

# Machine Learning Techniques in Keratoconus Classification: A Systematic Review

AATILA Mustapha<sup>1</sup>, LACHGAR Mohamed<sup>2</sup>, HRIMECH Hamid<sup>3</sup>, KARTIT Ali<sup>4</sup>

LTI Laboratory, ENSA School-University Chouaib Doukkali, El Jadida, Morocco<sup>1,2,4</sup>

LAMSAD Laboratory, ENSA School of Berrechid-University Hassan First, Settat, Morocco<sup>3</sup>

**Abstract**—Machine learning (ML) algorithms are being integrated into several disciplines. Ophthalmology is one field of health sector that has benefited from the advantages and capacities of ML in processing of different types of data. In a large number of studies, the detection and classification of various diseases, such as keratoconus, was carried out by analyzing corneal characteristics, in different data types (images, measurements, etc.), using ML tools. The main objective of this study was to conduct a rigorous systematic review of the use of ML techniques in the detection and classification of keratoconus. Papers considered in this study were selected carefully from Scopus and Web of Science digital databases, according to their content and to the adoption of ML methods in the classification of keratoconus. The selected studies were reviewed to identify different ML techniques implemented and the data types handled in the diagnosis of keratoconus. A total of 38 articles, published between 2005 and 2022, were retained for review and discussion of their content.

**Keywords**—*Ophthalmology; corneal disease; keratoconus classification; machine learning*

## I. INTRODUCTION

Keratoconus is a non-inflammatory bilateral corneal disease, characterized by a progressive deformation of the cornea which takes the shape of a cone [1]. The common symptoms of keratoconus are usually abnormally progressive myopia and astigmatism, vision poorly corrected by glasses, difficulty adapting to lenses, visual fatigue, and headaches. Other specific symptoms may be associated with each stage of keratoconus. The prevalence of keratoconus can range from 0.2 to 4.790 per 100 000 people [2]. Keratoconus can affect only one eye or both eyes at the same time, with different degrees of evolution, and repetitive eye rubbing is considered the most involved factor in the progression of this disease [3]. The diagnosis of keratoconus is generally made by examining the topography of the cornea as well as analyzing certain biomechanical characteristics of the cornea [4].

The detection of keratoconus, especially in its early stage, is a task that is not obvious in the absence of a set of uniform criteria describing this keratoconus stage. Considering the importance of the diagnosis of keratoconus, many contributions that aim at the classification of keratoconus have been published. The authors of a significant number of research works have opted for the adoption of ML techniques in their keratoconus classification systems, with the aim of achieving a good level of precision in the discrimination of this disease and assisting clinicians in patient diagnosis.

Generally, the diagnosis of keratoconus is done manually by specialists, who must analyze the different corneal characteristics to collect sufficient information to confirm the presence of keratoconus. However, to better support specialists in keratoconus detection task, many researchers have adopted ML algorithms to consolidate the decisions of ophthalmologists regarding the presence of keratoconus in patients [5]. The combination of the specialists' expertise and the advantages of ML, in processing different types of data, will certainly allow to detect keratoconus, particularly in its subclinical stage, with a high level of confidence and accuracy [6], to offer patients more choice of treatments and to avoid surgical interventions.

This paper proposes a systematic review concerning the use of ML techniques in the detection and classification of keratoconus. The main objective of this systematic review is to identify and evaluate the previous scientific literature relating to the classification of keratoconus using ML techniques, thus enabling researchers to learn about the state of research in this field. Moreover, this study will identify the commonly ML techniques used for the classification of keratoconus, the data types most used by ML-based systems in keratoconus classification and the corneal features most used in keratoconus classification.

## II. RELATED WORKS

The detection of early or even preclinical forms of keratoconus will allow appropriate patient care and anticipate vision problems. Some research teams have focused on producing systematic reviews to present the latest advances in research concerning keratoconus disease to researchers. The Authors of systematic review [7] aimed to survey and critically evaluate the literature on the algorithmic detection of subclinical keratoconus. Measured parameters and the design of the machine learning algorithms reported in 26 papers were compared following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations. As conclusion, authors reported that ML can potentially improve the detection of subclinical or early keratoconus. In the review [8], authors conducted the study to determine the prevalence and risk factors for keratoconus worldwide, including eye rubbing, family history of keratoconus, atopy, allergy, asthma, eczema, diabetes type I and type II, and sex. In this review 29 articles included 7 158 241 participants from 15 countries were analyzed. Results showed that the prevalence of keratoconus in the whole population was 1.38 per 1000 population and eye rubbing, family history of keratoconus, allergy, asthma, and eczema were the most important risk factors for keratoconus

according to the available evidence. Authors in [9] presented a systematic review to discuss new approaches to the early detection of keratoconus and recent investigations regarding the nature of its pathophysiology. Authors in this study reviewed the evidence for keratoconus complex genetics and evaluate the identified genes/loci and potential candidate gene/loci. Generally, there is a remarkable lack of reviews highlighting the different uses of ML techniques for the classification of keratoconus.

### III. METHOD

This systematic review was conducted in Scopus and Web of science scientific databases, adhering to PRISMA guidelines in its most recent version 2020. For the proper conduct of this review, a list of research questions (RQ), that the Systematic Literature Review (SLR) should answer, has been listed in Table I. The collection of works studied in this systematic review aims to select as much as possible of related scientific papers, on detection and classification of keratoconus using ML tools, while excluding irrelevant studies that do not provide enough information related, thus aiming for high precision. In order to achieve the objectives, already cited, of this systematic review with good levels of precision, a well-extended search strategy is therefore necessary.

The terms considered in the selection of studies in this systematic review are “Keratoconus” and “Machine learning”. The research query used in this study is structured as follows:

**Research query** = ( TITLE-ABS-KEY ( keratoconus ) AND TITLE-ABS-KEY ( machine AND learning ) ).

TABLE I. RESEARCH QUESTIONS OF THE STUDY

No.	Research Question (RQ)
RQ1	What are the main objectives of using ML techniques in the classification of keratoconus?
RQ2	What are the ML techniques used in the classification of Keratoconus?
RQ3	What are the data types used by the different classifiers for the classification of keratoconus?
RQ4	What are the most used corneal features in keratoconus classification by the different ML models?
RQ5	What is the impact of ML use on the classification accuracy of keratoconus compared to traditional techniques?
RQ6	What is the number of keratoconus classes retained for each study included in this review?
RQ7	What are the limitations of the current literature and the opportunities for future research?

To produce a relevant systematic review, regarding the use of ML algorithms in keratoconus classification, a set of inclusion criteria (IC) and exclusion criteria (EC) was adopted in the process of selection of the considered documents. Included studies are the original articles, published between 2005 and 2022, which contributed on keratoconus detection using ML techniques. Selected works must use ML algorithms, trained and tested in different datasets, with a distribution of the data in training and testing datasets using different techniques such as cross-validation. In addition, the full text of the selected papers must be available, and only studies published in English were considered. Conference papers, conference reviews, letters, books, book chapters and editorials

were excluded from this study. The inclusion and exclusion criteria are summarized in the Table II below.

