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Review

A Survey of the Diagnosis of Peripheral Neuropathy Using Intelligent and Wearable Systems

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Abstract: In recent years, the usage of wearable systems in healthcare has gained much attention, as they can be easily worn by the subject and provide a continuous source of data required for the tracking and diagnosis of multiple kinds of abnormalities or diseases in the human body. Wearable systems can be made useful in improving a patient's quality of life and at the same time reducing the overall cost of caring for individuals including the elderly. In this survey paper, the recent research in the development of intelligent wearable systems for the diagnosis of peripheral neuropathy is discussed. The paper provides detailed information about recent techniques based on different wearable sensors for the diagnosis of peripheral neuropathy including experimental protocols, biomarkers, and other specifications and parameters such as the type of signals and data processing methods, locations of sensors, the scales and tests used in the study, and the scope of the study. It also highlights challenges that are still present in order to make wearable devices more effective in the diagnosis of peripheral neuropathy in clinical settings.

Keywords: wearable systems; peripheral neuropathy; intelligent systems; sensors

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1. Introduction

One of the major causes of disability worldwide is peripheral neuropathy (PN). It is described as the damage of peripheral nerves that includes both sensory and motor nerves, which can cause severe motor impairments, and 2.4% of the total world population suffers due to the prevalence of peripheral neuropathy [1]. There are various causes of this disease; however, the most affected ones are those people who have a prolonged history of diabetes. Almost half of diabetic patients develop neuropathy at some stage of diabetes [2]. Other causes of peripheral neuropathy include chemotherapy-induced peripheral neuropathy (CIPN) [3], nerve compression, injury, alcohol use, hereditary diseases, toxin exposure, and vitamin deficiencies [4]. Globally, USD 375 billion were spent in 2010 for the treatment of peripheral neuropathy in diabetic patients, and it is expected to reach USD 490 billion by 2030 [5]. The impact of peripheral neuropathy on healthcare costs and quality of life due to pain, gait instability, foot ulceration, amputation, and injury due to risk of fall demand an effective strategy or method for the diagnosis and treatment of the disease as early as possible [6]. Peripheral neuropathy has become the most common neurologic condition that is faced by physicians in almost all medical specialties. The main challenge for physicians is to effectively screen an asymptomatic patient for peripheral neuropathy since the symptoms of peripheral neuropathy are not prominent in its early stages, which makes it difficult to diagnose by physicians and requires careful and expert analysis for the diagnosis process [7,8]. Peripheral neuropathy is the main reason for foot ulceration and amputation in diabetes patients [9]. For this purpose, nerve conduction studies (NCS) along with electromyography (EMG) are the most widely and effectively used tool for the screening of peripheral neuropathy; however, these techniques are time-consuming, costly, and labor intensive, and it is also not practical to use NCS/EMG in clinical settings [10].

In recent years, rapid advancement in the field of information and communication techniques has enabled us to model, design, and produce compact mobile devices with efficient processing capabilities and battery life [11]. The physical sizes of wearable devices have significantly reduced due to modern fabrication techniques, such as microelectromechanical (MEM) techniques, which play a very important role in the improved productivity, and the high accuracy and sensitivity of wearable devices [12]. The concept of wearable technology was first introduced by a mathematics professor "Edward O Thorp" in the early 1960s to predict roulette wheels [13]. Wearable devices are designed with specific electronic functions, and they come in various materials depending upon their use [14]. Due to their feasibility and low cost, applications of wearable devices are growing rapidly in many research areas such as healthcare [15], education [16], sports medicine [17], military purposes [18,19], and social networking [20]. In Ref. [21], different applications of wearable sensors in consumer sports are discussed. Wearable devices are also commercially available for healthcare purposes, such as different commercially available devices from different brands for measuring step counts and heart rates that are compared in [22] with respect to their accuracy. Wearable devices have proven to be reliable in some applications such as step counts and distance measuring. However, further investigation, research, and improved algorithms are needed to make wearable devices more accurate for clinical diagnosis and to explore more applications in the healthcare field [23,24].

This survey paper summarizes the state-of-the-art research work that has been carried out for the diagnosis of peripheral neuropathy using wearable devices that may assist physicians and help maintain the health of patients who are suffering from peripheral neuropathy. This research article has the following aims: (i) presenting recent research techniques based on wearable devices for the diagnosis of peripheral neuropathy, and (ii) highlighting the research gaps and open challenges in the diagnosis of peripheral neuropathy. The main purpose of this survey paper is to present the effectiveness of wearable technology in the diagnosis of peripheral neuropathy, to address the issues that are still present in using wearable devices for the diagnosis of peripheral neuropathy, and to highlight the gap that needs to be addressed in the future in order to make wearable devices more suitable for the diagnosis of peripheral neuropathy. The following questions are answered in this paper:

1. What research has been carried out towards developing systems based on wearable devices for the diagnosis of peripheral neuropathy?
2. Which types of wearable devices are the most suitable or commonly used for the diagnosis of peripheral neuropathy?
3. How can wearable technology assist physicians and contribute to improving the health of patients having peripheral neuropathy or at risk of developing peripheral neuropathy?
4. What are the challenges that wearable devices are facing in the diagnosis of peripheral neuropathy?

These questions led us to identify the role of wearable devices in the diagnosis of peripheral neuropathy and to highlight the potential future work that is needed to make wearable devices more accurate and commercially available for the diagnosis of peripheral neuropathy in clinical settings. This paper is organized as follows: Section 2 discusses the criteria for the selection of research papers; Section 3 describes the recent research work in the field of wearable devices for the diagnosis of peripheral neuropathy using only the same type of wearable sensors; Section 4 describes the systems based on multiple types of sensors in order to diagnose PN; Section 5 discusses the research gaps in the field of wearable technology for the diagnosis of peripheral neuropathy; and Section 6 concludes the paper.

2. Methodology

The selection of papers was carried out in three steps: (i) initial search in different digital libraries to identify relevant research papers based on their title and abstract; (ii) filtering out of papers based on defined criteria; and (iii) selection of most appropriate research papers. First, an extensive search was carried out to find research papers that were based on noninvasive techniques for the diagnosis of peripheral neuropathy using wearable technologies on IEEE Xplorer, Science Direct, the ACM digital library, and Google Scholar. These databases were selected, as they possess a collection of indexed publications, journals, and conference proceedings that include wearable technology in healthcare. Research papers that were included from each database were published between the years 2013 and 2023. The following terms were used to search research articles in these databases: peripheral neuropathy and wearable systems/devices/sensors combined in different ways with the words non-invasive, screening, diagnosis, intelligent, automated, and machine learning. The initial search list after removing duplicates included 33 papers from IEEE Xplorer, 12 papers from Science Direct, 10 papers from the ACM digital library, and 21 papers from Google Scholar.

