A real-time system to aid clinical classification and quantification of tremor in Parkinson's Disease

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Abstract— **The availability of an objective clinical evaluation in the diagnosis and monitoring of parkinson's disease is a primary importance objective in neurology. Furthermore, in many patients next to resting tremor typical of the disease are also found other types of tremor as kinetic and postural tremor so making the diagnosis difficult. The ability to classify the different types of tremor specific for each patient through an examination of the instrumental, non-invasive and very simple and fast is a great tool to aid the clinical diagnosis of the disease.**

Our system meets the above requirements. It consists of an inertial sensor that allows the acquisition of the quantities of interest, and by a series of algorithms able to provide an objective and quantitative assessment of the type and severity of tremor in patients with Parkinson's disease. The availability of an objective report on the severity of the disorder developed according to a strict correlation with the valuation provided by the UPDRS scale is a good starting point towards the personalization of care as well as being a useful tool in the analysis of the course of the disease.

I. INTRODUCTION

Parkinson's disease (PD) is a widespread illness second in incidence only to Alzheimer's disease over age 40. It is estimated that in 2030 there will be about 9 million sick only in the countries of Western Europe [1]. It is due to chronic and progressive degeneration of the nervous structures that make up the extrapyramidal system. It is a disorder characterized by the degeneration and death of dopamine producing neurons. When they decreased of 30% appear the first symptoms of the disease such as bradykinesia, rigidity and tremor [2].

The tremor is certainly one of the most disabling symptoms of the disease. It is defined as involuntary and rhythmic contraction of the muscles that determines a state oscillatory of all or a part of the body. It can be classified into various types, the most notable in PD are resting tremor (RT), postural tremor (PT) and kinetic tremor (KT). RT occurs when the subject under examination does not voluntarily contracted muscles and maintains the affected part resting on a support such as his own leg. PT occurs primarily in the upper extremities of the body and is characterized by fluctuations faster than the RT. It can be observed when the patient keeps the limb and lying stationary in opposition to the force of gravity as holding the arm in front of the body and tends to disappear when the muscles are relaxed. KT occurs during the execution of voluntary movements such as those can be made to grasp an object, writing or touching the tip of the nose. The characteristic tremor of PD is undoubtedly the resting tremor but it is extremely important to analyze the possible presence of other types of tremor as may be the PT or KT. Approximately 80% of patients PT and KT occurs in addition to RT [3]. It tends to get worse with age.

Currently, the clinical diagnosis of PD, the evaluation of the severity of symptoms, the time evolution of the disease, the positive or negative effect observed after administration of a specific drug, are carried out through the UPDRS (Unified Parkinson's Disease Rating Scale) [4].Each parameter used for the diagnosis and estimation of the evolution of the disease is classified according to a numerical scale from 0 to 4 where 0 represents the absence of the disorder or not difficult to perform a certain movement while 4 represents the marked presence of the disorder or the marked difficulty to perform a precise movement. The scale allows to obtain an assessment of numerical type through which it is possible to compare the tests results in the course of time and follow the evolution of the disease. Diagnosis and classification of the disease and specifically tremor is still error prone due to personal interpretations without any objective reference uniquely applicable to all cases. Therefore, it is essential to develop technological systems that allow objective analyses of the characteristic parameters of tremor and provide comparability of data gathered over time in order to intervene pharmacologically in the most appropriate way possible. The goal of developing techniques and equipment that can give an objective, rapid, and reproducible disease classification has been strongly pursued in the past, but with poor results because the evaluation of the patient with Parkinson's disease is difficult for a number of variables to be taken into account. Furthermore, any instrumental method formulated for outpatient visit should provide required data by means of simple and non-invasive techniques in the shortest possible time. Moreover, it should be able to evaluate the patient's symptoms at home varying the drug therapy.

Many studies have as objective clinical monitoring of patients with motor dysfunction through the use of inertial sensors . In particular, for patients with Parkinson's disease, accelerometers and gyroscopes have been used to quantify bradykinesia [5], rigidity [6] and tremor [7] [8] . In all these studies data analysis is done offline and the medical does not have the ability to immediately view the results of the tests. Therefore it is essential to have a tool which enables the real-time reporting so that the doctor can get immediate feedback. The ability to save the captured data for each medical examination allows us to immediately compare it with previous examinations and evaluate the time

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evolution of the disease together with the effectiveness of drug treatment. Consequently, a device capable of evaluating the tremor is a useful aid in diagnosis and therapy of PD.