TABLE II. INCLUSION CRITERIA (IC) AND EXCLUSION CRITERIA (EC)

No.	Criteria
IC1	Papers published in a peer reviewed scientific journal.
IC2	Works published in English.
IC3	Testing of algorithms on test datasets.
EC1	Reviews, conference papers, conference reviews, letters, books, book chapters and editorials.
EC2	Works that do not provide enough information on the methodology adopted and that do not report results in a clear way.
EC3	Articles whose full text is not available.

According to the previous research query, a total of 175 documents were identified from Scopus and Web of science databases. After eliminating Reviews, conference papers, conference reviews, letters, books, book chapters and editorials, this number is reduced to 110 scientific articles. Among these 110 papers, 47 duplicate documents were removed. After reading titles and abstracts of different papers, 17 articles were excluded, 3 of which were not written in English and 14 others were not related to the classification of keratoconus using ML techniques. The other inclusion and exclusion criteria were applied on a total of 46 articles, of which two documents did not clearly detail the adopted methodology and did not report obtained results, and six other articles are not relevant, since they do not focus on the use of ML in keratoconus classification. The final number of articles included in this systematic review is 38 articles as shown in Fig. 1 below.

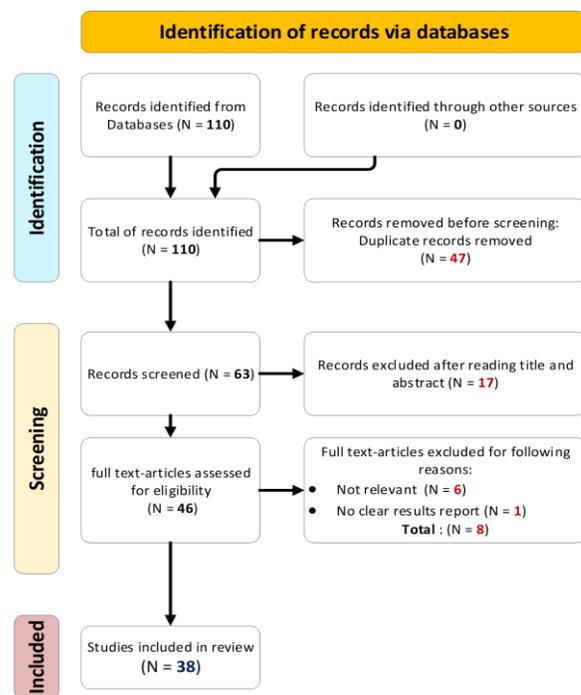


Fig. 1. PRISMA flow chart of the process of papers collection.

Once the articles were selected, based on the different inclusion and exclusion criteria already mentioned, an in-depth analysis of the selected articles was carried out. A set of information was extracted including the year of publication of each paper, the ML techniques used in the classification step of keratoconus, the number of inputs used by each technique and the technique performance in terms of accuracy, precision, recall, f1-score, sensitivity, specificity and area under the curve ROC. For the datasets, retained information represented the types of data used by different methods, the size of the dataset and the number of corneal classes considered during the classification process.

#### IV. RESULTS

Retained articles, related to keratoconus classification using ML tools, were published from 22 different countries. The countries representing the origin of the greatest number of publications are Belgium with 5 articles, followed by China and Spain with 4 articles each country, followed by USA and Romania with 3 articles each country. Belgium, China, Spain,

USA, and Romania represent the origin of 50% of the papers included in this study with a total of 19 papers. Fig. 2 below shows the distribution of included works by countries of publication and Table III reports the Literature Review Matrix (LRM) of reviewed articles.

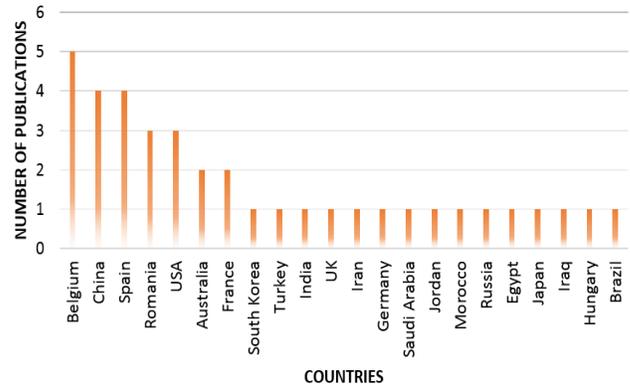


Fig. 2. Distribution of selected papers by countries.

TABLE III. DETAILS OF STUDIES INCLUDED IN THE CURRENT SYSTEMATIC REVIEW

Ref.	Year	Technique	Data type	Dataset size	Classes number	Inputs number	Performance
[10]	2022	Five-layer feedforward network	Biomechanical parameters calculated from corneal raw videos	276 samples	2 classes	4 biomechanical characteristics	Accuracy: 98.7%, Sensitivity: 97.4% Specificity: 100% Precision: 100%
[11]	2022	FcNN, XGBoost & TabNet (Voting)	Corneal parameters	2613 samples	3 classes	18 variables	Accuracy: 90.6% to 95.6% Sensitivity: 67.6% to 90.5% Specificity: 90.9% to 97.9%
[12]	2022	SVM Classifier applied to selected features, extracted using AlexNet & TabNet	Corneal topographic images	682 images	2 classes	1x1000 features	Accuracy: 98.53% Sensitivity: 98.06% Specificity: 99.01%
[13]	2022	GoogLeNet Classifier applied to segmented image using PSO, DPSO & FPSO	Corneal topographic images	1500 images	3 classes	224x244x3 images	Accuracy: 95.9% Sensitivity: 94.1% Specificity: 97%
[14]	2021	Random Forest & decision tree	Pentacam topographic Corvis biomechanical variables	80 eyes	2 classes	27 parameters	Accuracy: 89% Sensitivity: 86% Specificity: 93%
[15]	2021	VGG-16	Corneal topographic images	1926 images	2 classes	224x224 corneal maps	Accuracy: 97.85 % Sensitivity: 98.46 % Specificity: 90% AUC: 94.23%
[16]	2021	Multilayer perceptron (MLP), neurofuzzy & Naïve Bayes	Pentacam measurements	450 eyes	4 classes	19 parameters	Accuracy: 98.2% Sensitivity: 98.5% Specificity: 99.4%
[17]	2021	Linear discriminant analysis (LDA) & random forest (RF)	Corneal tomography DCR & pachymetric parameters	434 cases	4 classes	11 parameters for RF. 6 parameters for LDA.	LDA Accuracy: 71% RF Accuracy: 78%
[18]	2021	Time delay neural network	Pentacam data	743 patients	2 classes	6 features	Sensitivity: 70.8% Specificity: 80.6%
[19]	2021	Convolutional neural Network (CNN)	Corneal frontal and lateral images	450 images	4 classes	Two 2D images	Accuracy: 97.8% Sensitivity: 98.45% Specificity: 96%
[20]	2021	Logistic regression, decision tree, random forest, MLP, Fast-Large Margin, KNN & Naïve Bayes	Images	Iraq base: 448 images. Europe base: 692 images.	2 classes	140 vectors of 400 dimensions	Accuracy: 91.33% Sensitivity: 88.58% Specificity: 94.39%
[21]	2021	RF, SVM, KNN, DT, NB, LR & LDA on selected features	Corneal parameters	3162 rows Harvard Dataverse Keratoconus dataset	2 classes 4 classes	10 variables 420 variables	Accuracy: 4 classes: 95.32% 2 classes: 98.1% AUC: 100% (4 classes)
[22]	2021	RF using PCA for	Pentacam parameters	267 eyes		267 parameters	Accuracy: 98%

