



REVIEW ARTICLE - ENGINEERING

Image-Based Face Recognition Techniques Used in Disease Detection Approaches: A Survey

Ghalib Ahmed Salman¹, Inas Jawad Kadhim^{1*}, Ahmed Husham Al-Badri²

¹Electrical Engineering Technical College, Middle Technical University, Baghdad, Iraq

²Faculty of Computing, Universiti Teknologi Malaysia, Johor Bahru, Malaysia

* Corresponding author E-mail: inasjk@mtu.edu.iq

Article Info.	Abstract
<p><i>Article history:</i></p> <p>Received 07 September 2023</p> <p>Accepted 01 November 2023</p> <p>Publishing 31 March 2024</p>	<p>Facial diseases lead to noticeable changes on the human face, and some of them extend beyond internal effects or organ-based disorders. Indeed, certain types of facial diseases result in visually noticeable abnormalities on the human face. These alterations in facial patterns can serve as potential indicators for corresponding diseases, particularly in the fields of endocrinology and metabolism, Muscles-Nervous disorders, Chromosomes, and Genetic disorders, among others. Technologies used in Face Recognition (FR) have been developed over the past few decades; however, only a limited amount of research has been applied in recent years to FR-based disease detection for clinical purposes. FR applications relying on Artificial Neural Network (ANN) techniques have recorded higher accuracy rates in diagnosing facial diseases. This field of recognition holds promising potential for optimizing facial diagnosis approaches and supporting medical staff in evaluating detections. In practice, only a few research ideas have been translated into medical products, emphasizing the need to identify and integrate future applications. As a primary focus, this paper centers on the key applications and technologies for detecting various types of facial diseases, along with a discussion of prospects.</p>
<p>This is an open-access article under the CC BY 4.0 license (http://creativecommons.org/licenses/by/4.0/)</p>	
<p>Publisher: Middle Technical University</p>	
<p>Keywords: Face Recognition; Disease Detection; Artificial Intelligence; Convolutional Neural Network; Face Disorders.</p>	

1. Introduction

One of the unique bio-identifications for a human is the face, as it contains a considerable amount of information that can identify gender, age, race, health status or even the psychological [1]. Due to its easy accessibility and costly-efficient, the human face was widely adopted as a competitive biometric identification with the iris and fingerprint [2]. Many kinds of disease affect not only functional abnormality and internal structures but also facial characteristics. These diseases that influence facial attributes are generally associated with metabolic and endocrine disorders [3], neuromuscular effects [4], and genetic syndromes [5], where some of them are rare or complex diseases. Early detection and recognition of such diseases are timely crucial for alert and better treatment. Fig. 1 contains a collection of computer-based generated images for infected faces that summarizes some types of diseases that can be detected through human face analysis.

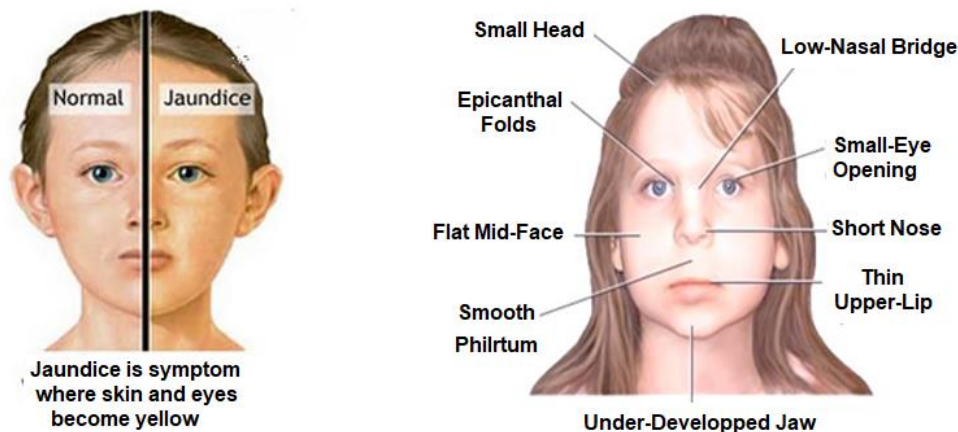


Fig. 1. Illustrates some kinds of face disease

Nomenclature & Symbols			
AD	Alzheimer Disease	HoG	Histogram of Oriented Gradients
AI	Artificial Intelligence	KNN	K-Nearest Neighbor.
AlexNet	Alex Krizhevsky Network	LBP	Local Binary Patterns
ANN	Artificial Neural Network	LDA	Discriminant Analysis
AUC	Area Under Curve	LSTM	Long Short-Term Memory
BPN	Back-Propagation Network	MIP	Medical Image Processing
CNN	Convolutional Neural Network.	NHGRI	National Human Genome Research Institute
DCV	Discriminant Common Vectors	ML	Machine Learning
DDS	Disease Detection System	PCA	Principal Component Analysis
DL	Deep Learning	PD	Parkinson Disease
DS	Down Syndrome	PDBNN	Probabilistic-Decision-Based Neural Networks
EBG	Elastic Bunch Graph	ResNet	Residual Network
EBGM	Elastic Bunch Graph Matching	RBF	Radial Basis Function
FDNA	Facial Dysmorphology Novel Analysis	SLR	Systematic Literature Review
FR	Face Recognition	SVM	Support Vector Machine
GWT	Gabor Wavelet Transformations	TGF	Topographical Features
ICA	Independent Component Analysis	TS	Turner Syndrome
HMM	Hidden Markov Model	VGGNet	Visual Geometry Group Network

Automation in Face-Recognition (FR) technologies started rising in the early 1970's, and effective algorithms were subsequently developed to address various real-world applications. These applications covered wide area of researches such as personality identification, forensic science, security surveillance, gender and age identification, crime fighting, etc. [2]. Novel approaches in face recognition that considered facial diseases had significant occurrence in the early 2000's. Genetic-based children's syndromes [6] and neuromuscular-based facial dysfunction [7] represent the early types of disease that were identified using knowledge-based recognition techniques. Recently, considerable developments in Artificial Intelligence (AI) have enhanced human life by leading to noticeable contributions in computer-based healthcare. Medical Image Processing (MIP) has witnessed significantly advancements within AI medical applications, contributed to fields such as dermatology, radiology, ophthalmology, pathology, and gastroenterology [8, 9]. As a significant application of auto-image analysis, FR algorithms display outstanding effectiveness in AI-related tasks, including age estimation. Subsequently, the number of published works in the field has witnessed a dramatic increase, especially within (2013- 2020), which can be presented in an exponential curve. More specifically, FR was adopted to assist disease detection, particularly in cases where human face exhibit abnormal facial features. Furthermore, a wider variation of research was conducted in AI medicine such as racial recognition, male/ female discrimination, victim-age estimation in forensics and other related areas [1-3]. Due to the rising importance of medical diagnosis based on face image, research in face recognition for disease diagnosis is witnessing growing innovations and new research ideas in medical applications. This accelerated viewing and inspection of human-face diseases, enhancing an early notification for comprehensive treatments. Despite that some facial diseases can be simply detected by the patient's appearance, some of them are complex (have unnoticeable characteristics by human eyes) with low levels of occurrence. In traditional methods of diagnosis, the awareness about such diseases is a challenge for the patients or even for doctors with low experience. In addition, selecting the appropriate tests and achieving accurate result analysis poses a secondary challenge. Therefore, AI-based recognition technologies offer promising opportunities for reducing time and cost consumption in diagnosis procedures and minimizing empirical errors. However, published research in this field has covered a huge number of developments in ideas, algorithms and applications, with some providing cutting-edge updates deeply or broadly. Therefore, this review aims to analyzes face recognition applications in the field of disease detection. The primary goal of this work is to discuss the achievements of technology with a specific focus on the advantages of face-based recognition techniques detecting facial diseases.

This study provides an overview of the conducted research, fostering cooperation between clinical and computer-based views of science, and stimulating new ideas for future works in engineering and medicine.

2. The Components of Face Recognition Schemes

Different systems of facial recognition (FR) have been developed using various schemes, yet most of them share common major components that are essential for constructing a systematic FR model. Generally, these components consist of Data Acquisition, Recognition Schemes, and Recognition Algorithms, with the possibility of some systems incorporating additional internal components.

2.1. Data acquisition

Different types of devices were used for capturing face images such as specialized cameras, ordinary (mobile) cameras, and video frames from captured movies, which were connected to the suitable software [5]. In the more recent research, 3D-image cameras (or scanners) were also used in capturing and analyzing facial features [10]. Mostly, the environmental settings are found in medical centres (Hospitals), where in some types of settings, adopted applications have patient terminals. Via the cloud connection, patients are used to capturing themselves locally for viewing, analyzing and providing medical advice by the specialists in these centres [11]. Capturing devices have some factors that can affect captured-image quality for the face such as low resolution, occlusion, illumination, noise, face rotation, and facial expressions [12]. In addition, the conditions of the patient's face, capturing environment, camera quality, and camera-user-position setting produce other types of error. To capture high-quality images, patients are asked the clinicians, to expose all face areas (from ear to ear), to look directly and open his/ her eyes, shut their mouths, tie up their hair, and to relax and show No-expression face [13, 14]. In neural disease, patients are asked to perform specific face tasks that can evaluate the neuromuscular function of their face [18]. Some studies controlled capturing angle, patient-camera distance, light source, and face expression to eliminate effects of illumination, scale and rotation [2, 3], which are ideal conditions that ignored real situations of the human face.

