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(Research Article)

The use of artificial intelligence for early detection of acromegaly from patients' photographs

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Abstract

Acromegaly is a rare endocrine disease. It manifests with a metabolic disorder and typical physical changes. It evolves gradually and the first obvious signs appears between 7 to 10 years. The effects on patients are both physical and psychological. The diagnostic delay is associated with increased mortality and disability and the drastic changes, in many cases, are irreversible. Early diagnosis will help patients with acromegaly live better lives and reduce the financial burden of their condition. We aim by this survey to investigate the ways artificial intelligence where used for the early detection of acromegaly from photographs. No literature survey was conducted, to our knowledge, that tackle the different artificial intelligence techniques used for this purpose, their results and limitations.

Keywords: Machine Learning; Deep Learning; Acromegaly; Photographs

1. Introduction

Advances in Artificial Intelligence (AI) have found applications in different fields, especially for health which has open opportunities for early diagnosis of many diseases. One of the reasons that enhance the growth of AI is the demand in big data processing and to empower doctors with instruments that will assist them in their profession and patients with their healing process. In addition, the demand for automated image processing has pushed forward the application of AI for the interpretation of medical image and results particularly in major advancements in Machine Learning (ML) and Deep Learning (DL).

Acromegaly is a rare pathology with a prevalence of 2.8- 13.7 cases per 100000 and an incidence of 0.2- 1.1 cases/ 100000/year [1]. It is one of the rare disorders with an insidious course, resulting in a delay of 7 to 10 years in diagnosis. Patients seek care after observing changing in their appearances. Even if the first signs and symptoms has begun to settle early, it is not evident for every doctor or even for the patient's family to recognize. Acromegaly is characterized by widening tooth spacing, prognathism, frontal bone enlargement, nose enlargement, prominence of the zygomatic arch, prominence of the brow ridge and forehead, swelling of the soft tissues, and thickening of the skin[2].

Acromegaly is the result of excess secretion of growth hormone (GH) and therefore an increase in insulin-growth factor (IGF1) [3], [4], [5] .In 95% of cases, acromegaly results from the presence of a pituitary adenoma, usually a macro-called that secretes GH. In less than 5% of cases, excess GH is the result of excessive somatoliberin secretion (GHRH), either by a hypothalamic tumour or exceptionally by neuroendocrine tumour (lung, digestive) [3], [4], [5]. The clinical manifestations of acromegaly are multiple and affect all systems. Generalized visceromegaly (heart, thyroid tongue, prostate) is always present. cardiovascular impact, which can range from high blood pressure, cardiomyopathy to heart

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failure, increasing the risk of mortality. Gastro-intestinal manifestations (intestinal disorders, polyps), respiratory (dyspnea, sleep apnea syndrome), neurological (headaches, aneurysms), musculoskeletal (arthralgia, carpal tunnel syndrome) as well as metabolic especially diabetes and dyslipidaemia, make that the patient suffering from acromegaly spend months and years consulting different specialists (cardiologist, neurologist, pulmonologist, rheumatologist, etc.) In order to relieve his symptoms, which exacerbates the delay in diagnosis [3], [4], [5] Facial and extremity bone deformities are specific and typical of acromegaly, enlargement of the extremities is the result of soft tissue swelling associated with bone deformities, this causes the hands to be wide and sulky with a positive ring sign, and the feet to be widened with a regular change in size. The deformation of the face is very characteristic, it includes a protrusion of the eyebrows, a prominence of the frontal bumps, a widening of the root of the nose, thickened lips and ears, wrinkles and the nasogenic furrow very marked. Mandibular development causes prognathism with dental malocclusion and enlarged interdental space [5-7]The use of these typical changes in the face and extremities by artificial intelligence will lead to a reduction in diagnostic time.

2. Material and methods

Researchers leveraged the benefits that AI offers to early diagnosis of many diseases from images such as the diagnosis of ocular diseases from fundus images or detection of bones fractures. Other researchers focused on patients photography for the detection of certain illness such as Down syndrome[8], Angelman syndrome[9], Turner syndrome[10,11]. Many publications present AI solutions and architectures that assist medical practitioner in diagnosis but not many are conducted for early diagnosis of rare disease and this is partially due to lack of data. We believe that this paper can serve as a reference for those who would like to explore the use of AI for the early diagnostic of acromegaly.

