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Design And Implementation Of Early Detection Of Glaucoma, Integrated With Deep Learning Models On Fundus Images

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Abstract- The early detection of some diseases can be a decisive factor in postponing or stabilizing their most adverse effects on the people who suffer from them. In the case of glaucoma, which is an ocular pathology that is the second leading cause of blindness in the world, early detection can make the difference between a patient's complete losses of vision, or preserve their sight, as well as improve their subsequent treatment. It is for this reason that there are currently medical campaigns for the early detection of pathologies with these characteristics in a certain study population, called screening, which have shown very good results. In addition, the application of telemedicine to these processes has allowed remote evaluation of cases by clinical experts and numerous initiatives have emerged for its use in new screening strategies. On the other hand, biomedical image processing techniques based on deep learning have undergone great development in recent years, and there are several works that have demonstrated their possible application in the automatic detection of glaucoma with fundus images. The article has consisted of the development of a web platform that integrates both scenarios: on the one hand, the remote evaluation of fundus images by medical specialists, and on the other, the application of a tool based on Deep Learning for the automatic detection of glaucoma in the case studies.

I. INTRODUCTION

Glaucoma is a disease characterized by specific changes in the visual field and the papilla, usually accompanied by ocular hypertension and which, if not treated in time, leads to blindness. The vision proceeds in several stages. Light enters the eye, the retina transforms this stimulus into an electrical signal that is conducted as a nerve impulse that the brain is able to process.(14) The optic nerve connects the eye with the cerebral cortex. In glaucoma, nerve cells and fibers progressively die as a result of the increase in intracular tension (TO), as a consequence the eye continues to see light but the transmission of this information to the brain is interrupted, and this is the heart of the problem called glaucomatous damage (Figure 1).

Fig. 1. Optic disc excavation in a glaucomatous eye

In the early stages of the disease, visual function remains surprisingly intact. As the pathology evolves, it causes visual defects in the patient's vision. Before the patient is aware of this loss of vision, it can be detected by the ophthalmologist. This is what makes glaucoma dangerous: by the time the patient realizes their vision loss, the disease is already at an advanced stage.

Early detection of glaucoma can postpone the most adverse effects of the disease, as well as to improve its subsequent treatment. Its diagnosis is based on structural tests of the optic disc, as well as functional ones. In recent years, numerous initiatives have emerged for the detection of glaucoma based on remote evaluation by clinical experts, using, among others, fundus images acquired with digital retinographs. . In addition, the advancement of biomedical image processing techniques has been revolutionized in recent years with the development of deep learning techniques and there are several works that have demonstrated its possible application in the automatic detection of glaucoma with eye fundus images.

II. LITERATURE REVIEW

The application of screening for the early detection of retinal diseases is one of the most successful cases in ophthalmology [13-16], its use being especially relevant in the detection of diabetic retinopathy (DR) and age-related macular degeneration (AMD). Both are asymptomatic in their early stages and respectively represent a growing cause of vision loss in middle-aged and elderly people. In addition, there are also studies that demonstrate the effectiveness of screening for Glaucoma detection.

It was found that it was not necessary for the machine to exceed the precision of the human eye in order to provide useful information that would support specialists in their decision. The steps followed by CAD technologies in the process of classifying an image [3] are: (1) preprocessing and adaptation of the image to improve its quality before being processed, (2) segmentation of the image in the regions of greatest interest for analysis, to centralize the detection process in these regions, (3) identification of findings that may contribute to the classification of the pathology sought, and finally, (4) classification of the image based on the findings found. A great challenge currently facing CAD technology research is the extraction of not only quantitative, but also qualitative information from images, with the aim of contributing, in addition to the result of the classification, information on the findings that have contributed to the final decision established in the process. The review has been made on the observations and tabulated in Table 1.

