Automatic Diagnosis of Carpal Tunnel Syndrome by applying existing and novel signal characteristics

A Thesis

submitted to the designated
by the General Assembly of Special Composition
of the Department of Computer Science and Engineering
Examination Committee

by

Prokopios Kontogiannis

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE IN COMPUTER SCIENCE

WITH SPECIALIZATION
IN TECHNOLOGIES - APPLICATIONS

University of Ioannina

February 2017

Dedication

To my family..

Acknowledgements

In all sincerity, I would like to thank my supervisor George Manis, for his substantial advice during this nice journey of playing.
I would also like to thank the doctors, Dr Sarmas I. (Neurologist at Neurological Clinic Manager at University Hospital of Ioannina) for giving me remarkable tips and Dr Tsamis K. (Neurologist) for his continual aid and unlimited resolving of my questions.
Also I thank my friends Paris Tsantarliotis, Mitsos Zavantis and Ermh Mastora for the awesome brainstorming and companionship during our courses and projects.

Table of Contents

List of Figures

List of Tables

List of Algorithms

Abstract

Prokopios Kontogiannis, M.Sc. in Computer Science, Department of Computer Science and Engineering, University of Ioannina, Greece, February 2017.
Automatic Diagnosis of Carpal Tunnel Syndrome by applying existing and novel signal characteristics.
Advisor: Georgios Manis, Assistant Professor.

Carpal Tunnel Syndrome (CTS) is a medical situation where the median nerve is compressed while traveling through the tunel of human wrist. The resulting symptoms affect the 5% of the general population and the diagnosis of the syndrome is mainly based on Nerve Conduction Studies (NCS), a procedure of electrical conduction of finger nerves. The resulting signals are inspected by the neuro-physiologists and specific characteristics are measured in order to decide about the existence of the syndrome.

The diagnosis of CTS is still controversial. Many researchers claim that since no more accurate method has been found, the NCS (Nerve Conduction Studies) should be considered as the gold standard of CTS diagnosis, while others insist that the remarkable instances of false negative results and the absence of correlation between NCS findings and clinical symptoms should lead to the establishment of an alternative method of CTS grading scale.

In this thesis, after evaluating the existing signal features, we propose two additional techniques to the diagnosis of CTS; the first one consists of more geometric characteristics of the signal than those that are applied today and the second one is a feature which arises from the implementation of an algorithm called Dynamic Time Warping and examine if it can identify patterns in our time-series data.

Our results show that geometric characteristics in addition to Dynamic Time Warping feature can ameliorate the accuracy of our model to predict the CTS grading severity and also increase the sensitivity and specificity values of today methods.

Εκτεταμενη Περιληψη

Προκόπιος Κοντογιάννης, Μ.Δ.Ε. στην Πληροφορική, Τμήμα Μηχανικών Η/Υ και Πληροφορικής, Πανεπιστήμιο Ιωαννίνων, Φεβρουάριος 2017.
Αυτόματη Διάγνωση του Συνδρόμου του Καρπιαίου Σωλήνα με Εφαρμογή υπαρχόντων και Νέων Χαρακτηριστικών από το σήμα.
Επιβλέπων: Γεώργιος Μανής, Επίκουρος Καθηγητής.

Το Σύνδρομο του Καρπιαίου Σωλήνα, αποτελεί την πιο συχνή πάθηση του μέσου νεύρου και αφορά μία μεγάλη μερίδα του γενικού πλυθησμού (περίπου το 5%). Το μέσο νεύρο διέρχεται μέσω ενός τούνελ που υπάρχει στον ανθρώπινο καρπό, ονομάζεται Καρπιαίος Σωλήνας και αποτελείται από τένοντες, χόνδρους και το μέσο νεύρο. Έτσι, ενώ το ωλένειο νεύρο διέρχεται από τον καρπό αλλά έξω από τον καρπιαίο σωλήνα, το μέσο νέυρο είναι το μόνο νεύρο το οποίο διασχίζει τον καρπιαίο σωλήνα.

Αυτός ακριβώς είναι και ο λόγος που ο νευροφυσιολογικός έλεγχος θεωρείται σήμερα η πιο αποτελεσματική μέθοδος διάγνωσης του συνδρόμου. Με τη διενέργεια ηλεκτρικής αγωγιμότητας των νεύρων, επιθεωρούνται κάποια χαρακτηριστικά από τα προκύπτοντα σήματα και πραγματοποιείται σύγκριση μεταξύ των χαρακτηριστικών του μέσου και του ωλένειου νεύρου. Επειδή το μέσο νέυρο επηρεάζεται ενώ το ωλένειο δεν επηρεάζεται από το σύνδρομο, η μεταξύ τους σύγκριση αναμένεται να καταδείξει την ύπαρξη του συνδρόμου.

Παρόλα αυτα όμως η αποτελεσματικότητα του ΗλεκτροΝευροΓραφήματος είναι αρκετά αμφισβητίσιμη. Αφενός δεν είναι αμελητέα τα περιστατικά που, ενώ εμφανίζουν την κλινική εικόνα του συνδρόμου, έχουν φυσιολογική ηλεκτρική αγωγιμότητα, αφετέρου δεν παρουσιάζεται σημαντική συσχέτιση μεταξύ αγωγιμότητας και κλινικών αποτελεσμάτων. Μόλις το 2000, παρουσιάστηκε και θεωρήθηκε αποδεκτή η κλίμακα του J. Bland, η οποία δείχνει μία συσχέτιση κάποιων χαρακτηριστικών των σημάτων με τα κλινικά συμπώματα των περιστατικών και έγινε δεκτή (στα κύρια

σημεία της) από την AAN (American Association of Neurology) ως βάση για την ευρέως χρησιμοποιούμενη κλίμακα από τότε και στο εξής σε κάθε έρευνα που αφορά τη σοβαρότητα του συνδρόμου.

Έτσι, πρόσφατες έρευνες έχουν στραφεί στην μέθοδο του Υπερηχογραφήματος του καρπού για τη διάγνωση του Συνδρόμου του Καρπιαίου Σωλήνα, χωρίς ωστόσο να αποδεικνύουν ότι το υπερηχογράφημα αποτελεί από μόνη της αξιόπιστη μέθοδο διάγνωσης.

Σε αυτή τη διατριβή, ερευνούμε την απόδοση των χαρακτηριστικών που χρησιμοποιούνται σήμερα. Ελέγχουμε τη συσχέτιση κάθε χαρακτηριστικού χωριστά με την υπάρχουσα κλίμακα καθώς και την απόδοση των πιο γνωστών ταξινομητών με το σύνολο αυτών των χαρακτηριστικών.

Επίσης ακολουθούμε την ίδια διαδικασία για νέα χαρακτηριστικά που προκύπτουν από τα σήματα της ηλεκτρικής αγωγιμότητας των νεύρων, και δεν έχουν αξιολογηθεί μέχρι σήμερα, με σκοπό την εύρεση χαρακτηριστικών που δεν εξαρτώνται από τον ανθρώπινο παράγοντα.

Τέλος χρησιμοποιώντας τον αλγόριθμο της Δυναμικής Στρέβλωσης του Χρόνου, ελέγχουμε τη συσχέτιση του χαρακτηριστικού που προκύπτει, με τη χρησιμοποιούμενη κλιμάκωση, καθώς και με την κλινική εικόνα των ασθενών και αναλύουμε τα αποτελέσματα. Η εμφανής αποτελεσματικότητα του αλγορίθμου στην αναγώριση ομοιοτήτων μεταξύ των σημάτων μας αλλά και αυτή κάποιων εκ των γεωμετρικών χαρακτηριστικών των σημάτων, βελτιώνει την απόδοση των ταξινομητών, και δημιουργεί προυποθέσεις για τη συνδρομή του στην καθιέρωση μιας νέας πιο αποτελεσματικής κλιμάκωσης της σοβαρότητας των περιστατικών του Συνδρόμου του Καρπιαίου Σωλήνα και άλλων παθήσεων.

Chapter 1

Introduction

1.1 Objective

Carpal Tunnel Syndrome despite being a medical situation that affects the 5% of the general population, it still cannot be thoroughly diagnosed and current techniques have significant values of both false negatives and false positives subjects.

The objective of our thesis is to examine the existing features in order to evaluate a potential automatic diagnosing tool and novel features that outcome from the resulted signals of Nerve Conduction Studies, the most accurate method of electrical conduction of human nerves, and propose these features to be detected for the diagnosing , treating and understanding of other complicated cases too.

1.2 Contribution

Diagnosing of CTS is still problematic and NCS although the most reliable method, is not yet an undeniable technique of standardizing the grading scale of CTS' severity. Besides, the actual machines do not make any prediction about the existence of the

syndrome and thus, the doctor is not given any kind of diagnosis. In this thesis, through classification methods, we try to automate the procedure of diagnosing the CTS.

In our research we propose several novel signal geometric characteristics and a novel method by applying DTW (Dynamic Time Warping) algorithm. Both procedures have never been tested before in the diagnosis of CTS. More specifically DTW is rarely used before for time-defined diseases; although DTW is implemented only for time series data, it is not used in diagnosing a syndrome that is totally defined by the time a curve (or more) turns up.

The novel geometric features and the DTW algorithm can be implemented in many other cases on future, driving the researchers to focus on more than the usual extracted features of signals and time series data. Besides, the grading of the severity of CTS is not yet fully established and our proposals give more options to those who will do this in the future.

1.3 Structure

This thesis is structured as follows:

In Chapter 2 we present the basic concepts for understanding the Carpal Tunnel Syndrome. We explain the Nervous System by emphasizing on the difference between motor and sensory nerves and then we focus on carpal tunnel, the passage through which travels the median nerve. We also present the symptoms of the syndrome, its diagnostic methods and finally the Nerve Conduction Studies, which are the process of electrical conduction of the nerves and their different techniques of conducting sensory and motor nerves to evaluate the existence of CTS. Most important studies and reviews are also presented during the analysis of the diagnosis of CTS.

Chapter 3 presents our case study; the descriptive statistics of our sample, the clinical symptoms, potential exclusions and resulted NCS findings. Hence, we describe our groups of severity.

In Chapter 4, we describe the common features that are used today as outputs of the NCS in order to decide about the presence of the syndrome. Then, we analyze each one separately in purpose of examining their contribution to the final diagnosis.

In Chapter 5, we use five very popular and up-to-date classifiers in order to

evaluate their accuracy and determine the possibility of automatic diagnosis of the syndrome.

In chapter 6, we present novel features for the resulted signals. They are geometric characteristics with physical meaning that may play significant role in the diagnosis of the syndrome. Finally, we use the classifiers of Chapter 4 to evaluate their accuracy.

Chapter 7 examines another new feature, that has never also be tested in the diagnosis of CTS: the Dynamic Time Warping (DTW) algorithm. We present the algorithm, its logic, studies that focus on it and finally we experiment with it as a feature of NCS in our case study. At the end, we propose the wavelet transform for decomposition of the resulted signal before applying the DTW algorithm.

The last Chapter displays the conclusion and a discussion of our results, especially those of DTW algorithm, and potential future work on several time-series cases.

Chapter 2

The Carpal Tunnel Syndrome (CTS)

2.1 The Nervous System

2.1.1 Definition

The nervous system is composed of the central nervous system (CNS) and the peripheral nervous system (PNS), plus several organs that play the role of sensors. Sensory nerve fibers transfer the sensory stimuli, which is processed and then delivered from the motor nerve fibers to muscles. The nervous system coordinates all these parts to retain balance, by transporting information to and from different functional parts of the body, through electrical and chemical signals. The brain and the spinal cord compose the CNS, while the PNS is composed of sensory and ganglia neurons, plus other nerves that connect the neurons to each other and to the CNS. The interconnection of these regions is implemented by composite neural trails.

2.1.2 Definition of Neuron

The human body is composed of billion neurons, electrically excitable body cells that consist of a dendrite, a short extension with branches that play the role of the antenna for receiving information into its cell body and an axon, a much longer extension that carries the signals for transmitting this information.

2.1.3 Motor and Sensory Nerves

In order to carry the information in the form of signal between the CNS and other regions of the body, nerves are divided into motor and sensory nerves. They are both path of the Peripheral Nervous System and they consist of motor and sensory neurons respectively.

Sensory nerves receive information from the sense organs, they carry the signal from the receptors to the Central Nervous System and then the signal could be carried to the brain or to a motor nerve. So while sensory nerves carry information to the CNS, Motor Nerves, on the other hand, carry signals from the CNS to a gland/muscle, which then contracts.

Mixed nerves are the nerves that consist of motor and sensory neurons, thus they have the ability to carry the stimuli information from the sensor to the CNS and then carry back the processed information from the CNS to the muscle. The whole transmission occurs in milliseconds and provides human body with the efficiency to fast react to environmental incentives.

2.2 The Carpal Tunnel

Carpal tunnel is a narrow canal which is structured by bones plus an upper strong layer of connective tissue, known as transverse ligament, and is situated on the palmar side of the wrist. It is a passageway (tunnel); several flexor tendons plus the median nerve, which is a mixed nerve, pass through it. The median nerve is the only nerve that travels through this canal in the wrist and is responsible for the feeling on palmar side of four fingers (dig1, dig2, dig3 and dig4).

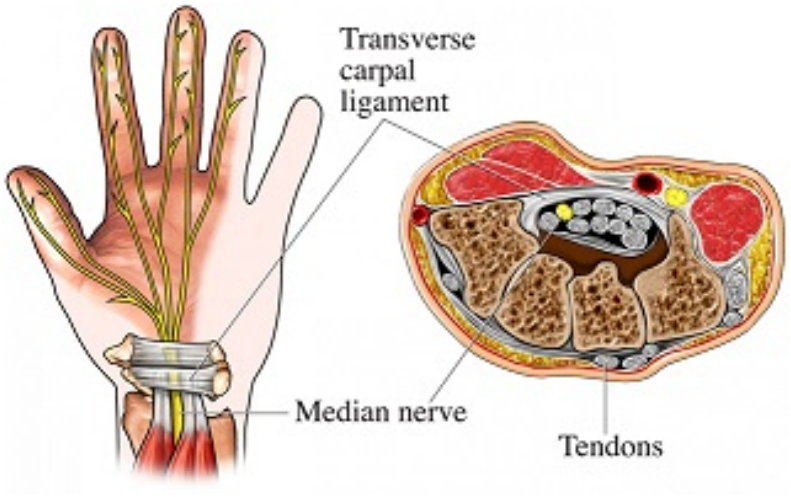


Figure 2.1: The tunnel; only median nerve passes through

As shown on figure 2.1 [1], the median nerve is branched into four fingers, but only at the left side of the 4th digit. This is because at the right side of this finger, it is the ulnar nerve that is branched into it.

2.3 The Syndrome

Carpal tunnel syndrome (CTS) is the most common of all entrapment neuropathies, since it affects almost the 5% of the general population [1] and is caused by the compression of the median nerve beneath the transverse ligament in the carpal tunnel. Since the canal is narrow, when any of the nine long flexor tendons passing through it become swollen or degenerated, the narrowing of the canal often results in the median nerve (the only nerve that passes through the tunnel) to squeeze or compress.

Carpal tunnel syndrome is often the result of a combination of factors that increase pressure on the median nerve and tendons in the carpal tunnel, rather than a problem with the nerve itself. Most likely the disorder is due to a congenital predisposition - the carpal tunnel is simply smaller in some people than in others. Other contributing factors include trauma or injury to the wrist that cause swelling, such as sprain or fracture; overactivity of the pituitary gland; hypothyroidism; rheumatoid arthritis; mechanical problems in the wrist joint; work stress; repeated use of vibrating hand tools; fluid retention during pregnancy or menopause; or the development of a cyst

[1] *nuevamentes.net*/2014/12/*el-sindrome-del-tunel-carpiano.html*

or tumor in the canal. In some cases no cause can be identified.

There is little clinical data to prove whether repetitive and forceful movements of the hand and wrist during work or leisure activities can cause carpal tunnel syndrome. Other disorders such as bursitis and tendonitis have been associated with repeated motions performed in the course of normal work or other activities. Writer's cramp may also be brought on by repetitive activity.

2.4 Symptoms of CTS

The compression of median nerve shown on figure 2.2 [2] results in:

- Pain and/or Numbness (Tingling)

  Carpal tunnel develops slowly. At first, the patient will notice it at night or in the morning. The feeling is similar to the "pins-and-needles" sensation one gets when a hand falls asleep. During the day, the patient feels pain or tingling when holding things, like a phone or a book, or when driving. Shaking or moving the fingers usually helps ameliorate the situation. Carpal tunnel syndrome can also cause a feeling of numbness in the hands. Some people feel like their fingers are swollen, even though no swelling is present, or they may have trouble distinguishing between hot and cold.

- Weakness

  As carpal tunnel syndrome progresses, the sense of weakness in the thumb and first two fingers will start, and it may be difficult to make a fist or grasp objects. The patient starts dropping things, or has problems doing things like holding a utensil or buttoning a shirt.

[2] $en.wikipedia.org/wiki/Carpal\_tunnel\_syndrome/media/File : Carpal\_Tunnel\_Syndrome.png$

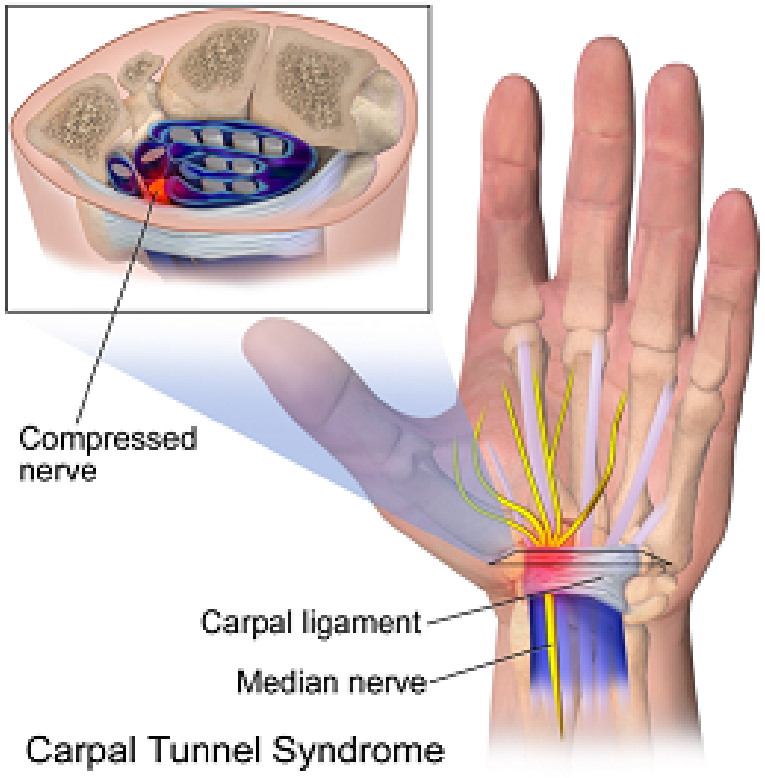


Figure 2.2: The carpal tunnel syndrome; the median nerve compressed

2.5 Diagnosis of CTS

Apart from the clinical examination, the doctor should confirm the existence of CTS by implementing electrodiagnostic test (EDX). In this test, electrodes are placed on the hands and wrists, and small electric shocks are applied to measure how quickly the median nerve transmits impulses.

