#### Automatic Tuberculosis Severity Scoring Using Machine Learning Techniques

Author: Noreddine BELHADJ CHEIKH Supervised by: Abdelkader HAMADI

A thesis submitted for the Master's degree in Engineering of Information Systems



Faculty of Exact Science and Informatics University Of Mostaganem Abdelhamid Ibn Badis Algeria 25 February, 2019

## Abstract

Abstract goes here here

# Contents

1	Pul	monar	y Tuberculosis and its types	5			
	1.1	Latent	Tuberculosis (TB) infection (Latent Tuberculosis Infection (LTBI))	5			
	1.2	Active	tuberculosis	Ę			
	1.3	Pulmo	onary Tuberculosis	7			
	1.4	Types	of Pulmonary Tuberculosis	7			
		1.4.1	Summary	8			
2	Med	dical Iı	maging and Machine Learning	10			
	2.1	Medic	al imaging	10			
		2.1.1	Medical imaging technologies	10			
		2.1.2	Medical imaging Archiving and Recording	11			
	2.2	Machi	ne Learning (ML)	12			
		2.2.1	Supervised learning	13			
		2.2.2	Ensemble learning	14			
		2.2.3	Deep learning	15			
		2.2.4	Transfer learning	16			
		2.2.5	Evaluation metrics	16			
	2.3	Applic	eation of deep learning in medical imaging				
		2.3.1	Niftynet	17			
		2.3.2	Summary	17			
3	Tuberculosis severity scoring using machine learning						
		3.0.1	Dataset	19			
		3.0.2	Participation and results	20			
4	Gen	neral C	Conclusion	21			
$\mathbf{A}$	Apr	oendix		22			

### Introduction

In recent decades, medical imaging has become indispensable in the diagnosis and therapy of diseases. With the enhancement of medical imaging databases, new methods are required to better handle this huge volume of data. However, because of the large variations and complexity of medical imaging data, it is generally difficult to deduce analytical solutions or simple methods to describe and represent objects such as lesions and anatomies in data. Therefore, medical imaging tasks require learning from the examples, and this is one of the key interests of the machine learning field.

Machine learning has become one of the main tools for medical image analysis. Machine learning techniques are solutions for developing tools to help physicians diagnose, predict, and prevent the risk of disease before it becomes too late in less time. Deep Learning is a new component in the field of machine learning that encompasses a wide range of network architectures designed to perform multiple tasks. The first use of neural networks for medical image analysis goes back more than twenty years, their use has increased by several orders of magnitude over the last five years. different, articles [1, 2, 3, 4, 5] have highlighted the application of deep learning to a wide range of medical image analysis tasks (segmentation, classification, detection, recording, image reconstruction, enhancement, etc.).

Tuberculosis is an infectious disease caused by a bacterium called Bacillus mycobacterium tuberculosis [6]. In 2018, 10 million people fell ill with TB, and 1. 6 million died from the disease [6]. This disease remained one of the top ten leading causes of death in the world in 2018 [6]. Tuberculosis attacks the lungs but can also affect other parts of the body [7]. Accurate and rapid diagnosis is the key to controlling this disease, but traditional TB tests produce inaccurate or time consumnig results to be definitive. Researchers have been interested in this disease, particularly in the context of the ImageCLEF 2018[8] international challenge [8] where two tasks have been reserved for it. Algorithms involving deep learning have been tested to diagnose the presence or absence of tuberculosis. The results obtained were interesting. Indeed, the algorithms have achieved an impressive accuracy rate up to 96% [9, 10] a result that is better than the intervention of many radiologists.

The goal of our project is to automatically give score of TB severity via Computed Tomography (CT) scan. One of the possible applications of this study is to accelerate the diagnosis of the disease from a radiology image without resorting to expensive medical tests. This work is part of the ImageCLEF2018 task of classifying types of TB, which has shown more promising results. We explore in this paper the different work and different concepts that link with this problem. Starting by giving an overview of tuberculosis and its types in chapter 1. Then, discuss the relationship between artificial intelligence and

medical images and give definition of some important parts of these fields in chapter 2. In chapter 3, the ImageCLEF Tasks are described and the related work of tuberculosis sever scoring is reviewed.

## Chapter 1

# Pulmonary Tuberculosis and its types

Tuberculosis is a chronic infectious disease caused by a bacterium. called "Mycobacterium Tuberculosis" or Bacillus Koch (Bacillus Koch (BK)). Its most current and most common form (85% of cases) is pulmonary tuberculosis, but there are also extrapulmonary forms such as bone tuberculosis, ganglion tuberculosis and renal tuberculosis.

Tuberculosis can develop rapidly after the first contact with the microbe, but it can also appear several years later.

#### 1.1 Latent TB infection (LTBI)

LTBI is the presence of tubercle bacilli within the body without manifestation of the disease. LTBI carriers are by definition non-contagious and pose no risk to those around them.

#### 1.2 Active tuberculosis

Active tuberculosis is a condition in which the body's immune system is unable to fight off or defend against the Mycobacterium tuberculosis bacterium. This inability causes an infection of the lungs, which is the most common presentation, or other parts of the body (tuberculosis is a multisystemic disease). Apart from the respiratory system, the organ systems most commonly affected include the gastrointestinal system, the musculoskeletal system, the lymphoreticular system, and the reproductive system, as well as the skin and the liver.

Globally, the best estimate is that 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017: 5.8 million men, 3.2 million women and 1.0 million children [11]. There were cases in all countries and age groups, but overall 90% were adults (aged 15 years), 9% were people living with Human Immunodeficiency Virus (HIV) (72% in Africa) and two thirds were in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). These and 22 other countries in World Health Organization (WHO)'s list of 30 high TB burden countries accounted for 87% of the world's cases[11]. Only 6% of global



Estimated TB incidence rates are shown in Figure 1.1.

