Decision support system for an early-stage keratoconus diagnosis

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Abstract. Currently, there is a wide variety of different diseases that exist, a lot of which can be hardly prompt diagnosed even by medical specialists. This paper presents a method for early-stage diagnosis of ophthalmologic disorder keratoconus. Working with medical imagery that was captured by a rotating Scheimpflug camera system for anterior segment analysis, the goal was to create a decision support system to aid ophthalmologists in prompt detection of the disorder to eliminate the chance of further surgical intervention. Given approach uses several steps to achieve that goal, such as find the region of interest on the medical imagery using a Single Shot MultiBox Detector, filter and binarize the image, locate the cornea and approximate the curve with least squares fitting, classify the stage according to the previously labeled dataset by medical specialists with a random forest method. The suggested approach achieves 76% precision on a dataset containing 500 images of the patients with the first stage of keratoconus and healthy patients. The final result was compared with modern existing medical methods that are usually used in ophthalmologic clinics by medical specialists.

1. Introduction

Information technologies are currently used in almost all possible areas of human activity. Medicine is especially actively developing, offering modern specialized means for the detection and subsequent diagnosis of various diseases. Often, as a result of the examination, the doctor receives a set of images that need to be studied, interpreted, draw conclusions about the patient's condition and outline a further course of treatment. Given the vast range of possible diseases, some of which are characterized by mild symptoms, even qualified doctors are not always able to notice the initial stages of the pathological process. This problem is particularly relevant to diseases of unknown etiology or less studied. In particular, ophthalmologic disease keratoconus [1], which is a degenerative non-inflammatory ophthalmopathy can be attributed to a change in the optical properties of the pupil due to a change in the thickness of the cornea and its deviation from the ideal spherical healthy form. Moreover, there are cases when the symptoms of the disorder in the early stages are confused for myopia or astigmatism due to similar visual sensations, while its progression can lead to severe visual impairment. Keratoconus has 4 different stages [2], numbered from 1 to 4 which are stated in Table 1.

In this regard, issues related to the development of processing tools obtained in the process of examining the cornea of images, identifying abnormalities and decision-making support in making the diagnosis as early as possible are of particular relevance.

Table 1. Keratoconus classification based on disease evolution. VA, visual acuity; D, dioptres.

Stage	*Description*
1	Frustre or subclinical form; diagnosed by corneal topography; ~6/6 VA achievable with spectacle correction
2	Early form; mild corneal thinning; corneal scarring absent
3	Moderate form; corneal scarring and opacities absent; Vogt's striae; Fleischer's ring; <6/6 VA with spectacle correction, but ~6/6 VA with contact lens correction; irregular astigmatism between 2.00-8.00 D; significant corneal thinning
4	Severe form; corneal steepening > 55.00 D; corneal scarring, <6/7.5 VA with contact lens correction; severe corneal thinning and Munson's sign

In this paper, the proposed mathematical apparatus, algorithmic and software tools can be used in the construction of an automated decision support system [3,4] for diagnosing and determining the stage of keratoconus based on the analysis of sets of medical imagery.

2. Image pre-processing

Before starting to work on the curve of the cornea, it is necessary to select a region of interest on the image, which includes only the corneal arc. This will considerably facilitate further image processing since the output image will not include many default white marks of the capturing device.

This pre-processing will also help to get rid of possible components of the images that can lead to an inaccurate finding of the contours of the cornea. Such areas include tears, part of the eyelid, as well as other random details in the picture. Besides, the selection of the working area will reduce the number of processed pixels. Considering the nature of cornea medical imagery, that is, there are not many objects on it, and the required arcs usually have similar appearance on different images, it is not important to determine the high accuracy of the working area in the image, the Single Shot MultiBox Detector [5] was chosen based on a single pass through the image. This pre-processing is carried out using the Tensorflow [6] machine learning library for building and training a neural network, which will automatically find the working area. It is necessary to provide that the cornea in the image can be presented in different sizes. In the given case, training and test datasets were prepared, containing 30% and 70% of the total number of images respectively. On the training set, the necessary areas of the image, which include the corneal arc was manually pre-marked. For the subsequent finding of contours, it is necessary to process the obtained region of interest. The main idea is to eliminate possible distortions on the image and bring it into a binary form.

For the most accurate results, the original image is pre-converted to halftone using the formula:

$$y(i,j) = 0.299 * R(i,j) + 0.587 * G(i,j) + 0.114 * B(i,j) \quad (1)$$

Where R, G, B are for red, green and blue components of the image respectively. It should be noted that medical imagery is sometimes quite noisy, which can negatively affect the results. For this, it was decided to use a Gaussian Blur [7], which would significantly reduce image noise, and prevent the possible case where the cornea would represent a somewhat rough arc.

