Machine Learning for Salivary Gland Ultrasound Scoring

Section 304

Product Design Specifications

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Background

Sjögren's syndrome (SjS) is a systemic autoimmune disease (SAD) that causes the dysfunction of the exocrine glands (mainly the salivary and lacrimal glands) with patients often showing persistent dryness of the mouth and eyes [1, 2]. According to estimations, two to four million people in the United States have SjS; however, only one million have been diagnosed, likely due to the nonspecific diagnostic guidelines and the heterogeneous nature of the disease [3]. The current standard of care of the client is to perform at least baseline salivary gland ultrasounds (of the submandibular and parotid glands) in SjS patients. For some higher-risk individuals, regularly scheduled salivary gland ultrasounds are performed.

Function

The problem arises within the current OMERACT ultrasound grading system, which requires subjective opinions and lacks nuance. As a result, a machine learning approach is proposed to rid of inter-reader variability and to strive to provide more exact prognostication. The proposed algorithm takes ultrasound grayscale images as input and outputs binary SjS positive or SjS negative.

Client requirements

The following is a list of client requirements:

- The algorithm needs to take ultrasound grayscale images as input and output binary SjS positive or SjS negative.
- It is preferable that the algorithm can be processed in real-time within a manageable time frame, where the physicians can receive the algorithm's output immediately after the patient's ultrasound procedure.
- Images must be de-identified before they can be used for training
- Generalizability to other Rheumatic diseases and EMT applications is preferable

Design requirements

1. Physical and Operational Characteristics

a. Performance requirements:

The product will be a machine learning program that is run on hospital computers and analyzes salivary gland ultrasound images. The program must provide an accurate classification of the images and determine whether the patient has SjS or not.

The program will be utilized in clinical settings post-ultrasound readings. This means that the device could potentially be used many times a day, depending on clinic hours and number of patients that need ultrasounds. To ensure that no long waits occur for patients, the machine learning algorithm should be relatively quick at analyzing the ultrasound images. A first-in-first-out (FIFO) queue structure will be used to ensure that no tasks are skipped due to processing time.

b. Safety:

As this is a machine learning program, there should not be any safety concerns for users; however, as this algorithm will be utilized in diagnosing SjS, it is very important that the algorithm works properly. Otherwise, any missed diagnosis could result in patient's not receiving proper treatment for SjS, which potentially can cause increased health risks and concerns [4].

c. Accuracy and Reliability:

Since this is a highly adaptable product, it will gain accuracy as it is presented with more data. Thus it has been created to increase in reliability with additional time and usage. The models will be evaluated by first partitioning the dataset into training and validation sets with a 7:3 ratio respectively. The model will then be trained on the training set and evaluated with the validation set. The output of which will be put into a confusion matrix and the ROC curve will be generated.

A baseline will first be assessed using a support vector machine (SVM), and the goal is to perform better than the baseline with either a more complicated deep neural network (DNN) or an established model like the ResNet-50. Ideally, the accuracy should be greater than or equal to 95%.

In practice, especially in the early stages of the product, a physician's opinion might be needed to supplement the output of the algorithm.

d. Life in Service:

In light of a better scoring system, or a software/hardware change this product is not compatible with, this product may become obsolete. As a result of its adaptive qualities, however; it is continuously capable of learning when presented with new data and will be relevant as long as ultrasound images need to be graded objectively for SjS.

e. Shelf Life:

Given that the system is updated in order to stay relevant with the software and hardware it will be run on, the shelf life of this product is infinite.

f. Operating Environment:

The product is designed to operate in clinical environments, primarily on computers that can run the code. The code can run on any operating system but requires Python to be installed on the computer for the program to run if the client prefers the program in a .py or .ipynb format. If the code is built as an executable software, no Python is required.

g. Ergonomics:

The sole restrictions would be the usage of an admissible computer, the requirement of Python dependent upon the client's preferred file format, and patient permission for their images to be run through the program.

h. Size:

As the product is software oriented, there are no physical size restrictions or requirements.

i. Weight:

The project design is software based, and thus weight is not applicable in terms of software. The weight required by the client ranges, as they require a workstation, whether a laptop or desktop, to run the software and process images.

j. Materials:

There only will be a software aspect to the product. So, since there will be no hardware, no physical materials are needed for this product. As for software, PyTorch will be used for the machine learning framework, and GitHub will be necessary for maintenance.

k. Aesthetics, Appearance, and Finish:

There is no hardware, so there will be no color, shape, or form texture requirements. This product consists of only software, so aesthetics, appearance, and finish are not applicable.

2. Production Characteristics

a. Quantity:

Only one program has to be written to fulfill the requirements. This program will then be used on any device the client wishes to use.

b. Target Product Cost:

Since this device only consists of software, there will be no manufacturing costs.

3. Miscellaneous

a. Standards and Specifications:

The project concerns human data; thus, a few issues must be addressed, namely the acquisition of human data, de-identification protocols, and working with de-identified data.

De-identified ultrasound images will be provided by the client; however, if any additional data acquisition is to take place, per 21 CFR 56.102, any data acquisition from human subjects shall fall under the definition of clinical investigation and:

> must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit [5].

Human subject shall be defined as an individual who is or becomes a participant in this project, as the subject of ultrasound imaging [5]. In such a case, informed consent of the participants and IRB approval must be obtained. Per FDA guidelines, adequate information that allows an informed decision must be provided, participants' understanding of the aforementioned information should be facilitated, adequate time must be allocated for the participants to ask questiosn and discuss protocols with family and friends, and voluntary participation agreement must be obtained, and the participants should be updated with more information as research progresses [6].

In the case of working with de-identified data, which is defined as there is no reasonable basis to believe that the information can be used to identify an individual under 45 CFR 164.514, HIPAA Privacy Rule "does not restrict the use or disclosure of de-identified health information, as it is no longer considered protected health information" [7, 8].

Per 45 CFR 164.514(b), HIPAA provides two de-identification methods: 1) Expert determination and 2) Safe harbor. The former requires "a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable" while the latter requires the removal of 18 types of identifiers, including but not limited to name, address, and phone number [7].

b. Customer:

The primary customers of this product are Hospitals, Rheumatologists, and EMTs. In addition, it is also preferred that the algorithm can be generalized to other rheumatic diseases.

c. Patient-related concerns:

This algorithm must provide accurate diagnoses to prevent the consequences of a false negative or false positive result. Minimizing the number of inaccurate results is crucial as false negatives can lead to a patient not receiving the treatment that they need and false positives can lead to patients being exposed to unnecessary treatments and medications. It is also important that patient health information is not disclosed without proper notice as outlined in 45 CFR 164.520 [9].

d. Competition:

Other methods of detecting SjS include blood and urine tests, Schirmer tear test, Sialography, Salivary scintigraphy, and biopsy [10-14]. While these tests are less subjective than the current OMERACT grading system, they are significantly more invasive and time consuming than ultrasound scans. Additionally, a patent titled 'Method for Developing a Machine Learning Model of a Neural Network for Classifying Medical Images' by Tienovix LLC claims protection for a machine learning model relating to Data Collection, Feature Definition, Image Analysis, Labeling, Data Splitting, Neural Network Training, Training Metrics, Threshold Evaluation, Validation Process, Validation Metrics, and Model Storage [15]. This patent describes a method for obtaining medical image data, including ultrasound images, and trains a machine learning model to analyze features in the image and validate that model's accuracy with a training set. This method can be applied to diagnose SjS by training a machine learning model to recognize features of salivary gland ultrasound scans and grade them based on their characteristics. Another patent titled "Machine-aided workflow in ultrasound imaging", protects the use of computer-aided classification to detect objects inside of the body [16]. While this patent describes the classification of organs in an ultrasound scan, a similar model could be used to distinguish the salivary glands in ultrasound scans of potential SjS patients.

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