In the next step, the authors reviewed the potentially relevant research papers based on the following criteria: (1) the technique used in the study should be completely non-invasive; (2) only wearable devices/sensors are used for data collection; (3) data acquisition method is provided; (4) physical prototype of the model exists; (5) studies based on wearable systems for the treatment or prediction of risk of falling in already diagnosed peripheral neuropathy patients are not included; and (6) only the literature published in English is included. Finally, 15 research articles were chosen which were purely focused on the diagnosis of peripheral neuropathy using wearable sensors. Among these, four articles focus on gait kinematics using inertial sensors for the diagnosis of PN; three research papers are based on the diagnosis of peripheral neuropathy through the analysis of foot plantar pressure; three studies are related to the diagnosis of peripheral neuropathy using electrocardiography (ECG) data; and five research studies are based on the use of multiple wearable sensors for the detection of peripheral neuropathy. In this paper, systems proposed by researchers for the analysis of PN are divided into two broad categories, which include single-type wearable sensor-based platforms and multiple-type wearable sensor-based platforms. Research platforms based on single-type sensors are subdivided into the following three categories: the first category includes the diagnosis of PN by studying human gait using inertial sensors; the second category includes foot plantar pressure-based systems; and the third category focuses on the analysis of the ECG signal in order to diagnose the damage of nerves responsible for proper heart functioning.

3. Intelligent Wearable Systems Using Single-Sensor Type for Diagnosis of Peripheral Neuropathy

The automated diagnosis of peripheral neuropathy (PN) has been performed in many studies [8,25–34] where only a single sensor or technique is used for the data acquisition purpose. These techniques are based on analyzing foot plantar pressure or gait analysis, vibration- and sensitivity-based confocal microscopic image processing, thermal image processing, ultrasound scanner, and nerve conduction studies (NCS) or electromyography (EMG). However, in order to diagnose peripheral neuropathy, a continuous source of data is necessary to diagnose and track the progression of PN. Image-based approaches can provide a feasible way of detecting PN. In a number of research studies [35–38], a subject's gait is analyzed using cameras, but, due to the camera's limited field of view, it cannot provide continuous data which can result in missed data points [39]. Similarly, other non-wearable techniques such as vibration- or perception-based methods and thermal images provide suitable ways for the detection of PN, but these types of methods are not suitable for long-term data collection which is vital for the diagnosis and progression of PN [40]. For this purpose, wearable sensors are the most suitable way to collect continuous data, as wearable devices are designed in such a way that they can be easily worn by patients and attached to the human body directly [41]. They also provide a way to collect and store patient activity data for later use [42].

In this paper, the research techniques for the diagnosis of peripheral neuropathy using a single-type wearable sensor are divided into three categories depending on the type of sensor, the placement of the sensor, and obtained biomarkers or feature points.

3.1. Wearable Inertial Sensor-Based Intelligent Systems for the Diagnosis of PN

Wearable inertial sensors are mostly used for activity recognition tasks such as human gait or postural positions with potential applications in healthcare and well-being, as they offer reliable and accurate methods for studying human motion [43]. There are different configurations of inertial sensors that can be used for recording and analyzing human gait for the purpose of diagnosis. In most cases, inertial sensors are attached to the leg, foot, or waist of the human body [44]. The most commonly used sensor in most studies is an accelerometer in order to study human motion [45]. The combination of an accelerometer and gyroscope or inertial measurement unit has also recently been used by many researchers [46–49] for studying human motion for different applications.

Chen and Shanshan [50] use a wearable inertial sensor, i.e., accelerometer for the early screening of peripheral neuropathy in diabetic patients and evaluate how much valuable information can be added by the wearable inertial sensor in the screening process of peripheral neuropathy. In this study, the authors focus on developing a wearable system based on inertial sensors that distinguish the gait of diabetic patients with and without peripheral neuropathy. The diagnosis of PN is based on the degradation in gait which results in a slower gait, limited knee and ankle mobility, and shorter steps. The experimental study was performed on 106 participants (aged 38 to 83 years old—54 female and 52 male); among those, 30 were diagnosed as confirmed diabetic peripheral neuropathic patients, and 76 healthy individuals were included. The study was approved by the Ethics Committee of Shanghai Ninth People's Hospital, China. The ground truth in this study was taken from the results of NCS studies and physicians' diagnoses. For data collection, an ear-worn 3three-axis accelerometer was used to capture movements in lateral, forward, and vertical directions at a sampling rate of 100 Hz. During walking trials, each participant had to walk 10 m for three rounds while capturing motion data.

The data were transmitted wirelessly to a tablet in real time. To obtain the gait feature, vertical acceleration was used to segment gait cycles. To identify heel-strike events, a customized peak detection algorithm was used by delineating each gait cycle from a heel-strike event to the instant before the next heel-strike event. The gait features that were used in this research include heel-strike events, toe-off events, variance, skewness, and kurtosis of the gait signal. Other features like the maximum amplitude of the gait signal, cadence per minute, and gait speed during the 10-m walk test were also included for analysis.

After data processing, five categories of logistic regression models (Model A to Model E) were used to predict the presence of peripheral neuropathy using different databases having different feature points. The first model, i.e., Model A, only used the total score from the Michigan neuropathy screening instrument (MNSI) history; the second model was based on physical examination of motor and sensory functions using nerve conduction studies (NCS). Model C used both the data from MNSI history and NCS studies. The fourth model, Model D, only used data from an ear-worn accelerometer, and the last model, Model E, was based on the combination of MNSI history and gait features from the inertial sensor. Age and gender were also used as feature points in all five proposed models. The main reason for creating different models was to quantitatively measure the contribution of wearable sensors to the early screening of PN. In order to compare the performance of the proposed models, the authors applied the likelihood ratio (LR) test to find the best possible gait features for the diagnosis of PN. Significant increased LR test stats show that the new feature or biomarker enhances the performance of the models and improves model fit statistically. To examine overfitting, the Brier score was calculated by observing the difference between the true probability and observed probability. The results of this study show that three gait features can play a great role in distinguishing abnormal walking in PN patients. These features include the skewness of lateral acceleration, the maximum amplitude of lateral acceleration, and the range normalized maximum amplitude of lateral acceleration. The overall results show that these three gait features can be used to diagnose PN, as they reveal that gait patterns in DPN patients are less extreme and exhibit less sway in the lateral direction. Additionally, step length and gait speed are relatively higher in PN patients compared to healthy individuals. Among all five proposed models in this research, Model E, which consists of inertial data as well as MNSI history, outperformed all other proposed models and suggests that valuable information can be added by wearable sensors in the screening of PN in order to make the diagnosis process more accurate and diagnose the disease in time.

