Steps Towards Intelligent Diabetic Foot Ulcer Follow-up based on Deep Learning

António Chaves[0000−0002−2449−2658], Regina Sousa[0000−0002−2988−196X], António Abelha[0000−0001−6457−0756] and Hugo Peixoto[0000−0003−3957−2121]

ALGORITMI/LASI, University of Minho, Braga, Portugal
antonio.chaves@algoritmi.uminho.pt, regina.sousa@algoritmi.uminho.pt, abelha@di.uminho.pt, hpeixoto@di.uminho.pt

Abstract. Diabetes is a chronic disease that affects the effective production of insulin in an individual. This incapacity leads to great damage to the cardiovascular system as well as the nervous system. Unfortunately this is a very present disease in today's population. Indeed, global diabetes prevalence is estimated to be between 9,5% and 10,5%. Diabetic patients have a need for constant monitoring and evaluation by the healthcare professional whenever diabetic foot wounds show symptoms of infection and ulceration. The high number of patients with this diagnosis makes follow-up a problem for health professionals as well as for the patient. Lack of communication and access to health care are major contributing factors to lower extremity amputations, high mortality and morbidity interventions. In order to solve this gap, the present work presents an architecture for the development of a collaborative and decision support tool, between not only health professionals but also patients, capable of rapidly and automatically identifying, assessing and treating ulcer and symptoms of the pathology. This automation will be implemented through classification models with Deep Learning.

Keywords: Diabetes, Computer Aided Diagnosis, Deep Learning, Ulcer Classification, Application Development

1 Introduction and Contextualization

Diabetes, a chronic disease that appears when the pancreas does not efficiently produce insulin or when the body is unable to utilize the insulin produced. Insulin is a hormone that deals with the regulation of blood sugar, and when uncontrolled for any reason it gives rise to an event of hyperglycemia (increased blood sugar). This is one of the most common effects of uncontrolled diabetes and over time leads to major damage to the cardiovascular system as well as the nervous system [1, 2].

The classification of this pathology is divided into two types: Type 1 Diabetes and Type 2 Diabetes. Type 1 diabetes is associated with a deficit in insulin production and is treated by the daily administration of insulin to the body. Symptoms that may appear include excessive urine excretion, thirst, constant hunger, weight loss, vision changes, and fatigue. These symptoms can occur suddenly or not at all [3]. Type 2 diabetes, on the other hand, is associated with the inefficient use of insulin produced by the body. A large proportion of diabetes diagnoses are related to type 2 [4]. These are more easily identifiable because the patients complain a lot of body weight gain. For both types early diagnosis can be made through affordable tests that calculate blood sugar levels [5]. The treatment of diabetes involves diet and physical activity along with lowering blood glucose and the levels of other known risk factors that damage blood vessels [6].

According to the world health organization the treatment of diabetes should include blood sugar control, for example with oral medication, blood pressure control, screening and treatment of retinopathy (which causes blindness), blood lipid control, and not least foot care. This last point is one of the most important since Diabetic Foot Ulcers (DFU) are one of the most common occurrences in diabetic patients due to lower limb nerve damage and reduced blood flow in the area. To this end, patients should maintain patient self-care by maintaining foot hygiene, seek professional care for ulcer management, and have their feet examined regularly by healthcare professionals [2]. In this way Lower Extremity Amputations (LEA), which itself is associated with high morbidity and mortality in patients, may be decreased. In order to minimize the risk of LEA, careful and thorough monitoring of the lower limbs is necessary [7].

The main objectives of this study are the understanding of Artificial Intelligence implementations capable of supporting decision making and analyzing images related to possible DFU complications. Primarily, the concerning topics surrounding the matter will be explained, as well as the supporting evidence for the importance of the present study, followed by a state of the art review on architecture and neural network models chosen across different implementations. Lastly, the present work will present a proposed architecture for developing a tool for implementing a Decision Support System (DSS) capable of reviewing images submitted by DFU users.

2 Background

To achieve greater knowledge over the topic covered hereby, it is of great importance to understand some major topics, that this manuscript covers. First, diabetes and wound classification importance and struggles, making decision support systems an important step to achieve more efficient patient treatments. One of the most up to date technologies applied in the healthcare domain is Machine and Deep Learning and more specifically CNN.

