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A Deep Learning Model to Assess and Enhance Eye Fundus Image Quality

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Never consider study as an obligation, but as an opportunity to penetrate the beautiful and wonderful world of knowledge.

Albert Einstein

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Resumen

La ingeniería busca diseñar, construir e implementar soluciones que permitan aumentar y/o mejorar la calidad de vida de los seres humanos. Igualmente, desde la medicina son generadas soluciones con los mismos fines, posibilitando que estas dos áreas del conocimiento convergan por un bien común. Con el trabajo de tesis "A Deep Learning Model to Assess and Enhance Eye Fundus Image Quality", se propuso e implementó un modelo que permite evaluar y mejorar la calidad de las imágenes de fondo de ojo, lo cual contribuye a mejorar la eficiencia y eficacia de un posterior diagnóstico basado en estas imágenes. Para la evaluación de estás imágenes, se desarrolló un modelo basado en una arquitectura de red neuronal convolucional ligera, la cual fue llamada Mobile Fundus Quality Network (MFQ-Net). Este modelo posee aproximadamente 90 % menos parámetros que aquellos de última generación. Para su evaluación se utilizó el conjunto de datos públicos de Kaggle con dos sets de anotaciones de calidad, binario (buena y mala) y tres clases (buena, usable y mala) obteniendo en la tareas de clasificación de la calidad de la imagen de fondo de ojo una exactitud de 0.911 y 0.856 en la modalidad binaria y tres clases respectivamente. Por otra parte, se desarrolló un método el cual realiza una mejora de la calidad de imágenes de fondo de ojo llamado Pix2Pix Fundus Oculi Quality Enhacement (P2P-FOQE). Este método está basado en tres etapas las cuales son; premejora: para ajuste de color, mejora: con una red Pix2Pix (la cual es una Conditional Generative Adversarial Network) como núcleo del método y postmejora: la cual es un ajuste CLAHE para contraste y realce de detalles. Este método fue evaluado en un subconjunto de anotaciones de calidad para la base de datos pública de Kaggle el cual fue re clasificado por un especialista de la Fundación Oftalmológica Nacional para tres categorías (buena, usable y mala). Con este método fue mejorada la calidad de estas imágenes para la clase buena en un 72,33 %. Así mismo, la calidad de imagen mejoró de la clase mala a la clase utilizable, y de la clase mala a clase buena en 56.21 % y 29.49 % respectivamente.

Palabras clave: Calidad de Imagen, Evaluación de Calidad, Fondo de Ojo, Calidad de Imagen sin Referencia, IA Móvil, Aprendizaje Profundo, Clasificación, Degradación Sintética de la Calidad, Mejora de la Imagen, Red de Adversarios Generativos Condicional.

Abstract

Engineering aims to design, build, and implement solutions that will increase and/or improve the life quality of human beings. Likewise, from medicine, solutions are generated for the same purposes, enabling these two knowledge areas to converge for a common goal. With the thesis work "A Deep Learning Model to Assess and Enhance Eye Fundus Image Quality", a model was proposed and implement a model that allows us to evaluate and enhance the quality of fundus images, which contributes to improving the efficiency and effectiveness of a subsequent diagnosis based on these images. On the one hand, for the evaluation of these images, a model based on a lightweight convolutional neural network architecture was developed, termed as Mobile Fundus Quality Network (MFQ-Net). This model has approximately 90 % fewer parameters than those of the latest generation. For its evaluation, the Kaggle public data set was used with two sets of quality annotations, binary (good and bad) and three classes (good, usable and bad) obtaining an accuracy of 0.911 and 0.856 in the binary mode and three classes respectively in the classification of the fundus image quality. On the other hand, a method was developed for eye fundus quality enhancement termed as Pix2Pix Fundus Oculi Quality Enhancement (P2P-FOQE). This method is based on three stages which are; pre-enhancement: for color adjustment, enhancement: with a Pix2Pix network (which is a Conditional Generative Adversarial Network) as the core of the method and post-enhancement: which is a CLAHE adjustment for contrast and detail enhancement. This method was evaluated on a subset of quality annotations for the Kaggle public database which was re-classified for three categories (good, usable, and poor) by a specialist from the Fundación Oftalmolóica Nacional. With this method, the quality of these images for the good class was improved by 72.33 %. Likewise, the image quality improved from the bad class to the usable class, and from the bad class to the good class by 56.21 % and 29.49 % respectively.

Keywords: Image Quality, Quality Assessment, Eye Fundus, Non-reference Image Quality, Mobile AI, Deep Learning, Classification, Synthetic Quality Degradation, Image Enhancement, Conditional Generative Adversarial Network.

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1 Introduction

The acquisition and analysis of images in fields such as astronomy, engineering and photography, among others make it possible to record, represent and study behaviors of natural and artificial phenomena. Likewise, in the medical field they constitute a valuable tool for specialists to improve their work, largely in terms of time and associated costs, generating a quick, accurate and economic diagnosis. Some of the most widely used medical imaging techniques and technologies today are computed tomography (CT), magnetic resonance imaging (MRI), ultrasound and ophthalmoscopy. Within ophthalmological studies, which consist of the exploration of the fundus through the pupil; the transparent means of the eyeball; the retina and the optic disc [1], the use of fundus images is essential for the diagnosis and treatment of various eye diseases such as diabetic macular edema, age-related macular degeneration and diabetic retinopathy, as well as for the detection of elements such as exudates, micro aneurysms and hemorrhages, among others [2]. Being Diabetic Retinopathy (DR) [3] the most common cause of vision loss among people with diabetes and the leading cause of vision impairment and blindness among working-age adults [3] converts this disease in one area of great interest for studies today.

There are various devices, fixed, portable, commercial and non-commercial for obtaining fundus images. Within these devices, the most used are: Retinograph [4], Slit Lamp [5], D-Eye Portable Retinal System [6], Smartphone y lente 20 D [6], Portable Eye Examination Kit [6], SmartScope/Pictor Plus [6], Horus Scope [6], Ocular CellScope [6] and iExaminer [6].

It is evident that, although fixed models are superior in terms of quality of the images obtained, they have disadvantages over mobile or portable models such as their high acquisition costs. Moreover, mobile devices, although they are cheaper than fixed devices, present a greater variability at the moment of capturing a fundus image, affecting the quality of these images, compromising their usefulness for an adequate study or diagnosis.

Currently, regarding the quality of fundus images according to the “Essential Elements in Developing a Diabetic Retinopathy Screening Program” [7], they have developed a series of guidelines on which ophthalmology specialists can rely to determine the quality of a fundus image.

In this thesis, an original application of DL techniques was developed, producing a general model both for eye fundus image assessment and enhancement as shown in Figure **1-1**. This model receives as an input an eye fundus image to verify its quality. Once the quality is verified, if the model classifies it as poor (bad) or partially good (usable), the quality enhancement model performs processing in order to upgrade its quality. Otherwise, the image is not enhanced and is presented in its original format.

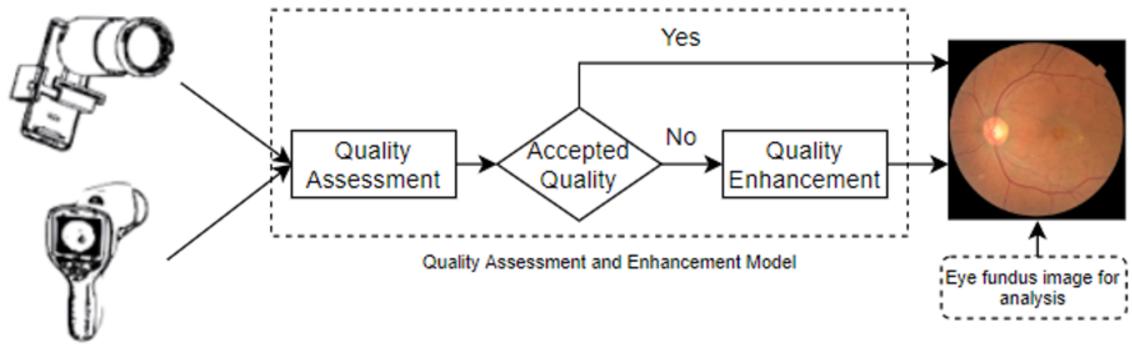

Figure 1-1: Graphical summary for the eye fundus assessment and enhancement end-to-end model

1.1 Problem Identification

According to the World Health Organization in 2015 around 415 million adults were living with Diabetes Mellitus (DM), 145 million suffer from some type of Diabetic Retinopathy (DR). The disease prevalence in 2040 is estimated to be 642 million people with DM and 224 million with complications related to DR.
Ophthalmology specialists have to perform the diagnosis process of ocular diseases using eye fundus images. Although ophthalmologist's centers define acquisition protocols, several problems are presented yet. In specific, the proper quality of fundus images that ensures a reliability diagnostic, mainly in scenarios where the acquisition is performed by mobile or portable camera devices is still a challenge.
In Colombia, the ocular screening of the population of hard-to-reach and rural areas is carried out ophthalmic brigades using these portable devices. However, an incorrect fundus image quality could lead to inappropriate health interventions in the people and poor public politics.
On the other hand, the design of methods to enhance public and private datasets of ophthalmologist's centers with regular or bad quality is poorly tackled by researchers. Besides, to our knowledge, no method integrates both evaluation and enhancement of the fundus image quality through deep learning techniques.
Therefore, the following research questions arise in the framework of this proposal:

- How can the quality of the fundus image be automatically evaluated and improved by means of models based on deep learning?

- Which method based on deep learning allows for an adequate evaluation of fundus images?
- How can the quality of the fundus image be improved automatically using deep learning models?
- How can quality assessment and quality improvement models be combined into a single end-to-end deep learning model?

1.2 Main and Specific Goals

1.2.1 Main Goals

To implement and to evaluate an end-to-end deep learning method to estimate and to improve fundus image quality.

1.2.2 Specific Goals

- To propose a pre-processing strategy for fundus images.
- To propose/adapt a deep learning method to evaluate the quality of the fundus images.
- To propose/adapt a deep learning method to improve retinal images with poor quality.
- To propose an end-to-end model that integrates the evaluation and enhancement of eye fundus images quality.
- Systematically validate and evaluate the proposed methods with real data.

1.3 Contributions

With this work culmination, it was contributed to diverse materials in terms of conference papers, software, and datasets. The following is the outline of the main contributions of this work.

1.3.1 Conference papers

The following is a list of papers that have been published and submitted during the development of this research:

- A lightweight deep learning model for mobile eye fundus image quality assessment [8].

- A conditional generative adversarial network-based method for eye fundus image quality enhancement [9].
- SOPHIA: System for OPHthalmic image acquisition, transmission, Intelligent Analysis and decision support of ophthalmic images [10].