Cohen et al. [51] proposed a framework for the diagnosis of peripheral neuropathy based on an inertial measurement unit (IMU) and tandem walking test. The main focus of this study was to determine whether the tandem walking test can be performed successfully for the screening of peripheral neuropathy. In the experimental study, both healthy subjects and subjects with peripheral neuropathy were recruited. All subjects could walk without any gait aid. The experiment included 21 subjects with PN (13 males, 8 females—age 60 $\pm$ 12.4 years) (mean $\pm$ SD) including small fiber, large fiber, or mixed large and small fiber neuropathy, and 61 healthy subjects (31 males, 30 females—age 49.6 $\pm$ 16.0 years). This study was approved by the Institutional Review Board for Human Subjects Research of Baylor College of Medicine, Houston, TX, USA. The ground truth was provided by a medical expert using electromyography (EMG). At the time of the walking trials, subjects wore only socks for hygiene purposes. The walking task consists of a 10-step walk on the industrial carpeting in two different phases. In the first phase, the subjects were asked to walk with their eyes open; in the second phase, the subjects were asked to perform the walking task with their eyes closed. The IMU sensor was mounted on the torso of each subject in order to collect gait data. From the raw sensor data, mean square values of resultant acceleration, angular velocity about the roll axis, angular velocity about the pitch axis, and angular velocity about the yaw axis were measured. To calculate the differences in the dependent measures, multilevel statistical techniques were used including separate models fitted to each dependent variable. Receiver operating characteristic (ROC) measures were taken into consideration for the statistical analysis of the sensor signal. Chi-square distribution was used to determine changes in eye open/closed conditions between pathological and non-pathological subjects. The experimental results in this study show that it is more likely for PN subjects to take significantly more consecutive steps with eyes open than eyes closed, while healthy individuals took more consecutive steps than PN subjects in both eyes open and closed conditions. The motion data analysis results indicated that PN subjects have higher angular velocity about the roll axis, angular velocity about the pitch axis, and angular velocity about the yaw axis. The results also showed that PN subjects show greater instability compared to healthy persons while performing the tandem task with their eyes closed.

Esser et al. [52] used a single IMU to analyze gait in order to diagnose peripheral neuropathy in diabetic patients. The main aim of the study was to analyze human gait using an IMU sensor during a 10-m walk test. The IMU was mounted on the lower back, and data from the accelerometer and gyroscope were recorded at the sampling rate of 100 Hz for further processing. By using the collected data, spatiotemporal gait parameters were extracted from the sensor data. The extracted parameters included step time, cadence, stride length, and walking speed. The data analysis for each group in order to find group differences was performed using the chi-square statistical method. This method compares the distribution of categorical variables in a sample with the distribution of categorical variables in another sample. For statistical analysis, this study uses ROC curves by means of the area under the curve (AUC). The experimental set-up included 17 participants (14 males, 3 females) with DPN, and 42 healthy participants (30 males, 12 females) aged around 63.2 $\pm$ 9.2 years. There was no difference in age, gender ratio, height, or BMI between groups. The participants were recruited from the Oxford Centre for Diabetes, Endocrinology and Metabolism at the Oxford University Hospitals NHS Foundation Trust

(Oxford, UK), and the study had approval from the National Research Ethics Committee (NRES: 11/SC/0218). The PN patients were confirmed using a monofilament test carried out by a specialist diabetes podiatrist. The obtained results in this study indicate that significant differences were found for all spatiotemporal parameters between PN patients and healthy subjects except for stride length. However, walking speed differed significantly in unhealthy and control subjects compared to any other gait-related parameters, while producing the largest discriminatory power (AUC = 0.975).

Wang et al. [53] proposed a framework for the diagnosis of peripheral neuropathy and other neurological disorders using two IMU sensors ((InvenSense MPU-6050) in order to analyze human gait. The two IMUs were used to measure five key kinematic and three spatiotemporal gait parameters that can help in distinguishing the type of neurological disorder. These parameters capture the kinematics of the ankle's linear motion and shank rotation, as dysfunction of lower-limb segments and joints would impact the motion of the ankle and shank. The IMUs were mounted on the ankle of each shank in the sagittal plane on the lateral side. The data were collected at a sampling frequency of 100 Hz. The study included 8 patients with PN (3 males, 5 females—age 49 + 8), 13 patients with post-stroke (PS) (9 males, 4 females—age 61 $\pm$ 15 years), 15 patients with Parkinson's disease (PD) (9 males, 6 females—age 76 $\pm$ 7 years), and 13 healthy subjects (HC) (7 males, 6 females—age 49 $\pm$ 20 years). Additionally, information about subjects' heights and weights was provided in [53]. The study was approved by the Medical Ethics Committee of the School of Medicine at Zhejiang University, China. As can be observed, the data between each group are not balanced based on age or female/male ratio. In walking trials, the participants were asked to walk at a convenient speed for more than 12 m on a flat surface. From the IMU data, eight features were extracted based on detected gait phases and calculated motion trajectories i.e., stride length (SL), gait cycle duration (GD), percentage swing phase (PSP), max ankle velocity (MV), max ankle height (MH), ankle horizontal displacement (MHD), range of shank motion (RS), and kinematic asymmetry (KS). Using extracted features, a support vector machine (SVM) classifier was used to distinguish among four classes. The algorithm for training and validation of the proposed system was carried out in MATLAB. The classification accuracy achieved was 93.9% in this case. In this study, the authors used separate SVM classifiers for each of the four classes. In this way, four SVM classifiers were trained to distinguish data points of one class of subject from another class. During the training process, linear kernel function and sequential minimal optimization (SMO) method were used.