2.1 Diabetes and Wound Classification

Diabetes is a chronic illness which, over time, leads to major damage to the body's cardiovascular and nervous system and is estimated to have been the direct cause of death of 6.7 million people in 2021, making it one of the top

10 leading causes of death in adults worldwide. Global diabetes prevalence is estimated to be between 9,5% and 10,5% of the population which amounts to 500 million cases, a number which has been steadily growing for the past two decades [8, 9].

Severe cardiovascular and nervous damage on a patient's body can result in poor wound healing, especially when present in the body's extremities. The detection of DFUs is usually a time consuming process done by experts and its correct classification and early detection detrimental in the reduction of LEA, which increase morbidity and mortality among diabetic patients.

2.2 Clinical Decision Support Systems

Clinical decision support systems (CDSS) are computerized frameworks implemented in order to improve healthcare delivery by enhancing medical decisions. To achieve this goal, the CDSS uses clinical knowledge that is built into the system which is used to analyze and explore data in order to discover patterns that may be useful for decision making, through Machine and Deep Learning techniques [10].

2.3 Deep Learning

Deep Learning is a subset of Machine Learning - and consequently Artificial Intelligence - aimed at automatically learning from knowledge without being explicitly programmed [11]. It differentiates itself from traditional ML techniques by applying successive layers of representation, often called Neural Networks, term derived from human physiology due to the similarity to our understanding of the brain. [12] The interest in Deep Learning has been continuously growing due to its success in Natural Language Processing and Image Recognition tasks, among others [13].

Up until 2012, Machine Learning algorithms made up most of the modern era solutions in the implementation of image recognition in computer vision. This was due to the fact that training Deep Learning methods was deemed complex and time consuming task and needed very large input quantities and computing power [14]. in its study and contribution to an image classification competition and the astonishing results obtained shifted the attention to the use of Convolutional Neural Networks for the task. The author proves at the time that CNN can set record breaking metrics in image recognition and some ground truth needs for the success of the implementation of such methodology. First and foremost, Deep Learning models must be trained with large scale datasets. The specificity of some image recognition tasks - as is the reviewed DFU classification problem - and the lack of quality datasets may impose early constraints to a models classification success rate. In order to minimize this issue, and to prevent the occurring of over-fitting issues, two techniques are usually employed. The first, Data Augmentation, is a simple task of converting each image in a dataset by applying a range of operations, such as rotation, pixel shifting and crop, to artificially increase the sampling size. This process can be automatically generated and is usually computationally inexpensive. The second relies on the use of pre-trained models, which should already be able to classify some image properties before being fine-tuned, so that further training may be focused solely the specific features on the classification task.

2.4 Convolutional Neural Networks

Convolutional Neural Networks are a subset Artificial Neural Networks, making use of the same neuronal architecture in order to self-optimize through learning. The main differences between CNN and ANN are the stacked layers that form the model, and their application to pattern recognition in images. The recognition of simpler defining aspects of images and their inclusion in the architecture allow for more precise image recognition tasks requiring fewer parameters for a correct model setup. CNNs are composed of three different types of layers: convolution, pooling and fully connected (FCL) layers. The first two serve the purpose of feature extraction, while FCL maps the outputs generated by the former into a result such as classification [15, 16].

3 State of the Art

The prevalence of diabetes worldwide, along with technological progress and computer aided diagnosis have resulted in new viewpoints to help aid segmentation and classification in diabetic foot ulcers.

The use of Neural Networks comes as a successor to more traditional computer vision and machine learning methods. More specifically, Convolutional Neural Networks have been directly associated with image recognition tasks [17] and are the most common subject of research within the realm of automatic DFU diagnosis. Recent research in the subject can be highlighted in three categories: wound segmentation and classification algorithms and architectural design for implementation of related applications.

The authors in [18, 19] respectively propose architectures based on the MobileNetV2 and MobileNet Convolutional Neural Networks for wound segmentation which substitute convolutional layers with depth-wise separable convolutional layers. It exponentially decreases computational cost compared to the traditional convolutional layers and suitable for applications where computing resources are limited with no observable trade-off in final results.

