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A new approach to study gait impairments in Parkinson's disease based on mixed reality

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Universidade do Minho
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DIREITOS DE AUTOR E CONDIÇÕES DE UTILIZAÇÃO DO TRABALHO POR TERCEIROS

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Muito obrigada a todos.

Bia

STATEMENT OF INTEGRITY

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration.

I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

ABSTRACT

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. PD onset is at 55 years-old on average, and its incidence increases with age. This disease results from dopamine-producing neurons degeneration in the basal ganglia and is characterized by various motor symptoms such as freezing of gait, bradykinesia, hypokinesia, akinesia, and rigidity, which negatively impact patients' quality of life. To monitor and improve these PD-related gait disabilities, several technology-based methods have emerged in the last decades. However, these solutions still require more customization to patients' daily living tasks in order to provide more objective, reliable, and long-term data about patients' motor conditions in home-related contexts. Providing this quantitative data to physicians will ensure more personalised and better treatments. Also, motor rehabilitation sessions fostered by assistance devices require the inclusion of quotidian tasks to train patients for their daily motor challenges. One of the most promising technology-based methods is virtual, augmented, and mixed reality (VR/AR/MR), which immerse patients in virtual environments and provide sensory stimuli (cues) to assist with these disabilities. However, further research is needed to improve and conceptualize efficient and patient-centred VR/AR/MR approaches and increase their clinical evidence.

Bearing this in mind, the main goal of this dissertation was to design, develop, test, and validate virtual environments to assess and train PD-related gait impairments using mixed reality smart glasses, integrated with another high-technological motion tracking device. Using specific virtual environments that trigger PD-related gait impairments (turning, doorways, and narrow spaces), it is hypothesized that patients can be assessed and trained in their daily challenges related to walking. Also, this tool integrates on-demand visual cues to provide visual biofeedback and foster motor training. This solution was validated with end-users to test the identified hypothesis. The results showed that, in fact, mixed reality has the potential to recreate real-life environments that often provoke PD-related gait disabilities, by placing virtual objects on top of the real world. On the contrary, biofeedback strategies did not significantly improve the patients' motor performance. The user experience evaluation showed that participants enjoyed participating in the activity and felt that this tool can help their motor performance.

Keywords: Parkinson's disease; Virtual reality; Augmented reality; Mixed Reality; Rehabilitation; Gait disabilities; Sensory cueing; Biofeedback.

RESUMO

A doença de Parkinson (DP) é a segunda doença neurodegenerativa mais comum depois da doença de Alzheimer. O início da DP ocorre, em média, aos 55 anos de idade, e a sua incidência aumenta com a idade. Esta doença resulta da degeneração dos neurónios produtores de dopamina nos gânglios basais e é caracterizada por vários sintomas motores como o congelamento da marcha, bradicinesia, hipocinesia, acinesia, e rigidez, que afetam negativamente a qualidade de vida dos pacientes. Nas últimas décadas surgiram métodos tecnológicos para monitorizar e treinar estas desabilidades da marcha. No entanto, estas soluções ainda requerem uma maior personalização relativamente às tarefas diárias dos pacientes, a fim de fornecer dados mais objetivos, fiáveis e de longo prazo sobre o seu desempenho motor em contextos do dia-a-dia. Através do fornecimento destes dados quantitativos aos médicos, serão assegurados tratamentos mais personalizados. Além disso, as sessões de reabilitação motora, promovidas por dispositivos de assistência, requerem a inclusão de tarefas quotidianas para treinar os pacientes para os seus desafios diários. Um dos métodos tecnológicos mais promissores é a realidade virtual, aumentada e mista (RV/RA/RM), que imergem os pacientes em ambientes virtuais e fornecem estímulos sensoriais para ajudar nestas desabilidades. Contudo, é necessária mais investigação para melhorar e conceptualizar abordagens RV/RA/RM eficientes e centradas no paciente e ainda aumentar as suas evidências clínicas.

Tendo isto em mente, o principal objetivo desta dissertação foi conceber, desenvolver, testar e validar ambientes virtuais para avaliar e treinar as incapacidades de marcha relacionadas com a DP usando óculos inteligentes de realidade mista, integrados com outro dispositivo de rastreio de movimento. Utilizando ambientes virtuais específicos que desencadeiam desabilidades da marcha (rodar, portas e espaços estreitos), é possível testar hipóteses de que os pacientes possam ser avaliados e treinados nos seus desafios diários. Além disso, esta ferramenta integra pistas visuais para fornecer biofeedback visual e fomentar a reabilitação motora. Esta solução foi validada com utilizadores finais de forma a testar as hipóteses identificadas. Os resultados mostraram que, de facto, a realidade mista tem o potencial de recriar ambientes da vida real que muitas vezes provocam deficiências de marcha relacionadas à DP. Pelo contrário, as estratégias de biofeedback não provocaram melhorias significativas no desempenho motor dos pacientes. A avaliação feita pelos pacientes mostrou que estes gostaram de participar nos testes e sentiram que esta ferramenta pode auxiliar no seu desempenho motor.

Palavras-Chave: Doença de Parkinson; Realidade virtual; Realidade aumentada; Realidade mista; Reabilitação; Desabilidades motoras; Pistas sensoriais; Biofeedback.

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List of Abbreviations and acronyms

A

AR	Augmented Reality
A	Assessment
ABC	Activities-specific Balance Confidence scale

B

BBS	Berg Balance scale
BDI	Beck Depression Inventory

C

CoA	Cue-oriented assistance
CoT	Cue-oriented training
CAVE	Cave automatic virtual environment

F

FoG	Freezing of Gait
FI	Fully immersive
FAB	Frontal Assessment Battery
FOG-Q	Freezing of Gait Questionnaire
FC	Final contact

G

GEQ-post game	Game experience questionnaire-post game

H

HMD	Head-mounted display
H&Y	Hoehn and Yahr scale

I

IMI	Intrinsic Motivation Inventory
ITC-SOPI	Independent Television Commission Sense of Presence Inventory
IC	Initial Contact

K

KPI	Key Performance Indicators

M

MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
Mini-BESTest	Mini-Balance Evaluation Systems Test
MR	Mixed Reality
M1	Monitoring test 1 - dice
M2	Monitoring test 2 - door
M3	Monitoring test 3 – narrow spaces

P

PD	Parkinson's Disease
PIGD	Postural Instability and Gait Disorder
PTF	Percentage of time frozen
PC	Personal computer
PD-f	Parkinson's Disease patients with freezing of gait (freezers)
PDQL	Parkinson's Disease Quality of Life questionnaire

Q

QoL	Quality of Life

S

SI	Semi immersive
SSQ	Simulator Sickness Questionnaire
SUS	System Usability Scale
SAC	Stress Arousal Checklist

T

T	Training
TUG	Timed Up and Go test
TC1	Control test 1
TC2	Control test 2
T1	Training test 1 – dice with arrows
T2	Training test 2 – door with footprints
T3	Training test 3 – narrow spaces with footprints

U

UPDRS Unified Parkinson's Disease Rating Scale

UPSRS-III Unified Parkinson's Disease Rating Scale part III

V

VR Virtual Reality

VGoT Videogame-oriented training

1 Introduction

This dissertation presents the work carried out over the past year, integrated in the scope of the Master Degree in Biomedical Engineering at the Biomedical Robotic Devices Lab (BiRDLAB) included in the Centre of MicroElectroMechanical Systems (CMEMS), a research centre of the Department of Industrial Electronics (DEI) of University of Minho.

The project main goal was to develop and validate a mixed reality (MR) tool for the assessment and training of gait disabilities in Parkinson's disease. This solution was developed to bring a new paradigm shift. Thus, by triggering PD-related gait impairments, patients can be assessed and trained in everyday situations. The potential of mixed reality, integrated with a motion tracking system, to mimic everyday environments, was tested, aiming a more objective medical assessment, and enhanced and motivational rehabilitation exercises. All the steps performed to achieve this solution are detailed in this document.

1.1 MOTIVATION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease [1]. It is believed that PD physiopathology lies in the loss of dopamine-generating neurons in the basal ganglia, which is related to human movement control. The first dyskinesias appear when there is a deficiency in dopamine release by these cells [1], [2]. Its average onset is at 55 years-old and its incidence increases with age [1].

This disease is characterized by several symptoms with gait impairments being the most common and disabling ones. Motor symptoms include **freezing of gait (FoG)**, **bradykinesia (movement slowness), hypokinesia (reduced movement amplitude), akinesia (problems initiating movement), festination (tendency to speed up when performing repetitive movements), rigidity, postural instability**, and **reduced movement automaticity**, all of them **diminishing patients' quality of life** [1]–[7]. Usually, patients start by reducing their walking velocity, taking shorter steps, and presenting some gait asymmetries and eventually suffering motor freezing events. FoG is defined as the "*sudden inability to continue walking despite the intent to maintain locomotion" and "it is episodic and variable by nature*", being one of the most debilitating and difficult impairments to assess [3], [4], [7]. **FoG events are typically triggered by specific situations**, such as initiation of walking, turning during steady-state walking, facing objects, stress, distraction, and nearing doorways. Even if these environments did not trigger a complete moment of gait blockage, they contributed to a decrease in the step length and velocity, occurring festination and akinesias. Moreover, these gait disabilities can be aggravated by dual-task attentional requirements [2], [3], [6]–[8].

Motion tracking systems make it possible to monitor patients' motor function using **wearable sensors** [9], while **electromyography systems** acquire electrical muscle activity, reflecting motor fluctuations [10]. Both systems are at the forefront of motor function's monitoring, enabling to gather data with **low-cost**, **portable**, and **miniaturized sensors**. It has been possible to monitor kinematic and electromyography-driven information about patients' motor conditions, such as their **gait spatiotemporal parameters** [2], [11], [12], **FoG events duration** and **occurrence** [2], [13]–[15]**, muscles activity** [10], or **postural changes** [11], [12]. Indeed, **this information represents trivial data for physicians to monitor**, over time, **the motor state of their patients**, **controlling the progression of the disease**, especially if they can access these data collected on patients' home environments, during their daily tasks. This would result in **greater supervision of the development of the disease** and would allow **treatments to be personalised to the patient**. Despite the continuous progress of these technological solutions in the continuous monitoring of PD-associated gait disabilities, **it is still difficult to feasibly assess and train patients for their common daily tasks**.

Several researchers have dedicated themselves to the study of the neurological origin of these impairments in order to customize treatment methodologies for PD-related gait disabilities [16]. Despite the scientific advances, different hypotheses are still pointed out. It is only known that there may be **a failure in the activity of nerve messages between the central nervous system and the efferent muscles, responsible for movement, that can cause motor symptoms in PD** [17]–[19]. To overcome these motor symptoms, **researchers pointed out cueing-based interventions** [5]. These strategies involve the use of external temporal or spatial stimuli to facilitate movement, in the form of visual, auditory and vibrotactile cues. **These cues contribution consists in bypassing faults in nervous messages that may be at the origin of gait impairments** [17]–[19]. Indeed, these sensory cueing strategies are integrated into biofeedback devices, which have already been explored in the PD field. These systems make use of wearable technology to provide sensory acquisition and trigger a cue information (biofeedback). They can detect a decrease in cadence or a change of the lower leg muscle activity, and through the detection of such motor behaviors deliver sensory cues [8], [17]. Thus, these interventions could lead to a change in postural control, step pattern, and unfreeze gait freezing events, prevent falls, and consequently could promote less variability in gait and a more goal-oriented gait. Further, wearable systems allow their integration into patients' everyday tasks, ensuring greater freedom of movement and comfort [9]. However, to the best of knowledge, the **effectiveness of these technologies for rehabilitation has seldom been investigated and validated in real-life situations.** Thus, the use of virtual environments to immerse patients in those situations could potentiate

the biofeedback interventions. Further, these studies **did not follow a patient-centred approach**, some **did not use fully wearable systems** and **did not include modular systems**, meaning they **are not easy to integrate with other technologies** [2], [17]. Lastly, patients and physicians were rarely included in the development phase and there were very few accurate and objective evaluation metrics, plus it was unusual to use functional movement training.

Virtual, augmented, and mixed reality emerged in the last decades as a promising strategy to allow patients' immersion in customized virtual environments. In fact, these personalised virtual and interactive environments allow patients to be placed in situations where they can perform daily tasks, obtaining more feasible and natural motion data. When a modular development architecture is used, this VR/AR/MR equipment may be integrated with other monitoring and actuation devices, fostering patients' motor assessment and training. In this sense, in order to overcome the limitations encountered, this dissertation aims to explore the use of mixed reality (MR) in the assessment and training of PD patients during their motor tasks. **By developing a robust system of MR integrated with a high technological motion tracking device**, capable of assessing PD-related gait disabilities, it is expected to show how immersive, interactive MR technology can offer a new methodological framework for monitoring and training gait-related behaviours in PD.

1.2 PROBLEM STATEMENT

More reliable assessment and consistent training geared towards daily tasks are needed, and this can be achieved by immersing PD patients in virtual environments to improve their motor function assessment and training.

It is expected to *(i)* explore the use of MR to develop and design virtual environments closer to patients' daily reality; *(ii)* develop a modular architecture capable of integrating the MR approach with a motor assessment device; *(iii)* investigate the potential of sensory cues in improving gait impairments through augmentative cues.

To address these problem statements, it is crucial to follow a user-oriented approach capable of developing a motor assessment and training strategy closer to patients' daily needs. This dissertation will adopt a systematic approach to answer these key constraints.

1.3 GOALS

The ultimate goal of this dissertation was to design, develop, test, and validate three different virtual environments, which recreate everyday situations, to assess and train PD-related gait disabilities using MR smart glasses and a motion tracking system. One of the most distinguishable features of this dissertation is its multi-disciplinary nature spanning from neurosciences to algorithms for MR, modular architectures, wearable sensors, and biofeedback strategies. Thus, this work required dealing with existing and front-end hardware, designing virtual environments, gait analysis and segmentation, validating protocols with end users, and data analysis.

To reach this main goal, the following step-goals and Key Performance Indicators (KPI) needed to be defined and achieved:

Goal 1: Gather knowledge about VR/AR/MR strategies used in PD for motor training and assessment, through literature reviews, to answer the following questions: *(i)* "How have the VR/AR/MR-based approaches been applied in PD to help patients mitigate gait disabilities?"; *(ii)* "Which technologies have been used to support VR/AR/MR-based approaches in PD?"; and *(iii)* "How have the VR/AR/MR-based approaches been clinically validated in PD?". This goal relates to **KPI 1**: summarising the literature through at least twelve articles; what are the most common gait disabilities in PD; what are the real-world situations that most cause PD-related gait disabilities. **Chapter 2** presents these surveys.

Goal 2: Implementation of a modular, user-customised, technological solution based on mixed reality to immerse patients in scenarios that can trigger PD-related gait disabilities. Based on the literature review, virtual environments that evoke PD-related gait disabilities and that are customisable according to the users' height will be developed. This will address the limitations identified in VR/AR/MR-based approaches in PD. This goal relates to **KPI 2**: development of three virtual environments that represent situations that typically cause PD-related gait disabilities. **Chapter 3** and **Chapter 4** describe the materials and procedures of this solution.

Goal 3: Implementation of a modular, user-customised, technological solution based on mixed reality integrated with another high-technological motion tracking device to help patients overcome PD-related gait disabilities. Outcomes cover the integration of a motion tracking system with MR technologies based on combined visual sensory cues, motion analysis and augmented reality. This goal relates to **KPI 3**: development of on-demand visual biofeedback strategies integrated in HoloLens 2; development of a real-time initial and final contact detection algorithm with a performance higher than 96% for accuracy. **Chapter 3** and **Chapter 4** detail the materials, methods and algorithms used and developed to achieve this solution.

Goal 4: Validation of the proposed MR strategy with end-users. It is intended to collect and analyse data to assess the usability, efficiency, and acceptability of implemented strategies (user-centred approach). This goal relates to **KPI 4**: validation of the solutions with at least ten end-users; statistically significant differences in spatiotemporal parameters between control and monitoring tests, and later between monitoring and training tests; SSQ score lower than sixteen points; IMI score greater than five points. **Chapter 5** will reveal the obtained results.

1.4 Research Questions

Considering the ultimate goal of this dissertation and the step-goals presented, relevant research questions (RQs) were identified, as follows:

RQ 1: How have the VR/AR/MR-based approaches and technologies been applied to support PD patients and how have they been clinically validated? This question relates to **Goal 1** and is answered in **Chapter 2**.

RQ2: How to implement a modular, user-customised, mixed reality-based technology solution that immerses patients in environments that (1) cause PD-related gait impairments; and that (2) help overcome these impairments with the aid of a motion tracking system and biofeedback strategies? This issue considers **Goal 2** and **Goal 3**. The answer is developed throughout **Chapter 3** and **Chapter 4**.

RQ3: How does the implemented modular technological solution, based on mixed reality integrated with a motion tracking system and with biofeedback strategies, affect the motor performance of PD patients during assessment and training? This question is linked to **Goal 4** and is answered in **Chapter 5**.

The presented RQs are summarized and answered in **Chapter 6**.

1.5 Contributions to Knowledge

The main contributions of this dissertation to knowledge are:

- Review on VR/AR/MR-based approaches currently deployed in PD to train and assess gait disabilities.
- Development of three virtual environments and virtual tasks that cause gait impairments, customisable to each participant.

- Implementation and validation of an algorithm for detecting initial and final contacts, in real time. Also, in this scope, an algorithm to estimate spatiotemporal metrics was implemented, based on gait segmentation.
- Development of two visual biofeedback strategies, customisable to each participant, to help overcome PD-related gait impairments.

It is expected that the developed work will lead to the elaboration of a journal article.

During this period, I had the privilege of guiding two students of the Integrated Masters in Electronic Engineering, in a project of the curricular unit "Projeto Integrador". In addition, I applied for a grant from the "Verão com Ciência" programme of the Fundação para a Ciência e Tecnologia (FCT).

1.6 Dissertation Structure

This manuscript is organized into six chapters, as follows.

Chapter 1 presents the motivation, problem statement and the ultimate goals of this work.

Chapter 2 outlines a comprehensive review of current literature about VR/AR/MR-based approaches to study PD-related gait disabilities. The VR/AR/MR-based approaches are presented and discussed, regarding the VR/AR/MR technology, embedded sensors, virtual tasks, and clinical outcomes. The chapter finishes with a summary of the findings.

Chapter 3 addresses the overview of the solution. It starts by describing the problem. Then, project +sense and its modules are presented, as well as a description of the hardware included in the strategy, mentioning its need and technical characteristics.

Chapter 4 outlines the solution description. Firstly, an introductory insight is presented, describing the setup to be used. Secondly, the user-centred design of the solution is presented, identifying the virtual tasks and environments designed. Thirdly, the integration of the sensory system is described, starting by explaining the real-time initial and final contacts detection algorithm, up to the estimation of spatiotemporal metrics, performed offline. Finally, the integration of the biofeedback strategies is explained.

Chapter 5 presents the validation protocol, results, and a critical discussion of the solution. Furthermore, it presents their limitations and possible explanations, along with research suggestions and improvements.

Chapter 6 concludes the dissertation, while providing a brief analysis of the project and its results, along with future research insights.

2 Literature Review

The development of a mixed reality tool for assessment and training of gait disabilities in PD patients can promote more personalised and reliable patient monitoring and rehabilitation. Nonetheless, it is crucial to first understand the state of the art of related works and identify their limitations and challenges, as well as their innovations that will drive this work.

2.1 Introductory Insight

Monitoring and assessing PD-related gait disabilities is a major step to study patients' disease progression and illness stage. However, it is still a challenge for physicians. Besides these disabilities are episodic and variable, they often occur on patients' daily living, so a **limited and subjective assessment is performed**. Therefore, it is necessary to investigate which devices and algorithms would be able to provide a continuous monitoring and gait assessment of daily motor tasks, and subsequently, gait-related metrics. On other hand, as an alternative motor treatment, biofeedback devices have gained particular interest in this field since they integrate the use of motor metrics to provide sensory cues whose role consists in bypassing faults in nervous messages that may be at the origin of gait impairments. Nevertheless, these technologies lack to immerse patients in a home environment, resulting in a failure to assess and train motor daily tasks, such as climbing stairs, get out of bed and grab weights. **It is crucial to produce more reliable** and **continuous data in order to obtain more trustworthy information** so that **physicians can evaluate more accurately their patients' motor conditions**.

VR/AR/MR technology has proven to be a promising and **innovative tool in healthcare** as a **complementary rehabilitation tool**. This technology **enables patients to immerse themselves in interactive virtual environments**, **closer to their daily living**, while in an unknown laboratory/hospital setting. Moreover, **it can provide sensory cues**, as a biofeedback mechanism, to assist PD patients. In fact, this technology is widely used in rehabilitation **promoting more personalized workouts** and **accelerating motor training**. Therefore, it is required to critically analyze in literature how VR/AR/MR technologies have been used in PD to provide motor monitoring and rehabilitation.

This review aims to determine how VR/AR/MR strategies have been used in PD to assess and train gait impairments, over the last ten years, and with which goals and effectiveness. The following questions were investigated and answered: *(i)* How have the VR/AR/MR been applied in PD to help patients mitigate gait-associated disabilities?; *(ii)* Which technologies have been used to support VR/AR/MR-based

approaches in PD?; and *(iii)* How have the VR/AR/MR-based approaches been clinically validated in PD?. The first question offers a revision with focus on the use of VR/AR/MR strategies. The second question identifies the implemented systems and their constituent parts. The last question offers a review of experimental methodologies to validate the VR/AR/MR approaches, which to the best knowledge, have not yet been identified. The holistic view of this review enables to identify the areas of methodologies employed and clinical practice for its validation.

2.2 METHODS

2.2.1 DATA SOURCES, SEARCH STRATEGY AND STUDIES SELECTION

An electronic systematic search was carried out on databases like Google Scholar and PubMed. The survey was conducted according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), as illustrated in **Figure 2-1**. For that purpose, keywords matching headings were used: ["Parkinson's Disease AND Gait Impairment"]; ["Parkinson's Disease AND Virtual Reality"]; ["Parkinson's Disease AND Augmented Reality"]; ["Parkinson's Disease AND Mixed Reality"]; ["Parkinson's Disease AND Rehabilitation"]; ["Parkinson's Disease AND Smart glasses"]; ["Parkinson's Disease AND head-mounted display"]; ["Parkinson's Disease AND HoloLens"]; ["Augmented Reality AND Freezing of Gait"]; and ["Parkinson's Disease AND Cueing"].

