
BIOIMAGE INFORMATICS

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MORPHOLOGICAL ANALYSIS OF IMAGES OF DRIED DROPLETS OF SALIVA FOR DETERMINATION THE DEGREE OF ENDOGENOUS INTOXICATION

Research article

Abstract

Endogenous intoxication (EI) is an integral pathology which gives the general information about state of health of the patient. There is a correlation of biochemical data (costly, require long-term invasive studies) and morphological indicators based on image analysis of the visual image of a droplet of saliva dried in standard conditions (a simple and cheap non-invasive procedure). It is important to develop cheap, fast, non-invasive, computerized morphological methods for a medical diagnostics of EI based on the unique clinical experience obtained in the past decade to apply for mass rapid screening and monitoring of patients during the clinical examination, and also for individual checkup the health of any patient. The method is proposed and laboratory setup is elaborated for determination of the EI by determination of morphological properties of dried pattern of evaporated saliva droplet. The set of microphotographs of the salivary dried patterns is formed taking into account the degree of EI. Criteria for expert evaluation of the EI degree from images of saliva dried pattern image are proposed. For the first time, computer software was created and tested to determine the EI degree. This makes it possible to process a large number of digital images of saliva patterns, which allows evaluating the monitoring of the patient health. Proposed method is a combination of bioinformatics and biochemistry approaches for obtaining diagnostic information from a morphological analysis of standardized dried patterns of saliva.

Keywords: dried pattern, saliva, microstructural bio-liquids' analysis, quantitative microscopy, automatic expert system, descriptors, bioinformatics.

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МОРФОЛОГИЧЕСКИЙ АНАЛИЗ ИЗОБРАЖЕНИЯ ВЫСОХШЕЙ КАПЛИ СЛЮНЫ ДЛЯ ОПРЕДЕЛЕНИЯ СТЕПЕНИ ЭНДОГЕННОЙ ИНТОКСИКАЦИИ

Научная статья

Аннотация

Эндогенная интоксикация (ЭИ) является интегральной патологией, которая дает общую информацию о состоянии здоровья пациента. Существует корреляция биохимических данных (дорогостоящих, требующих долгосрочных инвазивных исследований) и морфологических показателей, основанных на анализе изображения капли слюны, высушенной в стандартных условиях (простая и дешевая неинвазивная процедура). Важно разработать дешевые, быстрые, неинвазивные, компьютеризированные морфологические методы для медицинской диагностики ЭИ,

основанные на уникальном клиническом опыте, полученном в последнее десятилетие, для массового скрининга и мониторинга пациентов во время клинического обследования, а также для личного контроля здоровья пациентом. Предложен метод и разработана лабораторная установка для диагностики ЭИ путем определения морфологических свойств высушенного образца (паттерна) испаренной капли слюны. Набор микрофотографий паттернов формируется с учетом степени ЭИ. Предложены критерии для экспертной оценки степени ЭИ по паттернам высушенной слюны. Впервые было создано и протестировано компьютерное программное обеспечение для определения стадии ЭИ. Это позволяет обрабатывать большое количество цифровых изображений паттернов слюны. Это дает возможность проводить мониторинг здоровья пациента. Предлагаемый метод представляет собой комбинацию подходов биоинформатики и биохимических исследований для получения диагностической информации из морфологического анализа стандартизированных высушенных образцов слюны.

Ключевые слова: сухой паттерн, слюна, анализ микроструктуры биожидкостей, количественная микроскопия, автоматическая экспертная система, дескрипторы, биоинформатика.

1. Introduction

By today there has been accumulated a large amount of actual data on specific features of structure formation of different bio-liquids of human body in the normal state and during the pathological state development. Dried pattern sample is formed by evaporation of small drop of the biological liquid on a flat substrate. Such a pattern can be used for the diagnosis of various diseases. A study of mechanisms for bio-liquids structure formation by a method of optical microscopy is of specific interest [1], [2], [3], [4], [5].