After filtering, it is necessary to binarize the image, which will uniquely divide the pixels into foreground and background. The most suitable for this is binarization with setting the global intensity threshold. This method is the most primitive. Since the original images have a similar set of colours and pixel intensity, as part of the development of the software, the images after binarization were inspected to determine the most suitable threshold value.

3. Finding the arc of the cornea

After binarization of the image, the contours of the cornea can already be distinguished, since it is possible to determine the boundaries between the background of the image and its foreground, which are the cornea and the adjacent parts of the eye. Boundaries were detected by using the algorithm of

Suzuki and Abe [8], which allows determining the external boundaries on the binary image. The resulting contours are presented in the form of an array of points that clearly define the arc of the cornea.

Images are often not centred so to find the arc it necessary to find a point as far as possible from the pupil of the eye. It can be accomplished by ignoring the edges of the image since they can be distorted which negatively affects the final result. The resulting contour is divided into three equal sections. In the middle section, the chosen point is the farthest from the pupil.

Considering the standards of capturing the eye of a human and the characteristics of the human eye, the maximum distant point from the pupil will be the middle of the cornea, given this fact this point will be chosen as the starting point for analysing its upper surface of the cornea and highlighting the corresponding arc. Since the cornea is bounded by the upper and lower arcs, it is necessary to choose only the nearest points corresponding to the upper part of the cornea. The resulting point is further considered as a reference point. Using the Manhattan distance, the coordinates of neighbouring points nearest to the reference point are found. Considering the angle of inclination between the points, the left and right parts of the arc can be distinguished. Due to the nature of the human eye, if the point is not the border of the image, then an abrupt change in the angle of inclination between the points of the cornea will be a clear indication that the end of the arc has been reached. As a result of the operations performed, an array of points describing the arc of the cornea will be obtained.

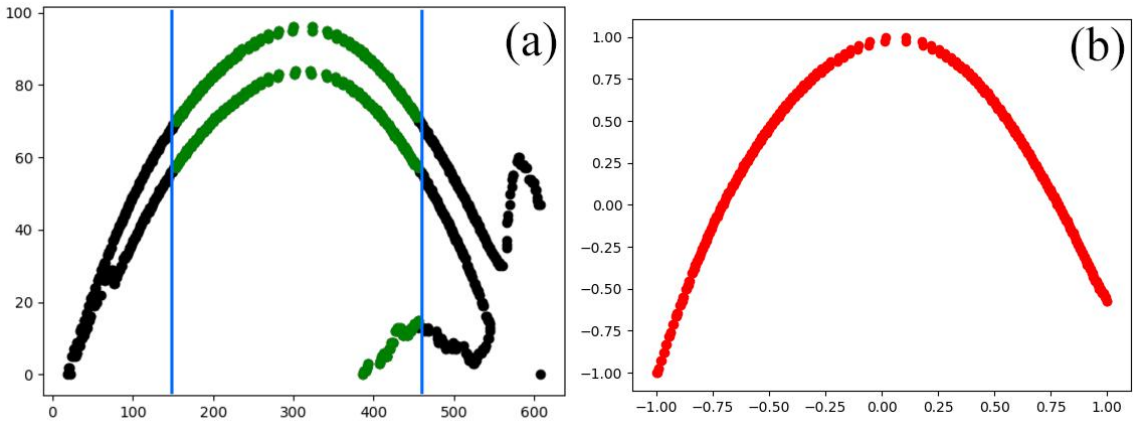

Figure 1. (a) The Initial array of points describing all contours of the image. The section inside the blue bounding lines highlights the points from which reference point is found. (b) The array of points describing the outer corneal arc, which was obtained after processing the initial array of points.

4. Curve fitting

To have a correct approximating function, it is necessary to provide for the possibility to consider the left and right parts of the cornea arc separately.

The slope will take a negative value if the points represent the left half of the arc and a positive value otherwise.