Studies were included if they fulfilled the following inclusion criteria: *(i)* studies of idiopathic PD; *(ii)* VR/AR/MR-based technologies were used as part of assessment or rehabilitation strategies; *(iii)* applicability to evoke or mitigate PD-related gait disabilities on lower limbs; *(iv)* the interventions were implemented with individuals with PD (both sexes, all ages, and any disease duration/scale) and *(v)* results were published in the English language and within the past 10 years. The exclusion criteria were: *(i)* studies not validated with PD patients; and *(ii)* studies that assessed interventions to improve upper limbs impairments. The articles' reference lists were searched for additional reports.

2.3 RESULTS

2.3.1 GENERAL RESULTS

A total of 172 articles were identified through Google Scholar (n=109) and PubMed (n=63) databases. Duplicates were removed (n=76). Articles were excluded if they had the following keywords on titles (n=9) and abstracts (n=8): upper extremity motor impairments, deep brain stimulation, electrical stimulation, magnetic resonance imaging (MRI) and motor imagery. From the 96 titles and abstracts

retrieved, 53 full-text articles were assessed for eligibility. Studies that did not meet the predefined inclusion criteria were excluded. 17 articles met the eligibility criteria and were included in this review. This approach is represented in **Figure 2-1**.

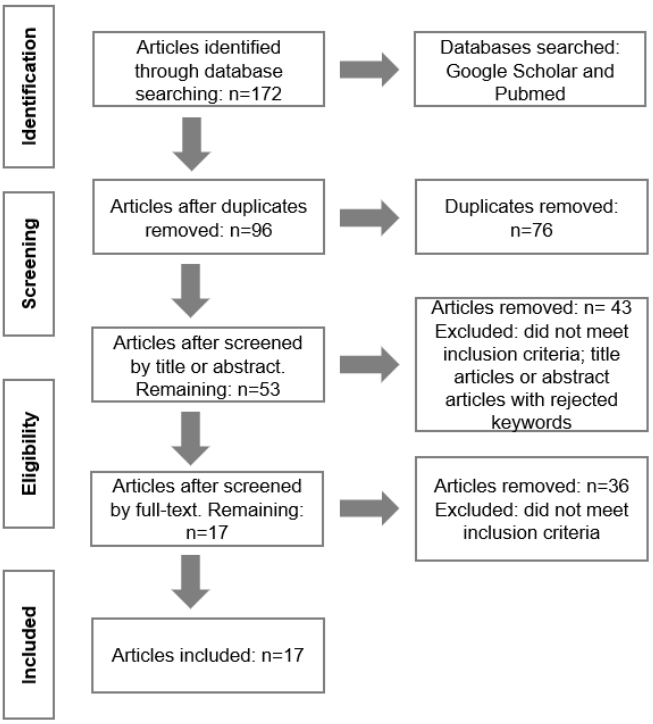


Figure 2-1 - Flowchart for the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

2.3.2 VR/AR/MR IN PD

From the literature search, seventeen original studies were included for analysis, presented in **Table 2-1**. Three studies aimed to evoke gait disabilities [2], [12], [20], while fourteen aimed to mitigate them [11], [13]–[15], [17], [18], [21]–[28], all of them through the use of VR, AR or MR. These reports were grouped and discussed according to their intervention strategy, *i.e.,* VR/AR/MR used: **1. Assessment (A):** to assess motor function (without any kind of training); **2. Cue-oriented assistance (CoA):** to assist motor function through the use of sensory cues; **3. Cue-oriented training (CoT):** to train motor function through cues; **4. Videogame-oriented training (VGoT):** to train motor function by performing one or several tasks in a videogame; and **5. Training (T):** to train motor function.

Table 2-1 - Developed VR/AR/MR technologies for PD patients and their intervention strategies, over the last ten years

	Ref	Objective
1	Gómez-Jordana et al. [2]	A
2	Lheureux et al. [11]	A
3	Yamagami et al. [12]	A
4	Besharat et al. [20]	A
5	Zhao et al. [13]	CoA
6	Geerse et al. [18]	CoA
7	Badarny et al.[21]	CoT
8	Janssen et al. [14]	CoT
9	Gómez-Jordana et al. [17]	CoT
10	Janssen et al. [15]	CoT
11	Wang et al. [22]	CoT
12	Tunur et al. [23]	VGoT
13	Calabrò et al. [24]	VGoT
14	Finley et al. [25]	VGoT
15	Campo-Prieto et al. [26]	VGoT
16	Wang et al. [27]	VGoT
17	Kim et al. [28]	T

To better visualize the contribute of VR/AR/MR in PD, **Figure 2-2** depicts a pie chart that reflects the articles' distribution according to their intervention strategy. It is observed that 29.4% of the selected articles were classified as VGoT, whereas 29.4% were classified as CoT, 23.5% as A, 11.8% as CoA, and finally 5.9% as T.

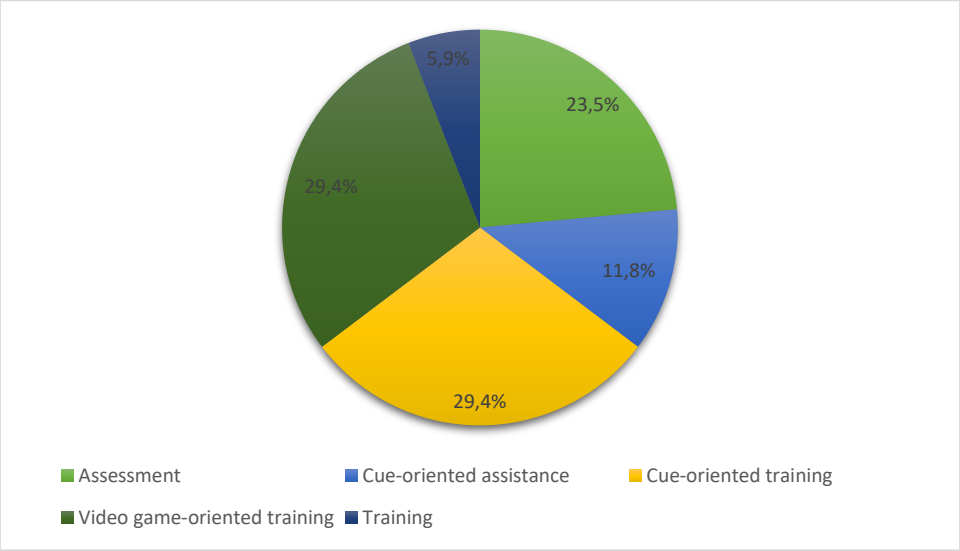


Figure 2-2 - Pie chart on the classification of articles according to their intervention strategy.

2.3.3 TECHNOLOGY SUPPORTING VR/AR/MR-BASED APPROACHES IN PD

Table 2-2 presents the VR/AR/MR technologies developed over the past ten years to evoke or mitigate PD-related gait disabilities, highlighting the equipment used, the virtual environment developed and the virtual task to be performed. In addition, the acquisition and actuation modules were discriminated.

The virtual environment describes the immersion of the environment created. Virtual environments can be classified as ***(i)*** **non-immersive** if using a personal computer (PC), ***(ii)*** **semi-immersive** assuming the use of large monitors, and ***(iii)*** **fully immersive** in the case of cave automatic virtual environment (CAVE) rooms or head-mounted displays (HMD) [26].

The virtual task corresponds to the task performed by the patient when immersed in the virtual environment.

The actuation system is responsible for providing tactile, visual, or auditory cueing, whereas the acquisition system acquires a physiological measurement of the patient. An actuation module was considered when systems provided sensory cues as a biofeedback mechanism: use acquired patients' sensory physiological information (*bio*) to deliver external sensory cues as vibrotactile, visual, and/or auditory cueing (*feedback*). Gonçalves et al. [29] described three roles for biofeedback mechanisms: stabilizing role which provides biofeedback to preserve or improve gait parameters or balance; **augmentation role** which corresponds to delivering sensory cueing, *i.e.*, provide biofeedback as a technique of re-integration and coupling postural control with stepping; and replacement role, known as sensory substitution, which provides sensory cueing to facilitate motor response generation.

Table 2-2 - Developed VR/AR/MR technologies for PD patients, over the last ten years

Goal	Paper	VR/AR/MR Equipment	Virtual Environment	Virtual task	Acquisition module			Actuation module		
					Built-in?	Type	Which one?	Built-in?	Type	Which one?
A	[2]	VR: Oculus Rift DK2	FI	Cross virtual doors	N	Tracking system	InterSense IS900	-	-	-
	[11]	VR: HTC Vive	FI	Walk	N	3D motion	IMU	-	-	-
	[12]	VR: HTC Vive	FI	Walk, cross virtual doors	-	-	-	-	-	-
	[20]	VR: HTC Vive	FI	Walk, cross virtual doors	N	Motion Capture System	Qualisys	-	-	-
CoA	[13]	AR: Google Glass	FI	Walk (turnings and doorways)	N	3D motion	IMU	Y	Audio	Glasses
									Flashing light	Glasses
									Optic flow	Glasses
	[18]	MR: HoloLens 1	FI	Walk	-	-	-	Y	Visual	Glasses
CoT	[21]	AR: microdisplay attached to glasses	FI	Walk	N	NI	NI	Y	Visual	Glasses
	[14]	VR: prototype of custom-made smart glasses	FI	Climb stairs, walk and turning	N	3D motion	IMU	Y	Visual	Glasses
	[17]	VR: Oculus Rift DK2	FI	Walk on hallways	N	Tracking system	InterSense IS900	Y	Visual	Glasses
	[15]	AR: HoloLens	FI	Turning	N	3D motion	IMU	N	Audio	Speaker
								Y	Visual	Glasses
	[22]	VR: HTC Vive Pro	FI	Cue-oriented game	N	3D motion	Vive Trackers	Y	Visual	Glasses
VGoT	[23]	AR: Google Glass	FI	Dance	-	-	-	NI		
	[24]	AR: CAREN	FI	Walk	Y	Accelerometer	G-Sensor	Y	Visual	CAREN
									Audio	
									Vestibular	
									Tactile	
	[25]	VR: HTC Vive	FI	Complete words	N	3D motion	Vive Trackers	-	-	-
	[26]	VR: HTC Vive Pro	FI	Box	-	-	-	-	-	-
	[27]	AR: C-Mill VR+ treadmill	SI	Walk	-	-	-	-	-	-
T	[28]	VR: Oculus Rift DK2	FI	Walk	-	-	-	-	-	-

[Ref.]: study reference; A: assessment; CoA: cue-oriented assistance; CoT: cue-oriented training; VGoT: videogame-oriented training; T: training; AR: Augmented reality; VR: Virtual reality; MR: Mixed reality; FI: fully immersive; SI: semi-immersive; N: no; Y: yes; IMU: Inertial Measurement Unit; CAREN: computer assisted virtual reality environment; NI: not identified.

It was observed that the VR/AR/MR equipment used by the selected studies were the Oculus Rift DK2 [2], [17], [28], HTC Vive [11], [12], [20], [25], Google Glass [13], [23], HoloLens [15], [18], and HTC Vive Pro [22], [26]. Furthermore, in [21] a micro display was attached to the eyeglasses frame and in [14] a prototype of custom-made smart glasses was designed. Finally, in [24] and [27] smart glasses were not worn, on the contrary, a computer assisted virtual reality environment (CAREN) and a C-Mill VR+ treadmill was used, respectively.

The virtual environment immersion ranged from fully immersive [2], [11]–[15], [17], [18], [20]–[26], [28] to semi-immersive [27], being frequently used head-mounted displays.

Virtual tasks included motor activities, like climbing stairs [14], turning [14], [15], and walking straight [11], [13], [14], [18], [21], [24], [27], [28], (*i.e.,* on a hallway as in [12], [17], [20]), or specific contexts that could trigger PD-related gait disabilities, such as crossing virtual [2], [12], [20] or real doors [13]. Additionally, when VR/AR/MR was applied for motor training strategies, a cue-oriented game was used in [22], while in [23]–[26] patients followed the tasks indicated on the virtual game, namely, dance [23], navigate a virtual boat [24], drive a ball to the finish line [24], smash flying objects [24], complete virtual words [25] or play a box game [26]. An overview of some virtual tasks and environments developed are shown in **Figure 2-3**.

Regarding the acquisition module, three systems were found: InterSense IS900 [2], [17], Qualysis [20], IMU [13]–[15], accelerometer (G-Sensor) [24] and Vive trackers [22], [25], with none of them being built in. IMUs were placed in both full body [14], [15] and lower body [11], [13] configurations.

With respect to the actuation module, it was identified the type and which device were used, and whether it was built in. All systems which had an actuation module used built-in actuators, such as augmentative visual cues or earphones [13]–[15], [17], [18], [21], [22], [24]. However, [15] also had a non-built-in actuator, namely, a speaker for auditory cueing. Furthermore, [24] used four types of actuators (visual, audio, vestibular and tactile), [13] used three types of actuators (audio, flashing light and optic flow), [15] used two types of actuators (visual and audio) whereas [14], [17], [18], [21], [22] only used one type of actuator, visual. Besides, visual cues were used more than auditory cues.

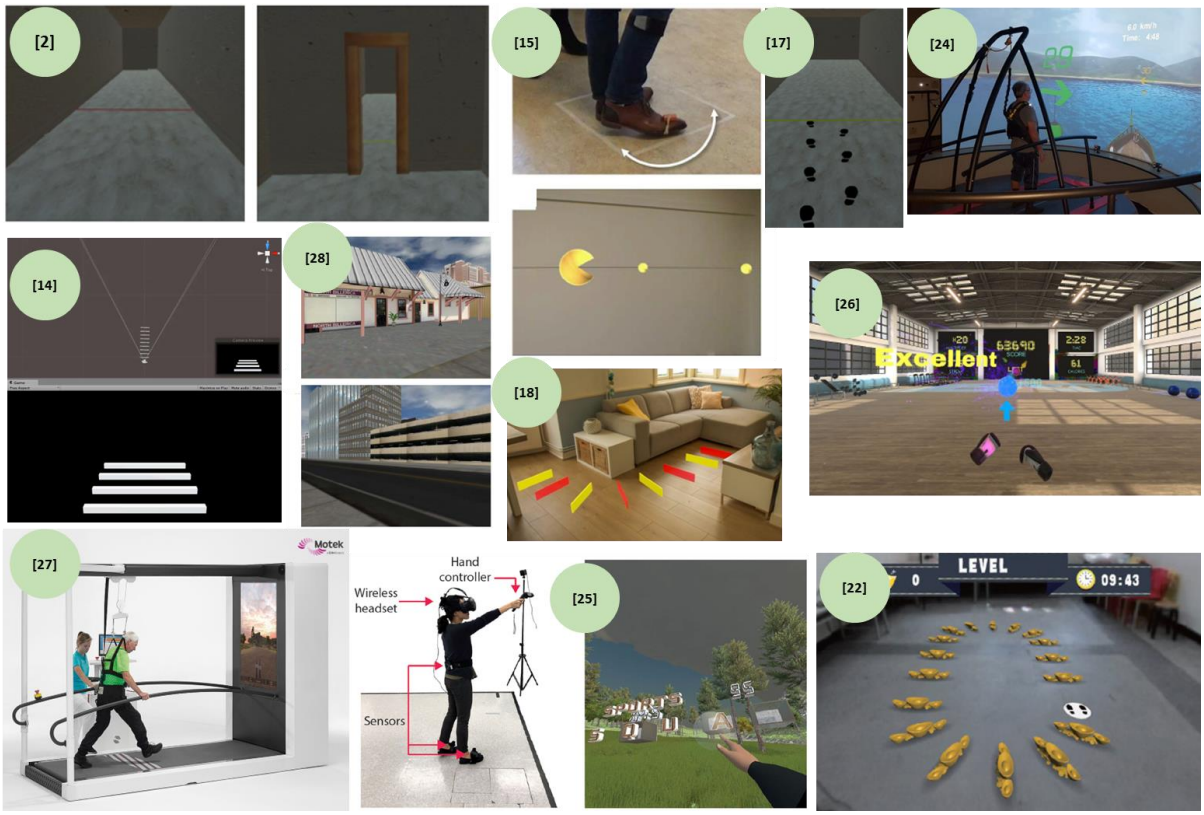


Figure 2-3 - Overview of some virtual tasks and environments taken from [2], [3], [12], [13], [19], [20], [22]–[26].

2.3.4 Validation methodology highlights: participants, criteria study, setting, protocols, Schedule, metrics

Table 2-3 summarizes the validation methodology of the selected studies. It highlights the participation and evaluation of PD patients, inclusion and exclusion criteria for participants selection, setting, experimental protocols, schedule, and the research evaluation metrics.

Unified Parkinson's Disease Rating Scale part III (UPDRS-III) [2], [12]–[15], [17], [18], [20], [23]–[25], [27], [28] and Hoehn and Yahr scale (H&Y) [11], [12], [14], [15], [18], [20], [21], [23]–[25], [27], [28] were the most commonly used rating scales for symptoms of PD. Along with UPDRS-III, Postural Instability and Gait Disorder sub-score (PIGD) [14], Activities-specific Balance Confidence (ABC) scale [11], [12], [22], [23], [28], Mini-Balance Evaluation Systems Test (Mini-BESTest) [11], [12], [20], [25], [28] and UPDRS-II [24] were used to reflect the evolution of motor function. To indicate the patients' cognitive and mental state, the Mini-Mental State Examination (MMSE) scale was used in [11], [14], [15], [27], Montreal Cognitive Assessment (MoCA) in [12], [18], [20], [23], [28] and Frontal Assessment Battery (FAB) scale in [13]–[15]. FOG-questionnaire (FOG-Q) was used in [2], [12]–[15], [17], [18], [20]. To assess simulator sickness symptoms, the Simulator Sickness Questionnaire (SSQ) was used [25].

Table 2-3 – Clinical Highlights of the developed VR/AR/MR technologies to PD patients, over the last ten years

Goal	Paper	Participants		Criteria Study		Setting	Protocol	Schedule	Metrics
		N	Scales	Inclusion	Exclusion				
A	[2]	10	- UPDRS-III; - FOG-Q;	-	-	Laboratory	Walk under 3 different virtual conditions: (1) no door; (2) narrow doorway; (3) standard doorway.	Single visit: (1) familiarisation phase; (2) 18 trials (6x each condition). Total: 20min	- step cadence (mean and CV); - step velocity (mean and CV); - step length (mean and CV); - duration of FoG episodes (mean and SD); - % trials with a FoG episode
	[11]	10	- UPDRS; - Mini-BESTest; - ABC scale; - H&Y; - MMSE;	- Diagnosis of PD; - - H&Y≤3; - MMSE > 24/30; - No other pathology interacting with gait or causing dizziness; - No uncorrected visual deficiency; - Ability to walk 512 consecutive strides (±10– 15 min);	-	Laboratory	Walk in a randomized order in 3 conditions: (1) Overground Walking; (2) Treadmill Walking (3) immersive Virtual Reality on Treadmill Walking	Single visit	- speed; - step length; - cadence; - SSQ
	[12]	10	- MDS-UPDRS-III; - NFoGQ; - MoCA; - Mini-BEST; - ABC Scale; - H&Y;	- Diagnosis of PD; - Self-reported FoG; - Self-reported ability to walk 400m without assistance from a device or another person; - No diagnosis of dementia; - No uncorrected vision or hearing problems;	-	Laboratory	Walk in 5 environments: (1) Physical laboratory without VR; (2) virtual laboratory without obstacles; (3) virtual doorway; (4) virtual hallway; (5) virtual street scene with crowds	Single visit	- gait speed; - step length (mean and CV); - step width; - step time; - step time asymmetry; - festination; - SSQ
	[20]	12	- MoCA; - NFOGQ; - Mini-BEST;	- Diagnosis of PD without dementia;	-	Laboratory	Walk under 4 conditions: (1) physical laboratory; (2) virtual laboratory; (3) virtual doorway;	Single visit	- kinematic variables; - gait speed; - step length (mean and CV); - step time;

			- MDS-UPDRS-III; - H&Y;	- Self-reported or clinician-observed FoG; - Ability to walk 400 m without assistance from a device or another person; - No uncorrected vision or hearing deficits;			(4) virtual hallway.		- step time asymmetry; - step width; - DLS; - festination; - SSQ
CoA	[13]	12 "end-of-dose"	- UPDRS-III; - NFOGQ; - FAB;	- Presence of FoG more than twice per day; - Able to walk 20m over a flat surface without walking aids;	- Significant cognitive impairments; - Comorbidities that impaired gait, or visual impairments;	Laboratory	Walk on 4 different walking courses in combination with 4 cueing conditions: (1) metronome; (2) flashing light; (3) optic flow; (4) no cue.	Single visit: (1) familiarization phase; (2) 16 different cue-course combinations (2 trials each). Total: 2.5h	- no. of FoG episodes; - duration of FoG episodes; - stride length (mean and SD); - speed; - cadence (mean and SD); - interview (user experience)
	[18]	24 "on state"	- UPDRS-III; - H&Y; - MoCA; - NFOGQ;	- Older than 18 years; - Diagnosis of PD; - Experience FOG in the dopaminergic "ON" state;	- Additional neurological diseases and/or orthopedic problems; - Inability to walk independently;	Home/Laboratory	(1) HOME: walk a freezing provoking route multiple times with and without wearing the HoloLens (without Holocue); (2) LABORATORY: familiarize participants to walking with the (on-demand) holographic cues; (3) HOME: equal to session 1 but wearing the HoloLens with and without the Holocue	3 sessions of 1.5h, one week apart	- no. of FoG episodes; - average duration of FoG episodes; - total duration of FoG episodes; - % time frozen (PTF)
CoT	[21]	20	- H&Y	-	- considerable visual deficit not compensated by correction; - ocular movement dysfunction; - gait disturbances due to neuromuscular diseases;	Laboratory	Walk a straight track of 10 m: (1) baseline; (2) online display off; (3) online display on; (4) residual effects; (5) examination;	Single visit	- speed; - stride length
	[14]	25 "end-of-dose"	- UPDRS-III; - UPDRS-PIGD;	- Diagnosis of PD; - Older than 18 years old;	- History of stroke; - Psychiatric disease;	Laboratory	Walk on 3 different walking courses in combination with 5 cue conditions:	Single visit:	- no. of FOG episodes; - % freezing time; - stride length (mean and SD);

