

Although previous scientific work devoted to this topic already exists, it is scarce at a national level, and it tends to resort to small datasets, limiting the applicability of its results. Hence, the main advantage of this project is the partnership with IPO Porto – Portugal's largest oncological hospital, and one of the largest in Europe –, which allowed obtaining over 10 years of duly protected medical records, containing information about over 795 808 unique patients and 7 791 918 clinical episodes, and with 2000 records created or updated on a daily basis. As a contribution to society, we expect the methods developed in the context of this project to be able to help healthcare professionals in the decision-making process, thus exploring the potential of the clinical experience of IPO Porto, and assisting decision making with specific recommendations and guidelines for each patient. Among many other possible applications, this tool can assist in performing patient stratification according to the risk of relapsing, developing metastases or undergoing a certain treatment or intervention, and reduce the need for invasive exploratory procedures.

By being based on all relevant information and providing up-to-date recommendations – that is, according to the most recent and scientifically validated oncological techniques – this tool will have the potential to avoid unnecessary expenses by significantly reducing the number of misdiagnoses and misprescriptions, to reduce the workload suffered by clinicians and even detect subtle markers that might not typically be considered by physicians. The products of this work can also be transferred to other oncological facilities, as well as to generalist hospitals with medical oncology services, national and international, which will encourage sharing practices between centers and facilitate future cancer research.

Finally, and despite all the efficiency gains, this tool can be translated into faster and more accurate diagnoses, personalized treatments according to the patient's biological characteristics and his/her specific cancer, a better understanding of his/her diagnosis and therapeutic options, and better health care for the population as a whole.

ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

ARTIFICIAL INTELLIGENCE AND THE SCREENING OF DIABETIC RETINOPATHY

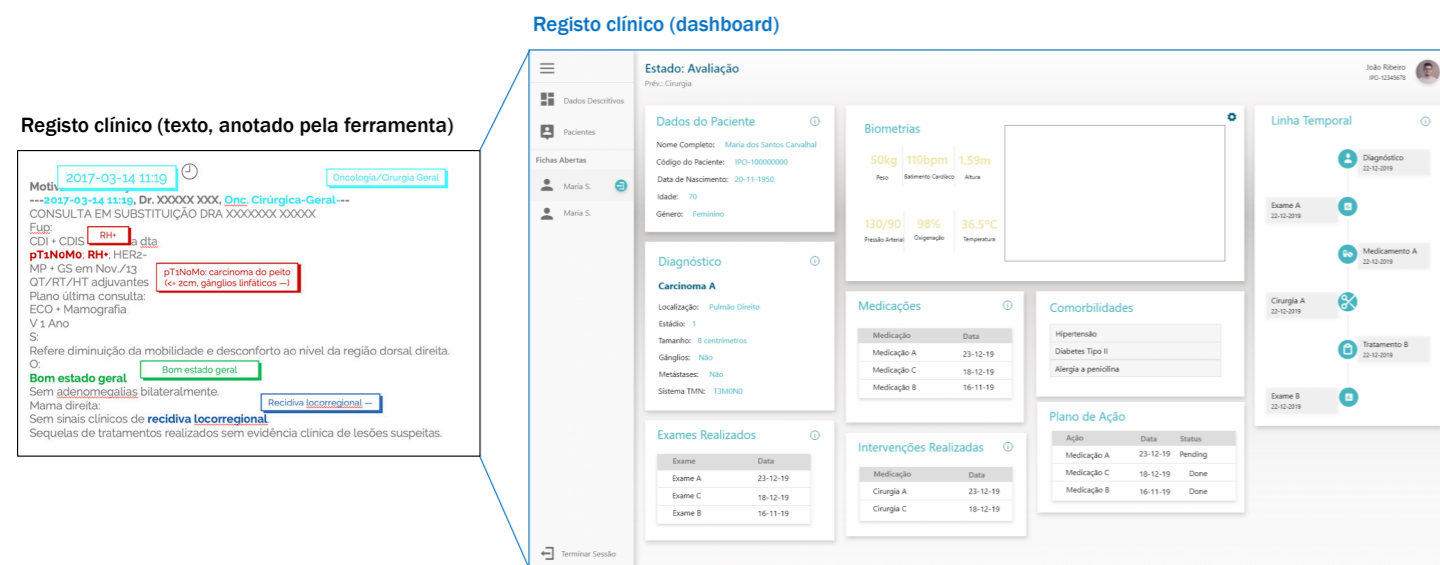


Figure 1. Example of the extraction of structured data to be used for building dashboards.

