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Early Detection of Parkinson's Disease – Simulation and Assessment

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***Abstract*— It is important to note that all tremors are not considered as symptoms Parkinson's disease, nor is a tremor proof Parkinsonism. Recent developments in the diagnosis of PD, necessitate thorough investigation of the disease etiology and pathophysiology. Moreover, the clinicians are aware that the present diagnostic tools and guidance need to be updated considering latest knowledge of PD to optimize its early detection. Tremors are visible indicators of the disease prognosis. Systematic study by monitoring tremor could reveal the early symptoms of PD. Therefore, the primary objective of this paper is to research for a simple and quick review of procedure to detect the disease in its early stages. Further, a tremor simulator for assessment of hand tremors is designed and developed in this investigation.**

Keywords*— *Parkinson's disease; Alzheimer's disease; tremors; muscular rigidity; complications

I. INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder of the brain that would progress slowly in several people. PD is the second most common disease after Alzheimer's disease (AD) which is much worried among aged population group [1]. It is estimated that about 7 to 10 million people worldwide are suffering from PD and 27 per 100,000 populations have the disease in Saudi Arabia [2]. The disease initially effects on motor activities of the patient. Normal movement of the body is controlled by a chemical called dopamine which is produced by billions of nerve cells present in the brain. It is believed that when the dopamine producing brain cells are damaged, the production of the dopamine chemical decreases that affects on movements and coordination of the body. The symptoms of the disease include tremors, muscular rigidity, changes in gait, and complications in speech [3]. Though the disease itself is not fatal, but the complications from the disease are serious. Proven treatment to cure the disease is presently not available yet [4,5], but the timely detection and diagnosis in early stages can help to plan for available medication to relieve from the symptoms. Tremor is physically observable motor symptom of the disease. A tremor is a rhythmical, involuntary shaking of the body or the parts [6]. It can happen in aged people also. It is therefore, tremor due to Parkinsonism need to be differentiated from the physiological tremor in aged people.

II. BRIEF HISTORY OF PARKINSON'S DISEASE

This Section narrates briefly about historical background of Parkinson's disease and relevant physiological system. The disease was mentioned much earlier to 200 years ago with the title as "An Essay on the Shaking Palsy" [7], henceforth an uncontrolled or involuntary shaking of the body was named by the author of that article. The motor symptoms, which are regarded as core symptoms of the disease include shaking of the body or its parts by their own, rigidity, and slowness in the movement of the limbs [8,9]. Charcot contributed significant discovery in the PD research by observing tremor at wrist through zymography, which is actually a tool to record arterial pulses [10]. Continued their research, Charcot depicted typical Parkinsonism through his famous drawings [11] in which various postures are shown which are resulted from motor deformity. Then, the Nobel laureate Arvid Carlsson reported that dopamine, which is a neurotransmitter in could be the reason behind PD [12]. It has been reported that the loss of dopamine cells present in substanta nigra in the brain could be the primary cause of PD and attempted to manipulate it by successfully administering a pharmaceutical drug called levodopa through the patients [13]. Despite of dedicated research by several neurologists and engineers, succinct cause and physiology of the disease is yet to know and there is no treatment to cure the disease till today.

III. ETIOLOGY

Etiology of PD is still unclear. Several studies presumed several risk factors that could be reason in the development of PD [14], thus increasing the disease complexity. Few of the risk factors are exposure to public water sources, chemicals, wood cutting dust, farming and rural environment. Broadly, they can be categorized as environmental. factors, aging, genetic factors, and combination of factors. Aging is a natural phenomenon. The pathogenesis of PD occurrence is usually in late middle age and its prevalence increases further with older age [15]. In the aging population (with mean age of 70 years), the neurodegenerative disorders pose higher challenge to the clinicians [16]. Cigarette smoking, caffeine consumption, pesticides, herbicides, and rural living also considered as potential risk factors of PD.

IV. SYMPTOMS OF PARKINSON'S DISEASE

As the PD is a multi-factorial disease, hence its symptoms are also having shared conditions. Because of this, the diagnosis of the disease became more complicated which necessitates long time observations of the patient. Although the symptoms are typical, they can vary from person to person. Generally, movement of a person is considered as common sign of PD;

however, there are several other symptoms are the clue for the disease which is not related to the movement. Few important motor and non- movement symptoms are given below. Figure 1 shows a typical symptomatic appearance of a PD patient. In early phases of PD, six major cardinal symptoms are identified. They are; akinesia, bradykinesia, hypokinesia, rigidity, tremor and postural instability [18]. The symptoms resembling PD was mentioned earliest in 1000 BC by ancient Indian and Chinese documents [19, 20].

