ОРИГИНАЛЬНАЯ СТАТЬЯ

THE CONSTITUTION SYSTEM OF DIAGNOSTIC CHARACTERS USING OUTCOME ANALYSIS OF BOUNDARY CIRCULAR-SHAPED MASSES IN LUNGS

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Purpose. The article investigates the possibility of using the information about the images contour characteristics of pathological spherical formations in lungs for differential illness diagnosis.

Materials and methods. The two-dimensional array of densitometric parameters obtained during the processing of tomographic medical images of patients with verified diagnoses of lung diseases (cancer and tuberculosis, 49 and 26 patients respectively) was analyzed. The technique of constructing the contours of images of such formations is developed. To introduce quantitative characteristics of the contour, the conditional center of mass of the pathology image is calculated and two one-dimensional signature functions are constructed: of the radius-vector module drawn from the center of the image of the spherical formation to its boundary, as well as the polar angle of rotation of the radius-vector. The argument of both functions is the conditional number of the pixel belonging to the path. With the help of spectral analysis of the signature function, such characteristics of contours as spectral entropy, multiplicity, number of local maximums, signature functions of the polar angle of rotation of the radius vector are proposed and calculated in the paper. The statistical significance of differences in values of these characteristics of contours of spherical formations in different diseases (cancer and tuberculosis) was analyzed.

Results. There were statistical differences in the characteristics of the contour for different pathologies proposed in the work, which can allow to perform differential diagnosis of the investigated lung diseases.

Conclusion. The obtained quantitative characteristics of the spherical formations in lungs can enter the system of assistance to the doctor in diagnosis. It should be remembered that there is no single diagnostic feature based on the quantitative characteristic of the image, which would immediately determine the type of pathology. Only a set of such features will allow to carry out high-quality diagnostics.

Keywords: computer tomography, medical images, contour characteristics, differential diagnosis, cancer, tuberculosis.

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СИСТЕМА ФОРМИРОВАНИЯ ДИАГНОСТИЧЕСКИХ ПРИЗНАКОВ ПО РЕЗУЛЬТАТАМ АНАЛИЗА КОНТУРА ШАРОВИДНЫХ ОБРАЗОВАНИЙ ЛЁГКИХ

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Цель. Исследовать возможность использования информации о свойствах контуров изображений патологических шаровидных образований легких в целях дифференциальной диагностики заболеваний.

Материалы и методы. Проанализирован двумерный массив денситометрических показателей, полученный при обработке томографических медицинских изображений пациентов с верифицированными диагнозами заболеваний легких (рак и туберкулез, 49 и 26 пациентов соответственно). Разработана методика построения контуров изображений таких образований. Для введения количественных характеристик контура рассчитан условный центр масс изображения патологии и построены две одномерные функции-сигнатуры: модуля радиуса-вектора, проведенного из центра изображения шаровидного образования к его границе, а также полярного угла поворота радиуса-вектора. Аргументом обеих функций является условный номер пиксела, принадлежащего контуру. С помощью спектрального анализа функции-сигнатуры в работе предложены и рассчитаны такие характеристики контуров, как спектральная энтропия, мультиплетность, количество локальных максимумов, функции-сигнатуры полярного угла поворота радиуса-вектора. Проведен анализ статистической значимости различий значений этих характеристик контуров шаровидных образований при различных заболеваниях (рак и туберкулез).

Результаты. Обнаружены статистические различия предложенных в работе характеристик контура для различных патологий, что может позволить осуществлять дифференциальную диагностику исследованных заболеваний легких.

Заключение. Полученные количественные характеристики шаровидных образований лёгких могут войти в систему помощи врачу в постановке диагноза. Необходимо помнить, что не существует единственного диагностического признака, основанного на количественной характеристике изображения, который бы сразу позволил определить тип патологии. Лишь совокупность подобных признаков позволит проводить качественную диагностику.

Ключевые слова: компьютерная томография, медицинские изображения, характеристики контура, дифференциальная диагностика, рак, туберкулёз.

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Introduction.

Medical images of lung diseases are usually diagnosed with qualitative description, often ambiguous. The radiologist, considering such images, analyzes their features relying on their diagnostic experience, which is supported by objective quantitative characteristics of the image only to a small extent [1–6].

The main quantitative characteristic obtained by the diagnostician during computer tomography is Hounsfield numbers belonging to certain voxels. Image processing programs report the diagnostician of the densitometric values for the selected area of interest and their statistical characteristics (usually, the mean value and the standard deviation). As a rule, the last two characteristics are not enough to diagnose correctly. In most cases, it is impossible to make the correct diagnosis based on just one statistical characteristic of the Hounsfield numbers totality for the medical image, and it is required to increase the number of objective characteristics that will allow differential diagnosis of diseases [7–11].