The structure of the biological liquid pattern is an integrating image of all the complex molecular relationships that exist in it, which are transformed to a macroscopic level. Consequently, a medical expert of high qualification can provide a diagnostics of the EI by the morphologic analysis of pattern of a dried droplet of saliva. There is only a small number of unique medical experts in the world who, based on own many years of experience in practical research, could exactly determine the presence of the pathology by studies of the pattern structure.

EI is an integral pathology which gives the general information about state of health of the patient, then the diagnostics of this disease requires high sensitivity with much lower requirements for selectivity. This is in optimal correspondence with diagnostic ability of the dry pattern morphologic analysis.

The idea of our project is to determine the degree of the EI without expertise of unique medical experts, but with use of automated (computer) expert system based on the numerical values of the morphological markers and descriptors with statistical analysis of the diagnosis in the training sample of images. Then a simple diagnostic procedure will be available to the average medical staff and even the patient himself.

The solving problem is to create a hardware and software system that implements the principle of diagnosis based on the digital recognition of dried saliva drop image and its computer analysis based on specially developed algorithms by comparing with the expert database descriptors.

Our investigations shown, that such medical expert has sensitivity to the EI degree determination by recognition of saliva dried pattern morphology is about 80%. Theoretically, the sensitivity of the computerized method based on bioinformatics algorithms can be reached the same value approximately.

2. Methods

The method of non-invasive determination of the degree of EI is based on transformation of drop of the saliva sample from liquid to a solid phase (pattern) through dehydration on a flat substrate and study of digitized image of the pattern by computerized expert system.

During evaporation of saliva drop, molecules and permolecular complexes are distributing in strictly defined locations over the pattern area in the form of concentration zones (Figure 1).

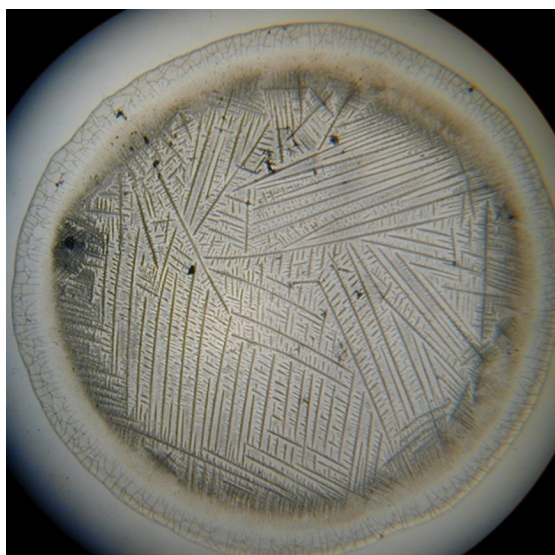


Figure 1 – Dried pattern of the saliva which corresponds to the 2-nd degree of EI (real size of the sample is 7 mm)

As a result, the film is formed, possessing a structure, whose specificity is defined by chemical composition and character of presented in bio-liquid substances interaction. Pathological changes lead to violation of qualitative and quantitative composition of saliva. These violations appear in solid phase morphology and can be described by quantitative descriptors [2], [3], [6].