Figure 1. Typical symptomatic appearance of a patient with Parkinson's disease.[17]

- Akinesia: a delay in the beginning of movements with long reaction times.
- Bradykinesia: slowness of voluntary movement.
- Hypokinesia: poor, incomplete, or simplified movements.
- Rigidity: rigidity of muscles causing pain and hampering certain actions and postures.
- Tremor: involuntary shaking which can be postural or resting.
- Postural instability: imbalance of body while standing or walking.

Few common non-motor symptoms are given below [21]:

- Depression and anxiety,
- constipation,
- olfactory malfunction,
- communication problems like trembling,
- dementia, sleeping disorders and
- sexual problems.

PD is a chronic and irreversible disease which is; therefore preventive measures need to be taken. Detection of the disease at its early stages might help the patients to lead a quality of life thereby increasing the span of life [22]. At present, diagnosis of PD is only based on the symptoms observed over a long period. There is no specific laboratory test, like blood test; neither imaging technique (such as x-ray or MRI) which can confirm the disease. Despite advances in radiology, the diagnostic imaging can only support a doctor in the diagnosis [23]. Since it is difficult to treat the disease with medicines or surgery, physiotherapy is considered as effective follow up treatment procedure for the patient [24].

V. Simulation and Assessment of Parkinsonian Tremor

The most obvious symptom of PD is tremor. Generally, tremor may be described as non-voluntary controlled rhythmic oscillations of body or limbs at specific frequency and amplitudes. Parkinsonian tremor is of two kinds; resting tremor and postural tremor. Resting tremor of hand has a typical range frequency of 3-7 Hz [25], which can occur when the patient is in relaxed state and the limbs are supported firmly [26,27]. Postural tremor is due to muscle contraction which occurs while the patient is voluntarily maintaining a position against gravity [28]. The displacement amplitude of resting tremor and postural tremor is in the range of ±5 mm [29,30]. It has been reported in the literature that the range of frequency of these two kinds of tremor is from 3 Hz to 12 Hz [31]. The resting tremor is very common and is considered as an important diagnostic parameter for PD [32]. Thus, the PD can be considered as a clinical syndrome of movement disorder which happens in the form of tremor and it is most often affects the hands.

A. Hand tremor:

Literature shows that hands are more often affected with tremor than any other parts of the body in PD patients (hands-94%, head-33%, voice-16%, jaws-8%, facial-3%, legs- 12% and trunk-3% among the PD patients) [33]. Figure 2 shows sketches of trembling hands which are shaking uncontrollably, which is a common characteristic of PD.

Figure 2. Sketch showing hand tremors featuring Parkinson's disease.[34]

Handwriting is usually unclear with tremulous hands. During writing task, oscillatory motions of wrist and fingers can

be noticed through the writings. Each letter written by tremulous hand will have larger length than the similar task with normal hand. Figure 3 shows an example of writing from a particular PD patient. We developed a device to induce voluntary movements capable of triggering Parkinsonian tremor. Idea of the device is to limit the real patient's data during validation of tremor assessment tool.

B. Parkinsonian Tremor simulator:

A simulator is a device which reproduces or represents testing conditions phenomena that would likely to occur during actual performance. Briefly, the simulator resembles to the reality under pre-defined conditions that can replicate the realism and unpredictability of actual situations. Simulators and modeling plays important role in biomedical research. They are also being efficiently used for flight simulation, vehicle road driving tests, gaming and medical educational purposes. Newly developed medical diagnostic and therapeutic systems are usually tested for their expected output performance, reproducibility and safety issues in the laboratory before applying on patients under clinical conditions. During the procedure, the patient models are simulated characterizing specific diseases or abnormalities. Hence, the simulated models are more important in the biomedical research for the complex disease systems that is to be conquered, and for preclinical testing of preventive or therapeutic approaches. Model based simulation give scope for exploration, generation and testing of hypotheses [36]. For creating simulated models, engineering and technological skills are required in their construction to target accomplishments.

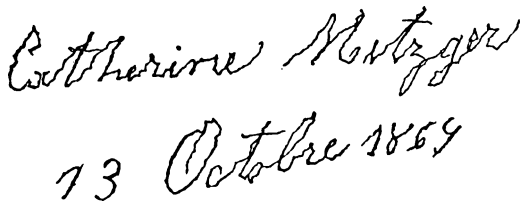


Figure 3. Example of handwriting from a PD patient (Source Jean-Martin Charcot, 1879 through Wikipedia [35]).