In addition to assessing the densitometric characteristics of the main area of interest, the radiologist pays great attention to the contour of the image of the spherical formation in the lung (SFL). Externally, diagnosticians divide them into "smooth", "scalloped", "bosselated", etc. [12–17]. From this we can conclude that the radiologist perceive the characteristic look of the contour of the SFL as a diagnostic parameter, but assesses subjectively. Quantitative characteristics of the contour should be presented and the dependence of these contour characteristics on the type of disease should be assessed. Only in this case, it will be possible to use this characteristic in differential diagnostics using automated systems of assistance to the doctor.

The paper calculates and uses quantitative characteristics of the image contours of the area of interest for patients with verified diagnoses and performs a statistical analysis of the dependence of these characteristics on the type of disease. This can make it possible to use the obtained characteristics for automated differentiation of the type of pathology in the lung with a more reliable diagnosis.

Materials and methods.

For the study, a database of patients with verified diagnoses was created: lung cancer and tuberculosis. The specialists of the RSHI "Diagnostic Center of Altai Krai" confirmed the diagnosis of patients undergoing examination on CT scanners. Confirmation of the lung cancer diagnosis was carried out by the histologist, and to confirm the tuberculosis diagnosis, culture sputum from the lungs was carried out.

Patients were scanned on a computer tomograph Asteion 4 (Toshiba Medical Systems). The scanning pitch was 2.0 mm, the voltage and current on the tube amounted to 80 kV and 160 mA respectively, the convolution kernel was FC01. Matrix was of 512×512 elements, DFOV 40×40 cm. Reconstruction of sections with thickness of 2 mm, pixel size of 0.4×0.4 mm was carried out. Visual analysis of images was carried out on the professional monitor PA301W (Japan), screen diagonal was 29.8 inches, resolution 2560×1600 pixels.

Visualization of medical images was carried out using the Merg eFilm Workstation© program, with the help of this program, the radiologist analyzed the medical image: found the focus of pathology, estimated the scale and the necessary volume in which the mentioned focus is enclosed. Then, the patient's data were processed in the Rentgenolog+ program [18] which converted the data of the area of interest from the DICOM format to a text file containing a rectangular matrix of Hounsfield numbers (densitometric densities in each voxel of the studied section). The area of interest (now it is a rectangular matrix of numbers) is considered by a doctor and physicist to select the optimal boundaries of the program workspace, as it is necessary that the entire contour was included in the selected area and, if possible, though not always achievable, did not touch the boundaries of that area. The area of interest was usually chosen so that on each section (i.e. in each rectangular matrix of numbers) there was one focus of disease.

A set of sections of the tomographic image containing the entire volume of SFL of the patient under study was obtained for each patient. Assuming that these sections contain information about the patient's disease, each section will contain this information separately. Thus, the database consisted of 982 sections for cancer (taken from 49 patients) and 493 for tuberculosis (taken from 26 patients).

A rectangular matrix of Hounsfield numbers for each section was used to construct the contour of spherical formations in lungs (SFL). A visual evaluation of the contour was performed on the reconstructed image, and the value of the densitometric indicator corresponding to the voxel of the studied contour was chosen according to the doctor ($Z0$). After that, all voxels which densitometric values are more than $Z0$ were assigned the value of 1, and those voxels which value is less than $Z0$ were assigned the value of 0. The problem of automating the selection of the $Z0$ contour boundary has not been satisfactorily solved yet. It is easy to create a program for automatic selection of the pathology contour boundary, but we believe that for now, the doctor makes it more reliable. Thus, according to the threshold value of $Z0$, the separation of SFL from other tissues by densitometric indicator was achieved. The selected $Z0$
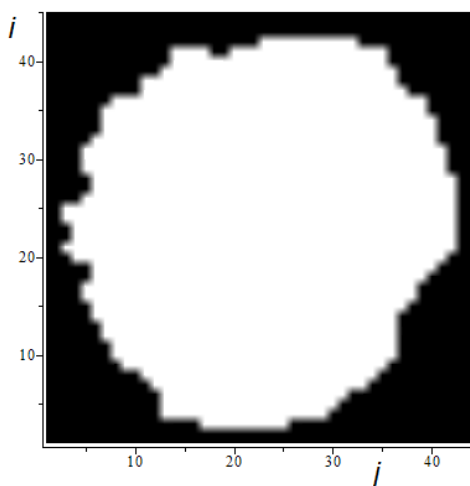
Fig. 1 (Рис. 1)