2.2. Recognition scheme

After ensuring fair quality of the captured face image, the recognition scheme processes the image through three steps: image pre-processing, feature extraction, and classification using Machine Learning (ML) approaches [1]. In this process, face analysis techniques are categorized into appearance-based and feature-based methods. Deep Learning (DL) approaches combine the second and third steps into single step using DL-based networks [5]. Firstly, the image is normalized (pre-processed) to enhance suitability for subsequent steps. Another widely adopted procedure in previous works is Face Detection which localizes and crops the face within the image [15]. After cropping the face from the image, its representing features are extracted using statistical analysis or pre-knowledge ML, while DL classifiers extract suitable features [16]. Then using these features, a similarity test is conducted to find the matching face in the database and a determination is made if the similarity level exceeds the designated threshold [17]. The input (suspected) face image is processed in the designed recognition system to decide whether the face is normal or exhibits a specific disease. Fig. 2 illustrates the generally followed steps in ML and DL recognition systems. Patient face images are collected, taking into account-controlled variables such as gender and age, along with the presence or absence of face disease. These images are then divided into training and testing subsets. The training subset images are utilized to train the system, allowing the classifier to learn image weights based on previously known labels (disease types). Once the learning stage is complete, the system becomes capable of recognizing the test subset of images without requiring knowledge of their labels. As all dataset images are potential candidates for both training and testing, cross-validation algorithms are applied. This ensures that each image is included in the training subset during a specific period and in the testing subset during another period [14, 18].

2.3. Recognition algorithms

Adopted algorithms in face recognition systems have different types and categorizing bases. Yet they can be divided, depending on feature extraction technique, into holistic-feature and local-feature techniques within ML networks, or DL-network techniques [12, 15]. Table 1 summarizes the components of FR systems (ML & DL) and the adopted feature types.

2.3.1. Machine-learning techniques

Holistic-Feature (also called appearance-based) techniques depend on the global face appearance to extract the relevant features, where they deal with the human face as an integral object. They extract holistic features and globally match their face to their corresponding in the dataset images. Without requiring a detailed knowledge about the inner components, the human face is converted into major or principal features (vectors). The standard types of holistic feature extraction algorithms were adopted in the form of Linear Discriminant Analysis (LDA), Principal Component Analysis (PCA), Independent Component Analysis (ICA), and Discriminant Common Vectors (DCV). Support Vector Machine (SVM) is widely adopted for classifying the extracted features, where it optimizes ICA and PCA performance [2, 12, 15].

By ignoring the holistic appearance and digging for more-detailed features, local features were also adopted in other methods, they divided the face image into segments regarding the differences in biological face components (eyes, nose, cheeks and mouth). These methods were provided with high result accuracy. Different types of face features were adopted in ML networks like Local Binary Patterns (LBP), Geometric Features, Histogram of Oriented Gradients (HoG), Elastic Bunch Graph Matching (EBGM), Elastic Bunch Graph (EBG), and Hidden Markov Model (HMM). Such types of features depend on prior knowledge to accomplish the selection for the suitable face features, which, in some cases, provides a significant challenging [2, 12, 15].

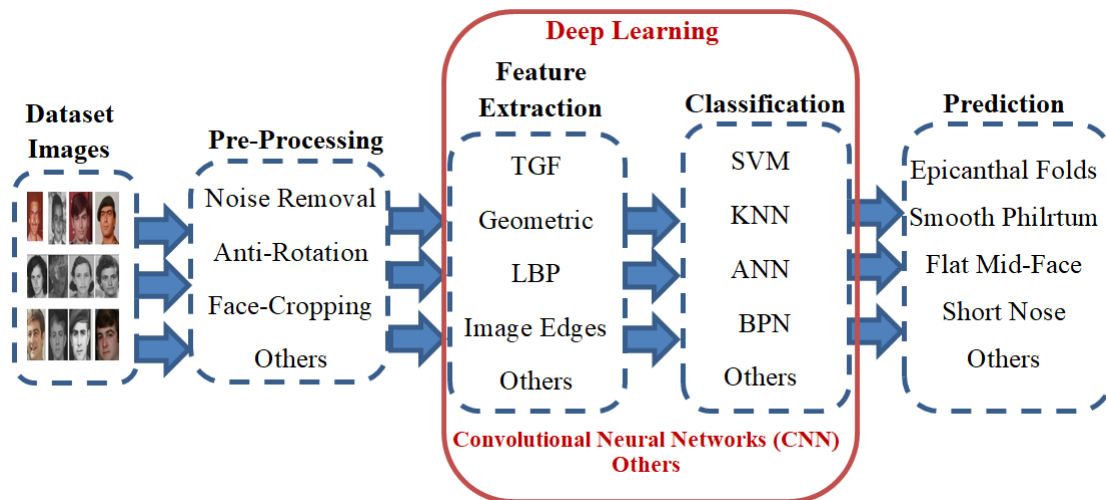


Fig. 2. The major steps adopted in face recognition system using ML and DL networks

Table 1. Summarizes adopted approaches and feature types used FR systems

Types	Approaches
Feature Extraction	Elastic Bunch Graph (EBG)
	Elastic Bunch Graph Matching (EBGM)
	Hidden Markov Model (HMM)
	Histogram of Oriented Gradients (HoG)
	Local Binary Patterns (LBP)
Classifiers	2D-Image Principal Component Analysis (2D Image IPCA)
	Discriminant Common Vectors (DCV)
	Eigen-face-Based Methods PCA Algorithm

	Independent Component Analysis (ICA)
	Kernel Principal Component Analysis (Kernel PCA)
	Linear Discriminant Analysis (LDA)
	Principal Component Analysis (PCA)
	Super Vector Machine (SVM)
	Alex Krizhevsky Network (AlexNet)
Deep Learning Approaches	Visual Geometry Group Network (VGGNet)
	GoogLeNet
	Residual Network (ResNet)

2.3.2. Deep learning networks

ML and DL networks have addressed and highlighted problems related to multidimensional data processing. Radial Basis Function (RBF) and Probabilistic-Decision-Based Neural Networks (PDBNN) were designed using Artificial Neural Network (ANN), and they demonstrated considerable levels of performance when applied to relatively small datasets. As an example of DL networks, Convolutional Neural Networks (CNN) were widely adopted in FR research, showing different levels of accuracy based on the architecture of the CNN networks used. Another advantage of DL networks their ability to eliminate illumination effects and emotional variance in facial images [3, 15]. Similar to conventional images, DL algorithms were developed to have the ability to analyze video frames that record human-face movements to indicate specific diseases. Three-dimensional Convolutional Neural Network (3D-CNN) is an adaptation from conventional CNN, extracting information provided by successive video frames [19]. 3D-CNN was adopted for detecting specific diseases (neurological) that cause dysfunction in the human face. Other researchers developed another version of DL models by combining conventional DL algorithms with Long Short-Term Memory (LSTM) to classify infected faces [20].

2.3.3. Advance recognition algorithms

Advancements in face recognition research have gradually been integrated into medical applications, particularly in the field of the face diagnostic field. An exemplary application in this field is the OpenFace 2.0 software, an open-source analyzer for facial behavior equipped with tools available for both researchers and users. It provides a facial framework for head pose tracking, landmark detection, facial action unit, and eye gaze recognition [21]. Some researchers have built their model using direct dependence on this software [4, 22]. The availability of such software enhances the capabilities of medical application researchers, allowing them to focus on improving their methods concerning disease attributes.

3. FR Techniques and Utilities

3.1. Disease variety performance

3.1.1. Endocrinology and metabolism

Endocrine disorders were identified by abnormal levels of hormones, where patients have metabolic diseases causing noticeable modifications in face features (muscles, bones, or soft tissues). In the early stages, the general signs of such diseases have high confusion with other signs of metabolic. A standard process of diagnosis is generally complex, with different examples of imaging examinations and hormone testing [23, 24]. The significant levels of performance in face recognition (for diagnosis approaches) made it accessible, screening and fast application.

As another example a high level of growth hormone causes Acromegaly disorders, characterized by patients having bigger nose sizes, rectangular faces, bigger lips, a bulging forehead, and prognathism [23]. A wide range of algorithms were built for detecting acromegaly cases in the human face. One of the early studies conducted in 2006 by Learned-Miller et al. [25] involved building a 3D detection model that classified frontal views of the patient faces into several classes, but their method was not a fully automated application. They handled 49-face dataset of patients with acromegaly, and their results yielded a considerable (85.7%) accuracy. Following that, another detection method was developed using Gabor Wavelet Transformations (GWT), which was a robust manner against undesired noise. Their dataset handled 57 images of patient faces with about 60 controls (age-matched and gender-matched). Considerably, their results yielded less accuracy level than the previous study reaching 81% level [26]. In another work, the authors handled LBP features using and Manhattan distance classifiers, where the results yielded (97%) accuracy. Using bigger datasets to be handled in ML techniques increases the efficiency of FR systems [27]. Kong et al., (2018) [28] adopted their own constructed dataset, which contains 596 controls dataset for 527 images of patients with acromegaly cases. The ML-based systems provided effectiveness, specificity and sensitivity (96%). Other acromegaly cases were handled in another work based on the (1131-image) dataset, which contains (1131infected & 12,598 normal) faces. The performance of their work yielded (94.79%) accuracy and (0.9556) for Area under Curve (AUC) [29].