1.3.2 Software

It was contributed with two developed Python-based systems which can work both independently and together as follows:

- A system for eye fundus image quality assessment. This system besides being developed for two modalities (binary and three-class) it also has its respective mobile version.
- A system for eye fundus image quality enhancement.

1.3.3 Datasets

- A processed and re-classified Kaggle [1] sub-sampled dataset. The dataset comprises 5,628 eye fundus images with different resolutions and quality levels spread in three-class category annotations provided by the specialist in Ophthalmology, Hernán Andrés Ríos.
  The annotations file is publicly available at https://github.com/adpzz/Eye-fundus-image-quality-assessment-and-enhancement.

1.4 Thesis Structure

This thesis is structured as follows: The first chapter presents the thesis introduction, the problem identification, the main and specific goals and the study contributions as well. The second chapter presents the background and related works. The third chapter presents the first problem tackled: the automatic assessment of the eye fundus images quality. The fourth chapter presents the second problem: the enhancement of the eye fundus images quality. Finally, the fifth chapter presents the thesis conclusions and ideas for future work.

[1] https://www.kaggle.com/c/diabetic-retinopathy-detection

2 Related Works

2.1 Quality Assessment

Image quality assessment is a fairly important research topic which has been studied for a long time from diverse viewpoints. Some of these viewpoints are embodied in works such as the one done by Yeadon et al. [11] in 1972 describing the modulation transfer function (MTF) measurements on channel image intensifiers (one of the most important ways for image quality during that time). Hopkins [12] in his 1974 work talked about some of the basic aspects of geometrical and diffraction optics that were relevant during the time for image evaluation problems. Finley et al. [13] in 1977 presented a system which automatically matches scene edge to a physical matrix of test edges for the purpose of estimating image quality. Gliatti et al. [14] presented a review for the usual USAs' Air Force-methods used to measure image resolution which includes Tribar-Resolving Power, Maximum Magnification Factor (MMF), Visual Edge Matching (VEM), Edge Trace Methods and Modulation Transfer Function (MTF) Analysis. In this line, Tiziani [15] in 1978 proposed an image quality criteria for aerial survey lenses based on MTF measurement. In 1980, Kuperman [16] realized a review comparing twelve quality estimators among which are Inverse Square Law (ISL), MTF, Sun's Equation, Resolving Power (RP), Visual Image Evaluation (VIE), Acutance, Edge Width, Reciprocal Edge Spread (RES), and two MTF/Aerial Image Modulations (MTF/AIM). In this regard, Overington [17] in 1981 analyzed the image quality and observer performance with relative visual efficiency which is based on modulation transfer function (MTF).

Later, in 1985 Nill [18] proposed a visual model weighted cosine transformation for image compression and quality assessment based on an image cosine transformation with a Human Visual - system model which used a Mean square error (MSE) measurement between the original unprocessed image and the processed image. In addition, Buffett [19] in 1986 studied the visual perception of simultaneous luminance contrast for subjective quality measures. In 1990, Sharp [20] published a study named Quantifying Image Quality. In this study, the main goal was to look for mechanisms to solve the problem of measuring only the performance of the displayed data. It is important to keep in mind that during that time, there was no accepted way of quantitatively assessing image quality. In the same year, Barrett et al. [21] presented a study related with the effects of quantum noise and object variability in terms of SNR's and ways for choosing and calculating appropriate SNR's, both, for system evaluation and optimization. As a continuation of this previous study, three years later, in 1993, Barrett et al. [22] divulged a model based on linear discriminant analysis termed the

Hotelling Observer.

Related to the quality requirements, there are different works and methods regarding its minimums. In this respect, one of the most notable works was carried out in 1994 by Eskicioglu et al. [23] which evaluates diverse quality measures such as: Average Difference, Structural Content, N. Cross-correlation, Correlation Quality, N. Mean Square Error, Hosaka plot, and Histogram, among others. The authors found out an interesting relation by combining numerical and graphical measures in grayscale image compression. Five years later, Månsson [24] published an interesting and complete review of image quality evaluation methods which are classified in physical, psychophysical and observer/diagnostic performance categories. Keeping this research line, in 2002 Wang et al. [25] proposed an universal objective image quality index to calculate and apply to various image processing applications. In 2004, Wang et al. [26] introduced an alternative framework for evaluating image quality based on the degradation of structural information. Additionally, in 2006, Sheikh et al. [27] induced an information fidelity criterion that quantifies the Shannon information shared between the reference image and the images distorted in relation to the information contained in the reference image itself.
So far, it has seen that there is a tendency for image quality assessment which involves reference images for the analysis. Nevertheless, reference fundus images do not usually exist when a diagnosis is made, therefore, an image quality assessment/rating can be performed without reference (NR-IQA / IQG).

In 2011, there is a methodology transformation proposed by Marrugo et al, [28]. In a comparative study, they implemented the use of non-reference quality metrics for fundus imaging concentrating on autofocus and quality assessment as applications. This was key to the correct operation of a fundus imaging system. With this new methodology in mind, Mittal et al. [29] developed an algorithm for evaluating the quality of the natural scene NR that operates in the spatial domain. In 2013, Köhler et al. [30], also, presented a non-reference quality metric to quantify image noise and blur and its application to the evaluation of the quality of the fundus image. Besides that, in 2014, Sevik et al.[31] developed a two-step based retinal image quality assessment method using classical image processing and feature extraction techniques. In the same year, Pires et al. [32] presented a general framework with eye fundus quality assessment capabilities, based on a field definition and blur detection strategy. Likewise, Yan et al. [33] introduced a no-reference quality assessment method for retinal image based on supervised classification using a random forest classifier after a custom preprocessing strategy. Mahapatra et al. [34] published a classification of retinal image quality using neurobiological models of the human visual system, that combines unsupervised information from local salience maps and supervised information from trained convolutional neural networks (CNNs) to make a final decision on the image quality. Similarly, Tennakoon et al. [35] proposed a method that leverages learned supervised information using CNN, thus avoiding hand-engineered features. Abdel-Hamid et al. [36] introduced a quality index without reference for retinal color images from the decomposition of wavelet images as well.

Meanwhile, Sun et al. [37] presented a jointly fine-tuned CNN with a total loss equal to the summation of the losses of all channels. Costa et al. [38] suggested an explainable evaluation of the image quality of the retina. In the same year, Yu et al. [39] proposed an algorithm that combines unsupervised features from saliency maps and supervised features coming from convolutional neural networks (CNN).
Furthermore, in 2018, Zhou et al. [40] presented a central loss weighted softmax activation function to resolve the unbalanced distribution of data in medical imaging. Zago et al. [41] implemented an Inception-V3 [42] along with a fine-tuning strategy. Saha et al. [43] used an Alexnet [44] CNN architecture by using a hinge loss as the loss function. Lately, Coyner et al. [45] presented the implementation of a deep CNN for automated evaluation of the quality of the fundus image in retinopathy of prematurity and Fu et al. [46] developed a deep network based on the integration of different representations of color spaces.
It is really interesting the potential and the capacity of adaptability that these new models have achieved when allowing to abstract the characteristics of non-referenced fundus images for the execution of tasks like the quality assessment of these images. With regard to its results, those have become more generalizable, thus reliability and validity rates have increased.

2.2 Quality Enhancement

Image quality enhancement can be defined as a pre-processing technique that aims to suppress factors that affect image quality, while preserving the characteristics and other relevant image information. To pursue this, Drago et al. [47] came up with a fast, high-quality tone mapping technique based on logarithmic compression of luminance values, which imitates the human response to light. In 2004, Mecocci et al. [48] combined one of the most effective Retina algorithm (McCann99 [49]) with the Gray World transformation applied at a multiple resolutions with an additional post-processing which improved color balance and range results.
Stoica et al. [50] presented a two parts methodology: in the first part, they performed a laboratory evaluation of the HVS model by the contrast sensitivity function (CSF), meanwhile, in the second part, they implemented a technique of visual weightings for the JPEG2000 scheme using the evaluated HVS model in the Fourier domain of the color image. Two years later, Aibinu et al. [51] developed a new method of compensating uneven illumination in fundus images termed global-local adaptive histogram equalization, which used partially-overlapped windows (GLAPOW). In 2009, Cvetkovic et al. [52] presented a multi-scale high-frequency enhancement scheme, using as gain a non-linear function of the detail energy.
Fundus images are generally degraded by noise suffering from low contrast problems. These problems make it difficult for an ophthalmologist to detect and interpret diseases in the fundus images (Sahu et al., [53]). In cases where these factors affect the recording of the fundus image and poor quality images are obtained, it is necessary to provide alternative solutions to

guarantee the best conditions for an accurate diagnosis. Therefore, some related works have been developed such as the one proposed by Qidwai et al. [54] in 2010, in which he presented a blind deconvolution method using the maximum probability estimation approach. Similarly, in 2011 Kolar et al. [54] discussed how to correct non-uniform illumination of fundus images based on a surface approximation with the B-Spline technique. Likewise, in 2011, Marrugo et al. [55] presents how to restore the retinal image to color using a multi-channel blind deconvolution approach.

Also, Yi et al. [56] in 2011, published a method of not uniformly luminosity and contrast normalization present in the background retina images for quality enhancement. In 2013, Datta et al. [57], shares what he defines as an effective approach for quality enhancement in fundus images with non-dilated retina for detection tasks of microaneurysms using the CLAHE technique. Lu et al. [58] presented a method to improve the quality of fundus image using mathematical morphology, together, with a mixture of combined filters and Gabor operations. In 2018, Vu et al. [59] publishes a study on fast and efficient enhancement of image quality through desubpixel spiral neural networks as well. Wahid et al. [60], in 2018, developed a two-step approach by combining a histogram-based enhancement algorithm (FHBE) and contrast-limited adaptive histogram equalization (CLAHE) to improve the visual quality of fundus images. Also, in 2018 Joshi et al. [61] performed a detailed review of preprocessing techniques that can be used to reduce blur in fundus images as they are captured. Mitra et al. [62] in 2018, in turn, carried out work to improve and restore fundus images with non-uniform illumination of the retina obtained through a thin layer of cataracts.

Finally, among the recent works (2019) on fundus images quality enhancement, there are those developed by Qureshi et al. [63] and Sahu et al. [53] where the first one focuses on the development of a hybrid multi-stage image processing framework for quality enhancement. Sahu focused on addressing noise and contrast using the CLAHE filter to improve fundus image quality. In the same manner, Yoo et al. [64] presented a cycleGANs-based method for fundus quality enhancement which consists of the use of non-paired eye fundus images with good quality to extract its latent features to apply those features over bad quality eye fundus images.