The same test can be omitted to Ulnar and Radial nerves, for both sensory and motor parts of each nerve. These diagnostic tests that evaluate the electrical conduction of both Motor and Sensory nerves for the Ulnar, Median and Radial Nerves are called Nerve Conduction Studies (NCS) and they considered to be the gold standard [1], although argued [2, 3], in the diagnosis of CTS.

The most significant concept of NCS is the comparison of the median nerve NCS features with another nerve's same features. The accuracy relies upon the fact that only the median nerve travels in carpal tunnel and the comparison with a nerve that passes outside the canal could provide reliable results. So given the NCS features, the difference of the value from one feature of the Median nerve minus the value of the corresponding feature of the Ulnar nerve provides significant information about the

presence and the severity of CTS, especially when comparing different nerves at the same finger (i.e. dig4).

Another field of interest in the diagnosis of the syndrome is the Ultra/Sound of the carpal tunnel, but the results are not yet very promising and U/S is applied as an additional method to ensure the existence of the CTS [4].

2.6 Nerve Conduction Studies (NCS)

As mentioned above, Nerve Conduction Studies (NCS) are the electrodiagnostic tests that are performed to nerves in order to examine their ability of electrical conduction. From the resulting signal, the neurologist, nowadays, pays attention to the following features:

- Conduction Velocity
- Onset Latency
- Amplitude and/or Area

The most important measures are considered to be the velocity and the onset latency [5, 6, 7]. Very often the term NCV (Nerve Conduction Velocity) is used because of misunderstanding, since velocity is referenced as the gold standard of NCS [8].

2.6.1 Performing Sensory NCS

To perform a Sensory Nerve Conduction Study (S-NCS) one stimulates the peripheral nerve from a finger and the electrodes are recording the response, as presented on figure 2.3 [3]

The Onset Latency is defined as the time it takes (in milliseconds) for the electrical signal to travel from stimulus to response site where we placed the electrodes. The CV is the velocity of that traveling, measured in mm/ms (same as meters/sec).

2.6.2 Performing Motor NCS

To perform a Motor Nerve Conduction Study (M-NCS) one stimulates the peripheral nerve and the electrodes are recording the muscle response. Usually we perform the

[3] *clinicalgate.com/nerve-conduction-studies-and-electromyography*

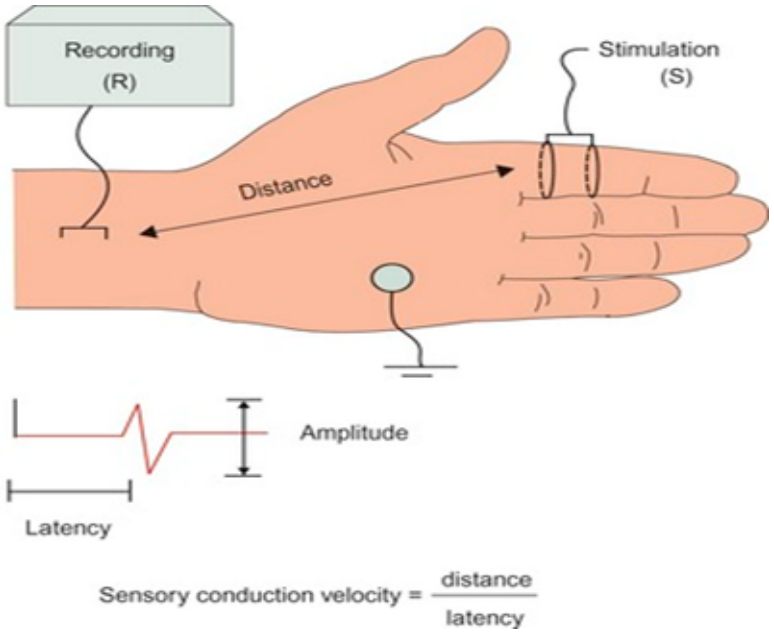


Figure 2.3: Sensory Nerve Conduction Studies

M-NCS twice, once the stimulus is placed at the elbow and then at the wrist. The recording site is always the same so as to be able to calculate the velocity between segments using the difference between the latencies, as presented on figure 2.4 [4]

2.6.3 Issues of NCS

Despite being the most accurate test, NCS current tests lack of standardized diagnostic criteria resulting to false positives and false negatives since NCS cannot detect abnormality in 16-34 % of subjects with clinical CTS [1].

Another disadvantage of NCS is that the current extracted features do not correlate with symptoms [3] and thus a commonly accepted grading scale has not yet been defined. Additional to this, each laboratory has different values of features referenced as normal and this results to increasing the necessity of a standard method of grading [2].

The absence of a widely approved grading scale, motivate many scientists to use arbitrary grading scales [5] and others to choose one among the most commonly approved grading scales, such as J Bland's scaling [9]. Thus the American Association of Neuro-muscular and Electro-diagnostic Medicine offered a proposal [10] as a starting point to develop consensus for a non-arbitrary grading scheme.

[4] *clinicalgate.com/nerve-conduction-studies-and-electromyography*

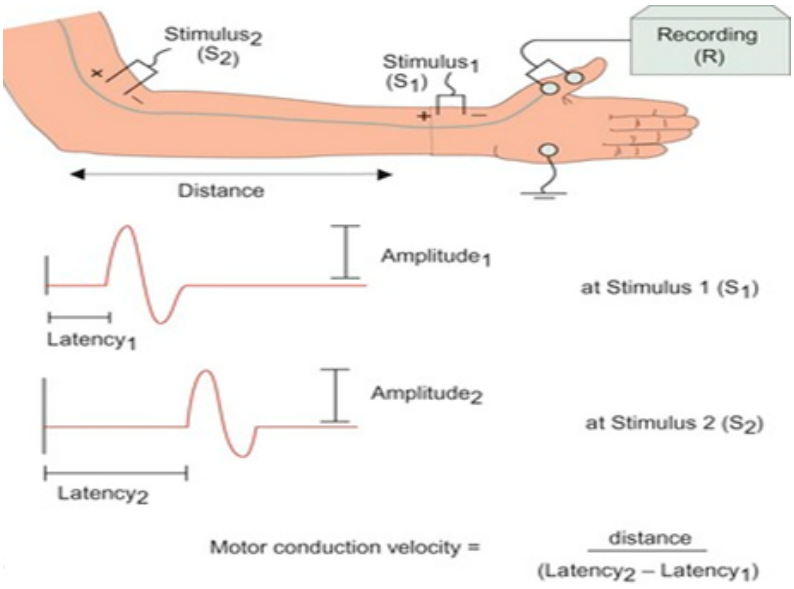


Figure 2.4: Motor Nerve Conduction Studies

This starting point was also the basis of the decision made by the doctors and neuro-physiologists of our case that is presented on next chapter, and is following these main rules:

- Mild CTS
  - Prolonged Distal Sensory Latency
  - Normal Distal Motor Latency
  - All amplitudes are normal
- Moderate CTS
  - Prolonged Distal Sensory and Motor Latencies
  - Probability for Decrease of Amplitudes
- Severe CTS
  - Undetectable or very Prolonged Sensory Potentials
  - Low Amplitudes of Mixed Response
  - Very Prolonged Distal Motor Latencies

In this thesis this proposal is used to grade the CTS hands, in order to evaluate the new methods and characteristics of the resulted signals. Only in cases where one

instance had issues of more than one category (e.g. normal distal motor latency - mild CTS, but significant decrease of amplitudes - moderate CTS), the severity of the syndrome is decided in combination with clinical symptoms, else only NCS findings where taking into account.

Chapter 3

Our Case Study

3.1 Case Study

In our study we included 39 volunteers, 29 patients and 10 healthy subjects (control group). The patients visited the Neurological Clinic at the University Hospital of Ioannina between 2013 and 2015 because of Carpal Tunnel Syndrome's symptoms in any of their hands and they agreed to have their results used for research purposes. The control group consists of 10 volunteers who were apparently healthy.

Subjects of both groups have signed that they agree to get their anonymous results (clinical symptoms and NCS findings) used for research purposes. The collection of all included data has been approved by the administration of the clinic.

3.1.1 Clinical Symptoms and Exclusions

Clinical diagnosis of CTS required the presence of at least one of the following symptoms:

- Pain
- Numbness
- Weakness

Table 3.1: Sample Statistics.

Characteristics	CTS Patients (n = 29)	Control Subjects (n = 10)
N (%)		
Women	26 (89)	7 (70)
Mean (SD)		
Age (years)	47.93 (12.92)	41.3 (9.14)
Weight (kgr)	72.55 (13.97)	66.50 (10.23)
Height (cm)	163.35 (7.68)	166 (8.94)
BMI (kgr/cm^2)	27.23 (5.15)	24.13 (3.16)

Among the 29 patients we excluded one woman who suffered from MS. Rest patients did not suffer from any other relative disease such as diabetes mellitus, endocrine or neurological disorders.

The final study included 53 CTS hands and 19 healthy hands.

3.1.2 Descriptive Statistics

Our subjects' physical characteristics are shown on table 3.1

3.1.3 Grading Scale

All hands were categorized according to their NCS findings and according to their symptoms also. For the symptoms' categorization, three pair of factors were counted;

- Pain Presence and Pain Duration (in months)
- Numbness Presence and Numbness Duration (in months)
- Weakness Presence and Weakness Duration (in months)

For NCS categorization, the recent literature was took into account.

3.1.4 Resulting Signals

Nerve conduction studies were applied to all subjects at the laboratory of the clinic, using their EMG/NCS product, a Dantec Keypoint from Natus.

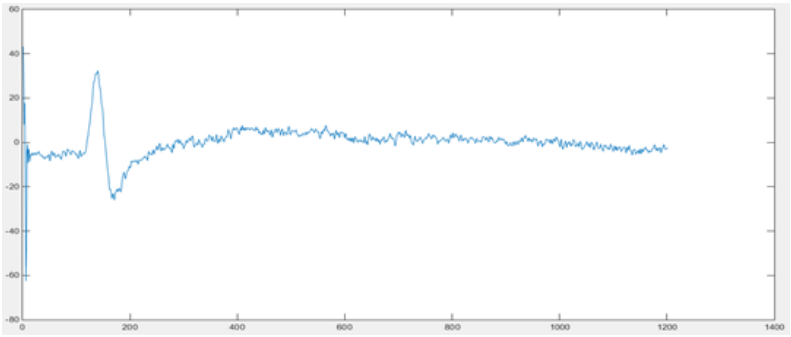


Figure 3.1: Typical form of a Sensory NCS signal.

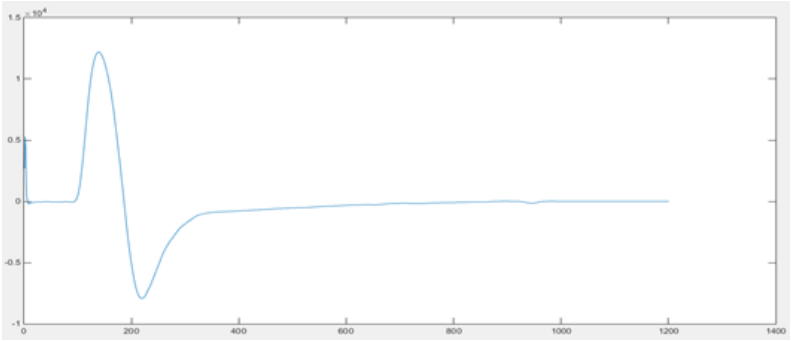


Figure 3.2: Typical form of a Motor NCS signal.

Motor nerve conduction studies performed for both ulnar and median nerves at both sides and Sensory nerve conduction studies performed at digits 2 and 4 for the median nerve and at digits 4 and 5 for the ulnar nerve. Also Sensory nerve conduction studies were performed for radial nerves at both sides.

The applied Nerve Conduction Studies (NCS) resulted in a set of signals for each study as shown in table 3.2.

Sensory Nerve Conduction Studies For digits 2, 4 and 5 (median and ulnar sensory nerves) the sensory conduction studies result signals of the form of figure 3.1.

The motor distal and proximal signal of both median and ulnar nerves, have the typical form of figure 3.2.

The sampling frequency of sensory and motor signals are 48 kHz and 24 kHz, respectively.

3.1.5 Resulting NCS Groups

The 72 hands were divided by the doctor in 4 groups using the recommended grading scale mentioned above (section 2.6.3):

- 19 hands from control group A (no CTS)
- 10 hands from group B (mild CTS)
- 17 hands from group C (moderate CTS)
- 19 hands from group D (severe CTS)

Apart from the control group, there are more 3 hands of patients that had one-hand CTS and so the other hand was included in control group.

Additionally there are 4 hands of patients with CTS clinical symptoms, who visited the hospital complaining for pain and/or numbness, but doctor found no NCS abnormalities. These hands were also included in control group, making 26 the hands of group A.

Chapter 4

Common Features

4.1 Introduction

In this chapter we focus on the main features that are extracted from Nerve Conduction Studies (NCS), since they are considered today as the most significant ones, in neurophysiology, for the diagnosis of Carpal Tunnel Syndrome (CTS).

To analyze them deeply, we examine each feature separately and also in combination with every other corresponding feature. That means, we compare all features for both median and ulnar sensory nerves and also we compare all features for both

distal and proximal motor nerves. The sensory nerve comparison is made for every pair of available NCS fingers:

- median vs ulnar at digit 4
- median at digit 4 vs ulnar at digit 5
- median at digit 2 vs ulnar at digit 5
- median at digit 2 vs ulnar at digit 4

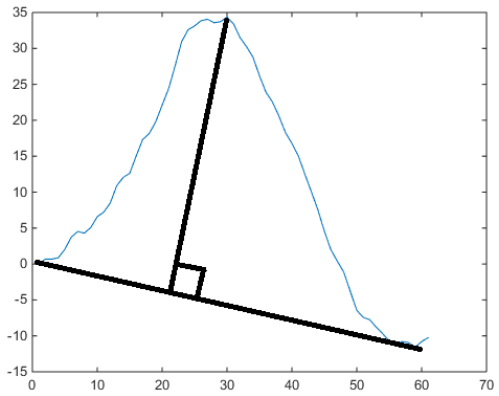
Since the basis of hands' grouping was the comparison between median and ulnar nerves at digit 4, the bias against other finger comparison certainly exists.

4.2 Sensory Amplitude (μV)

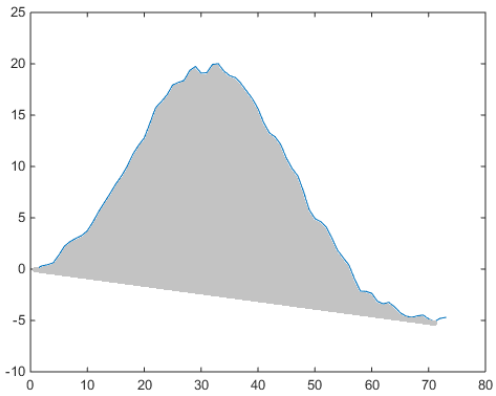
4.2.1 Amplitude Definition

There are multiple amplitudes of conduction that can be calculated when referring to curves with no-opposing edges. The machine gives to the doctor the amplitude defined as the length of the perpendicular to the line connecting the two edges, as shown on figure 4.1a.

Figure 4.1: Machine's Amplitude and Area.



(a) The Machine-given Amplitude.



(b) The Sensory Area.

In this section, we examine all alternative definitions of amplitude and we propose the one that fits best our data.

4.2.2 The machine-given amplitude

The machine calculates the amplitude described in figure 4.1.

4.2.3 Maximum Value Amplitude

Another definition of amplitude could be the maximum value, meaning the distance from the onset point. This definition ignores the existence of the negative curve and indicates the physical meaning of max μV a nerve conducted.

4.2.4 Maximum minus Minimum Value Amplitude

An alternative definition of amplitude is to estimate the distance between the max and min peaks of a curve. In this definition, the negative amplitude is weighted equal to the positive one.

4.3 Sensory Conduction Velocity (CV in m/s)

Conduction Velocity is calculated by dividing the distance between the stimulator and the recorders by the duration before the conduction started; it is considered to be the gold standard of Nerve Conduction Studies (NCS) so that very often the term NCS is replaced by the term NCV (Nerve Conduction Velocity).

4.4 Sensory Onset Latency (in ms)

Onset Latency is the time in milliseconds the stimulus travels through the nerve. It is common to claim the existence of the syndrome if the difference of latencies at dig4 between ulnar and median nerves exceeds 0.5 ms.

4.5 Sensory Peak Latency (in ms)

The Peak point is always following the onset point and its latency is defined as the time the stimulus need while travelling through the nerve to achieve the maximum

conduction value. Actually, it is the peak value of the signal.

4.6 Sensory Peak - Onset Latency (in ms)

A rare feature that is measured is the difference between the two latencies, meaning the Peak minus the Onset latency.

4.7 Sensory Area (in ms*uV)

The area given by the machine is calculated by the borders of the curve as shown on figure 4.1b.

4.8 Motor Distal and/or Proximal Amplitude

In motor nerves the amplitude of the curve is defined as the total distance between the two edges. It is equal to the maximum minus minimum value difference.

4.9 Motor Distal and/or Proximal Takeoff Latency

The take-off point of motor nerves is in accordance to the onset point of the sensory nerves; the point where the stimulus conducts the muscle at the recording area.

4.10 Motor Conduction Velocity

The conduction velocity of a motor nerve is not defined for both the distal and proximal NCS; it comes from the combination of both of them. So, there is one velocity that can be measured and is defined as the velocity (m/s) with which the stimulus travels through the motor nerve.

4.11 Results

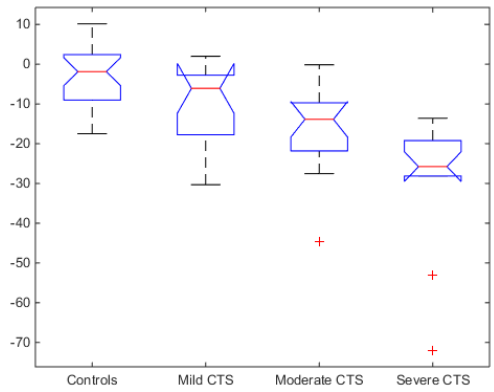
Due to few number of subjects for each group, we used the Kruskal-Wallis statistical test to get our p-values. It equals to a non-parametric one-way ANOVA test that does not assume normal distribution and is an appropriate method for ordinal (for 3 groups and more) data-sets. The alpha level was set to .01.

The results of our experiments are as follows:

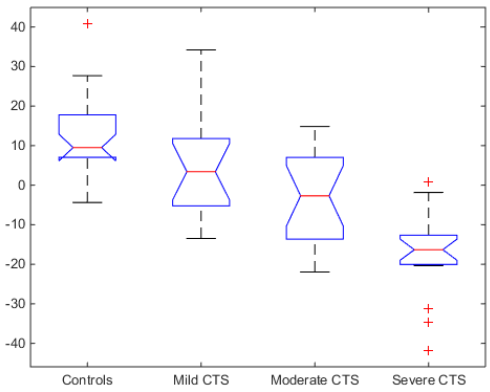
- Sensory Amplitude

  The results of our testings between all possible comparisons indicated that the comparison between median at digit 2 and ulnar nerve at digit 4 gave the best discrimination between most groups (figure 4.2).

