   a) regular distributed;
   b) basophilic clumpy;
   c) highly dispersed;
3) form of nucleus:
   a) ovoid;
   b) round;
   c) bizarre;
4) sizes of a cell;
5) presence of symplaste.

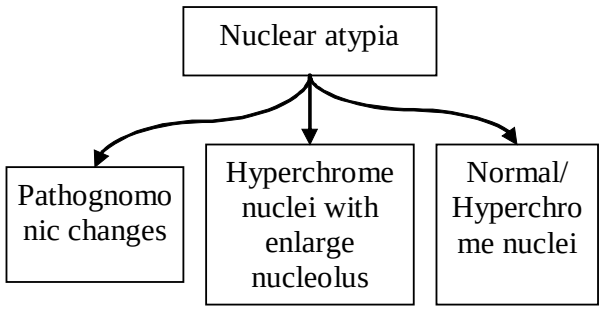


Fig.10– The colour image of cell with a nuclear

Pathognomonic changes are found out in a nuclear (fig. 11) and are presented by cytoplasmatic inclusions and grooves.

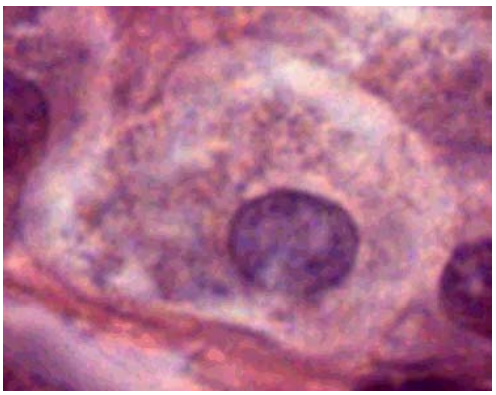


Fig.11– The colour image of cell

Grooves look like narrow extensive objects crossing a nuclear from one edge to another (fig. 12). Inclusions are characterized by vials-like objects. Object’s contents are painted the same as cytoplasm (fig. 12).

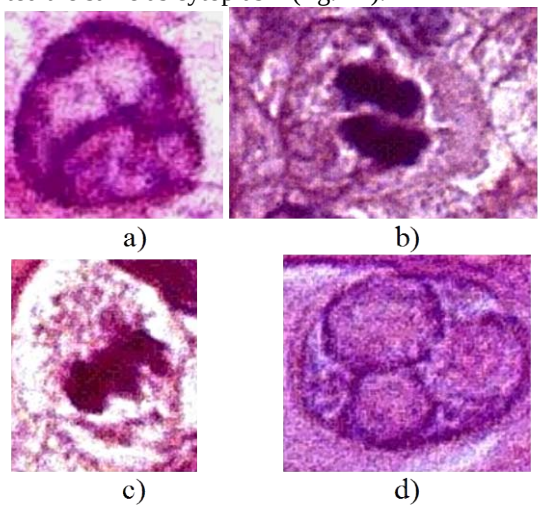


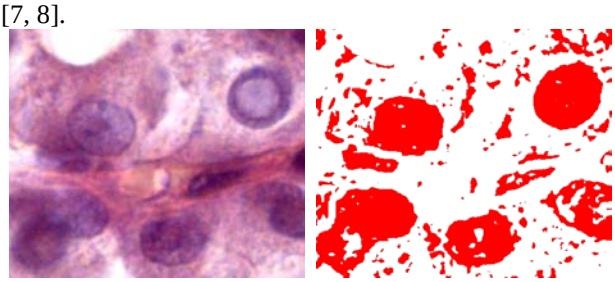
Fig.12 – Pathological changes of a nuclear: a) groove, b) mitosis, chromosome backlog in body, c) a mitosis, backlog of a fragment of a chromosome in a metaphase, d) inclusions.

Nuclear analysis brings Topological properties of objects which allow to define pathognomonic structure type for a papillary thyroid cancer:

- groove – If there are more than 2 points of crossings with nuclear border ;
- mitosis – if there are more than one large object;
- mitosis – if camber of object is less 0, 8;

- inclusion – if the brightness of object is high .