			- H&Y; - NFOGQ; - MMSE; - FAB;	- Presence of FoG more than once per day;	- Severe uncorrected visual or hearing impairments; - Comorbidity limiting ambulation; - Inability to walk unaided; - Deep brain stimulator or apomorphine pump; - Jejunal levodopa gel infusion; - MMSE score < 24;		(1) augmented visual cue bars; (2) augmented visual cue staircases; (3) conventional 3D transverse bars on the floor; (4) metronome; (5) no cueing.	2 sessions separated by 30min break Total: 2.5h-3h	- cycle time (mean and SD); - cadence; - speed; - interview (user experience)
	[17]	12	- UPDRS-III; - FOG-Q;	-	-	Laboratory	Walk using visual cues: (1) 2 spatial conditions: 115% and 130% of an individual's baseline step length and; (2) 3 different temporal conditions: spatial only condition, 100 and 125% baseline step cadence.	Single visit: (1) familiarisation phase; (2) 6 different cueing conditions (8x each condition). Total: 40min	- Step length (mean and CV); - Step cadence (mean and CV); - Step velocity (mean and CV); (at baseline and post intervention)
	[15]	16 "end-of-dose"	- UPDRS-III; - H&Y; - MMSE; - NFOGQ; - FAB;	- Diagnosis of PD; - Presence of FoG more than twice per day;	- MMSE score < 24; - FAB score < 13; - Comorbidity causing severe gait impairments; - Severe bilateral visual or auditory impairments; - Inability to perform a 180◦ turn unaided;	Laboratory	Perform a series of 180° turns under: (1) an experimental condition with AR visual cues and; (2) two control conditions: auditory cues and no cues.	Single visit: (1) 1 training session: 3 blocks (15 trials each); (2) 2 experimental sessions: 3 blocks (15 trials each).	- PTF; - no. of FoG episodes; - duration of FOG episodes; - cadence; - peak velocity; - stride time (mean and CV); - step height (mean and CV); - max head-pelvis separation; - time to max head-pelvis separation; - max medial CoM deviation; - turn time; - interview (user experience)
	[22]	5	-	- Diagnosis of PD; - H&Y I-III; - Able to walk independently;	- Conditions that could have affected exercise function;	Laboratory	Play the game "Treasure Island Adventure" with and without obstacles in combination with 3 levels: 35, 40, and 45cm between the visual cues	1 session per week of 30min, over 3 weeks	- BBS; - ABC; - Step distance; - Leg raising; (at baseline and post intervention)

VgoT	[23]	7 "ON"	- UPDRS-III; - H&Y; - MoCA;	- Diagnosis of PD;	- H&Y > III; - MDS-UPDRS-III > 57; - Unable to wear or operate Google Glass; - Dementia;	Home	Complete at least 3 modules of MTG per day	Every day for 3 weeks	- Mini-BESTest; - one-leg stance; - TUG; - dual-task; - ABC scale; - BDI; - PDQL; - interview
	[24]	22	- UPDRS-II; - UPDRS-III; - H&Y; - Mini-BESTest; - MMSE;	- Diagnosis of PD; - H&Y≤3; - MMSE ≥ 24	- age > 85 years; - presence of severe medical and psychiatric illness potentially interfering with the VR training	Laboratory	Complete four scenarios: (1) Navigate a virtual boat through a slalom course; (2) walk across the board; (3) drive a red ball, moving the oad up to the finish line; (4) swat at flying objects that emerge along the path	20 conventional physiotherapy sessions + 3-month rest + 20 sessios of CAREN training	- BBS; - TUG; - UPDRS-II; - UPDRS-III; - FES-I; - H&Y; - 10MWT; - stride length; - cycle time; - stance phase/time; - swing phase/time; - percentage of single- and double-limb support; - speed; - cadence; - step length; - step width
	[25]	9 "ON"	- UPDRS-III; - H&Y; - Mini-BESTest; - SSQ;	- Diagnosis of PD; - No motor fluctuations; - H&Y I-III; - Older than 18 years old; - Walking independently; - Stable medication;	- Uncontrolled, involuntary movements (dyskinesia); - Musculoskeletal injuries; - Pain that limited movement;	Laboratory	Complete a puzzle that consisted of a word with missing letters located at eye level in the virtual environment	3 sessions of 30min each, over 1 week Total: 1h30	- SSQ; - ITC-SOPI; - IMI; - SUS;
	[26]	4	-	- H&Y II;	- Inability to correctly respond to the assessment protocol; - Presence of cardiovascular, pulmonary, or	Laboratory	Play the game BOX VR	2 sessions, 2 weeks apart; 1ª session: (1) familiarization phase with Steam VR Home (9min);	- SUS; - SSQ; - GEQ-post game; - interview (user experience)

					musculoskeletal condition; - Presence of severe visual loss; - Vertigo, epilepsy, and psychosis;			(2) training: game gym (3min); 2nd session: (1) familiarization phase with TheBlue; (2) training: game gym.	
	[27]	29 PIGD + 23 non-PIGD 2h after medication	- UPDRS-III; - H&Y; - MMSE;	- Diagnosis of primary PD; - <75 years old - H&Y stage I–III ("on" period); - MMSE>24 (>20 for those with only primary school education);	- Serious complications or comorbidities; - Special treatment required for other comorbidities; - Deep brain stimulation or in vivo implants; - Atypical or secondary PD; - Comorbidities affect walking; - severe cognitive, visual, and hearing impairment; - Using a psychotropic substance;	Laboratory	Complete 5 modules of C-Mill training in each training session	1 session of 30min per day for 7 days: (1) familiarization phase; (2) modules of C-Mill training.	- 10-meter walking test; - TUG test; - BBS; - Posture sway; - Gait adaptability; - Borg 6-20 Questionnaire; - perceived risk of falling; - PDQL
T	[28]	11 "ON"	- UPDRS-III; - H&Y; - MoCA; - ABC; - Mini-BESTest;	- Able to walk for 30 min on a treadmill; - 19<MoCA<30; - No other neurological disorders;	-	Laboratory	Walk for 20 min on a treadmill while viewing a virtual city scene	Single visit Total: 20min	- CoP excursion; - SSQ; - SAC; (at baseline and post intervention)

[Ref.]: study reference; A: assessment; CoA: cue-oriented assistance; CoT: cue-oriented training; VGoT: videogame-oriented training; T: training; UPDRS-III: Unified Parkinson's Disease Rating Scale part III; FOG-Q: Freezinf of Gait questionnaire; FAB: Frontal Assessment Battery; H&Y: Hoehn and Yahr scale; MMSE: Mini-Mental State Examination; UPDRS-PIGD: Unified Parkinson's Disease Rating Scale - Postural Instability and Gait Disorder ; Mini-BesTest: Mini-Balance Evaluation Systems Test; SSQ: Simulator Sickness Questionnaire; MoCA: Montreal Cognitive Assessment; ABC: Activities-specific Balance Confidence scale; CV: coefficient of variation; SD: standard deviation; PTF: percentage time freezing; DLS: double limb support; CoM: Centre of Mass; BBS: Berg Balance Scale; ITC-SOPI: Independent Television Commission Sense of Presence Inventory; IMI: Intrinsic Motivation Inventory; SUS: System Usability Scale; GEQ-post game: Game experience questionnaire-post game; TUG: Timed Up and go Test; BDI: Beck Depression Inventory; PDQL: Parkinson's Disease Quality of Life questionnaire; CoP: Centre of Pressure; SAC: Stress Arousal Checklist.

Inclusion criteria included the diagnosis of PD [11], [12], [14], [15], [18], [20], [22]–[25], [27], ability to walk independently [11]–[14], [18], [20], [22], [25], motor fluctuations absence [13]–[15], [25], musculoskeletal injuries absence [21], [25], lack of other neurological disorders [14], [18], [24], [28], lack of severe bilateral visual or auditory impairments [11]–[15], [20], [21], [26], [27], ability to perform a 180° turns unaided [15], lack of cognitive impairments [13], [23], lack of deep brain stimulation [27] or apomorphine pump and jejunal levodopa gel infusion [14], presence of stable medication [25]. For the studies that evaluated FoG, the presence of this symptom was also an inclusion criteria [12]–[15], [18], [20]. Additionally, specific scores of PD scales were used to include participants: 19<MoCA>30 in [28]; MMSE>24 in [11], [14], [15], [24], [27]; FAB score>13 in [15]; H&Y stage I-III in [22], [25] , H&Y stage I-III while on medication in [27]; H&Y stage II in [26]; H&Y stage<III in [11], [23], [24]. Moreover, some studies used clinical characteristics as inclusion criteria, namely, age: older than 18 years old in [14], [18], [25]; younger than 75 years old [27] and younger than 85 years old [24].

Regarding the validation scenarios, all [2], [11]–[15], [17], [20]–[22], [24]–[28] articles conducted an intervention in a laboratory setting apart from [18], [23] which followed a home-based approach.

Those articles that evaluated FoG used the following metrics: duration of FoG episodes [2], [13], [15], [18], percentage of trials with a FoG episode [2], number of FoG episodes [13]–[15], [18] and percentage of freezing time [14], [15], [18]. Moreover, gait-related metrics were used, such as step cadence (mean [2], [11], [13]–[15], [17], [24], coefficient of variation (CV) [2], [17] and standard deviation (SD) [11], [13]), step velocity (mean [2], [11]–[14], [17], [20], [21], [24], CV [2], [17] and SD [11], [24]), step length (mean and CV [2], [11], [12], [17], [20], [24]), stride length (mean and SD [13], [14], [21], [24]), peak velocity [15], step time (mean and asymmetry [12], [20]), stride time (mean and CV [15]), step width (mean [12], [20], [24] and SD [24]), festination [12], [20], kinematic variables [20], double limb support (DLS) [20], step height (mean and CV [15]), maximum head pelvis separation [15], time to maximum head-pelvis separation [15], maximum medial centre of mass (CoM) deviation [15], turn time [15], cycle time (mean and SD [14], [24]), step distance [22], leg raising [22], stance and swing phase [24], percentage of single limb support [24], posture sway [27], gait adaptability [27], 10-meter walking test (10MWT) [24], [27] and centre of pressure (CoP) excursion [28], in order to analyse gait performance.

In terms of balance analysis, Berg Balance Scale (BBS) [22], [24], [27], ABC scale [22], [23], Timed Up and Go Test (TUG) [24], [27] and dual-task [23], one-leg stance [23], Mini-BESTest [23], Falls Efficacy Scale International (FES-I) [24] and perceived risk of falling [27] were assessed. Furthermore, Simulator Sickness Questionnaire (SSQ) [11], [12], [20], [24]–[26], [28] was conducted to evaluate simulator

sickness symptoms, Independent Television Commission Sense of Presence Inventory (ITC-SOPI) [25] to check perceived sense of presence, Intrinsic Motivation Inventory (IMI) [25] to score levels of motivation, System Usability Scale (SUS) [25], [26] to evaluate system overall usability, Parkinson's Disease Quality of Life Questionnaire (PDQL) [23], [27] to evaluate quality of life (QoL), Beck Depression Inventory (BDI) [23] to assess depressive disorder status, Borg 6-20 Questionnaire [27] to check participants' perceived exertion and fatigue and Stress Arousal Checklist (SAC) [28] to assess stress. Finally, in [13]–[15], [23], [26] an interview was conducted on user experience, and in [26] a game experience questionnaire-post game (GEQ-post game) was also undertaken.

Gómez-Jordana et al. [2] proposed a study to assess if the presence of virtual doorways in a virtual environment could induce FoG the same way real doorways do. For experimental protocols, there were three groups, a group of healthy participants as a control group, a group of PD patients without FoG and a group of PD patients with FoG, named as freezers (PD-f). All groups walked along a hallway under three different virtual conditions (no door, narrow doorway (100% of shoulder width) and standard doorway (125% of shoulder width)). The presence of virtual doors resulted in a reduction on step length and velocity and an increase on gait variability, with the worst values occurring for PD-f. The narrow door was the one that provoked the most FoG.

Lheureux et al. [11] aimed to assess the effects of adding an optic flow displayed through an immersive virtual reality headset during treadmill walking on gait. PD patients were instructed to walk in a randomized order in 3 conditions: (i) overground walking; (ii) treadmill walking; and (iii) immersive virtual reality on treadmill walking. As a result, a greater step length and lower cadence were obtained. SSQ was similar between the (ii) and (iii) conditions.

Yamagami et al. [12] intended to investigate whether virtual environments that replicate FoG-provoking situations would exacerbate gait impairments associated with FoG compared to unobstructed VR and physical laboratory environments. Participants performed a series of walking tasks on five different environments (physical laboratory without VR; virtual laboratory without obstacles; virtual doorway; virtual hallway; virtual street scene with crowds). The results showed that FoG-provoking VR environments could exacerbate gait impairments that are related to FoG.

Besharat et al. [20] aimed to examine the effects of virtual doorways and hallways on gait kinematics among people with PD and FoG. Participants performed a series of walking tasks on four different conditions (physical laboratory; virtual laboratory; virtual doorway; virtual hallway). As a result, kinematic changes commonly associated with FoG episodes were obtained.

Zhao et al. [13] intended to evaluate rhythmic visual and auditory cueing in a laboratory setting. Participants performed a series of walking tasks on four different walking courses (wide turn, narrow turn, full turn, and doorway) in combination with three cues (metronome, flashing light and optic flow). A more stable gait pattern with the aid of these cues was obtained but FoG did not diminish significantly. The metronome was more effective than rhythmic visual cues and preferred by more participants.

Geerse et al. [18] explored unfamiliarity and habituation effects associated with wearing the HoloLens on FoG and evaluated the potential immediate effect of Holocue on alleviating FoG in the home environment. Patients performed three sessions of 1.5h, scheduled one week apart. In the first session, participants walked a freezing provoking route multiple times with and without wearing the HoloLens (without Holocue), in their homes. Session 2 took place in a laboratory and consisted of individually customise the cues of the Holocue application in terms of intercue distance and preferred type of cues and familiarize participants to walking with the holographic cues. Finally, the last session took place again at the patients' home. Participants walked the same route with the same conditions as in session 1, while wearing the HoloLens with and without the Holocue application. Wearing the HoloLens (without Holocue) did significantly increase the number and duration of FOG episodes, but this unfamiliarity effect disappeared with habituation over sessions. Holocue had overall no immediate effect on FOG, although objective and subjective benefits were observed for some individuals, most notably those with long and/or many FOG episodes.

Badarny et al. [21] studied the effects of visual feedback cues on gait. The virtual environment consisted of a virtual tiled floor in a checkerboard arrangement. The experimental protocol was divided into 5 phases: (i) walking without the device; (ii) walking with the device placed on but with the display turned off; (iii) walking with the display turned on; (iv) walking without the device after a 15-minute break; and (v) re-evaluation of baseline performance without the device one week after the first examination. The results suggested that wearing the device turned off resulted in a negligible effect of about 2%. With the display turned on, 56% of the patients improved their gait speed or stride length or both. After removing the device, 68% of the patients showed over 20% improvement in either gait speed or stride length or both. One week later, 36% of the patients showed over 20% improvement in baseline performance with respect to the previous test.

Janssen et al. [14] investigated the usability of 3D augmented reality cues compared to conventional 3D transverse bars on the floor and auditory cueing, in reducing FoG and improving gait parameters. Patients were presented to three walking courses (walking straight, stop and start and turning) with five cue conditions (two experimental conditions: AR visual cues bars, AR visual cues staircase; and three

control conditions: conventional 3D transverse bars on the floor, auditory cues via a metronome and no cues). None of the first four conditions reduced the number of FoG episodes or the PTF. However, the conventional bars increased stride length (mean and SD), cycle time and decreased cadence and speed. In addition, the auditory cues via metronome were the preferred ones among all cues.

Gómez-Jordana et al. [17] aimed to develop visual cues that could be presented in an immersive VR environment. In addition to choosing an experimental group of PD patients, a control group of healthy people was also included. Both groups walked back and forth on a virtual hallway with visual cues that were tailored at their own gait performance. These cues consisted of two spatial conditions (115% and 130% of an individual's baseline step length), and three temporal conditions (spatial only condition, 100% and 125% baseline step cadence), and were crossed with each other, resulting in six different cue conditions. Results showed that both groups were able to match their gait performance to the information in all the visual cue conditions apart from the 125% step cadence conditions. The experimental group decreased gait variability, step length CV, cadence, and velocity, unlike the control group. Additionally, for both groups, step velocity increased in the temporal conditions, the spatial conditions and the interaction between the two.

Janssen et al. [15] aimed to assess whether augmented reality visual cues improved FoG and turning in place in PD patients with FoG. For that purpose, patients were encouraged to perform a series of 180° turns under an experimental condition with AR visual cues and two control conditions: auditory cues and no cues. The results showed that AR visual cues did not reduce the PTF neither the number nor duration of FoG episodes in comparison with the no cues control condition. Moreover, all FoG parameters were higher when using AR visual cues than with auditory cues. Compared to both control conditions, AR visual cues reduced the peak angular velocity and step height and, on the other hand, increased the step height CV and time to maximum head-pelvis separation.

Wang et al. [22] evaluated improvements in gait and sense of balance after three weeks of training. Participants played a game which consisted of stepping on the visual cues, with or without obstacles. Increases in ABC scale were observed, and the patients' stability was improved. Furthermore, patients were satisfied with the use of AR equipment, not having felt any discomfort apart from the weight of the HMD.

Tunur et al. [23] evaluated the feasibility, safety and acceptability of a mobile dance intervention with four modules: "warm me up", "balance me", "unfreeze me" and "walk with me". The outcomes of this study suggested that it was safe and accepted by patients, who rated usability with a high value.

Calabrò et al. [24] intended to test the efficacy and feasibility of balance and gait training based on the CAREN to reduce the risk of falls and improve balance and gait in PD patients. Patients performed 20 sessions of conventional physiotherapy and, three months later, 20 sessions of CAREN training. This last training made it possible to shorten the gait cycle duration, the step width and cadence and increase gait speed, step length and single limb support percentage, presenting an overall greater clinical improvement, in relation to the conventional physiotherapy.

Finley et al. [25] studied the usability assessment and development of a VR training application, which allowed PD patients to practice a wide range of skills such as turning and problem-solving. This study integrated the participation of physical therapists who also rated the system usability and intrinsic motivation. Participants completed a puzzle, in the virtual environment, which consisted of a word with missing letters. High ratings on interest, motivation and usability were obtained, not only by the participants but also by the physical therapists.

Campo-Prieto et al. [26] explored the potential of fully immersive videogames as a rehabilitation tool for PD patients. To achieve this goal, participants played a box virtual game performing different boxing techniques. Patients did not demonstrate any adverse effects nor any SSQ symptoms. SUS score was above 75% and GEQ scores were high.

Wang et al. [27] studied the efficacy of C-Mill training on walking ability, in PD motor subtypes. In this sense, a group of PIGD and a group of non-PIGD participants were recruited. Patients walked on a treadmill performing various modules, among which, obstacle avoidance. Both groups improved overall score in C-gait assessment and TUG test. The non-PIGD group reported a less exertion after the intervention and an improvement in their QoL at three-month follow-up.

Kim et al. [28] investigated the safety of using an HMD for longer bouts of walking in fully immersive VR. This study included a group of healthy young adults, a group of healthy older adults and a group of PD patients. Participants walked on a treadmill while visualizing a virtual city scene. No discomfort was found along the intervention, neither symptoms of simulator sickness or measures of static and dynamic balance were reported after exposure to the virtual environment, in all groups. Furthermore, measures of stress decreased in all groups, while the level of arousal increased in PD group.

2.4 Discussion

2.4.1 How have the VR/AR/MR-based approaches been applied in PD to help patients mitigate gait disabilities?

VR/AR/MR-based approaches have been applied mainly in five types of interventions: *(i)* Assessment; *(ii)* Cue-oriented assistance; *(iii)* Cue-oriented training; *(iv)* Videogame-oriented training; and *(v)* Training. It was verified that frequently VR/AR/MR-based approaches were applied in PD for cue-oriented training [14], [15], [17], [21], [22], and videogame-oriented training [23]–[27], which corresponded to performing a training session through the use of visual/auditory cues or playing a videogame, respectively. However, VR/AR/MR-based approaches have also been used to immerse patients in specific environments aiming to assess motor performance, through reliable motor outcomes as in [2], [11], [12], [20]. In [13], [18] VR/AR/MR-based approaches were implemented aiming the use of smart glasses daily, as assistance, in patients' home (cue-oriented motor assistance). Furthermore, [28] explored the safety of wearing VR googles during walking training sessions on a treadmill, while viewing a landscape in a video game.

It was observed that the **main goal of these studies was to immerse patients in virtual environments** to **assess motor metrics** or **lead them to perform specific tasks oriented by cues or games**. VR has been used to change the users' reality aiming to take patients from real world to other immersive environments (*e.g.*, virtual doors, staircases, or games). However, when applied for long periods can cause nauseas, vertigo, and disorientation. On the other hand, AR used additional virtual objects in patients' reality to lead them to perform specific tasks by interacting with those objects. However, these digital objects need further studies to improve their application, *i.e.,* it should be analysed which objects can lead patients to perform a specific and gait disability-oriented interactive daily task (*e.g.,* carry out virtual bags, walking in narrow places or open and cross virtual doors) or even which visual cues (colour, size, and shape) can be better associated with motion (e.g., green footprints).

Mixed reality could overcome these constraints, by combining the best of both worlds (VR and AR), real-world immersion and digital objects interaction.

2.4.2 Which technologies have been used to support VR/AR/MR-based approaches in PD?

The VR/AR/MR-based approaches identified in the literature, besides using **VR, AR, or MR equipment**, also **integrated acquisition** and **actuation modules**.

The VR/AR/MR equipment used were Oculus Rift DK2 [2], [17], [28], HTC Vive [11], [12], [20], [25], HoloLens [15], [18], Google Glass [13], [23], HTC Vive Pro [22], [26], a micro display attached to the eyeglasses frame [21], prototype of custom-made smart glasses [14], CAREN [24], and a C-Mill VR+ treadmill [27]. Ten studies used virtual reality [2], [11], [12], [14], [17], [20], [22], [25], [26], [28], six studies applied augmented reality [13], [15], [21], [23], [24], [27] and only one study employed mixed reality [18]. Furthermore, only study [27] did not use fully immersive equipment since it did not use smart glasses or CAVE rooms. Virtual tasks consisted mainly of gait tasks: walking [2], [12]–[14], [17], [18], [20]–[22], [24], [27], [28], walking with turning [13], [14], [22], turning in place [15], crossing doorways [2], [12], [13], [20], climbing stairs [14], boxing [26], and dancing [23].

Regarding the acquisition module, only study [24] used built-in sensors, namely, the CAREN system which used an accelerometer, G-Sensor. The remaining studies that presented acquisition modules, did not use built-in sensors, and used 3D motion capture systems such as, InterSense IS900 [2], [17], Qualisys [12], and IMU [11], [13]–[15], and Vive trackers [22], [25]. These modules may be intrusive to the patient, so low volume technology should be selected.