3.2. Pressure Sensor-Based Intelligent Wearable System for Diagnosis of PN

Foot plantar pressure is the distribution of the pressure field that acts between the foot and the surface [54]. It plays a very important role in the diagnosis of peripheral neuropathy. As in most cases, due to the damage of foot nerves which is common in diabetic patients, the patient cannot feel the right amount of plantar pressure required to walk smoothly. Due to nerve damage, the sensitivity of the foot decreases. Hence, patients having peripheral neuropathy in the lower limb will always exert more pressure than the healthy person while walking [55]. This makes it important for diabetic patients to have regular check-ups, as symptoms of PN will appear in later stages of the disease where it is not possible to recover the organ, and it may result in amputation of the foot [56]. By using a wearable pressure sensor, the early diagnosis of PN can be made possible, as wearable systems can be used in clinical settings as well as remotely [57]. Further, it is difficult for doctors to examine patients by simply observing the gait of the patients. Wearable sensors can provide an objective measurement and detailed knowledge about the physiology of the patient which is necessary to keep people's lives healthy [58]. There are a variety of pressure measurement systems available; however, they are broadly classified into two types: (1) platform systems and (2) in-shoe systems. This section of the paper summarizes the research related to recording and analyzing foot plantar pressure for the diagnosis of peripheral neuropathy.

Cao et al. [59] proposed a method for the diagnosis of PN based on foot plantar pressure distribution. The main aim of the study was to analyze foot plantar pressure changes while measuring foot plantar pressure distribution in order to prevent ulcers in elderly diabetic people. The study further investigates the role of plantar pressure in elderly diabetic patients with and without PN and compares pressure distribution between healthy subjects and diabetic patients with and without peripheral neuropathy. This study includes foot plantar pressure data from 19 diabetic patients with peripheral neuropathy (DPN) (10 males, 9 females—age 65.7 $\pm$ 2.4 years), 17 diabetic patients without peripheral neuropathy (D) (9 males, 8 females—age 65.2 $\pm$ 6.8 years), and 20 healthy subjects (H) (11 males, 9 females—age 65.2 $\pm$ 5.4 years). Patients were recruited from Tianjin Medical University Chu Hsien-I Memorial Hospital in China. All subjects agreed to participate and signed informed consent after being fully informed of the study's procedure. The data were collected by using an insole wireless plantar pressure monitoring system designed by Medilogic, USA, at a sampling frequency of 300 Hz. The sensor can provide continuous data up to 10 m. The sensor was placed between the sole and the socks. The experimental protocol consisted of 10 m of walking trials at a speed suitable and comfortable for the subject. From plantar pressure data, the authors divided the plantar area into seven regions based on anatomical structure.

After collecting the plantar pressure data, the changes in peak pressures in segmented areas were analyzed while the subject was performing the walking task. In this study, the peak pressure was taken as the highest pressure in each segmented area during one gait cycle. A value of pressure higher than 200 KPa was considered high pressure. In this study, two insole pressure sensors were used to record pressure distribution in both feet. From sensor data, average pressure values of the right and left foot were calculated for each segment area in order to find statistical differences in each subject. The value of peak pressures in normal and DPN patients were investigated, clearly showing that DPN patients tend to have higher pressure in every segmented area of the foot compared to healthy or diabetic subjects without DPN. However, no differences were found in the peak pressure of healthy subjects and diabetic patients without PN. Results showed that the most sensitive areas related to the change in foot plantar pressure include the inner forefoot and medial forefoot region. Additionally, the peak pressure of the forefoot region in DPN patients is much higher compared to the peak pressure in the rear foot region. The overall study suggests that a significant increase in plantar pressure at the forefoot region was observed in DPN patients in the standing position, while healthy individuals in the standing position put more pressure on the rear foot.

Corpin et al. [60] proposed a model for the prediction of DPN by analyzing foot plantar pressure data. The Tekscan Medical Sensor 3000E hardware and Tekscan F-Scan 7.50 Research Software were used to collect the plantar pressure distribution of healthy subjects and DPN patients and to train different machine learning classifiers to distinguish between pathological and non-pathological subjects. The data collection step included 36 normal and diabetic volunteers and both female and male volunteers; however, the ratio between female and male volunteers was not provided. The volunteers' ages were between 49 and 56 years. The study was approved by the Ethics Committee under the supervision of the University of Santo Tomas Hospital (USTH), Manila, Philippines. The ground truth about the diagnosed case was obtained by using the Michigan Screening Instrument-questionnaire (MNSI-q). Nerve conduction velocity studies (NCV) were also conducted on each subject in order to find the ground truth. This research aims to classify among three classes: (1) healthy individuals (N); (2) individuals with diabetes but without peripheral neuropathy (DM); and (3) diabetic patients with peripheral neuropathy (DPN). Both male and female volunteers were included in these experimental trials. During walking trials, each subject had to walk 7 m in a straight line. Each subject had to perform the same walking trial eight times in order to obtain a sizable dataset. The subjects were asked to walk in their normal style during the trial. The Tekscan Medical Sensor 3000E hardware consists of 960 individual pressure sensing points to collect dynamic plantar pressure data. The overall system was based on an in-shoe pressure measurement system. The output of each sensor point was divided into 256 increments to make the visualization better. The software divided the foot into 13 different regions by mapping the pressure data to accurately form the outline of the foot.

The parameters that were calculated by the software included peak pressure (PP), the instant of maximum force (IMxF), the instant of peak pressure (IPP), pressure–time integral (PTI), force–time integral (FTI), length of contact (LC), and contact area (CA). The data were then analyzed statistically using one-way ANOVA. Two different datasets were created for each leg separately, as some features were significantly different between the left and right foot. Principle component analysis (PCA) was also used to determine potential features and to remove those features that contributed less to the learning process by reducing the dimension of the dataset. From 208 features, PCA reduces the dimension of the dataset to only 29 new features that can successfully represent the overall data, i.e., 95%. Different machine learning classifiers such as SVM, random forest, multilayer perceptron (MLP), K-nearest neighbor (KNN), and Gaussian process (GP) were trained and tested in order to distinguish between three given classes. The k-fold cross-validation algorithm was also used to validate the system's performance. The results of this research showed that the parametric difference between the right and left foot is an indication of asymmetric plantar pressure distribution. Hence, separate datasets were used to compare parameters from both feet. The results also stated that instant maximum force time (IMxFT) and contact area (CA) on the right foot exhibit multiple significance in different regions. However, if there is a significant difference in the contact area between the left and right foot, it indicates the presence of DPN. For classification purposes, among the five classifiers, the SVM classifier outperforms other classifiers, with the highest accuracy of 91.91%.