Fig. 1. Sample binary image.
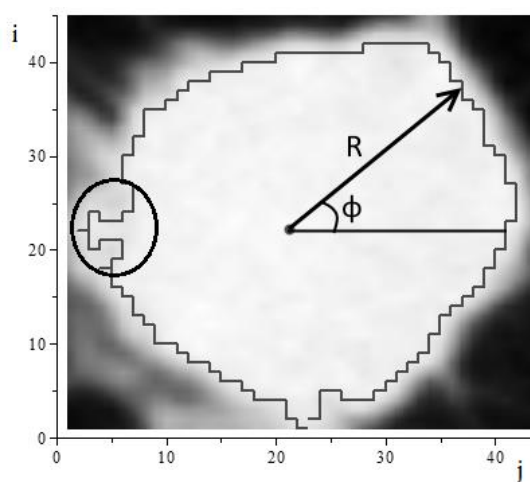
Рис. 1. Образец бинарного изображения.

Fig. 2 (Рис. 2)

Fig. 2. Example of "loops" forming in a CSM contour and its description in polar coordinates.

Рис. 2. Пример формирования «петель» в контуре CSM и его описание в полярных координатах.

value was applied to all the sections of the patient. The result is a binary image from the source image, in which the boundary of the contour is already clearly represented (Figure 1). Figure 1 shows a visual binary image of the area of interest, which shows the contour of the SFL (i, j – coordinates overlaid on the image).

$$x_c = \frac{\sum i \cdot Z(i,j)}{\sum Z(i,j)}, y_c = \frac{\sum j \cdot Z(i,j)}{\sum Z(i,j)}$$

(1)

In (1), Z (i, j) is the densitometric indicator of the tissue at the point of the flat section with the coordinates i, j, and summation occurs for all in and jn.

The values of the radius-vector module R(n) and the polar angle φ(n) (2, 3) were calculated for this vector:

$$R(n) = \sqrt{(j_n - x_c)^2 + (i_n - x_c)^2}, n = 1 \dots N;$$

$$\varphi(n) = arccos\left(\frac{j_n}{R_n}\right), n = 1 \dots N.$$

(2), (3)

This procedure was performed automatically for each contour by a program written in the Maple © mathematical package environment. A set of the radius-vector modules R(n) and polar angles φ(n) was named signatures of the selected contour [19]. Based on the received signatures, it was possible to enter quantitative characteristics of the features of the studied contours.

For more information on the quantitative characteristics of medical image contours we used, see article [20]. In particular, one of the methods is based on the calculation of the spectral power density of the centered radius signature. This power density helps calculate the entropy H(S(k)) for harmonics k of radius signatures (4).

$$H(S) = -\sum_{k=0}^{(N-1)/2} S(k) \cdot \ln S(k)$$

(4)

When using the second signature – angle φ(n), one can get another quantitative characteristic of the contour: the number of local maximums M, which corresponds to the change in the direction of rotation of the radius-vector R(n). In addition, in our study, the maximum S(k) value of the normalized spectral power density and the value of the entropy product H(S) and number of local L maximums were taken as the SFL contour characteristic, as we thought these characteristics could "react more sharply" to the type of disease. Local maximums are formed by passing the radius-vector along the contour in areas similar to those shown in Figure 2 (the area is highlighted by a circle).

The center of mass of the figure was defined as follows:

This path changes the direction of motion of the radius-vector along the left part of the selected area of the contour, thus, a "loop" is obtained. Very often, anatomically, the presence of a loop indicates the presence of a vessel entering the area of pathology and can serve as a diagnostic sign.

The number of such "loops" will be denoted as L and the characteristic obtained in the ratio (5) will be called multiplicity.

$$M = L \times H(S) \tag{5}$$

The above characteristics, i.e. the entropy of the signature of the contour radius-vector, multiplicity, the maximum value of the normalized spectral power density, and the number of local maximums, were calculated by the values of the densitometric indicator of each voxel belonging to the contour.

Calculations were performed automatically on a personal computer using programs written in Maple© and LabVIEW© [21].

fied quantitative characteristics of the contours are statistically indistinguishable for different types of diseases. If the null hypothesis is accepted, the proposed characteristics are not suitable as diagnostic parameters.

The results of the Student's t-test are presented in Table 1.

Discussion.