2.3 Deep Learning

The study of artificial neural networks begins with the work of Warren McCulloch and Walter Pitts in 1943 [65], where they proposed a theory on the functioning of neurons, thus succeeding in modeling a simple neural network by implementing electrical circuits. In recent years, Deep Learning (DL) [66], which corresponds to neural network models with a large number of layers for extraction and abstraction of higher-level features on raw data, have had great success in a diverse range of problems including: text analysis, voice analysis,

sequence analysis, image analysis.
One of the most important characteristics of DL is the possibility of being able to learn the representation of raw data directly. Models with this capability are generally denoted as end-to-end models as they directly receive the data in its original representation. They are also capable of simultaneously learning the representation while solving the specific task (eg. image classification).
One crucial component in DL-based modeling is the use of Convolutional Neural Networks (CNN), which basically consist of networks that perform mathematical convolution operations across the different layers of the network. These are two-dimensional representations of batch matrices that are windowed on the input data received by each layer of the network, resulting in an abstracted representation of the original information [67].
Deep Learning, in ophthalmology, thanks to its surprising compatibility with regard to its combination with medical domain images, has been implemented in fundus photographs, optical coherence tomography, and visual fields achieving a robust classification in the detection of diabetic retinopathy and retinopathy of prematurity, glaucoma disc, macular edema, and age-related macular degeneration [68]. A great advantage of DL in ocular imaging lies in that it can be used in conjunction with telemedicine as a possible solution to examine, diagnose and monitor the main ocular diseases of patients in primary care and community settings [69].

Below, in Tables **2-1** and **2-2** are summarized the last 20 years of state-of-the-art works related with eye fundus image quality assessment and enhancement respectively.

Table 2-1: State-of-the-art summary for eye fundus image quality assessment

Year	Reference	Modality	Method	Dataset
2000	Lalonde et al. [70]	Eye-fundus image	Decision score based on edge magnitude and intensity distribution	Private
2001	Gagnon et al. [71]	Eye-fundus image with masking, vessel extraction and macula detection	Histograms comparison	Private
	LalondeÝ et al. [72]	Eye-fundus image	Histogram matching for discriminator classification	Private
2003	Usher et al. [73]	Eye-fundus image with vessel segmentation	Classification based threshold vessel relevance	Private
2005	Toniappa et al. [74]	Retinal Image	Histogram asymmetry measurement	Private
2006	Fleming et al. [75]	Retinal Image	Image clarity and field definition scoring	Private
2007	Wen et al. [76]	Retinal Image	Vessels driven quality score	CDHB
2009	Bartling et al. [77]	Eye-fundus image	Quality score based on sharpness and illumination	Private
	Davis et al. [78]	Retinal Image	Feature based scoring	Private Public: MESSIDOR
2010	Giancardo et al. [79]	Retinal Image with vessel segmentation	SVM based on elliptical local vessel density features	Private
	Paulus et al. [80]	Retinal Image	SVM based on clustering, sharpness metric and Haralick texture features	Private

Table 2-1 continued from previous page

2011	Moscaritolo et al. [81]	Optic Disc Images	Image sharpness score	Private
	Marrugo et al. [28]	Eye-fundus image	No-reference metrics	Private
	Hunter et al. [82]	Retinal Image	Contrast and vessel quantification	Private
2012	Yu et al. [83]	Retinal Image with vessel segmentation	Partial Least Squares classifier based on vessels, histogram, textural and local sharpness features	Private
	Dias et al. [84]	Retinal Image	Multiple Feed-Forward Backpropagation Neural Network based on color, focus, contrast and illumination features	Public: DRIVE, MESSIDOR, ROC and STARE
2013	Huang et al. [85]	OCT images	Maximum tissue contrast index, histogram density modeling and decomposition score	Private
	Pires et al. [86]	Retinal Image	SVM based on similarity features	Private
	Köhler et al. [30]	Retinal Image with vessel segmentation	Quality metric Q_v based on noise and blur	DRIVE
	Katuwal et al. [87]	Retinal Image based on vessel segmentation	SVM based on vessel features	Private
2014	Dias et al. [88]	Retinal Image	Generic image indicators	Private Public: DRIVE, MESSIDOR, ROC and STARE
	Fasih et al. [89]	Retinal Image	SVM based on generic features	Private
	Nugroho et al. [90]	Retinal Image	Contrast measurement	Public: HEI-MED
	Sevik et al. [31]	Retinal Image with vessel segmentation	SVM based on vessels, fovea and optic disc features	Public: DRIMDB
2015	Veiga et al. [91]	Eye-fundus image with masks representations	Fuzzy classifier using Wavelet, Moment and Statistics-based focus measures features	Private Public: MESSIDOR
	Fasih M. [92]	Retinal Image	SVM	Private
	Wang et al. [93]	Eye-fundus image	SVM and Decision Tree based on three features of the visual human system	Private Public: DRIMDB and DRIVE
	Imani et al. [94]	Retinal Image	Shearlet Transform	Public: MESSIDOR and Khatam-Al-Anbia
	Giraddi et al. [95]	Eye-fundus image	SVM based on energy, mean and variance features	Public: DIARETDB0
2016	Hamid et al. [96]	Retinal image	Wavelet score	Public: DRIMDF and HRF
	Welikala et al. [97]	Retinal Image with vessel segmentation	SVM based on vessel segmentation	Public: UK Biobank dataset
	Yao et al. [98]	Eye-fundus image	SVM based on generic features	Private
	Abdel-Hamid et al. [99]	Retinal image	SVM based on sharpness, illumination, homogeneity, field definition, and content features	Public: DRIMDB, DR1, DR2, HRF and MESSIDOR
2017	Mahapatra et al. [100]	Retinal image	DL CNN: Custom network	Public: DRISHTI
	Galdran et al. [101]	Eye-fundus image	Mean-Subtracted Contrast-Normalized scoring	Public: DRIMDB
	Costa et al. [38]	Eye-fundus image	DL CNN: Multiple Instance Learning	Public: ARSN and DRIMDB
	Saha et al. [102]	Eye-fundus image	DL CNN: Alexnet	Public: EyePACS
	Yu et al. [39]	Eye-fundus image	Saliency Map and DCNN and SVM	Kaggle
	Costa et al. [103]	Eye-fundus image	$\mathrm{Q}_v andImageStructureClustering$ scores	Public: DRIVE and MESSIDOR

Table 2-1 continued from previous page

2018	Shao et al. [104]	Eye-fundus image and vessel segmentation	SVM, Decision Tree and Dictionary Learning based on Illumination, Naturalness and Structure levels	Public: MESSIDOR, STARE, MUMS-DB, CHASE_DB, DRIVE, DRIMDB and EyePACS
	Zago et al. [41]	Retinal image	DL CNN: Inception-V3	Public: DRIMDB and ELSA-Brasil
	Saha et al. [43]	Eye-fundus image	DL CNN: Alexnet	Public: EyePACS
	Rodrigues et al. [105]	Retinal image	DL CNN: Custom network	Private Public: IDRiD, EyePACS, STARE, ROC and HRF
2019	Zhou et al. [40]	Eye-fundus image	DL CNN: Inception-ResNet-V2 with multitask approach	Public: Kaggle
	Raj et al. [106]	Eye-fundus image quality assessment survey, challenges and future scope	State-of-the-art review	-
	Fu et al. [46]	Retinal image	DL CNN: Multiple color-space fusion	Public: EyePACS
	Coyner et al. [45]	Retinal image	DL CNN: Inception-V3	Private
	Lauermann et al. [107]	OCT image	Multi-layer DCNN	Private
	Wang et al. [108]	Eye-fundus image	DL CNN: DenseNet	Public: DRIMDB and DR1
2020	Jimenez et al. [109]	Retinal image	MLP Network based on hand-extracted features	Private
	Pérez et al. [8]	Eye-fundus image	DL CNN: lightweight MFQ-Net	Public: Kaggle
	Alais et al. [110]	Retinal image	DL CNN: lightweight based on fovea location	Public: e-ophtha
	Bhatkalkar et al. [111]	Eye-fundus image	DL CNN: Custom network	Public: STARE, DRIMDB, ONHSD and KMC
	Liu et al. [112]	Eye-fundus image	Gcforest for small samples based on color and texture features	Public: DRIMDB and ACRIMA
	Oraá et al. [113]	Eye-fundus image	DL CNN: InceptionResNetV2-based	Private Public: DRIMDB
	Shen et al. [114]	Eye-fundus image	DL: Semi-tied adversarial discriminative domain adaptation model	Private Public: IDRiD

Table 2-2: State-of-the-art summary for eye fundus image quality enhancement

Year	Reference	Modality	Method	Dataset
2001	Asmuth et al. [115]	Slit lamp biomicroscopic fundus	Pairwise image alignment	Private
2002	Lin et al. [116]	Retinal vessels images	Background subtraction of retinal blood vessels	Private
	Wanas et al. [117]	Retinal vessels images	Set of cascaded linear directional filters	Private
2005	Sander et al. [118]	OCT images	Multiple scan averaging	Private
2006	Belkacem et al. [119]	Retinal image	Multi-scale spatial decomposition	Private
	Youssif et al. [120]	Eye-fundus image	Contrast and illumination equalization	Public: DRIVE and STARE
	Chang et al. [121]	OCT images	Intensity Demodulation of the Interlayer, compensation of phase-shifting error and camera calibration	Private

Table 2-2 continued from previous page

2007	Bueno et al. [122]	Eye-fundus image	Mueller matrix elements based	Private
2008	Joshi et al. [123]	Retinal image	Domain knowledge for non-uniform sampling to estimate the degradation and produce a correction factor	Public: DIARETDB1
	Intajag et al. [124]	Retinal image	Indices of fuzziness	Public: DRIVE
2009	Gu et al. [125]	Eye-fundus image	Rough set to enhance subgraphs from image wavelet equivalent	Private
2010	Qidwai et al. [54]	Retinal image	Blind deconvolution using maximum likelihood estimation	Public: STARE
2011	Giancardo et al. [126]	Retinal image	Multiple images for high quality image	Private
2012	Russell et al. [127]	Retinal image	Scattering based model	Private
2013	Datta et al. [57]	Retinal image	CLAHE per patches	Private
	Sree et al. [128]	Retinal image	Brightness control, Contrast stretching and Histogram equalization on FPGA	Private
2014	Setiawan et al. [129]	Retinal image	CLAHE over G channel	Private
	Ab Rahim et al. [130]	Eye-fundus image	Histogram Equalization, CLAHE and Mahalanobis Distance	Public: DRIVE
	Kulcsár et al. [131]	Eye-fundus image	Fast optical flow estimation compensation	Private
	Jintasuttisak et al. [132]	Retinal image	Nonlinear hue-saturation-intensity color modeI with Rayleigh CLAHE	Public: DIARETDB
2015	Ravichandran et al. [133]	Vessel image	Gabor filtering based and CLAHE	Public: DRIVE and STARE
	Datta et al. [134]	Retinal image	Fuzzy histogram over green channel and intensity and brightness equalization	Public: DRIVE, STARE, DIARETDB0 and DIARETDB1
2016	Bartczak et al. [135]	Eye-fundus image device assisted	Spectrally tunable light source based on a digital micro-mirror device	Private
	Yadav et al. [136]	Eye-fundus image comparative study	HE, ADHE, CLAHE and ESIHE	Private
	Lu et al. [58]	Vessel enhancement	Morphological filtering, CLAHE, Multi-scale morphological bottom-hat transformation and weighted sum	Private
2017	Soomro et al. [137]	Fundus Fluoresce in Angiogram images	Morphological operation with threshold based stationary wavelet transformation and CLAHE	Public: Fundus Fluorescein Angiogram Photographs of Diabetic Patients, HRF and Colour Fundus Images of Healthy Persons and Patients with Diabetic Retinopathy Database
	Krylov et al. [138]	3D fundus image	Grid warping based	Private
	He et al. [139]	Retinal image	Scale-invariant feature transformation based	Private
	Bandara et al. [140]	Retinal image	Speeded up adaptive contrast enhancement	Public: STARE and DRIVE