The actuators combined with the VR/AR/MR-based approaches were all built-in [13]–[15], [17], [21], [22], [24] with the exception of [15] that used a speaker for auditory cueing. Moreover, [24] used four types of actuators, namely, visual, auditory, vestibular, and tactile cues, [13] used three types of actuators (two of them visual (flashing light and optic flow) and one auditory cue), [15] used two types of actuators (visual and auditory cues) whereas [14], [17], [18], [21], [22] only used one type of actuator, in this case, visual cues. Visual cues were used more often than auditory cues. Indeed, **visual cues indicate spatial information**, whereas **auditory and vibrotactile cues give only temporal information** [14], [17]. However, it is still unclear which cues are suitable for a particular motor task or even for a specific symptom. Future research should address these shortcomings, aiming to **develop virtual environments and tasks, highly personalized to patients, integrated with motion tracking and biofeedback devices, with clear and specific motor aims.** It is important to study which virtual scenario/activity can best immerse patients in everyday scenarios to study a specific motor symptom (e.g., FoG), or even which technology can best assess or train that symptom.

2.4.3 How have the VR/AR/MR-based approaches been clinically validated in PD?

All studies recruited less than thirty participants, corresponding to an insufficient sample to be representative of the PD population, requiring **greater clinical evidence**. Based on the scales used by the researchers to monitor patients' disease degree, it is possible to organize them as follows: *(i)* clinical

assessments – H&Y, FOG-questionnaires; *(ii)* cognitive assessments – MoCA, MMSE, FAB test; and *(iii)* motor assessments – PIGD, ABC, UPDRS-III [2], [12]–[15], [17], [18], [20], [22], [23], [25]–[28]. **A complete evaluation of PD participants must include all types of assessments**. Moreover, **the study criteria for the participants' selection should consider the same evaluation**, and, ideally, all external factors that may affect participants' motor functions should be eliminated.

Tunur et al. [23] and Geerse et al. [18] were the only studies conducting a home-based approach demonstrating the potential of AR and MR as a training strategy. In addition, only [2], [17], [28] studies considered an age-matched control group constituted by the same number of participants, submitted to the same test conditions. **Case control design studies should include participants with match features aiming to decrease the analysis bias**. A single study [26] included a group of physical therapists who assessed a post-test of SSQ, SUS, and IMI (from the perspective of a player). In fact, **it is crucial to perform long-term retention tests to evaluate the sensory integration on patients' motor behaviors, after an extensive period of usage**. Moreover, only three studies [23], [24], [27] carried out a follow-up evaluation, which shows to be an important quality factor of systems, strategies and even for the results obtained. Finally, [11], [12], [20] assessed the simulator sickness questionnaire and only [25] assessed the usability, simulator sickness symptoms, sense of presence and levels of motivation questionnaires. **These usability questionnaires are important to assess patients' acceptability to VR/AR/MR strategies**. To develop a motor assessment and training strategy closer to the patients' daily living, these concerns should be addressed, and a user-oriented approach should be conducted. Gathering knowledge about **how to motivate patients and physicians during the sessions to monitor or train their gait parameters reveals an impactful approach to accelerate patients' motor improvements**.

2.5 Conclusions and Future directions

By reviewing the current literature review of VR/AR/MR-based approaches for motor assessment and training, in PD, it is verified that these approaches have been used to immerse patients in specific virtual environments (VR) or interact with virtual objects overlaid on the real world (AR). Positive results have been observed by the application of these approaches for motor assessment, cue-oriented assistance/training, and videogame-oriented training. Despite the scientific progress of using VR/AR/MR-based approaches in the last decades as a methodological framework to monitor or train PD-related gait disabilities, some limitations can be pointed out to the reviewed literature review. VR/AR/MR strategies

have been applied in PD to immerse **patients in virtual environments** in order to **assess motor performance** or **lead them to perform specific tasks oriented by cues or games**.

VR has proven effective in completely immersing patients in other scenarios, by replacing their reality. However, it should not be used for long periods of time as it causes motion sickness symptoms in users. On the other hand, AR was used to add digital elements in patients' reality, requiring more real and robust objects to provide a reliable near-home environment. Thus, it will be **beneficial to use a mixed reality experience, which combines elements of both AR and VR, where real-world and virtual objects interact**. Furthermore, when using AR to provide sensory cues it is observed a non-focused approach on the user, *e.g.,* a study used monocular smart glasses, however, in order to improve the effects of visual cueing, the **visual information should be projected binocularly** or **towards the centre of the visual field** (especially, considering the visual impairments verified in these patients).

In AR, **to help with scaling**, the direction and size of the foot displacement should be provided, *e.g.*, **through footprints**. Most of the studies demonstrated an **insufficient familiarisation with the smart glasses** and, **games** or **sensory cues**. Therefore, **it is required an adequate period of familiarisation with the VR/AR/MR equipment to better integrate the user with the virtual** and **interactive environments**. Also, to complement this approach focused on the user, the **usability** of the system and the **motivation of patients** and **physicians** should be documented for future evaluation. Further, it was observed that it is required to obtain a **larger sample size and a larger range of disease severity** that is more representative of the PD population. A **randomized control group** is also another fault in these studies. Overall, **more clinical evidence is required**.

Bearing this in mind, the following future challenges and unanswered research questions were identified: analyse which virtual environment/task can better assess and train patients regarding their gait symptomatology; smart glasses should be more lightweight, comfortable, with a user-friendly design, binocular and with an adequate field of view; VR/AR/MR technologies should integrate a control group, to study the effects of them; VR/AR/MR should integrate a control condition, to distinguish distraction by the smart glasses; the experimental group should be assessed before and after the intervention; assessment of the VR/AR/MR-based approach should include usability, safety and feasibility questionnaires and more objective tests; and finally VR/AR/MR should incorporate treatment protocols of several sessions per week, for several weeks with longer follow-up intervals. **Table 2-4** summarizes all identified limitations regarding technological and validation methodology issues.

Therefore, a systematic approach was followed to identify the requirements of the system, from the point of view of the user and the technologies, considering the limitations identified in the literature review, allowing to move on to the next tasks of the dissertation.

Table 2-4 - Identified limitations of current VR/AR/MR-based approaches and guidelines for their mitigation

	Limitations	Guidelines to be followed
Technological	Smart glasses characteristics: heavy, uncomfortable, monocular and with a narrow field of view	Smart glasses should be more **lightweight**, **comfortable**, with a **user-friendly design**, **binocular** and with an **adequate eye calibration** and **field of view**
		Explore the use of **mixed reality**
	Unknown monitoring systems' contribution	Explore the use and potential of other integrated monitoring systems specified for different gait impairments
	Unclear correlation between virtual environments and tasks and better assessment and training	Study which are the best virtual environments and virtual tasks to motor assessment and training
Validation	Failure to carry out usability, safety, and feasibility questionnaires	Assessment of the VR/AR/MR-approach should include **usability, safety and feasibility questionnaires** and more objective tests
		Implementation of a **suitable familiarization phase** with VR/AR/MR equipment
	Short-term interventions and follow-up absence	VR/AR/MR should incorporate treatment protocols of several sessions per week, for several weeks with longer **follow-up** intervals
	Control group absence	VR/AR/MR should integrate a **control group** to study the effects of it
	Control condition absence	VR/AR/MR should integrate a **control condition** to distinguish distraction by the smart glasses

3 SOLUTION OVERVIEW

The following chapter specifies the materials and methods used to develop the proposed strategy and to acquire and process all the data required. This includes **i)** an overview of the solution found, starting by summarising the problem raised; **ii)** a presentation of the project in which this dissertation is integrated; and **iii)** the respective project module to which this dissertation has contributed; and **iv)** an introduction to the devices and systems used.

3.1 PROBLEM DESCRIPTION

From the literature review it was concluded that VR/AR/MR strategies have the potential to not only **immerse patients in environments** that recreate daily situations which may trigger PD-related gait disabilities but also to **integrate biofeedback strategies to help patients emerge** from these disabilities. However, some limitations were identified, such as the fact that the smart glasses were heavy, no usability, safety or feasibility questionnaires were used, and the lack of control conditions in the protocols, preventing a clear discussion of the results obtained.

Thus, a new strategy **must include patients with Parkinson's disease as target audience** and will be implemented based on **MR technology**, i.e., the combination of real-world immersion and virtual objects interaction, **integrated with a motion tracking system**. Patients' motor performance will be recorded and assessed by the motion tracking system, which should present a **real-time synchronization with the MR technology**. Further, the analysis of users' motion will make it possible to provide on-demand visual cues, following a **visual biofeedback strategy**.

In this sense, this dissertation expects to **(i)** develop virtual environments that lead to gait impairments and **(ii)** integrate a biofeedback strategy that enables patients to overcome these episodes. Therefore, three different virtual environments were developed, in which patients were immersed and encouraged to perform motor tasks, that corresponded to three situations that typically cause PD gait impairments (turning, crossing doors, narrow spaces). In addition, a biofeedback strategy based on visual cues was proposed to improve patients' motor performance in the same virtual environments.

This solution is integrated in the +sImmersive module of the +sense project, which is presented in the next section.

3.2 +SENSE

This dissertation is integrated and intended to contribute to the **+sense** project. The project aims to improve patients' quality of life, promoting less dependence on third parties by improving their mobility

and motor autonomy. In this sense, +sense offers front-end high-tech solutions based on wearable biofeedback devices which rely on acquisition, interpretation, and feedback of patients' sensorimotor information. Currently, +sense is divided into four modules, as shown in **Figure 3-1**: **(1)** +sBiofeedback; **(2)** +sMotion; **(3)** +sC-support and **(4)** +sImmersive. The development of this dissertation contributed to the fourth module.

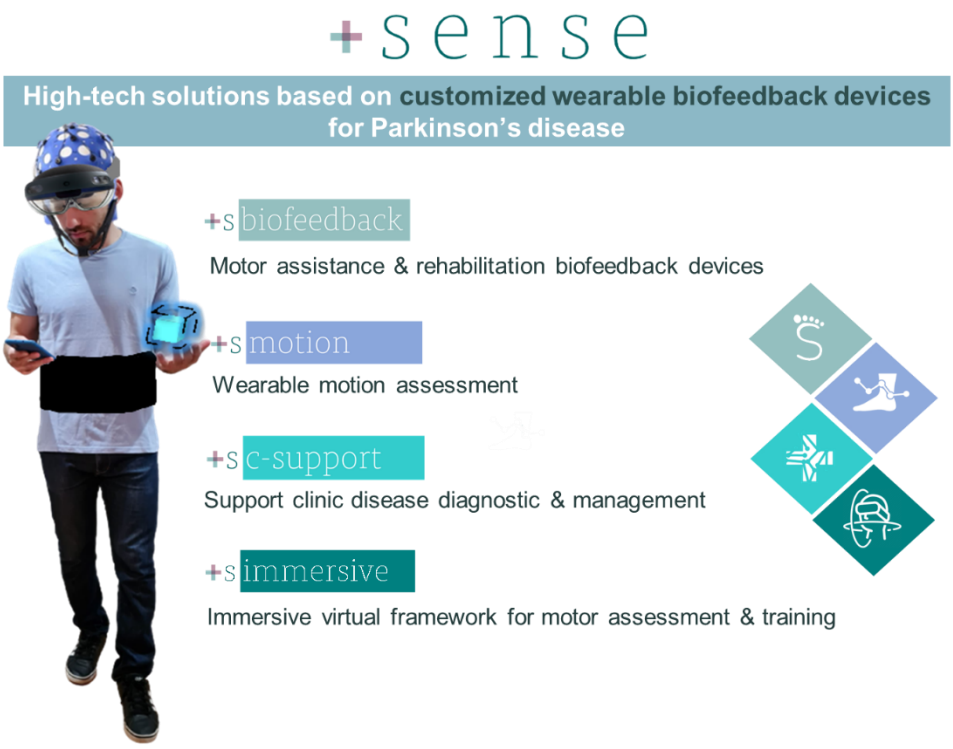


Figure 3-1 - +sense modules.

3.3 +sIMMERSIVE

This module brings a new paradigm shift by using mixed reality approaches, integrated with a motion tracking device and biofeedback strategies, as a complementary tool for motor monitoring and training of PD-related gait disabilities. The three virtual environments allow the immersion of the user in everyday situations, having to perform daily motor tasks, in order to achieve a more reliable motor assessment and rehabilitation. Thus, this dissertation brings a step forward in the knowledge of how mixed reality-based motor assessment and training can be applied in Parkinson's disease. The +sImmersive considers the multifactorial nature of PD and innovates by contributing with a patient-centred approach. Bearing this in mind, two devices were used: (1) mixed reality smart glasses; and (2) motion tracking system, explained in detail in the following sections.

3.3.1 MIXED REALITY SMART GLASSES: MICROSOFT HOLOLENS 2

In order to implement the mixed reality strategy, the Microsoft HoloLens 2 was used, a fully immersive, portable, and wearable commercial setup device of augmented/mixed reality, **Figure 3-2**. It consists of an AR/MR headset and a USB Type-C cable, which allows to charge the smart glasses and connect them to other devices such as computers.

Figure 3-2 - Microsoft HoloLens 2.

Some of the HoloLens 2 system specifications are mentioned in **Table 3-1** [30]. HoloLens 2 presents see-through holographic lenses, enabling to see the real world, never losing the sense of reality. Moreover, they have several sensors that allow head and eye tracking, making it possible for the glasses to always know where the user is in space. These smart glasses have built-in speakers and microphone. In this sense, beyond the visual feedback, they can also provide auditory feedback to users. One of the biggest strengths is that they can understand the human and the environment through hand tracking, eye tracking, voice, 6DoF tracking and spatial mapping, making these glasses user-friendly. In addition, they only need a USB Type-C cable to connect to a computer, they are lightweight (556g), one can wear glasses under them, and their battery lasts up to 3 hours of active use.

This vast range of features of HoloLens 2 motivated its selection, as it was intended to use mixed reality smart glasses that allow holograms to be placed in real space, while still seeing the real world.

Table 3-1 - Specifications of HoloLens 2 smart glasses [30]

HoloLens 2 Technical Specifications		
Display	*Optics*	*See-through holographic lenses (waveguides)*
	Resolution	2k 3:2 light engines
	Holographic density	2.5k radiants (light points per radiant)
Sensors	Eye-based rendering	Display optimization for 3D eye position
	Head tracking	4 visible light cameras
	Eye tracking	2 IR cameras
	Depth	1-MP time-of-flight (ToF) depth sensor
	IMU	Accelerometer, gyroscope, magnetometer
Audio and speech	Camera	8-MP stills, 10800p30 video
	Microphone array	5 channels
	Speakers	Built-in spatial sound
Human understanding	Hand tracking	Two-handed fully articulated model, direct manipulation
	Eye tracking	Real-time tracking
	Voice	Command and control on-device; natural language with internet connectivity
	Windows Hello	Enterprise-grade security with iris recognition
Environment understanding	6DoF tracking	World-scale positional tracking
	Spatial Mapping	Real-time environment mesh
	Mixed Reality Capture	Mixed hologram and physical environment photos and video
Compute and connectivity	SoC	Qualcomm Snapdragon 850 Compute Platform
	HPU	Second-generation custom-built holographic processing unit
	Memory	4-GB LPDDR4x system DRAM
	Storage	64-GB UFS 2.1
	Wi-Fi	Wi-Fi: Wi-Fi 5 (802.11ac 2x2)
	Bluetooth	5
	USB	USB Type-C
Fit	Single size	Yes
	Fits over glasses	Yes
	Weight	566g
Software	Windows Holographic Operating System	
	Microsoft Edge	
	Dynamics 365 Remote Assist	
	Dynamics 365 Guides	
	3D Viewer	
Power	Battery life	2–3 hours of active use
	Charging	USB-PD for fast charging
	Cooling	Passive (no fans)

HoloLens 2 has some recommended system requirements (**Table 3-2**)[31] that the host computer must meet to properly enjoy the experience. A computer TUF Gaming with a NVIDIA GeForce GTX 1060 GPU was used to run and connect the software needed to build the mixed reality tool. According to **Table 3-2,** the computer TUF Gaming comprises all the minimum and recommended requirements to use HoloLens 2 system.

Table 3-2 - Comparison of recommended system requirements for using HoloLens 2 [31] and the specifications of the used computer (TUF Gaming FX505GM_FX505GM)

Component	**Recommended system requirements**	**TUF Gaming FX505GM_FX505GM**
CPU	64-bit with 4 cores or equivalent	Intel® Core™ i7-8750H CPU 2.20GHz
GPU	DirectX 11.0 or later WDDM 1.2 driver or later	NVIDIA GeForce GTX 1060
RAM	8 GB or more	32 GB
Operating system	64-bit Windows 10 Pro, Enterprise, or Education (Hyper-V support)	Windows 11 Home 22H2

3.3.2 Motion tracking system: Xsens MVN Awinda

The IMU-based motion capture system relies on MVN Awinda (Xsens, Enschede, The Netherlands) [32], [33] given its reliability for body motion analysis in free-living conditions. The lower body configuration (**Figure 3-3a**) comprises a total of 7 wearable Wireless Motion Trackers (MTw) sensors (**Figure 3-3b**) which are placed on the body through adjustable straps **(Figure 3-3c**). This system collects the lower-body kinematic data that will be used to study the participants' motor performance and act accordingly. Furthermore, this system was used to communicate with Unity software, providing information about the occurrence of gait initial or final contact (IC/FC) so that the biofeedback could act in HoloLens 2.

Figure 3-3 – Xsens MVN Awinda components. (a) lower body configuration; (b) MVN Motion Tracker (MTw); (c) MVN Awinda straps; (d) MVN Awinda station.

The MTw sensors have embedded accelerometers, gyroscopes and magnetometers that provide 3D acceleration, 3D angular velocity and 3D magnetic field, respectively [32], [33]. These measurements become particularly interesting for position and orientation estimation of human body segments. Thus, it was possible to develop an algorithm (**Section 4.3**) for detecting initial and final contacts, according to the data coming from Xsens, namely the angular velocity in y and the linear velocity in z of the foot sensors. Data from the MTw sensors are wirelessly transmitted and synchronised by the Awinda Station (**Figure 3-3d**).

During the data acquisition sessions, it was used the **MVN Analyze Pro 2021.2**, an easy-to-use software for real-time viewing and recording, which allows the export of motion capture data to third party applications [32]. Furthermore, this software has a **streaming feature** which **enables computers to stream the captured data over a network to other client computer**, in **real-time**, **Figure 3-4**. This real-time network streaming protocol is based on User Datagram Protocol (UDP). The UDP Protocol is unidirectional, is stateless and does not require the receiver to answer incoming packets, which allows greater speed. Upon this, Xsens has developed plug-ins, available for Unity3D, for free at asset store, for usage with third party tools as a client application, allowing to receive motion capture data in real-time. The data content in the datagram is defined by the specific protocol set. Each datagram starts with a 24-byte header followed by a variable number of bytes for each body segment, depending on the selected data protocol. All data is sent in 'network byte order', which corresponds to big-endian notation. The header contains the type of the data and some identification information, so the receiving end can apply it to the right target [34].

Thus, a new session was created for each "equipped" volunteer and anthropometric data was measured and registered to build the person's biomechanical model. After, a calibration method is performed to align the MTw sensors with the user's body segments by the "Npose + Walk" task. When a successful calibration is achieved and the "stream" feature is on, as well as the "Linear Segment Kinematics", "Angular Segment Kinematics" and "Time code" datagrams selected, it is finally possible to start recording a real-time session according to the defined protocol.

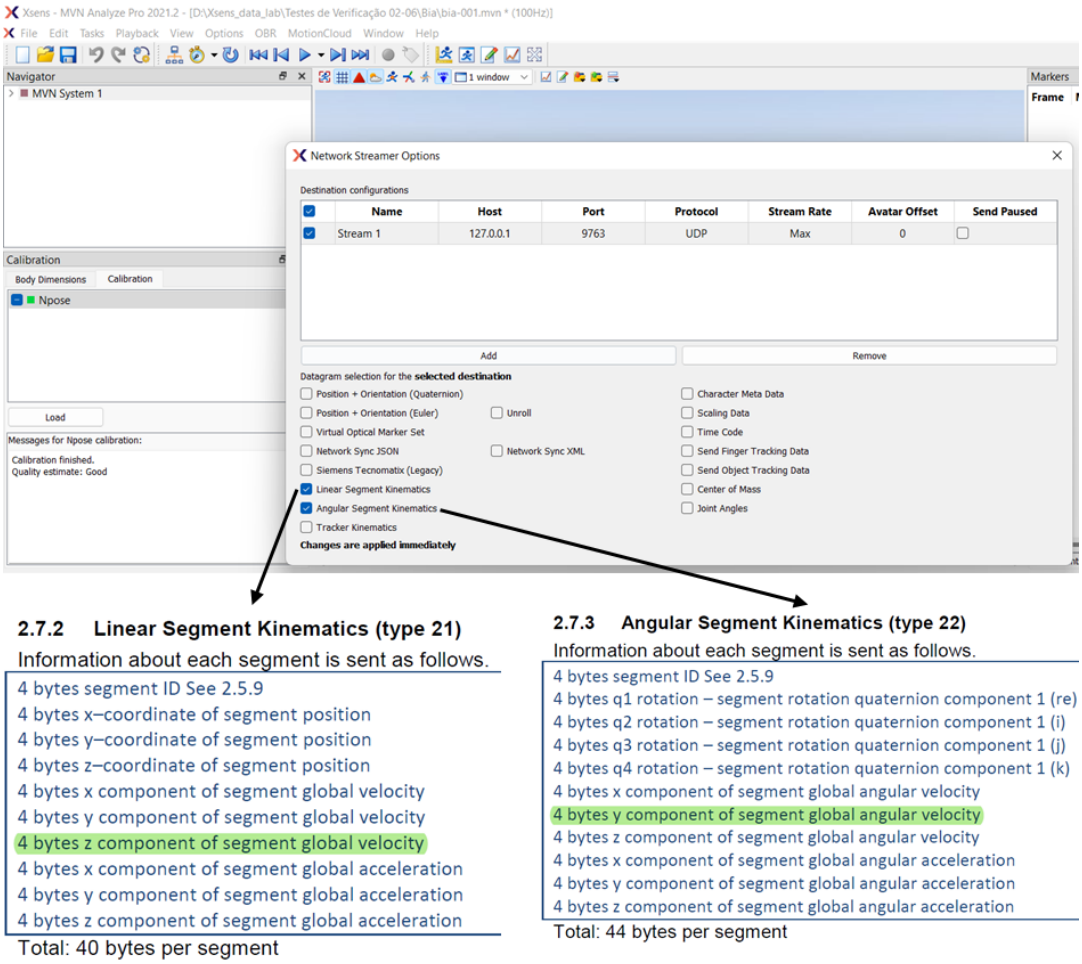


Figure 3-4 – Real-time streaming feature in MVN Analyze Pro.