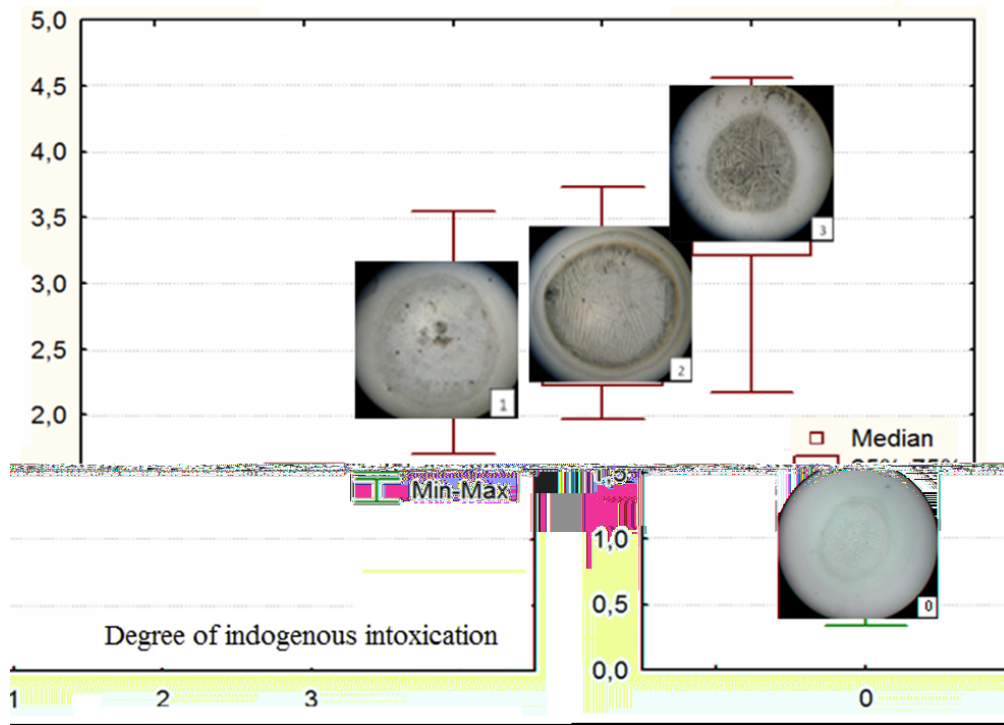


Figure 2 – Degrees of EI and correlation between the morphology of the dried pattern of a droplet of saliva and the biochemical parameter of the patient (see the text)

There is a correlation of biochemical data (costly, require long-term invasive studies) and morphological indicators based on image analysis of the visual image (pattern) of a droplet of saliva dried in standard conditions (a simple and cheap non-invasive procedure). Figure 2 demonstrates such a correlation between the morphology (zonal structure) of the dried pattern and biochemical parameter of the patient (medium mass molecule concentration in the saliva). In Figure 2, each characteristic image of the dry pattern on the graph corresponds to some degree of EI, from 0 to 3. Every degree of the EI manifests by the saliva dried pattern morphology with characteristic features which gives the opportunity to determine the EI degree by pattern morphology automatic recognition.

Thus, we can to determine the degree of EI of the patient by morphological analysis of the saliva dried pattern. This is a basis of the diagnosis of the pattern without the involvement of biochemistry by computer microscopy investigation of morphology of saliva dried pattern.

Laboratory setup for diagnostics by the saliva pattern morphology (Figure 3) consists of three basic systems: sample preparing system, digital recognition of the pattern image system, automated expert diagnostic system (computer program). The setup represents a research computer system for routine analysis in medical and biological applications and fundamental studies in the field of functional bio-liquids morphology [3], [6], [7].

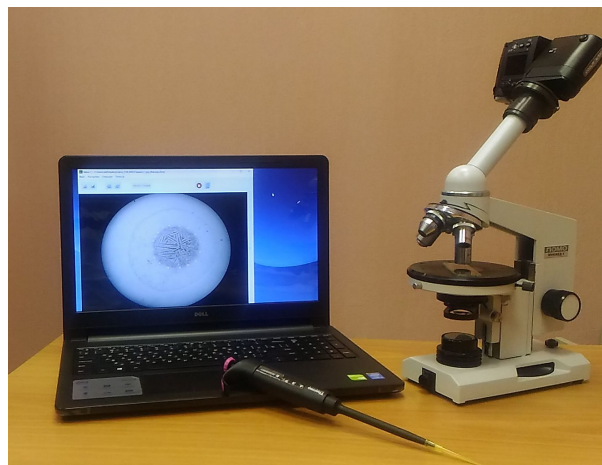


Figure 3 - Laboratory setup is formed by microscope, web-camera, computer, and sample preparation devices and materials (pipette-dispenser, microscope slides, etc)

Sample image processing includes:

1. *Sample preparing by pipette-dispenser obtaining of dried patterns.* Samples were prepared by drop dehydration on substrate (microscope slide). Drop of saliva (volume of 0.01 ml) is deposited to the substrate surface. This sample is dried at the room temperature from 20 to 25 Celsius degrees and relative humidity of 25-35 % with minimal mobility of ambient air. After evaporation of free water, a saliva drop fully goes over into a solid phase and forms a dried pattern. Diameter of the droplet and its dried pattern on the substrate belongs to the interval of 5-7 mm approximately.