		dimensionality reduction			2 classes	from 1692 parameters	Sensitivity: 97% Specificity: 98%
[23]	2021	24 machine learning models	Pentacam measurements	3 datasets of 5881 samples	5 classes 3 classes 2 classes	Elevation dataset: 5 features from 18	AUC (SVM): 5 classes: 88% 3 classes: 96% 2 classes: 99%
[24]	2021	Quadratic discriminant Analysis (QDA)	Pentacam data	12647 rows	6 classes	7 parameters	AUC: 95% to 100%
[25]	2020	CNN	Corneal tomography images	3218 images	3 classes	Images of 256x256 pixels	Accuracy: 95.8%
[26]	2020	Logistic regression	Demographic, optical & geometric data	178 eyes	3 classes	5 variables	Accuracy: 73%
[27]	2020	Logistic regression	Demographic, optical, pachymetric & geometrical parameters	169 samples	6 classes	17 variables	Accuracy: 69.8%
[28]	2020	RF, SVM, KNN, LR, LDA, Lasso Regression, DT & MLP	Corneal parameters	88 eyes	2 classes	11 parameters	Accuracy: 87% (RF) Sensitivity: 92% (SVM) Specificity: 88% (KNN) Precision: 89% (RF) AUC: 96% (RF)
[29]	2020	LR & Artificial Neural Network (ANN)	Corneal morphological features using Scheimpflug camera and UHROCT	121 eyes	3 classes	49 parameters	Sensitivity: 95.1% (LR), 98.5% (ANN) 1-Specificity: 94.8% (LR), 94.7% (ANN) AUC: 90% (LR), 93% (ANN)
[30]	2020	Feedforward Neural Network (FNN)	Anterior and posterior corneal elevations & minimum pachymetry value	812 subjects	5 classes	2 vectors of 46 anterior and 46 posterior parameters	Accuracy: 99.9%
[31]	2020	InceptionResNetV2	Corneal topographic images	6465 images	5 classes	Images of axial curvature, front and back elevation & corneal thickness	Accuracy: 95% Sensitivity: 91.9% Specificity: 98.7% AUC: 99.3%
[32]	2020	CNN	Raw data of the Pentacam HR system	854 samples	3 classes	Five matrices, each of a size 141x141	Accuracy: 94.74% Recall: 93.71% Precision: 94.1% F1-score: 93.89%
[33]	2020	CNN based on ResNet with fewer hidden layers and 4 input channels	Corneal topographic images	3000 images	3 classes	56x56x4 matrix	Accuracy: 99.3%
[34]	2020	25 machine learning models	Corneal parameters	3151 samples	2 classes 3 classes	8 features	Accuracy (Cubic SVM) : 2 classes: 94.0% 3 classes: 62%
[35]	2019	CNN	Corneal topographic images	3000 images	2 classes	180x240x3 pixels	Accuracy: 99.33%
[36]	2019	ResNet-18	Corneal topographic maps using anterior segment optical coherence tomography (AS-OCT)	543 images	5 classes	224x224 corneal maps	Accuracy: 87.4%
[37]	2019	Conditional linear Gaussian Bayesian network	Topographic indices, calculated from the Placido ring images	60 eyes	2 classes	16 parameters	Sensibility: 100% Specificity: 100%
[38]	2019	Feedforward neural network, Grossberg-Runge Kutta	Topographic data	851 subjects	4 classes	1x117 features	Accuracy : 99.58% Sensitivity: 99.91% Specificity: 99.90% Precision: 99.90%
[39]	2019	SVM & DT	Corneal Topographic images	40 cases	2 classes	16 features	Accuracy (SVM): 90% Accuracy (DT): 87.5%
[5]	2019	Density-based clustering	Corneal parameters	3156 eyes	4 classes	420 corneal parameters	Specificity: 94.1% Sensitivity: 97.7%
[40]	2017	SVM	Pentacam parameters	131 eyes	5 classes	25 parameters	Accuracy: 88.8%
[41]	2016	SVM	Pentacam data	860 eyes	5 classes	22 parameters	Accuracy: 88.8% Sensitivity: 89% Specificity: 95.2%
[42]	2016	MLP	Tomographic data, topographic data & keratoconus indices	135 eyes	3 classes	15 parameters	AUC: Unilateral: 88% Bilateral: 96%
[43]	2014	LDA & ANN	Maps of the corneal epithelial and stromal	204 subjects	5 classes	6 variables	Sensitivity: 94.6% (LDA), 98.9% (ANN)

			thickness				Specificity: 99.2%(LDA), 99.5%(ANN)
[44]	2013	DT	Corneal Topographic images	372 eyes	2 classes	55 features	Sensitivity: 100% Specificity: 99.5%
[45]	2010	SVM, MLP & Radial Basis Function Neural Network (RBFNN)	Corneal topographic maps using OrbscanII	318 maps	4 classes	11 variables	SVM & MLP: AUC: 99% Sensitivity: 100% Specificity: 100% RBFNN: AUC: 98% Sensitivity: 98% Specificity: 98%
[46]	2005	DT C4.5	Videokeratography data	244 eyes	2 classes	4 Zernike polynomial coefficients	Accuracy: 92% AUC: 97%

Considering publication dates of selected articles, a large part of the retained documents was published during the period 2019 to 2022, with a total of 31 papers; the seven remaining articles were published in the period from 2005 to 2017. Fig. 3 below represents the curve of the publication's evolution per years between 2005 and 2022.

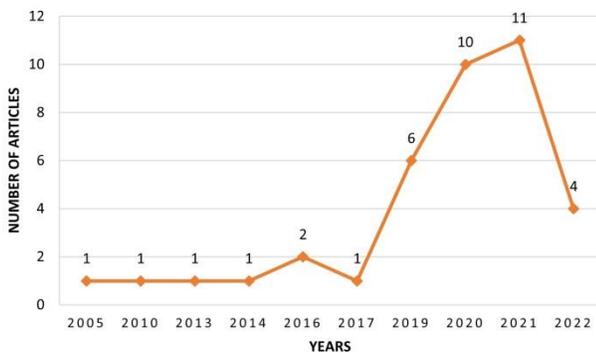


Fig. 3. Number of articles by years of publication.