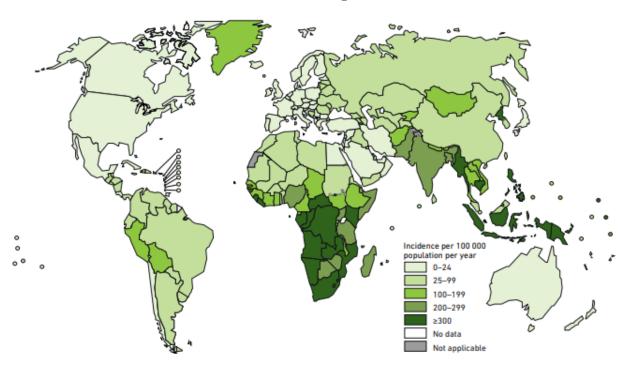


FIGURE 1.1 – Estimated TB incidence rates, 2017 [11]

#### 1.3 Pulmonary Tuberculosis

Pulmonary TB is caused by the bacterium Mycobacterium tuberculosis (M tuberculosis). It affects the lungs and it may spread to other organs. Pulmonary TB is highly contagious as a person may get TB by breathing in air droplets of an infected person [12].

#### 1.4 Types of Pulmonary Tuberculosis

There exist five types of pulmonary tuberculosis namely (infiltrating, focal, tuberculoma, miliary and fibro-cavernous). A 2D slice of CT scan for each type of pulmonary TB is shown in Figure 1.2.

Miliary TB Miliary tuberculosis (TB) is the widespread dissemination of Mycobacterium tuberculosis via hematogenous spread. Classic miliary TB is defined as millet-like (mean, 2 mm; range, 1-5 mm) seeding of TB bacilli in the lung, as evidenced on chest radiography. This pattern is seen in 1-3% of all TB cases. Symptoms may include fever, night sweats, and weight loss. It can be difficult to diagnose because the initial chest x-ray may be normal. Patients who are immunosuppressed and children who have been exposed to the bacteria are at high risk for developing miliary TB.[13, 14, 15, 16]

**Focal TB** Focal TB is diagnosed in the event of lesions not exceeding two lung segments. A small number of pathological foci with a diameter of about 1 cm are formed in the lung, which occurs at different times. [17]

**Infiltrative Tuberculosis** infiltrative tuberculosis is characterized by the fuzzy outlines of shadows on radiography. This often happens when forming new cavities. infiltration appears on radiography as rounded, or shade of homogeneous structure. All spots are divided into small, medium and large. The small ones have a size of 1 to 2 cm, the means 2-4 cm, the large ones up to 6 cm.[18]

**Tuberculoma TB** A tuberculoma is a clinical manifestation of tuberculosis which unites tubercles into a solid chunk, and so can mimic cancer tumors of many types in medical imaging studies.[19, 20]

Fibrous-cavernous TB Distinctive features of cavernous form of lung tuberculosis are the presence of the thin-walled cavity located on a background of slightly changed lung tissue at absence of the expressed infiltrative and fibrotic changes. Cavernous tuberculosis develops among patients with, disseminated, focus lung tuberculosis, at disintegration of tuberculomas; at late revealing of disease, when the phase of disintegration is finished by formation of cavities, and the attributes of the initial form disappear. At radiographic examination rounded cavity is defined, with a thin two-layer wall and usual localization in subclavicular area. [21]

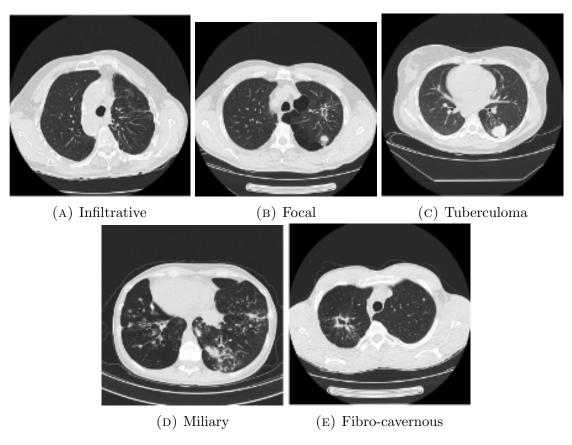


FIGURE 1.2 – CT slices of the five pulmonary TB types.[8]

#### 1.4.1 Summary

As shown in this chapter, tuberculosis is a chronic and may result in the death of the infected person. Furthermore, TB has several types that are diagnosed and treated diffrently. In the next chapter, the diffrent medical imaging technologies used to diagnose TB are presented along with the role of machine learning to analyse medical imaging. A particular focus will be put on deep learning and its architectures and diffrent evaluation metrics.

## Chapter 2

# Medical Imaging and Machine Learning

#### 2.1 Medical imaging

Medical imaging encompasses the technologies and processes of creating visual representations out of an anatomical volume in a form of images to be used for clinical diagnosis, medical intervention, and disease monitoring.

#### 2.1.1 Medical imaging technologies

Common medical imaging technologies include ones which use electromagnetic radiations such as X-ray imaging and Computed Tomography (CT) imaging, others use sound waves and magnetic field such as ultrasound an magnetic resonance imaging.

X-ray imaging this technology is the oldest and the most frequently used, it works on wavelengths and frequencies that can penetrate through the skin creating a visualization of the inner body. It used to detect skeletal system malfunctioning, cancer through mammography, and other diagnoses that involve the visualization of the inner body. This technique comes with risks associated with the use of X-ray radiation.

CT imaging is a form of X-ray imaging that produces a 3D visualization of for diagnosis, providing greater quality and detailed imaging of the internal organs, bones, blood vessels, soft tissues within the body. it also inherits the risk of X-ray imaging whereas the benefits exceed its risk where in many cases the use of CT scans prevents the need for exploratory surgery.

**Ultrasound imaging** uses High-frequency sound waves that are transmitted from the probe to the body via the conducting gel, those waves then bounce back when they hit the different structures within the body and that is used to create an image for diagnosis. This technology is considered the safes without any recorded side effects of its usage and is the most cost-effective. Due to its low risk, it is the first choice for pregnancy.

Magnetic resonance imaging uses a strong magnetic field and radio waves it enables an in-depth view of the inside of a joint or ligament to be seen, rather than just the outside as in the case of CT scans and X-ray. It has risks associated with the use of a

strong magnetic field where any kind of metal implant, artificial joint could be moved or heated up within the magnetic field.