3.1.2. Muscles- nervous disorders

Face topography is essential in detecting infections and changes in Muscles- Nervous (Neuromuscular) diseases. Different AI algorithms were widely designed and applied to detect facial neurological diseases. Although FR applications still have their limitations compared to other applications [30], they have shown considerable utility for diagnosing different diseases. Loosing face muscles or motion ability is called Facial Paralysis. Diagnosing such disease requires doctor's ability to rank scale for face topography and features that can be measured by muscle movement [31]. Conventional techniques were related to the asymmetry and 2-side face extraction. Captured clips from patient videos, consisting of 75 infected and 10 controls cases, were processed using a combination of LBP, Gabor filter, and Adaboost methods and they yielded relatively low accuracy value (60.7%) using ML networks [32]. However, considerable enhancements have been achieved in assessment objectivity with the use of DL networks. Gou et al. [33] proposed an end-to-end solution for direct analysis of face images using fine-tuned Deep CCN networks. Their experiments considered the facial expressions 105 images for patients and 75 ones for controls, resulting in a considerable classification accuracy (about 91%). Additionally, full 3D-CNN networks are used to build 3DPalsyNet as a grading software for motion recognition and face palsy. This framework showed an accuracy rate of 86% in motion detection and 82% in face palsy [34].

Degenerative diseases cause death or damage of neurons, which called as (neurodegenerative diseases), and they affect the central nervous system. The most widely spread type of dementia is Alzheimer Disease (AD), where the patient progressively lose thinking skills and memory. It is commonly a result of the death of brain cells and brain atrophy. Another disease is the Parkinson's Disease (PD) which results from a significant lack of dopamine secretion, where usually, PD patients have a masked face. Amyotrophic Lateral Sclerosis (ALS) has low occurrence rate, yet it causes a significant loss in motion neurons controlling voluntary muscles [35]. Tau, et al (2021) [36] reviewed the published papers in the field of Neurodegenerative Diseases and discussed them in detail. Table 2 summarizes the methods, dataset sizes, infection type, and performance results of the published papers. As a contribution to the field of ordinary diagnosis approaches, adopting an FR approach showed considerable performance. Realistic datasets were collected and offered freely available to provide considerable images to study like Public Datasets Efforts and Real-World. In addition, a recent dataset was collected from static images showing face diseases. Different sources from the Internet were used to collect these images, forming the In-The-Wild dataset. This dataset provides intensity features and face landmarks that help in classifying morbid cases [37]. Bandini et al. (2021) [38] constructed an open-source dataset collected from video frames to show the weakness in facial motions. Despite the availability of these datasets, more face-case images are needed to provide significant data and to ensure accuracy.

Table 2. A summary of published papers regarding Degenerative diseases

Method	Dataset Size	Infection Type	Performance
XGBoost & Random Forests [39]	100	PD & HC	Accuracy= 67%
LSTM & tremor extraction [20]	64	PD & HC	Precision = 86%
SVM & OpenFace 2.0 [4]	604	PD & HC	Accuracy = 96%
CLM,AAM, SDM, ERT, FAN [38]	22	ALS & HC	Accuracy= 89%
SVM, Random Forests, HOG, LBP, KNN, [40]	140	PD & HC	F1 = 88%
Deep CNN [41]	238	AD & HC	Accuracy = 94%

3.1.3. Abnormality in muscles-nervous chromosomes and genetic

Disorders in chromosomes and Genetic affect the general internal components and the outer shape of the human face. Genetic changes have direct effects on the fetal development of face components or indirect effects on face phenotype due to the abnormality in the systemic environment. Standard methods for disease detection include chromosome karyotyping and genome sequencing, which confirm the abnormality of genetic subjects. In such processes, clinicians must have an early knowledge about the probability as well as the analysis and detection techniques. Early acknowledgement of the infection is highly useful for the patient to consider starting an early therapy or to have a long-period support [42].

One of the common aberrations of chromosomes is Down Syndrome (DS), which is usually a result of trisomy 21. On the other side, it's the occurrence probability is still small (1/800) among newborns worldwide [43]. Extracted features from the human face of infected persons with DS include upward slanting palpebral fissures, a flattened face, epicanthus, protruding tongue and small ears. Some of DS studies [44], (ML methods) were designed for small-size datasets. In another work [45], ICA was adopted to design a hierarchical local model. The authors studied 50 under-age DS patients (80 controls) and accurately extracted face landmarks. Their classification experiments yielded an accuracy measure of about 97%.

An automatic identification system for DS was built using DL approach with CNN networks, requiring a larger image dataset. The adopted dataset contained of 10562 face images of healthy and infected persons with DS [46]. The experimental results yielded an accuracy of approximately 96% and a specificity of 97%, highlighting the potential of AI-based DS detection systems. The authors trained their proposed system using Caucasians face images, while other studies utilized similar algorithms on Asian and African faces [47-49]. These studies demonstrated considerable performance of AI algorithms due to the race variety whereas DS is global disease.

In another type, Turner Syndrome (TS) represents a partial or complete loss of the 'X' chromosome, making it wider prevalent in women with an occurrence possibility ratio of (1/200). Infected persons have phenotypic disorders in face systems. Ordinary type of TS is represented by ear deformity, epicanthus, micro-gnathia, multiple nevus, and high-arched palate [50]. Song et al. (2018) [13] handled TS by constructed model based on 68 face landmarks that were extracted using medical observations. Their experimental results yielded about 85% for accuracy rate. A disease detection system from face image was developed using DCNN [51]. The authors collected a 207-image dataset for female TS patients with 1074 controls. Where most of dataset subjects were photographed more than one time, the frame work of their research was designed using different image selection method to decrease bias effects. Their system yielded considerable accuracy ratio (97%), where AUC value was (0.95+). Furthermore, they conducted a prospective study with small size of sample 2- patient sample with 35 controls. The authors used sensitivity and specificity to evaluate their experimental results with similar results (97%) for both of them. Their dataset images were captured, in general, for Chinese subjects.

Both DS and TS genetic diseases are chromosomal Disorders. Different researches were conducted to build efficient FR methods in recent years to detect genetic diseases. An automatic face-disease detection method was conducted depending on LBP features and Bayesian networks called Facial Dysmorphology Novel Analysis (FDNA) [52]. Gurovich, et al (2019) [4] provided an analysis framework for face image named DeepGestalt using DL algorithms, and it was designed as a smartphone application named. Deep CNN networks were also proposed to build an assessment for human-face morphologic features, which was used to help TS patients [18]. Table 3 summarizes set of previous works in the field of genetic diseases regarding followed technique, dataset size, and performance. Most of the discussed works yielded higher than 90% accuracy indicating high performance in disease detection. Although some of them are relatively old, we tried to discuss all available literatures in the field of genetic diseases detection.

3.1.4. Disease seriousness

Recently, FR algorithms were applied to determine the seriousness of diseases in emergency rooms. A CNN network was proposed to classify real illnesses from fabricated once in individuals. The experimental results yielded a sensitivity of 100% and a specificity of 42% [60]. Lin et al. (2020) [61] designed a deep CNN network for identifying patients that have coronary artery for severe illnesses. They conduct a multicenter

cross-study analyzing a 5796-patient dataset, where their results yielded (0.80) for sensitivity, (0.54) for specificity, and (0.73) for AUC. In another study, researchers built another CNN model to distinguish the faces of patients with asymmetric strokes [37].

Table 3. Face recognition works in genetic disease detection based on the human face

Followed Technique	Dataset Size	Handled Disease	Performance	
			Accuracy	AUC
Deep CNN [18]	246	Congenital adrenal hyperplasia	92%	--
FDNA [52]	48	Cornelia de Lange syndrome	94%	--
Face2Gene [53]	49	Cornelia de Lange syndrome	84%	--
Face2Gene [54]	853	X-linked hypohidrotic ectodermal dysplasia	--	0.98+
Face2Gene [55]	1102	Emanuel syndrome & Pallister-Killian syndrome	--	0.98+
Face2Gene [56]	53	Aymé-Gripp syndrome	--	0.994
Face2Gene [57]	223	Mucopolipidosis type IV	--	0.853
Face2Gene [58]	14	Kabuki syndrome	93%	--
SVM +LBP[59]	447	Noonan syndrome	86%	--
		Williams-Beuren syndrome		

3.1.5 Non-genetic syndromes

Some type of syndrome, such as Fetal Alcohol are a result of higher rates of alcohol consumption during a woman's pregnancy months. In study, human face images were used to extract facial features from 60 cases of Fetal Alcohol patients [62]. For other alcohol-related disorders, FDNA was also applied, which showed higher performance than manual inspection [63]. Another complex disease is inveterate stress syndrome, which manifests as dark images and Gamma Correction was used to create the uniform image. These images were then handled using Cascaded CNN with face landmark extraction. Their system was proposed to help long-distance drivers if they are fatigued or alert [64].