Artificial Intelligence can be useful in scenarios where skill labour fails to meet needs. This article describes the challenges and solutions found to face the diagnosis of diabetic retinopathy considering the increasing prevalence of diabetes in the Portuguese population.

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The diabetes and the diabetic retinopathy

Diabetes is a metabolic disease characterized by the presence of high levels of glucose in the blood over long periods of time. It is one of the diseases with the highest growth rates, affecting over 415 million people worldwide. Recent estimations point out that by 2040 there will be over 642 million people affected by such diseases. Portugal has one of the highest prevalence rates of diabetes among European countries, with 13.3% of Portuguese people aged between 20 and 79 years old having diabetes, which corresponds to more than 1 million people.

Diabetic retinopathy (DR) is a complication of diabetes, which affects more than 25% of the diabetic population, and which is characterized by damage to the blood vessels in the retina (layer of the eye where the images we see are formed). It is a silent pathology that gradually decreases the patients' visual acuity, being the main cause of blindness in the working age population. However, it can be successfully treated if diagnosed at an early stage. Current DR screenings implemented across the country are essential to identify cases of this disease in a timely manner and prevent its progression.

Screening for diabetic retinopathy

During the screening of DR, photographs of the fundus of the patient's eyes are captured. The procedure is noninvasive and, since the eyes are windows to the body, such photographs allow a direct observation of the blood vessels and the detection of diseases such as DR. The diagnosis of DR is made by detecting various lesions in the retina, such as microaneurysms, hemorrhages, exudates and neovessels (Figure 1). The diagnosis of DR is made by detecting various lesions in the retina, such as microaneurysms, hemorrhages, exudates and neovessels (Figure 1). Depending on the presence and number of different types of lesions, a degree of severity of DR can be associated with the patient.

Annually, an appreciable portion of the diabetic population is examined in primary health care units. In the north of Portugal, the Northern Regional Health Administration (ARSN) is the entity responsible for managing and implementing the DR screening process. The acquired images (retinographies) are stored in the ARSN archive, being the first medical decision taken at the Reading Center, where ophthalmologists analyze the retinography and conclude about their normality. If the retinography is normal, a re-screening of the patient is recommended after one year. If it is abnormal, the ophthalmologist determines the severity of the condition and the patient is referred for treatment. Current screening practice implies that ophthalmologists at the Reading Center analyze all images, including those of poor quality, impossible to diagnose, and images without signs of pathology, which represent about 80% of the total number of acquired images.

The SCREEN-DR platform: Artificial Intelligence for diagnosing DR

O aumento da prevalência de diabetes coloca alguns desafios aos processos de rastreio da RD visto que têm de estar preparados para acomodar uma população em constante crescimento. Para ajudar os oftalmologistas neste processo, automatizando parte dele e reduzindo a carga de trabalho dos especialistas e a subjetividade do diagnóstico de RD, o INESC TEC desenvolveu a plataforma SCREEN-DR (Figura 2).

The increase in the prevalence of diabetes poses some challenges to the screening processes for DR since they have to be prepared to accommodate a constantly growing population. To help ophthalmologists in this process, automating part of the process, thus reducing the workload of specialists and the subjectivity of RD diagnosis, INESC TEC developed the SCREEN-DR platform (Figure 2).

SCREEN-DR offers two advanced artificial intelligence (AI) solutions: one for the evaluation of image quality (EyeQualDR) and another for the detection of normality (EyeDetectDR). Besides this, a tool that allows to classify pathological images according to the DR severity is provided (EyeCadDR). This tool assists the ophthalmologist in the decision making, working as a second opinion.

When the acquired images display insufficient quality, EyeQualDR advises the technician to perform a new image capture. By its turn, the good quality images are stored in the ARSN and processed by EyeDetectDR, which distinguishes normal from pathological images.

The pathological images are classified a posteriori by an ophthalmologist, with the help of EyeCadDR. By removing from the pool of images to analyse the ones that correspond to non-pathological situations, the SCREEN-DR platform makes the screening and diagnosis process more efficient.

The advances in the AI area, namely in Deep Learning techniques, allowed to obtain truly promising results in the automatic diagnosis of medical images. These techniques "learn", like humans, through experience and trial and error. For that, the algorithm observes a large quantity of ophthalmological exams with the respective medical diagnosis. The algorithm tries to imitate the specialist's decision, learning to identify the patterns in the images which are signs of pathology.