2.1. Artificial intelligence, machine learning and deep learning

First, let's define artificial intelligence, machine learning and deep learning and what they share. Artificial Intelligence first appears in the 1950's when scientists wondered if computers can think independently. It is a general field that englobe machine learning and deep learning. Starting from the chess programs made by a large set of rules written by human experts, scientists thought they could develop an intelligence by coding as much as possible rules for transforming inputs to specific outputs. IA proved to be suitable to solve logical problems, but it turned out to be limited to solve more complex and fuzzy systems such as image classification. So, a new approach has been developed: machine learning.

In the 1950, Alan Turing introduced the Turing test as well as other main concepts that shaped the AI of today. In his work, he came to the conclusion that machines could be capable of learning and originality. Thus, machine learning arose from the assumption that computers would be able to learn and go beyond what we know about how to perform a specific task or learn from available data. So, the difference between IA and ML is that for IA programmers code the rules and the operations that manipulate inputs in order to generate outputs. In ML, the machine needs both inputs and the expected outputs to deduce the rules. Thus, Machine Learning looks for statistical structure and meanings in both inputs and outputs fed to the system. This rule can then be applied to new datasets to generate impressive results. For ML, machines are not programmed but trained. Although machine learning is tightly related to statistics, but it has the advantage of dealing with more voluminous and complex data that can't be handled using classical statistics such as Bayesian analysis, for example ML is applied for big image datasets with millions of pixels that is impossible to handle using traditional statistic techniques. In other words, we can define machine Learning as a procedure of predictions or decisions guided by the data. Many techniques are englobed in ML and have been the subject of many articles such as the work of [12] where the authors compared the performance of Naive Bayes, 1-Nearest Neighbor, Trees Random Forest, Support Vector Machine, AdaBoost, RBF Network and multi-layer perceptron techniques. ML techniques widely used are Naive Bayes Decision Tree, nearest neighbor, set classifiers and Support Vector Machines [13,14].

DL is a subclass of ML. It's very popular technique to extract information from images and have proved its efficiency especially in medical imaging where it achieved considerable performance compared to experts. DL is known for image segmentation and classification use cases. Figure 1 illustrate the fundamental component of neural network: the individual neuron where X represents the features of the model and Y the output and w the weight that connect the features.

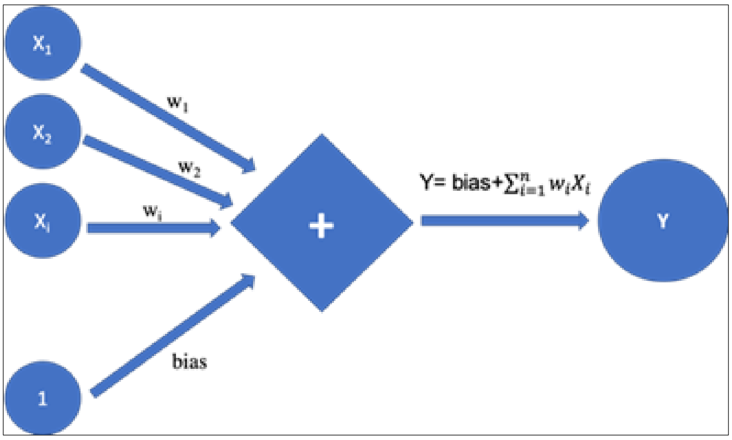

Figure 1 Single Neurone

Neurons are organized into layers in Figure 2, each layer perform a specific transformation. Through those layers' inputs are processed in different ways to approach the desired solution.