3.2. Clinical applications

Automatic algorithms for face analysis were adopted to build corresponding software like Face++ [65], and they were used in security surveillance, identity recognition, age estimation, etc. applications of real life. Researchers in the clinical field tended to develop such technologies where the face image of the patient is analyzed and handled using software applied on smart phones. Using such software, the patient can send his face image and receive the medical diagnosis in no time. Face2Gene is a standard application that is widely installed on smartphone apps for diagnosis using FR algorithms [5]. It's designed training on 216 types of genetic syndrome and a dataset of (17,106) face images for (10,953) cases, and it recorded high performance where employed in different studies. Another tool for face assessment is AutoFACE that depends on Deep CNN networks to handle facial expression [66].

Other related programs had their share of attention from researchers in face recognition at National Institutes of Health (NIH). Researchers in this institute developed identification software for DiGeorge syndrome, which is also called 22q11.2 Deletion Syndrome [67]. Fig. 3 shows that patient images from different perspirations such as Latin Americans, Caucasians, Asians, and Africans were chosen to train this software [68]. Both of specificity and sensitivity were higher than 96% for all perspiration groups.



Fig. 3. Different populations for recorded cases of Deletion Syndrome [4]

3.3. Characteristics of FR methods

Diagnosis methods using FR applications provided the possibility of resolving obstacles faced by traditional approaches. Many detectable diseases are characterized by various non-typical clinical appearances, making accurate and clear diagnoses challenging, particularly during late stages of infection. For example, in some cases, Cushing's syndrome and acromegaly are diagnosed after (2- 6) and (6) years delay respectively [69]. Due to the rarity of these diseases, clinical inspectors and apprentice doctors need extensive knowledge and experience to recognize their symptoms. Distinguishing between symptoms of similar diseases poses an additional challenge. Furthermore, conventional

techniques have their complexities as well as time and cost implications. Thus, as a comparison, FR techniques record higher accuracy, more informative results, and reduced time and cost requirements.

3.3.1. Significance

Significant FR-studies showed that, as a comparison with human inspectors, FR-based systems yielded better rates of accuracy in recognizing similar face images. Regarding early inspection for the acromegaly disease, computer-based diagnosing techniques yielded 86% accuracy rated against over 26% rate for human inspectors [70]. Another system for acromegaly detection yielded better performance than technician expertise and general-specialist internists (temperate-feature patients) [71]. Different-level medical technician from different were to perform online experiment [72]. Medical students and physicians were asked to test face images for Turner Syndrome disease that were previously tested by computer algorithm for FR diagnosis. The results of automatic FR classification yielded better specificity and sensitivity than human judgments. ML-based FR classifier of Cushing's syndrome and acromegaly was benchmarked with the visual classification made by residents, medical students, and clinical workers. Auto FR system recorded higher accuracy than visual tests by humans [29].

The practicality of FR applications was also explored by comparison with different other diagnosis approaches. Since the 2000s, Novel studies of FR systems benchmarked their results with other manual measurements to demonstrate the objectivity of FR applications using ML basis. In ordinary diagnosis, measurements of FR-based anthropometric accomplished using a hand-held ruler by skilled dysmorphologists recorded the best results. An automation-based method was conducted to analyze and classify facial motion. The authors built their study as consistency with the manual-tracking analysis of the disorders in facial nerves [8]. AI disease detectors also recorded considerable accuracy to rely the face disorders on subjective assessment. Different studies were also conducted on AD disease and facial paralysis [33 & 35]. Diagnostic systems based on FR provided close predictions to the grading system of the facial nerve (House-Brackmann) and Mini-Mental State Examination (MMSE) in these face disorders.

3.3.2. Inclusivity

Besides the significance of diagnosis results, the auto-analysis of face images had high clinical informative characteristics. Regarding the evolution of 3D facial technologies, face phenotypes could have higher-accuracy quantification with a predictor role. Due to acromegaly disorder, face-image features were accurately illustrated regarding the disorder progression, severity, and occurrence after some kinds of surgery. Some researchers [10] provided set of pivotal measures that are discrimination in disease classification regarding male/ female differentiation. Some of such features were proved to be linearly connected to Insulin Growth Factor 1 (IGF-1) levels [67]. Other researchers conducted a study on 668 patients [73], and they showed the superiority of face features in providing high-accuracy anticipation of responses for transsphenoidal surgical (TSS) patients. They compared their results with the ordinary invasive grading using the examination of pituitary image.

The novelty of such screening technologies has more than the differentiation of healthy from infected individuals, where they provide holistic diagnostic utilities. By studying an input face image, the standard application (Face2Gene) provides a list containing 30 possible types of genetic diseases, where the accuracy rates were about (91%) for a list of 10 diseases [5]. The same application (Face2Gene) was also applied on Japanese patients and yielded considerable accuracy also [74]. In another work [75], the authors invented a similar deep phenotyping monitoring technique that provides an early classification for potential risks to enhance global care for populations.

3.3.3. Contribution

The assemblage of AI- based techniques and medicine requirements provides considerable assistance to clinicians and patients, besides, it supports the applied systems in healthcare fields [76]. Despite the insufficiency of direct evidences for the studies of face analysis, previous works recorded significant improvements for AI techniques in the workflow that decreases the medical errors. There are many outstanding utilities from using ML-based face recognition algorithm for disease diagnosis such as reaching the knowledge edges. Where the number of face cases in the dataset is highly more than the total number of cases inspected by a skilled inspector, such a number provides to any-level inspector the accessibility to an accurate diagnosis. Furthermore, due the easiness of system installation on a portable device (mobile) and handle case images within seconds, the time consumption by traditional diagnosis ways is decreased to the minimum.

4. Suggestions for Contribution

4.1. Enlarging data size

Most of the previous works showed the utility of studying larger datasets, especially in ML-based techniques. It is approved that training ML systems with larger datasets record higher performance and reduced error rates. Moreover, human faces naturally exhibit different features due to the variation in gender, race and age. Studying the demographic effects of FR-based diagnoses systems suggested that the younger ages, females, and colored persons had less performance levels [2, 12, 16]. Simultaneous identification is crucial for disorders (dysfunction or disfigurements) of the limbs and stem. Langevin et al. [77] constructed a computer framework (PARK) for diagnosing PD disease with posterior healthcare. Such a considerable framework asks the patient to apply 1 audio task and 6 oral motor exercises on the webcam. The ordinary ATLAS system was designed to inspect patients from the ancestry of northern European only. In contrast, the National Human Genome Research Institute (NHGRI) applied ATLAS to individuals from various ancestral backgrounds in Diverse Populations [78]. This version of ATLAS aims to collect images of geometric features caused by different types of inherited diseases across different regions. Besides genetic syndromes, integrated information about face details is expected to cover a wide range of races, genders and diseases supporting the current systems.

4.2. Influencing factors in diagnosis accuracy

Many factors influence the analysis accuracy of face images, including age progression, different styles of head, facial expression, illumination, and face occlusion (caused by hair, glasses of hats) [12]. Detection techniques are continuously developed to avoid the influence of such factors. Medical technicians have also inspected possible critical factors that can influence the performance of FR-based Disease Detection Systems (DDS). Genetic disorders were also analyzed regarding overlapping facial patterns, which showed that the growing groups enhanced the

accuracy rate, while race and gender variation recorded insignificant effects [78]. Yet, only a smaller portion was searched and applied regarding the disease detection systems. An efficient evaluation of FR techniques in face-disease detection was performed by analyzing a set of participants (12,557) that have different diseases, where each participant has a single one [79]. The authors called their work “Facial Recognition Intensity” explaining how face features are complex. By increasing the size of the training dataset and using DL networks to enhance detection accuracy, they increase the diagnostic performance by (0.02).

4.3. Integrating the contributed technologies

Recently, 3D faces images have gained popularity in FR techniques due to their ability to provide more-depth information with less distortion in captured images. Different ML techniques have been developed for the classification of genetic syndrome types [80]. On the other side, 3D versions of CNN networks have been developed to handle face-motion attributes [81]. These innovative technologies provide wider ranges of interpretation and identification, especially for muscles-nervous disorders. Moreover, it is essential to consider real-time applications in disease detection and incorporate them into proposed systems for clinical use. Live capturing for the human face can detect eye blinking and distinguish between the face and a manipulated image [82]. An itemized facial analysis to handle each face organ can provide a contributed optimization and combined analysis for local features can provide higher-accuracy performance while identifying the whole face image. Guanjie et al. (2021) [83] proposed a clinical-aided diagnosis scheme to analyze eye images of serious eye myasthenia patients. Some disease can affect human movements, such that disease detection can depend, besides face images, on posture or motion analysis identified using DL techniques [84]. Facial expressions represent an additional set of factors that affect FR performance, which can be detected using DL & ML networks to enhance learning performance and detection generalization [85]. Patients, who have difficulties in communication with medical staff, make advantage of Auto-pain detection. Such an approach assists the role of medical staff to provide higher-quality medical help [86]. An auto-emotion detection system, which depends on face landmarks, was proposed to help some medical staff who have low-level abilities of understanding facial expressions. Responses of patients with AD disease, autism, and low-vision ability disorder can be also enhanced using auto-emotion detection systems [87]. The addition proposal is to assess face restoration after medical surgery, which was developed by Boonipat, et al [88]. On the other side, a Systematic Literature Review (SLR) was conducted to analyze algorithm refining within limited sizes of image datasets [89]. By analyzing the ML classifications of autism disorder, the proposed work determined that splitting the training/testing dataset stably (Nested Cross-Validation) provides unbiased and robust prediction regardless of the size of the image dataset. State-of-the-Art in the field of ML works keep producing improvements and expansion of applications.