Figure 4.2: Machine's Amplitude boxplots.



(a) Median - Ulnar at dig4.



(b) Median dig2 - Ulnar dig4.

All results are shown at table 4.1

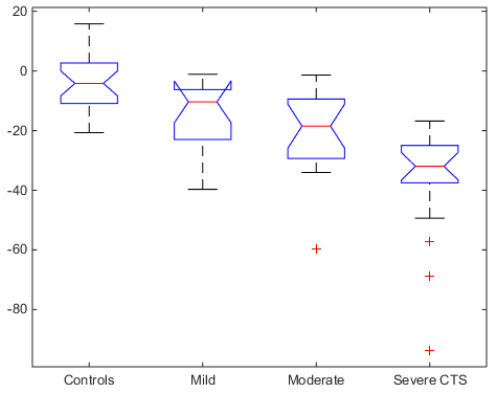
Table 4.1: Machine's Amplitude p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000013	0.03344378	0.08737528	0.00876483
median 2 - ulnar 4	0.00000000	0.01180829	0.13847672	0.00092576
median 2 - ulnar 5	0.00000282	0.12790785	0.34227921	0.00684216
median 4 - ulnar 5	0.00005327	0.11229830	0.28749542	0.05751940
median 4 - 2	0.56363495	0.41235518	0.93944001	0.54332693
ulnar 4 - 5	0.62226213	0.62976661	0.84936062	0.67053345

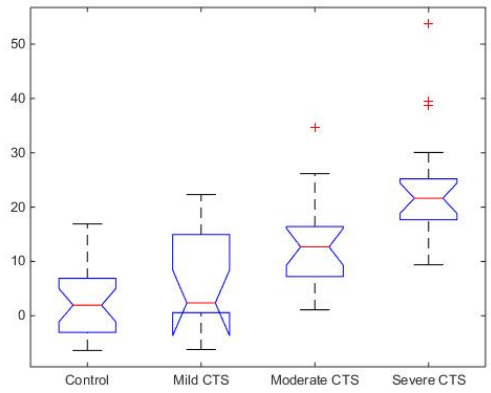
- Maximum Value Amplitude

  The results and boxplot are shown on figure 4.3a and on table 4.2. According to them, this amplitude is the most important among all the amplitudes that we discuss in this section, but still with overlapping notches.

Figure 4.3: Max and Max - Min Value Amplitude boxplots.



(a) Max Value Amplitude .



(b) Max- min Amplitude.

Table 4.2: Max Value Amplitude p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000001	0.00986819	0.12864314	0.00238703
median 2 - ulnar 4	0.00007637	0.13287038	0.70404297	0.03096931
median 2 - ulnar 5	0.01023459	0.34939958	0.96969816	0.05180401
median 4 - ulnar 5	0.00006823	0.19210231	0.49412454	0.01038538
median 4 - 2	0.74377622	0.65004536	0.34227921	0.87430472
ulnar 4 - 5	0.19776605	0.34939958	0.70404297	0.90325745

- Max minus Min Value Amplitude

  No significant results were extracted from the analysis of this kind of amplitude; the results are shown on table 4.3 and figure 4.3b.

  In conclusion, although the amplitude of the sensory nerves' signal is getting decreased as the CTS is grading, the confidence interval criterion of 99 per cent, is not met.

- Sensory Conduction Velocity

Figure 4.4: Conduction Velocity boxplot.

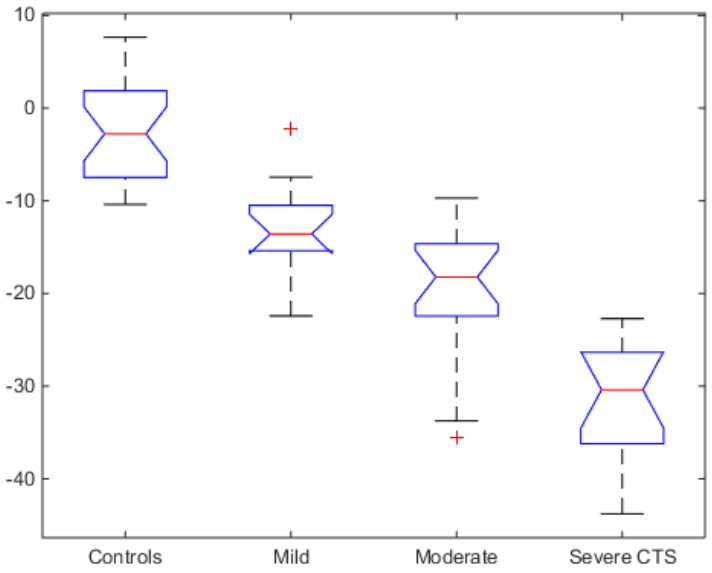


Table 4.3: Max - Min Value Amplitude p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000003	0.22272408	0.06269391	0.00089358
median 2 - ulnar 4	0.00002154	0.22272408	0.25445058	0.02092134
median 2 - ulnar 5	0.00051746	0.16469483	0.54332693	0.04490615
median 4 - ulnar 5	0.00000133	0.06127455	0.24657629	0.02272782
median 4 - 2	0.92254773	0.55152256	0.42503065	0.92503065
ulnar 4 - 5	0.90751846	0.84265906	0.76120799	0.52339298

The resulted p-values confirmed the recent literature about the importance of CV in grading the severity of the syndrome. The digit 4 comparison between median and ulnar nerves fitted best our group discrimination, as shown on figure 4.4 and on table 4.4

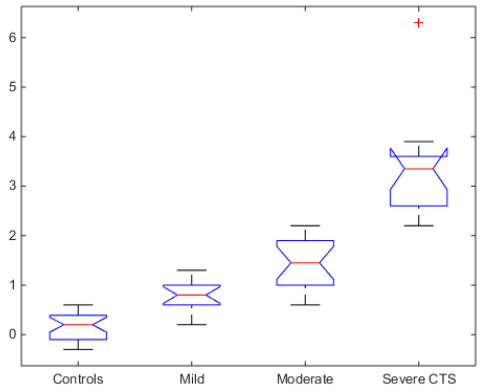
- Sensory Onset Latency
  Since this feature plays important role in grading scaling, the results shown on figure 4.5a and on table 4.5 are as expected, of the most discriminating.

- Sensory Peak Latency
  From our results, we can claim it is a significant feature in the diagnosis of CTS,

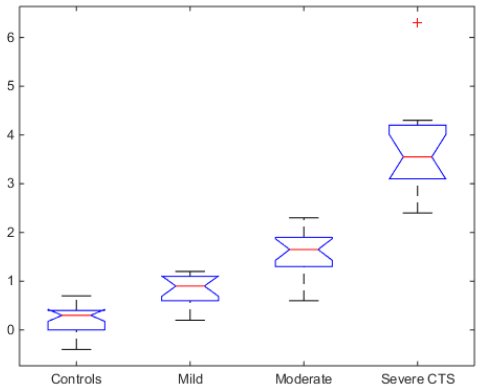
Table 4.4: Conduction Velocity p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000000	0.00001768	0.01630917	0.00016944
median 2 - ulnar 4	0.00000000	0.00010730	0.11061207	0.00023617
median 2 - ulnar 5	0.00000000	0.01010495	0.02499823	0.00023597
median 4 - ulnar 5	0.00000000	0.00047887	0.00305280	0.00047443
median 4 - 2	0.00023066	0.05628089	0.21460826	0.34227921
ulnar 4 - 5	0.09274439	0.11388761	0.07114651	0.20186788

Figure 4.5: Latencies Median - Ulnar at dig4.



(a) Onset Latency.



(b) Peak Latency.

and in some finger comparisons between groups, unexpectedly, we received better results than those that we received by the Onset latency measurement. The results are shown on table 4.6 and the box-plot on figure 4.5b

- Sensory Peak minus Onset Latencies
  The results in table 4.7 and figure 4.6a show that no significant discrimination can be determined, according to this feature's results.

- Sensory Area
  The results (table 4.8 and figure 4.6b) did not indicate any importance of the measurement of the area.

- Motor Distal and/or Proximal Amplitude
  The comparison between distal and proximal amplitudes, showed no signifi-

Table 4.5: Onset Latency p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000000	0.00000192	0.00046258	0.00000199
median 2 - ulnar 4	0.00000000	0.00002518	0.01184912	0.00001475
median 2 - ulnar 5	0.00000000	0.00018193	0.00488710	0.00000591
median 4 - ulnar 5	0.00000000	0.00000546	0.00046989	0.00000168
median 4 - 2	0.00000001	0.00065571	0.12769666	0.00026113
ulnar 4 - 5	0.54502994	0.45023424	0.96945660	0.18197572

Table 4.6: Sensory Peak Latency p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000000	0.00000344	0.00009658	0.00000168
median 2 - ulnar 4	0.00000000	0.00008261	0.00023927	0.00000512
median 2 - ulnar 5	0.00000000	0.00008310	0.00232174	0.00000509
median 4 - ulnar 5	0.00000000	0.00000444	0.00028188	0.00000169
median 4 - 2	0.00000004	0.00265028	0.34152598	0.00028297
ulnar 4 - 5	0.63336286	0.83014893	0.71589030	0.17062459

cant discrimination, confirming the recent literature that only the comparison between ulnar and median distal amplitudes is remarkable.

Because of the non-sensitivity of the motor ncs and in combination with the fact that the grading of CTS scaling assumes a motor decrease in order to bounce from mild to moderate group and a remarkable decrease to transit from moderate to severe group, we expected significant discrimination only between the two last groups, and that was verified by the results, as shown in figure 4.7a.

- Motor Distal and/or Proximal Takeoff Latency
  In addition to the amplitude, also the Takeoff latency between distal median and ulnar nerves, indicates a strong feature (figure 4.7b), while the comparison between distal and proximal measurements did not achieve any significant result at all.

  Our results verified that this feature is more important than the previous one.

- Motor Conduction Velocity

Table 4.7: Peak - Onset Latency p-values between groups.

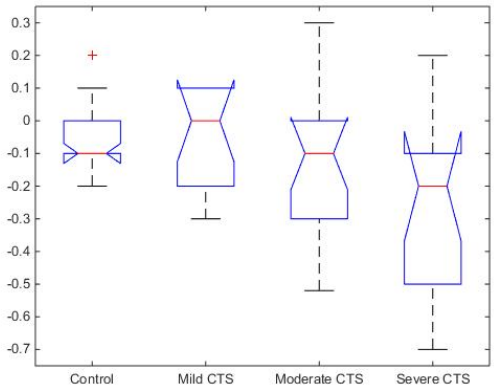
Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.03527300	0.34531717	0.14645245	0.17657217
median 2 - ulnar 4	0.00048542	0.63591522	0.13590321	0.03830345
median 2 - ulnar 5	0.00010043	0.26379900	0.26104989	0.02335438
median 4 - ulnar 5	0.01120085	0.55817997	0.35100282	0.08023567
median 4 - 2	0.00000004	0.00265028	0.34152598	0.00028297
ulnar 4 - 5	0.30489489	0.04605874	0.38079477	0.86567469

Table 4.8: Area p-values between groups.

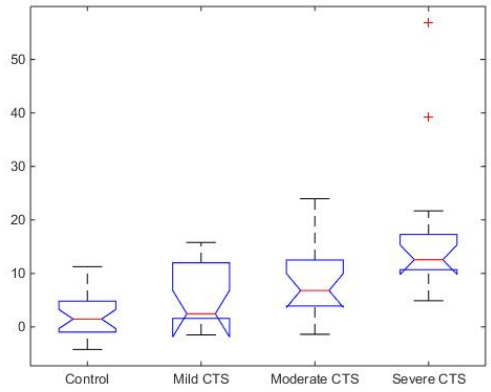
Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median 4 - ulnar 4	0.00000377	0.16469483	0.08056876	0.01505061
median 2 - ulnar 4	0.00001700	0.07411592	0.62142683	0.02266622
median 2 - ulnar 5	0.00510865	0.15993325	0.59485342	0.00896805
median 4 - ulnar 5	0.01129998	0.37937843	0.93944001	0.03668277
median 4 - 2	0.60212577	0.37977547	0.40331757	0.67605281
ulnar 4 - 5	0.45162710	0.65004536	0.59485342	0.71537845

Because of being robust (much less sensitive than in sensory nerves) the feature of motor conduction velocity did not give discriminant results. None of distal and proximal motor CV gave discriminant output for any of groups, figure 4.8

Figure 4.6: Motor Conduction Velocity (distal and proximal).

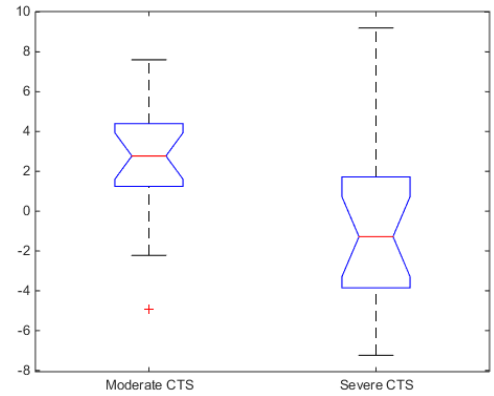


(a) Motor CV for median - ulnar distal nerves.

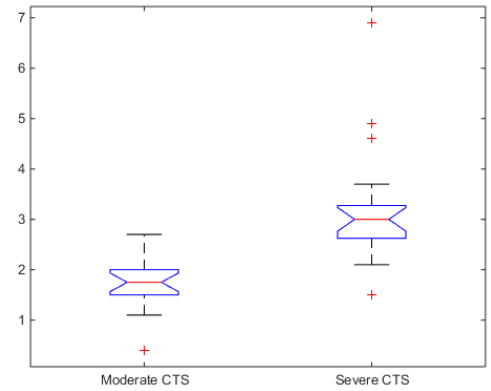


(b) Motor CV for median - ulnar proximal nerves.

Figure 4.7: Motor Amplitude and Takeoff Latency.

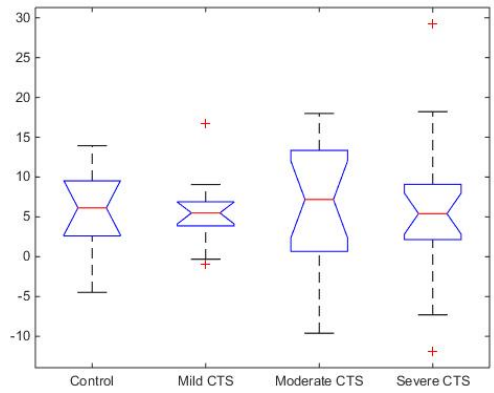


(a) Motor Amplitude for median - ulnar distal nerves.

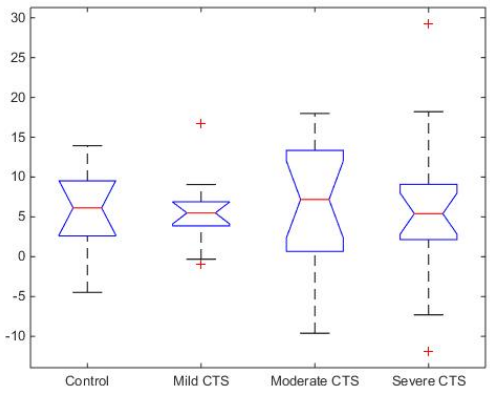


(b) Motor Takeoff Latency for median - ulnar distal nerves.

Figure 4.8: Motor Conduction Velocity (distal and proximal).



(a) Motor CV for median - ulnar distal nerves.



(b) Motor CV for median - ulnar proximal nerves.

Chapter 5

Classification

5.1 Introduction

Since automatic classification methods have never been applied to the existing features of Nerve Conduction Studies, in this chapter five main classifiers are being implemented in order to examine their results and create a model that can outcome the severity or even the existence of the syndrome:

- Logistic Regression
- K-nearest neighbor (KNN)
- Decision Trees

- Support Vector Machines
- Naive Bayes

To avoid multicollinearity problems, the most significant differences have been taken into consideration. The median - ulnar at digit 4 for the sensory nerves and the median - ulnar at distal for the motor nerves.

The labels assigned were of two kind; the doctor's grading scale and the clinical symptoms.

5.2 Logistic Regression

As a case of Generalized Linear Model, logistic regression can be seen from the same perspective of linear regression, but with two main differences:

- the label class is multinomial (binary or ordinal distribution)
- the outcome are probabilities in (0,1)

In our case, we use the Ordinal Logistic Regression, since our outcomes are ordinal labels of a syndrome severity. The name of the regression is obviously coming from the famous logistic function:

$$f(t) = \frac{1}{1 + e^{-t}} \tag{5.1}$$

which has the advantage of giving outcomes only between (0,1) that are interpreted as probabilities.

After implementing an Ordinal Logistic Regression model, we can handle the results to predict the outcome of an unseen observation. Besides, we can handle the results by interpreting the coefficients in the out-coming equations. In our case, because of the existence of four severity class labels, we will have to handle three equations. Each one expresses the log odds of the syndrome to be equal or less severe than a certain class. So, the first equation will give the coefficient of each predictor for the log odds to represent a healthy subject. The second equation will represent the log odds of the first two classes (healthy and mild CTS) against the last two classes (moderate and severe CTS). The third equation represent the log odds of the last class against the first three.

The reason why we are referring the log odds and not the probabilities term, is based upon the logit function, and there is no need for normalisation of our data:

$$\frac{f(t)}{1-f(t)} = e^{b0+b1*x1+..} \tag{5.2}$$

In order to compare the results between NCS grading and clinical symptoms, we also made one experiment with merged categories (the mild and the moderate CTS), because the clinical categorization should only have three categories in order not to be arbitrary: The category with no-symptoms, the severe category that felt weakness, and the middle category that felt only pain and/or numbness, but no weakness.

The accuracy of our model is shown on table 5.1. The classifier's results confirmed the literature in the field of non-correlation between symptoms and NCS findings.

5.3 K-Nearest Neighbor (KNN)

KNN is a classifier that implements a very simple algorithm, trying to find the k nearest observations of a new data point and label it according to the labels of these k observations. The majority, meaning the label with biggest population, wins. KNN belongs to lazy and instance-based learning algorithms. It is memory-based, because it uses the training instances that must always remember, so as to make a decision about a new entrance. Thus, it does not come with a generalization ready results, but decides after the receiving of a query. After the training phase the model stores the training data and in the testing phase the model assign a label to a data point according to the majority of most similar seen data.

The number k is defined by the user. In fact, the term 'nearest' is also defined by the user. In this chapter we use the default and most common similarity, the Euclidean Distance metric, which is defined as:

$$dist = \sqrt{\sum_{i=1}^{n}(x_i - y_i)^2} \tag{5.3}$$

while in next chapter we also implement a custom metric distance.

After making the decision about the metric distance, we examined many possible values of k. For the value of

$$k = 3 \tag{5.4}$$

our model showed the most significant results, especially in diagnosing the Carpal Tunnel Syndrome, the accuracy was almost 95 %.

5.4 Decision Tree

Decision tree is a classifier whose name came from its structure. The tree form of the classifier corresponds each input variable to a node and each target variable to a leaf. Thus, the path from the root to a leaf represents all the values of the input variables. Each node conducts a binary splitting of an attribute value.