Table 1. Review of Literature

Methods	Data	Preprocessing	Feature Extract	No. of features
[8]	Inception-v3	92	95.6	92.34
[58]	Disk-aware ensemble	91.83	83.80	83.80

	network (DENet)			
[62]	Eighteen layer CNN	98.13	98.3	98
[63]	U-net for segmentation and fully connected with dropout for classification	100	100	100
[65]	ResNet50	97	93	92
[68]	MB-NN	91.51	92.33	90.90
[69]	Four convolutional layers and fully connected layers.	87.40	85	71.17
[72]	ResNet	99.6	97.7	96.2

III. METHOD AND DEVELOPMENT

Development in Python of a Deep Learning model trained for the automatic detection of glaucoma in fundus images. The system reads the image to be analyzed and preprocesses it to be introduced into the model. The model returns two options as a result of the classification, positive or negative, being "positive" indicative that the fundus image contains suspicious signs of glaucoma and "negative" when the system classifies the image as normal or without signs of glaucoma. . The internal classification is based on a numerical score between 0 and 1 and the calculation of a threshold that optimizes the classification. The objective of this work block has been to integrate this trained model in the system. This section has consisted mainly in sending the images introduced in the platform automatically to the network, and storing the result of the automatic classification in the Database to be able to be used as help information for specialists. when evaluating studies. In addition, a qualitative information section has also been introduced in the images, which the evaluators can access, which will be discussed later.

A. Functional requirements and use cases

The screening strategy generally requires a large study population. This fact entails the need for an efficient classification of the data and an orderly control over the patients and the studies carried out. For this reason, the application must provide access to data in an intuitive and orderly manner.

Participating users are defined according to their roles in this process. To finish this section, a diagram has been included with the situations in which the application will make use of the mail server (Figure 2):

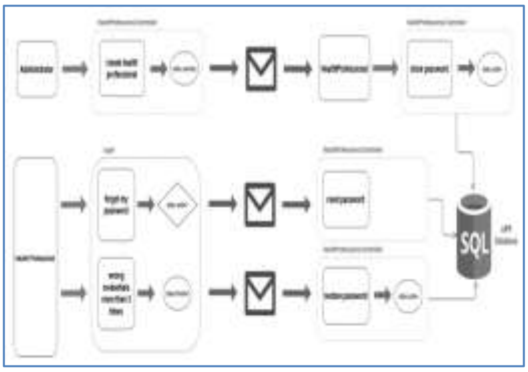

Fig. 2. Situations of sending emails by the application

B. Tools used in the work

- The Model-View-Controller (MVC)
- Laravel Homestead
- Bootstrap
- Relational database with MySQL

IV. TECHNIQUES USED FOR THE DEVELOPMENT OF THE SYSTEM

A. REST API server to deploy the Deep Learning model

A REST application interface is to be deployed on a remote server. This implementation has been based on the example taken as reference in [15]. Next, a diagram with the operation of this system is shown (Figure 3). The idea is that this interface contains the deep learning model loaded and available to process the REST type requests sent from the web platform. In our case of application, only POST type requests will be used, whose content will be the fundus images to be analyzed.

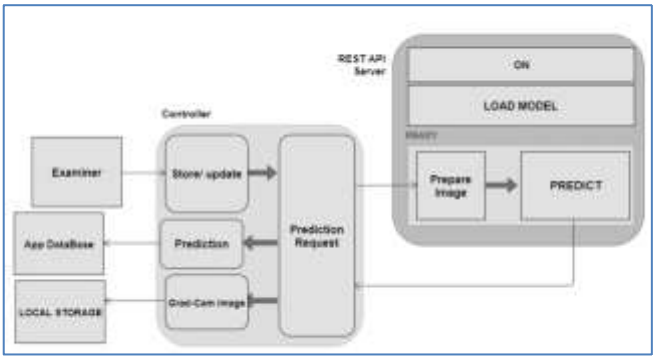

Fig. 3. Block diagram of the REST API

These images will be processed in the model loaded on the server side, and the interface will return a response in the form of a JSON serialized object with the results of the classification. This procedure will consist of two steps:

(1) Pre-processing of the image to adjust its characteristics (size, normalization of pixels) to the requirements of the network

(2) Processing of the image by the model, prediction of the classification results and obtaining the qualitative information of the study case using the Grad-CAM tool that will be explained later in this section.