#### 2.1.2 Medical imaging Archiving and Recording

due to the nature of a medical image, storing it is different from storing regular images. Medical image data set consists typically of one or more images representing the projection of an anatomical volume onto an image plane (projection or planar imaging), a series of images representing thin slices through a volume (tomographic or multislice two-dimensional imaging), a set of data from a volume (volume or three-dimensional imaging), or multiple acquisition of the same tomographic or volume image over time to produce a dynamic series of acquisitions (four-dimensional imaging).[22]

There exist several medical images file formats all of them sharing the goal of standardizing medical images storage and transmission. Major file formats widely used in medical imaging are Analyze, Neuroimaging Informatics Technology Initiative (Nifti), Minc, and Digital Imaging and Communications in Medicine (Dicom).

Analyze Analysis 7.5 was created in the late 1980s as a format used by the Analyze commercial software developed at the Mayo Clinic in Rochester, MN, USA. For more than a decade, the format was the standard for post-processing medical imaging. The big point of view of the Analyze format is that it was designed for multidimensional (volume) data. Indeed, it is possible to store 3D or 4D data in a file (the fourth dimension being typically the temporal information). An Analyze 7.5 volume includes two binary files: an image file with the extension .img which contains the raw voxel data, and a header file with the extension .hdr which contains the metadata (number of pixels in the three dimensions, voxel size, and data type). The header has a fixed size of 348 bytes and is written as a structure in C programming language. Reading, and editing the header requires a utility software. The format is now considered "old" but it is still widely used and supported by many processing software, viewers, devices, and conversion utilities.[22]

Nifti is a file format created in the early 2000s with the intention to create a format that preserves compatibility of the Analyze format but solving its weaknesses. Nifti may be considered a revised 'Analyze' format. NIfTI uses the "empty space" in the ANALYZE 7.5 header to add several new features such as image orientation with the intention of avoiding left-right ambiguity in the brain study. In addition, Nifti includes unsupported data type in the Analyze format as an unsigned 16-bit format. Although the format also allows the storage of header and pixel data in separate files, the images are usually saved as a single '.nii' file in which the header and data are stored. pixels are merged. The header has a size of 348 bytes in the case of data storage '.hdr' and '.img' and a size of 352 bytes in the case of a single file '.nii'. This difference in size is due to the presence of four additional bytes at the end, essentially to make the size a multiple of 16, and also to provide space for storing additional metadata.[23, 22]

Minc The Minc file format was developed in 1992 to provide a flexible data format for medical imaging. The first version of the Minc format (Minc1) was based on the standard common network format (NetCDF). Subsequently, to overcome the large data file support constraint and provide new features. Minc's development team chose to

upgrade from NetCDF to Hierarchical Data Format version 5 (HDF5). This new version which is not compatible with the previous one was called Minc2.[24, 22]

**Dicom** Dicom (Digital Imaging and Communications in Medicine), is the international standard for transmitting, storing, retrieving, printing, processing, and displaying medical imaging information. Dicom can only store pixel values as an integer. However, it supports various types of data, including floats, to store metadata. Whenever the values stored in each voxel are to be scaled, Dicom uses a scaling factor using two fields in the header defining the slope and the intercept of the linear transformation to be converted in real values. Dicom supports compressed image data through a mechanism that encapsulates a non-Dicom document into a Dicom file. The compression systems supported by Dicom are JPEG, Run-Length Encoding (RLE), JPEG-LS, JPEG-2000, and MPEG2 / MPEG4.[25, 22]

Table 2.1 shows a summary of file formats characteristic	Table 2.1	shows a	summary	of file	formats	characteristic
--	-----------	---------	---------	---------	---------	----------------

Format	Header	Extension	Data types
Analyze	Fixed-length: 348 byte bi-	.img and .hdr	Unsigned integer (8-bit),
	nary format		signed integer (16-, 32-bit),
			float (32-, 64-bit), complex
			(64-bit)
Nifti	Fixed-length: 352 byte bi-	.nii	Signed and unsigned inte-
	nary formata (348 byte in		ger (from 8- to 64-bit), float
	the case of data stored as		(from 32- to 128-bit), com-
	img and .hdr)		plex (from 64- to 256-bit)
Minc	Extensible binary format	.mnc	Signed and unsigned inte-
			ger (from 8- to 32-bit), float
			(32-, 64-bit), complex (32-,
			64-bit)
Dicom	Variable length binary for-	.dcm	Signed and unsigned in-
	mat		teger, (8-, 16-bit; 32-bit
			only allowed for radiother-
			apy dose), float not sup-
			ported

Table 2.1 – Summary of file formats characteristics [22]

#### 2.2 Machine Learning (ML)

Machine learning is a branch of artificial intelligence that encapsulates the methods and algorithms that automates analytical and mathematical model building. ML is based on the idea that machines can learn from a given data to solve or react to a certain input without being explicitly programmed[26]. One major task of machine learning, pattern recognition, and data mining is to construct good models from data sets.

Thanks to the rise of powerful and affordable computing power and the appearance of big data. machine learning is witnessing an exciting evolution. Nowadays, machine

learning techniques are being used in almost every field of research and application ranging from healthcare, medicine, agriculture, and finance . . . etc. As a result of these advances, systems which only a few years ago performed at noticeably below-human levels can now outperform humans at some specific tasks and complex games such as chess and Shogi[27, 28].

Machine learning algorithms are organized in categories based on the type of learning and whether data is available, labeled or not. Thus, we distinguish supervised learning, semi-supervised learning, unsupervised learning, Reinforcement learning algorithms.

#### 2.2.1 Supervised learning

Supervised learning is the machine learning task of learning a function that maps an input to an output based on example input-output pairs[29]. In supervised learning, the inference of a function is done from labeled training data [30]. Consequently, the availability of labeled training examples is mandatory.

There exist numerous supervised learning algorithms each has its strengths and weaknesses. for now, there isn't an algorithm that can perform best in every situation[31]. Support vectors machine (SVM) and decision trees are well-known examples of supervised learning algorithms and will be discussed next.

#### Support Vectors Machine (SVM)

A Support Vector Machine (SVMs, also support-vector networks) is a discriminative classifier formally, it constructs a hyperplane or set of hyperplanes in a high or infinite-dimensional space, which can be used for classification, regression, or other tasks like outliers detection. In other words, given labeled training data (supervised learning), the algorithm outputs an optimal hyperplane which categorizes new examples. SVMs are supervised learning models with associated learning algorithms that analyze data used for classification and regression analysis.[32, 33] SVMs are widely used in pattern recognition and classification tasks [34, 35, 36, 37, 38] and nonlinear regressions [39, 40, 41]

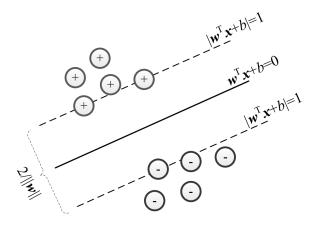


FIGURE 2.1 – An illustration of an SVM machine.