Table 2-2 continued from previous page

2018	Zhou et al. [141]	Retinal image	Luminosity and contrast enhancement by gain matrix and CLAHE over single channel	Private
	Anam et al. [142]	Eye-fundus image	Maximum entropy and Perona-Malik diffusion filter	Private
	Reddy et al. [143]	Retinal image	Piecewise gamma-corrected dominant orientation-based histogram equalization	Private
	Elloumi et al. [144]	Renita detction and image enhancement	Filter transformations and CLAHE equalization	Private: Smartphone-Captured Retinal Image Database
	Jin et al. [145]	Eye-fundus image	CLAHE over LAB color space representation	Private
	Mitra et al. [62]	Eye-fundus image	Blurriness subtraction, Hue Saturation Intensity and min-max color adjustment	Public: DRIVE and STARE
	Wahid et al. [60]	Eye-fundus image	FHBE-CLAHE and CLAHE-FHBE	Public: DIARETDB and DIARETDB1
	Krylov et al. [146]	Fundus Vessel Image	DL SRCNN	Public: DRIVE
2019	Dhal et al. [147]	Retinal image	Weighted and entropy-based thresholded histogram equalisation	Private
	Mazlan et al. [148]	Retinal image	Min filtering with morphological enhancement	Public: e-ophtha
	Sabri et al. [149]	Retinal image	A seven preprocessing steps method based on filters and transformations	Public: e-ophtha and MESSIDOR
	Sahu et al. [53]	Retinal image	Filters for noise removal and CLAHE transformation	Public: STARE
	You et al. [150]	Eye-fundus image	DL cycleGAN with attention block module	Private Public: EyePACS
	Wahid et al. [151]	Retina vessel Image	CLAHE - FHBE based	Public: DRIVE and STARE
	Subramani et al. [152]	Medical images with eye-fundus image	Fuzzy contextual dissimilarity adaptive histogram equalization	Private
	Zulfahmi et al. [153]	Retinal image	CLAHE with diverse filters	Public: STARE
2020	Xia et al. [154]	Medical images with eye-fundus image	Correction strategy in wavelet transform domain	Private
	Sharif et al. [155]	Retinal image	Histogram equalization, contrast stretching, image negative, brightness enhances, low light image and gray level slicing	Private
	dos Santos et al. [156]	Eye-fundus image	CLAHE and MLP	Public: DRIVE
	Palanisamy et al. [157]	Retinal image	Shearlet transform and adaptive gamma-correction with CLAHE	Private
	ElMahmoudy et al. [158]	Retinal image	Wavelet-based	Private
	Kandpal et al. [159]	Retinal image	Edge- based texture histogram equalization	Public: STARE, DIARET DB0, DIARET DB1 and CHASE
	Yoo et al. [64]	Retinal image	DL cycleGAN	Public: Custom

3 Eye Fundus Image Quality Assessment

This chapter explores the eye fundus quality assessment task, both for a binary and multi-class scenario. This classification aims to grade the image quality from Kaggle dataset. Previous works such as Saha et al. [102], who adapted the AlexNet [44] architecture (which is a 62M parameters and 8 layers CNN) performs an automated quality assessment of color. In like manner, Coyner et al. [45] presented a work with an Inception-V314 CNN implementation assessing the eye fundus image quality in retinopathy of prematurity. Likewise, Mahapatra et al. [34] described models that combine unsupervised information from local saliency maps and supervised information from trained CNNs for retinal image quality classification. Costa et al. [38] proposed for the image quality of the retina an explicable evaluation. Meanwhile, Zhou et al. [40] used a weighted softmax activation function with a central loss to resolve the unbalanced distribution of data in medical images. With this work, it was developed a deep learning-based method to analyze eye fundus image quality based on a light-weight CNN suitable to be run on mobile devices, termed Mobile Fundus Quality Network (MFQ-Net).
This work was published in the *International Symposium on Medical Information Processing and Analysis, 2019.*

3.1 Introduction

The acquisition and automatic analysis of images in fields such as astronomy, engineering, and photography, among others make it possible to record, represent and study the behavior of natural and artificial phenomena. In the medical field, images are a valuable tool for specialists to support their work in diagnosis tasks based on ophthalmological studies. These include the exploration through the pupil of the fundus of the eye; the transparent means of the eyeball; the retina and the optical disc [160]. The use of fundus images is essential for the follow-up and treatment of various ocular diseases such as diabetic macular edema, age-related macular degeneration, and diabetic retinopathy through the detection of elements such as exudates, microaneurisms and hemorrhages, among others [2].

The UK National Screening Committee [7] defines the guidelines which ophthalmologists can use to determine the fundus image quality. The main reason for this kind of guidelines is to report the minimum conditions to guarantee an appropriate exam so the specialists can perform a better diagnosis. The image quality is usually assessed by the specialist, however, having automatic methods for quality assessment may help to improve the overall quality of images taken by non-specialist (such as those acquired during medical brigades and screening studies) as well as to reduce the time invested on quality control.

3.2 Materials and methods

Figure **3-1** shows the overall architecture of MFQ-Net. The model is based on a CNN which is trained in a supervised fashion.

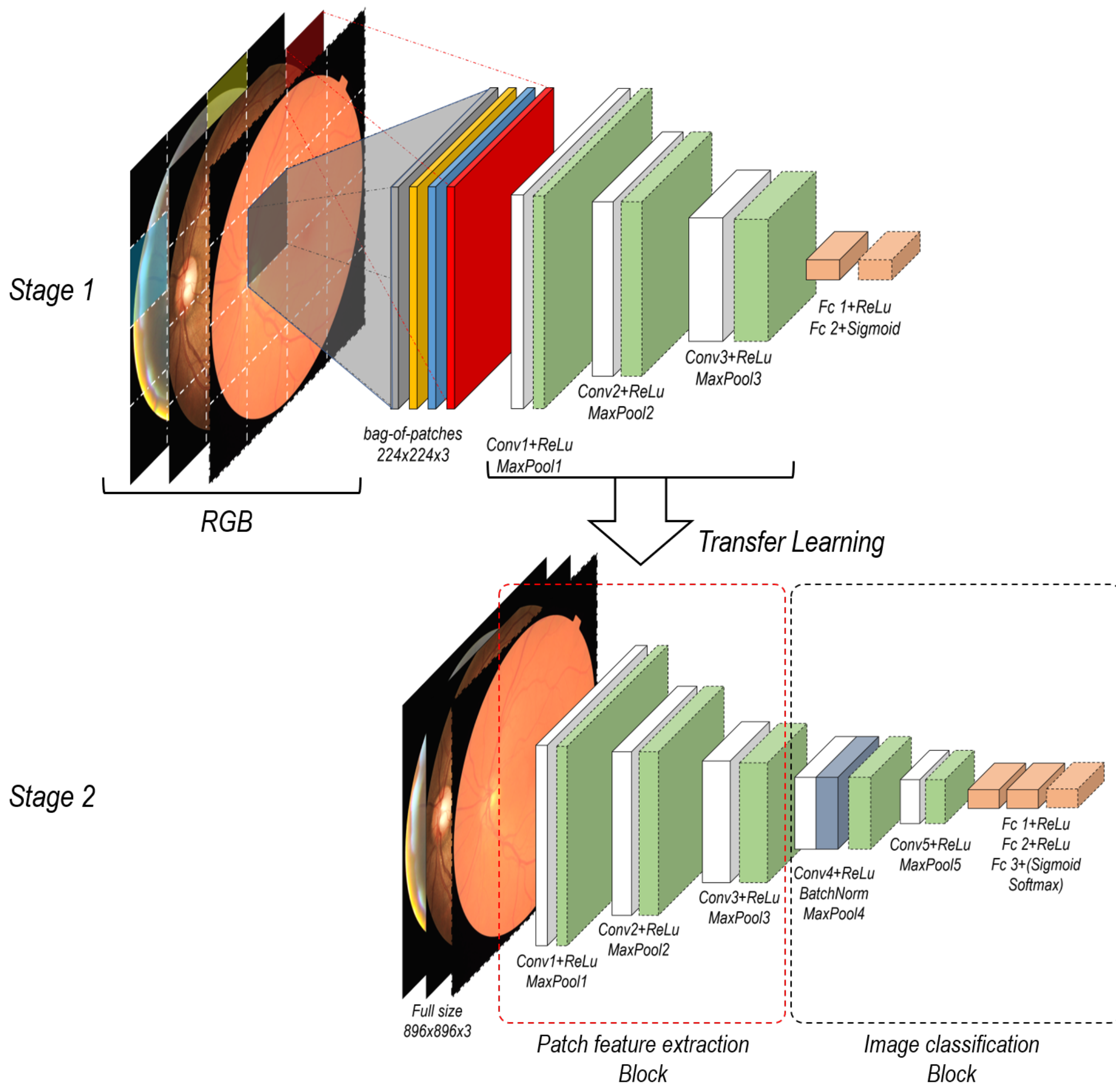

Figure 3-1: The graphical summary for the MFQ-Net architecture with two stages for the training process of the proposed method

3.2.1 Mobile Fundus Quality Network

This network consists of a fifteen CNN layers, which are structured on two main blocks: patch feature extraction (PFE) block and the image classification (IC) block. The first block is pre-trained with $224 \times 224 \times 3$ patches extracted from the original images. The second block takes the output of the first block, which is extended from patches to full images, and makes the prediction for a full $896 \times 896 \times 3$ image.
The overall architecture of the MFQ-Net is shown in Table **3-1**. The extended first block receives $896 \times 896 \times 3$ full images followed by three sub-blocks contains convolution/maxpooling layers with 16, 32 and 64 filters, and the kernel size for each sub-block was of 11×11, 9×9, and 7×7 respectively. The second block has a convolution/batchnormalization/maxpooling sub-block with 64 filters and a kernel size of 6×6, followed by a final convolution/maxpooling sub-block with 64 filters and a kernel size of 6×6 to finally incorporate two fully-connected layers of 256 and 64 respectively. The output classification layer has 1 neuron and a sigmoid activation function for binary classification and 3 neurons with softmax activation for three-class classification. In total, the network has approximately 607K parameters.

