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Mobile Systems as a Challenge for Neurological Diseases Management – The Case of Parkinson's Disease

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1. Introduction

Nowadays the importance of bio-medical engineering and mobile applications for healthcare is amazingly growing. During the last decades many devices and technological solutions have become available on the market and the interest in applying those technologies to the treatment of several kinds of pathologies has consequently increased. This chapter addresses the problem of continuous monitoring of patients affected by Parkinson's Disease (PD) and proposes a set of technologies to improve the following and management of such subjects.

PD is a neurodegenerative disorder of the central nervous system that affects motor skills and speech (Tolosa, 1998). The primary biochemical abnormality in PD is a deficiency of dopamine due to degeneration of neurons in the substantia nigra pars compact (D. G. Standaert & Young, 2001). The characteristic motor features of the disease include bradykinesia (i.e. slowness of movement), tremor, rigidity (i.e. resistance to externally imposed movements), flexed posture, postural instability and freezing of gait. Furthermore, PD is usually characterised by the loss of normal prosody of the speech (Darkins et al., 1988).

According to the World Health Organisation [WHO], 2002), there are more than six million people worldwide affected by PD. The syndrome typically appears around the age of 60. It affects Europeans and North Americans more often than Asians or Africans and it is more common in men than in women. PD affects about 2% of the population over the age of 65 years, figure that is expected to double by 2020 (de Lau & Breteler, 2006). For those reasons, PD poses a significant public health burden, which is likely to increase in the coming years. Annual medical care, including doctors' visits, physical therapies and treatment for co-occurring illnesses -such as depression- is estimated at $2,000 to $7,000 for people in early stages of the disease, and it is probably much higher for advanced stages. Surgical treatments for PD can cost $25,000 or more. As the disease progresses, institutional care at an assisted-living facility or nursing home may be required, and the related costs can exceed $100,000, per person annually.

Technology in general and specifically ICT might be an affordable alternative for PD's patients' treatment and management. The development of platforms for remote health

status monitoring, the qualitative and quantitative assessment and treatment personalization for people suffering from neurodegenerative diseases is expecting to provide in the future a remarkable improvement in patients' management as well as a substantial cutting-off of the economic burden generated by the disease. New technologies allow monitoring the evolution of the disease through the employment of a wide range of wearable and user-friendly micro-sensors. Moreover, the last advances in data processing and data mining algorithms is bound to provide more accurate information about the diverse aspects of PD evolution. Finally, it is important to highlight the huge potential in costs reduction that such platforms could yield. Furthermore, it is worth mentioning that the reduction in costs of hospitalization and treatment represents an attractive asset for the market forces involved in the development of biomedical applications.

2. Treatment

Current clinical treatment of Parkinson's disease is performed through ersatz dopamine administration or by using Deep Brain Stimulation (DBS) (Singh et al., 2007).

2.1 Dopamine treatment

Current therapy is based on augmentation or replacement of dopamine, using the biosynthetic precursor levodopa or drugs that activate dopamine receptors. These therapies are effective at the beginning of treatment. However, after a variable period of time, this initially excellent response is complicated by the appearance of MRCs. Complications include wearing-off, the abrupt loss of efficacy at the end of each dosing interval and diskinesias (de la Fuente-Fernández et al., 2004). Wearing off and dyskinesias produce substantial disability and frequently interfere with medical therapies (A.E. Lang & A.M. Lozano, 1998). Usually, motor fluctuations appear first, as a shortening of the initially smooth and long lasting dopaminergic response. In the typical case, few hours after drug intake the patients start to realize the re-emergence of signs and symptoms of the disease. This is known as end of dose deterioration or wearing off. This may happen several times a day; therefore the patient may actually several hours per day in the off state (Lees, 1989).

2.2 Deep brain stimulation

DBS is a surgical treatment involving the implantation of a medical device called a brain pacemaker, which sends electrical impulses to specific parts of the brain (Vaillancourt et al., 2003). The introduction of DBS as a therapeutic tool for advanced PD has revolutionised the clinical management of this condition. Due to its safety profile and efficacy, DBS has evolved from a last-resort therapeutic option to a modality that is now routinely offered to patients. Over the years, surgical candidates and the outcome expected with this procedure has become well established (Deuschl et al., 2006). Overall improvement that might be expected with surgery is similar to that provided by levodopa without the associated involuntary movements (Group, 2001). As the diseases progresses, however, non-dopaminergic symptoms (gait, postural instability, sleep disorders and depression, among others) become more prominent, leading to a significant increase in morbidity. To overcome some of the problems, the use of different surgical targets has been advocated. Perhaps the most promising application of DBS on this regards involves the use of Pedunculopontine Nucleus (PPN) stimulation for the treatment of gait and postural instability (Mazzone et al.,

2005). Recent studies suggest that this procedure might be suited for the treatment of falls and freezing. In addition to motor symptoms, an improvement in rapid eye movement sleep in patient with PD treatment with PPN DBS has been reported (Lim et al., 2009). In the future, a tailored approach to patient's specific symptoms may be possible (Lozano, 2009).

3. Assessment - state of the art

The assessment of PD can be performed through clinical and technological methods. Both types of solutions are reviewed.

3.1 Clinical solution

In Europe, each neurologist or general practitioner (GP) normally cares for 50 to 800 patients with PD. The range in workload is a result of diversity both in national health systems and in the availability of clinical resources across Europe. Even at 50 patients per clinician, this represents a serious challenge to homecare monitoring for specialised conditions. PD's patients normally visit their specialised clinician or GP every 4-6 months. As a result, any changes in the patient's conditions may not be recognised for several months, unless the patients themselves make contact (R. Greenlaw et al., 2009).

In clinical practice, information about motor fluctuations is usually obtained by asking patients to recall the number of hours of ON (i.e. when medications effectively attenuate tremor) and OFF time (i.e. when medications are not effective). This kind of self–report is subject to perceptual bias (e.g. patients often have difficulty distinguishing dyskinesia from other symptoms) and recall bias. Another approach is the use of patient diaries, which can improve reliability by recording symptoms as they occur, but does not capture many of the features useful in clinical decision making (Group, 2001).