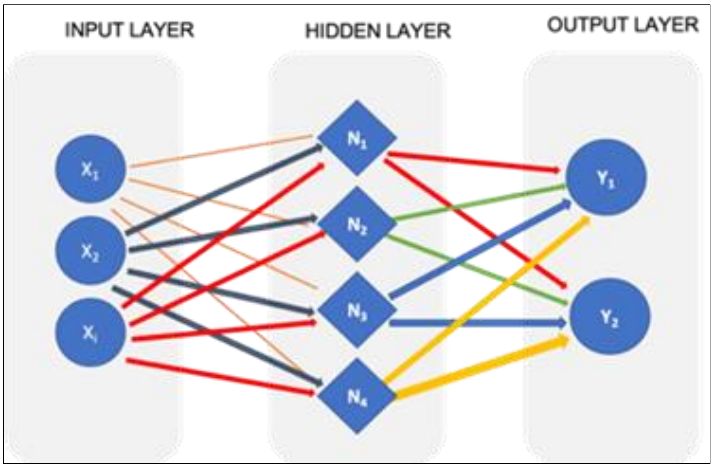

Figure 2 Deep Neural Network

The Convolutional Neural Network (CNN) are the most used techniques for imaging algorithms such as classification and segmentation. It aims to extract topological properties of an image and are widely used for problems such as identification and classification of tumors in radiology or detection of abnormalities in fundus images. Figure 3 illustrate a configuration of a CNN for a binary classification of a photographs into acromegaly or not acromegaly.

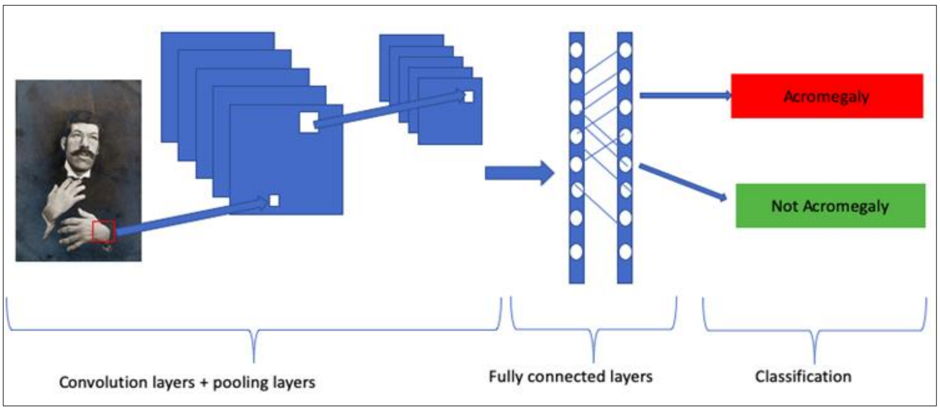

Figure 3 General configuration of a Convolutional Neural Network configuration for the detection of acromegaly photo used as a sample [15]

2.2. Study design

The scope of our work has been determined by the following questions: What AI solutions did researchers proposed for the diagnostic of acromegaly from photography? What are the issues and challenges encountered? To what extend those solutions are reliable?

The first phase of our strategy consisted of looking for existing surveys and publications that propose AI solutions for early diagnosis of acromegaly. The second phase was about finding relevant scientific papers on the subject, we used terminology like acromegaly, artificial intelligence, deep learning, machine learning and photography. We relied principally on Pubmed, Google Scholar, ACM Digital Library, IEEE Xplore, Springer Link and ScienceDirect. After removing duplicates and irrelevant articles from the screened papers, we were able to examine in detail and select the most suitable ones. These articles were satisfying the following eligibility requirements: Full text availability, writing in English, the articles cover details about how they used an AI technique on photography of acromegaly patient for early diagnosis.

2.3. Early diagnosis from patient's photography

Researchers developed architectures for early diagnosis of acromegaly based on photography of patients. The first concern was the detection of the disease using facial photographs of patients which can be considered as a binary classification problem. Table 1 represents the studies in the literature about the use of photographs for the detection of acromegaly using AI.