There are several modes of simulated models being used in biomedical studies. Mathematical models, computer models, animal models, mammalian models and hybrid simulators are few of well-known simulating models used by the medical researchers [37]. Human breast has been modeled from materials to evaluate newly developed imaging systems. For the detection of breast cancer, microwave imaging systems have been developed and tested its performance from simulated breast models. The models were made from materials representing human breast tissues [38]. Several researchers have investigated the effects of mammary gland density for dose calculation on simulated breast models [39,40]. Patient specific kidney was simulated for interventional urology studies [41,42]. Magnetic resonance imaging (MRI) technique is being continuously improving and the protocol has been updating to achieve superior images of body organs. To improve the diagnosis of cardiovascular diseases through MRI, dynamic heart models were developed and validated the technique [43]. From their reported studies, it is understood that any abnormal situation can be simulated to analyze and validate a new diagnostic system, before applying on actual cases. In our study, we developed a human hand tremor simulator to research a probable protocol for the diagnosis of Parkinsonism. The simulator will save the time and effort of accessing Parkinson's disease patients through hospitals

C. Previous related works:

Parkinson's disease is a long term progressive nervous disorder system affecting the movement of the patient. Parkinsonism, which is symptomatic sign of PD, includes trembling of the hands, arms, legs, jaw and face. It also causes stiffness in the arms, legs and trunk resulting in slow movement. The balance of body could be lost while walking and the coordination among limbs may be disturbed. There are no prescribed lab tests are available for PD which makes the physicians difficult to diagnose [44].

It is estimated that about 7 to 10 million people worldwide are suffering from PD and 27 per 100,000 populations have the disease in Saudi Arabia [45]. Signs and symptoms, characterizing PD are varied but the tremor is believed as motor symptom of the disease. A tremor is a rhythmical, involuntary shaking of the body or the parts. The shaking disorder usually begins in the hand or arm, though the limb is resting or relaxed [46]. Tremor is not fatal but it affects the quality of everyday activities. Most of the time, doctors refer the tremor as Parkinsonism which can be a visually noticeable symptom. Tremor can be of two types; either 'rest tremor' or 'action tremor' [47]. Resting tremor, which is at 4-7 Hz frequency, is considered as an important criterion for the diagnosis of PD [48,49]. More than 75% of PD patients experiences difficulties in eating, writing and holding objects [50] due to the tremor. Doctors routinely assess the tremor from writing and spiral drawing samples from the patients. It is then evaluated by a score of 0-9 which is based on visual rating score (VRS). The score is considered as clinical index from which the severity of the tremor is quantified [51]. However, the procedure of visual score assessment is an examiner dependent which is vulnerable to minor changes in the drawing and the measurement protocol. Therefore, the objective of this work is to evaluate the spiral drawings more precisely, considering small changes in tremor induced from the hand. To simulate hand tremor, a technical vibrating platform is designed to shake the hand while drawing spirals on paper at tremor frequency (4-7 Hz) simulating Parkinsonism in the normal hand. The tremor simulator will help to conduct as many experiments in the laboratory as possible. Usually the patients visiting hospitals are in trauma during which they feel discomfort when they are asked for repetition of experiments during assessment. Therefore, the designed simulator can be considered for preclinical trials to standardize the procedure of evaluating tremor.

VI. TREMOR SIMULATOR

A. Design and development of tremor simulator:

A small hand shaking table has been fabricated in order to simulate hand tremors that could be analogous to symptomatic Parkinsonism. The simulator has a horizontal sheet (100x60x4 mm) for keeping the hand and the plywood sheet is supported by four vertical stands, each carrying a linear spring to produce

dynamics on the sheet during compression action. The hand resting sheet is fitted such that it can make translational motion from a d. c. motor attached below the sheet. The motor powered by 12 V battery source, has a gear attachment so that the geared motor can rotate at 100 RPM speed. A cam shaped disc is firmly fixed at the motor shaft end. When the motor rotates, the disc pushes a metal pin which is fixed to the

bottom surface of the sheet. The sheet was drilled four holes for the supporting screws which carry four springs. The holes are of 10 mm long to allow the sheet to make back and forth movement.

The motor with 100 RPM speed can produce 1.67 Hz frequency by shaking the sheet. But the cam disc has four edges so that the frequency of our simulator is 6.67 Hz, which is same as tremor frequency. The four holes in the sheet are 10 mm long by which the tremor intensity can be envisaged. Figure 4 shows schematic of the designed simulator. When the forearm is placed on the sheet of the simulator, it allows the hand to shake at tremor frequency. The simulator has been designed and fabricated by the authors. This is a novel design and this type of tremor simulator did not find elsewhere. The frequency of the simulator was calibrated with a standard linear actuator.

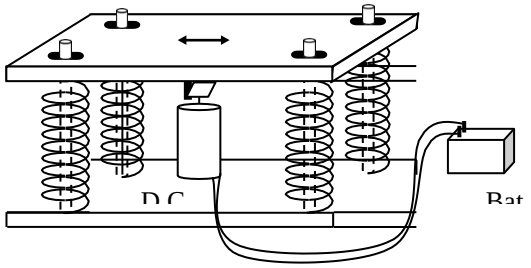


Figure 4. Schematic diagram of tremor simulator.