The main reason for using a remote interface with these characteristics is that the Deep Learning model will only be loaded when the server is started for the first time, making it available for use at any time by the application. Since the trained models usually have a high load cost, the use of this technique considerably reduces the operation times of each request, which is a great advantage for our work. The call to the REST server will be made from the web platform, between the process of sending the study by the examiner for its evaluation and the reception of the study by the evaluator. When the browser requests to send the data for evaluation, the images will be sent to the server. The images will be processed independently and the result will be returned from the network as a JSON object to the application.

Once the application receives these data, it will store the results of the classification of each image in the database together with the rest of the study data. The qualitative information, which is received in the form of a numerical matrix, will be converted into an image and stored in the same directory as the original images. Then, the process of sending the study for evaluation will end. The evaluator will receive the study and once the evaluation begins, they will have access to these data.

B. Tools used in Python to invoke the Deep Learning application

The most important libraries that have been used in the generated Python scripts have been keras, tensorflow, numpy, requests, JSON and matplotlib.

C. Grad-CAM tool to obtain qualitative information from the model

One of the most important challenges facing technologies based on deep learning is the fact that the system acts as a black box, that is, it does not explain the decisions made for the prediction to be made. For this reason, there are research branches of these technologies that focus on the study of mechanisms to extract qualitative information from the network, and approximations have been given with very good results. In this work, a technique called Grad-CAM has been used, applied to images, which locates the areas of the input image that have contributed with greater weight to the classification obtained at the network output, and relates the result to the pixels in these areas of the image using backpropagation and network deconvolution techniques [23]. The result is a numerical matrix that, if represented as an image, shows a color map over the original image with the regions that most influenced the final decision marked with greater intensity. There are different implementations of this technique in Python, and the one referenced in [24], which uses a network model based on Keras, has been used in the work.

V. PLANNING AND PHASES OF THE WORK

This development phase started from the Master version to create the OPH platform for specialized ophthalmology in the case of glaucoma, and consisted of the steps explained below.

A. Create a database for BitScreen OPH.

The model of this database will be the same as for BitScreen Master.

– Add a personal and family history of glaucoma section to the views for creating a study, and specialize the image upload section for the case of eye images, adding fields of image type, position and eye to which they correspond, with the options "left" or "right". Create the corresponding fields in the database.
– Modify the evaluation views of a study, adapting the section of visualization and analysis of the acquired images for eye images, and specializing the global evaluation section for the case of diagnosis of glaucoma.

B. Integration of the CAD model in BitScreen OPH.

This has been the last phase of the work and has consisted of five steps, (1) integration of the deep learning model in a REST API for deployment on a server. (2) Creation of an executable script on the client side that connects to the REST API server. This script will send the fundus images for classification and will receive the result of the model, also generating the images for the visualization of the qualitative information of the system to be stored on the platform. (3) Invocation of the script from the platform by the study control functions, when sending (store) or updating (update) the studies for evaluation. (4) Store the results (prediction and score) of the automatic classification in the database, associating them with each test image acquired in the study. (5) Add access to classification results from the evaluation form and retrieve results from the database and visualization of qualitative information.

C. Results and test plan

In this work the results of the work will be shown and a test plan divided into two blocks will be developed. On the one hand, a table will be defined with the technical requirements that the web application will have to meet and it will be checked one by one if it works correctly. On the other hand, a test of the success rates of the prediction model will be carried out on some test data, in order to draw conclusions about the sensitivity and specificity parameters of the system.