4.4. Advanced applications

Besides assessment and diagnose, face-image analysis plays a crucial role in determining target treatments and enhancing medical enlightenment. Ridha et al. (2020) [11] proposed a novel physical therapy for facial disability using a 3D printed head-accessory. An ML kit, provided by Google, was adopted for a disability prediction using ANN to anticipate the disability percentage. Combined with a headgear, such an ANN prediction scheme suggested an ordinary treatment period for physiotherapists. ANN-based facial analysis was adopted also in radiology and pathology education [90, 91]. As an example, pathologists have adopted face-image synthesis techniques for training purposes, which provides a useful tool to control the quality and eliminate visual and intellectual bias. In FR fields, face patterns can be in the 3D domain as models for the medical education of students, which helps to understand the occurrence chances and development stages of the disease.

4.5. Research- products path

The wide expansion of AI algorithms for image interpretation has been approved by the Food and Drug Administration (FDA) [76]. Although the number of published articles and reviews has been growingly extending recently, only a limited number of study articles have been successfully transformed into tools for diagnostic aiding. Mobile tools and applications with easy installation (Face2Gene for instance) represent the most effective research converted to end-user products. To ensure the sufficiency and efficiency of AI-base and ML-based products as devices for medical purposes, the FDA organization has released a framework of regulations with an attitude plan [92]. For future expectations, besides productizing research algorithms, the concentration will tend to eliminate practical bias and performance validation in medical research scenes.

4.6. Security and safety

In current works and research, human face images are considered as critical concern of privacy for individuals. When a patient is asked to capture a facial photo, a higher number of them demonstrate worry or hesitation considering the face's private information can be leaked [93]. Patients were asked by NHGRI to sign a copyrights form before capturing their face images on the Atlas website. Ethically, the implications of FR technologies require more regulating laws and rules. Safety, security, autonomy, privacy, and responsibility represent the major considerably aspects [94]. In an analytical study of regulations in Europe and the United States, FR technologies provide higher performance when assessing the impacts of data protection and human rights [95]. Roundtree et al. (2021) [96] conducted an integrative study by reviewing the published articles, in recent decades, that analyzed ethical aspects of FR issues. Regarding clinical issues, captured images of patient faces must be handled earnestly as significant records in medical studies. Considering another type of safety issue, internal or external intrusions into DL-based frameworks indicate another safety challenge [97].

Safety preparations must consider network vulnerability to hostile challenges, especially in DL-based systems. For adversarial robustness, hostile challenges have different types such as robust optimization, gradient masking, and detecting hostile examples [97]. In FR applications, assessing and testing are usually set to test current models, yet several optimization frameworks were proposed. Despite all paid efforts in face classification frameworks, deeper studies should be conducted to ensure FR classifier's safety for clinical applications.

5. Conclusions

Different technologies were developed in FR-based diagnosis over the recent decades, but the convergence of human face analysis and diagnosing of facial diseases remains a promising research branch. In clinical preparations, capturing processes for human face images need standardization to ensure high-quality images. Traditional detection methods (feature-based) and DL methods were proposed for FR-based face diagnosis. The detection systems that depended on facial recognition recorded considerable levels of accuracy in detecting different types of

facial disease, covering chromosomes and genetic, endocrinology and metabolism, muscles- nervous besides non-genetic syndromes and disease seriousness. Despite the numerous research algorithms proposed for face-based diagnosis, only a few of them were converted into practical clinical applications. As benchmarking with other ordinary diagnosis approaches, FR-based approaches for disease detection were higher objective, accurate, informative, and comprehensive. FR application also provides the ability to improve the efficiency of the healthcare system. Although different research ideas are applied in this field, several new areas can be considered for future research. Expanding the size of face image datasets can lead to higher accuracy and the factors affecting diagnostic accuracy levels should be analyzed and tested. Additional research ideas can be converted into products to provide more medical services. Other medical services rather than only diagnosis provide promising fields to be searched. Security and safety issues are considerable ethical aspects that need wider investigation to be organized under appropriate regulations.

Acknowledgement

It is our honor and pleasure to extend our heartfelt gratitude to the esteemed Editor and the diligent Reviewers for their invaluable contributions to the enhancement of our manuscript.

References

- [1] Naji, Maitham Ali, Ghalib Ahmed Salman, and Jasim Fadhil Muthna. "Face recognition using selected topographical features." *International Journal of Electrical and Computer Engineering* 10(5), 4695, 2020, DOI: 10.11591/ijece.v10i5.
- [2] Kaur, Paramjit, et al. "Facial-recognition algorithms: A literature review." *Medicine, Science and the Law*, 60(2), 131-139, 2020, <https://doi.org/10.1177/0025802419893168>.
- [3] Kosilek, R.P.; Frohner, R.; Würtz, R.P.; Berr, C.M.; Schopohl, J.; Reincke, M.; Schneider, H.J. Diagnostic Use of Facial ImageAnalysis Software in Endocrine and Genetic Disorders: Review, Current Results and Future Perspectives. *Eur. J. Endocrinol.* 173, M39–M44, 2015, DOI:10.1530/EJE-15-0429.
- [4] Ali, M.R.; Myers, T.; Wagner, E.; Ratnu, H.; Dorsey, E.R.; Hoque, E. Facial Expressions Can Detect Parkinson’s Disease: Preliminary Evidence from Videos Collected Online. *NPJ Digit. Med.* 2021, 4, 1–4. <https://doi.org/10.1038/s41746-021-00502-8> PMID: 34480109.
- [5] Gurovich, Y.; Hanani, Y.; Bar, O.; Nadav, G.; Fleischer, N.; Gelbman, D.; Basel-Salmon, L.; Krawitz, P.M.; Kamphausen, S.B.; Zenker, M.; et al. Identifying Facial Phenotypes of enetic Disorders Using Deep Learning. *Nat. Med.* 2019, 25, 60–64. <https://doi.org/10.1038/s41591-018-0279-0>.
- [6] Loos, H.S.; Wiczorek, D.; Würtz, R.P.; von der Malsburg, C.; Horsthemke, B. Computer-Based Recognition of Dysmorphic Faces.*Eur. J. Hum. Genet.* 11, 555–560, 2003, <https://doi.org/10.1038/sj.ejhg.5200997>.
- [7] Wachtman, G.S.; Cohn, J.F.; VanSwearingen, J.M.; Manders, E.K. Automated Tracking of Facial Features in Patients with Facial Neuromuscular Dysfunction. *Plast. Reconstr. Surg.* 2001, 107, 1124–1133.
- [8] Rajpurkar, P.; Chen, E.; Banerjee, O.; Topol, E.J. AI in Health and Medicine. *Nat. Med.* 2022, 28, 31–38. <https://doi.org/10.1038/s41591-021-01614-0>.
- [9] Yu, K.-H.; Beam, A.L.; Kohane, I.S. Artificial Intelligence in Healthcare. *Nat. Biomed. Eng.* 2018, 2, 19–731. <https://doi.org/10.1038/s41551-018-0305-z>.
- [10] Meng, T.; Guo, X.; Lian,W.; Deng, K.; Gao, L.;Wang, Z.; Huang, J.;Wang, X.; Long, X.; Xing, B. Identifying Facial Features and Predicting Patients of Acromegaly Using Three-Dimensional Imaging Techniques and Machine Learning. *Front. Endocrinol.* 2020, 11, 492. <https://doi.org/10.3389/fendo.2020.00492>.
- [11] Ridha, A.M.; Shehieb,W.; Yacoub, P.; Al-Balawneh, K.; Arshad, K. Smart Prediction System for Facial Paralysis. In Proceedings of the 2020 7th International Conference on Electrical and Electronics Engineering (ICEEE), Antalya, Turkey, 14–16 April 2020; pp. 321–327. DOI: 10.1109/ICEEE49618.2020.9102600.
- [12] Anwarul, S.; Dahiya, S. A Comprehensive Review on Face Recognition Methods and Factors Affecting Facial Recognition Accuracy. In Proceedings of the ICRIC 2019, Recent Innovations in Computing, Jammu, India, 8–9 March 2019; Springer: Berlin/Heidelberg, Germany, 2020; pp. 495–514. https://doi.org/10.1007/978-3-030-29407-6_36.
- [13] Song, W.; Lei, Y.; Chen, S.; Pan, Z.; Yang, J.-J.; Pan, H.; Du, X.; Cai, W.; Wang, Q. Multiple Facial Image Features-Based Recognition for the Automatic Diagnosis of Turner Syndrome. *Comput. Ind.* 2018, 100, 85–95. <https://doi.org/10.1016/j.compind.2018.03.021>.
- [14] . Hong, D.; Zheng, Y.-Y.; Xin, Y.; Sun, L.; Yang, H.; Lin, M.-Y.; Liu, C.; Li, B.-N.; Zhang, Z.-W.; Zhuang, J.; et al. Genetic Syndromes Screening by Facial Recognition Technology: VGG-16 Screening Model Construction and Evaluation. *Orphanet. J. Rare Dis.* 2021,16, 344. <https://doi.org/10.1186/s13023-021-01979-y>.
- [15] Jayaraman, U.; Gupta, P.; Gupta, S.; Arora, G.; Tiwari, K. Recent Development in Face Recognition. *Neurocomputing* 2020,408, 231–245. <https://doi.org/10.1016/j.neucom.2019.08.110>.
- [16] Wang, Xin, et al. "Gan-generated faces detection: A survey and new perspectives." arXiv preprint arXiv:2202.07145, 2022. <https://doi.org/10.48550/arXiv.2202.07145>.
- [17] Banerjee, D.; Yu, K. Robotic Arm-Based Face Recognition Software Test Automation. *IEEE Access* 2018, 6, 37858–37868. DOI: 10.1109/ACCESS.2018.2854754.
- [18] AbdAlmageed, W.; Mirzaalian, H.; Guo, X.; Randolph, L.M.; Tanawattanacharoen, V.K.; Geffner, M.E.; Ross, H.M.; Kim, M.S. Assessment of Facial Morphologic Features in Patients With Congenital Adrenal Hyperplasia Using Deep Learning. *JAMA Netw. Open* 2020, 3, e2022199. doi:10.1001/jamanetworkopen.2020.22199.
- [19] Bayouth, Khaled, Fayçal Hamdaoui, and Abdellatif Mtibaa. "An Attention-based Hybrid 2D/3D CNN-LSTM for Human Action Recognition." 2022 2nd International Conference on Computing and Information Technology (ICIT). IEEE, 2022. DOI: 10.1109/ICIT52419.2022.9711631.
- [20] Jin, B.; Qu, Y.; Zhang, L.; Gao, Z. Diagnosing Parkinson Disease Through Facial Expression Recognition: Video Analysis. *J. Med.Internet Res.* 2020, 22, e18697. doi: 10.2196/18697.
- [21] Baltrušaitis, T.; Zadeh, A.; Lim, Y.; Morency, L.-P. OpenFace 2.0: Facial Behavior Analysis Toolkit. In Proceedings of the 13th IEEE International Conference on Automatic Face & Gesture Recognition (FG 2018), Xi’an, China, 15–19 May 2018. DOI:

10.1109/FG.2018.00019.

- [22] Nam, U.; Lee, K.; Ko, H.; Lee, J.-Y.; Lee, E.C. Analyzing Facial and Eye Movements to Screen for Alzheimer's Disease. *Sensors*, 20, 5349, 2020, <https://doi.org/10.3390/s20185349>.
- [23] Colao, A.; Grasso, L.F.S.; Giustina, A.; Melmed, S.; Chanson, P.; Pereira, A.M.; Pivonello, R. Acromegaly. *Nat. Rev. Dis Primers*, 5, 20, 2019.
- [24] Savas, Mesut, et al. "Approach to the patient: diagnosis of Cushing syndrome." *The Journal of Clinical Endocrinology & Metabolism* 107.11 (2022): 3162-3174. <https://doi.org/10.1210/clinem/dgac492>.
- [25] Learned-Miller, E.; Lu, Q.; Paisley, A.; Trainer, P.; Blanz, V.; Dedden, K.; Miller, R. Detecting Acromegaly: Screening for Disease with a Morphable Model. *Med. Image Comput. Comput. Assist. Interv.* 2006, 9, 495–503. https://doi.org/10.1007/11866763_61.
- [26] Frohner, R.; Würtz, R.P.; Kosilek, R.; Schne der, H.J. Optimierung Der Gesichtsklassifikation Bei Der Erkennung von Akromegalie. *J. Klin. Endokrinol. Stoffw.* 2013, 6, 20–24.
- [27] Gencturk, B.; Nabiye, V.V.; Ustubioglu, A.; Ketenci, S. Automated Pre-Diagnosis of Acromegaly Disease Using Local Binary Patterns and Its Variants. In *Proceedings of the 36th International Conference on Telecommunications and Signal Processing (TSP)*, Rome, Italy, 2–4 July 2013; pp. 817–821. DOI: 10.1109/TSP.2013.6614052.
- [28] Kong, X.; Gong, S.; Su, L.; Howard, N.; Kong, Y. Automatic Detection of Acromegaly From Facial Photographs Using Machine Learning Methods. *EBioMedicine* 2018, 27, 94–102. <https://doi.org/10.1016/j.ebiom.2017.12.01>.
- [29] Wei, R.; Jiang, C.; Gao, J.; Xu, P.; Zhang, D.; Sun, Z.; Liu, X.; Deng, K.; Bao, X.; Sun, G.; et al. Deep-Learning Approach to Automatic Identification of Facial Anomalies in Endocrine Disorders. *Neuroendocrinology* 2020, 110, 328–337. <https://doi.org/10.1159/000502211>.
- [30] Gautam, R.; Sharma, M. Prevalence and Diagnosis of Neurological Disorders Using Different Deep Learning Techniques: A Meta-Analysis. *J. Med. Syst.* 2020, 44, 49. <https://doi.org/10.1007/s10916-019-1519-7>.
- [31] Wang, B.; Wu, X. Application of Artificial Intelligence in Recognition and Evaluation of Facial Paralysis. *Chin. J. Med. Instrum*, 46, 57–62, 2022. <https://doi.org/10.3969/j.issn.1671-7104.2022.01.012>.
- [32] Ngo, T.H.; Seo, M.; Matsushiro, N.; Chen, Y.-W. Quantitative Analysis of Facial Paralysis Based on Filters of Concentric Modulation. In *Proceedings of the 2015 12th International Conference on Fuzzy Systems and Knowledge Discovery (FSKD)*, Zhangjiajie, China, 15–17 August 2015; pp. 1758–1763. DOI: 10.1109/FSKD.2015.7382213.
- [33] Guo, Z.; Shen, M.; Duan, L.; Zhou, Y.; Xiang, J.; Ding, H.; Chen, S.; Deussen, O.; Dan, G. Deep Assessment Process: Objective Assessment Process for Unilateral Peripheral Facial Paralysis via Deep Convolutional Neural Network. In *Proceedings of the 2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017)*, Melbourne, Australia, 18–21 April 2017; pp. 135–138. DOI: 10.1109/ISBI.2017.7950486.
- [34] Storey, G.; Jiang, R.; Keogh, S.; Bouridane, A.; Li, C.-T. 3DPalsyNet: A Facial Palsy Grading and Motion Recognition Framework Using Fully 3D Convolutional Neural Networks. *arXiv* 2019, arXiv:1905.13607. DOI: 10.1109/ACCESS.2019.2937285.
- [35] Xing, Xin, et al. "Efficient training on Alzheimer's disease diagnosis with learnable weighted pooling for 3D PET brain image classification." *Electronics* 12.2 (2023): 467. <https://doi.org/10.3390/electronics12020467>.
- [36] Tau, tan, A.-M.; Ionescu, B.; Santarnecchi, E. Artificial Intelligence in Neurodegenerative Diseases: A Review of Available Tools with a Focus on Machine Learning Techniques. *Artif. Intell. Med.* 2021, 117, 102081. <https://doi.org/10.1016/j.artmed.2021.102081>.
- [37] Zhuang, Y.; McDonald, M.; Uribe, O.; Yin, X.; Parikh, D.; Southerland, A.M.; Rohde, G.K. Facial Weakness Analysis and Quantification of Static Images. *IEEE J. Biomed. Health Inform.* 2020, 24, 2260–2267. DOI: 10.1109/JBHI.2020.2964520.
- [38] Bandini, A.; Rezaei, S.; Guarin, D.L.; Kulkarni, M.; Lim, D.; Boulous, M.I.; Zinman, L.; Yunusova, Y.; Taati, B. A New Dataset for Facial Motion Analysis in Individuals With Neurological Disorders. *IEEE J. Biomed. Health Inform.* 2021, 25, 1111–1119. DOI: 10.1109/JBHI.2020.3019242.
- [39] Rajnoha, M.; Mekyska, J.; Burget, R.; Eliasova, I.; Kostalova, M.; Rektorova, I. Towards Identification of Hypomimia in Parkinson's Disease Based on Face Recognition Methods. In *Proceedings of the 2018 10th International Congress on Ultra-Modern Telecommunications and Control Systems and Workshops (ICUMT)*, Moscow, Russia, 5–9 November 2018; pp. 1–4. DOI: 10.1109/ICUMT.2018.8631249.
- [40] Hou, X.; Zhang, Y.; Wang, Y.; Wang, X.; Zhao, J.; Zhu, X.; Su, J. A Markerless 2D Video, Facial Feature Recognition-Based, Artificial Intelligence Model to Assist With Screening for Parkinson Disease: Development and Usability Study. *J. Med. Internet Res.* 2021, 23, e29554. doi: 10.2196/29554.
- [41] Umeda-Kameyama, Y.; Kameyama, M.; Tanaka, T.; Son, B.-K.; Kojima, T.; Fukasawa, M.; Iizuka, T.; Ogawa, S.; Iijima, K.; Akishita, M. Screening of Alzheimer's Disease by Facial Complexion Using Artificial Intelligence. *Aging* 2021, 13, 1765–1772. doi: 10.18632/aging.202545.
- [42] Gravholt, Claus H., et al. "The changing face of Turner syndrome." *Endocrine reviews*, 44(1), 33-69. The changing face of Turner syndrome, 2023.
- [43] Bull, M.J. Down Syndrome. *N. Engl. J. Med.* 2020, 382, 2344–2352. DOI: 10.1056/NEJMra1706537.
- [44] Agbolade, Olalekan, et al. "Down syndrome face recognition: a review." *Symmetry* 12.7 (2020): 1182. <https://doi.org/10.3390/sym12071182>.
- [45] Zhao, Q.; Okada, K.; Rosenbaum, K.; Kehoe, L.; Zand, D.J.; Sze, R.; Summar, M.; Linguraru, M.G. Digital Facial Dysmorphology for Genetic Screening: Hierarchical Constrained Local Model Using ICA. *Med. Image Anal.* 2014, 18, 699–710. <https://doi.org/10.1016/j.media.2014.04.002>.
- [46] Qin, B.; Liang, L.; Wu, J.; Quan, Q.; Wang, Z.; Li, D. Automatic Identification of Down Syndrome Using Facial Images with Deep Convolutional Neural Network. *Diagnostics* 2020, 10, 487. <https://doi.org/10.3390/diagnostics10070487>.
- [47] Srisraluang, W.; Rojnueangnit, K. Facial Recognition Accuracy in Photographs of Thai Neonates with Down Syndrome among Physicians and the Face2Gene Application. *Am. J. Med. Genet. A* 2021, 185, 3701–3705. <https://doi.org/10.1002/ajmg.a.62432>.
- [48] Vorravanpreecha, N.; Lertboonnum, T.; Rodjanadit, R.; Sriplienchan, P.; Rojnueangnit, K. Studying Down Syndrome Recognition Probabilities in Thai Children with De-Identified Computer-Aided Facial Analysis. *Am. J. Med. Genet. A* 2018, 176, 1935–1940. <https://doi.org/10.1002/ajmg.a.40483>.
- [49] Porras, A.R.; Bramble, M.S.; Mosema Be Amoti, K.; Spencer, D.; Dakande, C.; Manya, H.; Vashist, N.; Likuba, E.; Ebel, J.M.; Musasa, C.; et al. Facial Analysis Technology for the Detection of Down Syndrome in the Democratic Republic of the Congo. *Eur. J. Med. Genet.* 64, 104267, 2021. <https://doi.org/10.1016/j.ejmg.2021.104267>.