**A. RQ1. What are the Main Objectives of using ML Techniques in the Classification of Keratoconus?**

The early diagnosis of keratoconus is very meaningful to avoid heavy treatments or surgical interventions that can cause further damage to the cornea. Many technologies allow showing different aspects of the cornea, such as biomechanical features, wavefront aberrations, elevation maps and pachymetry [47]. To determine accurately keratoconus presence, ophthalmologists must be up to date and able to analyze, combine and interpret indices and information obtained by all these different technologies as diagnosis result. However, ML tools have shown great capacity in the analysis and processing of heterogeneous data, such as measurements, videos, images, etc. It is for these advantages that ML techniques have been used in systems of keratoconus classification. The main objectives of using ML in keratoconus classification are the optimization of keratoconus diagnosis process as much as possible by its early identification, the assurance of better care for patients and their follow-up, the proposal of adequate medical actions according to the identified stage, and the confirmation of the diagnosis carried out by specialists, by combining their expertise with the capacities of ML techniques. Moreover, ML is used in keratoconus classification to fix the limitations of existing diagnostic methods, including qualitative rather than

quantitative evaluations of parameters, coefficients, and observer bias [5].

**B. RQ2. What are the ML Techniques used in the Classification of Keratoconus?**

Various ML techniques were used for keratoconus classification in studied works. The unsupervised ML is represented in this review by the Density-Based Clustering technique which was used as keratoconus classifier.

For supervised ML, different methods were implemented in the contributions included in this review. Many works have adopted simple ML algorithms such as Support Vector Machine (SVM), K-Nearest Neighbors (KNN), Random Forest (RF), Linear Discriminant Analysis (LDA) or other algorithms [21]. Other studies have implemented some techniques, such as ensemble learning, based on Bagging, Boosting, Stacking,..., etc., allowing the combination of several machine learning algorithms to improve the performance of predictive systems in terms of classification accuracy [16]. Other techniques, such as DL were adopted in several works for classification of keratoconus. Generally, the different ML techniques commonly used in the studies included in this review are:

1) *Naive bayes (NB)*: The Naïve Bayes is a probabilistic classifier well suited to high dimensional datasets. Despite its simplicity, the NB algorithm can outperform other more efficient classifiers [37].

2) *K-Nearest neighbors (KNN)*: KNN method is a ML technique that classifies new observations, assigning them to the class most present in the neighbors of this observation based on similarity functions, such as distance functions [21], [28].

3) *Logistic regression (LR)*: LR is a probabilistic supervised ML algorithm using the sigmoid function as a decision rule, providing a probability of producing an event with values between 0 and 1 [21], [48].

4) *Linear discriminant analysis (LDA)*: It is a technique belonging to competitive machine learning methods, which is used for dimensionality reduction [49]. The idea behind LDA is to find a linear combination of variables that best separates different classes [50].

5) *Decision tree (DT)*: DT is a classifier algorithm of a tree structure. The nodes of the DT represent the evaluation tests of the observations attributes, while the arcs represent the responses to the tests associated with the nodes, and the leaves

correspond to the different classes [21]. Different variants of DT, such as Chi-square automatic interaction detection (CHAID) and classification and regression tree (CART), have been implemented for the discrimination of keratoconus [51].

6) *Artificial neural networks (ANN)*: It is a computational imitation of the way neurons work in the human brain, an ANN consists of three layers, input, hidden and output. Each neuron of a given layer is interconnected with the neurons of the next layer, and each connection has a weight which is used for the calculation of the output [52].

7) *Convolutional neural networks (CNN)*: Initially designed to process images more efficiently [53], CNNs are a particular type of ANN belonging to such a broad category of methods called DL. CNNs are designed using multiple building blocks, such as convolution layers, pooling layers, and fully connected layers. Deep learning techniques are based on the CNN architecture [35], [54].

8) *Ensemble learning*: Ensemble learning is a technique that consists of combining several individual ML classifiers to build a predictive system while improving the prediction

performance of the overall system. Random Forest is an example of ensemble learning techniques based on the bagging principle [28].

9) *Density-based clustering (DBC)*: It is an unsupervised ML technique based on local cluster criterion method, such as density connected points [5]. For this technique, the data points in the region separated by two clusters of low point density are considered as noise.

The emergence of the use of ML techniques in the medical field will undoubtedly impact the practice of health professionals, this diversity of ML algorithms used in the diagnosis of keratoconus, reflects the great interest of researchers in this disease and its treatment and management. However, it should be noted that the purpose of using ML in the medical field, ophthalmology in particular, is not to replace health professionals with automated systems, but rather to support them in the analysis and interpretation of voluminous and heterogeneous data collected, in order to make the right decisions by reducing the margin of error for specialists. Fig. 4 below represents different ML techniques identified in the papers included in the current review.