The learning of the tree is implemented by examining every possible split of each attribute. Then the best split is chosen according to the optimization criterion which is the Gini's Diversity Index. In general a diversity index reflects to the quantitative distinct types of a dataset and their ratio inside it. The gdi (Gini's Diversity Index) is an index of such a type, since it reflects to the probability that if two instances are taken from a dataset, these are of the same type:

$$gdi = 1 - \sum_{i} p(i)^2 \tag{5.5}$$

Building a decision tree from our data through recursive partitioning and creating the nodes corresponding to the attribute values by splitting them through the gdi criterion is the process of making a model of a tree shaped classifier.

Then to classify unseen data, the model passes the corresponding attributes to its decision maker process and without needing to remember all training data, assigns to it the analogous label, by just following the already made decision rules.

In our experiments, the decision tree classifier has an accuracy of 96% of diagnosing the Carpal Tunnel Syndrome.

5.5 Support Vector Machine (SVM)

The goal of an SVM classifier is to find a hyperplane that can discriminate the classes of our data. This hyperplane is a margin between each class and the bigger it is the better the differentiation has been conducted. To construct the best hyperplane, the algorithm uses a subset of the training instances that will be closest to the hyperplane.

The vector consisted of these instances is called support vector, since this subset of training dataset supports the creation of the hyperplane. The equation of the hyperplane is:

$$w^T * x_i + b = 0 \tag{5.6}$$

In order to differentiate the classes the following equation is being used:

$$f(x) = w^T * x_i + b \tag{5.7}$$

with the goal to achieve a positive sign for one class and a negative sign for the other class:

$$f(x) \geq 0, classA$$
$$f(x) < 0, classB$$

So, in order to maximize the margin, since the best discrimination is when the hyperplane's distance for both classes' instances is the biggest possible and in real world most classes are not perfectly separable, the problem is becoming a minimization cost function:

$$minf(w) = \frac{||w||^2}{2} + C\sum_{i=1}^{N}\xi_i \tag{5.8}$$

where

$$\xi_i = 0$$

for totally separable problems, as it provides an estimate error of the decision boundary, and the function is finally induced to the following objective function:

$$f(x) = sign\left(\sum_{i=1}^{l}(a_i y_i(x..x_i) + b)\right) \tag{5.9}$$

The most important advantage of an SVM classifier is that it can transform a nonlinear problem to a linear one, but in an alternative space. This can be done using the kernel trick. The kernel trick uses a new space $\Phi(x)$ and then a linear decision boundary make the instances separable in the transformed space. In fact, we replace the inner product with the kernel function and then the same methodology is

being applied to construct a linear decision boundary. The kernel function is actually a similarity function, decided by the user.

To train an SVM classifier for instances with more than two classes, we reduce the multiclass problem into multiple binary classifications. In our thesis we implemented the one class vs the rest classes approach, after normalizing all data.

5.6 Naive-Bayes

The naive Bayes classifier is based upon the famous Bayes theorem. For that reason the classifier is trying to model probabilistic relationships between the set of attributes and the classes. Although the model assumes no dependence between the attributes and in real world this assumption does not really exist, it is commonly accepted that NB classifiers works well.

The Bayes theorem states:

$$P(Y|X) = \frac{P(X|Y)P(Y)}{P(X)} \tag{5.10}$$

The classifier in the training phase calculates, through the Bayes Theorem, the posterior probabilities of an instance to belong to each class granted the attributes. By comparing these probabilities, the biggest value wins and its class is assigned to the unseen instance.

Its advantage is that there is no need of computing each combination's class-conditional probability of an instance X (given class Y), but only the conditional probability of each attribute X_i. Although, these attributes are supposed to be independent and they are not, the simplicity of computing each attribute separately usually gives significant accuracy. The final instance conditional probability is coming from the product of the attributes' conditional probability.

In our experiments, although there is a strong relationship between our data's attributes (for example latency and velocity are certainly strongly correlated), the NB classifier has an accuracy of 96% in diagnosing the syndrome.

5.7 Feature Selection

In order to ameliorate the performance of our models we applied a custom sequential feature selection. We performed the tests to a probabilistic model (naive Bayes) and a kernel based model (SVM).

At first, we started by defining as the initial set the one which is consisted of all the features. Starting from the motor NCS features we excluded each one from the original set and then tested the performance of the model. If none of the two models gave better results, we eliminated the feature from the current set. After proceeding so with every feature, we continued by defining as our initial subset the current set of features which came up after the examination of every feature and we started adding each one feature to our model following the same order of the previous step; we started adding the motor NCS features and we kept only the features that increased any of our models' performance.

5.8 Leave-one-out Cross Validation and Results

K-fold cross validation is called the technique of partitioning the data set into k subsets of equal size. One of these subsets is used as test data and the rest k-1 subsets are used as training data. The validation process is being repeated k times, since each subset must play the role of the test data exactly once. In the special case where k=N (N: number of instances) the k-fold cross validation is induced to leave-one-out cross validation, which means that we train all the data but one instance, which plays the role of the testing data. In this thesis, because of the small number of instances and the small probability of over-fitting the model, we used the leave-one-out process for each classifier.

The selected features that gave the best results after following the process described on the previous section are the following:

- Sensory Onset Latency
- Sensory Conduction Velocity
- Sensory Max Value Amplitude
- Motor Take-off Latency

Table 5.1: Accuracy of Classifiers.

4 classes	3 classes	3 classes-Clinical	Ctrl-Patients	Ctrl-Patients Clinical
Logit				
71.23 %	81.72 %	51.95 %	80.52 %	79.57 %
SVM				
82.43 %	94.04 %	68.67 %	95.13 %	86.91 %
KNN				
66.23 %	72.08 %	53.95 %	84.71 %	74.03 %
D-Tree				
70.68 %	80.52 %	55.39 %	96.10 %	77.92 %
Naive-Bayes				
80.92 %	90.13 %	65.49 %	94.81 %	85.32 %

The results in terms of accuracy, of each classifier are shown on table 5.1.

Chapter 6

Novel Features

6.1 Introduction

In this chapter we present the geometric features we extracted from the signal in order to evaluate them. The main goal (and also the motivation of finding such features) of the extraction process, was to keep the features independent from the manual detection of the curves by the doctor. In this way we exclude the human factor and we construct automatic features. We also excluded the common features and the alternative definitions of the amplitude that were presented in chapter 4 and have already been evaluated.

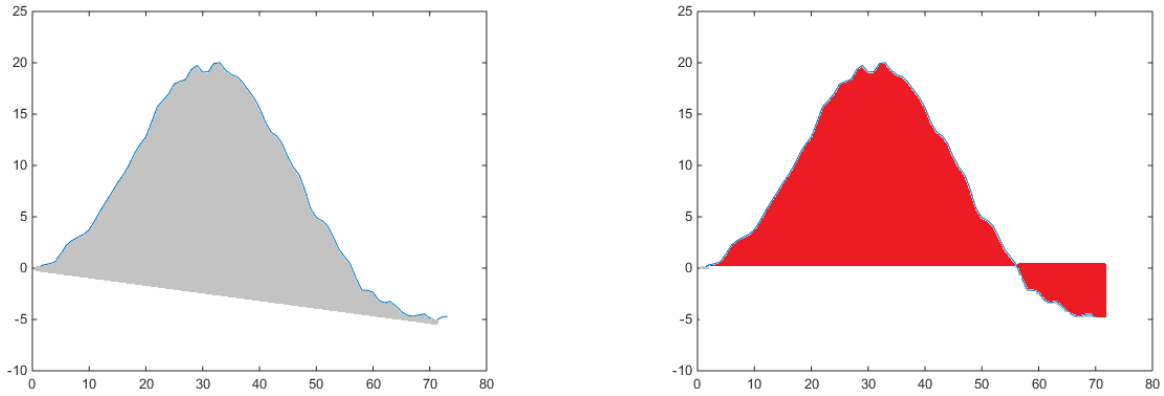
In order to characterize the result of an experiment as significant, a low p-value is not enough if it is only referred to the discrimination of two random groups. For example, if an area feature gives a significant differentiation for the severe CTS it

cannot be determined as remarkable, since the curve is being extremely distorted, and one can notice the severity of the syndrome without the aid of any automatic technique. On the contrary, if the discrimination exists between the control and the mild CTS groups, the result is absolutely significant because the early CTS is not obvious and the recent research has not made big steps in finding the gold standard of diagnosing the mild CTS.

6.2 Global Sensory Area

After examining the machine given area, we found that there is no significant results in diagnosing the Carpal Tunnel Syndrome. For this reason we defined a new type of area as shown in figure 6.1b. The new area is giving significance to the 'negative' curve and treats it as it was positive, since the physical meaning of this small negative curve is the depolarization of cells' membranes.

Figure 6.1: Definition of Machine's and Our Area.



(a) The Machine-given Area.

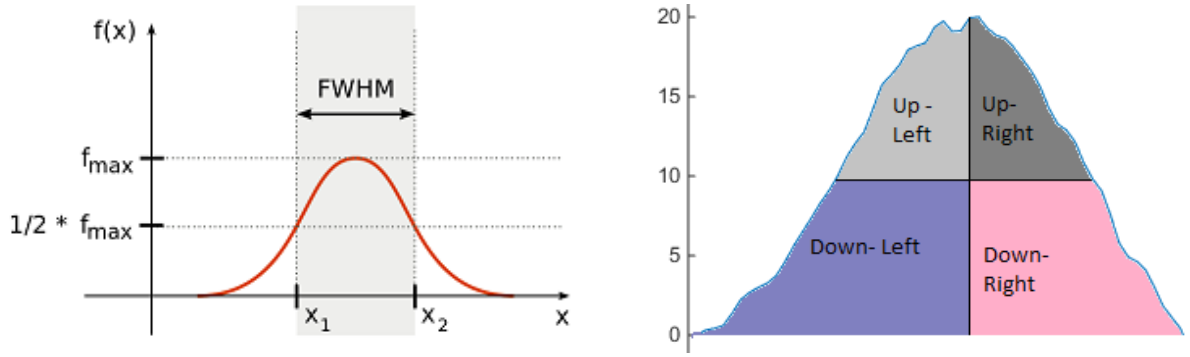
(b) New defined Area.

We can define the global area feature as the sum of A1 and A2, where A1 is the positive curve's area and A2 the negative one.

6.3 Full Duration at Half Maximum (FDHM)

FDHM is an alternative to FWHM (full width at half maximum), since we use the term duration because of time reference of our signals. It is defined as the duration (the width in x-axis) of the signal between the points where the y-values are taking the half of the maximum value, as shown on figure 6.2a.

Figure 6.2: FDHM and alternative sub-areas of a sensory curve.



(a) Full Duration at Half Maximum.

(b) New defined sub areas.

6.4 Left, Upper Left, Down Left and Right, Upper Right and Down Right Areas

From figure 6.2b, we present the definition of the four main subareas which are divided by the FDHM line of x-axis and the peak-to-zero line of y-axis:

- Upper Left Area
- Down Left Area
- Upper Right Area
- Down Right Area

and then, from these partitions of areas we define the following areas:

- Left Area as the sum of Upper and Down Left areas
- Right Area as the sum of Upper and Down Right areas

- Up Area as the sum of Upper Left and Upper Right areas and
- Down Area as the sum of Down Left and Down Right Area.

All these areas were considered as features, and also all the possible ratios between each other; then we experimented each one alone for the median nerve and then in comparison with the corresponding feature of the ulnar nerve.

We conducted this process for both sensory and motor nerves. The motor NCS consists of two curves, a positive and a negative one, so we implemented the process for both of them.

6.4.1 All other possible ratios

In order to complete the areas experiment, we computed the significance of all possible ratios between the areas:

- Upper Left Area/Left Area
- Down Left Area/Down Area
- Upper Left Area/Upper Area
- Left Area/Global Area
- Upper Area/Global Area
- Upper Left Area/Global Area

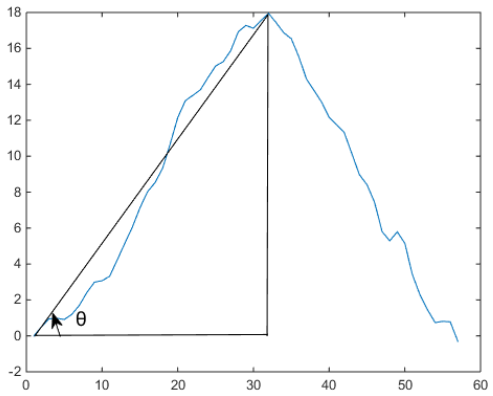
6.5 Tangents and Fitting Slopes

In this section the features of two kind of slopes are presented for both left and right side of each curve and their discriminating ability is being examined.

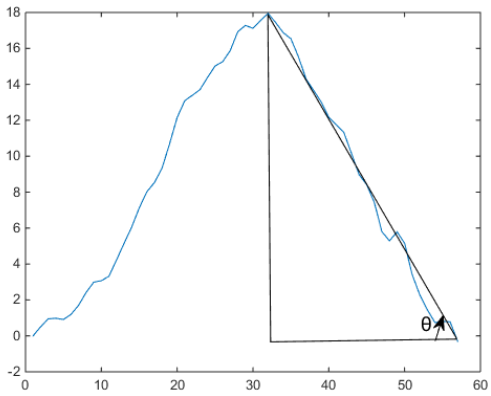
6.5.1 The tangent of theta

The first type of slope is defined as the tangent of the angle theta of the line that connects the onset (start) point and the peak (max-amplitude) point.

Figure 6.3: Left and Right TanTheta Feature definitions.



(a) Left Tangent.



(b) Right Tangent.

$$\tan(\theta) = \frac{f(peak) - f(onset)}{peak - onset} \tag{6.1}$$

and the analogous definition is coming from the right side of each curve. Both definitions are shown on figure 6.3, and were implemented also for the negative curves of the signals.

$$\tan(\theta) = \frac{f(offset) - f(peak)}{offset - peak} \tag{6.2}$$

The left negative tangent, however, can fairly differentiate the the syndrome groups from the control group, when compared the median - ulnar nerves.

On the contrary, the motor NCS findings did not serve any significant result by the tangents of every side of all curves.

The most significant results of sensory tangents are shown on table 6.1.

6.5.2 The fitting slope

Another extracted feature, is the fitting slope, meaning the line that best fits all the data points of the left and then the right side of the curve, using the least squares method, by minimizing the sum of squared errors of the fitting line.

Table 6.1: Sensory tangents features.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
Left Positive				
median-ulnar 4	0.00000064	0.15624627	0.06269391	0.02090932
median 4	0.00000000	0.10602875	0.00004812	0.00000598
Left Negative				
median-ulnar 4	0.00000130	0.00060187	0.93011051	0.03531743
median 4	0.00000003	0.31731051	0.00286375	0.04904607
Right Positive				
median-ulnar 4	0.00000011	0.02006083	0.14887949	0.02468220
median 4	0.00000000	0.22272408	0.00022895	0.00006634

6.6 Results for each Feature

In this section we present the results of our new features. In ratios instances, we display those which not demand human' s interference, e.g. upper left / upper area, except from cases of other ratios where there exist remarkable outcomes.

- Global Sensory Area

  The results showed no significance for all of the three type of areas: A1, A2 and Global Area = A1 + A2 alone and in every possible combination between median and ulnar nerves of all digits.

  In this experiment we also computed the expanded total area: we followed the curve until its end, meaning until the time when it becomes zero by crossing the x-axis, but again the area did show not at all significant result in diagnosing the syndrome or discriminating two categories of severity between each other.

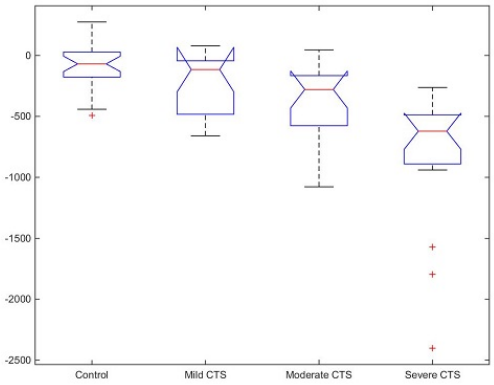
  To conclude, the feature of global area of any type, and in many possible alternative definitions of the term area, should not be considered as a significant feature in the diagnosis of CTS.

  Results are shown on figure 6.4.

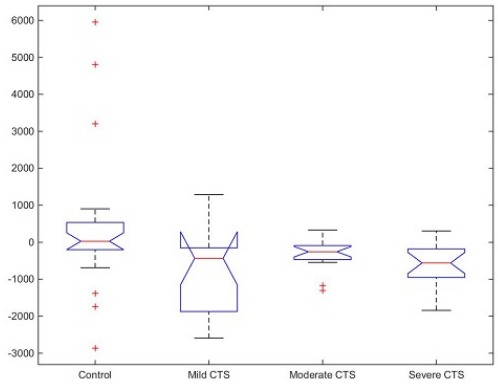
- FDHM

  The FDHM experimentation resulted in significant outcomes, not only from the comparison between fingers but also as a standalone feature. As shown on figure 6.5 and on table 6.2 the median - ulnar at digit 4 comparison gave the best

Figure 6.4: Area and Expanded Total Area comparison median - ulnar 4.



(a) New Defined Area median - ulnar at dig4.



(b) Expanded Area median - ulnar at dig4.

results, but also the median fdhm at digit 4 gave remarkable, even if they are not better than the comparison between median - ulnar, results. Until now this is the only feature that can give significant p-values and discriminant box-plots as solo, without the comparison of median and ulnar nerves. For both features, the last group, that of severe CTS, is not significantly discriminated.

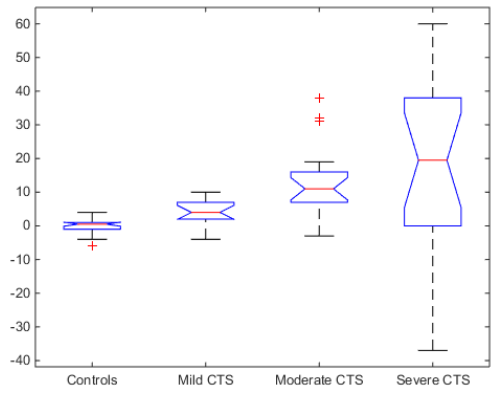
Table 6.2: Fdhm p-values between groups.

Comparisons	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
median-ulnar 4	0.00001594	0.00074779	0.00606262	0.17332437
median 4	0.00037206	0.04211000	0.02239443	0.24777272

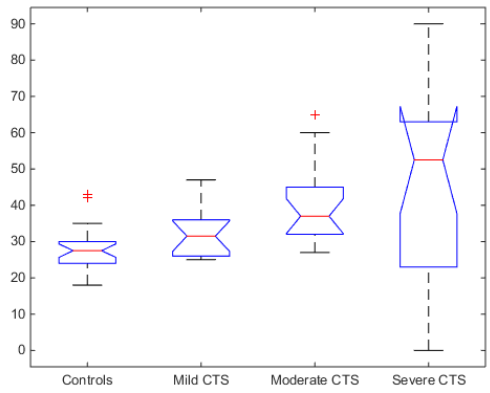
- Sensory Left and Right Areas
  These features did not give any significant result of the sensory nerves in differentiating any pair of the four levels of CTS (figure 6.6).