Following these approaches, it was possible to obtain a system capable of identifying simultaneously which images have enough quality for diagnosis and, from these, which should be forwarded to a medical doctor since they show signs of DR. This system learned from a large quantity of past screening data performed by ARSN, contemplating images from a large variety of patients and acquired by different machines, allowing the algorithm to obtain a quite complete experience.

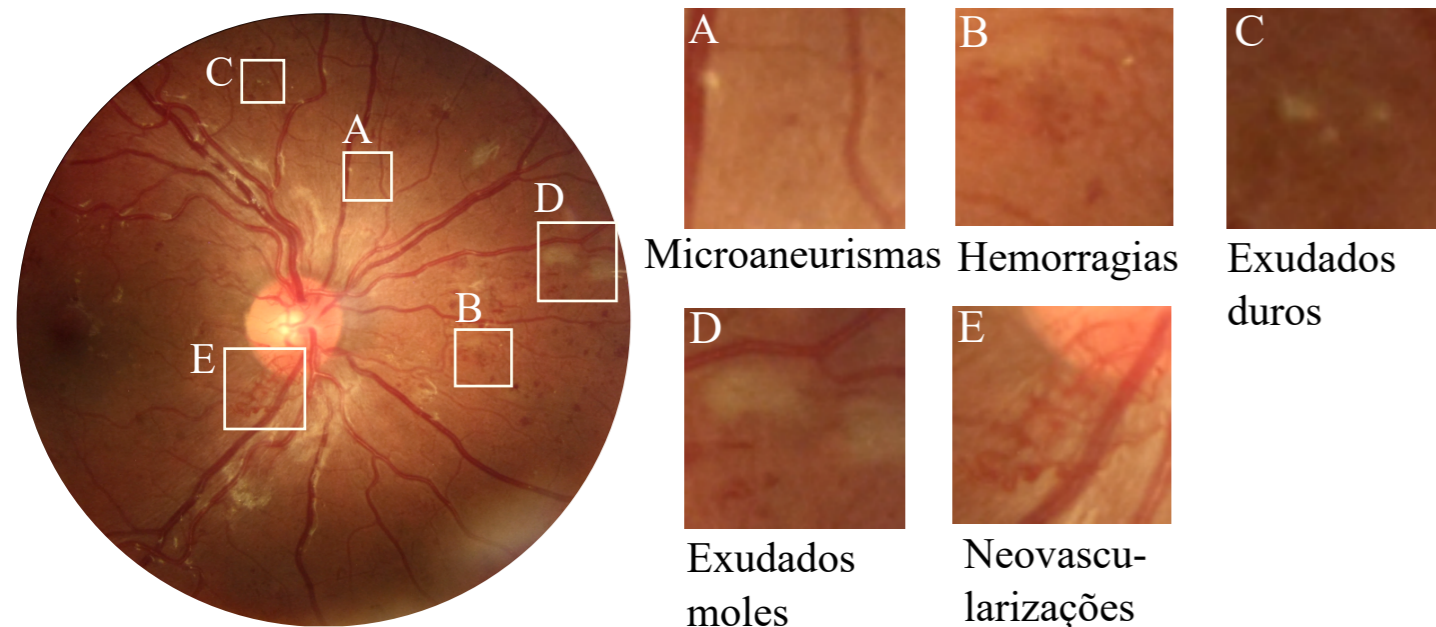


Figure 1 - Most common lesions associated with diabetic retinopathy found in the fundus photographs. Image taken from <https://doi.org/10.1016/j.media.2020.101715>.

Intuitively, the more experience a medical doctor has, potentially more accurate will be his decisions, and the same logic may be applied to this type of IA techniques. The solution proposed for the grading of the severity of the disease allows to obtain a DR grade, an explanation associated with the grade and an uncertainty of the diagnosis. This system was trained solely with the eye fundus images and the associated DR grade, attributed by the ophthalmologists. The association of an uncertainty to the system's prediction is of special relevance in computer assisted diagnosis, since it allows to establish which are the cases that need additional analysis by specialists. The explanation of the system's decision through the highlighting of the image regions which contributed the most for that decision allows to mitigate the "black-box" (term commonly used for a system that allows the access to the input and output, without any access to the inner information) behaviour associated with deep neural networks, which commonly

hinders the adoption of these automatic systems in clinical contexts. To evaluate this solution, the predictions of the AI systems were compared with the diagnosis from several medical doctors in past exams. We verified that the system is capable of identifying patients that need treatment with a level of reliability similar to the medical doctors, disagreeing with the specialists to the same degree in which they disagree between themselves. Additionally, as the system utilizes data generated during DR screening, it can continue to improve as more exams are performed. These results suggest that the implementation of this system in the process of DR screening could reduce the number of exams that the specialists need to analyse, allowing them to spend more time in the treatment of the most severe cases. Considering that only around 10% of the screened patients require treatment, this system could reduce in,