B. Why Spiral drawings in tremor assessment?

Investigators have been using simple tests like writing and drawing in the preliminary assessment of upper limb movement disorders. Spiral drawing approach has become significant and is considered as standard for clinical evaluation purposes and it has been recommended by the Movement Disorder Society. Mathematical definition of a spiral in words is a curve that emanates from a point, moving farther away as it revolves around the point. There are three types of spiral based on mathematical equations; Archimedean spiral, logarithmic spiral and hyperbolic spiral. Archimedes spiral drawing to detect tremor has become a standard method because the drawing captures frequency, amplitude and direction of hand tremor. They are simple to draw and appear symmetrical to observer. Distortions in the spirals drawn from the tremor hand can be quantifiable and the resulting values could be index of tremor severity. While drawing a spiral, there is continuous movement until an end point of the spiral. Such a continuous recording of the movement cannot be achieved during writing process. Therefore, Archimedean spiral drawing has become a gold standard in detecting tremor.

VII. RESULTS

Figure 5 shows arrangement of the simulator to acquire data from tremor hand. The subjects under investigation were asked to sit in relaxed position. Forearm of the right hand was placed on the horizontal sheet of the simulator. The center of mass of the writing forearm was made to rest on the simulator. This will overcome any artifacts in drawings occurred from imbalanced body segmental weights. For analyzing hand tremors, the spiral drawings were considered as our data. In the first stage, the data was acquired from the simulator, without running the motor which is considered as without tremor. During the second stage of data acquisition, the spiral drawings were obtained by switching on the motor. This data was considered as the drawings with hand tremor. The drawings, with and without tremor, were then analyzed to assess the tremor.

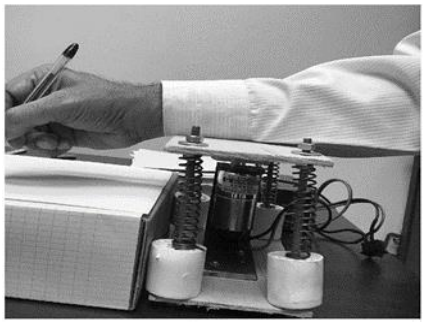
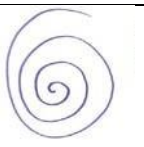
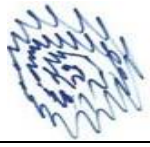
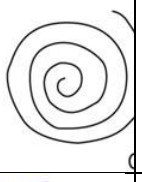
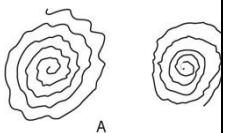
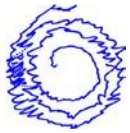
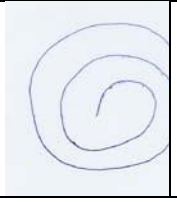


Figure 5. Spiral drawing data acquisition from the tremor simulator.

Table 1: Examples of spiral drawings from normal and PD patients appeared in the peer journals.

Reference	Normal	With Tremor
Ideal Archimedes Spiral		
Titel : *Essential tremor* [52].		
Title: *Diagnosis and treatment of hand tremor* [53].		
Title: *Discrete Cosine Transform for the Analysis of Essential Tremor,* Frontiers in Physiology [54].		
Normal and tremor spiral drawings obtained from our Tremor Simulator		

Archimedes Spirals were drawn on white papers by pen. All the drawing papers were scanned and saved in jpg file format. From image processing technique, the drawings were analyzed. Spiral drawings (with and without tremor) were validated by comparing with standard data which were published in peer journals.

Few examples of spiral drawings from normal and PD patients are shown in the table. Names of researchers and publication details are also given in the table. In the last row of the Table, the spirals drawn from the normal and tremor simulator, designed in this work are shown. Visually our results appear similar to the peer works. However, further analysis of this data will quantitatively differentiate and evaluate the tremor. This method is only for evaluation of data analysis and standardization method before taking the real data and clinical evaluation of tremor severity.

CONCLUSION

We have designed and developed a tremor simulator for assessment of hand tremors. The simulator is useful for repeated experiments in the laboratory and standardizing a protocol for evaluation of tremor. This will help to generate Archimedes Spiral drawings from the normal persons simulating tremor in their hands during data collection. We have collected the data in our laboratory from normal control group of ten young adults. The subjects were in the age group of 24 years (+/-2) years. We compared the spiral drawings taken from our experiments with standard database. Our data were found in good agreement with the standard data. The designed tremor simulator is intended to use in the laboratory, before going for real tests on PD patients in the clinical environment.

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