Table 3-1: MFQ-Net summary, were PFE and IC refers to the blocks for patch feature extraction and image classification respectively

Block	Layer	Size	Channels	Kernel size	Pool size
PFE	Input	896x896	3	-	-
	Conv_1	886x886	16	11x11	-
	MaxPool_1	443x443	-	-	2x2
	Conv_2	435x435	32	9x9	-
	MaxPool_2	87x87	-	-	3x3
	Conv_3	81x81	64	7x7	-
	MaxPool_3	27x27	-	-	3x3
IC	Conv_4	22x22	64	6x6	-
	BatchNorm	22x22	-	-	-
	MaxPool_4	11x11	-	-	2x2
	Conv_5	6x6	64	6x6	-
	MaxPool_5	3x3	-	-	2x2
	FullyCon_1	-	256	-	-
	FullyCon_2	-	64	-	-
	FullyCon_3	-	(1) - (3)	-	-

The model is trained in two stages. The idea is to train an initial smaller model on image patches and later extend it to full images. For the first stage, each image is scaled to $896 \times 896 \times 3$ size. Then it was split into 16 patches of $224 \times 224 \times 3$ pixel resolution. These patches are used to train the initial smaller model by adding an output binary layer that uses a sigmoid as an activation function and a binary cross-entropy as the loss function. For the second stage, the second maxpooling pool size in the initial smaller model is modified from 5×5 to 3×3 in order to avoid the float point number of parameters. Then, the model is extended by adding the IC block and trained with the $896 \times 896 \times 3$ scaled images as input, using for the binary classification task a binary output layer with a sigmoid as activation function and a binary cross-entropy as the loss function. For the three-class classification task a three output layer uses a softmax as activation function and a categorical cross-entropy as the loss function.

3.2.2 Dataset

There is a good variety of available eye fundus image datasets used commonly for pathology classification and segmentation tasks. However, the number of available/public eye fundus quality datasets is limited. Besides, some of them present issues such as category imbalance, a very low number of samples, and an extremely differentiated quality separability.

The Kaggle DR dataset [1] was selected due to its resolution diversity; a wider number of samples (35126 for training and 53576 for test sets); and its diverse images quality (good and bad image quality likewise image with artifacts such as bright areas). Based on the quality-labels reported for the Kaggle dataset, two different tasks were defined: a binary classification task [40] and a three-classes classification task [46].

For this task, each image was resized to a resolution of 896×896 pixel with RGB channels keeping its aspect ratio to later be split into 16 patches, of 224×224 pixel resolution each one. From the set of patches it was randomly sampled a subset for training, validation, and test keeping the class balance. A summary of the datasets used for this work is given in table **3-2**.

Table 3-2: Summary of used Kaggle annotation datasets

Dataset	Quality label	Training set	Validation set	Test set
Kaggle with binary labels [40]	Accepted	1285	226	873
	Rejected	1285	226	873
Kaggle with three-classes labels [46]	Good	6678	1669	8471
	Usable	1501	375	4558
	Bad	1856	464	3220

Some samples for `Accepted` and `Rejected` images from Zhou et al. [40] and `Good`, `Usable` and `Bad` images from Fu et al. [46] are shown in figures **3-2** and **3-3** respectively.

[1] https://www.kaggle.com/c/diabetic-retinopathy-detection

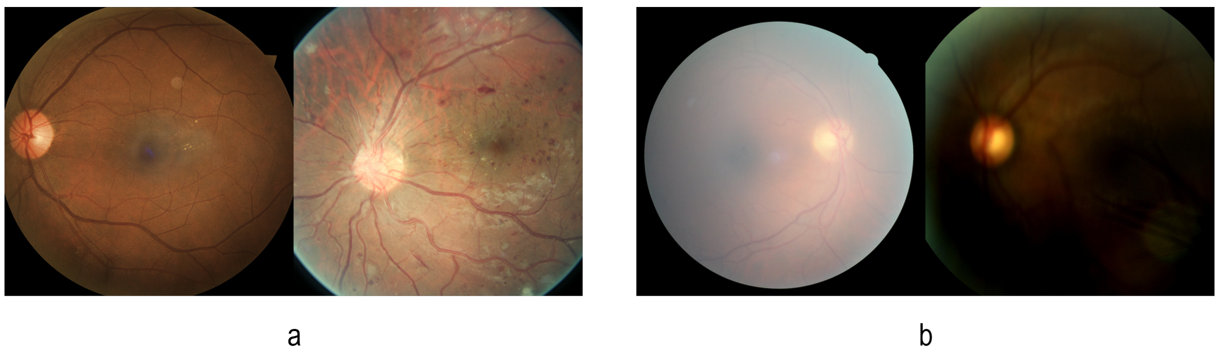

Figure 3-2: Image samples from Kaggle dataset with binary labels. a) Accepted quality. b) Rejected quality.

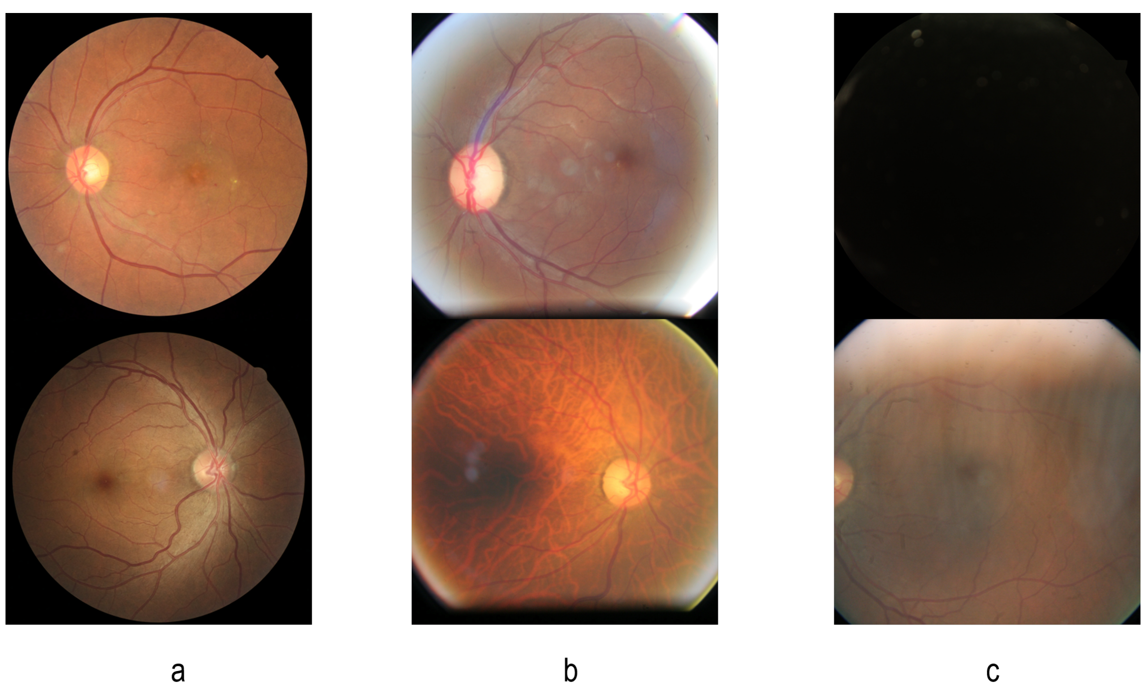

Figure 3-3: Image samples from Kaggle dataset with 3-class labels. a) Good quality. b) Usable quality. c) Bad quality.

3.2.3 Experimental Setup

As described in the Subsection 3.2.1, the model is trained in two stages. For the first stage, a hyperparameter exploration is carried out with a fix number of 20 epochs, varying both the batch size, 2^m for $1 \leq m < 6$ and the learning rate, between $7e^{-3}$ and $9e^{-7}$. This is only performed on the binary dataset.

In the second stage, two models are trained: one for the binary and the other for the three-classes classification task. In both cases, the patch feature extraction block is initialized with the weights obtained in the first stage. The models are trained with `Adam Optimizer` using a learning rate of $1e^{-6}$ along 25 epochs, freezing the first 6 layers to avoid weights updating. Later, a `fine-tuning` process is done during 150 epochs by unfreezing the whole architecture layers and using a learning rate of $1e^{-7}$. Each training was carried out using an Nvidia GeForce RTX 2080 Ti graphic card, completing the whole training for the binary classifier in approximately 6.10 hours and approximately 35.85 hours for the three-class classifier.

3.3 Experimentation and Results

This section has a tow parts approach in order to evaluate, both, effectivity and efficiency method performance.

3.3.1 Effectivity Evaluation

For each training stages and steps accuracy, loss, validation accuracy and validation loss (as shown in table **3-3**) were monitored. These gave as a result a learning rate of 8.496 e^{-5} and batch size of 8 for best hyperparameters in the exploration stage.

Table 3-3: Models training performance, here PFE refers to the patch feature extraction block

Model	Loss	Accuracy	Validation Loss	Validation Accuracy
PFE	0.3627	0.8401	0.3952	0.8303
MFQ-Net (Binary)	0.1701	0.9413	0.2614	0.9107
MFQ-Net (Three-class)	0.2236	0.9738	0.2412	0.9102

After the model's performance evaluation, the obtained results were: for binary classification tasks an accuracy of 0.9117 after *fine-tuning* and 0.8565 ACC for three-class classification after transfer learning. For the binary classification: sensitivity (SE), specificity (SP), accuracy (ACC), positive prediction value (PPV), negative prediction value (NPV), and area under the curve (AUC) were calculated, and for the three-class classification: ACC, precision (PS), recall (RC) and, f-score (FS) were determined as shown in table **3-4**.

Table 3-4: Performance for each method and model on testing sets

Model	SE	SP	ACC	PS	RC	FS	PPV	NPV	AUC
Zhou et al.	0.954	0.976	0.965	0.999	-	-	-	-	-
MFQ-Net (Binary)	0.9421	0.8853	0.9117	0.8774	0.9421	-	0.8774	0.9461	0.9595
Fu et al.	-	-	0.9175	0.8645	0.8497	0.8551	-	-	-
MFQ-Net (Three-class)	-	-	0.8565	0.8564	0.8564	0.8564	-	-	-

In the three-classes classifier, for the first class (good) just the 0.31% of the data was classified as `bad` quality and 5.32% as `usable` quality. Besides, for the `bad` class just the 1.71% were miss-classified as `good` quality and 12.33% as `usable` quality. However, the results for the class `usable` presented the highest miss classification results with 18.19% miss-classified samples as `good` quality and 12.59% of the images as `bad` quality.