Certainly for PD there is the additional complication of symptoms which vary throughout the day (swinging between ON and OFF states). During the short office visit in this neurologist the patient may appear very well and he misses to report symptoms of wearing off. As a result, treatment modifications are not undertaken in time. Besides, it is disempowering for the patient to be asked to present a true picture of their disease in a pre-scheduled one hour appointment (R. Greenlaw et al., 2009).

The actual emergence of dyskinesias throughout the day mainly depends on the intermittent dopaminergic drug intake, even in influence by timing and quantity of each individual dose of levodopa. While other phenomena, such as delayed response or no-response depends also on stress, food intake and many other factors. In this case, patients will greatly benefit from quantitative objective assessment of their motor status in daily life in relation to the dosing schedule.

In an attempt to solve these problems and to find more objective assessment, several rating scales have been designed and used. Among them, the Unified Parkinson's Disease Rating Scale (UPDRS) is the most widely used (Goetz et al., 2004). This rating tried to quantify selected symptoms and signs of Parkinsonism in a 5-points scoring system (with 0 for no signal and 4 for a marked severity of the sign). Unfortunately, the use of the UPDRS scale, like any other semi-objective rating scale presents some limitations like intra and inter observer inconsistencies. Besides, it can be time consuming and ca be biased by subjectivity issues related to historical information. Moreover, the pattern and severity of PD symptoms may vary considerably during the day, while clinical rating scales only provide moment-to moment assessment; and finally, measurements of motor fluctuations made in the clinic

may not accurately reflect the actual functional disability experienced by the patient at home.
The accurate assessment of speech quality is a major research problem that has attracted attention in the field of speech communications for many years. Subjective quality measures given by professional personnel who have received special assessment training are necessarily time consuming and costly (Lingyun Gu et al., 2005).

3.2 Technological solution: sensors for motion analysis

Over the past decades various technologies, methodologies and systems have been proposed for the monitoring and the assessment of the Parkinson's disease. A significant number of studies investigated various parameters of the gait of PD patients. Others focused on the evaluation and quantification of the patients' motor status and various disease symptoms by the use of computerized motion tests (e.g. handwriting, inserting pegs, and games). Table 1 describes some features of the human motion, as well as the characteristics which can be measured through the use of wearable sensors.

Features	**Characteristics**	**Sensor**
Gait	Speed of Locomotion	Motion sensor
	Variability of the gait	
	Rigidity of legs	
Posture	Trunk inclination	Motion sensor
Leg movement	Speed	Motion sensor
	Length of Step	Motion sensor
	Step Frequency	Motion sensor
	Stride	Motion sensor
Hand Movement	Speed	Motion sensor
	Angle Amplitude	Motion sensor
Tremor	Amplitude	Motion sensor
	Frequency	
	Duration	
	Asymmetry	
Fall	Fall detection	Motion sensor
Freezing of Gait	Leg movement analysis	Motion sensor
Levodopa-Induced Dyskinesia (LID)	Duration	Motion sensor
	Severity	
Bradykinesia	Duration	Motion sensor
	Severity	
	Asymmetry	
Aphasia	Pitch	Microphone
	EPE	

Table 1. Parkinson's disease – wearable sensors for human motion related measurements

The accuracy of measurements of the parameters above described depends on several technical features that are often in conflict with other needs such as usability, wearability, technical feasibility and the social acceptance of the devices used by the subjects.
In Table 2 a description of these desirable properties along with their conflicts is presented.

Desirable properties	Conflict
Small sensor	The size of sensor is definitely an important factor, especially for portability and mobility matters. However, small sensors may not have enough room for long-lasting battery or storage capacity.
Smart sensor	Sensors possessing many characteristics are often bigger in size, expensive and consume more power
Sensor storage capacity	Due to a limit in storage capacity, sensors have to upload data frequently to the data personal server. So it is important to employ a good wireless communication technology that does not drain excessive power from the sensors.
Sensor processing capability	Because sensors do not often have large processing capability, they may not be able to process all data before the upload to the personal server. This means that large amount of raw data should be stored and eventually sent. Therefore it is important to have an efficient communication channel.
Sensor communication range	Whilst sensors are only able to communicate over short range, it is crucial to define a specific radius of action.

Table 2. Wearable sensors desirable properties & conflicts

3.2.1 Systems for Parkinson's disease monitoring

Most of the research work carried out in the field of PD monitoring focuses on the assessment of the motor status of PD's patients. During the last decade, many research groups have been trying to develop a system able to objectively quantify the severity of the motor disturbances using motion sensors (Patel et al., 2010; 2009; 2007). An important number of these studies is based on the study of various parameters of motor behaviour, in particular features related to the gait (R. Greenlaw et al., 2009; Salarian et al., 2007; 2004).
Other studies focused on the identification of ON/OFF fluctuations through the assessment of tremor (Van Someren et al., 1993), dyskinesias (Keijsers et al., 2003; 2000) and bradykinesia (Papapetropoulos et al., 2010). Some groups are also committed to use electromyogram (EMG) or voice analysis (Kimura et al., 2007).
Additionally, in the literature there are examples of remote monitoring and patient management for PD (Tindall & Huebner, 2009), as well as the use of telematic services to facilitate the performance of motor tests remotely (Das, 2010; Dorsey et al., 2010; Giansanti et al., 2008; Westin et al., 2010).
Even though many advances have been done in the last years, it must be said that there is still a lack of an all-inclusive system able to provide reliable assessment of the status of PD patients being at the same time economically affordable. In particular it is crucial to provide:

- An effective evaluation of PD symptoms through monitoring and testing routines while not interfering with the patient daily life.
- A personalised profile of the patient allowing the correlation between those factors affecting the severity of symptoms (i.e. medication schedule and meals) and the evolution of the disease.
- The clinician with a system able to manage more efficiently the patient by providing timely indications on the effectiveness of the therapy and suggestions on therapy changes.