In this study we report results obtained by means an easily usable system constituted by a wearable IMU sensor node that can be employed for clinical diagnosis of tremor and real-time quantification of relative severity.

II. MATERIALS AND METHODS

A. Acquisition system

We used an inertial platform developed by us equipped with tri-axial accelerometer, tri-axial gyroscope and a tri-axial magnetometer. The device transmits the data to the PC via bluetooth.Additionally data storage can also be carried out locally via a mini SD card. The developed device performs calibration of inertial sensors to compensate for the drift due to temperature and any radiated emissions from other electrical equipment operating in the zone of influence of the instrument before running the core of our application. The device is settings with a sampling frequency of 128 Hz and the full-scale of the accelerometer of 2 g in order to detect even the smallest forms of tremor during the medical examination.

In order to make wearable the sensor it is inserted into a special bracelet fitted with a strap that allows an easy use. The bracelet is made from elastic material in such a way to be able to adapt to the different patient body and to enable it to remain perfectly integral with the limb on which it is placed avoiding unwanted vibrations that could be superimposed on the useful signal to be analyzed. The end result is a kind of wristwatch very comfortable and easy to wear.

In order to evaluate resting, postural, and kinetic tremor we have carried out three differents tests. For resting tremor evaluation the patient is sitting with both feet on the floor and closed eyes and must remain with his arms resting on the thighs (Fig. 1). The test duration is 1 minutes during which, if the tremor does not occur, the neurologist introduces complications for distract the patient (eg. count backwards from 100 to zero step x). Usually, this test is performed for both arms. For postural tremor measurement the patient is sitting with both feet on the floor and closed eyes and he must stretch his arms forward, trying to stay in this position for almost 1 min. Again, the test is performed for both arms. In kinetic tremor evaluation the patient was sitting with both feet on the floor and closed eyes and he must perform the so called index-nose test which consists in stretching forward the arms and then executing a series of forward and backward movements bringing index to the nose touching its tip. The test is performed for both arms.

B. Classification of tremor

1) Typology of tremor: An objective classification of tremor can be traced through the two parameters frequency and intensity extractable from previous signal. The frequency analysis is performed by means the extraction of the fundamental frequency through which classify the type of tremor. We assume the tremor of hand a periodic oscillation that is a reasonable assumption in these cases. The extraction of the fundamental frequency is essential for tremor classification. Depending on the detected frequency we can distinguish three fundamental tremor types [9]: low frequency tremor (2-6 Hz), medium frequency tremor (6-10 Hz), high frequency tremor ($>$ 10 Hz). The three basic types of tremor can be classified on the basis of the previous subdivision: resting tremor (3-6 Hz), postural tremor (6-9 Hz), kinetic tremor (9-12 Hz).

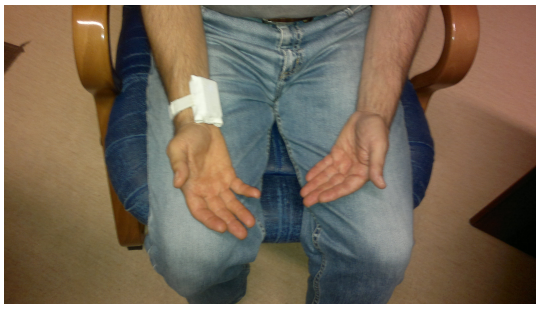

Fig. 1. Patient under test.

2) Intensity of tremor: The second characteristic that distinguishes the tremor between patients and that is particularly useful and significant for observing the temporal evolution of the disease is the amplitude of oscillation or rather its intensity. Starting from the accelerometer [10] data is possible to quantify the amplitude of oscillations and particularly the intensity of tremor at the various frequencies in the spectrum through the Power Spectral Density (PSD). This also allows an estimate of how much the tremor is disabling for the patient by limiting his normal activities into daily routine.

Each case is different from the other and many patients are suffering from multiple tremors characterized by a bandwidth spread so the introduction of further classification parameters like F50 and SF50 is necessary. F50 is the frequency at which half power frequency lying on the left of this while the other 50% is on the right. It provides an indication of the power distribution into the considered band. How much more F50 is close to the fundamental frequency more the intensity parameter will be trusted for estimation of the severity of tremor K.