[20, 21] utilize Encoder-Decoder based CNN models in their research, achieving state of the art scores in wound region mapping (Intersection over union and Data-based Dice). This NN architecture are mostly implemented due to their capability in data dimensionality reduction, noise suppression and data reconstruction. [22] Both studies make use of controlled images even though they differ in image quality sampling techniques. The first proposed the preprocessing of images by applying several augmentation techniques in the datasets supplied for model training while the second physically places a ruler with color markup in order to normalize color and enhance the precision of wound depth calculations.

While this may defeat the purpose of implementing a telemedicine application due to the controlled nature of image capture required, it shifts some attention to wound depth and size calculations, which may be difficult to infer, especially when keeping track of multiple stages of the same wound.

[23] proposes a binary classification method for DFU segmentation based on traditional CNN layers, with an AUC performance at 96%. The architecture of this method is split into three main sections, namely traditional GoogLeNet layers for cropping images of skin patching and normalization before transferring them to parallel convolutional layers for multi-level feature extraction followed by fully connected layers and a SoftMax-based output classifier.

Although not reporting the best metrics in reviewed literature, [24] offers good insight on a possible architecture for a fully working mobile platform consisting of a web application and a dedicated server for image processing and classification. Furthermore, the developed Multi-Label CNN Ensemble can classify most complications related to DFU such as infections and exudate.

4 Results

This study's goals can be divided into two main categories: an interoperable telemedicine application aimed at enhancing patient-doctor approximation, for rapid diagnosis of severe diabetic complications and a DFU segmentation framework based on Deep Learning, for rapid wound classification and medical decision support. As per noticed in reviewed literature, the implementation of a production ready system for DFU classification still faces the major problem of dataset suitability.

Model training requires a vast amount of records to be able to correctly serve its purpose. Most datasets observed in reviewed studies were imbalanced and lacked dimension and even when applying artificial augmentation were still far from desired proportions. These must also be backed by a manual classification done by professionals, a time-consuming task which requires cooperation from specialized DFU physicians. The heterogeneity of image capture devices will also impose a challenge to the model's classification prediction. Different devices, illumination settings and camera angles are all external factors to take into consideration.

Lastly, the implementation of the system is dependent on the patients' ownership of a smartphone or tablet device and its availability to run on different types of operating systems.

4.1 Proposed Architecture

The architecture proposition was based on [24] and [25] and is comprised of the following components:

- **Data Sources:** Different sources for data gathering for model training and testing;

- **Deep Learning Algorithm:** A Deep Learning Model capable of classifying submitted images of DFU, obtained from the optimization of a selected pre-trained algorithm;
- **Database:** Database for information storage. With patient permission, stored images may be supplied into the Deep Learning Model for further training and improvement on recognition tasks;
- **Back-end Server:** The architecture's business layer, a server for application login management and request routing;
- **Mobile Application:** Intended for patient's use, this part of the presentation layer should allow for image capture and submission as well as over time tracking of personal information and medical advice;
- **Web Application:** Management tool for physicians which allows them to review patient submitted images, along with the automatically generated classification and access to patient history.

The following figure 1 presents the applications components and their interactions.

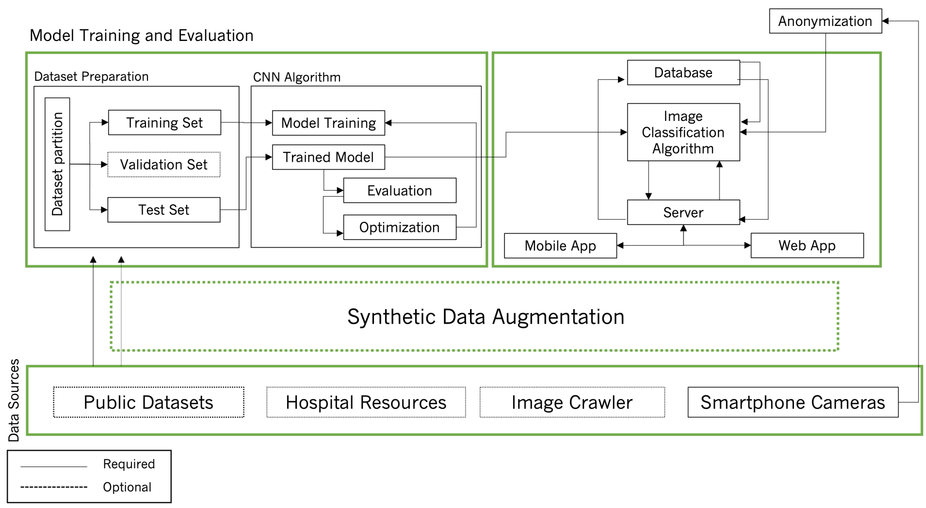

Fig. 1. Proposed architecture.