Wang et al. [61] proposed a wireless footwear system to monitor diabetic foot ulcers due to peripheral neuropathy in diabetic patients. The system consists of an insole pressure sensor array that captures pressure changes during walking and transfers data via Bluetooth to a mobile phone in real time. So, the proposed methodology offers the continuous monitoring of plantar pressure using an insole flexible pressure system. A composite piezoresistive flexible sensor was developed to fulfill long-term monitoring requirements. The construction of the sensor was composed of carbon black and silicon rubber. The functioning of the sensor was validated by a custom pressure testing platform, which consists of a keyboard testing machine, a pressure testing machine, and a desktop computer. The data of 5 healthy subjects (HC) (4 males, 1 female—age 48.5 $\pm$ 3.5 years), 5 diabetic patients without PN (D) (2 males, 3 females—age 55.8 $\pm$ 5.6 years), and 5 DPN patients (2 males, 3 females—age 59.00 $\pm$ 10.71 years) were recorded by the proposed pressure measurement system. All subjects were able to walk without any gait aids. The study was approved by the Research Ethics Committee of the Body Data Science Engineering Center of Guangdong Province and the First Affiliated Hospital of Jinan University of Guangdong Province in China. In the walking trial, subjects were asked to walk 20 m along the corridor and stairs for one minute at their regular speed. The data were captured at a sampling frequency of 20 Hz with a 12-bit sampling resolution. The application interface for smartphones was also designed to allow users to visualize the pressure distribution in real time. The final database consists of 2403 samples, including 779 samples from the HC group, 736 from the D group, and 888 samples recorded for DPN patients. From the raw sensor data, peak plantar pressure (PPP), the pressure–time integral (PTI), the maximum pressure gradient (MaxPG), the minimum pressure gradient (MinPG), the full width at half maximum (FWHM), the forefoot-to-rearfoot plantar pressure ratio (F/R), and the symmetry index (SI) were extracted for the database feature points. The feature points used in this study were calculated using the method given by Botros et al. [62]. Five different machine learning classifiers, support vector machine (SVM), K-nearest neighbors (KNN), RF (random forest), GBDT (gradient-boosted decision trees), and AdaBoost classifiers were trained, and they tested the performance of the proposed system. A 10-fold cross-validation was also used to validate the ML models. The overall average accuracy of all five classifiers used was 85%, with the highest accuracy of 94.7% in the case of the random forest (RF) classifier. It should be noted that the sample size of the participants (five per class) is a small number, and further evaluation is needed with a higher number of participants.

3.3. ECG-Based Intelligent Wearable Systems for Diagnosis of PN

According to [63], almost one-third of acute myocardial infarction patients have diabetes, which is one of the leading causes of peripheral neuropathy. The damage to these peripheral nerves that regulate the heart mechanism is called cardiac autonomic neuropathy (CAN) [64]. Electrocardiography (ECG) is a quick and non-invasive procedure for the early detection of CAN, which is caused by the damage of those peripheral nerves that are responsible for the proper functioning of the heart. This section of the paper focuses on the diagnosis of CAN by analyzing ECG signals.

In Ref. [65], an ECG-based platform for the diagnosis of peripheral neuropathy was proposed. The diagnosis was based on the fact that uncontrolled high glucose levels in diabetic patients cause cardiovascular diseases because they affect heart rate variability (HRV). This study is focused on analyzing HRV parameters in DPN patients so that normal and abnormal ECG can be distinguished. The HRV analysis has the capability to recognize variations in the autonomic nervous system (ANS), which is responsible for keeping the heart functioning properly [66]. The data collection method involved the recording of an ECG for all participants for 24 h using a four-channel Holter machine. Twenty subjects were enrolled for the data collection task. All 20 subjects (10 males and 10 females with a mean age of 55.7 years old) were type-II diabetes mellitus patients and were all 40 years old or above. Of the 20 subjects, 10 subjects were confirmed diagnosed with DPN using nerve conduction studies (NCS). The study was approved by the ethical committee of Bangladesh University of Health Sciences. The ECG data were collected at a 200 Hz sampling rate and then the signal was processed in order to remove any possible noise. The ECG signal was then processed in order to extract nine feature points related to HRV to distinguish between DPN-positive and DPN-negative groups. Both time-domain and frequency-domain parameters of the ECG signal were extracted for classification purposes. The Wilcoxon rank-sum test [67] was used to find statistical significance between these two classes. The obtained results showed the feasibility of ECG data for the purpose of diagnosing peripheral neuropathy related to the heart.

In Ref. [68], Jelinek et al. also used HRV attributes of the ECG signal in order to distinguish between the DPN group and the healthy control group. This study proposed a new classification technique for diagnosis purposes and compared the performance of other machine learning (ML) classifiers with the proposed one. The authors utilized their prior collected dataset called Diab Health [69] and selected a subset of 21 patients with severe diabetic neuropathy. However, no information was provided on how the subset was selected. The main aim of the study was to investigate the contribution of HRV parameters in an automated disease classification task. A multi-level clustering technique was used to improve diagnostic accuracy. The data collection procedure included 20 min of ECG recording in a supine position for all participants. The ECG signals were recorded at a sampling frequency of 400 Hz with a lead II configuration [70]. The ground truth for CAN patients was acquired from Ewing battery criteria [71]. The results of this study indicate the significance of HRV parameters for the diagnosis of cardiovascular diseases and the proposed graph-based machine learning classification algorithm (GBML) performed better compared to other conventional clustering techniques. The performances of ML algorithms were based on sensitivity and specificity, which are common metrics for ML algorithms [72]. The best sensitivity of 0.98 and the best specificity of 0.89 were achieved in the case of the GBML clustering technique.

Sharanya and Sridhar [73] proposed a system for the diagnosis of CAN that is based on a convolutional neural network (CNN) for prediction purposes. The aim of this study was to classify CAN-positive and CAN-negative subjects by analyzing ECG signals. In the experimental trials, 13 male and 6 female subjects participated. Among them, 9 subjects were confirmed positive for CAN, and 10 were healthy subjects, labeled as CAN-negative class. No information on the age of the participants or approval of the study from an institutional review board or an ethical committee was provided. The ECG signals were acquired at a sampling frequency of 400 Hz in lead II configuration for 20 min. After acquiring the ECG signal, the signal was processed to remove possible noise, and then feature points such as RR-intervals, etc., were extracted from the clean ECG signal. Using the extracted features, a CNN model was trained to distinguish between normal ECG and abnormal ECG, representing the presence of CAN. The overall results show that CNN can take care of analyzing the complexity of the ECG attributes for the early diagnosis of CAN. The overall accuracy for the diagnosis of CAN achieved in this study is 95.42%. Research work discussed in this paper for the diagnosis purpose using a single wearable sensor is summarized in Table 1.