To eliminate the possibility that the obtained halves could be having different lengths additional checking was implemented which compares both parts of the arc to only include equidistant points from the reference point, as a result, an array of points is obtained that uniquely describes the cornea. Based on the given points, it is possible to construct a mathematical function, which in general will help in further determining the keratoconus stage from the initial images. For the subsequent classifications of the disorder stages, it is worthwhile to single out certain parameters reflecting the properties of the cornea. To compare each point of the arc is time-consuming and not an accurate way. One of the possible ways of representing this array in another form is an approximation. Let there be N values of the argument x_i and corresponding values of the function F_i. The main task is to find a function from the class of algebraic polynomials of the Nth degree. For a set of N, the maximum

degree of a polynomial is $k = N - 1$. The maximum degree of a polynomial is determined by the number of data points used to generate it. However, it is generally recommended that you use the lowest degree as possible to accurately represent your data set, since higher-order polynomials passing directly through each data point may exhibit erratic behaviour between these points. A general polynomial regression model can be developed using the least squares fitting which can be defined as follows:

$$F(x) = a_0 + a_1 x + a_2 x^2 + \ldots + a_n x^n \quad (2)$$

The least squares fitting [9] is aimed to minimize the differences between the values estimated by a polynomial and the expected values from the data set. Given the characteristics of the polynomial coefficients, the general form of which is presented below, the value of the first coefficient can be ignored, since it only affects the position of the curve along the y-axis. In the given dataset 8th degree polynomial was sufficient.

5. Stage classification

Based on the polynomial coefficients obtained and similar works [10,11], a random forest method [12], which is using a collection of decision trees, was chosen to classify stages of the disorder. The number of trees was selected using an experiment that took into account the classification accuracy based on a prepared sample of 200 images: 100 with the parameters of the first stage of keratoconus and 100 without deviations from the norm. The training sample included 70% of the original sample, and the remaining 30% entered the test sample. Taking into account possible deviations in the accuracy values, it was decided to average the classification values, therefore as shown in figure 2, each point on the graph represents the average value obtained by the classifier in the five previous experiments.

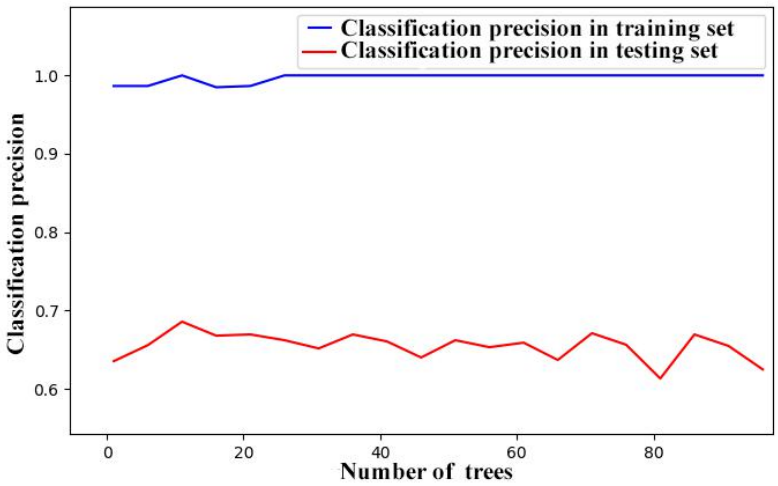

Figure 2. Classification accuracy of random forest method with different number of tress used.

The importance of certain coefficients of the polynomial was also examined. For evaluation, a Gini impurity index [13] was calculated, which is a measure of how often a random element is incorrectly classified. In general, the index is as follows:

$$G = \sum_{i=1}^{n_c} p_i (1 - p_i) \quad (3)$$

Where n_c is the number of classes in target variable and p_i is the ratio of this class.

As can be seen from figure 3, the most important coefficients of 8th degree polynomial are a_2, a_8, a_3, a_6 . But the remaining coefficients are also significant since their Gini impurity index > 0.050 $ and the value of the coefficient a_2 exceeds a_5 only 1.7 times, which cannot be considered a significant difference.