3.3.2 Efficiency Evaluation

Additionally, it was wanted to evaluate the performance of the MFQ-Net model in a mobile device. We measured the classification average elapsed time in milliseconds (AVG-ET) performance. For the binary and 3-classes models over 5 randomly chosen images per class by running on an Android 9.0 OS version smart-phone. It was compared against a MobileNet-v2 implementation with 64 neurons fully connected layer. It was also measured the size of each model in terms of the amount of Megabytes for both for Keras (K-S) and Tensorflow lite representation (TFLite-S), the number of parameters for each model (PMS), and the accuracy for each model (ACC) as shown in table **3-5**. The results show a difference around of 331 ms between models being the MobileNet-v2 model the faster one, however, in terms of size and effectivity our MFQ-Net presents a better performance for this type of task.

Table 3-5: Models performance on Android OS

Model	K-S	TFLite-S	PMS	AVG-ET	ACC
MFQ-Net (Binary)	5.89	2.32	607K	2195.80	0.9117
MFQ-Net (Three-class)			607K	2202.89	0.8565
MobileNet-v2 (Binary)	27.3	8.75	2.34M	1872.49	0.7399
MobileNet-v2 (Three-class)			2.34M	1863.45	0.7218

3.4 Discussion

The first approach proposed for quality assessment was based on full-sized direct image classification. However, this approach was, on one hand computationally expensive limiting its possibilities of being applied over mobile devices, and on the other hand, its capability to abstract significant patterns for acceptable image quality was limited. Nonetheless, it was noticed that a local-to-general transfer learning-fine tuned strategy produced even better results, which showed a useful starting point for fundus image quality classification tasks by complementing each other.

Second, the combination of the convolutional-maxpooling layers when performing a kernel reduction with a factor of two allows the network to emulate a multi-scale (bottle-neck) feature extraction refining in this way the type and characteristics learned about the image.

Third, the MFQ-Net was validated with two different datasets achieving accuracy results of 0.911 and 0.856 for binary and three-class classification respectively, which represents comparable results with the actual state-of-the-art methods and models in terms of effectivity.

Finally, regarding to the classification results for the `three-classes`, the usable class presented the most difficult decision criterion with similar miss classification results both on images classified as good quality and images classified as poor quality.

4 Eye Fundus Image Quality Enhancement

This chapter explores the eye fundus quality enhancement task for a multi-class scenario. This method aims to enhance the quality of a new reclassified (by a specialist) dataset, which is a sample from the Kaggle dataset [1]. Some works have been previously addressed these issues offering enhancement or adjustment methods in order to improve the available data to guarantee the specialist diagnosis. Recently, different deep learning techniques for the quality enhancement of natural images have been proposed. In particular, Yang et al. [161] developed a Multi-Frame Convolutional Neural Network (MF-CNN) to enhance the quality of the compressed video. Vu et al. [59] exposes a convolutional neural network for image quality enhancement which also can be trained for super-resolution imaging. Yoo et al. [64] presented a cycleGANs-based method for fundus quality enhancement. One of the most popular is the Pix2Pix, proposed by Isola et al. [162] which consists of a Conditional Generative Adversarial Network (cGAN) that generates new samples from a pre-establish (conditional) condition provided during its training. This approach requires paired images (`good` and `bad` quality) which is difficult to find in a common medical environment. With this work is presented a deep learning-based method for eye fundus quality enhancement termed Pix2Pix-Fundus Oculi Quality Enhancer (P2P-FOQE).
This work was published in the *Workshop on Ophthalmic Medical Image Analysis* from the *International Conference on Medical Image Computing and Computer Assisted Intervention, MICCAI 2020*.

4.1 Introduction

Deep learning models used for eye screening based on eye fundus images have obtained outstanding results in the classification of retinal diseases, such as Diabetic Retinopathy (DR), Diabetic Macular Edema (DME), and Age-Related Macular Degeneration (AMD) among others [163].
These models have improved the prognosis of ocular diseases, increasing the number of early and proper treatments positively impacting people's life quality [164]. For that reason, the need to ensure optimal working conditions in the screening facilities and medical devices

[1] https://www.kaggle.com/c/diabetic-retinopathy-detection

is mandatory. However, acquisition devices often are affected by external factors such as found noise, blurring, missed focus, illumination, and contrast issues hindering the detection by experts. The mishandling of these factors affects the ability of experts and deep learning model performance [53, 141]. Some works have been previously addressed these issues offering enhancement or adjustment methods in order to improve the available data to guarantee the specialist diagnosis. Sahu et al. [53] proposed a noise removal and contrast enhancement method based on contrast limited adaptive histogram equalization (CLAHE). Singh et al. [165] described the use of median filters with Histogram Equalization (HE) and CLAHE use with Curvelet Transformation for image enhancement in segmentation tasks. Bandara et al. [140] presented an enhancement technique based in a Coye [166] algorithm variant improved with a Hough line transform that is based on vessel reconstruction. Raja et al. [167] explains the use of multi-directional local histogram equalization. Wahid et al. [60] explained the combination of fuzzy logic and histogram-based enhancement algorithm with CLAHE for eye fundus visual quality enhancement. Finally, Zhou et al. [141] detailed a two steps method for eye fundus quality enhancement based on a color gain matrix with gamma correction factor adjustment and an L channel CLAHE implementation.

Recently, different deep learning techniques for quality enhancement of natural images have been suggested. In particular, Yang et al. [161] developed a Multi-Frame Convolutional Neural Network (MF-CNN) to enhance the quality of the compressed video. Vu et al. [59] exposes a CNN for image quality enhancement which also can be trained for super-resolution imaging. One of the most popular networks for image reconstruction and image generation due to its versatility and adaptability to different tasks is the Pix2Pix model proposed by Isola et al. [162]. This method consists of a Conditional Generative Adversarial Network (cGAN) that generates new samples from a pre-establish (conditional) condition provided during its training. With regards to eye fundus quality enhancement, one of the newest and relevant works is proposed by Yoo et al. [64]. His method is based on CycleGANs that provide a solution for quality enhancement without the need for paired images (good and bad quality) which is difficult to find in a common medical environment.

4.2 Materials and methods

Figure **4-1** shows the overall pipeline of the proposed method for eye fundus image quality enhancement. P2P-FOQE has three sequential stages. The first stage deals with the image resizing and luminosity-contrast adjustment. The second stage handles the core image enhancement. Finally, the third stage applies a CLAHE transformation for limited contrast adjustment. The following subsections discuss the details of the three stages.

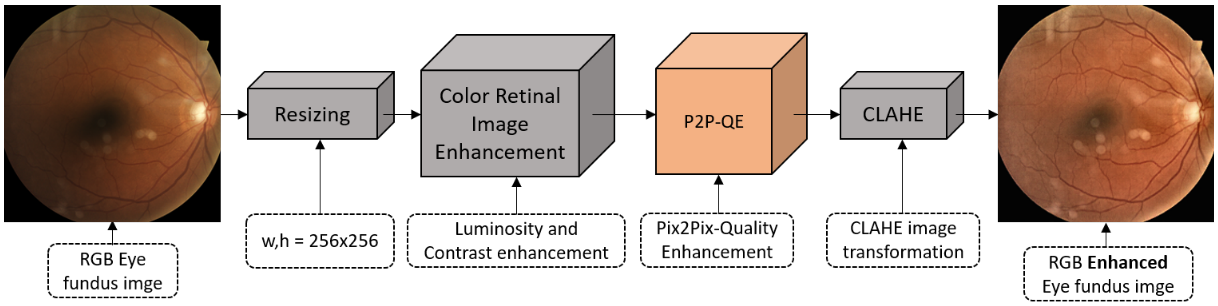

Figure 4-1: Box diagram for our suggested P2P-FOQE. Stage 1) Pre-enhancement; Stage 2) Pix2Pix Enhancement; Stage 3) Post-enhancement

4.2.1 Pix2Pix-Fundus Oculi Quality Enhancer

- Pre-enhancement
  This stage receives a resized color fundus image to a resolution of $256 \times 256 \times 3$ keeping its aspect ratio. Then, the image pre-enhancement is performed using our implementation from the color retinal image enhancement method presented by Zhou et al. [141]. First, the method focuses on luminosity enhancement, working over the value channel from the HSV color space representation together with a gamma correction to ensure the luminosity-channel independence generating a luminance gain matrix. In specific, that is applied over the original R(x,y), G(x,y) & B(x,y) image components, obtaining the r'(x,y), g'(x,y) & b'(x,y) luminosity enhanced. Then, the second step enhance the contrast, by applying a CLAHE transformation over the L channel from a LAB color space by obtaining a new split channel representation designated as follows: r''(x,y), g''(x,y) & b''(x,y). Finally, these arrays are stacked into one single array obtaining a final pre-enhanced image shape of $256 \times 256 \times 3$. This pre-enhanced image is used as input for the P2P-FOQE model which consists of a Pix2Pix architecture.

- Pix2Pix Enhancement
  Pix2Pix is one of the most widely used deep learning models in the last years. It has been used for synthesizing photos from label maps, colorizing images and reconstructing objects from diverse representations, among others. The Pix2Pix model was used for eye-fundus image enhancement by mapping good quality features from good quality images to bad quality images. In this process, a quality enhanced representation is transferred from one image to a bad quality image. The architecture is summarized in two blocks: the conditional GAN Generator (G) is constituted by a modified U-Net following skip connections, helping the generator to avoid the information bottleneck. Then, the conditional GAN Discriminator (D) is a GAN termed as Patch-GAN which is based on patches scale, similar to obtain local styling. This Patch-GAN forces low-frequency correctness by the use of an L1 term to avoid noise such as blurring over the enhancement. At last, a discriminator output patch size of $30 \times 30 \times 1$ is obtained to

classify a $70 \times 70 \times 1$ image portion aiming to produce the enhanced eye fundus image.

- Post-enhancement
  This final stage receives a partial enhanced fundus image with a $256 \times 256 \times 3$ resolution, where a CLAHE is applied through the RGB channels to limit its contrast amplification by a factor of 1.5 (this value was obtained in a grid search) to reduce the problem of noise-amplification commonly noticeable in adaptive histogram equalization (AHE).