3.2.2 Available systems in the market/research

There are several products produced by certain research groups or commercially available for the assessment of PD. Some examples follow:

Cleveland Medical Devices

Cleveland Medical Devices Inc. commercialises Kinesia, a compact wireless system for monitoring the severity of PD motor symptoms. The system includes miniature motion sensors worn on the hand and it wirelessly transmits motor symptom information to a personal computer. Data is collected while patients follow computer based video instructions.



Fig. 1. Kinesia, Cleveland Medical Devices Inc. system for PD monitoring based on motor sensors (Jovanov et al., 2001)

Cleveland Medical Devices Inc. also commercialises Kinetisense, a compact wireless system for monitoring gait, posture or upper limb movement. The system integrates two channel Electromyography (EMG) and three orthogonal accelerometers and gyroscopes collecting data on three dimensional movements. The system is wearable and lightweight and is wirelessly connected to a computer for real-time data transmission. As alternative, data can be stored on a memory card for 12 hours recording and transmitted asynchronously. The system can be linked to different software tools for movement and posture analysis, detection of slips and falls and for the performance and monitoring of rehabilitation exercises.



Fig. 2. Kinetisense, Cleveland Medical Devices Inc. system for PD monitoring based on motor sensors and electromyography (Jovanov et al., 2001)

Intel Corporation

Intel Corporation has developed a system called At home Telemonitoring Device (AHTD), based on nonlinear speech single processing methods around the use of discrete variational integrator. It could be used to perform speech analysis detect abnormalities and telemonitor neurological disorders with voice singles.

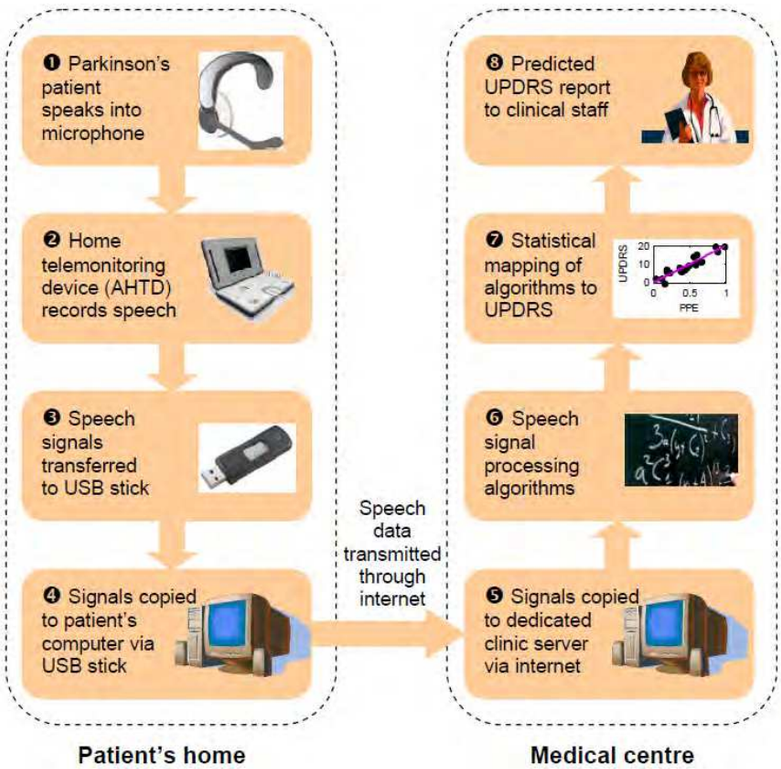


Fig. 3. At Home Telemonitoring Device (AHTD), Intel Corporation system for PD monitoring based on speech processing (Tsanas et al., 2010b)

Karolinska Institute

The Karolinska Institute, Sweden, has developed a prototype test battery for evaluating fluctuation motor symptoms in PD together with a decision support system as part of the Movistar TEVAL project (Westin et al., 2010). The system is based on a handheld device with built-in mobile communication, where combined patient diaries with on-screen motor tests are implemented. The data collected from the patient are transmitted to a central system where they are analysed through Artificial Intelligence methods. Besides, it originates alerts and advice via a web interface.

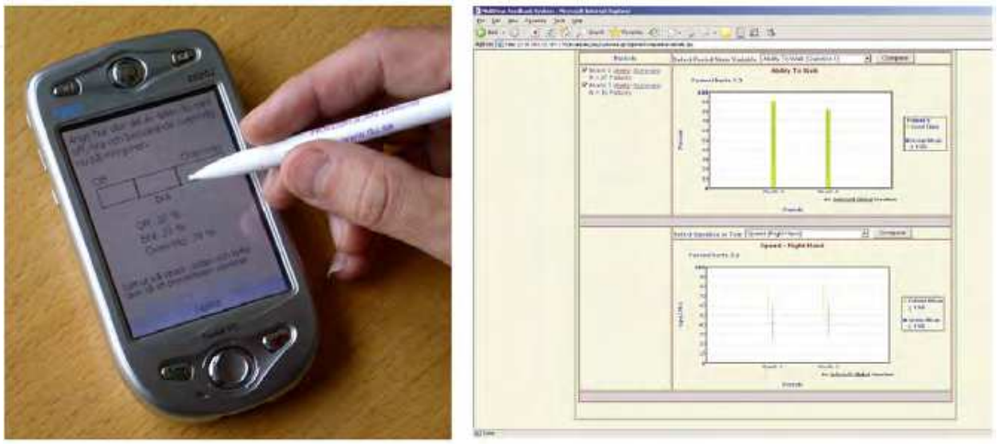


Fig. 4. TEVAL project prototype, Karolinska Institute, Sweden, based on patient diaries together with on-screen motor tests

Twente University

The University of Twente, Enschede, in the Netherlands, has developed a system called SensorShoe that is a mobile gait analysis tool. It is composed by a low-power sensor node equipped with movement sensors (3D accelerometers and 2D gyroscopes) connected to a PDA which provides immediate feedback to the patient while walking and suggest physical



Fig. 5. Sensor Shoe, University of Twente, Enschede, The Netherlands. Gait analysis based on movement sensors (Kauw-A-Tjoe et al., 2007)

exercises based on the personal rehabilitation and training program defined for the patient and stored in the PDA. The system can connect to the hospital or to the physician through the PDA and transmit daily motion data, which can be analysed by physicians and be used to improve the physical therapy.