VI. TOOL FOR THE EARLY DETECTION OF GLAUCOMA: BITSCREEN OPH

The platform allows remote evaluation by clinical experts of fundus images for the detection of glaucoma in them. This process is carried out following a store-and-forward technique, which consists of storing in the application the medical data and the images acquired from the patients, to later be used by the evaluators of the cases. The platform offers different functionalities according to the role that the user has. The administrator will be able to register medical centers that use the platform, add patients and register and manage active medical users; the technician or examiner will open the study cases associated with each patient and send them for her evaluation; and finally, the evaluator will make use of the data and images acquired by the examiner to study the case and diagnose if there are signs of pathologies.

A. Results of the web application

Machine learning has been referred to on numerous occasions as belonging to the framework of Artificial Intelligence (AI) technologies. This has been the term used by simplicity in the web application to refer to this technology, so from now on the document will refer to this concept in the same way.

4.1.1 Login

The welcome screen appears as Login page (Figure 4).

Fig. 4. Welcome screen

The first view that will be had when starting the platform is the welcome view, and this will give access to the registration form for the user (Figure 5).

Fig. 5. User registration

In case the user has forgotten his password, he can request via e-mail the sending of a form to choose a new one, activating the Forgot your password? button. This request will be feasible as long as the user is not blocked**.**

B. Login as administrator user

The first page users have access to is the one shown below, which is common for all and only differs in the dropdown options menu located at the top right of the screen. This menu contains the options that the user can access, and they will be different depending on the skills they have (Figure 6).

Fig. 6. Home view for the administrator user

After saving the data of the created user, the platform will automatically send an email to the user to complete the registration process. The image shown below contains the view corresponding to the edit form of a user already created. It is important to highlight the Send restore password link option located in the upper right corner of the screen. With this option, the administrator will allow the user to reactivate his account if he has been blocked by the application, sending the platform an email with the corresponding form. In the two situations mentioned in this point, the form of the emails and the structure of the forms sent are very similar to those already seen in the Login section of this work. If the administrator clicks the

Medical Centers option in their dropdown menu, they will be redirected to the list of registered medical centers in the application. Both patients and medical users registered on the platform will belong to a medical center. From this view, the administrator can introduce a new center by clicking on the Create button, or edit the data of an existing center by clicking on the edit button for each item. If the administrator clicks the Contact option in the dropdown menu, they will be able to see the contact details of the administrative staff of the platform, as well as a map with the location. On the other hand, from My Profile you will access the view shown below, where the user can add or change the personal data associated with their profile. These options will also be available to medical users. Finally, the option Patients from the menu will give access to the list of patients registered on the platform. From this view, the administrator can create a new patient associated with a specific medical center, edit the data of an existing patient or view the studies associated with this patient. The table can be sorted in alphanumeric order according to the data in the Patient ID and Registration Date columns. The administrator will be able to visualize the studies created by any of the technical users, regardless of their status: pending sending to evaluation, in evaluation or closed, but he will not be able to modify no data on these. Only technical users will be able to edit the data of the studies to which the administrator has access.

C. Login as technical user or examiner

The technical user, or examiner, will have access to the menu options shown at the top right of the following image (Figure 7). The menu option Studies will allow the user to access a list with all the studies created, either saved without sending, sent or closed, for which he is responsible. On the other hand, if the user clicks on Patients, they will access the same list of patients as the one shown with the administrator. From this you will be able to obtain the list of studies associated with each patient, and you will be allowed to create, edit new studies, and view the closed studies with the results of the evaluations. The previous images show the form for creating a new study and the result of pressing the option to save the data. The fields marked with an asterisk are required fields for the application to send the study to the evaluator. In addition, in order to send the form for evaluation it is necessary to have uploaded at least one test image. In the event that some mandatory field is missing or that no test file has been inserted, it will give an error in the form and mark these fields in red or indicate the problem in a message, retrieving the data you had already selected so you don't have to start over using the session.