SF50 represents the frequency band within which the 68% of the total power of the signal is contained. Because SF50 is centered on F50, it is fair to say that SF50 represents the dispersion of the frequency around the central frequency. If SF50 is very tight, we can consider the resting tremor as unique contribution without committing a significant error. Otherwise the error is not negligible if SF50 is very wide and F50 deviates from the fundamental tremor frequency F0. In this case, it is necessary the introduction of a corrective factor H. This correction is weighted by the PSD contributions from KT e PT and from SF50 broadness.

C. Algorithms description

The signal processing is performed using MathWorks MATLAB tool.

The input signals are the three accelerations components one for each spatial axis.The RMS is calculated because our sensor node can not attached in a defined position to the wrist.

The obtained signal is then filtered to eliminate all contributions outside the band of interest. There is the possibility of choosing between many different filters that allow to eliminate all the noise components and focus the analysis in the band of interest. We tested several type of filter and the best results are provided from a FIR equiripple.Initially, a filter from 3 to 12 Hz is applied allowing to identify the typical frequencies of tremor. Subsequently, we redefine the filtering into the band of interest through others more selective filters. In detail, a band-pass filter from 3 to 6 Hz in case of RT or a band pass filter from 6 to 9 Hz in case of PT or a band-pass filter from 9 to 12 Hz in case of KT is applied.

The algorithm works in real-time through Hanning windows of 4 s of duration and with overlap 25%. The windows where the tremor not occurred are not considered in the classification of tremor. The weighted average of the contribution in each window provides the typical frequency tremor for each subject (F0). Starting from filtered signal we compute the PSD for each frequency bands (low, medium and high) to have an objective estimation of the tremor severity K. We have also calculated the parameter F50 and SF50 and we check if we have to apply a corrective factor H. In particular if the signal is narrowband ($|F0\text{-}F50| < 0.5$ Hz and $|SF50| < 1$ Hz) the error assuming the maximum value of the spectral density within the band considered as a parameter for the assessment of the severity of the disorder is negligible and no correction is required as shown in Fig. 2 where only RT is detected. In all the other cases a correction factor is required in order to estimate the severity of tremor in each band and to evaluate the correlation with UPDRS as shown in Fig. 3 where PT and KT also occur. This correction factor is calculated according to the amplitude of SF50, the difference between F0 and F50 and the PSD in the other bands each one appropriately weighted. The calculation of the weighting coefficients of the different contributions used for the determination of factor H is done by a preliminary analysis of the trend of the signal in frequency so that the correction factor applied is automatically adapted to each patient.

Correlation with the UPDRS is based on the PSD in each band. The algorithm calculates the mean power on the bands analyzed and introduces the factor H if is necessary. Finally it compares the result with the UPDRS scale to provide an estimation of the severity of tremor.

III. RESULTS

For the validation of our model and algorithms developed, we performed two differents series of tests. All the subjects are Parkinson's disease affected (patients of the Department

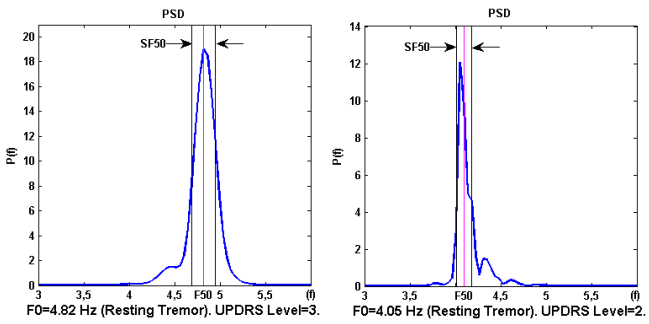

Fig. 2. RT detection. $|F0\text{-}F50| < 0.5$ Hz and $|SF50| < 1$ Hz, the corrective factor H is not applied for severity estimation.

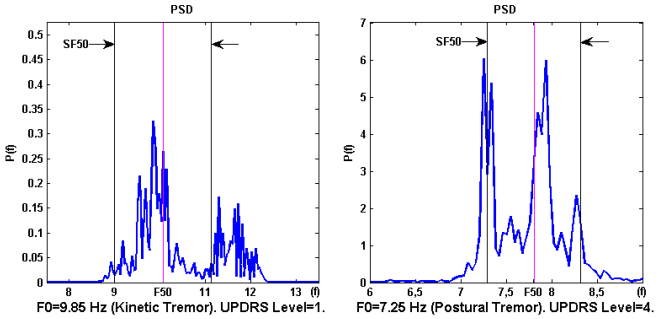

Fig. 3. KT and PT detection. In the first $|F0\text{-}F50| < 0.5$ Hz but $|SF50| > 1$ Hz, the corrective factor H is applied for severity estimation. In the second $|F0\text{-}F50| > 0.5$ Hz and $|SF50| > 1$ Hz, the corrective factor H is applied for severity estimation.

of Neurology at the Medicine Faculty of Ancona, Universitá Politecnica delle Marche) and they agreed to participate in the study voluntarily. Our system allowed us to realize a real-time evaluation of the tremor during outpatient visits.