3.4 Conclusions

After an extensive literature review about the currently VR/AR/MR-based approaches used in PD, it was noticed that mixed reality may be the best technology to be used with individuals with Parkinson's disease, as it allows virtual and interactive objects to be added to the real world, without ever losing the sense of reality.

Thus, this dissertation aims to explore this technology not only for the assessment but also for the training of PD-related disabilities. To this end, this dissertation is inserted in the +sense project, contributing to the +sImmersive project module and makes use of two high-tech equipment, namely the HoloLens 2 mixed reality smart glasses and the Xsens motion tracking system.

4 SOLUTION DESCRIPTION

This chapter presents the methods used to develop the virtual environments and the biofeedback strategy, answering **RQ2**. This includes **I)** an introductory insight and conceptual overview of the strategy; **II)** a description of the virtual environments developed, and virtual tasks chosen; **III)** a detailed description of the data acquisition system integration; and **IV)** an explanation of the biofeedback integration implemented.

4.1 INTRODUCTORY INSIGHTS & CONCEPTUAL OVERVIEW

The fact that, until today, PD is an incurable disease, leads to the search and development of strategies that improve the accuracy of motor assessment and allow for more consistent rehabilitation processes. Thus, this dissertation aims to further explore the contribution of mixed reality in these assessment and training strategies. To this end, two technological devices were used, HoloLens 2 and Xsens. The contribution of the HoloLens 2 consisted in the creation of the virtual environments in which the participant is immersed and the display of visual cues. In turn, Xsens was used to monitor the participant's motor performance and also to detect the occurrence of initial and final gait contacts for the use of on-demand visual cues to implement the biofeedback strategy.

4.2 VIRTUAL TASKS AND ENVIRONMENTS IN HOLOLENS 2

After conducting the literature review, the most adequate scenarios and tasks were discussed, *i.e.*, the scenarios that may trigger gait disabilities and motor tasks that portray the patient's daily life. In this sense, situations that most provoke PD-related gait disabilities according to [2], [11], [12], [20] are walking through doors, walking in narrow places, and turning. Thus, three virtual environments were designed and developed using **Unity software** to address these contexts (**Table 4-1**): **1) corridor presenting two dice**, one on each side of the corridor, in which the patient has to carry the dice to the corresponding coloured box on the other side of the corridor by turning around; **2) corridor with a door** in the middle in which the patient has to walk to the finish line, crossing the door; and **3) narrow corridor** in which the patient has to walk to the finish line. It is expected that when immersed in these environments, the gait of the patients will be a gait representative of PD, i.e., small and slow steps.

Table 4-1 - Developed virtual environments and their motor tasks

Virtual Environment	Description	Task	Virtual environments
Scenario 1	Corridor with two dice, one on each side of it	Walk, pick up the dice, turn around, land in the corresponding coloured box, walk, pick up the other dice, turn around, land in the corresponding coloured box, walk to the finish line	
Scenario 2	Corridor with a door in the middle of it	Walk through a doorway to the finish line	
Scenario 3	Narrow corridor	Walk in a narrow corridor to the finish line	

On the other hand, it was also aimed to use biofeedback strategies to obtain the opposite effect, that is, a more fluid gait, longer and faster steps. Thus, visual cues were added to these three scenarios. In the case of scenario 1, **arrows of the same colour as the dice** were used, representing the path to be travelled between the dice and the box. Each set of arrows displayed the colour relative to the playing dice so that the user would not be confused. For scenarios 2 and 3, **right and left green footprints** were drawn to anticipate the next step that the person must take, that is, as the patient walks, left and right footprints appear. Green was chosen since the eye is most sensitive to a yellowish-green colour under normal lighting conditions [35], [36] and, beyond that, green is related to "being right", "proceeding", unlike de colour red, as in traffic lights. These environments can be visualised in **Figure 4-1**.

It is important to mention that the virtual environments are customisable to each patient in terms of patient's height, i.e., at the beginning of each session, the patient's height is set in Unity so that the

scenario adjusts to it. Furthermore, by means of the participant's height, the distance between the visual cues in the footprint tests (biofeedback) is adjusted by a trial-error adjustment.

Figure 4-1 - Biofeedback virtual environments.

4.3 Sensory system integration: from MVN Analyze Pro to Unity

Xsens MVN Awinda was used for 2 purposes: **(1)** to **stream the kinematic data to Unity** so that it was possible to **detect initial and final contacts of the subject's gait in real-time**, in biofeedback/training trials; and **(2)** to **acquire the lower body kinematic data** to later **calculate metrics** related to motor performance, i.e., **spatiotemporal metrics**.

Regarding the first purpose mentioned above, it was necessary to detect the initial and final contacts of the subject's gait because these are the events that are associated with the beginning and end of a gait cycle, and these are often affected in PD. It is expected that providing biofeedback at these moments may help to bypass the failures in nerve messages that may be at the origin of PD-related gait impairments.

4.3.1 Real-time initial and final contact detection

MTw sensors have embedded accelerometers, gyroscopes and magnetometers that provide 3D acceleration, 3D angular velocity and 3D magnetic field, respectively [30], [31].

The various signals that Xsens provides, such as speed, position, angular velocity, acceleration, among others, in the three directions, were observed and compared to the foot contact (FC) signals that represent the "heel strike" (or initial contact) and "toe off" (or final contact) of both feet. After a detailed analysis, it was concluded that a **heel strike (HS or IC) could be represented by a local minimum after a global maximum of angular velocity in the y direction**, and a **toe off (TO or FC) could**

be represented by a global maximum of velocity in the z direction, for both feet, as can be depicted in **Figure 4-2**. These findings were supported by [37].

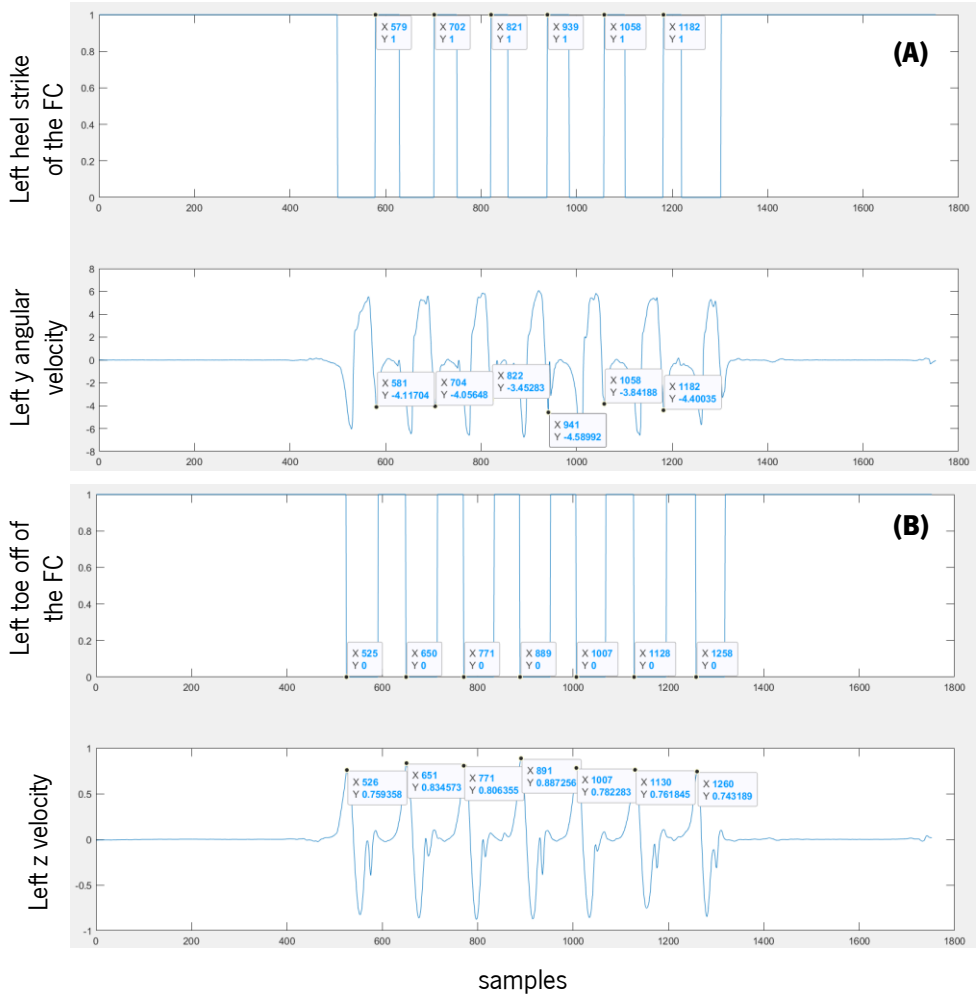


Figure 4-2 - Comparison of (A) left heel strike signal of FC signal with angular velocity signal in y direction; (B) left toe off signal of FC with velocity signal in z direction.

Thus, code was developed in C#, using Visual Studio 2022 in Unity software, for the development of this algorithm, divided into four steps: **(1)** arrival of kinematic data from MVN Analyze Pro; **(2)** first derivative computation; **(3)** finite state machine (FSM); and **(4)** adaptive thresholds calculation, discriminated in the flowchart in **Figure 4-3**.

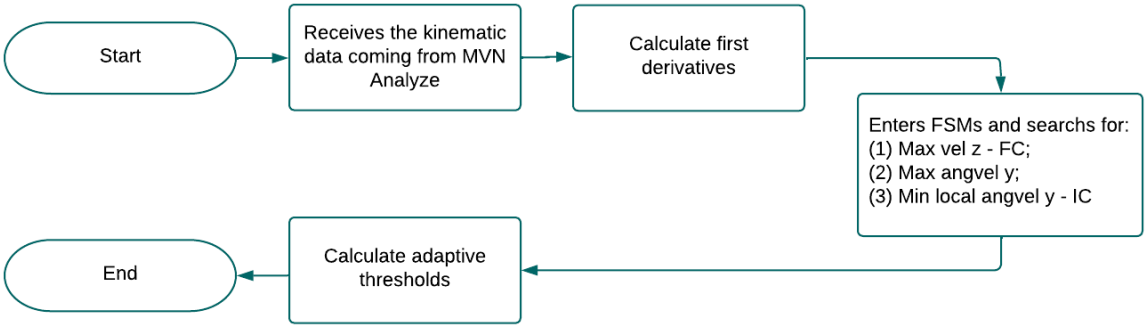


Figure 4-3 - Flowchart representing the real-time initial and final contact detection algorithm, which runs on Unity.

Regarding the **first step**, the values of velocity in the z direction (*velz*) and angular velocity in the y direction (*angvely*), for both feet, were received in bytes and converted to floats.

In a **second step**, the first derivatives of the values mentioned above were calculated and saved since, throughout the algorithm, the current and previous samples acquired will be needed. When the first sample is acquired, the previous one is assumed to be zero.

In order to distinguish the occurrence of an IC and a FC, a **FSM** was implemented (**third step**) that works by means of a **switch case statement**. This statement changes state according to the decision rules presented in **Table 4-2**. Three decision rules were specified, which correspond to **(1) finding a global maximum of the linear velocity in z direction** that corresponds **to a FC**; **(2) finding a global maximum of the angular velocity in y direction**; **(3) finding a local minimum after the global maximum of the angular velocity in y direction** that corresponds **to an IC**. These decision rules were defined, based on curve tracing techniques, including the **evaluation of signal derivatives** and **adaptive thresholds**. Evaluating signal derivatives allowed the detection of maximum and minimum peaks (maximum: *velz_diff* < 0 & *velz_diff_prev* > 0; or *angvely_diff* < 0 & *angvely_diff_prev* > 0; and minimum: *angvely_diff* > 0 & angvely_diff_prev < 0). In turn, the use of thresholds eliminated local unclear peaks (maximum: *velz* > velz_th or *angvely* > angvely_th). Each decision rule presented allowed triggering from one event to the next. It is important to note that two FSM were implemented, one for each foot (*FSM_left* and *FSM_right*).

Conventional FSMs present a static behaviour that does not address common changes in gait. In fact, the duration of a gait cycle and the amplitude of the inertial signals are affected by variations in spatiotemporal gait metrics, such as gait speed and stride height. In order to overcome this limitation, a fourth step added **adaptive thresholds** to FSMs, instead of static thresholds, based on [38]. This strategy enables to reduce intra and inter subject variability. The threshold values used in the FSMs decision rules were changed every five gait cycles (*count_gaitcycle* = 5) and defined as 40% of the average

value of the velocities and as 10% of the average value of the angular velocities of the previous events. The initial values and percentages defined to update the adaptive thresholds and also the number of gait cycles were found empirically after testing with several participants and several gait conditions.

Table 4-2 - Gait events and corresponding decision rules of FSM

Condition	**Gait Event**	**Decision Rules**
1	$TO_{L,R}$	(velz_diff < 0) && (velz_diff_prev >= 0 && velz > velz_th)
2	-	(angvely_diff < 0) && (angvely_diff_prev >= 0) && (angvely > max_angvely_th)
3	$HS_{L,R}$	(angvely_diff > 0) && (angvely_diff_prev <= 0) && (angvely > angvely_th)

4.3.2 VERIFICATION TESTS OF REAL-TIME IC AND FC DETECTION

To verify the performance of the real-time IC/FC detection algorithm, gait kinematic data were collected from healthy individuals to accomplish a benchmarking analysis of the real-time analysis versus the foot contact signals provided by the MVN Analyze Pro software. The following subsection presents the methodologies adopted in the verification tests.

4.3.2.1 PARTICIPANTS, MATERIAL, EXPERIMENTAL PROTOCOL AND DATA ANALYSIS

Four healthy subjects (two males and two females) were recruited and accepted to participate in this data collection. A list of inclusion criteria was outlined to conduct the experimental data collection. Participants were recruited if they had: **I)** 18 or more years old; **II)** height within 150 and 185cm; and **III)** healthy locomotion. **Table 4-3** presents the participants' detailed anthropometric data.

Table 4-3 - Metadata of the participants included in the acquired dataset

Participant ID	**Gender (M/F)**	**Age (years)**	**Body height (cm)**
S1	M	19	182
S2	M	19	179
S3	F	23	166
S4	F	29	160
Mean and STD	-	22.5 (± 4.09)	171.75 (± 9.07)

During this data acquisition the two aforementioned devices were used, the HoloLens 2 smart glasses and the Xsens motion tracking system. This last equipment was placed in the lower body plug-in configuration. **Figure 4-4** represents the position of these devices in the participant.

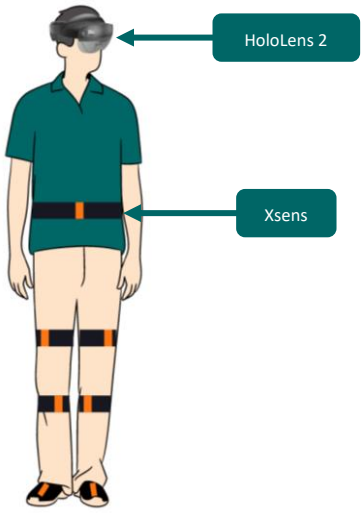


Figure 4-4 –Representation of the devices used in the verification tests.

The data acquisition protocol consisted of performing two different trials, three times each, which consisted of walking in a straight line along 10 meters: **(1) with the smart glasses OFF**; and **(2) with the smart glasses ON, showing a virtual scenario (scenario 3, narrow spaces)**. In total each patient performed 6 trials.

After the experimental protocol was completed, the acquired data was analysed in offline. To do this, the trials were exported in MVN Analyze Pro and then the exported trials (**mvnx files**) were loaded into MATLAB. Afterwards, the real-time IC/FC detections were compared with the Xsens foot contact signals (ground truth), as depicted in **Figure 4-2**. Thus,

(1) The angular velocity signal in the y-direction from both feet was compared with the respective foot contact signal to assess the performance of real-time identification of IC;

(2) The velocity signal in the z-direction from both feet was compared with the respective foot contact signal to assess the performance of real-time identification of FC.

Detected gait events were evaluated considering their **accuracy** (Equation 4-1), **precision** (Equation 4-2), **sensitivity** (Equation 4-3), and **specificity** (Equation 4-4). These metrics portray the performance of the developed algorithm. **True positives** (TP) corresponded to the gait events correctly identified, **true negatives** (TN) represented gait events that the algorithm correctly detected as a non-event, **false positives** (FP) corresponded to gait events not correctly identified and **false negatives** (FN) the events that should had been detected. Furthermore, **advance and delayed detections** were also assessed based on their percentage of occurrence and duration. Advance and delayed detections were considered from the TP detections.

Equation 4-1

$$Accuracy\ (\%) = \frac{TP + TN}{TP + TN + FP + FN}$$

Equation 4-2

$$Precision\ (\%) = \frac{TP}{TP + FP}$$

Equation 4-3

$$Sensitivity\ (\%) = \frac{TP}{TP + FN}$$

Equation 4-4

$$Specificity\ (\%) = \frac{TN}{TN + FP}$$

4.3.2.2 RESULTS AND DISCUSSION

Table 4-4 presents the performance of the real-time IC and FC detection algorithm. It shows the accuracy, precision, sensitivity, specificity and, advance and delayed detections (by means of their percentage of occurrence and duration).

Table 4-4 – Results of the verification tests

Metric	**Mean (±SD)**
Accuracy (%)	98.93 (± 1.38)
Precision (%)	100.00 (± 0.00)
Sensitivity (%)	97.87 (± 2.75)
Specificity (%)	100.00 (± 0.00)
Delays (freq %))	0.27 (± 0.52)
Delays (time (s))	0.01(± 0.02)
Advances (freq %))	0.19 (± 0.37)
Advances (time (s))	0.02 (± 0.03)

The proposed algorithm showed to be significantly accurate (mean of 98.93%), sensitive (mean of 97.87%), precise (100%), and specific (100%) for the tests performed, meaning that the developed algorithm is able to detect, without much error, the initial and final contacts, presenting sufficient capacity to integrate the biofeedback strategy, having reached the **KPI3**, which defined 96% as the percentage of accuracy to be met, that is, in a space of 10 meters where 20 steps are taken, the algorithm detects 19 IC/FCs. However, an adjustment to the thresholds was subsequently made using existing data from the

project database for 9 PD patients. Nevertheless, further modifications may have to be made in the future considering the heterogeneity of PD and the intra- and inter-subject variability.

4.3.2.3 CONCLUSIONS

The proposed real-time IC and FC detection algorithm has shown to be accurate, sensitive, precise, and specific. The adaptability introduced in the IC and FC detection ensures greater robustness of the system in the eventual occurrence of perturbations. These aspects make this algorithm suitable to be integrated with an actuation system, i.e., with a biofeedback strategy. However, there are some future challenges such as the need to validate this algorithm with (1) data collected from PD patients; (2) data collected from PD patients at various stages of the disease; and (3) data collected over time.

4.3.3 SPATIOTEMPORAL METRICS ESTIMATION

In order to assess whether the immersive virtual environments were able to trigger PD-related gait disabilities and whether the visual biofeedback was able to help patients overcome these impairments, **spatiotemporal metrics were estimated using the motion data captured by Xsens**. Thus, a code was developed in **MATLAB** for this estimation.

Table 4-5 presents the calculated spatiotemporal parameters, as well as the definition and formula of each and the units of measurement. Furthermore, the **variability (SD) and asymmetry (AS)** of these metrics were also calculated.

Table 4-5 - Spatiotemporal parameters: description, formula and units [39]

Spatiotemporal parameter	*Definition*	*Formula*	*Measured units*
Step duration	Time between the contact of two consecutive limbs in ground	$IC_{i+1} - IC_i$	Seconds
Stride duration	Duration of one gait cycle, i.e., the interval between two sequential initial contacts on the ground by the same limb	$IC_{i+2} - IC_i$	Seconds
Stance phase duration	Duration of stance phase or ratio of stance phase duration with stride duration	$\frac{(FC_{i+1} - IC_i) \times 100}{Stride\ duration}$	Seconds or percentage
Swing phase duration	Duration of swing phase or ratio of swing phase time with stride duration	$\frac{(StrideTime_{i+1} - StanceTime_i) \times 100}{Stride\ duration}$	Seconds or percentage
Double support phase duration	Interval of time of the double support phase or ratio of double support phase duration with stride duration	$\frac{(IC_{i+1} - FC_i) \times 100}{Stride\ duration}$	Seconds or percentage
Step length	Distance that one part of the foot moves in front of the same part of the other foot during each step	$2\sqrt{2Lh - h^2}, h = \iint_{IC_i}^{IC_{i+1}} acceleration_{vertical}$	Meters
Stride length	Distance between two consecutive initial contacts on the ground by the same limb	$step\ length_i + step\ length_{i+1}$	Meters
Velocity	Distance covered by the whole body in a given time	$\frac{step\ length_i}{step\ duration_i}$	Meters per second
Cadence	Number of steps taken in a specific time	$\frac{velocity_i \times 60}{step\ length_i}$	Steps per minute
ROM	Range of the signals	$max\left(acceleration_{x,y,z}\right) - \min\left(acceleration_{x,y,z}\right)$	Meters per second squared
RMS	Relates to the vibration levels of a signal	$rms\left(acceleration_{x,y,z}\right)$	Meters per second squared
JERK	First time derivative of acceleration	$diff\left(acceleration_{x,y,z}\right)$	Meters per second cubed

ROM: range of motion; RMS: Root mean square.

Figure 4-5 is a representation of the gait cycle of a healthy subject, for easier interpretation of the concepts.

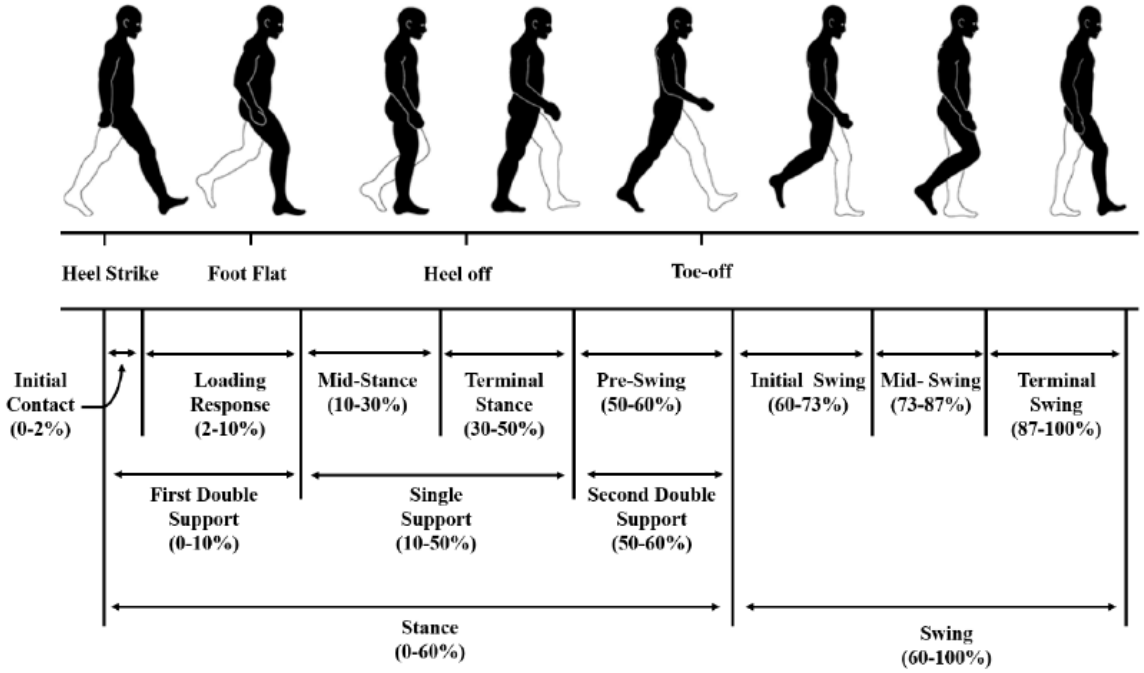


Figure 4-5 - Gait cycle of a healthy subject.