2. *Obtaining of digital image of the pattern by microscope or slide-scanner.* To obtain the digitized image of dried pattern, the microscope Polam R211-M (LOMO, Russia) was used.

3. *Processing of image by the program (automated expert system) and obtaining of the diagnostic information.*

Mathematical algorithm for computation the degree of EI by image of saliva pattern was elaborated [8], [9]. It is based on scientific researches in the field of analysis of structural changes in saliva pattern depending on the EI degree. The most important problems which we have solved is specifying of structures characteristics of the pattern which are most informative to determine the EI degree. We used the quantitative markers [7] and new computer descriptors taking into account the color and zonal structure.

3. Results

In framework of development of our algorithm we analyzed saliva probes belonged to 60 patients (training set, correlation coefficient $R^2=0.72$, see Figure 4) and received medical expert scores for these probes. After regression analysis of the training set, we obtain the scoring function to determine EI degree. After that the developed computer algorithm was tested on 40 saliva probes belonged to the others patients (test set, correlation coefficient $R^2=0.70$).

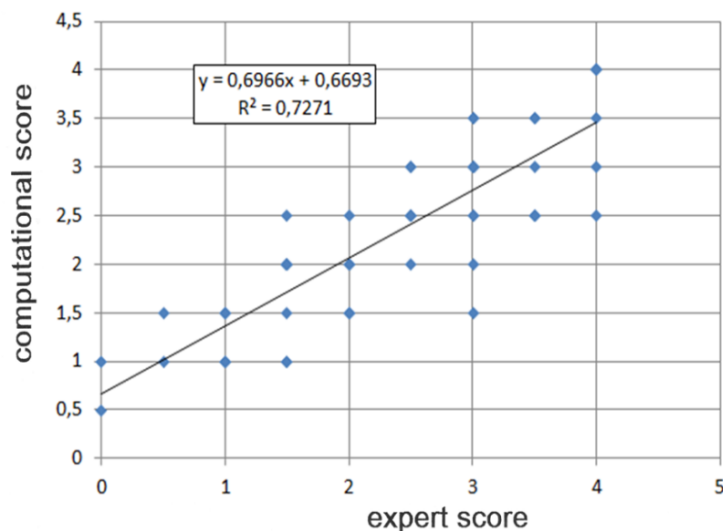


Figure 4 – Training set to determination of the scoring function for EI degree

Comparing the correlation coefficients of the training and the test sets, we can conclude that our markers and computer descriptors possess a well-defined interrelation with EI degree of the patients. Therefore the study of quantitative characteristics (color and zonal distribution) provides diagnostic information.

On the basis of saliva patterns samples library (obtained from different patients with EI) we have elaborated the automated expert system for EI numerical diagnostics. The principle of diagnostics bases on the procedure of saliva pattern preparation including digital recognition of pattern image and its computer analysis based on specially developed algorithms by comparing with the expert descriptors and extensive database of dried pattern samples obtained from clinical treatments which include more than 100 samples were validated. We have carried out own research in collaboration with medical diagnostic centers and formed the electronic database. It was shown the regular specific connection between the specific change in the pattern structure from normal to pathological state which corresponds to some EI degree.

Progressive features of the method are:

- simplicity of sample preparation and rapid analysis;
- objectivity of diagnostics: an automated quantitative analysis of the sample is used, the conclusions are based on an electronic database;
- this is non-invasive method of sampling;
- possibility of revealing pathological abnormalities at early stages and controlling changes in the dynamics of the disease;
- possibility of using telemedicine technologies which is compatible with smartphone and personal computer.

EI is an integral pathology which gives the general information about state of health of the any patient. Currently, solutions for rapid diagnostics of EI are absent in the market. Product's competitive advantages of our methods give the opportunity to propose an innovative device that is in demand by a wide range of consumers, as well as for medical clinics.

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Финансирование

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Conflict of Interest

None declared.

Конфликт интересов

Не указан.

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