- Sensory Upper and Down Areas
  For the sensory nerve, only between the obviously separated groups these features gave significant results, between the control and the moderate CTS and between the mild and the severe CTS. However this is not a requesting potential of an automatic process. The most significant issue in our thesis should be to recognize two nearby classes and specifically the Control against the Mild CTS

Figure 6.5: FDHM comparison median - ulnar 4 and FDHM solo median 4.

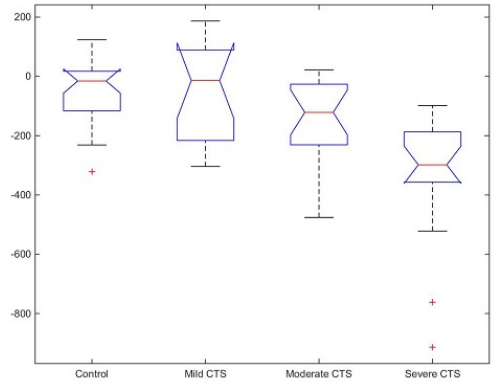


(a) FDHM median - ulnar at dig4.

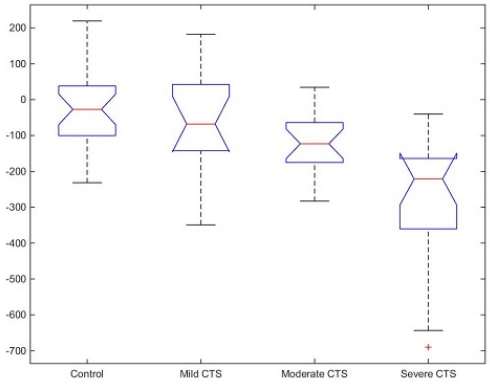


(b) FDHM only median at dig4.

Figure 6.6: Left and Right Areas comparison median - ulnar 4.



(a) Area Left median - ulnar at dig4.



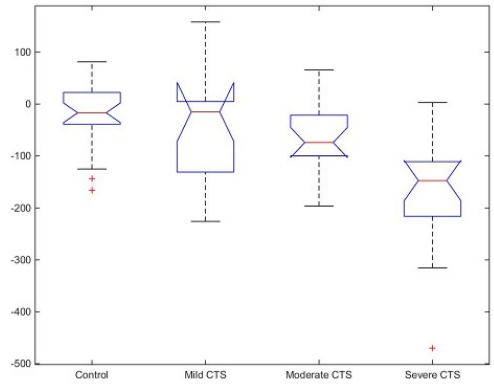
(b) Area Right median - ulnar at dig4.

class. This would lead to an almost perfect diagnosing of the syndrome. Results are shown on figure 6.7.

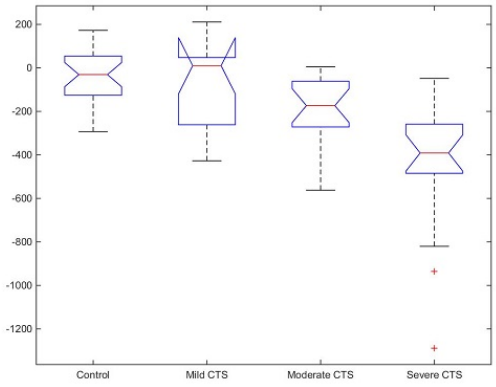
- Sensory Upper Left and Right Areas
  Due to broaden variance of the Upper areas for the mild CTS group, none feature gave remarkable results (figure 6.8).

- Sensory Down Left and Right Areas
  No differentiation between controls and CTS groups was obtained, as shown in figure 6.9.

Figure 6.7: Upper and Down Areas comparison median - ulnar 4.



(a) Upper Area median - ulnar at dig4.



(b) Down Area median - ulnar at dig4.

- Sensory Upper Left / Upper Area
  No discrimination between controls and CTS groups was obtained, as displayed in figure 6.10a

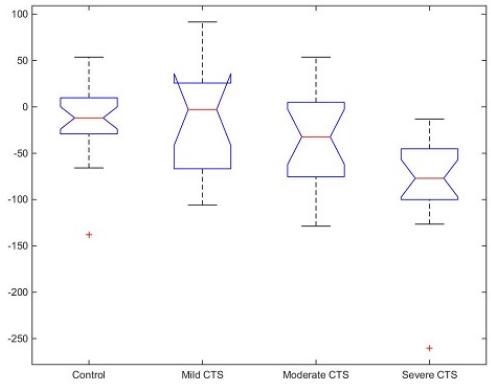
- Sensory Upper Left / Left Area
  No differentiation between controls and CTS groups was obtained, as shown in figure 6.10b

- Sensory Upper Left /Global Area
  Analogous to previous features' results (figure: 6.11a).

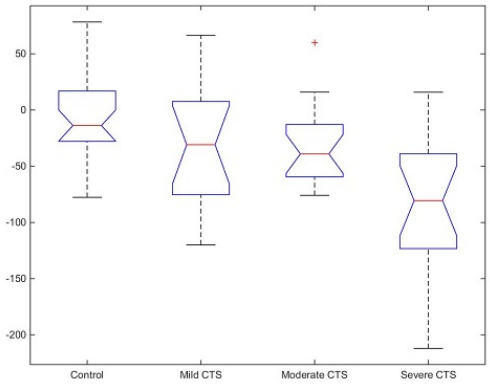
- Sensory Upper /Global Area
  No detection of CTS was achieved, figure 6.11b.

- Sensory Left and Right Tangent Theta
  The results of sensory nerves' tangent gave significant discrimination between the most nearby classes of CTS severity. The best results were given by the left tangent of the solo median nerve at digit 4. The comparison between median and ulnar nerves also gave remarkable results, but not as such of the median standalone corresponding feature. On the other hand, the median - ulnar comparison for the left tangent of the negative curve of sensory nerves gave better outcomes than the solo median feature. For all comparisons there always exists a pair of groups that there is no discriminating ability between them. The results are shown on figures 6.12 and 6.13

Figure 6.8: Upper Left and Right Areas comparison median - ulnar 4.



(a) Upper Left Area median - ulnar at dig4.



(b) Upper Right Area median - ulnar at dig4.

- Sensory Left and Right Fitting Slope
  The sensory NCS left and right slopes gave analogous but worst than the corresponding tangents results. 6.14 and 6.15

- Motor Distal and Proximal Left and Right Areas
  The motor Right Area for both Distal and Proximal NCS, of positive curves, gave significant outcomes. The importance of the results comes from the fact that it performs a significant separation between the control group and the rest. This is a surprise, because the motor nerve is known as robust and non-sensitive in early CTS, while the outcome is totally unbiased, since for the construction of the grading scale the motor findings do not play any role between the no-CTS and the mild CTS groups. The motor NCS findings are used to separate the mild from the moderate and the moderate from the severe group.

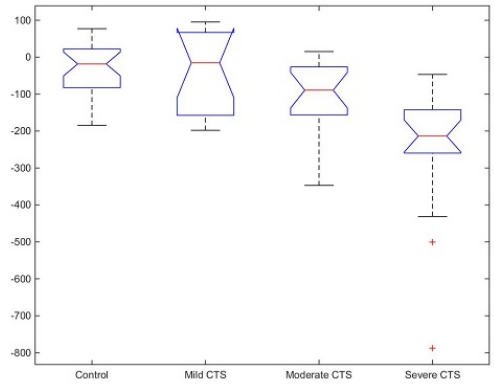
  The results are shown on figure 6.16.

- Motor Distal and Proximal Up and Down Areas
  The motor nerve did not either give significant results for any of these features in any of its curves.

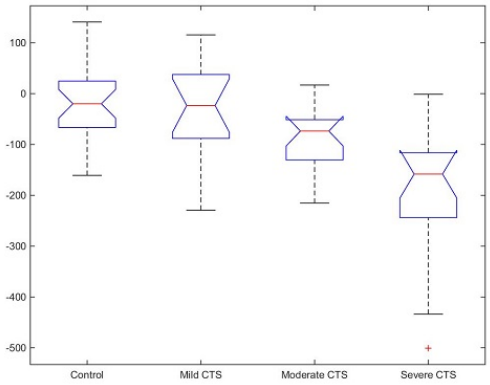
- Motor Distal and Proximal Upper Left and Right Areas

  The experiments lead to similar to the Right Areas results: The sensory nerve did not outcome significant results while the motor distal and proximal NCS

Figure 6.9: Down Left and Right Areas comparison median - ulnar 4.



(a) Upper Left Area median - ulnar at dig4.



(b) Down Right Area median - ulnar at dig4.

of Upper Right areas can decide for the existence of the syndrome. As before, the comparison between median and ulnar nerve do not come with significant results.

The results are shown on figure 6.17.

- Motor Distal and Proximal Down Left and Right Areas
  The results for these features were analogous to the previous experiments. The motor distal and proximal Down Right Area gives significant discrimination between the control group and the rest syndrome groups.

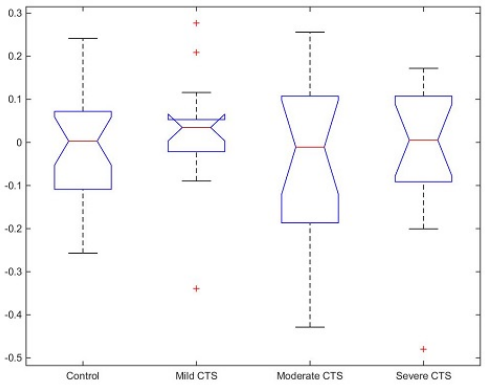
- Motor Distal and Proximal Upper Left / Upper Area
  This ratio is not depended upon human' s detection of the curve, but did not outcome any important conclusion, as shown on figure 6.18.

- Motor Distal and Proximal Left and Right Tangent Theta
  The tangents of all kinds did not give good results (figure 6.19).

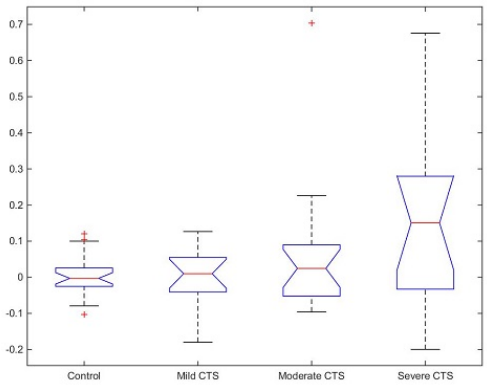
- Motor Distal and Proximal Left and Right Fitting Slope
  The slopes did not give powerful results (figure 6.20).

- Motor Distal and Proximal FDHM
  For both curves the FDHM feature did not output significant results (6.21).

Figure 6.10: Upper Left to Upper and Upper Left to Left Area Ratio comparison median - ulnar 4.

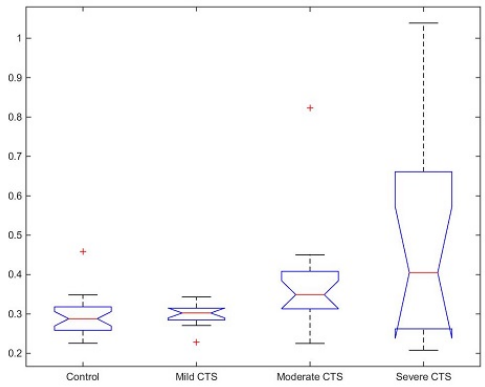


(a) Upper Left Area median - ulnar at dig4.

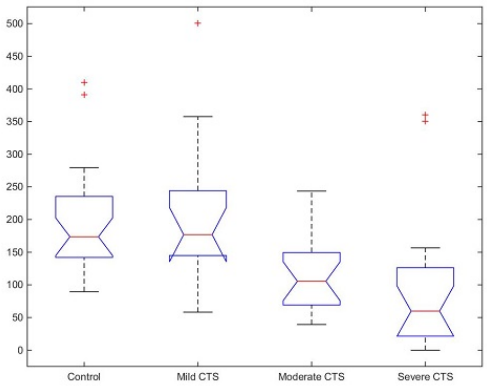


(b) Down Right Area median - ulnar at dig4.

Figure 6.11: Upper Left to Upper and Upper Left to Left Area Ratio comparison median - ulnar 4.

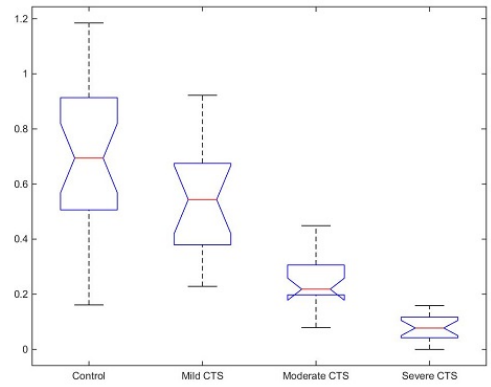


(a) Upper Left Area median - ulnar at dig4.

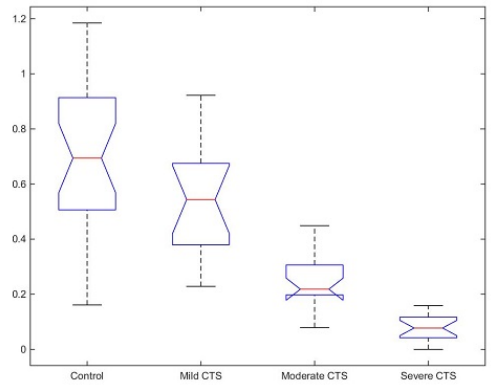


(b) Down Right Area median - ulnar at dig4.

Figure 6.12: Sensory Left TanTheta median 4 and comparison median - ulnar 4.

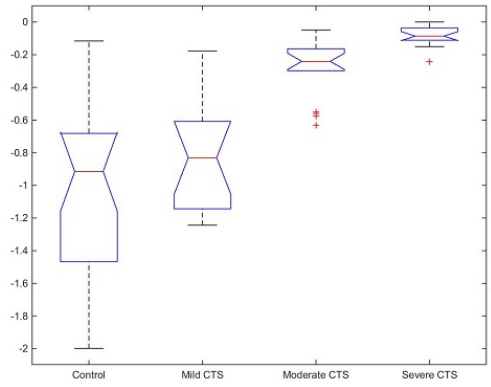


(a) Left TanTheta median at dig4.

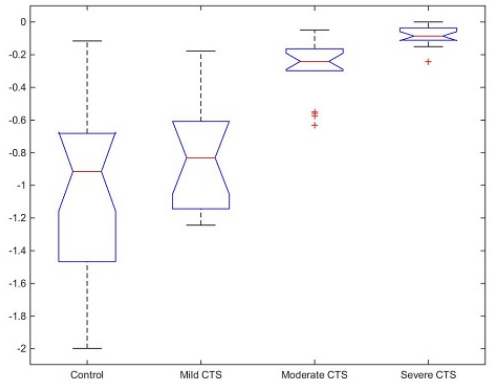


(b) Left TanTheta median - ulnar at dig4.

Figure 6.13: Sensory Right TanTheta median 4 and comparison median - ulnar 4.

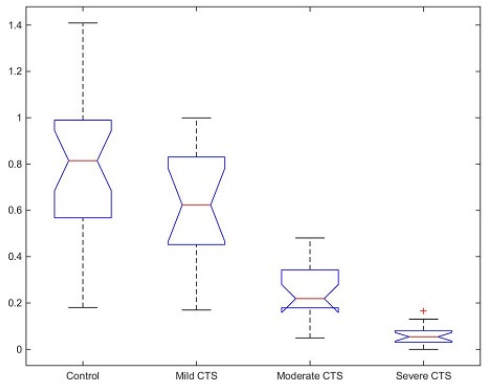


(a) Right TanTheta median at dig4.

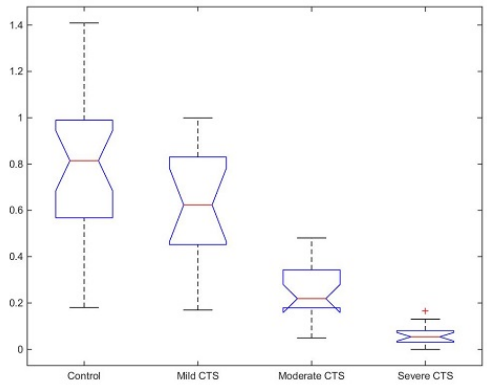


(b) Right TanTheta median - ulnar at dig4.

Figure 6.14: Sensory Left Slope median 4 and comparison median - ulnar 4.

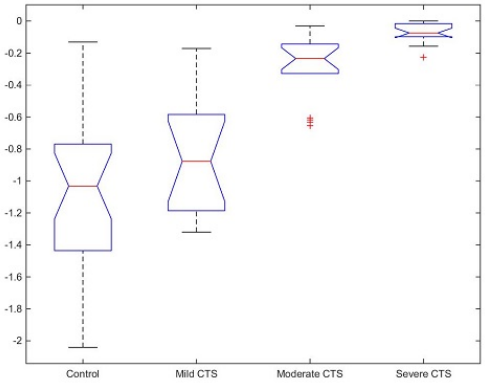


(a) Left Slope median at dig4.

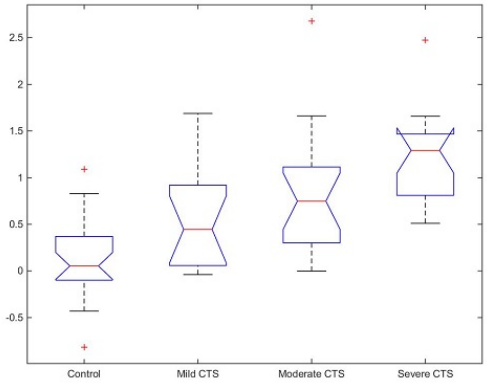


(b) Left Slope median - ulnar at dig4.

Figure 6.15: Sensory Right Slope median 4 and comparison median - ulnar 4.

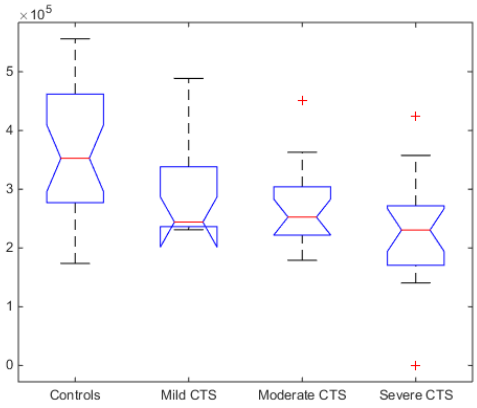


(a) Right Slope median at dig4.

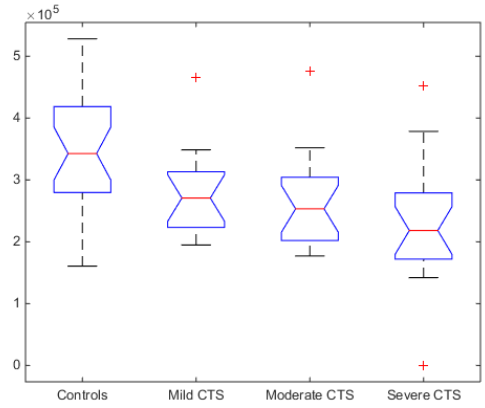


(b) Right Slope median - ulnar at dig4.

Figure 6.16: Right Motor Areas from Distal and Proximal NCS.