In order for a complete sample gathering of data, the combination of multiple data sources is optimal, so long as the dataset's content is balanced. The combined data gathered through public datasets and partner hospitals' own image databases can be run through an automatic Synthetic Data creation process so that the initial training and test data sample can be artificially increased. Healthcare facilities' data sources, which collect data for every patient making it a powerful tool in decision making, [26] can be an empowering factor in the image classification accuracy, in part due to their complete manual labelling and the opportunity to corroborate DFU with other types diagnosis. For example, DFU infections are usually difficult to diagnose without the support of specific blood tests.

This sample is then split in three subsets, for model training, validation and testing. The model's training process is recurrent until the error margin in testing images is deemed sufficient. The computational power required for a full training of DL architectures as well as the impact of the images' diverse characteristics can be diminished through the adoption of a pre-trained network, such as ImageNet, which allow an increase of the more specific local learning rate [27].

As is suggested, the architecture's back-end server is the core structure of the application and has a significant importance in request handling, database access, authentication and security. The application's end goal architecture relies on the centralized deployment of the back-end server and classification algorithm and, as such, the idea of a micro service implementation arises. This decision needs to be assessed before implementation and its analysis is substantially reliant on the amount of potential healthcare partners and patients. While scalability must be addressed, a monolithic architecture may be in order if survey data shows the number of potential users not to be a deciding factor also maintaining a lower relative computational cost and averaging faster response times. [28]

The heterogeneity of nowadays users' devices implicitly guides the development of the mobile application into cross-platform ready development frameworks. The excessive cost of native development does not compensate for the drawbacks of cross platform such as limited access to functionality - as long as smartphone camera access is granted - and poorer performance.

User submitted images, gathered directly from personal devices, are sent for classification purposes through the designated Back-end Server routes. Their response should be quickly presented to the user and stored for user history and comparison. An important aspect of user images is their usefulness for further model training although subject to user permission for personal image use.

5 Discussion

The suggested architecture is based on [24]'s contribution, however, the suggestion of a embedded DL model within the Mobile Application, seems to be far from desired, especially taking into consideration modern era smartphone processing power. The trade off between performance metrics when comparing computer and smartphone systems is still noticeable [29] and should only be considered as a last resort for implementation. The pinpointed advantages of the embedded model such as offline usability and better responsiveness when compared to the use of an internet connection are still far outweighed by a 10% drop off in performance metrics.

The improvement of the models classification should be done through data augmentation and transfer learning techniques and further fine tuning by adding user submitted images to the training dataset, not only increasing its size but also in the anticipation of shaping the models capability of DFU identification, diminishing the aforementioned external factors' influence. If training data is still deemed insufficient or having an unbalanced distribution, the combination of different datasets can be set in place. The concept of dataset merging for training in segmentation networks proves NN performance can be boosted and thus provide better results [30, 31].

On another note, the application's success is also highly dependent on its adoption from healthcare services and patients alike as recent cybersecurity issues can be have detrimental social impact and consumer trust.

6 Conclusions

Diabetes is undoubtedly one of the most common diseases in developed countries, and lower limb nerve damage, due to low blood flow in such areas, can lead to severe complications such as DFU. Being a chronic disease, contributions to long term treatment, prevention, patient follow-up as well as better and more reliable treatment decisions are of great importance. In this study a framework for the implementation of a fully interoperable application capable of automatic DFU classification for rapid assessment is proposed. Indeed, this architecture has the potential to shift the paradigm of the treatment of severe diabetic complications, with an end goal of improving patients' lives. Main contributions vary from recognizing the main obstacles towards implementation to provide adequate solutions for these issues. Furthermore, the proposed architecture paves the way for the fulfillment of the DL model's training and optimization. It's design is scalable and modular, proposing a cross-platform framework with web and mobile capabilities settled in incremental development and overall usability.

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