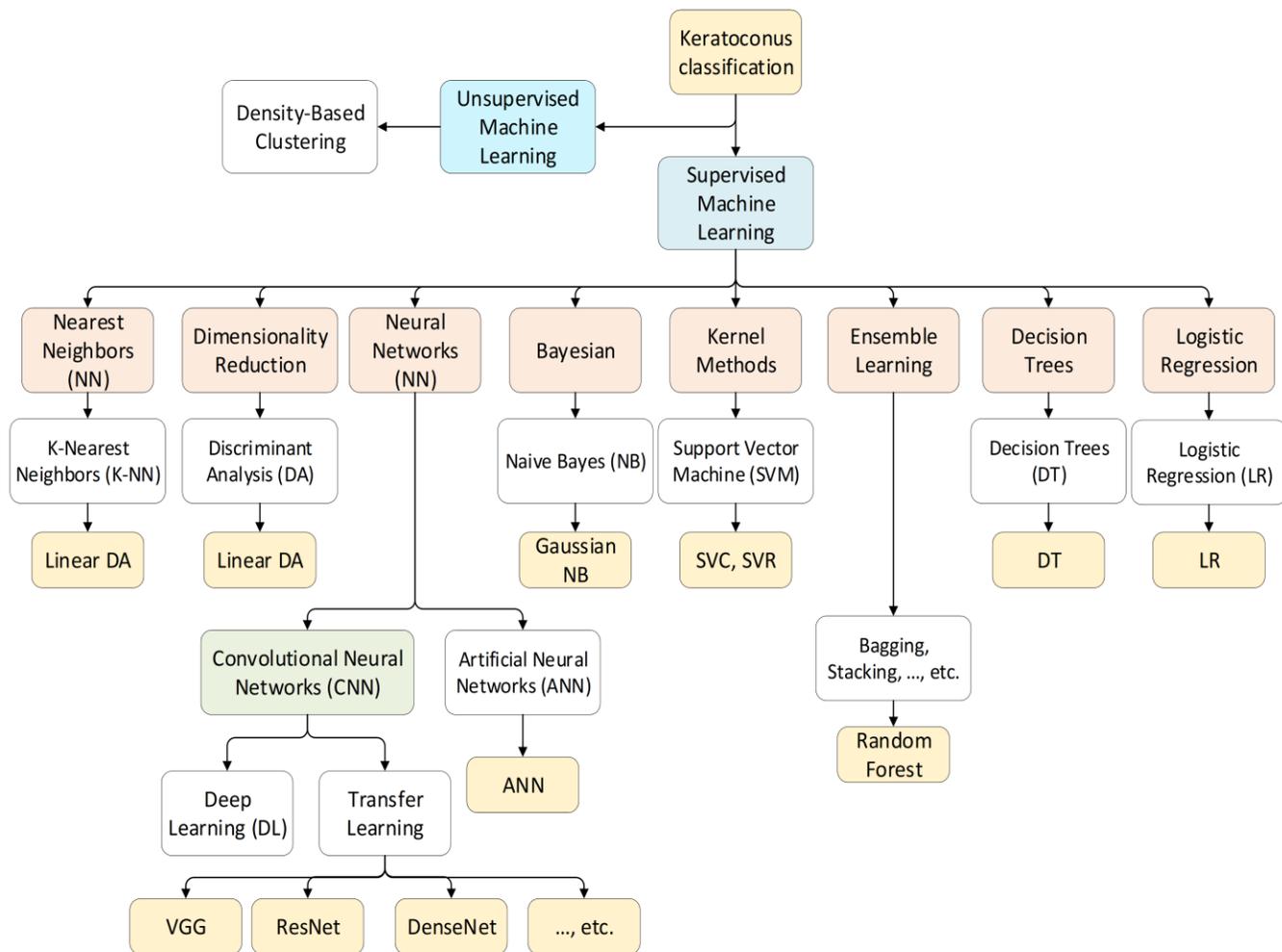


Fig. 4. Explanatory diagram of the commonly used ML techniques in the classification of keratoconus.

Fig. 5 below represents the rates of ML and DL classifiers use in the included papers.

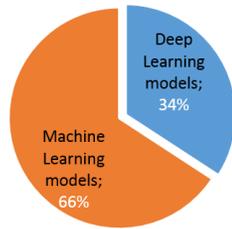


Fig. 5. ML and DL use percentages in selected papers.

### C. RQ3. What are the Data Types used by the Different Classifiers for the Classification of Keratoconus?

The diversity of ML algorithms is accompanied by a variety of data types handled by these algorithms. The data types used in the works selected in this study are:

1) *Images*: In most of contributions, using deep learning architectures, authors have used image type data for the classification of keratoconus. Processed images are in different types, such as corneal topography [12], tomography [25], and Placido disc [37].

2) *Corneal parameters*: A set of measurements, obtained using specific devices such as Pentacam, describing the cornea in detail on different aspects (geometric, topographic, ..., etc.). A total of 15 studied documents have handled corneal data and parameters as input data for the classification of keratoconus [16], [28], [21], [17], [18], [22], [23], [24], [30], [32], [34], [38], [40], [41], [42].

3) *Biomechanical data*: Biomechanical parameters refer to the distortion responses of the cornea to an applied force such as corneal hysteresis (CH) and corneal resistance factor (CRF). Biomechanical parameters are generally integrated in the corneal parameters already cited as inputs [14].

4) *Demographic data*: Age and gender are the demographic parameters the most integrated in studied articles as input data [14], [18], [29].

5) *Morphological data*: Morphological data make it possible to describe the morphology of the cornea and to identify any structural anomaly of the latter. Indeed, the thickness of the cornea varies from one individual to another, due to the difference in the radius of curvature of its anterior and posterior faces [29].

6) *Geometric data*: Correspond to information essentially describing the geometry of the anterior and posterior corneal surfaces to diagnose any pathology linked to an alteration in corneal morphology [55]. Among these data the total corneal volume, the anterior corneal surface, the posterior corneal surface, the total corneal surface, the deviation of the anterior apex and the deviation of the posterior apex [26].

Other papers, not included in this review study, introduced other forms of data such as the ethnic properties of patients [56]. Fig. 6 indicates the data types used by the different models of keratoconus classification proposed in the papers treated in this study.

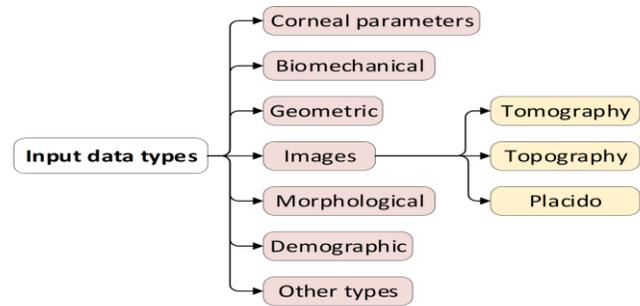


Fig. 6. Types of data adopted as inputs for different ML classifiers used in the studied papers.

### D. RQ4. What are the Most used Corneal Features in Keratoconus Classification by the Different ML Models?

Between 38 analyzed documents, 22 papers have reported the list of features used as inputs by the different classifiers implemented for the classification. The 10 most used features in different papers are:

- Radius of the corneal curvature (Radius), used in 10 documents.
- Flat simulated keratometry (Kf), declared in 7 papers.
- Steep keratometry (Ks), appeared in 6 articles.
- Age, reported in 6 different works.
- Astigmatism, reported in 5 different papers.
- Inferior-Superior value (I-S), used in 5 articles.
- Index of height decentration (IHD), used in 5 papers.
- Index of surface variance (ISV), declared in 4 papers.
- Index of vertical asymmetry (IVA), used in 4 works.
- Gender, used in 4 papers.

### E. RQ5. What is the Impact of ML use on the Classification Accuracy of Keratoconus Compared to Traditional Techniques?

The detection of keratoconus in its first stage will make it possible to follow its evolution closely and try to slow down, or even stop, it by following adequate measures on a case-by-case basis. The detection of keratoconus in its advanced stages can be ensured by evaluating certain symptoms and clinical signs of the cornea, visibly clear for specialists, given the advanced stage of the disease. For subclinical keratoconus, this operation is not possible, this is due to the similarities in signs with normal eyes. However, the early diagnosis of keratoconus is made using video technologies performing corneal topographies. Thus, the large number of parameters describing the cornea and the difficulties in analyzing corneal topographic images represent the greatest difficulty in the identification of subclinical keratoconus. It is to overcome all these obstacles and to distinguish keratoconus in its early phase in patients, that the ML is used for the analysis of corneal topographies, showing great precision when classifying keratoconus compared to traditional diagnostic methods [14].

F. RQ6. What is the Number of Keratoconus Classes Retained for Each Study Included in this Review?

The number of corneal classes retained in each of the different studies included in the current review varies between 2 and 6 corneal classes. The articles considering 2 and 3 corneal classes for keratoconus classification represent the large part of the papers studied in this systematic review, with a total of 26 papers (15 papers and 11 papers for keratoconus classification considering 2 and 3 corneal classes respectively). Table IV indicates the distribution of studies by the number of corneal classes considered in keratoconus classification.