#### **Decision Trees**

A decision tree represents a function that takes as input a vector of attribute values and returns a "decision"—a single output value[29]. It is one of the predictive modeling approaches used in statistics, data mining and machine learning. It works as decision support tool. A decision tree is a flowchart-like structure, works by recursively splitting training data into subsets based on the value of a single attribute. Each split corresponds to a node in the tree representing a test on the attribute/features, each branch represents the outcome of the test, and each leaf node represents a class label (decision taken after computing all attributes). A basic structure of a decision tree is shown in Figure 2.2.[42, 43] There exist different algorithms for building a decision tree, namely ID3 (Iterative Dichotomiser 3), C4.5 (successor of ID3), CART (Classification And Regression Tree), CHAID (CHi-squared Automatic Interaction Detector) and MARS. The algorithms and techniques of building decision trees are an exciting research domain, where the speed, efficiency, and accuracy are improved [43]. Decision trees are used in many fields including medecine[44, 45], astronomy[46], and genetics[47]...etc.

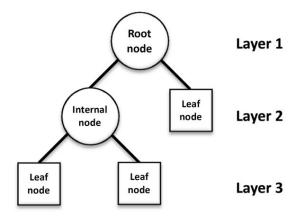


Figure 2.2 – Basic structure of a decision tree.

#### 2.2.2 Ensemble learning

In ordinary machine learning algorithms, the intention is to learn one hypothesis from training data. Whereas, in ensemble methods[48] multiple learners that are called base learner. Base learners are trained to solve the same problem. Thus, a collection of hypothesis is constructed and being combined for a prediction. For instance, during cross-validation, we might generate twenty different decision trees, and have them vote on the best classification for a new example. Ensemble learning is also called committee-based learning or learning multiple classifier systems[29]

Figure 2.3 shows a common architecture of ensemble learning. There exist two types of ensembles, those that use a single base learning algorithm to produce homogeneous base learners, leading to homogeneous ensembles, i.e, an ensemble of decision trees. The second type consists of the use of different base learning algorithm to produce heterogeneous base learners, leading to heterogeneous ensembles, i.e, an ensemble of neural networks and SVMs.

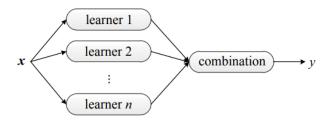


Figure 2.3 – A common ensemble architecture.

The use of an ensemble leads often to a much stronger generalization than the use of a single learner. Ensemble methods are proven to boost weak learners and turn them to strong learners with more accuracy. [49]

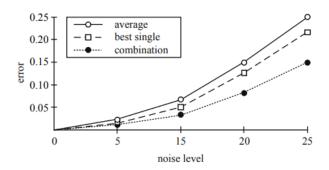


Figure 2.4 – A simplified illustration of Hansen and Salamon [1990]'s observation: Ensemble is often better than the best single.

Boosting and bagging are methods of ensemble learning which are used to improve the stability and accuracy of base learners. They're briefly described below.

Bagging stands for bootstrap aggregation which is a method for generating multiple versions of a predictor and using these to get an aggregated predictor[50]. Random forest is a well-known example of an ensemble learning algorithm. It uses the combination of bagging technique[51] and random selection of features on the decision tree as the base learner to produce a collection of decision trees thus constructing a random decision forest.

**Boosting** consists of iteratively learning weak classifiers with respect to a distribution and adding them to a final strong classifier. Moreover, boosting is based on the question "Can a set of weak learners create a single strong learner?" [50].

**Stacking** it is a technique that is used to ensemble a diverse group of strong learners by training a second-level machine learning algorithm called a "meta-learner" to learn the optimal combination of predictions of the base learners.

#### 2.2.3 Deep learning

Deep learning is a method of machine learning based on learning data patterns and representations for the goal of artificial intelligence it is also known as deep structured

learning or hierarchical learning. The hierarchy of nature enables the computer to learn complicated concepts by building them out of simpler ones through the use of layers. the graphical representation of these concepts shows deep graphs, with many layers. That is why it's called deep learning.

There exist many architectures involving deep learning such as deep neural networks, deep belief networks, deep Boltzmann machines and recurrent neural networks which have been applied in a wide range of domains, like Computer vision, natural language processing, education, finance . . . etc. due to the vast domain of deep learning, A particular focus is given to deep neural networks architecture in this paper.[52]

Deep neural networks have shown a state of the art performance that has beaten many ML algorithms, especially in computer vision. Deep networks could be categorized into four major network architectures groups: Unsupervised Pretrained Networks (UPNs), Convolutional Neural Networks (CNNs), Recurrent Neural Networks, Recursive Neural Networks[53]. Widely used examples of CNN architectures are GoogleNet[54], ResNet[55], VGGNet[56], AlexNet[57].

#### 2.2.4 Transfer learning

Transfer learning is a machine learning method where a model developed and trained for a task is reused as the starting point for building and training a model on another task. Transfer learning is meaningful to be used when the target Task dataset is relatively smaller than the dataset that the model was pre-trained on and when the inputs are homogeneous, i.e, images and X-ray scans. It helps to take advantage of the pre-learned structures and features and decrease the time of training the model.

#### 2.2.5 Evaluation metrics

Evaluation metrics are used to measure the performance of a machine learning model. There exist different evaluation metrics used for benchmarking or fine-tuning a model. Classification accuracy, confusion matrix and receiver operating characteristic (ROC) are briefly described in the next section.

Classification Accuracy Classification Accuracy is the ratio of the number of correct predictions to the total number of input samples. It is calculated by Equation 2.1.

$$Accuracy = \frac{\text{Number of Correct predictions}}{\text{Total number of predictions made}}$$
(2.1)

Confusion Matrix A confusion matrix is a table that is often used to describe the performance of a classification model (or "classifier") over a set of test data for which the true values are known. In the case of a binary classifier, we get Table 2.2.