It can be seen from the table that the Student's t-test allows to reject the null hypothesis for all characteristics, provided that the distributions of the studied characteristics are subject to normal law. In this case, all the described charac-

Table №1. Values of the studied parameters for certain types of the disease.			
Investigated parameters	Type of disease	Mean value	Standard error of the mean
The amount of local maximum, M	Cancer	5.789	0.174
	Tuberculosis	5.012	0.098
An entropy of the radius-vector signature, H	Cancer	1.337	0.014
	Tuberculosis	1.117	0.011
Multiplicity, MH	Cancer	7.797	0.259
	Tuberculosis	5.758	0.140
A maximum value of normative power of spectral density, S	Cancer	0.573	0.006
	Tuberculosis	0.647	0.004

For non-parametric statistic test, we used the Mann–Whitney test, the results are presented in Table 2.

Results.

All the characteristics were analyzed for normal distribution in the STATISTICA© program by the Shapiro–Wilk test and it turned out that these samples were not likely to be taken from normal distribution (in common terms, the normality test was not passed). This test for the entropy of harmonics radius-vector signatures is graphically presented below (Figure 3). Visually, we saw similarities to normal distribution and it seemed strange to us. However, a statistical assessment using the chi-squared test also argues that it is unlikely that the characteristics studied belong to a normal distribution. In this regard, it was proposed to test the possibility of using the studied characteristics for differential diagnostics of the SFL using parametric (due to visual similarity with normal distribution) and non-parametric statistics (due to lack of normality).

The null hypothesis consisted in the belonging of the studied parameters for different verified diagnoses to one general population, i.e. the speci-

teristics of the contour can be diagnostic parameters.

The Mann–Whitney test was used for verification by non-parametric method, the results of which are shown in Table 1.

As can be seen from Table 1, now the result of verification of the null hypothesis on the possible belonging of the studied parameters of one general population to another one is ambiguous. Only the last three characteristics for these diseases are statistically distinguishable and can serve as diagnostic parameters. According to the Mann–Whitney test, the "number of local maximums" parameter has too much probability of type I error (more than Pcrit=0.05).

As a result, it can be seen that the characteristics studied can be used in the differential diagnosis of SFL. However, the "amount of local maximum" characteristic requires additional research. The proposed system for the formation of diagnostic signs has proved its viability and can be safely applied in clinical practice of radiation

Table №2. Results of testing the null hypothesis (STATISTICA©)			
Investigated parameters	t-statistics	The probability of type I error for the t-test	The probability of type I error for the Mann-Whitney test
The amount of local maximum, M	2.82	4.9×10^{-3}	0.14
An entropy of the radius-vector signature, H	8.57	0	0
Multiplicity, MH	5.01	0	0
A maximum value of normative power of spectral density, S	7.43	0	0

diagnosis.

Conclusion.

• Without using the hypothesis about the normality of the contour characteristics (it is not statistically confirmed), the "number of local maximums" parameter has too much probability of type I error (0.14), i.e. it cannot be argued that it is statistically distinguishable for different diseases. This circumstance does not allow this parameter to be used in differential diagnostics.

• The remaining three parameters for different diseases are statistically distinguishable and can be used for differential diagnosis.

• When making a diagnosis, it is necessary to rely on the indications of a set of diagnostic parameters, this approach can be implemented in automated systems of assistance to the doctor. At the moment, there is a set of parameters available for the system of assistance to the doctor, which include both already well studied: densitometric indicator, RMSD of densitometric indicator, and new: fractal dimension, entropy of the contour radius-vector signature, the number of local maximums, multiplicity, the maximum value of the normalized spectral power density. Increasing the quantitative characteristics of medical images will also improve the reliability of differential diagnostics.

• The diseases considered in this article are not the only ones where studies of images of local manifestation of pathology are used. The characteristics of the image contour described above can be used in differential diagnosis and other diseases.

The obtained quantitative characteristics of spherical formations in lungs can enter the system of assistance to the doctor in the diagnosis. It must be remembered that there is no single diagnostic feature based on the quantitative characteristic of the image, which would immediately allow to determine the type of pathology. Only a combination of such signs will allow for a qualitative diagnosis.Pregnant patients diagnosed with symptomatic MM need prompt therapy. Immunomodulatory drugs such as thalidomide and lenalidomide may induce marked teratogenicity, and should be avoided during the whole pregnancy period. Also, bortezomib cannot be recommended in pregnant patients, as there are few data about its safety.

Corticosteroids are the safest therapy of MM during pregnancy and can be used as a monotherapy in patients with the mildly symptomatic disease until delivery. In rapidly progressive disease, intensive combination therapy is usually required. If this progressive disease is diagnosed in the first trimester, termination of pregnancy is recommended. If the patient has an extensive pelvic or vertebral bone disease, Cesarean section is preferred to avoid trauma resulting from a vaginal delivery [5].

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