Table 1. Summary of the wearable systems for detecting peripheral neuropathy (PN) using a single-type sensor. H: healthy; DPN: diabetic PN; CAN: cardiac autonomic neuropathy; PD: Parkinson's disease; ACC: accelerometer; IMU: inertial measurement unit; N/A: not available.

References	No. of Participants	Distribution of Participants	No. of Sensors and Placement	Data Collection Procedure	Methodology	Results
Chen and Shanshan [50]	106	PN: 30 H: 76	3-axis ACC	Single ear-worn ACC	10-m walking test	Gait analysis using logistic regression models for training and testing
Cohen et al. [51]	72	PN: 21 H: 61	IMU	Single torso-mounted IMU	Tandem walking test	ROC and Chi-square methods were used to evaluate the gait data.
Esser et al. [52]	56	PN:14 H: 42	IMU	Single IMU attached to lower back	Standard 10-m walking test	Chi-square distribution using IMU Sensor data for classification. Statistical analysis was conducted using ROC.
Wang et al. [53]	49	PN: 9 Stroke: 13 PD: 14 H: 13	IMUs	Two IMUs were attached to the ankle of each shank	12-m walking trail	The gait parameters were extracted using method [74] based on wavelet analysis.
Cao et al. [59]	56	DPN: 19 Diabetic: 17 H: 20	Insole wireless plantar pressure monitoring system designed by Medilogic	The sensor was placed on one foot between the soles and socks of the participants	10-m walking test recorded at 300 Hz sampling	Peak pressure was recorded in each case by dividing the foot into seven segments and then comparing the pressure distribution of each region in each of the two classes
Corpin and Ryan Rey A. [60]	36	N/A	Tekscan Medical Sensor 3000E	Single Tekscan Medical sensor placed on the right foot only.	7 m walking in a straight line and repeat the procedure eight times	In-shoe pressure monitoring system was used. The Tekscan software provides a number of gait and pressure parameters that can be used as features for ML algorithms
Wang et al. [61]	20	DPN: 5 H: 5	Insole piezoresistive pressure sensor array	Two insole pressure sensors that each contained eight pressure measuring points were placed on both feet.	20-m walking test	Using the proposed insole system, the pressure data were collected from each sensing point, and peak pressures were recorded to create a database of healthy and unhealthy subjects. Five different classification algorithms were then trained for the diagnosis, and the model was validated by using k-fold validation.
Morshed et al. [65]	20	DPN: 10 H: 10	Holter device	Four-channel (RA-LA, LA-LL, LL-RA, and Vx-RL) Holter device	24-h ECG recording at 200 Hz	HRV parameters were extracted from ECG data using a method in [75]. Both time-domain and frequency-domain features of the ECG signal were used in the diagnosis of PN.
Jelinek et al. [68]	21	DPN: 21	ECG	ECG sensor with lead II configuration	20-min ECG recording in spine position	Using HRV attributes of the ECG signal, a new multi-level clustering technique was proposed and implemented to distinguish between two classes.
Sharanya, S. and P.A. Sridhar [73]	19	CAN: 9 H: 10	ECG	ECG sensor with lead II configuration	20-min ECG recording	A CNN network was used to distinguish between PN and healthy subjects. A 20-min-long ECG was recorded for each subject.

4. Intelligent Wearable Multisensory Systems for Diagnosis of PN

Due to their multiple benefits over conventional devices, wearable sensors have gained tremendous interest in the clinical and medical fields [76]. The main features of wearable sensors are their size and flexibility. Due to their small size, multiple wearable sensors can be worn by the subject without feeling bulky. This provides continuous real-time data and simultaneously offers a way to collect data from multiple body parts [77]. This section describes the research work that is based on multiple sensors attached to different locations on the human body in order to diagnose peripheral neuropathy.

Sejdic et al. [78] used accelerometer data to model the human gait by extracting gait parameters from the raw accelerometer signal and showed the effectiveness of gait analysis by extracting clinically valuable information from a three-axis accelerometer signal for the diagnosis of peripheral neuropathy (PN) and Parkinson's disease (PD). The accelerometer was attached to the torso of the human subjects. The placement of the sensor was at the torso due to the sensitivity of torso dynamics to age and disease-related gait changes. The main purpose of the study was to comprehensively examine multiple gait features provided by the accelerometer signal in multiple domains across healthy and unhealthy subjects. The features from time, frequency, and time–frequency domain were extracted in order to distinguish among three considered groups, i.e., subjects with PN or PD or healthy subjects. The experimental procedure included a walking trial of subjects aged 65 years or above on a custom computer-controlled treadmill. Among the participants, there were 14 healthy subjects, 11 subjects with peripheral neuropathy, and 10 subjects with Parkinson's disease. The authors did not provide information about the gender of the participants. The study was approved by the Institutional Review Board at the University of Pittsburgh, USA. Dynamic and static reflective biomarkers were also placed on the bony landmarks in order to measure heel and toe trajectory data for stride segmentation using a 3D optical motion capture system (made by Natural Point, Inc., Corvallis, OR, USA). A three-axis accelerometer (MMA7260Q, Freescale Semiconductor, Austin, TX, USA) was firmly attached over the L3 segment of the lumbar spine to measure linear acceleration along vertical, anterior-posterior, and medial-lateral axes. In each waking trial, the data were recorded at 100 Hz for 3 min after the subject reached the optimal or preferable speed. From the toe and heel trajectory data, strides were calculated by using 3D optical motion capture system data. The system used coordinates of the heel and the toe markers in the direction of progression in order to calculate the actual instantaneous speed and strides, a method proposed by Fusco, N. and Cretual, A. [79]. From the stride data, gait speed, mean stride intervals, and coefficient of variations were calculated. From the acceleration signal, statistical features such as standard deviation, skewness, and kurtosis were calculated. Different frequency domain parameters were also extracted, such as cross-entropy, centroid frequency, bandwidth, wavelet bands, and wavelet entropy. The overall results showed that a person with peripheral neuropathy walks more slowly compared to healthy individuals. The features extracted from the acceleration signal proved to be quite suitable for detecting peripheral neuropathy and other neurological disorders.