- [50] Gravholt, C.H.; Viuff, M.H.; Brun, S.; Stochholm, K.; Andersen, N.H. Turner Syndrome: Mechanisms and Management. *Nat. Rev. Endocrinol.* 2019, 15, 601–614. <https://doi.org/10.1038/s41574-019-0224-4>.
- [51] Pan, Z.; Shen, Z.; Zhu, H.; Bao, Y.; Liang, S.; Wang, S.; Li, X.; Niu, L.; Dong, X.; Shang, X.; et al. Clinical Application of an Automatic Facial Recognition System Based on Deep Learning for Diagnosis of Turner Syndrome. *Endocrine* 2021, 72, 865–873. <https://doi.org/10.1007/s12020-020-02539-3>.
- [52] Basel-Vanagaite, L.; Wolf, L.; Orin, M.; Larizza, L.; Gervasini, C.; Krantz, I.; Deardoff, M. Recognition of the Cornelia de Lange Syndrome Phenotype with Facial Dysmorphology Novel Analysis. *Clin. Genet.* 89, 557–563, 2016. <https://doi.org/10.1111/cge.12716>.
- [53] Latorre-Pellicer, A.; Ascaso, Á.; Trujillano, L.; Gil-Salvador, M.; Arnedo, M.; Lucia-Campos, C.; Antoñanzas-Pérez, R.; Marcos-Alcalde, I.; Parenti, I.; Bueno-Lozano, G.; et al. Evaluating Face2Gene as a Tool to Identify Cornelia de Lange Syndrome by Facial Phenotypes. *Int. J. Mol. Sci.* 2020, 21, 1042. <https://doi.org/10.3390/ijms21031042>.
- [54] Hadj-Rabia, S.; Schneider, H.; Navarro, E.; Klein, O.; Kirby, N.; Huttner, K.; Wolf, L.; Orin, M.; Wohlfart, S.; Bodemer, C.; et al. Automatic Recognition of the XLHED Phenotype from Facial Images. *Am. J. Med. Genet. A* 2017, 173, 2408–2414.
- [55] Liehr, T.; Acquarola, N.; Pyle, K.; St-Pierre, S.; Rinholm, M.; Bar, O.; Wilhelm, K.; Schreyer, I. Next Generation Phenotyping in Emanuel and Pallister-Killian Syndrome Using Computer-Aided Facial Dysmorphology Analysis of 2D Photos. *Clin. Genet.* 2018, 93, 378–381. <https://doi.org/10.1002/ajmg.a.38343>.
- [56] Amudhavalli, S.M.; Hanson, R.; Angle, B.; Bontempo, K.; Gripp, K.W. Further Delineation of Aymé-Gripp Syndrome and Use of Automated Facial Analysis Tool. *Am. J. Med. Genet. A* 2018, 176, 1648–1656. <https://doi.org/10.1002/ajmg.a.38832>.
- [57] Pode-Shakked, B.; Finezilber, Y.; Levi, Y.; Liber, S.; Fleischer, N.; Greenbaum, L.; Raas-Rothschild, A. Shared Facial Phenotype of Patients with Mucopolidiosis Type IV: A Clinical Observation Reaffirmed by next Generation Phenotyping. *Eur. J. Med. Genet.* 2020, 63, 103927. <https://doi.org/10.1016/j.ejmg.2020.103927>.
- [58] Wang, Y.; Li, N.; Su, Z.; Xu, Y.; Liu, S.; Chen, Y.; Li, X.; Shen, Y.; Hung, C.; Wang, J.; et al. The Phenotypic Spectrum of Kabuki Syndrome in Patients of Chinese Descent: A Case Series. *Am. J. Med. Genet. A* 2020, 182, 640–651. <https://doi.org/10.1002/ajmg.a.61467>.
- [59] Porras, A.R.; Summar, M.; Linguraru, M.G. Objective Differential Diagnosis of Noonan and Williams-Beuren Syndromes in Diverse Populations Using Quantitative Facial Phenotyping. *Mol. Genet. Metab.* 2021, 9, e1636. <https://doi.org/10.1002/mgg3.1636>.
- [60] Forte, C.; Voinea, A.; Chichirau, M.; Yeshmagambetova, G.; Albrecht, L.M.; Erfurt, C.; Freundt, L.A.; Carmo, L.O.E.; Henning, R.H.; van der Horst, I.C.C.; et al. Deep Learning for Identification of Acute Illness and Facial Cues of Illness. *Front. Med.* 2021, 8, 661309. <https://doi.org/10.3389/fmed.2021.661309>.
- [61] Lin, S.; Li, Z.; Fu, B.; Chen, S.; Li, X.; Wang, Y.; Wang, X.; Lv, B.; Xu, B.; Song, X.; et al. Feasibility of Using Deep Learning to Detect Coronary Artery Disease Based on Facial Photo. *Eur. Heart J.* 2020, 41, 4400–4411. <https://doi.org/10.1093/eurheartj/ehaa640>.
- [62] Blanck-Lubarsch, Moritz, et al. "Simplifying diagnosis of fetal alcohol syndrome using machine learning methods." *Frontiers in Pediatrics* 9 (2022): 707566. <https://doi.org/10.3389/fped.2021.707566>.
- [63] Valentine, M.; Bihm, D.C.J.; Wolf, L.; Hoyme, H.E.; May, P.A.; Buckley, D.; Kalberg, W.; Abdul-Rahman, O.A. Computer-Aided Recognition of Facial Attributes for Fetal Alcohol Spectrum Disorders. *Pediatrics* 2017, 140, e20162028. <https://doi.org/10.1542/peds.2016-2028>.
- [64] Das, Sancharee, and Rupal Bhargava. "Vision-Based Fatigue Detection In Drivers Using Multi-Facial Feature Fusion." 2023 15th International Conference on Developments in eSystems Engineering (DeSE). IEEE, 2023. DOI: 10.1109/DeSE58274.2023.10099741.
- [65] Jung, S.-G.; An, J.; Kwak, H.; Salminen, J.; Jansen, B. Inferring Social Media Users' Demographics from Profile Pictures: A Face++ Analysis on Twitter Users. In *Proceedings of the International Conference on Electronic Business (ICEB)*, Dubai, United Arab Emirates, 4–8 December 2017.
- [66] Miller, M.Q.; Hadlock, T.A.; Fortier, E.; Guarin, D.L. The Auto-eFACE: Machine Learning-Enhanced Program Yields Automated Facial Palsy Assessment Tool. *Plast. Reconstr. Surg.* 2021, 147, 467–474. DOI: 10.1097/PRS.00000000000007572.
- [67] Guo, X.; Meng, T.; Huang, J.; Wang, X.; Lian, W.; Deng, K.; Gao, L.; Wang, Z.; Xing, B.; Long, X. 3D Facial Analysis in Acromegaly: Gender-Specific Features and Clinical Correlations. *Front. Endocrinol.* 2018, 9, 722. <https://doi.org/10.3389/fendo.2018.00722>.
- [68] Kruszka, Paul, et al. "22q11. 2 deletion syndrome in diverse populations." *American Journal of Medical Genetics Part A* 173.4 (2017): 879-888. <https://doi.org/10.1002/ajmg.a.38199>.
- [69] Qiang, Jiaqi, et al. "Review on facial-recognition-based applications in disease diagnosis." *Bioengineering*, 9(7), 273, 2022, <https://doi.org/10.3390/bioengineering9070273>.
- [70] Slagboom, Tessa NA, et al. "Prevalence of clinical signs, symptoms and comorbidities at diagnosis of acromegaly: a systematic review in accordance with PRISMA guidelines." *Pituitary* (2023): 1-14. <https://doi.org/10.1007/s11102-023-01322-7>.
- [71] Kong, Xiangyi, et al. "Automatic detection of acromegaly from facial photographs using machine learning methods." *EBioMedicine* 27 (2018): 94-102. <https://doi.org/10.1016/j.ebiom.2017.12.015>.
- [72] Chen, S.; Pan, Z.-X.; Zhu, H.-J.; Wang, Q.; Yang, J.-J.; Lei, Y.; Li, J.-Q.; Pan, H. Development of a Computer-Aided Tool for the Pattern Recognition of Facial Features in Diagnosing Turner Syndrome: Comparison of Diagnostic Accuracy with Clinical Workers. *Sci. Rep.* 2018, 8, 9317. <https://doi.org/10.1038/s41598-018-27586-9>.
- [73] Fan, Y.; Li, Y.; Li, Y.; Feng, S.; Bao, X.; Feng, M.; Wang, R. Development and Assessment of Machine Learning Algorithms for Predicting Remission after Transsphenoidal Surgery among Patients with Acromegaly. *Endocrine* 2020, 67, 412–422. <https://doi.org/10.1007/s12020-019-02121-6>.
- [74] Mishima, H.; Suzuki, H.; Doi, M.; Miyazaki, M.; Watanabe, S.; Matsumoto, T.; Morifuji, K.; Moriuchi, H.; Yoshiura, K.-I.; Kondoh, T.; et al. Evaluation of Face2Gene Using Facial Images of Patients with Congenital Dysmorphic Syndromes Recruited in Japan. *J. Hum. Genet.* 2019, 64, 789–794. <https://doi.org/10.1038/s10038-019-0619-z>.
- [75] Porras, A.R.; Rosenbaum, K.; Tor-Diez, C.; Summar, M.; Linguraru, M.G. Development and Evaluation of a Machine Learning-Based Point-of-Care Screening Tool for Genetic Syndromes in Children: A Multinational Retrospective Study. *Lancet Digit. Health* 2021, 3, e635–e643. [https://doi.org/10.1016/S2589-7500\(21\)00137-0](https://doi.org/10.1016/S2589-7500(21)00137-0).
- [76] Topol, E.J. High-Performance Medicine: The Convergence of Human and Artificial Intelligence. *Nat. Med.* 2019, 25, 44–56. <https://doi.org/10.1038/s41591-018-0300-7>.
- [77] Langevin, R.; Ali, M.R.; Sen, T.; Snyder, C.; Myers, T.; Dorsey, E.R.; Hoque, M.E. The PARK Framework for Automated Analysis of Parkinson's Disease Characteristics. *Proc. ACM Interact. Mob. Wearable Ubiquitous Technol.* 3, 1–22, 2019, <https://doi.org/10.1145/3328925>.