- true positives (TP): These are cases in which the predicted class is 1, and the actual class is 1.
- true negatives (TN): These are cases in which the predicted class is 0, and the actual class is 0.

	Predicted	Predicted
	0	1
Actual 0	TN	FP
Actual 1	FN	TP

Table 2.2 – A confusion matrix of a binary classification.

- false positives (FP): These are cases in which the predicted class is 1, and the actual class is 0.
- false negatives (FN): These are cases in which the predicted class is 0, and the actual class is 1.

**ROC** curve The ROC curve is created by plotting the true positive rate (TPR) against the false positive rate (FPR) which are calculated from the output of confusion matrix at various threshold settings. The true-positive rate is also known as sensitivity, recall or probability of detection in machine learning. The false-positive rate is also known as the fall-out or probability of false alarm and can be calculated as (1 specificity).

#### 2.3 Application of deep learning in medical imaging

Recent advancements in deep learning have revolutionized medical image analysis by allowing discovering morphological and/or textural patterns in images directly from data. As deep learning models have achieved state of the art performance over different medical applications. This achievement took the attention of researcher and practitioners where many methods and frameworks gathering the field of medical imaging and deep learning were created. Niftynet is one example of the platforms that we will discuss next.

#### 2.3.1 Niftynet

NiftyNet is a deep learning platform for medical imaging built on top of The TensorFlow framework[58]. It comprises several modular components that eases and abstracts the model building pipeline. The NiftyNet works by connecting four components: a Reader to load data from files, a Sampler to generate appropriate samples for processing, a Network to process the inputs, and an output handler (comprising the Loss and Optimizer during training and an Aggregator during inference and evaluation). These components are briefly depicted in Figure 2.5.[59]

#### 2.3.2 Summary

In this chapter, the different medical imaging technologies used to diagnose TB were presented along with the role of machine learning in medical imaging analysis. A particular focus was put on deep neural networks and its architectures. In the next chapter, the severity scoring subtask organized by the evaluation campaign ImageCLEF will be presented along with the oragnizer. Moreover, the dataset, evaluation metrics used will

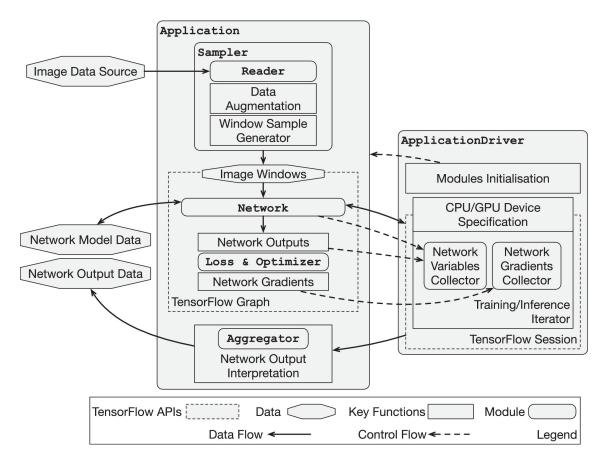


FIGURE 2.5 – A brief overview of NiftyNet components[59].

be looked at with f the top 3 and MostaganemFSEI teams approaches to automatic tuberculosis severity scoring.

## Chapter 3

# Tuberculosis severity scoring using machine learning

The severity score is a cumulative score of severity of TB case assigned by a medical doctor. Originally, the score varied from 1 ("critical/very bad") to 5 ("very good"). In this subtask, the score value is simplified so that values 1, 2 and 3 correspond to "high severity" class, and values 4 and 5 correspond to "low severity". In the process of scoring, the medical doctors considered many factors like the pattern of lesions, results of microbiological tests, duration of treatment, patient's age and some other.

This task was proposed by ImageCLEF 2019 which is an evaluation campaign that is being organized as part of the CLEF initiative labs. SVR task lays under the Image-CLEFmed Tuberculosis category of tasks along with CT report task (CTR) which consists of generating an automatic report based on the CT image of a patient.

This task possesses different difficulties and challenges. The small amount of dataset and examples for the use of deep learning, the large dimensions of the image slices without the availability of an expert to assist in reducing the irrelevant slices and decreasing the dimensions. The lack of powerful computation resources makes it difficult to train a machine learning model, particularly a deep neural network.

In the next sections, we will describe the dataset being used for ImageCLEF 2019 SVR task and discuss the participating teams' approaches and the results obtained for the severity scoring of ImageCLEF 2018.

#### 3.0.1 Dataset

The dataset contains 335 chest 3D CT images with an image size per slice of 512\*512 pixels and number of slices varying from about 50 to 400 of TB patients. All the CT images are stored in NIFTI file format with .nii.gz file extension (g-zipped .nii files). In addition to the CT images, a set of clinically relevant metadata was given. The selected metadata includes the following binary measures: disability, relapse, symptoms of TB, comorbidity, bacillary, drug resistance, higher education, ex-prisoner, alcoholic, smoking, severity. Moreover, automatically extracted lung masks where provided along with a set of tools for loading/saving niftii files. 218 patients are used for training and 117 for test.

#### 3.0.2 Participation and results

In 2018 there were 7 teams that participated and submitted their result in the SVR task. Each team used its own approach to build a solution for the SVR task. the participants were allowed to submit up to 10 runs for the task. A run consists of submission of the results of the developed model when applied on a test set provided by imageCLEF. The runs submitted for the severity scoring subtask were evaluated in two ways. One used the original severity scores from 1 to 5 and the task was to predict those numerical scores as precise as possible (a regression problem). Here, Root Mean Square Error (RMSE) was computed between the ground truth severity and the predicted scores provided by the participants. Alternatively, the original severity score was transformed into two classes, where scores from 1 to 3 corresponded to "high severity" and the 4 and 5 scores corresponded to the "low severity" class. In this case, the participants had to provide the probability of TB cases to belong to the "high severity" class. The corresponding results were evaluated using AUC. in this section we present the 3 top performing approaches in terms of Root Mean Squared Error (RMSE) along with the approach used by MostaganemFSEI team.