When the participant is exposed to virtual environments intended to assess motor performance, temporal metrics, such as step duration, are expected to increase and spatial metrics, including step length and velocity, to decrease, as these patients tend to present a more cautious behaviour in performing these tasks, leading to slower and smaller steps [2], [12], [20]

Conversely, when biofeedback is used, temporal metrics are expected to decrease, and spatial metrics are expected to increase, i.e., more stable gait pattern, faster, and bigger steps [1], [13]–[15], [17].

4.4 BIOFEEDBACK INTEGRATION

Regarding biofeedback strategies, two modalities were developed, one in open loop and the other in closed loop, which are explained below.

4.4.1 OPEN LOOP STRATEGY

The biofeedback strategy for virtual scenario 1, corridor with dices, consisted of using visual cues that indicated the path to be taken by the hand with the dice, from the initial location of the dice to the corresponding coloured box. To this end, arrows were drawn in the air, in the colour of the corresponding

dice, to help the user to turn. Arrows were chosen because they represent direction and movement, trying to facilitate the turning of the body. Each set of arrows displayed the colour relative to the playing dice so that the user would not be confused about which dice is carrying. This strategy is intended to make turning a more fluid and easier task, by providing visuospatial cueing information. **Figure 4-6** presents the strategy mentioned.

Figure 4-6 - Biofeedback strategy for scenario 1.

4.4.2 CLOSED LOOP STRATEGY

The closed-loop biofeedback strategy was achieved by the **communication protocol between MVN Analyze Pro and Unity**, using the **real-time IC/FC detection algorithm** (**Section 4.3.1**).

This way, the strategy for virtual scenarios 2 (virtual door) and 3 (narrow spaces) consisted of presenting visual cues on the floor in front of the user in a closed loop. In this case, it was chosen to use footprints since they show relevance in the gait. The green was chosen since the eye is most sensitive to a yellowish-green colour under normal lighting conditions [35], [36] and, beyond that, green is related to "being right", "proceeding", unlike de colour red, as in traffic lights. Thus, when the user places the right foot on the floor, a right IC or heel strike is detected, and the system will place a left green footprint to serve as a spatial guideline, indicating where to place the left foot. On the contrary, once the user places the left foot on the floor, a left IC or heel strike is detected, and the right green footprint is displayed. Therefore, a more fluid and continuous gait is motivated. **Figure 4-7** shows a green footprint of the right foot after detection of a heel strike from the left foot.

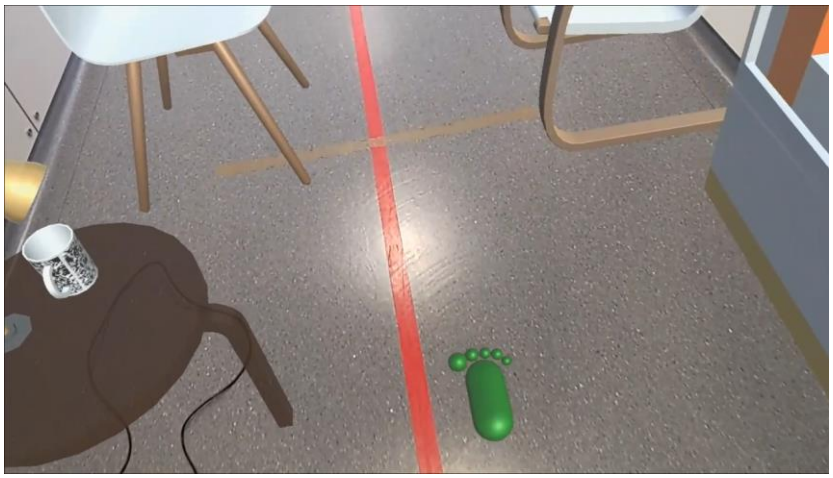


Figure 4-7 – Display of the right green footprint.

4.5 Conclusions

This chapter has presented the methods used to implement a modular, user-customised, mixed reality-based technology solution that (1) immerses patients in environments that cause PD-related gait impairments; and (2) immerses patients in environments that help overcome these impairments with the aid of HoloLens 2, Xsens and biofeedback strategies (**RQ2**).

The virtual environments and tasks were defined, having developed three different environments that aimed to represent the real-life situations that most cause PD-gait disabilities in PD patients, namely (1) turning (scenario 1); (2) walking through doors (scenario 2); and (3) walking in narrow spaces (scenario 3).

Regarding biofeedback strategies, arrows and footprints were added to the virtual environments, and it would be expected that the user would follow these visual cues. The footprints were provided in closed loop, i.e. as the user walks, more footprints will appear which are activated by the occurrence of ICs. Thus, when the user puts one foot on the ground, the HoloLens projects the footprint relative to the opposite foot in order to promote a more continuous and fluid gait. To make this possible, an algorithm was developed to detect ICs and FCs in real time, based on adaptive thresholds.

Furthermore, a MATLAB code was developed for the estimation of spatiotemporal metrics in offline, so that it was possible to evaluate the motor performance after exposure to the virtual environments and after exposure to the biofeedback strategies in these patients.

5 SOLUTION VALIDATION

This chapter describes the methodologies for validating the solution. Firstly, the protocol used in the validation of the mixed reality strategies with individuals with PD is presented. This validation protocol followed a pre-post experimental study design aiming to evaluate the subjects' motor performance. The participants and their characteristics are specified, as well as the inclusion and exclusion criteria. Next, the materials used in the intervention are described, followed by the data acquisition methods and the study variables. The data processing conducted to achieve the intended outcomes measures is exposed, as well as the statistical analysis performed. Finally, the results obtained are presented, as well as a detailed discussion of them, answering **RQ3**.

5.1 Introduction

5.1.1 Hypothesis, research question and study design

PD is currently incurable, so its treatment consists of applying interventions that slow down the rapid progression of the disease. The mixed reality strategies developed in this dissertation aim to bring the day-to-day reality of the patient closer to the medical appointment. In fact, it becomes critical that these patients are correctly and objectively assessed, since disease progression is very fast. In addition, it is intended to verify whether this strategy could complement rehabilitation sessions, through a more fun and disease-focused training, using visual cues, with the aim of improving their mobility and autonomy.

In that sense, the research question to be answered is **RQ3**: "How does the implemented modular technological solution, based on mixed reality integrated with a motion tracking system and with biofeedback strategies, affect the motor performance of PD patients during assessment and training?"

The study in question consisted of a **cross-sectional study** as an observation of a defined population was conducted at a single point in time. Exposure to the intervention and outcome were determined simultaneously [40].

5.2 Methodology

The validation protocol with pathological end-users was conducted in Hospital of Braga, with the collaboration of the physicians from 2CA-Braga, following the principles of the Declaration of Helsinki and the Oviedo Convention, in accordance with the ethical guidelines of the Ethics Committee in Life and Health Sciences (CEICVS 147/2021). All participants filled out an informed consent to participate in the current research.

5.2.1 PARTICIPANTS

Eleven subjects (six females and five males) were recruited and accepted to participate in this data collection. A list of **inclusion and exclusion criteria** was outlined in order to select the participants. Participants were recruited if they had: **I)** diagnosis of PD according to the UK Parkinson's Disease Society Brain bank criteria; **II)** presence of freezing of gait; **III)** Hoehn and Yahr stage between 1 and 4; **IV)** age between 45 and 85 years old; and **V)** able to walk without assistance. Exclusion criteria were: **I)** presence of comorbid disorders likely to affect gait, including stroke, orthopaedic disease, rheumatologic disease, other neurological and musculoskeletal disorders, cardiovascular and pulmonary diseases; **II)** significative cognitive impairment (MMSE<24); **III)** obvious motor impairments; **IV)** visual acuity deficits; **V)** audiometric deficits; **VI)** pain that may affect walking; and **VII)** inability to perform a 180° turn without assistance. **Table 5-1** presents the participants' detailed clinical characteristics and anthropometrics.

Table 5-1 - Demographic information about the PD participants

Participant ID	Gender (M/F)	Age (years)	Body height (cm)	Body mass (kg)	Clinical State	NFoG-Q	UPDRS, Part III	H&Y
PD-f 01	F	74	160	62	ON	27	66	4
PD-f 02	F	48	166	65	ON	24		4
PD-f 03	F	67	164	73	ON	24	71	3
PD 04	F	59	155	71	ON	0	18	2
PD 05	M	75	168	80	ON	0	12	2
PD-f 06	M	71	163	85	ON	24	19	2
PD-f 07	M	65	172	60	ON	25	15	1
PD-f 08	F	70	163	77	ON	13	22	2
PD-f 09	F	47	169	64	ON	12	14	1
PD-f 10	M	83	160	75	ON	26	57	4
PD-f 11	M	84	162	62	ON	26	42	3
Mean (±STD)	-	67.55 (± 11.71)	163.82 (± 4.55)	70.36 (± 7.96)	-	18.28 (± 9.88)	31.86 (±22.03)	2.29 (±1.08)

ID: identification; PD: individual with Parkinson's disease; PD-f: individual with Parkinson's disease and freezing of gait; M: male; F: female; NFoG-Q: New freezing of gait questionnaire; UPDRS-III: Unified Parkinson's disease rating scale – part III; H&Y: Hoehn and Yahr scale; STD: standard deviation.

5.2.2 MATERIALS

The materials used in the validation phase were the HoloLens 2 mixed reality smart glasses and the Xsens motion tracking system. In addition, a document recording the participants' demographic and clinical information was also used. HoloLens 2 was used to display the virtual environments and to provide the visual cues (arrows and green footprints). In turn, Xsens was used to stream inertial data to Unity at

maximum stream rate. In Unity, the real-time IC/FC detection algorithm script was added to provide on-demand visual biofeedback. Later, data from Xsens was used to estimate spatiotemporal metrics in MATLAB. **Table 5-2** outlines the equipment used during the validation phase, as well as the purpose, metrics and software of each material. **Figure 5-1** shows all equipment and software used, by acquisition protocol and how they interact with each other.

Table 5-2 Material used, its purpose, metrics and its software

Material	Purpose	Metrics	SW
Demographic registration document	Write down the demographic and clinical information of the participants		Microsoft Excel
HoloLens 2	Create virtual-augmented environments	FoG, bradykinesia, hypokinesia, akinesia, rigidity, festination	Visual Studio 2022
	Delivering visual cues	FoG	
Xsens	Gait kinematic data	FoG, bradykinesia, hypokinesia, akinesia, festination	MVN Analyze Pro
	Detect initial and final contacts	FoG	Visual Studio 2022

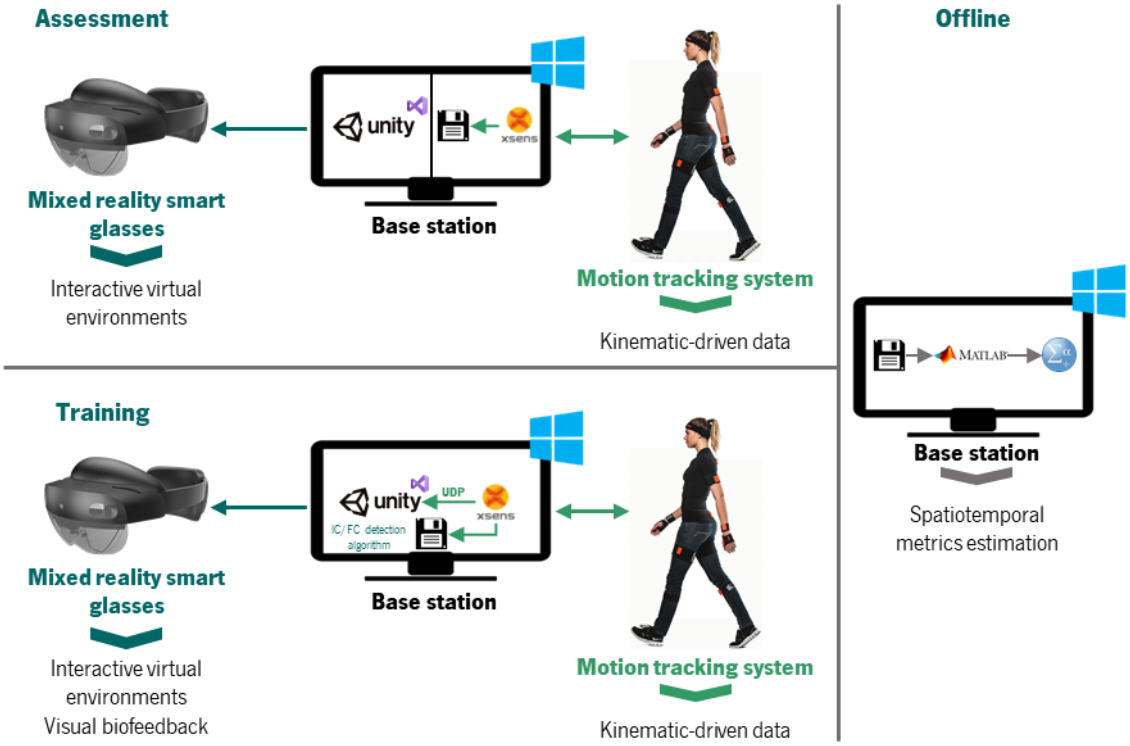


Figure 5-1 – Outline of the system, equipment and software used and how they interact.

5.2.3 DATA COLLECTION METHODS

In order to acquire the dataset that will allow testing the hypothesis under analysis, a protocol was outlined describing the participant selection criteria, the tasks to be followed and the evaluation to be carried out, **Appendix A – Experimental Protocol**. **Figure 5-2** presents a diagram of the steps followed throughout the experimental protocol.

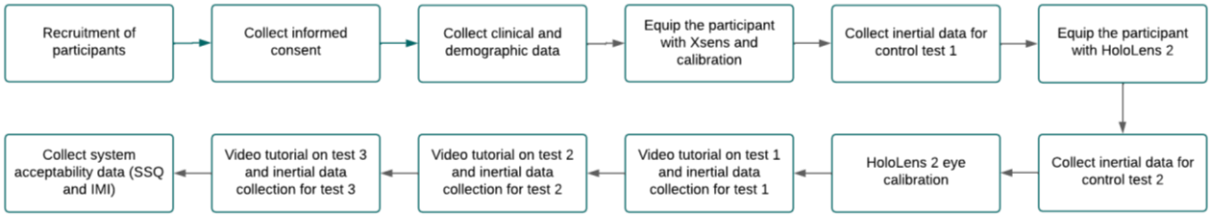
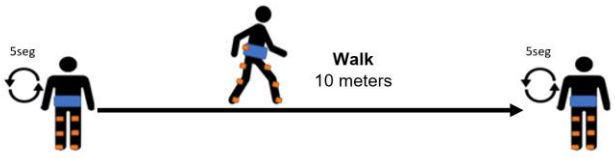
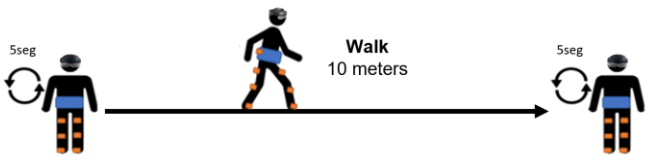


Figure 5-2 - Diagram representing the various steps of the experimental protocol.

The first step of the experimental protocol consisted of **selecting and recruiting volunteers**. Subsequently, **informed consents** were obtained, and the **clinical** (NFoG-Q, UPDRS-III, and H&Y) **and demographic data** (gender, age, height, weight) of each participant were collected.

The next step was to **equip the participant** with the Xsens acquisition system in the lower body configuration and proceed to **calibrate** it. After a successful calibration, the **first control test (TC1)** was performed, which consisted in walking in a straight line for 10 meters. It should be noted that all the tests were performed twice. Then, the HoloLens was placed, and the **second control test (TC2)** was carried out, which consisted of walking 10 meters in a straight line, with the glasses on but disconnected (represented in **Table 5-3**). The HoloLens was then connected and calibrated.

Table 5-3 - Control tests 1 and 2 and representation of their tasks

Test	Task
TC1	
TC2	

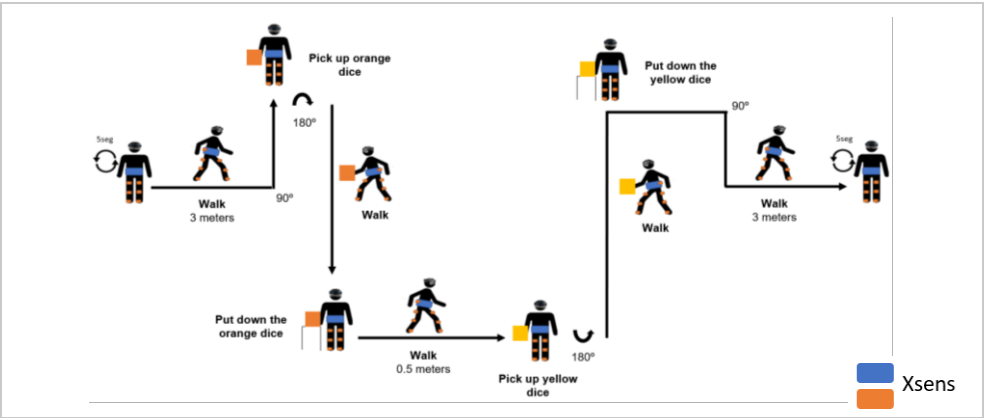
The next phase consisted of showing a **video tutorial** (**Figure 5-3**) explaining how to interact with a virtual playing dice, which was referred to as the **familiarisation phase (FP) (Figure 5-3)**. Next, a virtual environment was placed that contained two tables and a dice. In this environment the participant was encouraged to interact with the dice: increase and/or decrease the size, rotate it, and move it.

Tutorial FP

Figure 5-3 - Tutorial video shown to the participants and familiarization phase performed by the patient 7.

After the familiarisation phase the tests for data acquisition began. A tutorial video explaining the tasks to be performed in the first virtual environment was shown and then the virtual environment was placed on HoloLens and the participant performed the test. This test aimed to study the "turning" event of these patients, since this is a task that we perform on a regular and daily basis, and it is a trigger for gait freezing episodes. In this way, this **monitoring test 1 (M1)** was performed twice and then the same test but using biofeedback (visual cues, arrows), that is, **training test 1 (T1)**, also twice. The tasks to be completed are shown in **Table 5-4**.

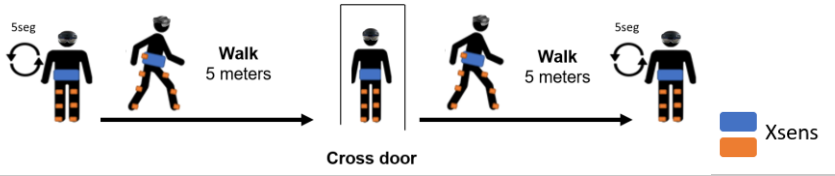
Table 5-4 - Monitoring and Training tests 1 and representation of the respective tasks

Test	Task
M1/T1	

Following test 1, a video tutorial representing the virtual environment 2 and the task to be completed was shown (**Table 5-5**). Then, the participant performed the test, which consisted in walking in a straight line, passing through a virtual door, placed in the middle of the 10-meter corridor, first without biofeedback (**monitoring test 2 (M2)**) and, later, with the visual cues (**training test 2 (T2)**), namely the green

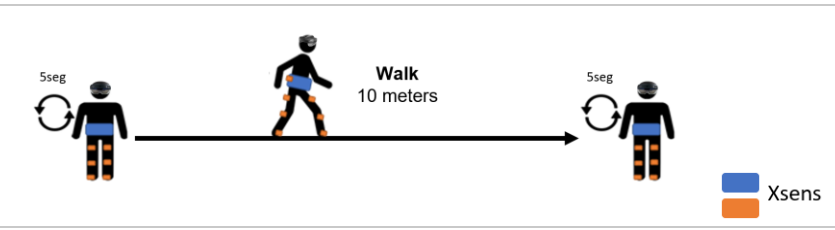
footprints provided in closed loop when foot contacts were detected. Each test was performed twice for a higher statistical significance during movement evaluation.

Table 5-5 - Monitoring and Training tests 2 and representation of the respective tasks

Test	Task
M2/T2	

Finally, a video tutorial of the virtual environment 3 was shown and the patient performed the test, first without visual cues (**monitoring test 3 (M3)**) and later with biofeedback (**training test 3 (T3)**). The task of environment 3 (represented in **Table 5-6**) consisted of walking straight to the finish line, passing through narrow places, always trying not to step on the virtual objects.

Table 5-6 - Monitoring and Training tests 3 and representation of the respective tasks

Test	Task
M3/T3	

After all the tests had been carried out, the equipment was removed from the participant.

Finally, the participants answered two acceptability questionnaires, namely the **Simulator Sickness questionnaire (SSQ)** and the **interest/enjoyment and value/usefulness subscales** of the **Intrinsic Motivation Inventory (IMI)**. The SSQ assesses the levels of symptoms associated with simulator sickness, i.e., assesses any adverse effects from exposure to the virtual environments, it detects changes in symptoms, such as nausea, oculomotor discomfort or disorientation. Participants answered each of the 16 questions based on the severity of symptoms they experienced using a four-point scale from 'none' to 'severe' (0–3) [12], [20], [25], [26], [28], [41]. In turn, the IMI questionnaire assesses participants' subjective sense of interest and value of the experience [25], [42]. This scale was scored on a seven-point Likert scale. Subscale scores were calculated by averaging across all items on each subscale and a higher score indicates a greater contribution from the concept described in the referred

subscale [25]. Three items on each subscale were customized to make them specific to this case, and an overall IMI score was calculated by averaging the subscales mean values. A formal statistical analysis of these metrics was not performed because the main interest was to use the scores for a qualitative evaluation of the mixed reality tool. The registration documents of the responses to both these questionnaires are in **Appendix B – Subjective questionnaires**.