TABLE IV. DISTRIBUTION OF STUDIED WORKS BY NUMBER OF CORNEAL CLASSES CONSIDERED IN THE CLASSIFICATION

Number of Classes	References	Total of papers
2 classes	[24], [37], [28], [35], [10], [12], [14], [15], [18], [20], [22], [23], [34], [39], [46]	15
3 classes	[11], [13], [23], [25], [26], [29], [32], [33], [34], [42], [44]	11
4 classes	[5], [21], [16], [17], [19], [38], [45]	7
5 classes	[15], [23], [30], [31], [36], [40], [41], [43]	8
6 classes	[24], [27]	2

G. RQ7. What are the Limitations of the Current Literature and the Opportunities for Future Research?

The objective of the current literature review study is to identify scientific studies aimed at the classification of keratoconus using machine learning tools. One of the limitations of this study is the exclusion of certain studies during the execution of the query for selecting papers from Scopus and Web of science databases, the poor choice of titles and keywords of articles by the authors may exclude the article, even if it is a work in the context of this study. Also, the exclusion of certain types of papers, such as conference papers and book chapters for example, may cause the loss of a large number of contributions aimed at the classification of keratoconus. Another limit of this study is that the period from 2005 to 2014 is represented by only four papers, this is perhaps due to the inclusion rules already mentioned and the low number of contributions, using ML techniques to the classification of keratoconus, published in this period. Moreover, this variety of ML techniques and types of data used in different studies makes the comparison of these systems more difficult, if not impossible, in the absence of a referential dataset to test these different systems implemented.

V. DISCUSSION

Based on the current systematic review, concerning the adoption of ML techniques for keratoconus classification systems, reported results show a remarkable increase in scientific productions, according to the selection criteria already cited, these last four years (2019, 2020, 2021 and 2022). This growth is maybe due to the interest of researchers in the use of ML techniques in the objective to take full advantage of the capabilities of these techniques in data analysis, especially in classification problems in several domains. This growth in the use of ML techniques in ophthalmology can be justified by the strong bond of this field

to image processing for the diagnosis of several diseases including keratoconus. As illustrated in Fig. 3, amongst 38 selected documents, 31 papers have been published in the past four years, i.e., 81.56% of all papers.

Regarding the countries of publication of different documents, Fig. 2 shows that the 38 papers were published from 22 different countries. Belgium, China, Spain, Romania, and USA have published 5, 4, 4, 3 and 3 papers respectively, with a total of 19 papers, representing 50% of the studied articles. The 19 other papers were published from 17 other countries.

Table IV indicates that over the 38 retained documents in the current review, 15 papers allowed keratoconus classification considering just 2 classes, 11 papers have considered 3 corneal classes, 7 studies used 4 corneal classes in the classification, 8 articles considered 5 classes of keratoconus in the classification task and 2 papers retained 6 corneal classes. Generally, the adopted classes of cornea are included in the following classes, namely normal, subclinical, mild, moderate, advanced, and severe stages of keratoconus. Among the 38 selected papers, 26 (i.e., 68.42%) opted for a classification of keratoconus by considering only 2 to 3 corneal classes (normal, subclinical and keratoconus). The idea behind is to ensure early detection of keratoconus in its subclinical stage, to treat it early and to stop its progression to advanced stages.

Fig. 4 shows that the authors have used two categories of ML algorithms, unsupervised ML, and supervised ML. Only one study over the studied papers implemented unsupervised ML, using the Density-based Clustering algorithm. In a total of 37 articles, authors proposed classification systems on the basis of supervised ML techniques. Authors of the different papers have proposed various architectures and several techniques to achieve high accuracy during classification. Thus, each of the works uses data, which are generally proprietary and not publicly accessible, which makes the comparison of these proposed methods difficult, if not impossible, in the absence of a public test platform to validate these works on the same dataset and under somewhat similar conditions.

To evaluate the classification performance of the proposed systems in the various works included in this literature review, the most used metrics are as follows:

- Accuracy: Described by “(1)”.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (1)$$

- Precision: Calculated using “(2)”.

$$Precision = \frac{TP}{TP + FP} \quad (2)$$

- Recall: Estimated using “(3)”.

$$Recall = \frac{TP}{TP + FN} \quad (3)$$

- F1-score: Depicted as “(4)”.

$$F1 - Score = 2 * \frac{Precision * Recall}{Precision + Recall} \quad (4)$$

- Area under ROC curve (AUC): Represents relationship between False Positive rate and True Positive rate of a test for all possible thresholds. The value of ROC lies between 0.5 and 1 and efficient classifier tend to maximize the ROC value towards 1 [21].

Where, True Positives (TP) represents the number of correct samples predicted as 'yes', True Negatives (TN) is the number of correct samples predicted as 'no', False Positives (FP) is the number of samples that are incorrectly predicted as 'yes' when they are actually 'no' and False Negatives (FN) represents the number of samples that are incorrectly predicted as 'no' when they are actually 'yes' [21].

## VI. CONCLUSION

This study presents a systematic review of machine learning (ML) tools for detecting and classifying keratoconus. It analyzes various data types including images, text, measurements, etc, and various ML classifiers, achieving good accuracy across different stages of keratoconus. However, the absence of a standardized dataset hinders the comparison of different approaches. Nonetheless, the study demonstrates that ML techniques, when combined with clinical expertise, can yield accurate results. In summary, ML techniques offer promise in enhancing the diagnosis and treatment of eye diseases like keratoconus, but their use should be accompanied by clinical expertise for reliable outcomes. It should be mentioned that the keratoconus classification systems proposed in the studies included in this review are intended to assist practitioners and not to replace them in the diagnosis of this disease. Future research should focus on developing standardized datasets to facilitate comparison and improve accuracy.