Fig. 7. Home view for the technical user

However, the user always has the possibility of saving the form to continue editing it later without having to enter all the mandatory data. Whether this option is selected or the form is sent for evaluation, the written fields and the test fields will be stored in the database used by the platform, associated with the created study, for later be retrieved by the evaluator or by the user himself if he wishes to edit or view them. Next, the form for the edition of the study that has previously been given as an example is shown. This form is the same both in the case that the study is pending completion and in the case that it has been sent for evaluation and the result is pending. Once the study is sent to the evaluator, it can be edited but not deleted. To end this section, captures from the example study are added after the evaluation process has been completed. The next section will cover the results of this process in detail.

D. Login as evaluator user

The evaluator will have access to the options from the drop-down menu shown in the following image (Figure 8).

Fig. 8. Home view for the evaluator user

If the user clicks on the Studies option, they will be redirected to the list with the evaluations assigned to them, whether in pending status, in the evaluation process, or completed (Figure 9). The different sections of the evaluation are drop-down, as in the studies, for greater user convenience. Below are the sectional assessment forms for an example assessment created. All selectable fields are required to close the case. However, and in the same way that occurred in the creation of the studies, the evaluator can save the evaluation in progress to continue editing it later, without having to write all these fields. The data will be temporarily stored in the session, and if the study is saved or closed, they are stored or updated in the database, associated with the corresponding evaluation.

Fig. 9. Section with the patient's clinical data, acquired by the technical user.

In the Tests section, the evaluator will be able to browse the different images uploaded, and in the event that there is an image of the eye fundus among them, they will be able to access the results of the classification automatically performed by the AI independently for each case. This can be done by clicking on the icon available for it, and a pop-up window will open that will show these results, as well as an image generated from qualitative information obtained by the network. From this window the user will be able to download the image by pressing the Download option enabled for it. AI results for Test 1 (Figure 10) and AI results for Test 2 (Figure 11).

Fig. 10. Evaluation form for Test 1 uploaded as an example.

Fig. 11. Evaluation form for Test 2 uploaded as an example.

The Global Assessment section will consist of a section for each case of analysis desired in the screening process (Fig. 12). The platform currently covers only the case of Glaucoma, but it is prepared to be able to add more pathological cases in the future if so desired.

Finally, the visualization of the study is shown for the evaluator user, once the evaluation has been completed and the case has been closed (Fig. 13).

VII. RESULTS OF THE REST API SERVER FOR THE DEEP LEARNING MODEL

This section shows an example of the operation of the REST API server that contains the Deep Learning model. The Python script used by the platform to make requests to the server has been executed in a user terminal. This script runs on the client side and needs two arguments:

The script sends the images to the server as a POST request. The server returns a response to each REST request in the form of a JSON dictionary. This object contains four messages: first, a confirmation message; second, the result of the prediction associated with the image sent as a key, which is displayed as output on the terminal; third, a numeric array containing the RGB values of the preprocessed input image; and finally, the qualitative information in the form of a numerical matrix. The client-side script gets an image in the form of heat map associated with the qualitative information, and stores it in the path added as an argument to the script, along with the original image, preprocessed by the server and reconstructed on the client side from the received RGB matrix.

A. BitScreen OPH Database Model

As already mentioned in the Planning and work phases section of Work 3, the database model used in the application has been fully inherited from the BitScreen Master platform, in turn based on in the model used by BitScreen PTB with the addition of five more tables due to the use of the Oauth2 package for sending mail. Only the oauth access tokens table of the new ones created will be used to store the tokens generated with the emails sent to the user. In this way, the structuring of the BitScreen OPH database consists of the relational use of 15 tables.

B. Test plan

The test plan carried out has been divided into two blocks: On the one hand, it has been proven that the web application meets the functional requirements and does not present technical failures. On the other hand, the Deep Learning model has been tested on a set of test images, which have not been used in the network training phase, and its behavior has been evaluated from the obtaining of the sensitivity and specificity parameters of the system.

C. Table of tests carried out for the application

It is shown in Table 2.