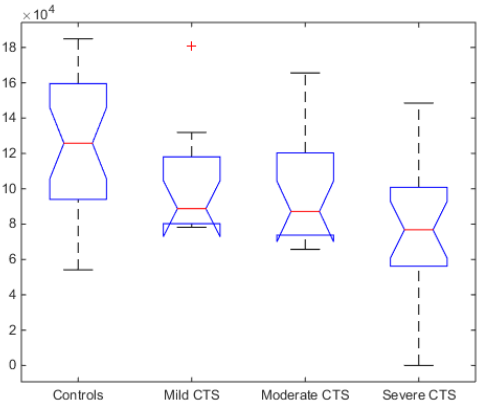


(a) Right Area for motor distal.

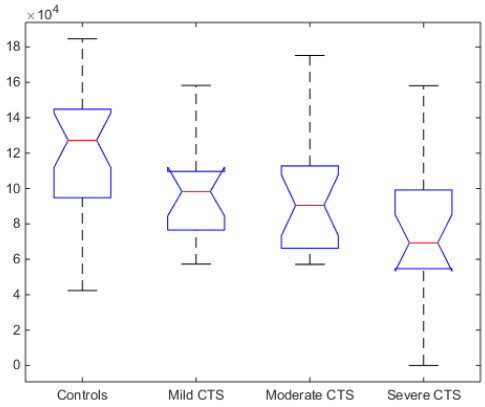


(b) Right Area for motor proximal.

Figure 6.17: UpRight Motor Areas from Distal and Proximal NCS.

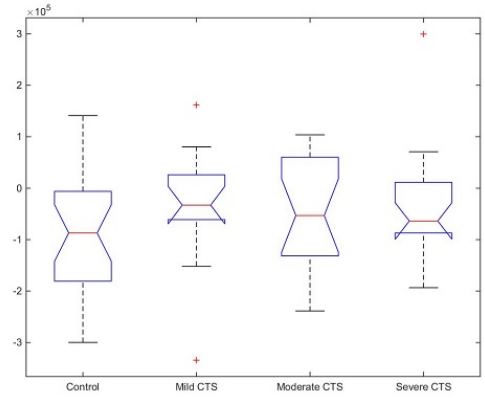


(a) UpRight Area for motor distal.

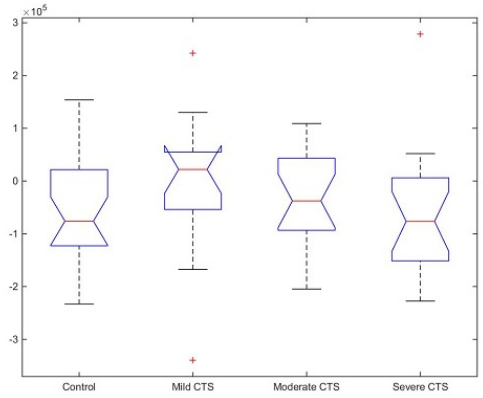


(b) UpRight Area motor proximal.

Figure 6.18: UpRight Motor Areas from Distal and Proximal NCS.

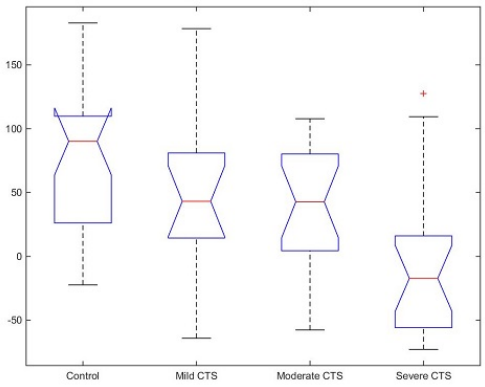


(a) Ratio of Upper Left to Upper for motor distal.

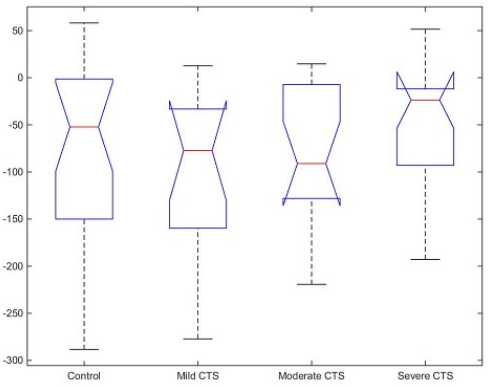


(b) Ratio of Upper Left to Upper for motor proximal.

Figure 6.19: Tangents for Distal and Proximal NCS.

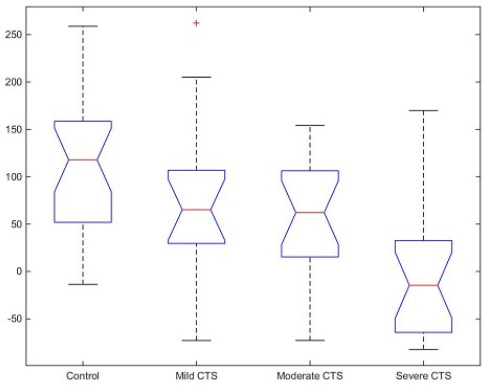


(a) Best tangent for motor distal (left).

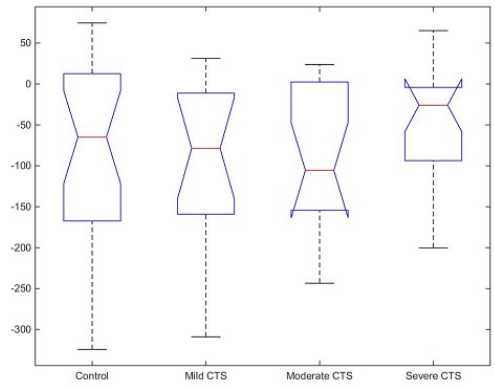


(b) Best tangent for motor proximal (left).

Figure 6.20: UpRight Motor Areas from Distal and Proximal NCS.

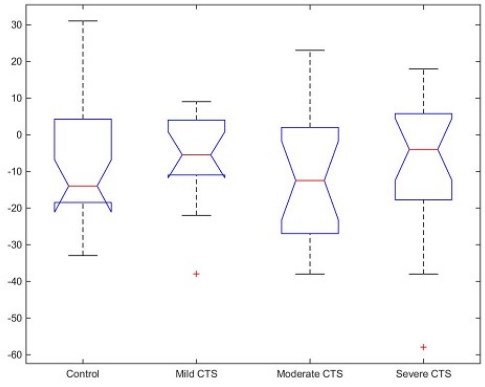


(a) Best slope for motor distal (left).

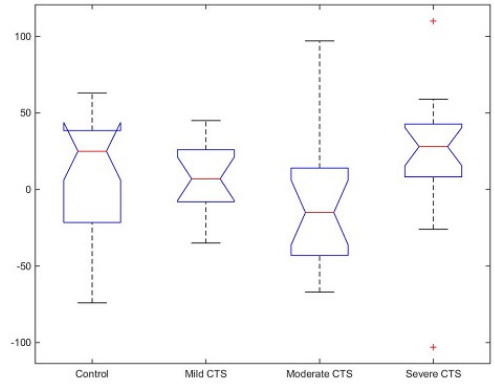


(b) Best slope for motor proximal (left).

Figure 6.21: FDHM for Distal and Proximal NCS.



(a) FDHM for motor distal.



(b) FDHM for motor proximal.

6.7 Classification Results

In order to evaluate again the findings of our experiments according to the new geometric features, we constructed the same classifiers of Chapter 5, using the same parameters. Our dataset firstly only consisted of the new features, but then we proceed with the addition of the main features that were presented to the previous chapter, so as to examine a potential amelioration of our model.

At the first part, all the features covered in previous sections of this chapter are used to construct an SVM and an Naive Bayes classifier. Then, we computed the cross-validation leave-one-out type and we started eliminating each feature one by one. Although we started from the high p-values features, only if the accuracy increased, after removing the variable, for all iterations, we eliminated that feature permanently. The result was such noticeable that from 31% accuracy (when all features were included) we ended up with three features and 71% accuracy.

From this process the remaining features are the same with the most significant features of our geometric characteristics, which means:

- the motor right area of the distal positive curve
- the sensory right tangent theta at digit 4
- the sensory FDHM for median - ulnar difference at digit 4

The accuracy of all classifiers as models with these three variables are presented on table 6.3

At the second part of our process, we added the remained attributes to the original common features of the previous chapter. As shown in the results at table 6.4 for most of the classifiers the model accuracy increased in the field of prediction of the exact class label of CTS severity.

However, the classifiers' accuracy values of the Controls vs rest groups of CTS comparison, has decreased after the addition of the geometric features. This would be flattering if it was combined with optimistic results from the perspective of clinical symptoms, but as we can notice at columns 3 and 5 of the referencing table, the differentiation between clinical classes also gave worst results. The target of finding a new set of features with remarkable enough results in NCS grading accuracy and better than the existing results in clinical correlation remains unsatisfied.

Table 6.3: The models of the three most important geometric features.

4 classes	3 classes	3 classes-Clinical	Ctrl-Patients	Ctrl-Patients Clinical
Logit				
54.55 %	63.64 %	59.09 %	81.82 %	82.47 %
SVM				
73.88 %	86.22 %	71.87 %	89.66 %	87.48 %
KNN				
57.14 %	66.54 %	51.69 %	84.42 %	83.12 %
D-Tree				
63.64 %	83.02 %	72.73 %	87.01 %	74.38 %
Naive-Bayes				
71.43 %	74.03 %	56.42 %	81.42 %	79.26 %

Table 6.4: Accuracy of supplementary Classifiers.

4 classes	3 classes	3 classes-Clinical	Ctrl-Patients	Ctrl-Patients Clinical
Logit				
77.92 %	83.12 %	55.19 %	83.77 %	74.03 %
SVM				
91.17 %	94.15 %	71.44 %	95.13 %	89.06 %
KNN				
74.03 %	79.22 %	56.10 %	88.05 %	87.01 %
D-Tree				
81.82 %	81.17 %	56.49 %	94.81 %	85.71 %
Naive-Bayes				
87.01 %	89.61 %	65.94 %	90.91 %	81.72 %

Chapter 7

Dynamic Time Warping (DTW)

7.1 Introduction

Dynamic Time Warping (DTW) is an algorithm implemented in times series on the purpose of finding similarities between signals. The goal of findings similarities is to recognize an individual shape, no matter the speed of its action. As its name defines, DTW warps the signals in the dimension of x-axis (time dimension) non-linearly.

In short terms DTW is trying to find the best alignment between two signals under certain conditions. It is widely used to recognize patterns in sound (voice) [11] and in activities (walking -running). Its implementation is based upon the fact that similar patterns indicate the same individual that takes an activity.

For example a person' s time series sound signal when speaking normally and when speaking rapidly is expected to give significant similarity when these two signals are been tested though DTW algorithm.

For the same reason, the tracking time series signal of a walking activity of a person and a running activity of the same person, should give high similarity, while the comparison between a walking activity of this person should output small similarity when compared with walking or running activity tracking of another person.

In other words, DTW abstracts the feature of speed from two signals and compares their shapes.

Apart from speech and activity recognition, the DTW algorithm is lately used for on-line signature recognition and shape matching applications.

In this chapter, we examine the implementation of DTW algorithm in the diagnosis of Carpal Tunnel Syndrome, by implicating it for every possible pair of signals, so as to determine if it can decide for similarities between time series signals of CTS affected and CTS non-affected nerves.

The main concept is that since DTW can match shapes, and we have data of nerves that have their NCS affected by the syndrome and other nerves that are not, the algorithm could detect high similarity between non affected nerves and small similarity between affected and non-affected nerves.

On the other hand, CTS is a syndrome for the diagnosis of whom the feature of speed is the most important. Conduction Velocity and Onset Latency are speed parameters and are nowadays considered to be the gold standard in the diagnosis of CTS, but DTW abstracts the time.

7.2 About Dynamic Time Warping (DTW)

Since, Euclidean distance between time series is not an appropriate distance metric to cluster and classify signals because of potential varying lengths, phase shifting and existence of delays the DTW algorithm is doing well in allowing (and ignoring) acceleration of signals along the time dimension [12]. The process of finding the best mapping between two signals by expanding or compressing works under certain restrictions.

The goal of DTW algorithm is to find the mapping path (along a distance matrix) with minimized overall cost.

Considering:

- two time series x and y of lengths m and n respectively,

- a cost matrix M of size $m * n$
- a path p as an ensemble of pairs of points x and y that starts from point [1,1] and ends to point [m,n] of the matrix M

Then the path $[p(1,1), p(x_i, y_j), ..., p(m,n)]$ is optimal, if it minimizes the overall distance of equation 7.1 with the following conditions:

- Boundary Condition: p_1=$p(1,1)$ and p_k=$p(m,n)$
- Monotonicity Condition: $n_k \geqslant ..... \geqslant n_2 \geqslant n_1$ and $m_k \geqslant ..... \geqslant m_2 \geqslant m_1$
- Step size Condition: For any pair (i,j) in the path, the possible next pairs are restricted to (i+1,j), (i,j+1), (i+1,j+1).

$$\sum_{i=1}^{k} |x(px_i) - y(py_i)| \tag{7.1}$$

In the algorithm 7.1 we present our implementation of DTW for finding the cost Matrix D, in Matlab. In the algorithm 7.2 we present the algorithm of finding the Optimal Warping Path.

In order to visualize the technique of DTW, we are going to implement the whole process to a sample of our data. The curves of a control subject (sensory median and ulnar nerves at digit 4) and of a patient, are been evaluated under the process of DTW, following these steps:

- Compute and Visualize Euclidean Distance Matrix.
- Compute and Visualize DTW (Accumulated) Cost Matrix.
- Backtracking for finding the optimal warp path.
- Visualize the optimal pair of time alignments.

7.2.1 Visualization of Distance and Accumulated Cost Matrices

To compute the euclidean distance matrix between two time series we calculate the equation of 7.2.

To compute the accumulated cost we calculate the equation 7.3 by implementing the algorithm 7.1

Algorithm 7.1 Dynamic Time Warping.

```
function D ⇐ mydtw(s1, s2)
n1 ⇐ size(s1, 1);
n2 ⇐ size(s2, 1);
D ⇐ zeros(n2, n1);
D(1, 1) ⇐ norm(s1(1, 1) − s2(1, 1));
for i=2:n1 do
    cost ⇐ norm(s1(i, 1) − s2(1, 1));
    D(1, i) ⇐ cost + D(1, i − 1);
end for
for i=2:n2 do
    cost ⇐ norm(s1(1, 1) − s2(i, 1));
    D(i, 1) ⇐ cost + D(i − 1, 1);
end for
for j=2:n1 do
    for i=2:n2 do
        cost ⇐ norm(s1(j, 1) − s2(i, 1));
        D(i, j) ⇐ cost + min([D(i − 1, j), D(i, j − 1), D(i − 1, j − 1)]);
    end for
end for
return D
end
```

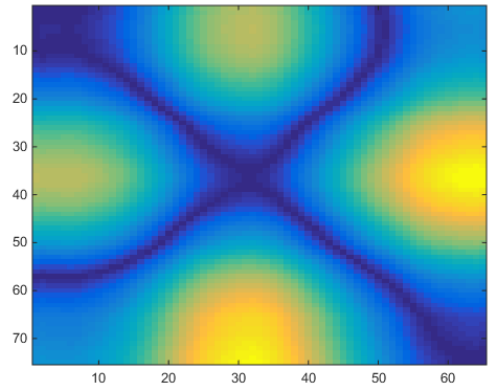
$$E(i,j) = \sqrt{(x(i) - y(j))^2} \tag{7.2}$$

$$D(i,j) = E(i,j) + min[D(i-1,j), D(i,j-1), D(i-1,j-1)] \tag{7.3}$$

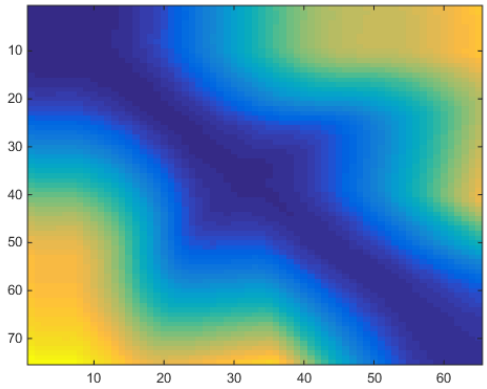
The distance matrices for euclidean and accumulated costs, are shown on figure 7.1 for the control and on figure 7.2 for the patient subject.

The darkest the blue is, the smaller the distance and the accumulated cost are. It is obvious that the diagonals of both the matrices consist of low cost cells, which means that the distance between similar points of the signals are closest than the points of large variance in time domain.

Figure 7.1: Control's Visualization of (a) Euclidean Distance and (b) Accumulated Cost.



(a) Euclidean Distance.



(b) Accumulated Cost (DTW).

7.2.2 Backtracking for finding the Optimal Warp Path

We can convert the problem of finding the path of minimum distance into a dynamic programming problem that can be solved in O(mn) time.

Since we have constructed the matrix of DTW using the algorithm 7.1, we can easily now use backtracking method to find the path with the minimal distance; we start form D(m,n) and we move backwards to the lowest cost cells. The algorithm of backtracking the optimal path is presented on algorithm 7.2

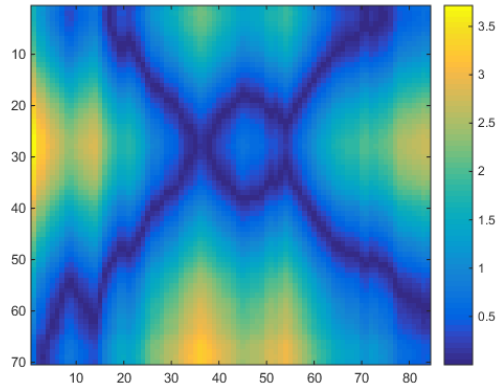
The visualization of the path alongside the matrices is shown on figures 7.3 and 7.4

7.2.3 Visualization of regarding alignments

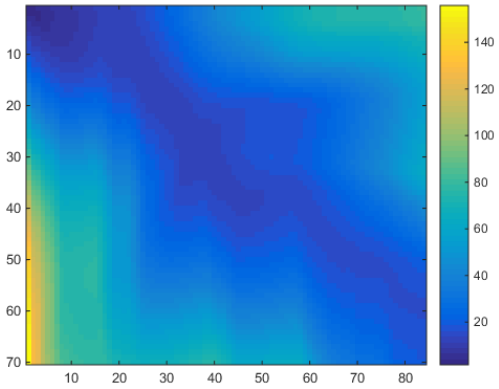
The presented process has as output a single path, the optimum one, from which every point of a signal is aligned with another point of the other signal. Using the extracted path, we can visualize the alignment for each pair of time series as shown on figure 7.5.

The last cell of the path, meaning the p(n,m) which is the most down-right cell of the accumulated cost (DTW) Matrix and is equal to D(n,m), is been extracted and used as a stand-alone feature to describe the similarity between two time-series. As shown on figure 7.6 this feature, one number, the value of the last cell of the D Matrix, can do very well in making decisions about the existence of the syndrome.

Figure 7.2: Patient Visualization of (a) Euclidean Distance and (b) Accumulated Cost.