5.2.4 Study Variables

To assess motor performance, some spatiotemporal metrics were calculated for all the tests performed. **Table 5-7** shows the metrics calculated as well as what is expected to happen after the **(1) monitoring tests, in relation to the control tests** and **(2) training tests, in relation to the respective monitoring tests**, based on [1], [2], [12]–[15], [17].

Table 5-7 - Spatiotemporal metrics and what is expected to happen to them in the different tests

Spatiotemporal Metric	*Monitoring tests M2 and M3*	*Training tests T1*	*Training tests T2 and T3*
Step duration	↑	-	↓
Stride duration	↑	-	↓
Stance phase duration	↑	-	↓
Swing phase duration	↓	-	↑
Double support phase duration	↑	-	↓
Step length	↓	-	↑
Stride length	↓	-	↑
Velocity	↓	-	↑
Cadence	↑	-	↓
ROM	-	↑	-
RMS	-	↑	-
JERK	-	↓	-

5.2.5 Data Analysis

The patients' kinematic data were used not only for the presentation of the visual cues but also for the **estimation of the spatiotemporal metrics** that will allow answering the hypotheses and RQs of the study. Thus, once the acquisition of the required data was completed, all trials were saved, and **pre-processing** of the acquired data was carried out before estimating the spatiotemporal metrics. This is a crucial step as it allows to eliminate irrelevant information.

For that purpose, firstly the Xsens mvn files were exported to **mvnx files** in the MVN Analyze Pro software so that it would be possible to analyse them later in MATLAB. Thus, several signals were visualised in MATLAB: angular velocity in y, linear velocity in z and foot contacts, from both feet sensors; and these were analysed in order to select the zones that are of interest to study, that is, **the region of interest (ROI)**.

In the case of the forward **walking tests**, namely, control tests (TC1, TC2), monitoring tests of scenarios 2 and 3 (M2, M3) and training tests of scenarios 2 and 3 (T2, T3), the FoG episodes and the initial and final moments of each acquisition were eliminated in order to maintain the region in which the patient is effectively walking.

In turn, in the **turning tests**, M1 and T1, the turning events were selected, i.e., two moments per test were selected, the turning to the left and the turning to the right, which corresponded to carrying the orange and yellow dice from their starting location to the final box.

After the ROIs were saved, the **spatiotemporal metrics were estimated based on IC/FC detections of foot contact signals**, also in MATLAB, and then **statistical analysis** was performed. **Figure 5-4** represents a diagram describing the various steps taken during data analysis.

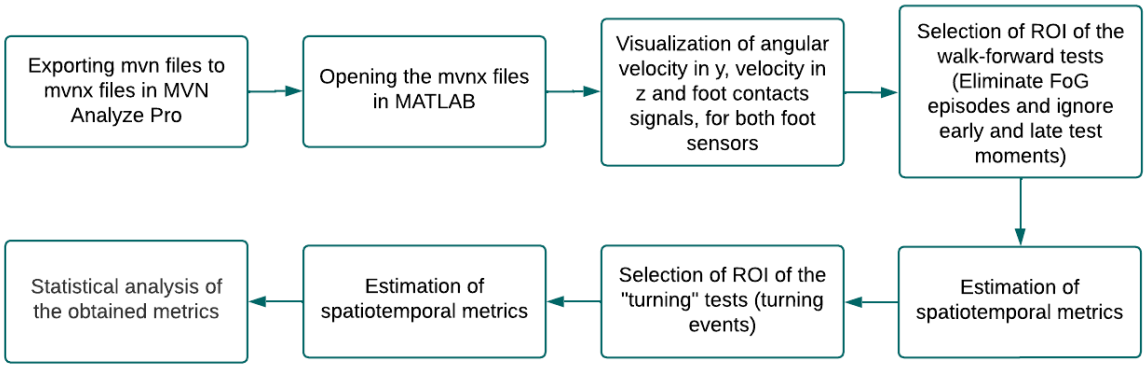


Figure 5-4 - Diagram representing the various steps of the data analysis.

5.2.6 STATISTICAL ANALYSIS

The statistical analysis was performed through **IBM SPSS software version 25.0** (for Windows) (IMP Corp, Armonk, NY, USA). Firstly, **descriptive statistics** were obtained to summarise the results (means and standard deviations) for each group and the **data normality** was assessed using **Shapiro-Wilk test**. The population was considered normally distributed if the significance value was higher than 0.05. This study presents **paired samples** as the samples are from the same participants, **Table 5-8**. In this sense, to compare two paired groups, paired t test was performed for the parametric metrics and the Wilcoxon signed-rank test was applied to variables where the assumption of normality was not verified. When more than two paired groups were to be compared, repeated-measures ANOVA was used for normal populations, on the contrary, the Friedman test was used for non-normal variables.

All statistical tests were executed considering a confidence level of 95% ($\alpha = 0.05$). The statistical tests were conducted to evaluate the following **null hypothesis (H0): "there are statistically significant differences between interventions"**. If *p*-value<0.05, the H0 is accepted.

Table 5-8 - Parametric and non-parametric tests

	Type of data	
Goal	**Measurement (of normal populations)**	**Order, result or measure (of non-normal populations)**
Compare two pared samples	Paired t test	Wilcoxon test
Compare more than two pared samples	Repeated-measures ANOVA	Friedman test

5.3 RESULTS

This subchapter aims to present the results from the validation protocol with PD patients. The results are divided into three sections. Firstly, the results concerning the motor assessment are presented, followed by the results related to the motor training. In addition, the results of freezing gait episodes (number and duration) per test are shown. Finally, the answers of the user's experience evaluation tests are depicted.

Eleven patients underwent the tests, with ten patients completing all tests. Patient 10 dropped out due to fatigue/no interest. Most participants successfully completed all the tests provided, in an average duration of 40 minutes.

5.3.1 IMMERSIVE VIRTUAL FRAMEWORK FOR MOTOR ASSESSMENT

Firstly, the aim was to check whether wearing the HoloLens 2 OFF would have any influence on the motor function of these patients. To this end, the TC1 and TC2 tests were compared. Regardless of the outcome of the comparison of these tests, the TC1 was selected to be compared to the other tests for the purpose of results analysis. Next, it was aimed to study the potential of mixed reality to cause PD-gait disabilities by comparing the TC1 with the M2 and, later, the TC1 with the M3.

Thus, the first step of the statistical analysis was to perform a descriptive analysis by test. The results of this step are shown in **Table 5-10**, for control tests 1 and 2 (TC1, TC2) and monitoring tests 2 and 3 (M2 and M3).

Afterwards, the normality of the features was verified using the Shapiro-Wilk test. As most of the features did not show a normal distribution, the **Wilcoxon test** was chosen for comparison of two paired samples. The results of this test are also shown in **Table 5-10**, in which the difference of a certain feature between the several tests is considered significant if the significance value is smaller than 0.05 and these are in bold.

Regarding **control tests TC1 and TC2**, only a few metrics, namely, step and stride length, velocity and AS swing time, presented statistically significant differences, since the p-value < 0.05, corroborating the null hypothesis. Afterwards, the **comparison between TC1 and M2** showed statistically significant differences in the metrics step and stride duration, stance, swing and double support phase, velocity, SD step and stride duration, SD stance and swing phase, SD step length, SD cadence and AS stance and swing time, corroborating the null hypothesis. Finally, the **comparison between TC1 and M3** showed statistically significant differences in almost all metrics, so the null hypothesis is corroborated. All these metrics are in bold.

Throughout data acquisition, the researchers visually assessed the existence of gait freezing episodes. Later, during data processing, these episodes were excluded and their number, average and total duration were counted per test. The results are presented in **Table 5-9**.

Figure 5-5 presents two QR codes showing videos of patient 7 performing tests M2 and M3.

Table 5-9 - Number, average and total duration os freezing of gait episodes in control tests and monitoring tests 2 and 3

Test	Number of episodes	Average duration (s)	Total duration (s)
TC1	0	0	0
TC2	0	0	0
M2	4	6.73	74
M3	0	0	0

Figure 5-5 – Videos of participant 7 performing the M2 and M3 tests.

Table 5-10 - Spatiotemporal metrics and their descriptive statistics, Shapiro-Wilk test and Wilcoxon test for control tests and scenarios 2 and 3

	TC1			TC2			Wilcoxon Test (sig)	M2			Wilcoxon Test (sig)	M3			Wilcoxon Test (sig)
Metric	Mean	Std deviation	Shapiro-Wilk (sig)	Mean	Std deviation	Shapiro-Wilk (sig)	(TC1-TC2)	Mean	Std deviation	Shapiro-Wilk (sig)	(TC1-M2)	Mean	Std deviation	Shapiro-Wilk (sig)	(TC1-M3)
Step duration	0.618	0.087	0.298	0.618	0.082	0.144	0.811	0.740	0.233	0.254	**0.022**	0.812	0.360	0.001	**0.003**
Stride duration	1.236	0.176	0.345	1.235	0.165	0.122	0.868	1.478	0.472	0.218	**0.025**	1.615	0.722	0.001	**0.005**
Stance phase	62.057	3.047	0.168	62.688	3.295	0.081	0.053	67.056	5.887	0.383	**0.000**	67.360	7.848	0.002	**0.000**
Swing phase	37.943	3.047	0.168	37.312	3.295	0.081	0.053	32.914	5.937	0.361	**0.000**	32.640	7.848	0.002	**0.000**
Double support phase	24.196	6.104	0.170	25.508	6.550	0.102	0.058	34.562	12.255	0.247	**0.000**	34.442	16.290	0.001	**0.000**
Step length	0.568	0.096	0.378	0.519	0.135	0.022	**0.004**	0.509	0.165	0.075	0.053	0.500	0.127	0.613	**0.003**
Stride length	1.143	0.199	0.265	1.046	0.257	0.033	**0.005**	1.019	0.344	0.108	0.053	0.994	0.258	0.596	**0.004**
Velocity	0.934	0.198	0.226	0.853	0.218	0.047	**0.012**	0.750	0.275	0.128	**0.002**	0.702	0.215	0.273	**0.000**
Cadence	99.395	13.881	0.149	99.988	13.399	0.035	0.744	95.866	27.003	0.399	0.396	89.104	21.928	0.042	**0.006**
SD step time	0.040	0.022	0.000	0.055	0.059	0.000	0.616	0.222	0.274	0.000	**0.001**	0.240	0.370	0.000	**0.002**
SD stride time	0.055	0.037	0.000	0.076	0.090	0.000	0.828	0.307	0.370	0.000	**0.002**	0.317	0.447	0.000	**0.003**
SD stance time	0.045	0.026	0.000	0.068	0.092	0.000	0.616	0.280	0.344	0.000	**0.001**	0.259	0.396	0.000	**0.002**
SD swing time	0.031	0.022	0.000	0.037	0.033	0.000	0.557	0.101	0.101	0.000	**0.005**	0.147	0.202	0.000	**0.003**
SD step length	0.139	0.067	0.049	0.119	0.052	0.043	0.184	0.180	0.102	0.043	**0.039**	0.159	0.105	0.001	0.420
SD stride length	0.182	0.121	0.002	0.134	0.089	0.000	0.145	0.252	0.166	0.072	0.133	0.211	0.171	0.002	0.528
SD velocity	0.229	0.119	0.008	0.191	0.084	0.087	0.170	0.247	0.126	0.259	0.396	0.204	0.125	0.004	0.231
SD cadence	6.170	2.530	0.002	7.453	5.207	0.001	0.500	19.854	19.948	0.000	**0.004**	13.895	15.022	0.000	**0.039**
AS step time	0.034	0.023	0.092	0.032	0.022	0.299	0.695	0.114	0.179	0.000	0.231	0.136	0.173	0.000	**0.017**
AS stride time	0.009	0.011	0.000	0.005	0.006	0.001	0.316	0.026	0.051	0.000	0.446	0.033	0.068	0.000	0.758
AS stance time	0.018	0.016	0.038	0.027	0.030	0.002	0.085	0.048	0.057	0.000	**0.031**	0.069	0.119	0.000	0.078
AS swing time	0.011	0.016	0.000	0.031	0.033	0.000	**0.004**	0.047	0.062	0.000	**0.011**	0.094	0.140	0.000	**0.008**
AS step length	0.112	0.079	0.053	0.121	0.092	0.044	0.777	0.102	0.071	0.080	0.845	0.109	0.077	0.058	0.983
AS stride length	0.043	0.043	0.002	0.026	0.031	0.001	0.085	0.038	0.040	0.003	0.586	0.039	0.043	0.002	0.472
AS velocity	0.176	0.130	0.023	0.184	0.132	0.111	0.349	0.159	0.090	0.103	0.913	0.173	0.104	0.158	0.616
AS cadence	5.546	3.910	0.241	5.768	3.701	0.176	0.557	7.072	8.293	0.000	0.845	9.726	7.091	0.006	0.071

5.3.2 IMMERSIVE VIRTUAL FRAMEWORK FOR MOTOR TRAINING

This subchapter presents the results of the biofeedback contribution to motor performance, i.e., tests **M1 with T1 (dice)**, **M2 with T2 (door)** and **M3 with T3 (narrow spaces)** were compared. Thus, a descriptive analysis per test was first performed and then the normality of the features was studied, using Shapiro-Wilk test. As most of the metrics did not present a normal distribution, the **Wilcoxon test** was used for comparison of two paired samples. The results of these tests are shown in **Table 5-12**, **Table 5-13** and **Table 5-14**, in which the difference of a certain feature between the several tests is considered significant if the significance value is smaller than 0.05.

Regarding **scenario 1**, no metrics showed statistically significant differences, rejecting the null hypothesis. In turn, **scenario 2** showed that only the metrics step duration, stride duration, velocity, cadence, and SD velocity, presented statistically significant differences, since the p-value < 0.05, corroborating the null hypothesis. Finally, **scenario 3** had two spatiotemporal metrics that showed statistically significant differences, namely step length and cadence. Thus, the null hypothesis is corroborated. All these metrics are in bold.

Throughout data acquisition, the researchers visually assessed the existence of gait freezing episodes. Later, during data processing, these episodes were excluded and their number, average and total duration were counted per test. The results are presented in **Table 5-11**.

Figure 5-6 presents six QR codes showing videos of patient 7 performing tests M1, T1, M2, T2, M3 and T3.

Table 5-11 - Number, average and total duration os freezing of gait episodes in monitoring tests 1, 2, and 3 and training tests 1, 2 and 3

Test	Number of episodes	Average duration (s)	Total duration (s)
M1	0	0	0
T1	0	0	0
M2	4	6.73	74
T2	6	9.78	107.6
M3	0	0	0
T3	4	3.13	34.4

Figure 5-6 - Videos of participant 7 performing tests M1, T1, M2, T2, M3 and T3.

Table 5-12 - Spatiotemporal metrics and their descriptive statistics, Shapiro-Wilk test and Wilcoxon test for scenario 1

	M1			T1			Wilcoxon Test (sig)
Metric	Mean	Std deviation	Shapiro-Wilk (sig)	Mean	Std deviation	Shapiro-Wilk (sig)	
ROM X (+)	3.630	1.427	0.049	3.472	1.269	0.002	0.390
ROM Y (+)	3.616	1.279	0.050	3.241	0.851	0.266	0.372
ROM Z (+)	4.720	3.046	0.000	3.985	3.422	0.000	0.168
RMS X (+)	0.478	0.217	0.003	0.508	0.214	0.018	0.178
RMS Y (+)	0.480	0.180	0.195	0.491	0.149	0.279	0.615
RMS Z (+)	0.380	0.157	0.092	0.383	0.222	0.001	0.833
JERK X (-)	0.002	0.006	0.007	0.001	0.005	0.005	0.158
JERK Y (-)	0.002	0.004	0.013	0.000	0.003	0.502	0.123
JERK Z (-)	0.000	0.004	0.054	0.001	.003	0.041	0.661

Table 5-13 - Spatiotemporal metrics and their descriptive statistics, Shapiro-Wilk test and Wilcoxon test for scenario 2

	M2			T2			Wilcoxon Test (sig)
Metric	Mean	Std deviation	Shapiro-Wilk (sig)	Mean	Std deviation	Shapiro-Wilk (sig)	
Step duration	0.758	0.228	0.274	0.848	0.298	0.000	**0.031**
Stride duration	1.513	0.463	0.230	1.696	0.606	0.000	**0.028**
Stance phase	67.517	5.724	0.536	69.522	5.243	0.393	0.064
Swing phase	32.451	5.775	0.505	30.478	5.243	0.393	0.071
Double support phase	35.519	11.918	0.252	38.728	10.415	0.524	0.170
Step length	0.518	0.165	0.093	0.499	0.189	0.135	0.948
Stride length	1.038	0.345	0.135	0.991	0.408	0.045	0.777
Velocity	0.747	0.283	0.118	0.630	0.268	0.008	**0.016**
Cadence	93.068	25.000	0.319	79.108	15.118	0.282	**0.002**
SD step time	0.227	0.282	0.000	0.209	0.257	0.000	0.446
SD stride time	0.315	0.380	0.000	0.285	0.278	0.000	0.327
SD stance time	0.292	0.351	0.000	0.261	0.255	0.000	0.332
SD swing time	0.098	0.103	0.000	0.118	0.146	0.000	0.231
SD step length	0.182	0.104	0.070	0.168	0.092	0.006	0.647
SD stride length	0.254	0.171	0.087	0.210	0.135	0.004	0.586
SD velocity	0.246	0.130	0.181	0.197	0.127	0.000	**0.028**
SD cadence	18.870	20.107	0.000	13.568	7.317	0.003	0.557
AS step time	0.118	0.183	0.000	0.090	0.075	0.044	0.616
AS stride time	0.027	0.053	0.000	0.025	0.029	0.002	0.845

AS stance time	0.048	0.058	0.000	0.064	0.102	0.000	0.983
AS swing time	0.047	0.063	0.000	0.060	0.119	0.000	0.286
AS step length	0.104	0.072	0.145	0.134	0.100	0.133	0.184
AS stride length	0.040	0.040	0.005	0.039	0.044	0.000	0.647
AS velocity	0.158	0.092	0.077	0.159	0.113	0.241	0.586
AS cadence	7.044	8.547	0.000	7.023	4.985	0.032	0.913

Table 5-14 - Spatiotemporal metrics and their descriptive statistics, Shapiro-Wilk test and Wilcoxon test for scenario 3

	M3			**T3**			**Wilcoxon test (sig)**
Metric	Mean	Std deviation	Shapiro-Wilk (sig)	Mean	Std deviation	Shapiro-Wilk (sig)	
Step duration (-)	0.762	0.229	0.022	0.821	0.398	0.000	0.147
Stride duration (-)	1.512	0.449	0.023	1.627	0.746	0.000	0.147
Stance phase	67.644	7.198	0.001	66.531	3.850	0.223	0.520
Swing phase	32.356	7.198	0.001	33.469	3.850	0.223	0.520
Double support phase	35.295	15.152	0.001	33.065	8.002	0.232	0.314
Step length (+)	0.483	0.107	0.418	0.544	0.128	0.229	**0.044**
Stride length (+)	0.960	0.217	0.539	1.071	0.263	0.146	0.070
Velocity (+)	0.693	0.191	0.652	0.744	0.263	0.686	0.841
Cadence	89.330	16.968	0.027	83.140	19.546	0.290	**0.024**
SD step time	0.192	0.303	0.000	0.161	0.236	0.000	0.811
SD stride time	0.277	0.393	0.000	0.199	0.239	0.000	0.809
SD stance time	0.220	0.343	0.000	0.203	0.324	0.000	0.936
SD swing time	0.122	0.164	0.000	0.123	0.215	0.000	0.841
SD step length	0.144	0.098	0.000	0.162	0.106	0.001	0.421
SD stride length	0.184	0.163	0.000	0.212	0.178	0.000	0.314
SD velocity	0.190	0.108	0.003	0.209	0.135	0.001	0.904
SD cadence	13.360	15.084	0.000	9.254	4.855	0.087	0.445
AS step time	0.124	0.174	0.000	0.136	0.294	0.000	0.421
AS stride time	0.030	0.070	0.000	0.037	0.103	0.000	0.557
AS stance time	0.047	0.078	0.000	0.142	0.403	0.000	0.445
AS swing time	0.069	0.097	0.000	0.115	0.300	0.000	0.825
AS step length	0.118	0.073	0.111	0.111	0.104	0.013	0.398
AS stride length	0.027	0.028	0.005	0.049	0.077	0.000	0.227
AS velocity	0.173	0.103	0.273	0.140	0.107	0.008	0.122
AS cadence	8.772	6.882	0.000	7.226	6.754	0.008	0.277

5.3.3 SSQ AND IMI QUESTIONNAIRES

At the end of data acquisition, participants completed the aforementioned acceptability questionnaires, SSQ and IMI (**Appendix B – Subjective questionnaires**). **Table 5-15** presents the results of these questionnaires.

Table 5-15 - SSQ and IMI questionnaires results

Participant ID	SSQ	IMI	
		Interest/Enjoyment subscale	Value/Usefulness subscale
PD-f 01	4	5.67	5.33
PD-f 02	3	5.67	5.33
PD-f 03	4	7	6.33
PD 04	0	7	5.67
PD 05	0	7	7
PD-f 06	4	5.33	7
PD-f 07	0	7	7
PD-f 08	3	6.67	6.67
PD-f 09	1	7	7
PD-f 10	1	7	6.67
PD-f 11	1	7	6.33
Mean (±STD)	1.91 (± 1.62)	6.58 (± 0.64)	6.39 (± 0.63)
		6.49 (± 0.64)	

5.4 DISCUSSION

This subsection discusses the results obtained in the previous subsection. The analysis is made for both "motor assessment" and "motor training" separately. In addition, a brief discussion is elaborated regarding the occurrence of FoG episodes and also the results of the acceptability questionnaires.

5.4.1 IMMERSIVE VIRTUAL FRAMEWORK FOR MOTOR ASSESSMENT

Looking at the mean values of the metrics of the **two control tests (TC1 and TC2)**, it can be seen that they hardly varied, with the exception of step and stride length and velocity. Actually, the referred metrics plus AS swing time presented statistically significant differences. Thus, it is concluded that the use of HoloLens influences motor performance in the mentioned metrics, even if they are switched off. This may be due to the presence of the HoloLens lenses that are not completely transparent, seeing some reflections.