- Training the P2P-FOQE model

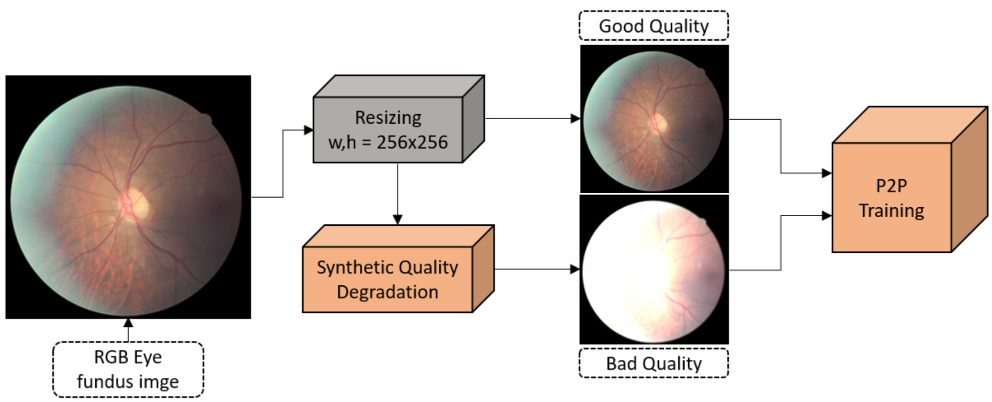

Figure 4-2: Box diagram for training our proposed P2P-FOQE method

The training of P2P-FOQE model requires as input two eye fundus images from the patient's eye with good and bad quality as shown in Figure **4-2**. However, free public data-sets of eye fundus images with these requirements is not available. Due to this limitation, it was devised a synthetic-quality-degradation strategy that generates bad quality versions of good quality images. The P2P-FOQE applies a set of transformations such as blurring and brightness at random levels to obtain noisy/degraded versions of the original good quality images. Besides, random areas were cropped for fovea-decentering and an outer light halo was added to create synthetical bad quality images. Then, the Pix2Pix enhancement model is trained using the pair of images: the original image and the synthetically degraded image. One of the main advantages of this approach is the possible use of both private and public datasets from previous studies. In the same manner, the generation of a synthetic controlled representation helps to minimize the risk of overfitting caused by the imbalance between the generator and discriminator during training.

4.2.2 Dataset

Kaggle dataset [2] provides a set of 88702 real-world eye fundus images with diverse resolutions and pathologies. In particular, the Kaggle dataset contains varied image quality features (such as luminance, contrast, and artifacts, among others). Fu et al. [46] defined three classes to evaluate the quality in this dataset (`good`, `usable` and `bad`). However, for this study the image quality is defined according to the compliance of specific characteristics with a more stringent criterion using the same three categories explained in details as follows:

- Good: Optimal quality focus on the foveal region and optic nerve, regular illumination of the entire field with full presence of the optic nerve and macula; with the presence of the entire route the temporal arches at the macular level. Without the presence of artifacts.

- Usable: Non-optimal quality focus on the foveal region and optic nerve, irregular illumination of the entire field with full presence of the optic nerve and macula; with the presence of at least 3/4 parts of the route the temporal arches at the macular level. It may have few artifacts that are not or confused with real injuries.

- Bad: Poor quality, there is no focus on the foveal or optic nerve regions, irregular illumination with the incomplete presence of the optic nerve or macula, with the presence of less than 3/4 parts of the temporal arches at the macular level. The significant presence of artifacts that avoid evaluating the macular region or optic nerve, or artifacts that simulate retinal lesions.

From the Kaggle dataset with Fu et al. [46] criterion, 1876 images per quality category, which were reviewed and re-classified (according to our classification criterion) as follows: 927-`good`, 1890-`usable` and 2811-`bad` by an ophthalmology specialist were randomly selected. When comparing the new labels to the ones provided by Fu et al. [46] the level of coincidence obtained, using Kappa measure, was 0.64.

4.2.3 Synthetical Image Degrading

The color fundus images were resized to a resolution of 256×256 pixels keeping its aspect ratio both to feed the Pix2Pix model and speed-up the training process. Images were transformed applying different quality degradation transformations: blurring, brightness, fovea-centering (randomly applied during the training), light halo, and a mixture of these previous transformations as presented in Figure **4-3**. This process produced a synthetic dataset of paired good-bad quality images with 927 images per category, which was randomly sub-sampled and divided into training and validation sets in an 80-20%-near ratio.

[2]https://www.kaggle.com/c/diabetic-retinopathy-detection

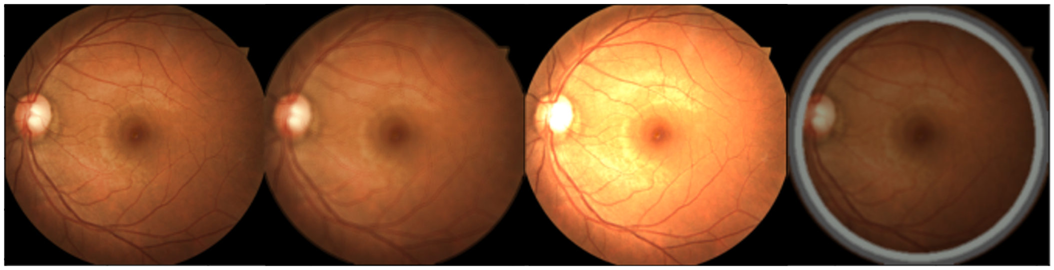

Figure 4-3: Synthetic quality degradation samples comparison. a) Raw image. b) Blurring degradation. c) Brightness degradation. d) Mixing of blurring, brightness and halo light

4.2.4 Experimental Setup

The Pix2Pix model was trained during 250 epochs using an Adam optimizer for generator and discriminator with a learning rate of $2e^{-4}$ and with a momentum of 0.5 and 0.999 for $beta_1$ and $beta_2$ respectively. This training was done using an Nvidia GeForce RTX 2070 Super with a runtime of approximately 9.02 hours.
The quality of enhanced images was assessed using two quality evaluation / classification baselines. The first one is a quality classifier method termed MFQ-Net by Pérez et al. [8], which was trained with images labeled with the new ophthalmology specialist criteria to estimate the quality of an input eye fundus image. This model classifies an image into three categories: bad, usable, and good. Besides, the quality of generated images was evaluated using the Automatic Quality Evaluation (AQE) method proposed by Bartling et al. [77] which focuses on sharpness and illuminance classifying the quality in four categories: very good, good, acceptable, and not acceptable.

4.3 Experimentation and Results

The whole dataset reported in subsection 4.2.2 was enhanced using our proposed method (P2P-FOQE) and six enhancement state-of-the-art methods such as CLAHE with 1.5 clip limit [168], color gain matrix with gamma correction factor adjustment and an L channel-CLAHE (L-CLAHE) by Zhou et al. [141], Pix2Pix enhancement by Isola et al. [162], Cycle-GANs enhancement by Yoo et al. [64], and combinations of channel-CLAHE plus Pix2Pix, and Pix2Pix plus CLAHE. Then, seven new data sets of images were generated with the application of the previous enhancement methods. The illustration over a sample image for these enhancements is shown in Figure **4-4**.
The generated seven data sets were evaluated using the MFQ-Net trained according to ophthalmologist criteria and, the AQE method that classifies according to sharpness and illuminance criteria as explained in detail in subsection 4.2.2.

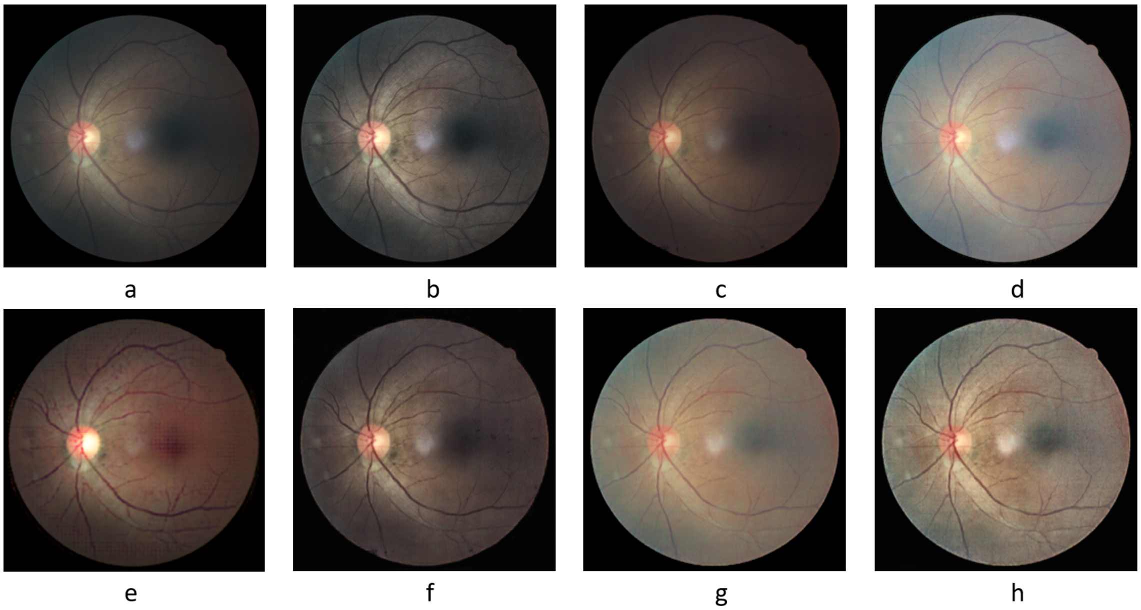

Figure 4-4: Illustration of different enhancement methods over the same image. a) Original color fundus image; b) CLAHE; c) color gain matrix with gamma correction and CLAHE; d) Pix2Pix; e) cycleGANs; f) Channel-CLAHE with Pix2Pix; g) Pix2Pix with CLAHE; and h) P2P-FOQE proposed method.

The generated seven data sets were evaluated using the MFQ-Net trained according to ophthalmologist criteria and, the AQE method that classifies according to sharpness and illuminance criteria as explained in detail in subsections 4.2.2 and 4.2.4.

The quality classification results obtained using the MFQ-Net on the seven enhanced data sets and the image dataset without enhancement (Non-enhance) are summarized in Table **4-1**. This table contains the percentage of samples for each original category: Original-Good (OG), Original-Usable (OU), and Original-Bad (OB), and the classification into three subcategories according to the re-classification given by the classifier. The first row corresponding to the no-enhance method, where the OG images were reclassified by the MFQ-Net classifier in 84.79 %, 14.89 %, and 0.32 % for good, usable, and bad categories respectively. The OU images were reclassified in 14.18 %, 75.03 %, and 10.79 %, for good, usable, and bad categories respectively. Finally, the OB images were reclassified in 0.85 %, 11.99 %, and 87.13 %, for good, usable, and bad categories respectively. The enhancement obtained with the P2P-FOQE method was the highest for Good label into the three main categories as reported in Table **4-1**. Moreover, the P2P-FOQE method outperforms the quality classification results of non-enhanced and state-of-the-art methods in OU and OB categories with percentages of 72.33 % and 29.49 % respectively, compared to the non-enhance method with 14.18 % and 0.85 % for OU and OB categories respectively, Pix2Pix + CLAHE method for OU category of 66.77 % and, cycleGANs method [64] in OB category of 23.94 % as reported in Table **4-1**.

Table 4-1: MFQ-Net evaluation results and enhancement methods comparison. OG, OU and OB refer to the original Good, Usable and Bad categories respectively. Each original category is subdivided into a new classification. In bold, the two highest percentages for each good subcategory.