A. UPDRS correlation

From a preliminary study over 30 different patients (18 males and 12 females aged from 57 to 86) we have obtained the correlation shown in Tab. I. Three neurologists were present during tests and provided us the UPDRS level for each patient.

The correlation is based on the PSD value. The calibration of the corrective factor H has been made on the basis of 60 acquisitions (one for each hand) appropriately weighting the contributions provided by the PT and KT with the width of SF50 in such a way as to obtain the 100% correct matches between the report provided by the algorithm and the evaluation of neurologists.

TABLE I
UPDRS CORRELATION OVER 30 PATIENTS

UPDRS Level	Estimated Level K
0	$K < 0.3$
1	$0.3 \leq K < 6$
2	$6 \leq K < 13$
3	$13 \leq K < 17$
4	$K \geq 17$

TABLE II

TREMOR EVALUATION OVER 12 PATIENTS

Patient	Tremor type	H (Y or N)	UPDRS
1 DX	RT	N	2
1 SX	RT	N	1
2 DX	RT-PT	Y	2
2 SX	RT-PT	Y	2
3 DX	RT	N	3
3 SX	RT	N	4
4 DX	RT-PT	Y	2
4 SX	RT-PT	Y	1
5 DX	RT-PT-KT	Y	3
5 SX	RT-PT-KT	Y	2
6 DX	RT	N	1
6 SX	RT	N	0
7 DX	RT	N	2
7 SX	RT	N	1
8 DX	RT-KT	Y	2
8 SX	RT-KT	Y	1
9 DX	RT	N	1
9 SX	RT	N	3
10 DX	RT-PT-KT	Y	2
10 SX	RT-PT-KT	Y	1
11 DX	RT-PT	Y	3
11 SX	RT-PT	Y	4
12 DX	RT	N	0
12 SX	RT	N	1

B. Tremor classification

The model validation and the convalidation of the proposed correlation with UPDRS has been performed on other different patients. We have enrolled 12 PD subject: 7 males and 5 females aged from 62 to 78.

The typology of tremor is correctly detected over all 12 patients for 24 acquisition (one for each arm). Results of frequency analysis are shown in the second column of the Tab. II. As we expected, in a lot of patients with PD not only RT but also PT and KT occur. The third column indicates whether or not the use of the correction factor H while the last column shows the instrumental quantification of tremor based on the correlation established by the UPDRS. These data have been analyzed by three neurologists in order to compare the UPDRS level provided by the system with the assessment made by them through the visual analysis of the patient during the test.

The results of the correlation with the UPDRS calculated by the proposed algorithm are faithful to the evaluation made of neurologists. The algorithm has 100% sensitivity and 100% specificity considering the sample of 12 patients.

IV. CONCLUSIONS

The developed system has characteristics that make it very appropriate for use in the diagnosis and control of neurodegenerative diseases such as Parkinson's both ambulatory and home monitoring. Our work is based on a simple IMU device and a set of algorithms for obtaining an objective real-time classification of tremor and a quantification of its severity according to UPDRS scale.

In addition, the system provides to the neurologist a certain methodology for the annotation of the severity and progression of the disease. The report is therefore not affected by subjective assessments that may depend, for example by medical personnel who alternates in subsequent analyzes of patient.

The classification of tremor is extremely important especially in the initial phase of the disease where it must be established if the patient presents RT typical onset of PD or if the cause of the tremor can be attributed to other neurological disorders. Moreover the proved correlation with the UPDRS allows to have a report objectively and universally recognized for the evaluation of patients with PD.

Our next aim is to automate the compilation of others UPDRS tabs and involve other aspects of the disease such as freezing or dyskinesias. The system so designed will make possible to monitor at home patients with Parkinson's disease allowing the doctor to calibrate drug therapy on the basis of a long-term observation rather than a simple outpatient visit. The implementation of the algorithm in a dedicated application for neurological use will provide automatic updating of a database containing the medical records of the patient. This is an additional tool to objectively diagnosis and monitoring of the disease.

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