Federal Polytechnic School of Lausanne

The Federal Polytechnic School of Lausanne, Switzerland, has developed a system for motion monitoring based on a portable data-logger with three body-fixed inertial sensors.

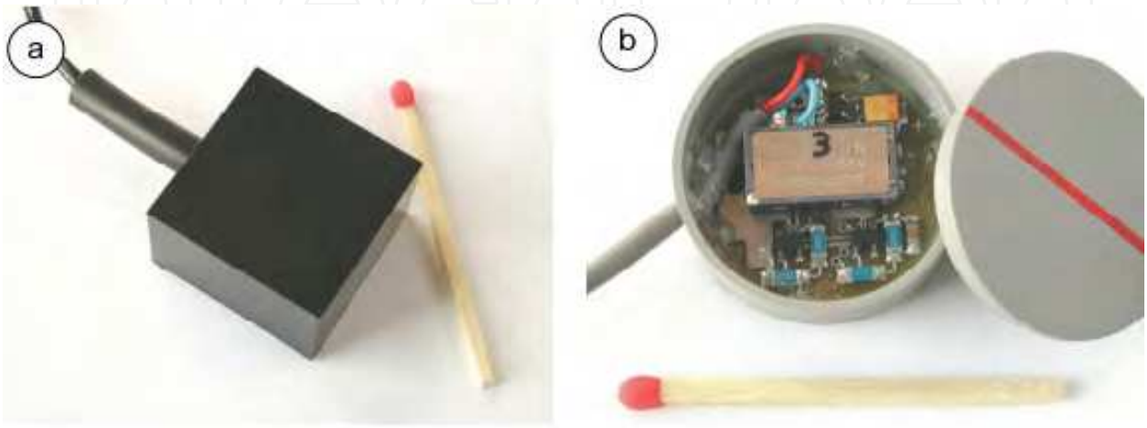


Fig. 6. a) The trunk sensor used for physical activity monitoring b) The uni-axial gyroscopes used for the gait analysis, The Federal Polytechnic School of Lausanne, Switzerland (Salarian et al., 2007).

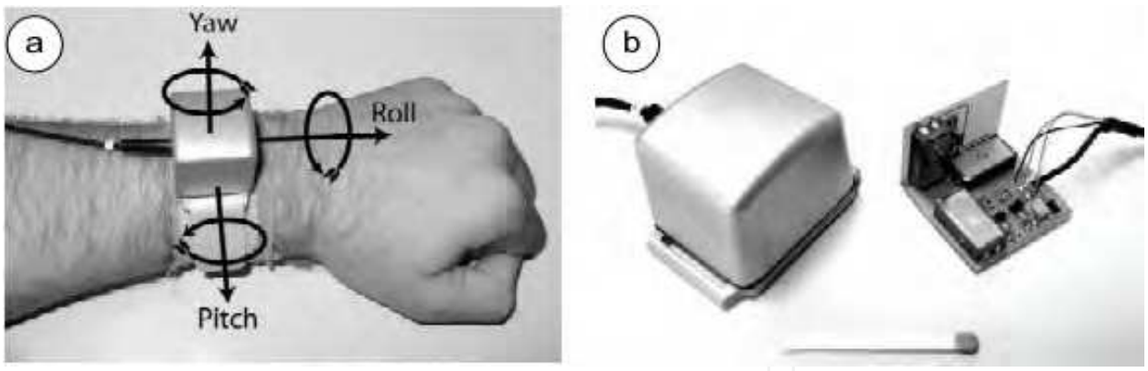


Fig. 7. a) Trunk sensor used for physical activity monitoring b) The uni-axial gyroscopes used for the gait analysis, The Federal Polytechnic School of Lausanne, Switzerland (Salarian, et al., 2007b)

Boston University

The Boston University National Institute of biomedical Imagining and Bioengineering has developed a wearable-sensor system for monitoring motor function. The system is composed by a device that can be worn unobtrusively by patients in their home to automatically detect the presence and severity of movement disorders associated with PD. The onset of the OFF status is based on the motor status of the patient that can be related to

the motor status of the patient with the medications assumptions. The system involves electromyographic (EMG) and accelerometric (ACC) body worn sensors, whose signals are analysed by a system using Artificial Intelligence methods.



Fig. 8. Boston University National Institute of Biomedical Imaging and Bioengineering, PD monitoring system through motor and EMG sensors (UB, 2011)

3.3 Technological solution: non autonomous home based monitoring closed loop systems

Close loop systems are those in which stimulation parameters are adjusted according to recorded signals. Talking about neurodegenerative diseases such as PD, close loop systems imply that medication doses and timing is adjusted based on the measurement of certain biomedical signals. Some examples follow.

3.3.1 PERFORM project

A sophisticated multi-paRametric system FOR the continuous effective assessment and Monitoring of motor status in Parkinson's disease and other neurodegenerative diseases research project has developed an intelligent system that monitors several motor signals of the patients that are analyzed in a medical centre by a medical professional. The system is able to propose treatment changes, based on the clinical assessment. Further explanations are provided later in this chapter (Perform, 2008).

3.3.2 HELP project

The HELP project (Home-based Empowered living for Parkinson's Disease Patients) aims at developing a comprehensive system able to administer drug therapy without patient intervention, in either continuous or on-demand basis in order to manage disease progression and to mitigate PD's symptoms (Help, 2011).

It is based on inertial sensors that capture inertial information about the patient's motion and compute spatiotemporal properties and Parkinson's related symptoms. At the point of care remote supervision of the patient is performed, together with Verification of the infusion algorithm and possible modification of its parameters. An intraoral device continuously administrates dopamine agonists to the mucosa from the mouth. Besides, a subcutaneous pump receives commands adapting the infusion rate of apomorphine, a non-selective dopamine agonist.