Top RMSE achieved was 0.7840, by the team UIIP\_BioMed with a single run. A Coder-Decoder Convolutional Neural Network trained on a third-party dataset of 149 CT scans with lesions labeled by a qualified radiologist was used as a Lesion-based TB-descriptor extraction method. The lesion-based TB-descriptors extracted from the patients CT scans were used to generate a random forest of 100 trees as a classifier [60]. This approach had the best RMSE 0.7840 and an AUC of 0.7708. The second best RMSE was 0.8513, achieved by the team MedGIFT among 9 runs. A graph model of the lung based on regional 3D texture features was used in an SVM classifier [61]. This method resulted in a better AUC than the previous approach.VISTA@UEvora team ranked 3rd with an RMSE of 0.8883 among 7 runs. The team used a 3D modeling approach with the multilayer perceptron algorithm. Finally, the team MostaganemFSEI used an approach that consists in extracting a single image semantic descriptor for each CT scan/patient instead of considering all the slices as separate samples [62]. The semantic descriptor was then passed as an input to bagging of a set of Random forest learners to perform a hierarchical classification of the severity score. By this approach, the team achieved an RMSE of 0.9721 and an AUC of 0.5987.

Group Name	Run	RMSE	Rank_RMSE	AUC	Rank_AUC
UIIP_BioMed	SVR_run_TBdescs2_zparts3_thrprob50_rf100.csv	0.7840	1	0.7025	6
MedGIFT	SVR_HOG_std_euclidean_TST.csv	0.8513	2	0.7162	5
VISTA@UEvora	SVR-Run-07-Mohan-MLP-6FTT100.txt	0.8883	3	0.6239	21
MostaganemFSEI	SVR_mostaganemFSEI_run3.txt	0.9721	12	0.5987	25

Table 3.1 – Results obtained by the top 3 participants and MostaganemFSEI team in the SVR subtask [8].

## Chapter 4

### General Conclusion

This report presents the results of the studies we conducted to obtain the knowledge needed to achieve our goal of automatically calculating the tuberculosis severity score via computed tomography (CT) image analysis.

As a first step, we conducted a bibliographic study on tuberculosis to get a clear idea about this disease and its impact, and its diffrent types. Then we introduced the concept of deep learning and its architectures. Afterwards, we talked about the field of medical imaging, focusing on a few applications of deep learning in the field of medical imaging and the file formats used to represent a medical image. Finally, we explored the work that has been done in the international challenge ImageCLEF2018[8] regarding the classification of tuberculosis severity scoring.

Through this bibliographic study, we have been able to make several conclusions. First, Tuberculosis disease continues to lead the list of mortal disease, so there is a need for ways to increase the rate of decline of the disease. Eventually, automated dignosis and scoring of tuberculosis severity would increase the availability and the time of diagnosis. Secondly, deep learning has imposed its supremacy and proven its efficiency in the field of image analysis. It is therefore worth the eandeavor to accelerate and improve image analysis. Finally, the work that has been done by the top performing teams to score pulmonary tuberculosis severity as part of the international ImageCLEF challenge showed the results obtained were very promising and yet there is still room for improvement.

In the practical part of this project we will try to apply deep learning and use the medical deep learning framework niftyNet to explore various ways to avert the weak points of the work of the state of the art. Eventually, reaching better results.

## Appendix A

# Appendix

#### Abbreviations

**3D** 3 Dimensions

AUC Area Under Curve

**BK** Bacillus Koch

CNN Convolutional Neural Networks

CT Computed Tomography

CTR CT report task

**Dicom** Digital Imaging and Communications in Medicine

FN False Negatives

**FP** False Positives

**HIV** Human Immunodeficiency Virus

JPEG Joint Photographic Experts Group

LTBI Latent Tuberculosis Infection

Minc Medical Imaging NetCDF

ML Machine Learning

MPEG Moving Picture Experts Group

Nifti Neuroimaging Informatics Technology Initiative

**RLE** Run-Length Encoding

RMSE Root Mean Squared Error

**ROC** Receiver Operating Characteristic

**SVM** Support Vector Machines

 $\mathbf{SVR}$  Severity scoring task

**TB** Tuberculosis

TN True Negatives

**TP** True Positives

 $\mathbf{UPN}$  Unsupervised Pretrained Networks

 $\mathbf{WHO}\ \mathrm{World}\ \mathrm{Health}\ \mathrm{Organization}$ 

# List of Figures

1.1	Estimated TB incidence rates, 2017 [11]	7
1.2	CT slices of the five pulmonary TB types.[8]	8
2.1	An illustration of an SVM machine	13
2.2	Basic structure of a decision tree	14
2.3	A common ensemble architecture	15
2.4	A simplified illustration of Hansen and Salamon [1990]'s observation: En-	
	semble is often better than the best single	15
2.5	A brief overview of NiftyNet components[59]	18

# List of Tables

	Summary of file formats characteristics [22]	
3.1	Results obtained by the top 3 participants and MostaganemFSEI team in the SVR subtask [8]	20

## **Bibliography**

- [1] J. Allard and N. Atalla, "Automatic segmentation of liver structure in ct images using a neural network," *IEICE TRANSACTIONS on Fundamentals of Electronics*, Communications, and Computer Sciences, vol. E77-A, no. 11, p. 892–1895, 1994.
- [2] H. A, L. SCB, L. JS, F. MT, and M. SK, "A shift-invariant neural network for the lung field segmentation in chest radiography," A Shift-Invariant Neural Network for the Lung Field Segmentation in Chest Radiography, vol. 18, no. 3, pp. 241–250, 1998.
- [3] O. Mehmed, D. B. M, and M. Robert, "Neural- network-based segmentation of multi-modal medical images: A comparative and prospective study," *IEEE Transactions on Medical Imaging*, vol. 12, no. 3, pp. 534–544, 1993.
- [4] K. J. E, N. FD, J. TK, and K. DL, "Abdominal organ segmentation using texture transforms and a hopfield neural network," *IEEE Transactions on Medical Imaging*, vol. 18, no. 7, pp. 640–648, 1999.
- [5] R. WE, G. JO, C. EN, and et al, "Automated segmentation and classification of multispectral magnetic resonance images of brain using artificial neural networks," *IEEE Trans Med Imaging*, vol. 16, no. 6, 1997.
- [6] W. H. Organization, "Tuberculosis fact sheet," September 2018. [Online; posted 18 September 2018].
- [7] A. L. Association, "Learn about tuberculosis," December 2018. [Online;Updated December 14, 2018].
- [8] Y. Dicente Cid, V. Liauchuk, V. Kovalev, , and H. Müller, "Overview of Image-CLEFtuberculosis 2018 detecting multi-drug resistance, classifying tuberculosis type, and assessing severity score," in *CLEF2018 Working Notes*, CEUR Workshop Proceedings, (Avignon, France), CEUR-WS.org <a href="http://ceur-ws.org">http://ceur-ws.org</a>, September 10-14 2018.
- [9] F. M. B. e. Puneet Sharma, *Image Analysis: 20th Scandinavian Conference, SCIA 2017, Tromsø, Norway, June 12–14, 2017, Proceedings, Part II.* Lecture Notes in Computer Science 10270, Springer International Publishing, 1 ed., 2017.
- [10] A. Menegola, M. Fornaciali, R. Pires, S. E. F. de Avila, and E. Valle, "To-wards automated melanoma screening: Exploring transfer learning schemes," CoRR, vol. abs/1609.01228, 2016.
- [11] W. H. Organization, "Global tuberculosis 2018 report," 2018.
- [12] U. N. L. of Medicine, "Pulmonary tuberculosis."