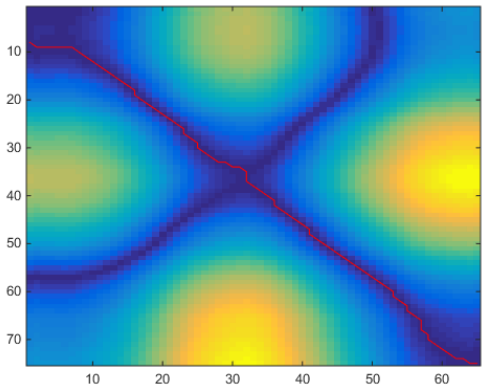
(a) Euclidean Distance.



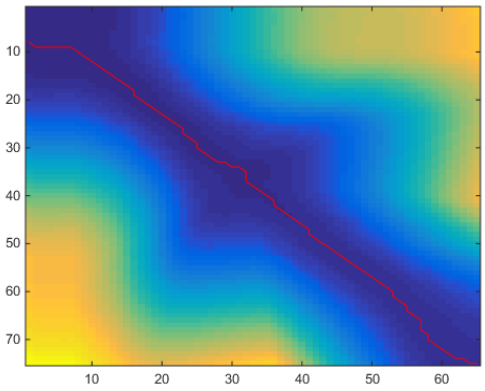
(b) Accumulated Cost (DTW).

In next section we examine this feature in all possible combinations of all existing signals.

Figure 7.3: Control's Visualization of Path Warping at (a) Euclidean Distance and (b) Accumulated Cost.

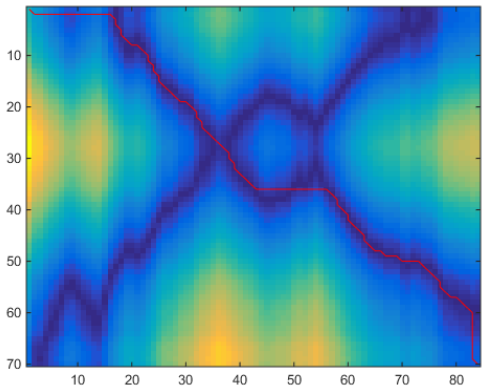


(a) Path Warping at Euclidean Distance.

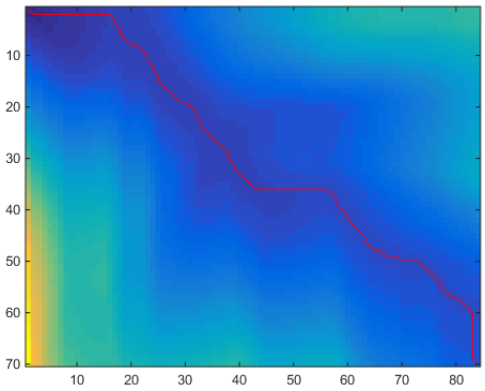


(b) Path Warping at Accumulated Cost (DTW).

Figure 7.4: Patient Visualization of Path Warping at (a) Euclidean Distance and (b) Accumulated Cost.



(a) Path Warping at Euclidean Distance.

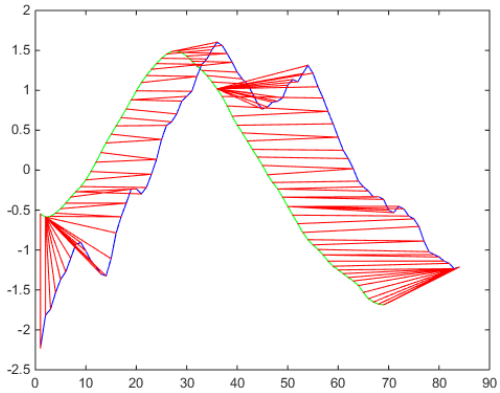


(b) Path Warping at Accumulated Cost (DTW).

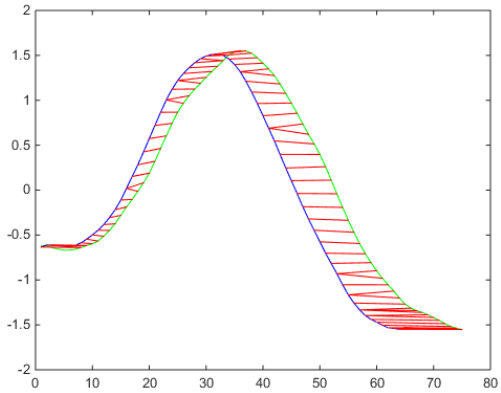
Algorithm 7.2 Optimal Warp Path.

1: $n1 \Leftarrow size(s1, 1)$;
2: $n2 \Leftarrow size(s2, 1)$;
3: $path \Leftarrow [n1, n2]$;
4: $s \Leftarrow size(path, 1)$;
5: $i \Leftarrow n1$;
6: $j \Leftarrow n2$;
7: while $(i > 1 \&\& j > 1)$ do
8: if $i == 0$ then
9: $j \Leftarrow j - 1$
10: else {if $j == 0$}
11: $i \Leftarrow i - 1$
12: else
13: if $D(i-1, j) == min([D(i-1, j), D(i, j-1), D(i-1, j-1)])$ then
14: $i \Leftarrow i - 1$;
15: else {if $D(i, j-1) == min([D(i-1, j), D(i, j-1), D(i-1, j-1)])$}
16: $j \Leftarrow j - 1$;
17: else
18: $i \Leftarrow i - 1$;
19: $j \Leftarrow j - 1$;
20: end if
21: end if
22: $s \Leftarrow s + 1$;
23: $path(s, 1) \Leftarrow i$;
24: $path(s, 2) \Leftarrow j$;
25: end while

Figure 7.5: Curves Alignments Visualization of a (a) patient and (b) a Control.

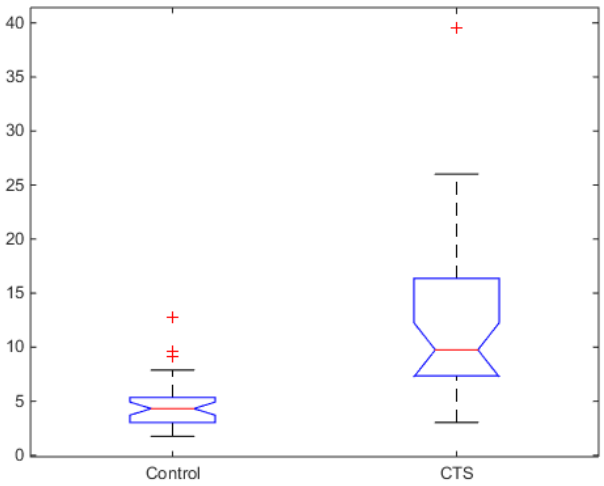


(a) Alignment of a patient's NCS Curves.



(b) Alignment of a control's NCS Curves.

Figure 7.6: Box-Plot of DTW for CTS and no-CTS groups.D(n,m) can effectively discriminate controls vs CTS subjects



7.3 DTW as feature of Nerve Conduction Studies

In this section we present the experiments that we implemented for the evaluation of DTW as a feature extraction method, customized to our data. For the unbiased evaluation of the DTW, several issues must be taken into account:

- Which part of signal to include.
- What normalization (if) must be done [13].
- Which are the candidate pairs for DTW implementation.

In order to construct a fair model of the best possible feature concerning the DTW, we have conducted every possible pair of digits, nerves, etc by implementing an exhaustive comparison for all pairs of every existing signal.

In addition, we experimented the DTW algorithm, for every kind of normalization, by trying both keeping and ignoring the size proportions between signals of each pair.

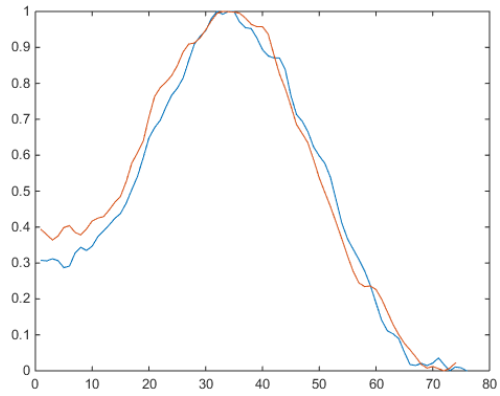
Finally, we concluded several different partitions of each signal; the complete signal, the complete filtered (detrended) signal, the curve between the onset and the offset point and a partition concerning an extension of the curve before and after its start and its end point respectively.

7.3.1 Implementing DTW

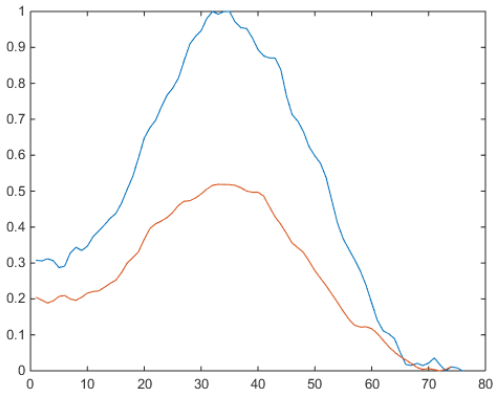
After making all possible experiments, we concluded that the median and ulnar nerves' curves at digit 4 is the most appropriate pair for implementing DTW and that during normalization, no proportional scaling should be kept. The results as shown on figures 7.7 and 7.8 and on table 7.1, indicated that the best discrimination between groups of CTS is being occurred when the curves are transformed to the same scale, confirming the recent literature [13]. It is remarkable to mention that the feature of DTW, when constitutes the only feature of our previous mentioned classifiers using one-leave-out cross validation, an average accuracy of 80% has been reached in diagnosing the existence of the syndrome.

Additionally, the implementation of DTW on motor nerves in every possible pair, is not appropriate for the discrimination of the CTS existence.

Figure 7.7: Ploting curves after (a) ignoring and (b) keeping their proportions.



(a) No Ratio scale.

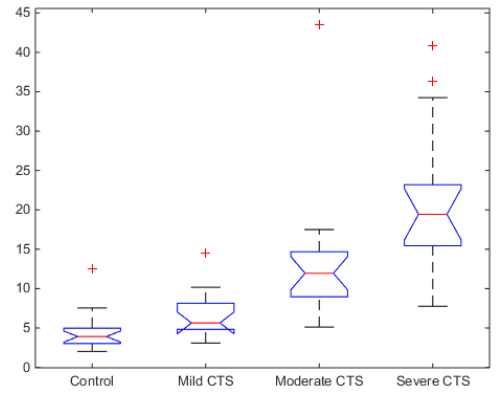


(b) Ratio scale.

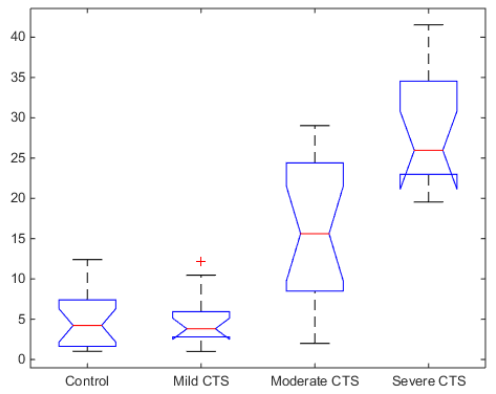
Table 7.1: DTW p-values after keeping and ignoring their proportions.

Ratios	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
No Ratio scale	0.00000000	0.00249993	0.00141832	0.00269128
Ratio scale	0.00000000	0.16630201	0.00209141	0.00010677

Figure 7.8: Ploting curves after (a) keeping and (b) ignoring their proportions.



(a) No Ratio scale.



(b) Ratio scale.

7.4 DTW and Clinical rating

It is widely acceptable that NCS do not correlate with symptoms. In this section we examine the correlation of DTW with the clinical data and the potential contribution of DTW in the increase of performance of NCS correlation with symptoms. To implicate this, we calculate Pearson and Spearman correlations for both DTW and Conduction Velocity features, at first separately and then in combination with each other. The Conduction Velocity is chosen because of being considered the gold standard in the diagnosis of the syndrome.

7.4.1 Spearman's Correlation

Spearman correlation is a ranking correlation; to examine the correlation between two attributes X and Y, Spearman technique ranks the attributes of both and replaces the values of attributes by its ranks. Then it calculates the difference between each pair and sums the squared results.

Its coefficient is calculated as Pearson's correlation but for the ranking values that have replaced the attribute values. When all ranking are distinct integers it is calculated by the type shown on equation 7.4.

$$\rho = 1 - \frac{6 * \sum {d_i}^2}{n(n^2 - 1)} \tag{7.4}$$

Since, the purpose of this approach is to compare two vectors, the one of dtw and the other of conduction velocity, we calculate the Spearman correlation for both and we compare the results.

Our clinical data are composed by the following three characteristics:

- Months of Pain
- Months of Numbness
- Months of Weakness

A custom way of performing reliable ranking for these data, since we already know that the weakness is the most severe symptom and the other two are of equal significance, is the following type:

$$severity = max(months(pain), months(numbness)) + months(weakness) * 1000 \tag{7.5}$$

By multiplying the duration of weakness, we ensure that the severe symptoms will rank after the others and in a logical order between them; the control group will certainly rank before the mild and moderate subjects since they have a value of zero; the intermediate groups will rank in the middle according to their duration of CTS symptoms.

The multiplication of weakness by one thousand times, does not play any negative role, but is used only for ranking latter. The scaling is not important in Spearman correlation, because it converts the values to rankings.

In order to confirm the contribution of DTW feature to the increase correlation of NCS with the clinical symptoms, we also calculated several logical symptoms' rankings (in months):

- each symptom's duration separately
- maximum duration of symptoms
- sum of symptoms' durations

Table 7.2: Spearman Correlation Coefficients for DTW, CV and Mutual rankings against Ranking of Symptoms.

Ranking Type	DTW	CV	Mutual
custom equation	.54	.55	.61
maximum duration	.55	.55	.60
sum of durations	.57	.59	.64
pain or numbness	.59	.57	.62
pain and numbness	.59	.60	.65
weakness duration	.31	.38	.42

7.4.2 Pearson's Correlation

Pearson's correlation is defined as the covariance of two attributes divided by their standard deviations.

Table 7.3: Pearson's Correlation Coefficients for DTW, CV and Mutual rankings against Ranking of Symptoms.

Ranking Type	DTW	CV	Mutual
custom equation	.34	.30	.36
maximum duration	.32	.42	.44
sum of durations	.34	.46	.47
pain or numbness	.36	.46	.47
pain and numbness	.31	.48	.47
weakness duration	.35	.31	.37

7.5 DTW after Wavelet Transformation

In this section we present the implementation of Dynamic Time Warping to the decomposed outcomes of the wavelet transforms of our signals for the most popular mother wavelets.

7.5.1 Definition of Wavelets

The need for a transform that could give enough information about the time resolution in frequency domain came up with the reveal of wavelets, an old idea - the first wavelet was introduced in 1910 by Haar - that is now used to many applications like the jpeg format of an image.

Wavelets are finite curves (waves) with amplitude that starts at zero and ends to zero. Its oscillation is symmetric about the y-axis and its area algebraic value is also zero, since it is symmetric about the x-axis too.

7.5.2 Wavelet Transform

Before discovering the wavelet transform, the researchers had only few options for the frequency resolution of time series data:

- Fourier Transform (FT)

  The most popular method for analyzing a signal in frequency domain is the Fourier Transform, which can interpret the original time-series as a sum of cosine functions and is defined by the equation 7.6

$$X(F) = \int_{-\infty}^{\infty} x(t)e^{-j2\pi Ft}dt \tag{7.6}$$

By multiplying the original signal with the analysis function, we can get the frequency resolution of it. However the final X(F) function, has no information about the time resolution, which in many cases is very important.

- Short Time Fourier Transform (STFT

  The requirement of time resolution in the frequency domain, has driven to an alternative to FT technique, the Short-Time FT. In this process we implement a window of fixed sized, for which we transform the signal alongside its width.

$$X(\tau, F) = \int_{-\infty}^{\infty} x(t)w(t-\tau)e^{-j2\pi Ft}dt \tag{7.7}$$

  The disadvantage of this method is the inflexibility of the window's size, which restrict the process to obtain only certain frequencies and time resolution analysis.

- Wavelet transform

  In contrast with the two previous methods. the wavelet transform can obtain both time and frequency resolution analysis. This is achieved by replacing the window size by a term called scaling; the wavelet can be stretched or shrink about x-axis and as a result we can obtain adequate resolutions for both time and frequency domains.

$$X(a, b) = \int_{-\infty}^{\infty} x(t)\Psi(a, b)dt \tag{7.8}$$

  Because of the inverse proportion between scaling and frequency value, if we stretch the wavelet we make the value of a larger than 1 and we obtain the low frequencies of the signal, however we have poorer time resolution. On the contrary, if we stretch the wavelet by making the value of a smaller than 1 we obtain high frequencies and very precise time resolution.

  This advantage can give us the power of using wavelets to detect smaller varying or abrupt changes of a signal, by using larger or smaller scaling factor of the chosen wavelet respectively.

Apart from scaling, the shifting property is used to align the wavelet with the desired extracted feature.

The wavelet transform is consisted of two main kind of transforms:

- The Discrete Wavelet Transform (DWT)

  Scaling: 2^j (j=1,2,3,4,..)

  Translation: $m * 2^j$ (m=1,2,3,4,..)

- The Continuous Wavelet Transform (CWT)

  Real positive values for both scaling and shifting properties.

These transforms categories are based on how the wavelets are scaled and shifted. The DWT accepts only integer values as the power of two for scaling property and integer values as multiplier for the translation property.

7.5.3 DTW for DWT

In our signals we performed the Discrete Wavelet Transform and then processed with Dynamic Time Warping algorithm in order to examine the appropriate wavelet and the best level of decomposition. To achieve this, we examined all existing popular mother wavelets:

- Morlet
- Daubechies
- Coifflets
- Biorthogonal
- Symlets

and we tested each one until the level of 9.

Table 7.4: DTW for DWT of Daubechies wavelets for level 2 (best level).

Mother	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
Haar	0.00000000	0.00970296	0.00072267	0.00237405
db2	0.00000000	0.00047072	0.00030767	0.00095025
db3	0.00000000	0.00173249	0.00108744	0.00699532
db4	0.00000000	0.00152936	0.00209141	0.00237405
db5	0.00000000	0.00317262	0.00141832	0.00555352
db7	0.00000000	0.00702795	0.00161652	0.00269128

Table 7.5: DTW for DWT of Coifflets and Biorthogonal for level 2 (best level).

Mother	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
coif1	0.00000000	0.00449412	0.00161652	0.00183993
coif2	0.00000000	0.00563377	0.00269128	0.00269128
coif3	0.00000000	0.00872450	0.00344469	0.00783543
coif4	0.00000000	0.00970296	0.00209141	0.01505061
bior1.1	0.00000000	0.00790297	0.00083277	0.00327496
bior1.3	0.00000000	0.00503486	0.00054662	0.00072267
bior1.5	0.00000000	0.00629621	0.00108744	0.00493836

Table 7.6: DTW for DWT of Symlets for level 2 (best level).

Mother	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
sym2	0.00000000	0.00047072	0.00030767	0.00095025
sym4	0.00000000	0.00503486	0.00209141	0.00269128
sym8	0.00000000	0.00783518	0.00399413	0.00493836
sym16	0.00000002	0.02884823	0.00072267	0.01670340

7.6 Results and Further Examination

In this section we examine which result gave the best performance for DTW feature, we compare the classifiers of DTW and CV to evaluate the importance of our new feature and finally we compute the Sensitivity and Specificity of both features. But at very first, we examine the homogeneity of the control group.