	OG			OU			OB		
Method	Good	Usable	Bad	Good	Usable	Bad	Good	Usable	Bad
Non-enhance	84.79	14.89	0.32	14.18	75.03	10.79	0.85	11.99	87.16
CLAHE [168]	**98.06**	1.94	0.00	64.44	33.92	1.64	12.20	32.23	55.57
L-CLAHE [141]	89.97	10.03	0.00	25.61	69.15	5.24	4.41	31.95	63.96
Pix2Pix [162]	77.02	22.22	0.76	13.97	74.13	11.90	0.92	18.43	80.65
L-CLAHE + Pix2Pix	85.44	14.56	0.00	24.60	70.95	4.44	3.91	41.66	54.43
Pix2Pix + CLAHE	97.95	2.05	0.00	**66.77**	32.17	1.06	18.25	40.66	41.09
cycleGANs [64]	88.46	11.43	0.11	47.78	50.79	1.43	**23.94**	61.86	14.19
P2P-FOQE	**98.06**	1.94	0.00	**72.33**	27.41	0.26	**29.49**	56.21	14.30

The classification results obtained using the AQE method on the seven enhanced data sets and the image dataset without enhancement are presented in Table **4-2**. Unlike the Table **4-1**, the Table **4-2** contains four sub-categories: Very Good (VG), Good (G), Acceptable (A), and Not-Acceptable (NA), for each category according to AQE criteria as presented in the subsection 4.2.4. The first row corresponding to the non-enhance method, where the OG images were reclassified by the AQE classifier in 0.22 %, 9.06 %, 85.87 %, and 0.00 % for VG, G, A, and NA categories respectively. The OU images were reclassified in 0.00 %, 3.28 %, 74.02 %, and 22.70 % for VG, G, A, and NA categories respectively. Finally, the OB images were reclassified in 0.00 %, 0.39 %, 35.75 %, and 63.86 % for VG, G, A, and NA categories respectively.

Table 4-2: AQE evaluation results and enhancement methods comparison OG, OU, and OB refers to the original Good, Usable and Bad categories respectively. Each original category is subdivided into a new classification. In bold, the two highest percentages for VG and G subcategories.

	OG				OU				OB			
Method	VG	G	A	NA	VG	G	A	NA	VG	G	A	NA
Non-enhance	0.22	9.06	85.87	4.85	0.00	3.28	74.02	22.70	0.00	0.39	35.75	63.86
CLAHE [168]	**48.87**	48.65	2.48	0.00	**26.83**	57.25	15.71	0.21	2.13	**25.86**	51.01	20.99
L-CLAHE [141]	0.11	25.03	74.33	0.54	0.00	9.79	77.30	12.91	0.18	3.45	59.84	36.54
Pix2Pix [162]	0.00	0.76	80.04	19.20	0.00	0.26	54.97	44.76	0.00	0.07	17.47	82.46
L-CLAHE + Pix2Pix	0.00	2.59	91.80	5.61	0.00	0.69	74.50	24.81	0.07	0.28	45.89	53.75
Pix2Pix + CLAHE	19.96	**70.77**	9.28	0.00	8.15	**63.97**	27.62	0.26	0.39	20.38	65.07	14.16
cycleGANs [64]	7.01	16.40	73.79	2.80	8.15	32.38	56.40	3.07	**3.59**	21.10	55.96	19.35
P2P-FOQE	**37.65**	**60.52**	1.83	0.00	**21.06**	**72.22**	6.67	0.05	**6.30**	**68.23**	25.15	0.32

The whole enhanced image data set obtained with our P2P-FOQE method was qualitatively evaluated by experts. The expert found that the proposed method enhanced some features in the color fundus images as depicted in Figure **4-5**

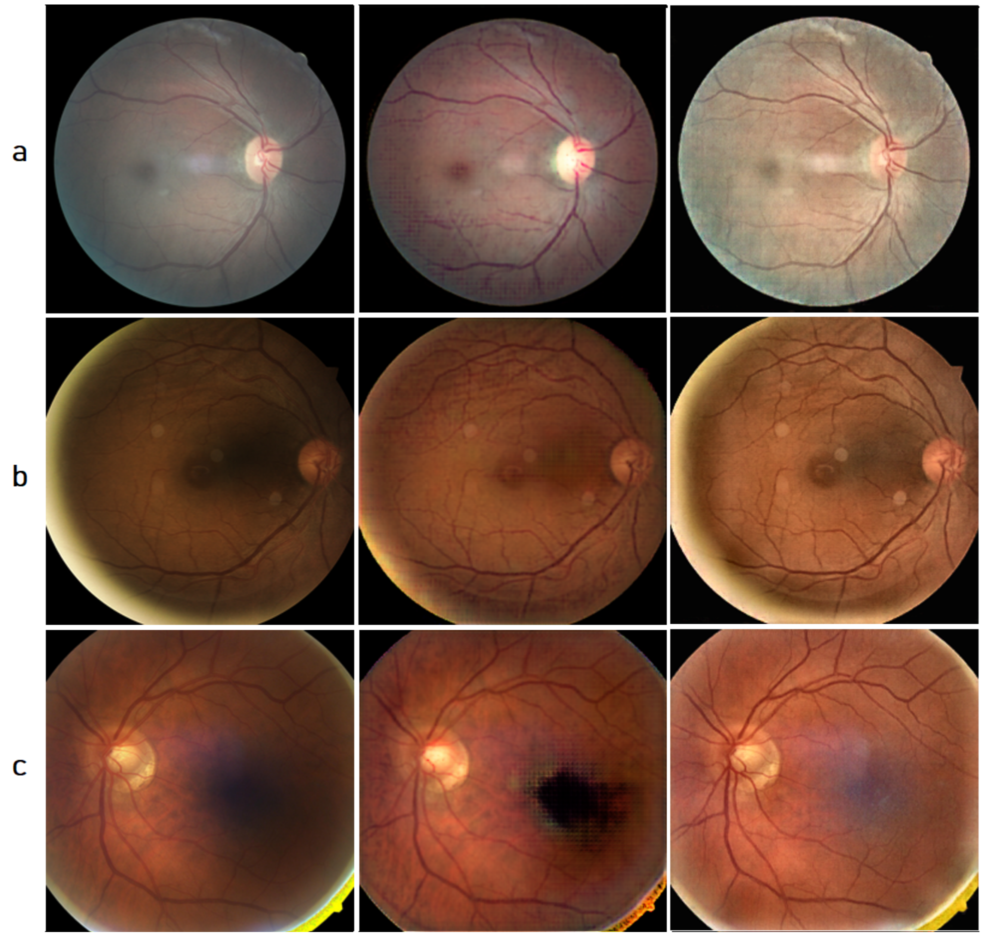

Figure 4-5: Expert comparison of enhanced images. [Left] Color fundus images; [Center] enhanced images using cycleGANs [64] and, [Right] enhanced images using P2P-FOQE proposed method.

4.4 Discussion

The P2P-FOQE method had an outstanding performance in the quality classification of VG and G classes compared to non-enhanced and state-of-the-art methods in OU and OB categories. Besides, the proposed method presented the best results in VG and G classes in the OB category and, the lowest percentages of NA class in the three categories as presented in Table **4-2**.

The application of a synthetic data degradation strategy allows the use of a paired model (good-bad quality) as well as contributing to the generalization of the Pix2Pix model with information related to the characteristic factors corresponding to the concept of bad quality.

This is evidenced by both the results obtained in Tables **4-1** and **4-2** as well as described by the specialist in the comparison between the improvement models.
It is important to use a post-processing stage using a CLAHE filter to ensure contrast enhancement and thus enhance and/or demarcate important details that may not have been enhanced or overshadowed either in the pre-upgrade or model enhancement stage.
The comparison has shown that L-CLAHE + Pix2Pix method is close to producing a detailed image, noise-controlling provided by CLAHE at near-constant regions of the image is required. On the other hand, the proposed method minimizes the negative impact of the images and preserves relevant quality features to support the proper diagnosis. The expert found that the proposed method enhanced some features in the color fundus images as depicted in Figure **4-5**. In particular, the two first fundus images (a-b center) generated patterns that looks like intraretinal hemorrhages and the vessels have irregular walls with interrupting paths. However, our proposed method (a-b right) presented hypo-pigmented findings accentuated and the neuroretinal ring is better preserved. Moreover, the fundus image (c-center) produced a notorious black spot that could be diagnosed as a melanoma-like lesion (cancer of the choroid) in comparison with the enhanced image obtained by our method that attenuates the black spot (c-right).

5 Conclusion and future works

This research studied and explored several deep learning approaches to provide a model for the eye fundus image quality assessment and enhancement tasks. Despite deep learning models require massive data amounts to obtain outstanding performances, the developed models tackle the lack of large datasets and involve the expert's knowledge to adjust the better quality and enhancement criteria of eye fundus images.

Making an objective image quality estimation based on subjective criteria is a considerably complex task. However, it was found that it is possible to assess the eye fundus image quality. Comparable state-of-the-art results were obtained using a significantly more lightweight model than the latest generation ones. This allows the possibility of its implementation in portable devices such as smartphones. In addition, this lightweight model performs the quality assessment task in execution times of the order of seconds.

A diverse set of annotations was crucial for the appropriate research development. Besides, existing annotations present a bias according to the specialist criteria who carried them out which affects the data quality and therefore the obtained results. With this in mind, it was decided to carry out a new annotation exercise with the help of one of the specialists from the Fundación Oftalmológica Nacional.

Eye fundus image quality enhancement represents another big challenge. The lack of paired (good-bad) quality datasets highly difficult this task. A reverse strategy of synthetic quality degradation (based on the quality criteria of the Fundación Oftalmológica Nacional specialist) was developed on the images marked as good quality. Considering a stricter quality criterion, it was found that, the characteristics referring to good image quality are enriched. This stricter criterion helps the image enhancement method to apply the enriched extracted features to better correct and enhance the deficient quality of the fundus images. This proved to be beneficial as assured both better datasets quality and better model performance. However, although the models are admirably adaptable to the different factors involved in these tasks, their individual use is not enough and requires a mixed strategy to achieve a broader problem generalization.

The obtained results were validated with the support from the Fundación Oftalmológica Nacional specialists. These results are evidence that the research goals which focus on eye fundus image quality assessment and enhancement have been successfully achieved, as well as the addressed research questions were answered. In addition, the public available eye fundus image annotations were released to help future research about these issues.

Finally, this work is the first stage of a telemedicine project which is in the clinical validation process. For future works, exploration with larger or different dataset modalities is suggested for both models. Another possible line of work is to integrate this work in a clinical workflow with health brigades (screening sessions, among others) and to incorporate it with other clinical diagnostic models of eye diseases for diagnosis support.

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