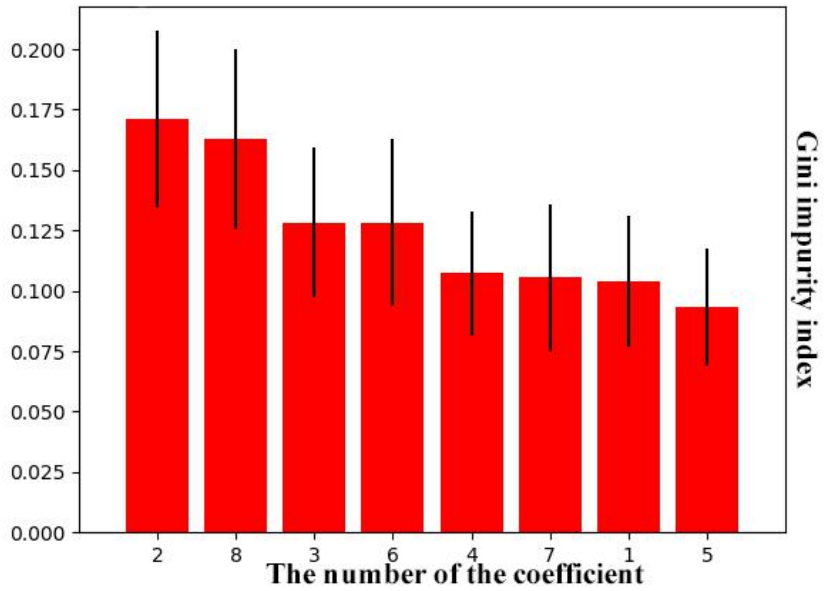

Figure 3. Coefficient importance of 8th degree polynomial. Black line is a standard deviation of the given coefficient.

6. Experimental results

For the experimental part, it was decided to test the results of the decision support system based on previously marked images by ophthalmologists.

In mathematical statistics to test statistical hypotheses concepts called type I and type II errors [14] were used. Type I error is the rejection of a true null hypothesis and type II error is the non-rejection of a false null hypothesis. In a given case, the medical specialist needs to confirm or deny the diagnosis of the disorder.

Results of the classification were based on the following measurements:

- Accuracy
- Recall
- F-score

The result of medical testing is often the doctor's verdict, which confirms the presence of the disease or denies it. Diagnosis of keratoconus is not an exception and the most important is the detection of corneal changes that occur in the first stage, which will prevent surgical intervention promptly. Given these characteristics of the disease, you can take the first stage of keratoconus and the absence of keratoconus as statistical hypotheses. Results of classifying 500 images of the eye with the first stage of keratoconus and healthy eye, which were equally divided evenly are given in table 2. The training set contained 70% of images, and the testing set contained 30% of the images.

Table 2. Precision, recall and F-score obtained for patients with the first stage of keratoconus and healthy patients.

	Precision	*Recall*	F-score
First stage	0.76	0.83	0.79
Healthy	0.73	0.62	0.67

Results of the suggested system were compared with modern medical approaches [15] and are given in figure 4.

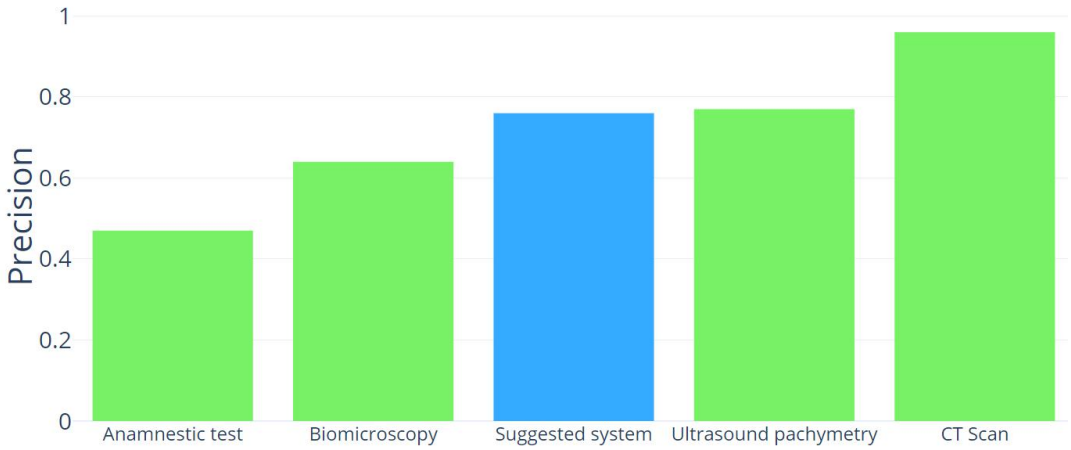

Figure 4. Comparisons of the different medical approaches used for diagnosing keratoconus.

7. Conclusion

As a result of the current research, a suggested decision support system was created for the diagnosis of keratoconus disease in its early stages. The developed system offers medical staff to import a set of medical images, based on which the program will give the textual and visual results with the information about the possible current stage of the disease the patient. Despite 76% precision, it is projected to take into account the inner part of the cornea, as well as the thickness between the inner and outer arcs. Increased precision could be achieved with further thorough research of the keratoconus disorder in its earliest form, especially the causes of occurrence. The designed software and the article will be useful for ophthalmologists not only to use but also to have a feedback for future discussions to produce a multifunctional decision support system, which can be used not only to diagnose ophthalmologic disorders but a wide range of human diseases by analysing medical imagery.

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