## REFERENCES

- [1] M. Aatila, M. Lachgar, A. Kartit, "Comparative study of optimization techniques in deep learning: Application in the ophthalmology fields," *J. Phys.: Conf. Ser.*, vol. 1743, pp. 1–12, 2021.
- [2] S. R. Jacinto, C. Gonzalo, S. Asaki, V. C. Cesar, S. J. Vincent and J. S. Wolffsohn, "Keratoconus: An updated review," *Cont. Lens Anterior Eye*, vol. 45, pp. 1–26, 2022.
- [3] L. Yong, X. Zhiqiang, L. Qiaoli, W. Yuzhou, L. Kan, X. Jiahui, C. Shihao and H. Liang, "Relationship between corneal biomechanical parameters and corneal sublayer thickness measured by Corvis ST and UHR-OCT in keratoconus and normal eyes," *Eye and Vis.*, vol. 8, pp. 1–12, 2021.
- [4] D. Kumar, V. K. Poojita, S. Rushad, K. Luci, L. V. Ganesan, G. Krati and K. Gairik, "Simplifying and understanding various topographic indices for keratoconus using Scheimpflug based topographers," *Indian J. Ophthalmol.*, vol. 68, pp. 2732–2743, 2020.
- [5] Y. Siamak, Y. Ebrahim, T. Hidenori, H. Takahiko, T. Hironobu, I. Satoru, A. Yusuke and A. Penny, "Keratoconus severity identification using unsupervised machine learning," *PLoS One*, vol. 13, pp. 1–11, 2018.
- [6] S. Shanthi, K. Nirmaladevi, M. Pyngkodi, K. Dharanesh, T. Gowthaman and B. Harsavardan, "Machine learning approach for detection of keratoconus," *IOP Conf. Ser.: Mater. Sci. Eng.*, vol. 1055, pp. 1–8, 2021.
- [7] H. Maile, J. P. O. Li, D. Gore et al. "Machine learning algorithms to detect subclinical keratoconus: systematic review," *JMIR Medical Informatics*, vol. 9, pp. 1–22, 2021.
- [8] H. Hashemi, S. Heydarian, E. Hooshmand et al. "The prevalence and risk factors for keratoconus: a systematic review and meta-analysis," *Cornea*, vol. 39, pp. 263–270, 2020.
- [9] V. M. Tur, C. MacGregor, R. Jayaswal et al. "A review of keratoconus: diagnosis, pathophysiology, and genetics," *Survey of ophthalmology*, vol. 62, pp. 770–783, 2017.
- [10] Z. Tan, X. Chen, K. Li, Y. Liu, H. Cao, J. Li, V. Jhanji, H. Zou, F. Liu, R. Wang and Y. Wang, "Artificial Intelligence–Based Diagnostic Model for Detecting Keratoconus Using Videos of Corneal Force Deformation," *Trans. Vis. Sci. Tech.*, vol. 11, pp. 1–8, 2022.
- [11] A. Hyunmin, K. N. Eun, C. J. Lim, K. Y. Jun, J. Ikhyun, S. K. Yul, "Patient selection for corneal topographic evaluation of keratoconus: A screening approach using artificial intelligence," *Front. Med. Lausanne*, vol. 9, pp. 1–9, 2022.
- [12] F. Murat, Ç. Cem, Ç. Ahmet and T. Taner, "Automatic detection of keratoconus on Pentacam images using feature selection based on deep learning," *Int. J. Imaging Syst. Technol.*, vol. 32, pp. 1548–1560, 2022.
- [13] P. Subramanian and G. P. Ramesh, "Keratoconus Classification with Convolutional Neural Networks Using Segmentation and Index Quantification of Eye Topography Images by Particle Swarm Optimisation," *Biomed. Res. Int.*, vol. 2022, pp. 1–9, 2022.
- [14] C. L. Gracia, J. R. Diana, C. F. Ana Belén and P. R. Antonio, "Diagnosis of subclinical keratoconus based on machine learning techniques," *J. Clin. Med.*, vol. 10, pp. 1–12, 2021.
- [15] C. Xu, Z. Jiaxin, I. C. Katja, B. Davide et al. "Keratoconus detection of changes using deep learning of colour-coded maps," *BMJ. Open Ophthalmol.*, vol. 6, pp. 1–8, 2021.
- [16] M. Ghaderi, A. Sharifi and P. E. Jafarzadeh. "Proposing an ensemble learning model based on neural network and fuzzy system for keratoconus diagnosis based on Pentacam measurements," *Int. Ophthalmol.*, vol. 41, pp. 3935–3948, 2021.
- [17] H. Robert, P. E. Lutz and R. Frederik. "Development of a classification system based on corneal biomechanical properties using artificial intelligence predicting keratoconus severity," *Eye and Vision*, vol. 8, pp. 1–11, 2021.
- [18] J. Marta, I. Issarti, E. O. Kreps, N. D. Sorcha et al. "Forecasting progressive trends in keratoconus by means of a time delay neural network," *J. Clin. Med.*, vol. 10, pp. 1–15, 2021.
- [19] M. H. A. Hosni and M. H. Abdullah. "Automated keratoconus detection by 3D corneal images reconstruction," *Sensors*, vol. 21, pp. 1–15, 2021.
- [20] M. B. Alazzam, A. S. AlGhamdi, S. S. Alshamrani et al. "Corneal biomechanics computational analysis for keratoconus diagnosis," *Comput. Math. Methods Med.*, vol. 2021, pp. 1–11, 2021.
- [21] M. Aatila, M. Lachgar, H. Hrimch and A. Kartit. "Keratoconus severity classification using features selection and machine learning algorithms," *Comput. Math. Methods Med.*, vol. 2021, pp. 1–26, 2021.
- [22] K. Cao, K. Verspoor, E. Chan, M. Daniell, S. Sahebajada and P. N. Baird. "Machine learning with a reduced dimensionality representation of comprehensive Pentacam tomography parameters to identify subclinical keratoconus," *Comput. Biol. Med.*, vol. 138, pp. 1–6, 2021.
- [23] A. Lavric, L. Anchidin, V. Popa, A. Al-Timemy et al. "Keratoconus severity detection from elevation, topography and pachymetry raw data using a machine learning approach," *IEEE Access*, vol. 9, pp. 84344–84355, 2021.
- [24] R. Malyugin, S. Sakhnov, S. Izmailova, E. Boiko, N. Pozdeyeva et al. "Keratoconus diagnostic and treatment algorithms based on machine-learning methods," *Diagnostics*, vol. 10, pp. 1–12, 2021.
- [25] H. Abdelmotaal, M. M. Mostafa, A. NR. Mostafa, A. Mohamed K. Abdelazeem. "Classification of color-coded scheimpflug camera corneal tomography images using deep learning," *Transl. Vis. Sci. Technol.*, vol. 9, pp. 1–12, 2020.
- [26] J.S. Velázquez-Blázquez, J.M. Bolarín, F. Cavas-Martínez, J.L. Alió. "EMKLAS: a new automatic scoring system for early and mild keratoconus detection," *Transl. Vis. Sci. Technol.*, vol. 9, pp. 1–18, 2020.
- [27] J. M. Bolarín, F. Cavas, J. S. Velázquez and J. L. Alió. "A machine-learning model based on morphogeometric parameters for RETICS