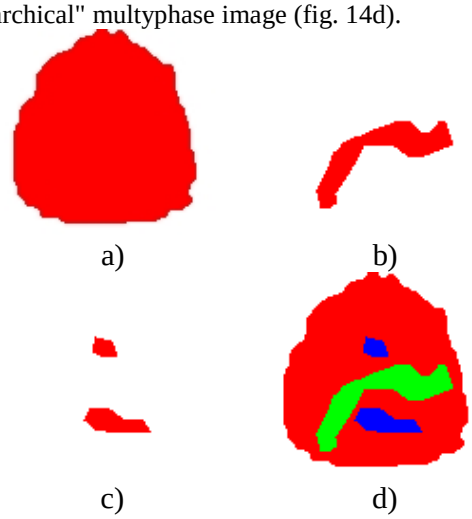
To study a nuclear structure it is suitable to use hierarchical image of its. Such an image can be obtained as a result of segmentation process. At the first stage the Otsu thresholding is performed (fig. 13) to binarize an image which has been obtained by difference of orthogonal components in LAB color coordinate system [7, 8].



a) b)

Fig.13 – Threshold segmentation of objects on the histological image: a) the original image, b) the result o binarisation.

Morphological opening operation divides then the merged objects to find topological characteristics . To connect broken lines of nucleus borders closing morphological operation must be carried out after. . Finally fillingoperation of the closed contours finish the process (fig. 14a). Geometrical noises are removed by the analysis of the sizes and the shape. For example, for identification of nuclear structure initial binary image is used. At this step subtraction of borders (fig. 14) define intranuclear objects. The result of such operation is "hierarchical" multyphase image (fig. 14d).



a) b) c) d)

Fig.14 – Binary image of a nuclear (a), grooves (b), nucleolus (c) and hierarchical image of a nucleus (d)

The idea of hierarchy of areas is easily realized with help of computer facilities

Table 1. Values of pixels for different elements in structure of cages

Object	Operation	Separate value	Values after association
Nuclear	1<<0	1	1
Grooves or inclusions	1<<1	2	3
Nucleolus	1<<2	4	7

It is possible to define about eight levels of hierarchy. Advantage of the described method lies in one hierarchical image. It allows to describe all levels of classification. As a result this image allows to receive the full information about nuclear.

Thus, if there are large objects, (furrows or inclusions) inside nucleus , the value of pixel corresponds to 3. For nucleolus or chromatin the pixel equal to 7. At the similar organization it is possible to operate easily with various nuclear components. It is possible to investigate topological structure of a nuclear by such association of bits in the hierarchical image. The nuclear characteristics are easy formalized for the chromatin description by using of such concepts as geometrical density of objects, intercept and the sum of chords.

4. NUMERICAL CHARACTERISTICS

The developed methods and algorithms have been tested on images of histological samples of the thyroid gland diseases: adenoma (15 cases), goiter (12) and papillary thyroid cancer (21). Following dependences have been received:

Table 2. Mean values of cell's nucleus

disease	area, 10^{-6}	Max. diameter, 10^{-6}	Min. diameter, 10^{-6}	Optical density	Optical range
adenoma	26.7	7.21	4.749	0.316	0.039
goiter	22.4	6.09	4.659	0.56	0.066
cancer	38.2	7.97	6.067	0.29	0.048
norm	21.0	6.68	4.11	0.47	0.057

Table 3. Dispersion of values of cells nucleus

disease	area, 10^{-6}	Max. diameter, 10^{-6}	Min. diameter, 10^{-6}
adenoma	121.10	2.00	1.66
goiter	87.63	1.38	1.05
cancer	138.98	2.05	1.49
norm	24.68	1.18	0.62

Table 4. Characteristics of follicles and intercellular space

disease	Mean diameter, 10^{-6}	Diameter dispertion, 10^{-6}
adenoma	146.6	3403.00
goiter	127.3	2847.38
cancer	42.5	421.05
norm	83.7	1606.3

Thus average values of nuclear area for a papillary thyroid cancer are much bigger than for thyroid cells in norm or at benign conditions. The dispersion of nuclear area for a papillary cancer is more than other. Therefore an extreme variety of nuclear changes for carcinomas are exists in this case. It is necessary to notice smaller diameter of follicles in a follicular variant of a papillary cancer in comparison with a craw and an adenoma. That feature can give additional criterion of differential diagnostics.

5. CONCLUSION

Histological characteristics are formalized by using of methods of the images analysis and calculations of characteristics for raster objects. The similar approach allows to automate histological research. It gains good results for quality and speed of diagnostics. The greatest problems are caused by process of structure definition of

nucleus and cells, because these images have small contrast and no accurate borders. But described methods allow constructing full functional of histology investigation without dependence on complexity of initial images by the expense of application of binarisation and segmentations methods.

6. ACKNOWLEDGEMENT

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