The results of Wavelet Transform are shown on tables 7.4, 7.5, 7.6 indicating that level 2 of the wavelets db2 give better results than the implementation of DTW without any filtering. Only the levels of significant results are presented.

On table 7.3 the correlation coefficients of Pearson correlation are presented. Despite the low value coefficients, DTW still contributes in increasing the coefficient of Conduction Velocity attribute.

For spearman correlation, the results indicated that DTW values gave almost equal correlation to conduction velocity, namely 0.53 vs 0.55 respectively. However, when normalizing the values of DTW and CV features, the combination of two is giving a correlation coefficient of 0.61, while the correlation coefficient between DTW and CV $\rho = 0.67$.

The Spearman's correlation coefficients are shown on table 7.2 for all grading clinical scales.

7.6.1 Differentiate Control and Patient Groups

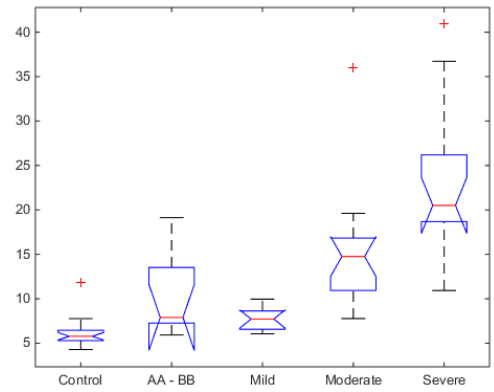
Since, at previous chapters, we accepted the labels given by the doctors as standard we, then, included 7 more hands in our control group. However, it is time to evaluate their importance according to DTW feature; we excluded these instances and we created two more tiny groups:

- group AA
  The three hands of non bilateral CTS (one-hand CTS gave the label of no-CTS to opposite "healthy" hand). Although NCS was applied to these hands and they were of no-CTS diagnosis, the fact of opposite hand' s dysfunction may affect the healthy too.

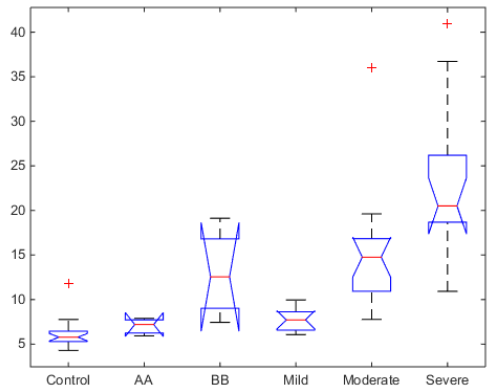
- group BB
  The hands of subjects which visited the hospital due to CTS symptoms, but they had no-CTS diagnosis.

The results of this experiment was noticeable (figure 7.9), indicating that both categories should not be taken into account considering the control labeling.

Figure 7.9: DTW boxplots for (a) mixed and (b) separated AA and AB groups.



(a) AA and BB groups are merged.



(b) AA and BB groups are separated.

7.6.2 Comparison of DTW vs CV

In order to evaluate the importance of DTW, we compare it with CV performance, since Conduction Velocity is considered as the gold standard in CTS diagnosis through NCS. We construct the same 5 classifiers of previous chapters and we compare their results. As shown on figure 7.10 and table 7.7, DTW gave some lower p-values and more discriminative results. If we take into account the bias in favor of CV, as the basis of group labeling, the DTW' s results are really notable.

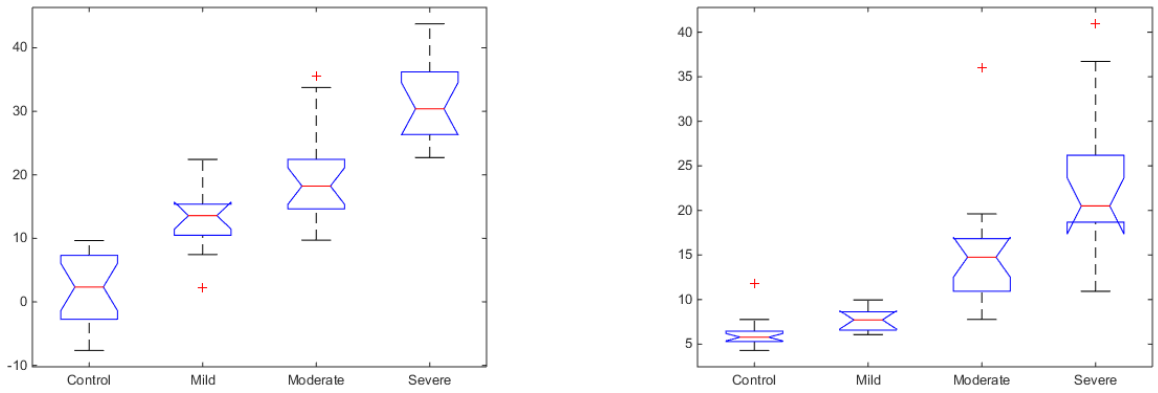
Table 7.7: DTW vs CV p-values.

Feature	All Groups	Ctrls vs Mild	Mild vs Mod.	Mod. vs Severe
DTW	0.00000000	0.00047072	0.00030767	0.00095025
CV	0.00000000	0.00008735	0.01630917	0.00016944

These impressive results prompted us to compare the DTW and CV features in terms of classification. In order to examine the sensitivity and specificity performance of DTW we present them on table 7.8.

The ROC curves for SVM classifier are presented in order to confirm the importance of DTW results against a biased feature, on figure 7.11 and table 7.9.

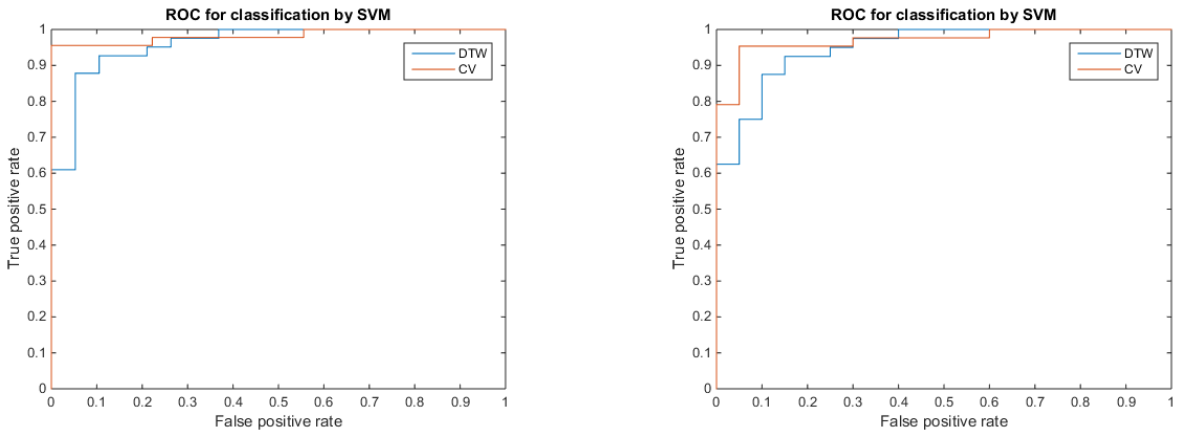
Figure 7.10: CV vs DTW boxplots.



(a) CV

(b) DTW

Figure 7.11: CV vs DTW ROCs.



(a) NCS grading

(b) Clinical grading

Finally, we examine the contribution of DTW feature to our classification model of chapters 5 and 6. The results are presented on table 7.10 and we should mention that after proceeding with the feature selection that we have explained to previous chapters, the geometric features did not play any important role; it seemed like the DTW feature overlapped the significance of our geometric features and gave better results when added to the models of chapter 5, while the addition of geometric features of chapter 6, did not ameliorate after the presence of DTW.

Table 7.8: Sensitivity and Specificity of DTW in comparison with CV.

	SVM	K-NN	N BAYES
Accuracy (4 groups)			
DTW	0.68	0.53	0.66
CV	0.59	0.55	0.63
Accuracy (Ctrls - CTS)			
DTW	0.89	0.88	0.82
CV	0.91	0.92	0.91
Sensitivity			
DTW	0.91	0.74	0.95
CV	0.72	0.83	0.83
Specificity			
DTW	0.89	0.93	0.73
CV	0.95	0.95	0.95

Table 7.9: Area Under Curve for DTW vs CV features.

Feature	AUC NCS	AUC Clinical
DTW	0.953	0.946
CV	0.989	0.961

7.6.3 DTW as distance metric of a KNN classifier

A state-of-the-art classifier in pattern recognition of time series data is considered to be the knn classifier using as distance metric the DTW distance [14].

In such cases the input data are the signals and then knn computes the DTW distance (D(n1,n2)) of each pair of them. In our case study the knn classifier that we implemented with DTW as distance metric, did not work; the accuracy of .35 and .74 for all classes and for control vs patients groups respectively is explained by the fact that two signals are necessary for the diagnosis of CTS, the median and the ulnar nerve NCS comparison. When one puts all signals to the classifier, the pairwise option for certain nerves cannot be detected. Thus, the classifier computes the DTW distances of all signals with each other, but this comparison makes no physical sense in our case.

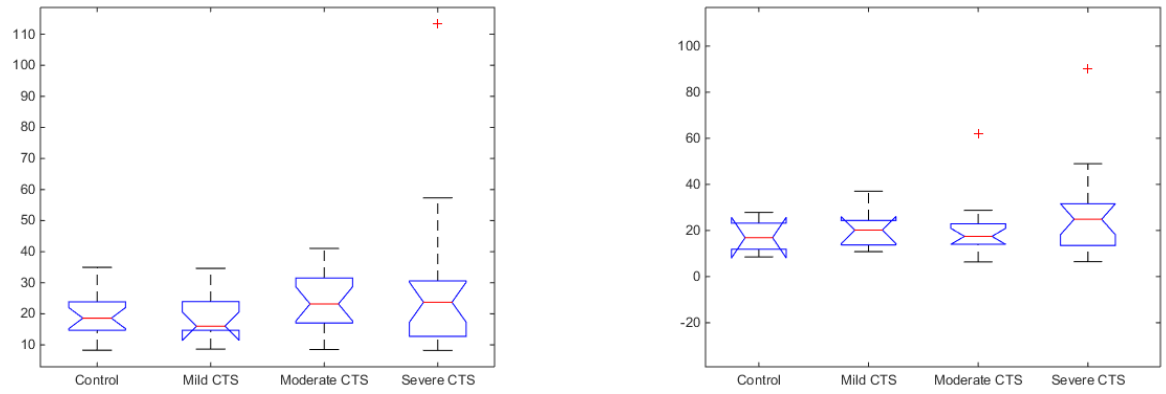
Table 7.10: Accuracy of our final Classifiers.

4 classes	3 classes	3 classes-Clinical	Ctrl-Patients	Ctrl-Patients Clinical
Logit				
74.58 %	89.56 %	62.26 %	88.24 %	84.43 %
SVM				
89.33 %	94.10 %	69.67 %	95.90 %	89.38 %
KNN				
67.86 %	78.64 %	56.45 %	88.48 %	78.32 %
D-Tree				
71.24 %	82.03 %	58.48 %	96.10 %	77.92 %
Naive-Bayes				
86.11 %	92.56 %	67.52 %	94.81 %	87.55 %

7.6.4 Motor Nerves' DTW Results

The process of sensory nerves, was also applied to the motor nerves, but no importance of DTW algorithm was obtained at distal or proximal signals (figure 7.12).

Figure 7.12: DTW for Distal and Proximal Curves.



(a) Motor Distal DTW Feature

(b) Motor Proximal DTW Feature

Chapter 8

Conclusion and Future Work

8.1 Discussion

The purpose of our research was to evaluate the existing characteristics for the diagnosis of CTS and also to propose more features that could ameliorate the accuracy of a diagnostic model. Besides, we aimed to contribute in the field of establishing a robust grading scale of the syndrome's severity.

We have extracted and presented several geometric features with indicating physical meaning of nerve compression and also Dynamic Time Warping (DTW) algorithm which are applied for first time for diagnosing of CTS.

Although the classification of CTS severity groups is biased, our results show that the existing features can do better in terms of accuracy, sensitivity and specificity. The groups were decided by the doctor taking into account the features that we used for our classification model.

On the contrary, some geometric features, gave significant results despite the fact of not been taken into consideration when the doctor made the groups of severity. This classification model is unbiased and indicated that some of these features can play important role in diagnosing the syndrome.

The most surprising feature, however, was not but the implementation of the DTW

algorithm. The non-linear alignment of two signals, those resulted from median and ulnar at digit 4 NCS, indicated a strong discriminating ability between all groups. Especially when the signals are decomposed by the wavelet transform on level 2, the dtw characteristic gave even more significant results.

Although CTS is defined, mostly, as the duration from the stimulus point until the response of the nerve, which means that is a time-defined case, DTW eliminated the time factor and identified pattern differences between affected (median) and non-affected (ulnar) curves. When time factor was added to dtw model, the accuracy was better than any other from our models. Additionally, DTW alone, gave same correlation with clinical symptoms that can give the existing (biased) features.

Hence, we can certainly claim our contribution to the improvement of the current methods in several fields of biomedical signals. Our novel signal characteristics and/or the DTW algorithm can be used as significant extracted features even for time-defined diseases, syndromes and medical situations.

8.2 Future Work

The future work that could be motivated by our thesis may be branched into three main directions:

- Evaluation of our results through a large database of CTS groups

  This is the most obvious continuation of our work, since the small amount of subjects in our case study cannot lead to a robust generalization of our results. However, the significant results of the DTW algorithm make us think that they can be confirmed at larger data-sets.

- DTW and geometric features' contribution to a robust CTS grading scale

  The controversial opinions about scaling the CTS severity can be decreased by the use of DTW algorithm to assist the establishment of an undeniable grading scale with eliminated false outputs.

- DTW and proposed geometric features for other time-series data

  The significant results of our experiments, especially those of DTW, can be used to diagnosing several medical situations. For instance, each ECG signal of a

patient and a healthy subject, when compared at their curves, instead of being compared at the whole signal (starting from QRS curve and ending to T curve) using DTW algorithm might discriminate the disease better than this happens nowadays.

Bibliography

[1] I. Ibrahim, W. Khan, N. Goddard, and P. Smitham, "Carpal tunnel syndrome: A review of the recent literature," The Open Orthopaedics Journal, vol. 6, no. 1, pp. 69–76, 2012.

[2] R. Senthooran and C. Adrian, Carpal tunnel syndrome - current controversies, vol. 29, issue 4, of Orthopaedics and Trauma. Elsevier, 2015.

[3] L. Robinson, We Should Not Use A Modifier To Describe The Severity Of Carpal Tunnel Syndrome, vol. 23 of ISSUES & OPINIONS. MUSCLE & NERVE, 2013.

[4] T.-T. Kuo, M.-R. Lee, Y.-Y. Liao, W.-N. Lee, Y.-W. Hsu, J.-P. Chen, and C.-K. Yeh, "Assessment of median nerve mobility by ultrasound dynamic imaging in carpal tunnel syndrome diagnosis," in IEEE International Ultrasonics Symposium, pp. 876–879, 2013.

[5] C. Jablecki, M. T. Andary, Y. T. So, E. Wilkins, and F. H. Williams, Literature Review of The Usefulness of Nerve Conduction Studies And Electromyography For The Evaluation Of Patients With Carpal Tunnel Syndrome, vol. 16. MUSCLE & NERVE, 1993.

[6] S. Swarna and J. Gonzalez-Cueto, "Conduction velocity distribution estimation using the collision technique for assessing carpal tunnel syndrome," in Conf Proc IEEE Eng Med Biol Soc., pp. 2373–2376, 2006.

[7] A. J. Metso, K. Palmu, and J. V. Partanen, Compound nerve conduction velocity – A reflection of proprioceptive afferents?, vol. 119 of International Federation of Clinical Neurophysiology. Elsevier, 1 ed., 2008.

[8] S. Swarna and J. A. Gonzalez-Cueto, "Selective activation of small nerve fibers for assessing carpal tunnel syndrome," in Conf Proc IEEE Eng Med Biol Soc., pp. 3668–3671, 2005.

[9] J. Bland, A neurophysiological grading scale for carpal tunnel syndrome, vol. 23. MUSCLE & NERVE, 2000.

[10] B. M. SUCHER, Grading Severity Of Carpal Tunnel Syndrome In Electrodiagnostic Reports: Why Grading Is Recommended, vol. 48 of ISSUES & OPINIONS. MUSCLE & NERVE, 2013.

[11] J. C. Lucero, K. G. Munhall, V. G. Gracco, and J. O. Ramsay, "On the registration of time and the patterning of speech movements," Journal of Speech, Language, and Hearing Research, vol. 40, no. 1, p. 1111–1117, 1997.

[12] F. O. Petitjean, A. Ketterli, and G. P, A global averaging method for dynamic time warping, with applications to clustering, vol. 44 of Pattern Recognition. Elsevier, 3 ed., 2011.

[13] T. Rakthanmanon, B. Campana, A. Mueen, G. Batista, B. Westover, Q. Zhu, J. Zakaria, and E. Keogh, Addressing Big Data Time Series: Mining Trillions of Time Series Subsequences Under Dynamic Time Warping, vol. 7 of Transactions on Knowledge Discovery from Data. ACM, 1 ed., 2013.

[14] D. Hui, T. Goce, S. Peter, X. Wang, and E. Keogh, "Querying and mining of time series data: experimental comparison of representations and distance measures," in Proc. VLDB Endow, p. 1542–1552, 2008.

Short Biography

Prokopios Kontogiannis was born in Lefkada, Greece in 1978.

EDUCATION

- High School - 3rd Lyceum of Ioannina, 1995
  Graduated from High School with a final grade of 17.3/20
- Hellenic Army Academy, 1996-2000, 8/10
- Hellenic Open University - Computer Science Department, 2005-2010, 7.2/10
- University of Ioannina - Department of Computer Science & Engineering
  (Currently) M.Sc. in Computer Science, Technologies - Applications

SKILLS

- Strong CS Experience
  - Administrator of Oracle Databases
  - Developer of Oracle Databases
  - Web Design
- Strong Programming Skills
  - PL/SQL
  - Javascript (client-side)
  - Matlab
  - Python
  - PHP

- Good Programming Skills
  - Javascript (server-side)
  - C
  - Java
- Languages
  - Greek (Native Language)
  - English (Proficiency)
  - French (DALF)
  - Italian (Diploma)

PROFESSIONAL EXPERIENCE

- Logistics Manager, 2002 - 2004
  Center of Army Logistics in Chios Island
- Logistics Supervisor, 2004 - 2007
  Center of Army Supply Chain in Ioannina
- Oracle DBA and Developer, 2007 - 2012
  HQ of Hellenic Center of Defence Logistics, Ag. Stefanos, Attiki
- Logistics Commander, 2012 - 2015
  Center of Army Supply Chain in Ioannina
- Commander of Ammunition Center, 2015 - 2017
  nearby Ioannina

OTHER INTERESTS

- Web design
- Windsurfing