Virtual environment 2 (doors) showed an increase in the mean values of step and stride duration, and a decrease in step and stride length, velocity, and cadence. These metrics behaved as expected (just like [2]) with the exception of cadence, which should have increased.

In fact, this virtual environment showed fourteen metrics out of twenty-five (step and stride duration, stance, swing and double support phase, velocity, SD step and stride duration, SD stance and swing phase, SD step length, SD cadence and AS stance and swing time) with statistically significant differences

between the control and monitoring tests. This means that the MR technology really disturbed the motor performance of the patients in the way that was expected, due to the presence of virtual objects and especially the virtual door that was able to recreate a real door.

In turn, **virtual environment 3 (narrow spaces)** showed an increase in the mean values of step and stride duration and a decrease in step and stride length, velocity, and cadence. Actually, these metrics behaved as expected with the exception of cadence, which should have increased.

Observing the results of the Wilcoxon test, sixteen out of twenty-five metrics showed statistically significant differences, demonstrating that the MR technology may in fact have triggered PD-gait related disabilities. This may be due to the presence of the various virtual objects that created a narrower corridor than the real corridor, acting as obstacles for the participant, making him take smaller and slower steps.

With regard to the occurrence of FoG episodes, the **monitoring tests should have increased their number and duration**. However, after analysing the results, it was found that monitoring test 2 was the only one that caused these episodes. This may be due to the fact that: (1) disease may be "masked" by medication, causing participants not to suffer from FoG, since data acquisition was performed 1h after medication intake on average, i.e., in "ON" phase; (2) heterogeneity in the origin of FoG, since some participants reported that they suffer from these episodes in stressful situations, other patients suffer right after waking up, as well as, other patients suffer when they are in crowded places.

5.4.2 IMMERSIVE VIRTUAL FRAMEWORK FOR MOTOR TRAINING

Regarding **virtual environment 1 (dices)**, one would expect the average ROM and RMS values to increase and the average JERK values to decrease with the use of the biofeedback strategy. However, by analysing the results one notices that the average ROM values for the three axes decreased, in turn the average RMS values for all axes increased and the same happened for the average JERK values. Thus, only the RMS behaved as expected.

From the results of the Wilcoxon test, no statistically significant differences were found, making it possible to mention that the visual biofeedback strategy, namely the coloured arrows, had no evident impact. This may have occurred because the smart glasses do not have a sufficient field of view (FOV), forcing patients to look in the direction of the floor. Another reason could be that there was little time in contact with the biofeedback strategy.

Virtual environment 2 (doors) showed an increase in the mean values of step and stride duration, a decrease in the mean values of step and stride length as well as a decrease in the mean values of velocity and cadence. Nevertheless, step and stride duration and cadence were expected to decrease,

step and stride length were expected to increase, just as velocity, since this biofeedback strategy aims to improve motor performance, obtaining larger and faster steps.

In fact, this virtual environment showed some metrics (step and stride duration, velocity, SD velocity and cadence) with statistically significant differences between the monitoring and training tests. Thus, biofeedback may have negatively affected these metrics once the mean values behaved contrary to what was expected. This may be due to (1) the participant was left waiting for the footprints, and (2) the real-time IC and FC detection algorithm was not suitable for these patients' gait causing the footprints not to appear right away, increasing their reaction time. On the other hand, the **cadence** values behaved as expected. This may be due to the fact that the footprints indicate spatial information to the participant, i.e., where to place the next foot.

In turn, **virtual environment 3 (narrow spaces)** showed an increase in the mean values of step and stride duration as well as step, stride length and velocity. On the other hand, the cadence decreased its mean value with the use of the footprints. Actually, step and stride length, velocity and cadence behaved as it was expected. On the contrary, step and stride duration should have decreased.

There are two spatiotemporal metrics that showed statistically significant differences, namely **step length and cadence**. This may be due to the intention of the footprints to "force" the participant to be aware of them and to help planning where to place his feet, guiding him to the finish line. In addition, the footprints had a pre-defined distance between them (dependent on the height of the participant), influencing the participant to follow and imitate the visual cues.

In what concerns the occurrence of freezing of gait episodes, the **number and duration of these episodes would be expected to reduce or disappear in the biofeedback training trials**. However, this did not occur and may be due to (1) unfamiliarity with visual cues, as participants reported that they had never interacted with these; (2) reduced field of view of the HoloLens 2 causing participants to sometimes fail to see visual cues.

5.4.3 SSQ AND IMI QUESTIONNAIRES

After analysing the results obtained for the SSQ it was concluded that they did not reflect any symptoms (nausea, disorientation, and oculomotor) after exposure to the virtual environments. Furthermore, no participants verbally indicated that they had symptoms of simulator sickness.

In turn, the results of the IMI questionnaire showed that the system received high ratings on the interest and value subscales. The participants were always happy and willing to participate in the tests,

and some said they would like to see this system in their rehabilitation sessions. Furthermore, a relative of a participant said that virtual environment 1 could be used not only for gait rehabilitation but also to train other symptoms such as tremors in order to decrease them or to keep them from worsening.

5.5 CONCLUSIONS

The validation phase with end users was crucial for the culmination of the project. Excellent results were obtained for the monitoring tests, having been able to provoke PD-related gait disabilities, proving that MR technology is capable of recreating real-life situations which alter PD patients motor performance. On the contrary, the biofeedback tests did not obtain the expected results, which could be due to several reasons: (1) HoloLens do not have a sufficient field of view (FOV), forcing patients to look in the direction of the floor and causing to sometimes fail to see visual cues; (2) unfamiliarity with visual cues; (3) little time in contact with the biofeedback strategy; (4) the real-time IC and FC detection algorithm was not suitable for these patients' gait pattern causing the footprints not to appear right away, increasing their reaction time. Participants reported no symptoms regarding the use of mixed reality and gave high ratings to the value and interest scales.

6 CONCLUSIONS AND FUTURE DIRECTIONS

A modular technological solution based on mixed reality and integrated with a high-technological motion tracking system was developed. The main goal was to design, develop, test, and validate different virtual environments to assess and train PD-related gait impairments using HoloLens 2 and Xsens. Using three specific virtual environments (turning, doorways, and narrow spaces) that trigger PD-related gait impairments, it was hypothesized that patients could be assessed and trained in their daily challenges. Thus, it proposed a new monitoring tool for physicians, by contributing to a more reliable assessment of patients' motor performance when faced with day-to-day motor tasks. Also, this tool integrated on-demand visual cues to provide visual biofeedback and foster motor training. This solution was validated with end-users to test the hypothesis.

After accomplishing the delineated objectives for this project and the respective KPIs, it is possible to answer the formulated research questions presented in Chapter 1:

RQ 1: *How have the VR/AR/MR-based approaches and technologies been applied to support PD patients and how have they been clinically validated?*

This question was answered in **Chapter 2**.

A literature analysis was conducted to access the current existing VR/AR/MR-based approaches and technologies used in PD patients for assessing and training PD-related gait disabilities, as well as how have these strategies been clinically validated. From the research it was concluded that VR/AR/MR-based approaches have been applied mainly in five forms of intervention: assessment, cue-oriented assistance, cue-oriented training, videogame-oriented training, and training. These approaches used various types of equipment, from VR, AR, MR glasses and even a treadmill with a screen and the CAREN system. In addition, they also used acquisition systems to monitor the participant's movement and some used actuation systems to provide visual, auditory, vestibular, or tactile biofeedback. Regarding the validation methods, all studies recruited less than thirty participants and used scales for disease's monitoring, such as H&Y, FOG-Q, MoCA, MMSE, FAB test, PIGD, ABC and UPDRS-III. However, some limitations were identified, such as the fact that the smart glasses were heavy, insufficient number of participants, no usability, safety or feasibility questionnaires, and the lack of control conditions in the protocols, preventing a clear discussion of the results obtained. Overall, it was observed that the main goal of these studies was to immerse patients in virtual environments to assess motor metrics or lead them to perform specific tasks oriented by cues or games.

RQ2: *How to implement a modular, user-customised, mixed reality-based technology solution that immerses patients in environments that (1) cause PD-related gait impairments; and that (2) help overcome these impairments with the aid of a motion tracking system and biofeedback strategies?*

This issue was answered in **Chapters 3** and **Chapter 4**.

Considering what was found in the literature, a modular technological solution was proposed. The HoloLens 2 were used to create the virtual environments and to provide the visual cues. Xsens was the motion tracking system chosen to obtain the kinematic data of the patients' gait and also to detect the occurrence of ICs and FCs in real time, so that biofeedback could be used. Three virtual environments were developed that corresponded to three real-life situations that usually cause disabilities in these patients, namely, turning, walking through doors, and walking in narrow places. The first scenario aimed at having the user carry two dices from one side of the corridor to the other. In the second and third scenarios the user had to walk in a straight line to the finish line, without stepping on the virtual objects. Furthermore, a real-time IC and FC detection algorithm was developed that receives the kinematic data, calculates the first derivatives, enters FSM and searches for the events mentioned and also calculates adaptive thresholds, making this algorithm adaptable intra and inter subject. A code for the estimation of the spatiotemporal metrics was also developed. Two biofeedback strategies were developed, open and closed loop. For scenario 1 the open loop strategy was used, which consisted of arrows of the colours of the dice, which followed the path between the dice and the corresponding box. For scenarios 2 and 3, the closed loop strategy was used, which was achieved by integrating the Xsens with the HoloLens through the real time IC and FC detection algorithm based on adaptive thresholds.

RQ3: *How does the implemented modular technological solution, based on mixed reality integrated with a motion tracking system and with biofeedback strategies, affect the motor performance of PD patients during assessment and training?*

This question was answered in **Chapter 5**.

The results showed that, in fact, mixed reality has the potential to recreate real-life environments that often provoke PD-related gait disabilities, by placing virtual objects on top of the real world.

Regarding biofeedback strategies, these did not bring about the desired effects since the results did not show a significant improvement in the patients' motor performance. This may be due to several factors, including unfamiliarity with visual cues, short time in contact with the biofeedback strategies, insufficient FOV of HoloLens and real-time IC and FC detection algorithm was not suitable for these patients' gait pattern causing the footprints not to appear right away, increasing their reaction time.

However, the user experience evaluation showed that participants enjoyed participating in the activity, they did not report any simulator sickness symptom and they felt that this tool can help their motor performance.

In addition, some limitations of the solution are pointed out: (1) small sample of PD patients, not being representative of the PD population; (2) short test time; (3) no follow up; (4) no control group.

The future work of this dissertation considers some aspects that should be carefully conducted to a further and deeper analysis. The most important refers to the need to integrate these strategies with the +sense waistband in order to obtain a lighter and easier to wear wearable system. This way, patients would be able to use the HoloLens and the waistband without the need to put several sensors on the body. Regarding the experimental protocol, a new phase could be added after the training tests in which the patient walks again without the HoloLens in order to understand whether the visual cues had any effect on walking. Furthermore, in order to better investigate the influence of biofeedback in these patients, other types of biofeedback should be studied, namely auditory and vibrotactile cues. At last, the developed real-time IC and FC detection algorithm should be adjusted to the patients' walking pattern by acquiring more data from several patients, at different stages of the disease.

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APPENDICES

Experimental Protocol

Mixed Reality in Parkinson's Disease

Purpose:

OB1: Study the possibility of using mixed reality as a complementary methodological framework to monitor gait associated disabilities in Parkinson's Disease (PD).

OB2: Study the possibility of using mixed reality as a complementary methodological framework to train gait associated disabilities in PD.

Study design:

- Cross-sectional study.

Local:

- Hospital of Braga – 2CA Braga Academic Clinical Center.

Study chronology:

- **T0:** Patients' selection and recruitment
- **T1:** Experimental procedure
- **T2:** Data analysis
- **T3:** Dissemination

Figure 1 - Study chronology (W: week).

Participants:

- **Number of participants**: 11 participants with PD

Table 1 - Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
- Diagnosis of PD according to the UK Parkinson's Disease Society Brain Bank criteria - Presence of Freezing of Gait (FoG) - Hoen & Yahr scale ≥ 2 and ≤ 4 - Age between 50-85 years old - Able to walk without assistance - No relevant cognitive deficit (MMSE > 24)	- Presence of comorbid disorders likely to affect gait, including stroke, orthopedic disease, rheumatologic disease, other neurological and musculoskeletal disorders, cardiovascular and pulmonary diseases - Cognitive impairment - Obvious motor impairments - Visual acuity deficits - Audiometric deficits - Pain that may affect walking - Inability to perform a 180° turn without assistance

Material:

- Participants demographic registration document
- Hoehn & Yahr scale (H&Y)
- Unified Parkinson's Disease Rating Scale part III (UPDRS-III)
- New Freezing of Gait Questionnaire (NFOG-Q)
- Simulator Sickness Questionnaire (SSQ)
- Intrinsic Motivation Inventory (IMI)
- Mixed reality smartglasses Microsoft HoloLens 2
- Xsens:
    - Lower-body configuration
    - MVN Awinda

Data acquisition and outcomes:

Table 2 - Acquired variables and respective necessary material

Type	**Variables**	**Material**
Demographic	Age [years]	Participants demographic registration document
	Gender [F/M/Non-binary]	
	Weight [Kg]	
	Height [cm]	
Clinic	Disease stage	H&Y
	Motor disability	UPDRS-III
	FoG level	NFOG
Motion	1. 3D motion data 2. Kinematic-driven gait parameters: ▪ Rhythm: step/stride time and stance/swing/double-support phase. ▪ Pace: step/stride length, velocity, and cadence. ▪ Variability: step length/time, velocity, and stance/swing phase standard deviation. ▪ Asymmetry: step length/time, velocity, and stance/swing phase asymmetry. 3. Postural related metrics: ▪ Trunk pitch and roll. ▪ Range of motion. ▪ Root mean square ▪ JERK.	Xsens
Acceptability	Cybersickness	SSQ
	Level of motivation	IMI

2

Experimental procedure:

Step 1. Participant recruitment.

Step 2. Participation informed consent signature.

Step 3. Record and assess participant clinic scales.

Step 4. Record participant demographic data: age, gender, weight, and height.

Step 5. Place Xsens to the participant.

Step 6. Calibrate Xsens.

Step 7. **Perform control test 1 (TC1)** (tables 3 and 4).

Step 8. Put HoloLens 2 on the participant.

Step 9. **Perform control test 2 (TC2)** (tables 3 and 4).

Step 10. Perform the eye calibration process on HoloLens 2.

Step 11. Show video tutorial "Dice".

Step 12. **Perform Familiarization trial (FT)** (table 4 and 5).

Step 13. Show the video tutorial "Scenario 1" (M1) and explain the trial task to be performed (table 3 and 4).

Step 14. **Perform monitoring test (M1) and start data acquisition** (table 3 and 4):

- **a.** Start data acquisition in MVN Analyze Pro.
- **b.** Indicate to the participant to stand still for 5 seconds.
- **c.** Indicate to the participant to perform the explained task.

Step 15. **Finish data acquisition:**

- **a.** Indicate to the participant to stand still for 5 seconds.
- **b.** Stop Xsens data acquisition via MVN Analyze Pro.

Step 16. Repeat the procedure from **step 13** until the completion of the tests indicated in table 3.

Step 17. Remove Xsens and HoloLens 2 from the participant.

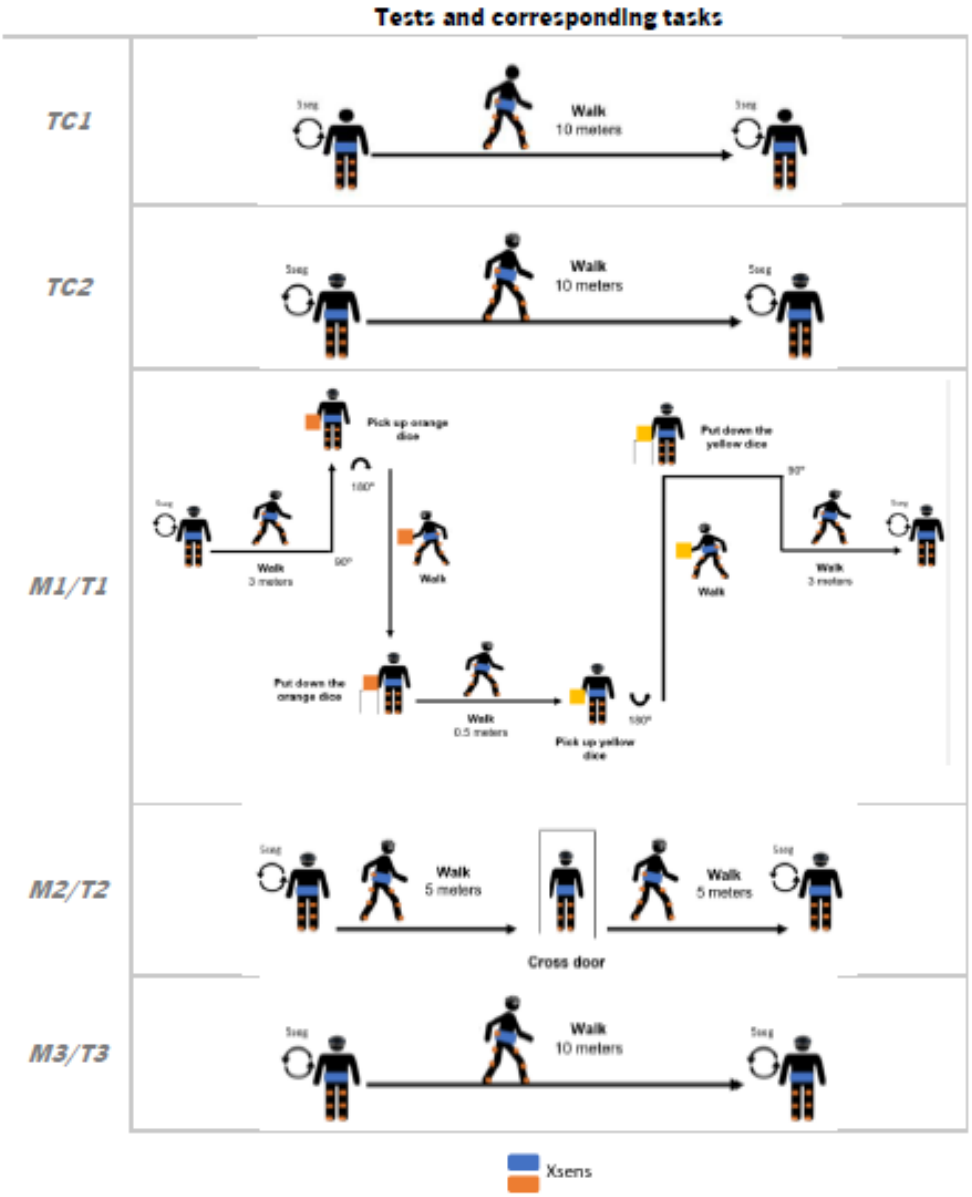
Step 18. Ask the participant to fill out IMI and SSQ questionnaires.

Estimated time per subject: ~40min

Table 3 – Tests, corresponding tasks, and estimated time

	Test	Tasks	Estimated time
Control conditions	(**TC1**) Walk without HoloLens 2	5sec stand + walk 10m + 5sec stand	1min
	(**TC2**) Walk with HoloLens 2 turned off	5sec stand + walk 10m + 5sec stand	1min
Familiarization	(**TF**) Interact with a virtual dice	Pick up dice + scale + rotate + move + place on face 6	3min
Monitoring	(**M1**) Turning	5sec stand + walk 3m + pick up orange dice + turn 180° + put the orange dice down + turn 180° + pick up yellow dice + turn 180° + put the yellow dice down + walk 3m + 5sec stand	4min
Training	(**T1**) Turning	5sec stand + walk 3m + pick up orange dice + turn 180° + put the orange dice down + turn 180° + pick up yellow dice + turn 180° + put the yellow dice down + walk 3m + 5sec stand	4min
Monitoring	(**M2**) Crossing virtual door	5sec stand + walk 5m + cross door + walk 5m + 5sec stand	2min
Training	(**T2**) Crossing virtual door	5sec stand + walk 5m + cross door + walk 5m + 5sec stand	2min
Monitoring	(**M3**) Walking in narrow spaces	5sec stand + walk 10m + 5sec stand	2min
Training	(**T3**) Walking in narrow spaces	5sec stand + walk 10m + 5sec stand	2min

Table 4 – Tests and corresponding tasks



5

Data analysis:

Table 5 - Variables and methods designation to achieve respective study purposes

Purpose	Variables	Method	
Compare motion metrics measured with and without MR framework.	Motion data	Paired sample statistical tests	OB1
Compare motion metrics measured with and without biofeedback.			OB2
Descriptive and visual analysis of clinic and demographic data.	Clinic and demographic data	Descriptive and visual statistics (mean ± standard deviation) *	
Motion sickness and Intrinsic Motivation	Acceptability	SSQ and IMI	
*SPSS will be used to accomplish the statistical analysis.			

Schedule:

Tasks	Week											
	1	2	3	4	5	6	7	8	9	10	11	12
Recruitment	■											
Experimental procedures		■	■	■	■	■	■	■	■			
Data analysis					■	■	■	■	■	■	■	
Dissemination								■	■	■	■	■

APPENDIX B – SUBJECTIVE QUESTIONNAIRES

B.1 SIMULATOR SICKNESS QUESTIONNAIRE

Name:		
Gender (F or M or non-binary):	Age:	Date:

Put a cross according to how well you agree with the sentence.

* Scale of 4 points: 0 – None. 1 – Slight. 2 – Moderate. 3 – Severe.

No.	**Symptoms**	Answer*			
		0	**1**	**2**	**3**
1	General discomfort				
2	Fatigue				
3	Headache				
4	Eyestrain				
5	Difficulty focusing				
6	Increased salivation				
7	Sweating				
8	Nausea				
9	Difficulty concentration				
10	Fullness of head				
11	Blurred vision				
12	Dizzy (eyes open)				
13	Dizzy (eyes closed)				
14	Vertigo				
15	Stomach awareness				
16	Burping				

B.2 Intrinsic Motivation Inventory Questionnaire

Name:		
Gender (F or M or non-binary):	Age:	Date:

Put a cross according to how well you agree with the sentence.

* Likert scale of 7 points: 1 – Strongly disagree. 2 – Disagree. 3 – More or less disagree. 4 – Undecided. 5 – More or less agree. 6 - Agree. 7 – Strongly agree.

Subscales	Items	Answer*						
		1	2	3	4	5	6	7
	1 - I really enjoyed doing this activity.							
Interest/Enjoyment	2 - This activity was fun to do.							
	3 - I would describe this activity as very interesting.							
	4 - I think that doing this activity is useful to help me with motor function.							
Value/Usefulness	5 - I would be willing to do this again because it has some value for me.							
	6 - I believe that this activity can be beneficial to me.							