Table 1 Aim of different studies related to acromegaly detection using photographs

Reference	Aim of the study
[2]	Detection
[16]	Detection and severity classification1-2-3
[17]	Detection and measure of facial parameters
[18]	Self-screening from hand photographs

Authors in [2] used 1123 bidimensional photography to train an ensemble learning model that will classify the patient into normal or acromegaly person. The model was trained on 596 normal photographs and 527 acromegaly patients and tested on a dataset of 128 normal and 114 acromegaly. Their method performed a 96% specificity and sensitivity and NPV 95% and PPV 96%, F1-score were 0.95 for normal and 0.96 acromegaly. In 2020 the same researchers applied Inception and Resnet V1 as a backbone for a CNN model on 1911 bidimensional photography for detection and severity classification (starter – mid - severe) [16]. The model was tested on 237 photos with scores between 1 and 3 and performed a good accuracy of 90.7% a precision of 94.1% 93.4% and 87.5% respectively for scores 1,2 and 3. The recall was 74.4%, 91.4% and 97% respectively for the same scores. In the same year, [17] investigated the detection of acromegaly and the measure of facial parameters of patients using 3D imaging techniques. The model was tested on 124 participants, 62 acromegaly patients and they matched 62 normal people with same age and sex. In another perspective, [18] used hand photographs of 192 normal people and 635 acromegaly patients to train a Dynamic CNN based on RESNET34. The testing dataset contained 50 normal hands and 115 acromegaly patients' hands. The model performed the same as the model of [2] with a PPV of 0.966 and NPV of 0.958 a better sensitivity of 0.983 and less specificity 0.920, the F1-score were better with 0.974. Those results arise a new possibility for diagnosis of acromegaly without using facial photos and instead using hands to protect the privacy of patients especially that the results of both models are more than acceptable. Table 2 summaries the studies around the detection of acromegaly from photographs and the results obtained.

Table 2 Different AI techniques used in the literature for the detection of acromegaly from photographs

References	AI techniques	Indicators
[2]	Machine Learning and Ensemble Learning	Accuracy = 96%
		F1-score = 96%
[16]	Inception-Resnet V1	Accuracy=90.7%
		F1-score:
		-Score 1= 83.1% -Score 2= 92.4% -Score 3= 92.0%
[18]	Dynamic CNN based on RESNET 34 performed the best	Accuracy = 96%
		F1-score = 97.4%

2.4. Challenges and open issues

Because the acromegaly is a rare disease, we can observe from Table 3 that only four papers were published on the use of AI on photographs for early detection and even the training datasets in all the studies were not large enough. To overcome this limitation authors in [16] used two techniques. First one consists on accumulating more photography and the second one involves adding 3D information in pre-processing step. Another limitation of the study [16] is using only photos of Asian patients and is not yet tested on other population which erase the question of its applicability for other ethnic or regional groups.

Table 3 Size of the dataset used for every study found in the literature for the detection of acromegaly from photographs

Ref	Type of Data	Training Dataset		Test Dataset	
		Normal	Acromegaly	Normal	Acromegaly
[2]	Faces 2D	596	527	128	114
[16]	Faces 2D	Total=1911		mild= 34	
				intermediate = 91	
				severe= 112	
				Total = 237	
[17]	Faces 3D	NA	NA	62	62
[18]	Hands 2D	192	635	50	115

Another constraint face in the discussed studies is the inexistence of enough control photography's of the same patient. The researchers in[2-17] have choose normal images with the same characteristics of gender, ethnic, age, weight,.. that match the acromegaly patients. Using self-control photography will contribute for the grading of the severity of acromegaly and might help for the detection in an early stage. But collecting self-control photos in more challenging since the patients and their families are not aware of the disease in its beginning especially if the study depends on collecting 3D images [17]. The study in [18] proposed the use of hands photographs to encounter the limits of privacy of patients.

3. Conclusion

The strength of using AI in the detection of acromegaly lies on performing same as medical practitioner and sometimes even better using only labelled images without adding information or any medical knowledge. AI provides promising tools to help detecting acromegaly especially in the first stages where the identification is crucial and even grading the severity of the disease, but the rarity of dataset handicaps the research. This is just the beginning of a project to create a dataset for acromegaly Moroccan patients. This will help to investigate the use of AI in the early diagnosis of this rare disease for Moroccan. In this perspective, we collaborate, endocrinology doctors and computer scientists, to provide a computer aided diagnostic tool that will contribute to early detection of acromegaly from photos of face, hands and feet of potential patients.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

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