Khandakar et al. [80] proposed a technique to diagnose foot ulcers in diabetic patients caused by peripheral neuropathy due to excessive amounts of glucose in the blood. The main technique in their study was based on monitoring temperature and pressure changes in the diabetic foot in order to detect any chances of a foot ulcer due to PN. Smart insole pressure sensor (force-sensitive resistor) and temperature sensors (flexible thermistor) were used to record data from both feet. The proposed system provides portable and wireless transmission of pressure and temperature sensor data and can be used for long-term monitoring of the foot. Each insole sensor for each foot contains sixteen force-resistive pressure sensors and eight temperature sensors. In the walking experiment, each subject was asked to perform a 20 m walk six times, and data were collected at the sampling frequency of 40 Hz. The total number of participants was 12, aged between 20 and 59 years and included both female and male participants; however, the gender ratio was not defined. The local ethical committee of Qatar University approved the study. After that, each gait cycle was segmented in order to obtain the mean and standard deviation of the segmented gait cycles. The overall results show that the proposed system combined with ML provides a low-cost solution to diagnose or monitor diabetic foot ulcers due to PN. It also offers a way to transmit pressure and temperature data wirelessly at a low cost and with an appropriate number of sensors.

Another similar approach for the diagnosis of peripheral neuropathy in the foot or foot ulcers was given by [81], which was also based on measuring foot temperature and pressure in order to find the presence of PN. However, the proposed system is IoT-based open source. The study was based on the fact that DPN patients usually lose sensations in their feet during walking and standing due to damage to peripheral nerves and have higher foot temperatures than healthy individuals. The proposed systems offer cloud access to real-time pressure and temperature data. The severity of DPN was measured by analyzing higher pressure and higher temperature values over multiple positions on the foot. The system consisted of a flat FlexiForce pressure sensor embedded in a shoe sole, and a couple of DHT11 temperature sensors were attached to record pressure distribution. The overall hardware set-up for data collection during walking trials and pressure and temperature values used in this research was based on a theoretical analysis of the foot representing different levels of severity of the disease. The proposed research showed how cloud-based monitoring of DPN patients can help diabetes patients stay healthy by avoiding ulcer that are caused by PN. The system can monitor patients for a very long time and is capable of sending alert warnings if the data show some abnormal signs or patterns.

Sempere-Bigorra et al. [82] also presented a technique to monitor and diagnose diabetic foot ulcers due to PN using a wearable inertial sensor. A single IMU in the lumbar region was used to model the gait; however, this research used additional data acquisition and diagnostic methods such as sensory and vibration tests to diagnose PN. Hence, the scope of this research falls into the multisensory system category. Spatiotemporal gait parameters were extracted from the IMU signal and the superficial sensitivity and vibration test. Superficial sensitivity was performed using nociception tests [83], and deep sensitivity was examined using vibration tests [84]. The similarities between gait parameters and each sensory test were analyzed using a logistic regression model to find the presence of PN in the subjects. In the walking experiment, each subject was asked to walk 15 m back and forth at their normal speed. A total of 85 subjects (46 males and 39 females) participated in the experiment. All participants were aged between 20 and 87 years with a mean value of 68.1 $\pm$ 1.3 years. The study was approved by the University of Bologna Ethics Committee for Human Research in Italy. The IMU used in this research was manufactured by Wiva Science and is capable of transmitting data wirelessly via Bluetooth. For data distribution analysis, the Kolmogorov–Smirnov test was used [85], which showed non-normal distribution among data from different tests. Logistic regression analysis of the data showed that the inertial data and other clinical parameters can be used to successfully diagnose PN, as they are associated with lower sensitivity which shows the signs of PN in its early stages. The main outcome of the study was to measure the relationship between sensitivity impairment and feasible gait parameters. The observed relationship showed that it can be used in non-laboratory settings for the diagnosis of peripheral neuropathy and that IMUs provide valuable information in the diagnosis process.

Z. Veličković et al. [86] presented an approach for the early detection of PN caused by systemic autoimmune rheumatic diseases (SARDs). The authors focused on the use of wearable sensors along with machine learning as a screening tool for the diagnosis of PN related to SARDs. In the experimental study, both healthy and SARD patients participated. The total number of participants was 23 (9 males and 14 females), among which there were 11 SARD patients, and the rest were healthy subjects. The experiment consisted of recordings of different types of data. First, nerve conduction study (NCS) results were obtained for each subject. The results of the NCS studies provided the conduction velocity of motor and sensory fibers. In the second stage, four IMUs attached to both legs and arms were used to model the motion of subjects while performing six different types of exercises with eyes closed and open. The raw IMU data were sent to a tablet through Bluetooth, which sent it to the central server through Wi-Fi for feature extraction such as acceleration and power. The proposed system used a binary machine learning classifier for the detection of the presence or non-presence of PN-related SARD. The performance of the proposed model showed fine sensitivity and specificity. The results of the study highlight the potential of using wearable technology for the accurate diagnosis of diseases related to peripheral neuropathy.

Table 2 shows the summary of research work using multiple sensors.

Table 2. Summary of the wearable systems for detecting peripheral neuropathy (PN) using multisensory systems.

References	No. of Participants	Distribution of Participants	No. of Sensors and Placement	Data Collection Procedure	Methodology	Results
Sejdic et al. [78]	35	DPN: 11 PD: 10 H: 14	Accelerometer (ACC) and 3D optical motion capture system (Natural Point, Inc., Corvallis, OR, USA)	Single ACC attached at the torso	3 m walking test	Accelerometer and 3D optical system captured the gait data at 100 Hz. Different spatiotemporal and frequency domain features were extracted.
Khandakar et al. [80]	12	N/A	Force-sensitive resistors and temperature sensors based on thermistor	Two in-shoe wireless pressure and temperature monitoring systems using 16 FSR and 8 temperature sensors for each foot.	20 m walking test at a sampling rate of 40 Hz	NodeMCU and multiplexer were used to send all the data wirelessly to the main computer.
Kukreja et al. [79,81]	N/A	N/A	FlexForce Sensor and two DHT11 temperature sensors	In-shoe flexi pressure sensor was placed in the sole of the shoe, and two temperature sensors were aligned parallel to the instep and sole.	The data were collected from the participant wirelessly using NodeMCU and in-shoe sensors	Threshold values for the discrimination between healthy and PN patients were evaluated and used to diagnose PN
Sempere-Bigorra et al. [82]		DPN: 8 Diabetic: 77	IMU, vibration test, and sensitivity test	IMU attached to a lumbar area on the L5 spinal segment	The gait data were collected by using an IMU sensor, and data from other tests such as vibratory and sensitivity tests were also collected	The data were analyzed in order to find a correlation between these data. Logistic regression was then used to find the similarities between different groups.
Z. Veličković et al. [86]		PN: 11 Healthy: 12	NCS and four IMUs	NCS electrodes were placed at the chest, and IMUs were attached to each leg and arm	First, NCS data were collected for all participants, and then six different exercises were performed to record and process IMU data	The obtained results show that wearable devices can be made useful in the diagnosis of PN. The overall results showed good specificity and sensitivity.