Table 2. Tests carried out for the application

Test performed	Outcome
If an examiner submits a study for assessment, but some required requirement is missing, the platform does not submit it and issues an error message	Yes
In the event of an error, the written study data is restored from the session	Yes
Study data successfully saved and retrieved from the database	Yes
After a study is submitted for evaluation, the AI results are stored in a database	Yes
After a study is submitted for evaluation, quality information images are stored in the same directory as the test images	Yes
The evaluator has access to the studies assigned to him for evaluation	Yes
The evaluator can run and edit studies, and view closed studies	
The evaluator has access to uploaded clinical data from patients in studies	Yes
Estimator has access to AI classification results	Yes
The assessor can view and download test images uploaded by the examiner	
The estimator can view and download images with AI quality information	Yes
The estimator can save an unfinished valuation without filling in the required fields	Yes
Assessment data is correctly stored and retrieved from the database	Yes
When an evaluator closes a study, the evaluator considers it closed and can access the evaluation results	Yes`

Users can access and modify their profile information	Yes

D. Testing the Deep Learning model on a test data set

To evaluate the behavior of the model and compare its precision in the results with the success rate of medical specialists, the model has been applied on a set of 66 test images, which have not been used in the tests. phases of training or validation of the network. The model classifies the results into two distinct classes: the class 0 which represents that the analyzed image is "normal" (there is no glaucoma) and class 1 which represents "glaucoma suspicion". The network represents the predicted result with two numerical scores, the first with the probability that the image belongs to class 0 and the second with the probability that it belongs to class 1. To simplify the result of the network, it is usually establish a threshold or comparison threshold with the second score, in such a way that if the score is greater than the threshold the result of the image classification is established as '1' and if it is less it is established as ' 0'. Thus, we have four possible outcomes [26]:

True positive (TP): if both the image reference value and the predicted classification result are '1'.

True Negative (TN): If both the reference value and the predicted result are '0'.

• False positive (FP): if the reference value is '0' and the predicted result is '1'.

• False negative (FN): if the reference value is '1' and the predicted result is '0'.

Finally, from these values, the parameters of sensitivity and specificity of the network have been calculated. Sensitivity represents the percentage of “positive” cases correctly classified by the network, and specificity shows the percentage of “normal” cases correctly classified. The parameters obtained for our model are shown below.

Sensitivity =TP/ (TN + FP) = 91.2% (1)

Specificity = TN/ (TN + FP) = 99.8% (2)

Table 3. Comparison of Proposed method with other methods

Methods	**Classifier**	**Acc**	**sp**	**sn**
[38]	N.B.	92.65	90.03	92.00
[39]	SVM	90.98	91.63	91.32
[40]	SVM	94.11	90	100
[45]	SVM	90.14	85.66	94.30
[47]	k-NN	94.75	100	90.91
[30]	LS-SVM	94.79	95.88	93.62
[48]	Fuzzy logic	90.15	94.80	97.80
[49]	RF	96.05	95.32	96.29
[50]	SVM	98.63	97.60	92.30
[51]	SVM	99.30	99.40	96.90
Proposed	CNN	99.42	91.2	99.8

VIII CONCLUSIONS

The work consisted of developing and implementing a telemedicine tool for the early detection of glaucoma, integrating a deep learning model that helps medical professionals diagnose this pathology from fundus images. In conclusion, the contribution that this work can make to glaucoma screening processes is enormous. On the one hand, it allows healthcare professionals to evaluate case studies remotely, be able to serve populations in remote locations, and manage a large number of cases. In addition, since it is a telemedicine platform, it provides the functionality presented by these methods, which are increasingly used, such as efficient data classification and organization, which is very important for the work of doctors, as well as material and environmental costs savings through the use of digital resources. On the other hand, an application-integrated detection assistance system can be of great help to specialists in their assessment of studies, and with it, in a deeper analysis of patient cases, the results of which can be crucial for the early treatment of glaucoma upon detection of this pathology.

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