potentially, 90% the number of cases that the specialists need to analyse. Systems like this are of special importance to ensure that the DR screenings continue to be viable in the future, since our diabetic population is in constant growth. The final goal is to save the sight of the largest number of people possible, ensuring that they can maintain their jobs, which translates in economic benefits to the country but, more importantly, allowing them to maintain their quality of life. The ophthalmologists who collaborated during the development of this project consider that "the implementation of the SCREEN-DR project, which aims at optimizing and simplifying the diagnosis and identification of at risk DR patients, through screening solutions using AI techniques, could have a very positive impact in the quality of life of several diabetic patients. Software like this greatly facilitate the medical doctors' task of identifying at early stages a greater number of patients at risk, thus accelerating their access to treatment."

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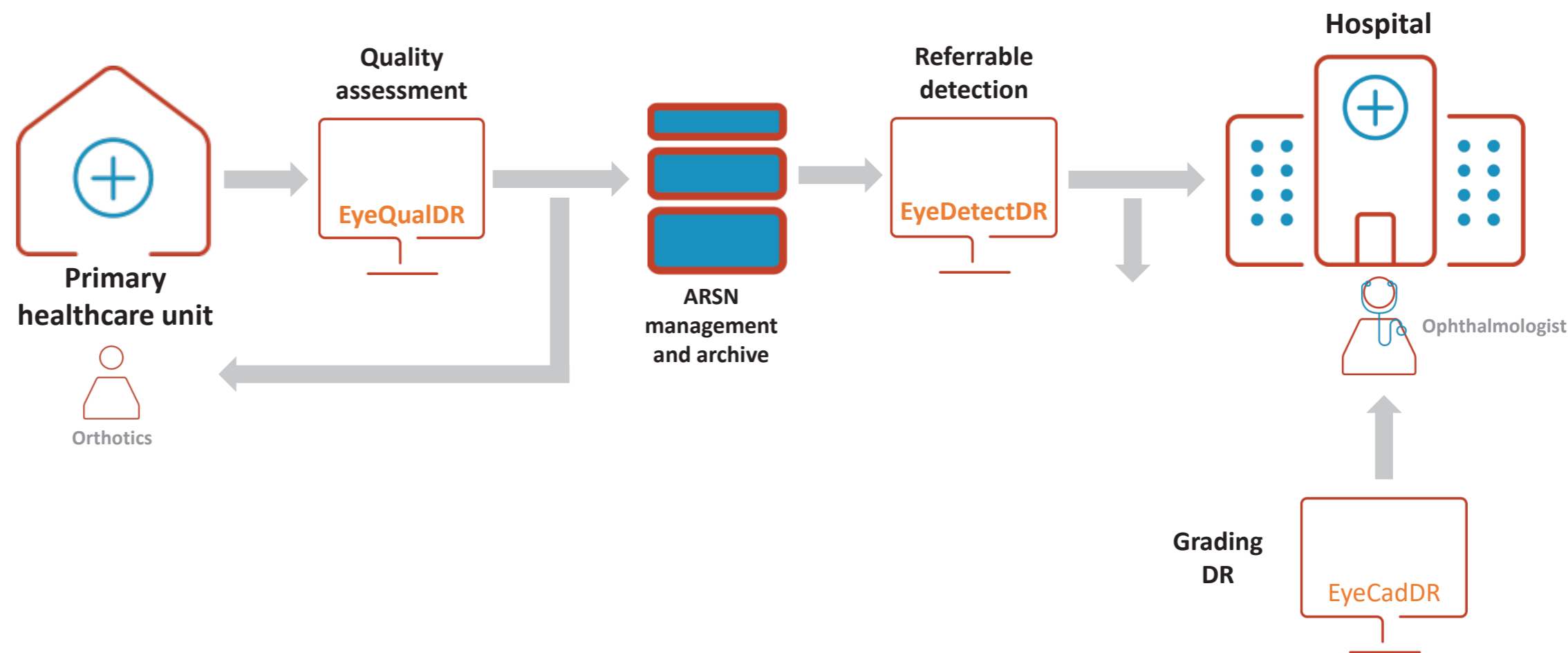


Figure 2 - SCREEN-DR platform for the diagnosis of diabetic retinopathy.