4. PERFORM system

4.1 Introduction

PERFORM is a project partially funded by the European Commission under the Seventh Framework Program, aiming at providing an innovative and reliable tool that is able to monitor and evaluate motor neurodegenerative disease patients, such as PD patients.
The PERFORM project is based on the development of an intelligent closed loop system that seamlessly integrates a wide range of wearable micro-sensors constantly monitoring several motor signals of the patients. Data acquired are pre-processed by advanced knowledge processing methods, integrated by fusion algorithms to allow health professionals to remotely monitor the overall status of the patients, adjust medication schedules and personalize treatment. Personalization of treatment occurs through PERFORM's capability to keep track of the timing and doses of the medication and meals that the patient is taking.

4.2 The PERFORM medical and technological vision

The information gathered by the inertial sensors (accelerometers and gyroscopes) is processed by several classifiers. As a result, it is possible to evaluate and quantify the PD symptoms that the patient presents as well as analyze the gait of the patient. Based on this information, together with information derived from tests performed with tests devices (e.g. virtual reality gloves) and information about the medication and food intake, a patient specific profile is built. Next steep is to compare the patient specific profile with his evaluation during the last week and last month, checking whether his status is stable, improving or worsening. Based on that, the system analyses whether a medication change is needed-always under medical supervision- and in this case, information about the medication change proposal is sent to the patient.

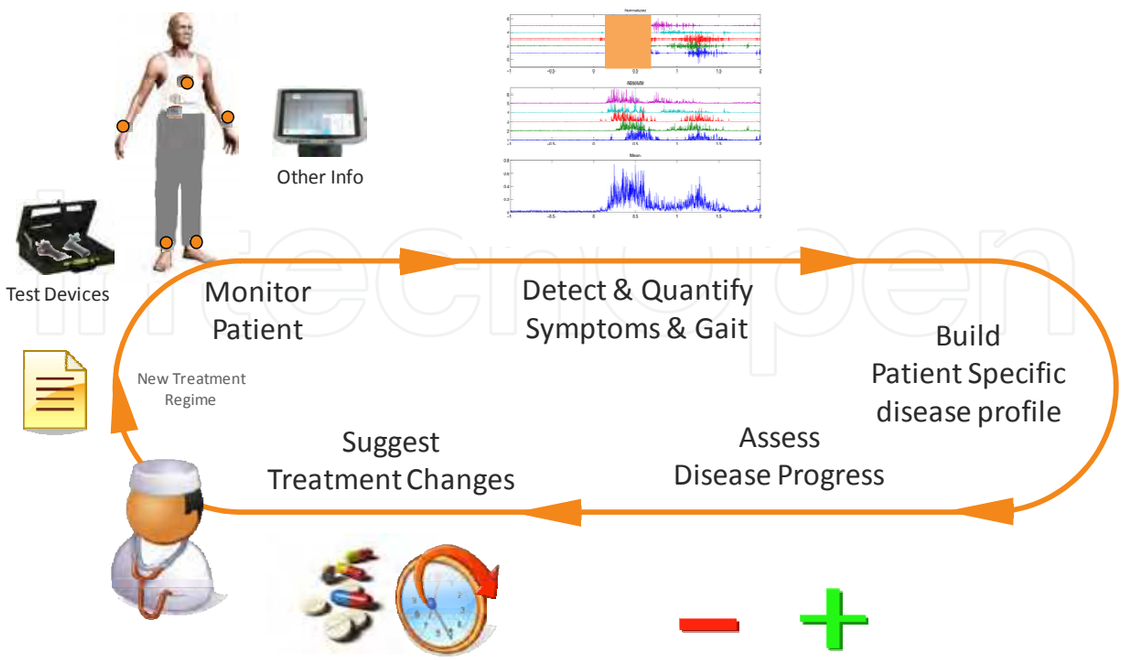


Fig. 9. PERFORM medical and technological vision

4.3 The PERFORM architecture

The system architecture proposed to meet the previously described medical and technological vision is presented in Fig. 10. It consists of two subsystems: the patient-side subsystem and the healthcare centre subsystem.