- [13] M. A, B. M, T. F, O. R, O. R, and S. H. et al, "Miliary tuberculosis: clinical manifestations, diagnosis and outcome in 38 adults," *Respirology*, vol. 6, p. 217–24, Sept. 2001.
- [14] S. SK, M. A, S. A, and M. DK, "Miliary tuberculosis: new insights into an old disease," *Lancet Infect Dis*, vol. 5, pp. 415–30, July 2005.
- [15] B. HM, B. WJ, C. RE, D. CL, E. SC, and F. L. et al, "American thoracic society/centers for disease control and prevention/infectious diseases society of america: treatment of tuberculosis," *Am J Respir Crit Care Med*, vol. 6, pp. 603–62, Feb. 2003.
- [16] R. L. Hunter, "Pathology of post primary tuberculosis of the lung: an illustrated critical review.," *Tuberculosis*, vol. 91 6, pp. 16–17, 2011.
- [17] M. Format, "Focal pulmonary tuberculosis causes, symptoms, diagnosis and treatment."
- [18] Respiratory, "infiltrative tuberculosis causes, symptoms, diagnosis and treatment."
- [19] S. D. Pitlik, V. Fainstein, and G. P. Bodey, "Tuberculosis mimicking cancer—a reminder," *The American Journal of Medicine*, vol. 76, pp. 822–825, May 1984.
- [20] S. Vento and M. Lanzafame, "Tuberculosis and cancer: a complex and dangerous liaison," *The Lancet Oncology*, vol. 12, pp. 520–522, jun 2011.
- [21] S. Jeffrey, H. Shen, K. Vadim, and J. Chinnawsamy, "Pathogenesis of post primary tuberculosis: immunity and hypersensitivity in the development of cavities," *Annals of clinical and laboratory science*, vol. 44, pp. 365–87, jun 2015.
- [22] M. Larobina and L. Murino, "Medical image file formats," *Journal of Digital Imaging*, vol. 27, pp. 200–206, dec 2013.
- [23] M. Jenkinson, "Nifti-1 data format," Oct 2007. [Accessed; posted 24 January 2019].
- [24] R. D. Vincent, L. Baghdadi, and V. S. FONOV, "Minc/softwaredevelopment/minc2.0 file format reference," Oct 2012. [Accessed; posted 24 January 2019].
- [25] O. S. Pianykh, Digital Imaging and Communications in Medicine: A Practical Introduction and Survival Guide. Springer Publishing Company, Incorporated, 1 ed., 2008.
- [26] J. R. Koza, F. H. Bennett, D. Andre, and M. A. Keane, Automated Design of Both the Topology and Sizing of Analog Electrical Circuits Using Genetic Programming, pp. 151–170. Dordrecht: Springer Netherlands, 1996.
- [27] M. Campbell, A. J. Hoane, Jr., and F.-h. Hsu, "Deep blue," *Artif. Intell.*, vol. 134, pp. 57–83, Jan. 2002.
- [28] D. Silver, T. Hubert, J. Schrittwieser, I. Antonoglou, M. Lai, A. Guez, M. Lanctot, L. Sifre, D. Kumaran, T. Graepel, T. Lillicrap, K. Simonyan, and D. Hassabis, "Mastering chess and shogi by self-play with a general reinforcement learning algorithm," 2017.

- [29] S. Russell and P. Norvig, Artificial Intelligence: A Modern Approach (3rd Edition). Pearson, 2009.
- [30] M. Mohri, A. Rostamizadeh, and A. Talwalkar, Foundations of Machine Learning (Adaptive Computation and Machine Learning series). The MIT Press, 2012.
- [31] D. H. Wolpert, "The lack of a priori distinctions between learning algorithms," *Neural Computation*, vol. 8, pp. 1341–1390, Oct 1996.
- [32] C. Cortes and V. Vapnik, "Support-vector networks," *Mach. Learn.*, vol. 20, pp. 273–297, Sept. 1995.
- [33] V. N. Vapnik, *The Nature of Statistical Learning Theory*. Berlin, Heidelberg: Springer-Verlag, 1995.
- [34] O. Chapelle, P. Haffner, and V. N. Vapnik, "Support vector machines for histogram-based image classification," *Trans. Neur. Netw.*, vol. 10, pp. 1055–1064, Sept. 1999.
- [35] H. Drucker, D. Wu, and V. N. Vapnik, "Support vector machines for spam categorization," *Trans. Neur. Netw.*, vol. 10, pp. 1048–1054, Sept. 1999.
- [36] S.-K. Woo, C.-B. Park, and S.-W. Lee, "Protein secondary structure prediction using sequence profile and conserved domain profile," in *Advances in Intelligent Computing* (D.-S. Huang, X.-P. Zhang, and G.-B. Huang, eds.), (Berlin, Heidelberg), pp. 1–10, Springer Berlin Heidelberg, 2005.
- [37] N. Cristianini and J. Shawe-Taylor, An Introduction to Support Vector Machines: And Other Kernel-based Learning Methods. New York, NY, USA: Cambridge University Press, 2000.
- [38] R. Kumar, A. Kulkarni, V. K. Jayaraman, and B. D. Kulkarni, "Symbolization assisted svm classifier for noisy data," *Pattern Recogn. Lett.*, vol. 25, pp. 495–504, Mar. 2004.
- [39] S. Mukkamala, A. H. Sung, and A. Abraham, "Intrusion detection using an ensemble of intelligent paradigms," *J. Netw. Comput. Appl.*, vol. 28, pp. 167–182, Apr. 2005.
- [40] R. K. Prasoona, A. Jyoti, Y. Mukesh, S. Nishant, N. S. Anuraj, and J. Shobha, "Optimization of gaussian kernel function in support vector machine aided qsar studies of c-aryl glucoside sglt2 inhibitors," *Interdisciplinary Sciences: Computational Life Sciences*, vol. 5, pp. 45–52, Mar 2013.
- [41] T. V. Gestel, J. A. K. Suykens, D. emma Baestaens, A. Lambrechts, G. Lanckriet, B. Vandaele, B. D. Moor, and J. Vandewalle, "Financial time series prediction using least squares support vector machines within the evidence framework."
- [42] O. Z. Maimon and L. Rokach, Data Mining with Decision Trees: Theroy and Applications (Machine Perception and Artificial Intelligence). World Scientific Pub Co Inc, 2007.
- [43] C. Manapragada, G. I. Webb, and M. Salehi, "Extremely fast decision tree," in Proceedings of the 24th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining, KDD '18, (New York, NY, USA), pp. 1953–1962, ACM, 2018.