- disease classification and GUI development,” *Appl. Sci. Basel*, vol. 10, pp. 1–19, 2020.
- [28] K. Cao, K. Verspoor, S. Sahebjada and P. N. Baird. “Evaluating the performance of various machine learning algorithms to detect subclinical keratoconus,” *Transl. Vis. Sci. Technol.*, vol. 9, pp. 1–11, 2020.
- [29] C. Shi, M. Wang, T. Zhu, Y. Zhang, Y. Ye, J. Jiang et al. “Machine learning helps improve diagnostic ability of subclinical keratoconus using Scheimpflug and OCT imaging modalities,” *Eye and Vision*, vol. 7, pp. 1–12, 2020.
- [30] I. Issarti, A. Consejo, M. Jiménez-García, E. O. Kreps, C. Koppen and J. J. Rozema. “Logistic index for keratoconus detection and severity scoring (Logik),” *Comput. Biol. Med.*, vol. 122, pp. 103809–103809, 2020.
- [31] Y. Xie, L. Zhao, X. Yang, X. Wu, Y. Yang, X. Huang et al. “Screening candidates for refractive surgery with corneal tomographic-based deep learning,” *JAMA Ophthalmol.*, vol. 138, pp. 519–526, 2020.
- [32] R. Feng, Z. Xu, X. Zheng, H. Hu, X. Jin et al. “KerNet: a novel deep learning approach for keratoconus and sub-clinical keratoconus detection based on raw data of the Pentacam HR system,” *IEEE J. Biomed. Health Inform.*, vol. 25, pp. 3898–3910, 2021.
- [33] P. Zéboulon, G. Debellemannièrè, M. Bouvet and D. Gatinel. “Corneal topography raw data classification using a convolutional neural network,” *Am. J. Ophthalmol.*, vol. 219, pp. 33–39, 2020.
- [34] A. Lavric, V. Popa, H. Takahashi and S. Yousefi. “Detecting keratoconus from corneal imaging data using machine learning,” *IEEE Access*, vol. 8, pp. 149113–149121, 2020.
- [35] A. Lavric and V. Popa. “KeratoDetect: keratoconus detection algorithm using convolutional neural networks,” *Comput. Intell. Neurosci.*, vol. 2019, pp. 1–10, 2019.
- [36] K. Kamiya, Y. Ayatsuka, Y. Kato, F. Fujimura, M. Takahashi et al. “Keratoconus detection using deep learning of colour-coded maps with anterior segment optical coherence tomography: a diagnostic accuracy study,” *BMJ. Open.*, vol. 9, pp. 1–7, 2019.
- [37] G. M. Castro-Luna, A. Martínez-Finkelshtein and D. Ramos-López. “Robust keratoconus detection with Bayesian network classifier for Placido-based corneal indices,” *Cont. Lens Anterior Eye*, vol. 43, pp. 366–372, 2020.
- [38] I. Issarti, A. Consejo, M. Jiménez-García, S. Hershko, C. Koppen and J. J. Rozema. “Computer aided diagnosis for suspect keratoconus detection,” *Comput. Biol. Med.*, vol. 109, pp. 33–42, 2019.
- [39] Z. M. Mosa, N. H. Ghaeb and A. H. Ali. “Detecting keratoconus by using SVM and decision tree classifiers with the aid of image processing,” *Baghdad Science Journal*, vol. 16, pp. 1022–1029, 2019.
- [40] I. R. Hidalgo, J. J. Rozema, A. Saad, D. Gatinel, P. Rodriguez et al. “Validation of an objective keratoconus detection system implemented in a Scheimpflug tomographer and comparison with other methods,” *Cornea*, vol. 36, pp. 689–695, 2017.
- [41] I. R. Hidalgo, P. Rodriguez, J. J. Rozema et al. “Evaluation of a machine-learning classifier for keratoconus detection based on Scheimpflug tomography,” *Cornea*, vol. 35, pp. 827–832, 2016.
- [42] I. Kovács, K. Miháltz, K. Kránitz, E. Juhász, A. Takács, L. Dienes, R. Gergely and Z. Z. Nagy. “Accuracy of machine learning classifiers using bilateral data from a Scheimpflug camera for identifying eyes with preclinical signs of keratoconus,” *J. Cataract Refract. Surg.*, vol. 42, pp. 275–283, 2016.
- [43] R. H. Silverman, R. Urs, A. Roychoudhury, T. J. Archer, M. Gobbe and D. Z. Reinstein. “Epithelial Remodeling as Basis for Machine-Based Identification of Keratoconus,” *Investigative Ophthalmology & Visual Science*, vol. 55, pp. 1580–1587, 2014.
- [44] D. Smadja, D. Touboul, A. Cohen, E. Doveh, M. Santhiago et al. “Detection of subclinical keratoconus using an automated decision tree classification,” *Am. J. Ophthalmol.*, vol. 156, pp. 237–246, 2013.
- [45] M. B. Souza, F. W. Medeiros, D. B. Souza, R. Garcia and M. R. Alves. “Evaluation of machine learning classifiers in keratoconus detection from orbscan II examinations,” *Clinics*, vol. 65, pp. 1223–1228, 2010.
- [46] M. D. Twa, S. Parthasarathy, C. Roberts, A. M. Mahmoud, T. W. Raasch and M. A. Bullimore. “Automated decision tree classification of corneal shape,” *Optom. Vis. Sci.*, vol. 82, pp. 1–22, 2005.
- [47] Y. Shi. “Strategies for improving the early diagnosis of keratoconus,” *Clin. Optom. (Auckl.)*, vol. 8, pp. 13–21, 2016.
- [48] E. S. Hwang, C. E. Perez-Straziota, S. W. Kim, M. R. Santhiago and J. B. Randleman. “Distinguishing highly asymmetric keratoconus eyes using combined Scheimpflug and spectral-domain OCT analysis,” *Ophthalmology*, vol. 125, pp. 1862–1871, 2018.
- [49] R. Kanimozhi and R. Gayathri. “Improvement In Keratoconus Diagnosis Using Morpho-Geometric Variables With Rnn Networks,” *Information Technology In Industry*, vol. 9, pp. 12–21, 2021.
- [50] R. Herber, E. Spoerl, L. E. Pillunat and F. Raiskup. “Classification of dynamic corneal response parameters concerning the topographical severity of keratoconus using the dynamic Scheimpflug imaging and machine-learning algorithms,” *Invest. Ophthalmol. Vis. Sci.*, vol. 61, pp. 5210–5210, 2020.
- [51] P. Song, S. Ren, Y. Liu, P. Li and Q. Zeng. “Detection of subclinical keratoconus using a novel combined tomographic and biomechanical model based on an automated decision tree,” *Sci. Rep.*, vol. 12, pp. 1–9, 2022.
- [52] P. T. Nguyen, D. H. Ha, A. Jaafari and H. D. Nguyen et al. “Groundwater potential mapping combining artificial neural network and real AdaBoost ensemble technique: the DakNong province case-study, Vietnam,” *Int. J. Environ. Res. Public Health*, vol. 17, pp. 1–20, 2020.
- [53] R. Yamashita, M. Nishio, R. K. G. Do, and K. Togashi. “Convolutional neural networks: an overview and application in radiology,” *Insights Imaging*, vol. 9, pp. 611–629, 2018.
- [54] A. H. Al-Timemy, N. H. Ghaeb, Z. M. Mosa and J. Escudero. “Deep transfer learning for improved detection of keratoconus using corneal topographic maps,” *Cognit. Comput.*, vol. 14, pp. 1627–1642, 2022.
- [55] F. Cavas-Martínez, D. G. Fernández-Pacheco, D. Parras, F. J. F. Cañavate, L. Bataille and J. L. Alio. “Geometric Modelling of the Human Cornea: A New Approach for the Study of Corneal Ectatic Disease. A Pilot Investigation,” *Bioinformatics and Biomedical Engineering: 5th International Work-Conference, IWBBIO 2017, Granada, Spain, April 26–28, 2017, Proceedings, Part I 5*, pp. 271–281, 2017.
- [56] S. Rafati, H. Hashemi, P. Nabovati, A. Doostdar, A. Yekta et al. “Demographic profile, clinical, and topographic characteristics of keratoconus patients attending at a tertiary eye center,” *J. Curr. Ophthalmol.*, vol. 31, pp. 268–274, 2019.