- [78] Pantel, J.T.; Zhao, M.; Mensah, M.A.; Hajjir, N.; Hsieh, T.-C.; Hanani, Y.; Fleischer, N.; Kamphans, T.; Mundlos, S.; Gurovich, Y.; et al. Advances in Computer-Assisted Syndrome Recognition and Differentiation in a Set of Metabolic Disorders. *bioRxiv* 219394, 2017, <https://doi.org/10.1101/219394>.
- [79] Wu, D.; Chen, S.; Zhang, Y.; Zhang, H.; Wang, Q.; Li, J.; Fu, Y.; Wang, S.; Yang, H.; Du, H.; et al. Facial Recognition Intensity in Disease Diagnosis Using Automatic Facial Recognition. *J. Pers. Med.* 11, 1172, 2021, <https://doi.org/10.3390/jpm11111172>.
- [80] Hallgrímsson, B.; Aponte, J.D.; Katz, D.C.; Bannister, J.J.; Riccardi, S.L.; Mahasuwan, N.; McInnes, B.L.; Ferrara, T.M.; Lipman, D.M.; Neves, A.B.; et al. Automated Syndrome Diagnosis by Three-Dimensional Facial Imaging. *Genet. Med.* 22, 1682–1693, 2020, <https://doi.org/10.1038/s41436-020-0845-y>.
- [81] Boualia, Sameh Neili, and Najoua Essoukri Ben Amara. "3D CNN for human action recognition." 2021 18th International Multi-Conference on Systems, Signals & Devices (SSD). IEEE, 2021, DOI: 10.1109/SSD52085.2021.9429429.
- [82] Khairnar, Smita, et al. "Face Liveness Detection Using Artificial Intelligence Techniques: A Systematic Literature Review and Future Directions." *Big Data and Cognitive Computing*, 7(1), 37, 2023. <https://doi.org/10.3390/bdcc7010037>.
- [83] Guanjie Liu, Y.W.; Guanjie Liu, Y.W. A Computer-Aided System for Ocular Myasthenia Gravis Diagnosis. *Tsinghua Sci. Technol.* 26, 749–758, 2021, DOI: 10.26599/TST.2021.9010025.
- [84] Arac, A. Machine Learning for 3D Kinematic Analysis of Movements in Neurorehabilitation. *Curr. Neurol. Neurosci. Rep.* 20, 29, 2020, <https://doi.org/10.1007/s11910-020-01049-z>.
- [85] Savchenko, Andrey V., Lyudmila V. Savchenko, and Ilya Makarov. "Classifying emotions and engagement in online learning based on a single facial expression recognition neural network." *IEEE Transactions on Affective Computing*, 13(4), 2132-2143, 2022, DOI: 10.1109/TAFFC.2022.3188390.
- [86] Hassan, T.; Seus, D.; Wollenberg, J.; Weitz, K.; Kunz, M.; Lautenbacher, S.; Garbas, J.-U.; Schmid, U. Automatic Detection of Pain from Facial Expressions: A Survey. *IEEE Trans. Pattern. Anal. Mach. Intell.* 43, 1815–1831, 2021, DOI: 10.1109/TPAMI.2019.2958341.
- [87] Zhao, X.; Zou, J.; Li, H.; Dellandrea, E.; Kakadiaris, I.A.; Chen, L. Automatic 2.5-D Facial Landmarking and Emotion Annotation for Social Interaction Assistance. *IEEE Trans. Cybern.* 46, 2042–2055, 2016, DOI: 10.1109/TCYB.2015.2461131.
- [88] Boonipat, T.; Asaad, M.; Lin, J.; Glass, G.E.; Mardini, S.; Stotland, M. Using Artificial Intelligence to Measure Facial Expression Following Facial Reanimation Surgery. *Plast. Reconstr. Surg.*, 146, 1147–1150, 2020, DOI: 10.1097/PRS.00000000000007251.
- [89] Vabalas, A.; Gowen, E.; Poliakoff, E.; Casson, A.J. Machine Learning Algorithm Validation with a Limited Sample Size. *PLoS ONE*, 14, e0224365, 2019, <https://doi.org/10.1371/journal.pone.0224365>.
- [90] Niazi, M.K.K.; Parwani, A.V.; Gurcan, M.N. Digital Pathology and Artificial Intelligence. *Lancet Oncol.* 20, e253–e261, 2019, [https://doi.org/10.1016/S1470-2045\(19\)30154-8](https://doi.org/10.1016/S1470-2045(19)30154-8).
- [91] Hosny, A.; Parmar, C.; Quackenbush, J.; Schwartz, L.H.; Aerts, H.J.W.L. Artificial Intelligence in Radiology. *Nat. Rev. Cancer*, 18, 500–510, 2018, <https://doi.org/10.1038/s41568-018-0016-5>.
- [92] U.S. Food and Drug Administration Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. 2021. Available online: <https://www.fda.gov>.
- [93] Katsanis, S.H.; Claes, P.; Doerr, M.; Cook-Deegan, R.; Tenenbaum, J.D.; Evans, B.J.; Lee, M.K.; Anderton, J.; Weinberg, S.M.; Wagner, J.K. A Survey of U.S. Public Perspectives on Facial Recognition Technology and Facial Imaging Data Practices in Health and Research Contexts. *PLoS ONE*, 16, e0257923, 2021, <https://doi.org/10.1371/journal.pone.0261738>.
- [94] Smith, M.; Miller, S. The Ethical Application of Biometric Facial Recognition Technology. *AI Soc.*, 37, 167–175, 2022, <https://doi.org/10.1007/s00146-021-01199-9>.
- [95] Almeida, D.; Shmarko, K.; Lomas, E. The Ethics of Facial Recognition Technologies, Surveillance, and Accountability in an Age of Artificial Intelligence: A Comparative Analysis of US, EU, and UK Regulatory Frameworks. *AI Ethics*, 1–11, 2021, <https://doi.org/10.1007/s43681-021-00077-w>.
- [96] Roundtree, A.K. Ethics and Facial Recognition Technology: An Integrative Review. In *Proceedings of the 2021 3rd World Symp. Artif. (WSAI)*, Guangzhou, China, pp. 10–19, 18–20 June 2021, DOI: 10.1109/WSAI51899.2021.9486382.
- [97] Hongsong Chen, Y.Z.; Hongsong Chen, Y.Z. Security Issues and Defensive Approaches in Deep Learning Frameworks. *Tsinghua Sci. Technol.* 26, 894–905, 2021, DOI: 10.26599/TST.2020.9010050.