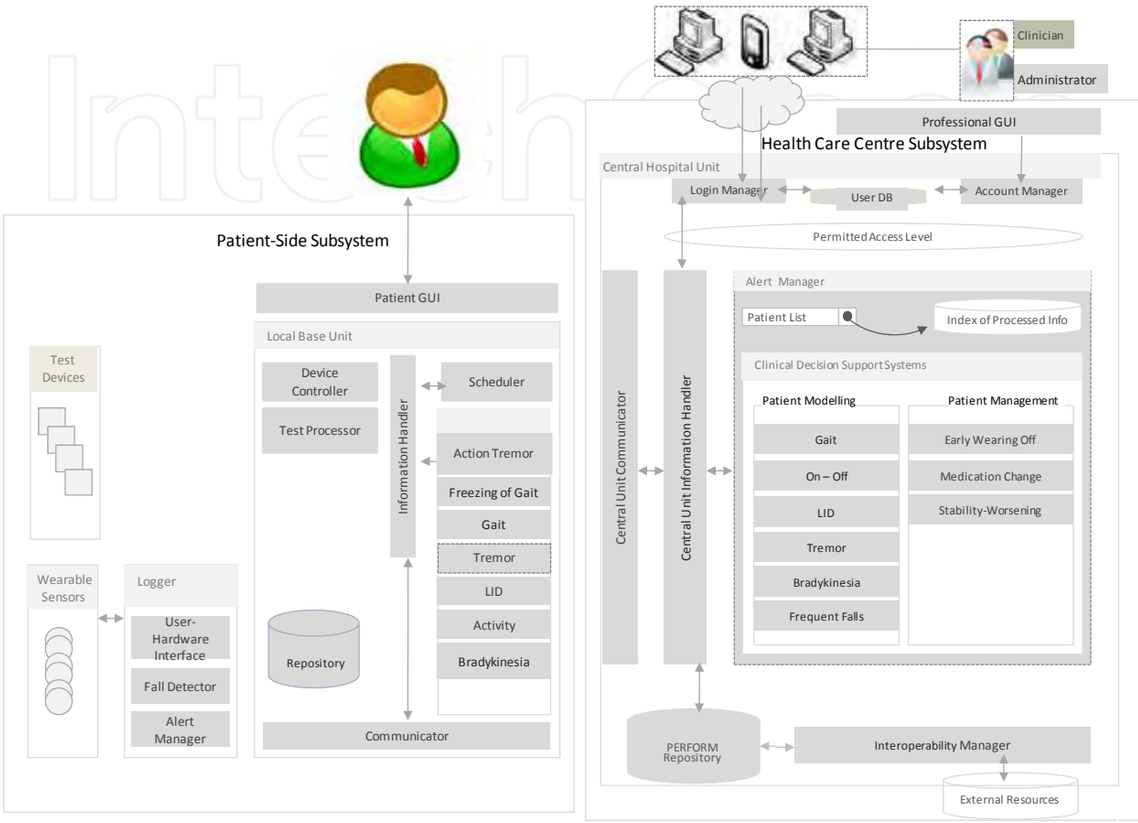


Fig. 10. PERFORM system architecture (R. Greenlaw et al., 2009)

The patient-side subsystem is responsible for the identification and quantification of the patient symptoms and the recording of other useful information for the evaluation of the patient status. The healthcare centre subsystem evaluates the disease progression and suggests appropriate treatment and changes, based on medical knowledge acquired from published medical guidelines.

The patient-side subsystem is composed by the following modules:

Continuous monitoring Module. It is used to monitor the patient motor status through the day. It consists of five accelerometers and a wearable device. The wearable device processes the recorded signals and detects patient falls in real time. The sensors position was hosen after careful examination and research on the targeted disease symptoms.

It is composed of four tri-axial accelerometers used to record the accelerations of the movements at each patient extremity, one accelerometer and gyroscope (on the trunk) used to record body/chest movement accelerations and angular body velocity during trunk and body turning, and a wearable device receiving all recorded signals. The sensors' position was chosen to allow all targeted symptoms detection and quantification with the minimum number of sensors.



Fig. 11. PERFORM System prototype including accelerometers, gyroscope and data logger (left) System placement on the body (right)

All sensors transmit using Zigbee protocol to the wearable device which is located on the patients' waist thus making up a body sensor network. Special attention is given to the sensors usage and the easy set up by the patient and the caregivers. The sensor size is no bigger than a small matchbox. Sensors on the arms and legs are attached on specially designed elastic Velcro bands, which allow fixation to any wrist or ankle size. The sensors are placed inside an elastic pocket on the band, which secures it firmly on the patient body avoiding motion artefact due to cloth movement. The sensor on the trunk in placed within a zipped elastic pocket on a vest. The vest is also equipped with Velcro straps to firmly adjust the sensor on the patient chest. The selected design allows the easy wearing and attachment/detachment of sensors.

Test Module. It consists of a set of devices (such as virtual reality gloves, microphones or video cameras) used to record patient information, while the patient is performing specific tests, as normally done at the clinician's office during an examination. The patient wears the test devices and performs the tests as instructed from the visual interface of the Base Module (Local Base Unit). The test module records the performed activities and identifies any abnormalities, such as wrong sensor or patient position. Finally, it processes the recorded data and extracts the information about the number of taps and hand movements per second, the detection of hypophonia and neutral face expression.

Patient interface. Emphasis is given in designing an easy to use interface for the patient, considering the patient motor disabilities and limited computer familiarity. The designed interface inherits the feel and tough of the phone dialling pad, and all system choices are based on it. Patient use the interface to declare their subjective estimation of their own status, to gain access to relevant disease information, to receive instructions on life-style interventions, such as medication and good intake and on the execution of tests. Moreover, PD's patients declare medication intake information, which is useful for the patient status assessment.



Fig. 12. PERFORM Patient Interface. Medication intake information (left). Food intake information (right)

Communication: the Base Module supports Bluetooth and Zigbee communication with the continuous monitoring system, and fixed line communication to the hospital centre over ISDN and xDSL.

Symptom Detection. This submodule processes received patient signals and detects the targeted patient symptoms (tremor, levodopa induced dyskinesia and off state). For each symptom dedicated submodule processes the relevant signals, detests the symptom episode and quantifies it into a severity scale from 1 to 4, according to the UPDRS scaling for PD patients (Cancela et al., 2010; Keijsers et al., 2000; Pansera et al., 2009). Other features such as duration, frequently and amplitude might also be provided for further clinician review and system evaluation.

The healthcare centre subsystem is composed of the following modules:

Patient Modelling Module. This module exploits the recorded patient information to build a patient symptom profile. For each main symptom (tremor, levodopa induced dyskinesia and on-off states), it produces a patient profile which describes the patient's common symptom features. When a new patient recording is processes, it is checked against the patient symptom profile. If significant differences are found, it might be due to two reasons: either a temporarily patient behaviour abnormality or a change to the patient profile. In the last case, the system checks whether a substantial number of similar situations are identified for the last time period for the specific patient and if that occurs, it creates an alert.

Patient Management Module. This module considers the detected symptoms and their characteristics, combines them with other recorded information and suggests appropriate treatment changes based on the accumulated specialists' knowledge on the management of PD.

Medical Interface: The system can be accessed either locally or remotely by the treating clinician and the general practitioner, using either a large screen access device (e.g. PC, laptop) or a small screen access device (e.g. PDA). Clinicians are directed to the home system screen, which presents the produced patient alerts to the patient specific screen, which provides the information needed to evaluate visually the patient condition. On request, the actual recorded signal and tests are downloaded from the patient-side to the healthcare centre for review. The focus is on the provision of an adequate visual description of the patient status within one screen, minimising the time spend by a clinician. Clinicians will access the system periodically to check patient status, but the option to be alerted when patient status changes are also available.