5. Discussion

In peripheral neuropathy, the gait of the patient is affected mostly due to pain, numbness, etc. Hence, all the studies given in this paper, except for the ones based on ECG, are based on the analysis of the human gait and foot plantar pressure for the diagnosis of PN in lower region muscles. Research studies [50–52] include the usage of a single inertial sensor placed at different body locations, such as the ear or leg in order to model the human gait. Each study had its own experimental protocol and extracted information that was relevant to the diagnosis. These studies show that an IMU or accelerometer may play an important role in the early diagnosis of PN, which is very crucial for human well-being. Research studies such as [53] show that the human gait can be modeled more accurately with the use of two inertial sensors attached to both legs. These studies also show how important the placement and number of sensors are to model gait exactly for such a task. Another important parameter in the diagnosis of PN is foot plantar pressure. To measure foot plantar pressure, mostly in-shoe-based systems are used. Research studies [59–61] discussed in this paper are all based on in-shoe pressure-measuring systems. However, these studies show the importance of measuring foot plantar pressure with the correct number of pressure points and locations. The gait parameters obtained from the in-shoe systems in all research studies were different, which shows the importance of recorded features for capturing gait using foot plantar pressure.

The research studies on the diagnosis of cardiac autonomic peripheral neuropathy (CAN) are also included along with gait analysis-based systems. The reason for this is that a strong connection or relationship can be modeled between the gait and ECG of the patient since the ECG patterns change during a walk. These patterns will differ in healthy persons compared to patients having PN at lower legs or CAN. The discussed research in this paper on the diagnosis of CAN is mostly based on analyzing heart rate variability which gives proper measures to diagnose CAN. The main difference in CAN-related studies is the use of different classifiers for the classification of disease.

It is also important to note that there is no universal protocol for data collection for PN. Therefore, each study defined its own experimental protocol for PN detection based on widely used methods by physicians. Therefore, the studies cannot be easily compared, as their protocols, heterogeneity in subjects, and data collection process were different. Additionally, since different sensors or sensor types are used in each study, there are differences in data, such as frequency, sample rate, range, and others, which contribute to the challenge of developing a benchmark dataset for PN detection.

6. Open Challenges and Conclusions

Recently, the usage of wearable devices has been increasing in many fields including healthcare. The prevalence of diabetes across the world contributes the most to causing peripheral neuropathy. Due to the increasing number of people suffering from peripheral neuropathy, there is a need to implement efficient methods based on modern technology and machine learning. In this section, the open challenges are summarized.

Readiness of wearable technology: Wearable devices can play a vital role in the diagnosis of many diseases, as they can be worn easily, multiple sensors can be used simultaneously, and continuous sources of data from the patient can be recorded for the investigations [87]. However, wearable systems are currently not that mature when it comes to the diagnosis of neurological diseases in clinical settings such as peripheral neuropathy [88]. There are a few commercially available wearable devices for healthcare purposes, but none of the wearable device systems has been used successfully for the accurate and early diagnosis of PN in clinical settings.

Easy-to-use systems for doctors and/or patients: Wearable sensor systems that are discussed in this paper are usually set up by engineers and researchers. To ensure that these systems are widely used, they need to take into account how doctors and/or patients (end-users) would use the systems. For example, a doctor should be able to set up the system, connect with the sensors, and understand what the data show (e.g., through a graphical user interface). Similarly, a patient should be able to wear the system at home and send the data to their doctor if remote and/or continuous monitoring is needed. Improving user experience is a critical factor for both patients and doctors.

Privacy concerns: Data privacy is an important issue when a system collects human data. Modern wearable technology has enabled us to combine information technology such as cloud medicine, big data, etc., to help monitor patients, but, at the same time, it also poses security threats since the data can be hacked and misused. Furthermore, companies can gather and trade data from smartphones or wearables to obtain potentially important information about users for different purposes, which compromises user privacy [89].

Ethical Considerations: Wearable devices provide new and innovative ways to help in the field of healthcare; however, certain ethical considerations are needed regarding the use of wearables in healthcare especially for third-party consumer tech. Ethical considerations should be clearly defined for how the data will be collected and what protocols have to be followed for the respective purpose so that companies will not misuse the data for their profits [90]. Additionally, data bias should also be addressed. In the papers presented in this survey, it is clear that very few studies had balanced datasets based on age or gender. For the US-based studies, race was not reported. Having datasets that are not distributed based on age, gender, race, etc., has the potential of creating ML models that are biased. AI models may increase mistrust and health inequality [91]. Explainable AI has the potential to address some of the biases [92,93]; however, it is important to have policies that would enable unbiased datasets [91].

User Awareness: Due to the relatively new technology, most users do not know the importance of the privacy of their data which are collected by wearable devices, especially in healthcare applications. Users need to understand the risks associated with wearable technology. In the future, this issue must be investigated extensively in order to ensure user privacy [93].

Accuracy and Reusability: Accuracy is one the most important factors when it comes to wearable systems for healthcare. If the accuracy of a wearable device is not sufficient, then this may lead to an incorrect diagnosis since the collected data will miss important vital signs. Another important factor is the reusability of the device. It is important to design wearable systems in such a way that they can be used continuously, and data must be collected with high precision. These two factors play a very important role in making wearable devices more suitable for healthcare [94].

Placement and Optimal Number of Wearable Devices: The correct placement of the wearable device on the human body is very necessary to collect accurate information about the user. The placement of wearable sensors affects accuracy, capability, and user experience. It is also important to use the right type of wearable device depending on the location of the body at which the system will be worn and the nature of the data [95]. It is also crucial to optimize the number of wearable devices that are needed and to define placement locations that are easily accessible. If a system has several devices and is complex to be worn, the physicians and/or the patients may be reluctant to use it. Recent work by Ha et al. [96] conducted a study to determine the optimal position for a pair of electrocardiography (ECG) and thermocouple (TC) sensors (for body temperature measurement) and a pair of photoplethysmography (PPG) and TC sensors. Therefore, additional research is required for the identification of optimal wearable devices, such as biosensors and motion sensors, and their placement while maintaining a high level of accuracy of PN detection.

Wearable devices are required to be at a high technology readiness level [97], but legislation and policy are also required to provide protections for human data [98]. Therefore, it is clear that more research is needed in the field of wearable devices to address these challenges so that they can be used effectively in healthcare [99], and policies are required to protect patients and to ensure trustworthy and unbiased systems.

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