- [44] V. Podgorelec, P. Kokol, B. Stiglic, and I. Rozman *Journal of Medical Systems*, vol. 26, no. 5, pp. 445–463, 2002.
- [45] E. Cantú-Paz and C. Kamath, "Using evolutionary algorithms to induce oblique decision trees," in *Proceedings of the 2Nd Annual Conference on Genetic and Evolution-ary Computation*, GECCO'00, (San Francisco, CA, USA), pp. 1053–1060, Morgan Kaufmann Publishers Inc., 2000.
- [46] Q. Ding, Q. Ding, and W. Perrizo, "Decision tree classification of spatial data streams using peano count trees," in *Proceedings of the 2002 ACM Symposium on Applied Computing*, SAC '02, (New York, NY, USA), pp. 413–417, ACM, 2002.
- [47] P. W. H. Wong, T. W. Lam, Y. C. Mui, S. M. Yiu, H. F. Kung, M. Lin, and Y. T. Cheung, "Filtering of ineffective sirnas and improved sirna design tool," in Proceedings of the Second Conference on Asia-Pacific Bioinformatics - Volume 29, APBC '04, (Darlinghurst, Australia, Australia), pp. 247–255, Australian Computer Society, Inc., 2004.
- [48] T. G. Dietterich, "Ensemble methods in machine learning," in *Proceedings of the First International Workshop on Multiple Classifier Systems*, MCS '00, (London, UK, UK), pp. 1–15, Springer-Verlag, 2000.
- [49] Z.-H. Zhou, Ensemble Methods: Foundations and Algorithms. Chapman & Hall/CRC, 1st ed., 2012.
- [50] M. Kearns, "Thoughts on hypothesis boosting." (Unpublished), Dec. 1988.
- [51] T. K. Ho, "Random decision forest," pp. 14–16, Proceedings of the 3rd International Conference on Document Analysis and Recognition, Montreal, Aug. 1995.
- [52] Y. Bengio, "Learning deep architectures for AI," Foundations and Trends® in Machine Learning, vol. 2, no. 1, pp. 1–127, 2009.
- [53] J. Patterson and A. Gibson, Deep Learning: A Practitioner's Approach. O'Reilly Media, Inc., 1st ed., 2017.
- [54] C. Szegedy, W. Liu, Y. Jia, P. Sermanet, S. E. Reed, D. Anguelov, D. Erhan, V. Vanhoucke, and A. Rabinovich, "Going deeper with convolutions," CoRR, vol. abs/1409.4842, 2014.
- [55] K. He, X. Zhang, S. Ren, and J. Sun, "Deep residual learning for image recognition," CoRR, vol. abs/1512.03385, 2015.
- [56] K. Simonyan and A. Zisserman, "Very deep convolutional networks for large-scale image recognition," *CoRR*, vol. abs/1409.1556, 2014.
- [57] A. Krizhevsky, I. Sutskever, and G. E. Hinton, "Imagenet classification with deep convolutional neural networks," in *Proceedings of the 25th International Conference on Neural Information Processing Systems Volume 1*, NIPS'12, (USA), pp. 1097–1105, Curran Associates Inc., 2012.

- [58] M. Abadi, A. Agarwal, P. Barham, E. Brevdo, Z. Chen, C. Citro, G. S. Corrado, A. Davis, J. Dean, M. Devin, S. Ghemawat, I. Goodfellow, A. Harp, G. Irving, M. Isard, Y. Jia, R. Jozefowicz, L. Kaiser, M. Kudlur, J. Levenberg, D. Mané, R. Monga, S. Moore, D. Murray, C. Olah, M. Schuster, J. Shlens, B. Steiner, I. Sutskever, K. Talwar, P. Tucker, V. Vanhoucke, V. Vasudevan, F. Viégas, O. Vinyals, P. Warden, M. Wattenberg, M. Wicke, Y. Yu, and X. Zheng, "TensorFlow: Large-scale machine learning on heterogeneous systems," 2015. Software available from tensor-flow.org.
- [59] E. Gibson, W. Li, C. Sudre, L. Fidon, D. Shakir, G. Wang, Z. Eaton-Rosen, R. Gray, T. Doel, Y. Hu, T. Whyntie, P. Nachev, M. Modat, D. C. Barratt, S. Ourselin, M. J. Cardoso, and T. Vercauteren, "Niftynet: a deep-learning platform for medical imaging," vol. 158, pp. 113–122, 2018.
- [60] V. Liauchuk, A. Tarasau, E. Snezhko, V. Kovalev, A. Gabrielian, and A. I. Rosenthal, "Lesion-based TB-descriptor for CT image analysis," September 10-14 2018.
- [61] D. Cid, M. Y., and H., "Texture-based graph model of the lungs for drug resistance detection, tuberculosis type classification, and severity scoring: Participation in ImageCLEF 2018 tuberculosis task," September 10-14 2018.
- [62] A. Hamadi and D. E. I. Yagoub, "Semantic descriptors for tuberculosis CT image classification," September 10-14 2018.