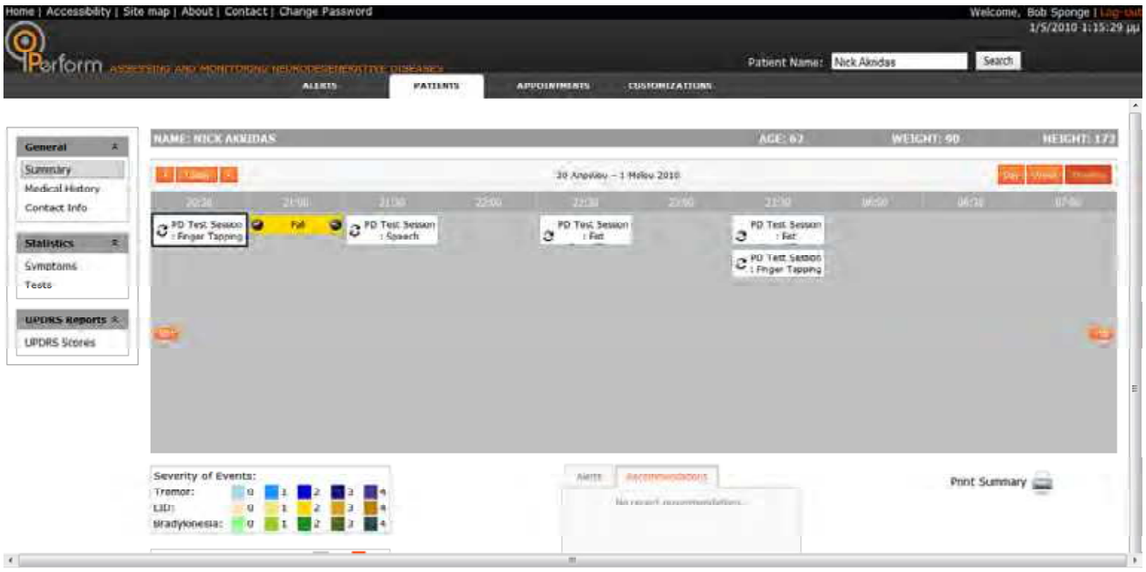


Fig. 13. PERFORM medical interface

Communication. All patient-side data (signal features and patient inserted information) are transmitted to the health-care subsystem once a day, through Internet.

4.4 Evaluation methodology

In order to test PERFORM system, several clinical trials have been arranged into 4 different phases, taking place between 2009 and 2011. Their description follows.

Phase 1: Data collection with SHIMMER

Eight subjects participated in this study, separated in two groups: four PD patients and four healthy subjects. The symptoms were rated by a professional neurologist with more than 20 years of experience with PD patients. Four accelerometers were placed on the right and left forearms and on the right and left calves, with a fifth accelerometer being placed on the trunk, at the base of the sternum. Motion data was collected using the SHIMMER platform (RealTime, 2011). SHIMMER is a small wireless sensor platform designed by Intel as a wearable device for health sensing applications. All sensors provide 3-axis accelerometer signals large storage, and low power-standards based communication capabilities. They also provide a Bluetooth protocol capability that allows SHIIMERs to stream the data to a computer. During the experiment, the accelerometry measurements were complemented by a reflective marker and a camera collection system. This complimentary analysis served as a support tool to validate the data used for this work.

Phase 2: Data Collection with ANCO first release trainer classifier

The data collection was performed with a network of wireless 3-axis ALA-6g sensors (Anco, 2011), located on the limbs, trunk and belt of the patient. During this phase, data were collected during tests with patients in a supervised environment, with the collaboration of the clinic's medical staff. Patients involved in this phase were required to be aged between 18 and 85 years old, suffering from PD, capable of complying with study requirements, receiving dopaminergic treatment and experiencing motor fluctuations. Dementia, Psychosis and significant systemic diseases (such as cancer) were the exclusion criteria

applied when selecting participants. The data set used in this study included trials with twenty PD patients, ten in Navarra (Spain) and ten in Ioannina (Greece). In order to comply with ethical requirements, all procedures were carried with the Clinic Institutional Review Board's permission. Data were collected following a standard clinical protocol in which patients carried out daily basic activities (i.e. walking, lying, sitting, etc.) during two cycles of on-off oscillations in response to levodopa during the same day and under the supervision of a clinician.

Phase 3: Long time recording

Data collection of phase 3 was performed with an updated version of the devices that includes a wearable and programmable logger that gave a better mobility to the patient and new ALA-6g accelerometers sensors equipped with an external battery allowing longer data collection session. Data were collected in a supervised environment and with the collaboration of the medical staff. Furthermore, patients involved in this phase, fulfilled with the age and medical specifications of the previous phase. The data were recorded with twenty-four PD patients, twelve in Navarra and twelve in Ioannina. Data were collected during a six-hour daily session in which patients carried out their normal daily activity. Moreover, four standard clinical protocol sessions were performed during two cycles of on-off oscillations in response to levodopa treatment and under the supervision of a clinician. At the end of the day, data were processed using the train set computed in the previous phase and the output were checked with the results provided by the clinicians

Phase 4: Final system testing

From March 2011, the integrated and final PERFORM system will be introduced to a new group of patients that will perform the final evaluation. The patient group will be constituted by 20 PD patients for regular tests and 4 PD patients for mid-term tests, all recruited from the Neurology Department from the Azienda Unita' Sanitaria Locale di Modena hospital in Modena, Italy.

4.5 Results

PERFORM project has released promising results in patients monitoring and status assessment. Due to the short-term nature of the clinic trials that have been carried out it is difficult to determine the future impact on patient treatment; however it is possible to at least provide a quantification of the performances of the modules of the Patient –Side Subsystem. It is designed to assess the motor status of the patients and establish a direct connection with the physician. Its basic functions are:

- to determine the activity of the subject
- to provide a quantification of symptoms severity based on the UPRDS scale and present such an information to the physician through remote communication
- to gather information about the daily life of the patient

The validation has proved that the first prototype of the Patient Side Subsystem is able to provide a very reasonable assessment of the daily activity of the patients using data classification techniques based on accelerometers. More specifically, the algorithms are able to discriminate activities such as walking, standing, laying or sitting with an accuracy of nearly 99%. The activity recognition is the base information needed to evaluate the symptoms related to movement. Besides, the clinical trials have proved that the algorithms are able to classify with an acceptable degree of accuracy the main symptoms of PD. General

body bradykinesia is quantified with a classification accuracy within the range of 70%-86% (depending on the number of sensors used in the measurements) compared to medical evaluation. Dyskinesia and tremor classification accuracy are respectively 93.6% and 97%. Those results are quite good in comparison with the subjective medical evaluation, with accuracy around 95%. The gait module has also proved to release useful information with acceptable level of accuracy. The gait analysis system provides a measure of stride length with a 7.3% of average error and a measurement of the complexity of movement through an analysis of the entropy of the walking.
Phase IV of the pilots is expected to provide a more accurate validation with long-term recording data.

4.6 Comparison with SoA systems

Compared to Kinesia system, a sophisticated multi-paRametric system FOR the continuous effective assessment and Monitoring of motor status in Parkinson's disease and other neurodegenerative diseases (PERFORM) presents the advantage of integrating other data from patient's monitoring, such as data from normal daily activity Kinesia monitors only upper extremity motor symptoms, while PERFORM is able to monitor the entire motor disorder, involving walking and moving in general, including freezing, falls risks, etc. The system is based on proprietary software and raw data may not be available.
In relation to Kinetisense commercial product, PERFORM links motion monitoring data to other information such as medication assumption, stress situations and historic data of the patient, in order to draw a complete picture and not only a snapshot such as Kinetisense does. The system is based on proprietary software and raw data may not be available. PERFORM integrates more data from continuous monitoring rather than on e-diary and voluntary motion exercises as the TEVAL Movistar system does.
Compared with SensorShoe system, PERFORM provides link to medication and enables complex data interpretation and analysis. On the other hand, PERFORM system is also able to detect abnormalities in motion, which the prototype built by the École Polytechnique Federale de Lausanne is not detecting.
In comparison with the system proposed by Boston university, PERFORM manages data from more devices and is able to correlate different data input.
Finally, in comparison with the project HELP, PERFORM is able to provide an assessment for specific symptoms such as dyskinesia, bradykinesia, tremor and akynesia, delivering a quantification based on the UPDRS scale, which HELP is not taking into consideration. On the other hand, the system is not providing a feedback to adjust the medication directly on the patients. In other word, PERFORM is not closing the loop of monitoring/assessment/medication adjustment in an automatic way, that is what HELP project has tried to do.

5. Conclusions

This chapter has presented a SoA review of the main methods used to monitor and assess PD's patients. On one hand, clinical assessment is usually performed through annotations in diaries and self-reports from the patient during the short office visit in this neurologist the patient may appear very well and he misses to report some symptoms, as a result, treatment modifications are not undertaken in time. The UPDRS is a scale that tries to quantify selected symptoms and signs of Parkinsonism in a 5-points scoring system (with 0 for no

signal and 4 for a marked severity of the sign). Unfortunately, the UPDRS like any other semi-objective rating scale has limitations like intra and inter observer inconsistencies, can be time consuming and ca be biased by subjectivity issues related to historical information.
On the other hand, technological solutions are able to provide quantitative objective information, including the use of motor sensors, electromyography, position transducers, and speech recognition systems.
This chapter has presented PERFORM, a project partially funded by the European Commission under the 7th Framework Program, aiming at providing an innovative and reliable tool that is able to monitor and evaluate motor neurodegenerative disease patients, such as PD patients.
The PERFORM project is based on the development of an intelligent closed loop system that seamlessly integrates a wide range of wearable micro-sensors, constantly monitoring several motor and signals of the patients. Data acquired are pre-processed by advanced knowledge processing methods, integrated by fusion algorithms to allow health professionals to remotely monitor the overall status of the patients and adjust medication schedules and personalize treatment. Personalization of treatment occurs through PERFORM's capability to keep track of the timing and doses of the medication and meals that the patient is taking. The system architecture has been presented. A comparison with available related systems has been performed.
The system has already been tested in hospitals in Navarra (Spain) and Ioannina (Greece). The integrated tests of the system will be performed in Modena (Italy) from March 2011.
Obtained results so far suggest an overall valid closed loop system, able to detect PD symptoms based on motor signals and additional information, evaluate with a high accuracy level the overall status of the patient and propose medication changes accordingly. However, to achieve more improvements especially in the automation of close-loop mechanism, further improvements are needed in order to provide a complete reliable assessment system for symptoms severity.

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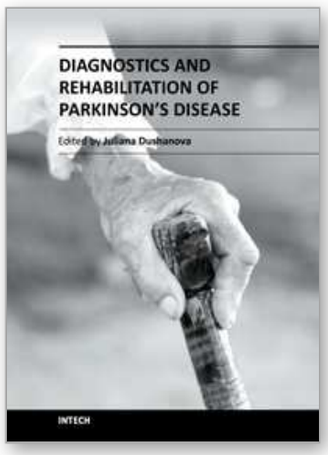
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Diagnostics and Rehabilitation of Parkinson's Disease presents the most current information pertaining to news-making topics relating to this disease, including etiology, early biomarkers for the diagnostics, novel methods to evaluate symptoms, research, multidisciplinary rehabilitation, new applications of brain imaging and invasive methods to the study of Parkinson's disease. Researchers have only recently begun to focus on the non-motor symptoms of Parkinson's disease, which are poorly recognized and inadequately treated by clinicians. The non-motor symptoms of Parkinson's disease have a significant impact on patient quality of life and mortality and include cognitive impairments, autonomic, gastrointestinal, and sensory symptoms. In-depth discussion of the use of imaging tools to study disease mechanisms is also provided, with emphasis on the abnormal network organization in parkinsonism. Deep brain stimulation management is a paradigm-shifting therapy for Parkinson's disease, essential tremor, and dystonia. In the recent years, new approaches of early diagnostics, training programmes and treatments have vastly improved the lives of people with Parkinson's disease, substantially reducing symptoms and significantly delaying disability. Written by leading scientists on movement and neurological disorders, this comprehensive book should appeal to a multidisciplinary audience and help people cope with medical, emotional, and practical challenges.

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