POLITECNICO DI TORINO

Master's Degree in Biomedical Engineering

Master's Degree Thesis

Pilot study on upper limb motor control evaluation: a XR approach on PwMS

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Summary

This Master's Thesis, conducted in collaboration with AISM (Associazione Italiana Sclerosi Multipla) and the REHAB section of the Italian Institute of Technology, explores the evaluation of upper-limb motor control using a mixed-reality (MR) approach with the Microsoft HoloLens2, a head-mounted display.

The research investigates the effectiveness of Microsoft HoloLens2 in providing quantitative assessments of upper-limb movements, standardizing the kinematics of hand movements during interactions with physical objects in a pick-and-place task. By leveraging the tracking capabilities of HoloLens2, this study provides detailed analyses of hand and eye movements, facilitating an in-depth evaluation of motor behaviors.

The study is centered on people with multiple sclerosis (PwMS) and examines three categories of movements: two in the frontal plane (upward and downward) and one in the transverse plane. The primary objectives are to extract, process, and compare the data with those of healthy subjects to create a clinical portfolio for the tested patients, and understand how hand trajectories are influenced when moving against or with gravity while interacting with physical objects—an essential aspect of daily living activities and upper-limb rehabilitation strategies.

Key kinematic features associated with the motor performance of impaired subjects were identified, addressing the current gap in quantitative tools necessary for monitoring recovery in rehabilitative processes. Metrics such as movement smoothness, efficiency, and accuracy were evaluated, which are vital for assessing motor performance in individuals with multiple sclerosis.

The study's exploration of common patterns in the behavior of patients with multiple sclerosis offers significant insights into improving upper-limb assessment and rehabilitation through innovative methods and technologies.

The experimental results revealed that people with multiple sclerosis exhibit significantly different performance compared to healthy individuals, especially in movements against gravity. This distinction was evident across several kinematic metrics, including Symmetry, Kurtosis, PTPV, and TPE. However, not all metrics showed significant differences, highlighting that each metric provides a unique perspective on the effects of the disease. In conclusion, the findings suggest that complex tasks, such as vertical pick-and-place movements, are more likely to reveal motor impairments in multiple sclerosis patients.

This study underscores the importance of using this novel type of complex, gravity-influenced tasks to gain a comprehensive understanding of the impact of multiple sclerosis on motor control. The differences between healthy and impaired subjects were most pronounced in movements against gravity, suggesting that these tasks could be particularly useful in assessing and addressing the motor impairments associated with the disease. The unique characteristics and specific utilities of these tasks provide a broader perspective on the consequences of the pathology, offering valuable insights for the development of more effective rehabilitation strategies.

Summary

Questa tesi di laurea magistrale, condotta in collaborazione con AISM (Associazione Italiana Sclerosi Multipla) la sezione REHAB dell'Istituto Italiano di Tecnologia, esplora la valutazione del controllo motorio dell'arto superiore utilizzando un approccio di realtà mista (MR) con il Microsoft HoloLens2, un display montato sulla testa.

La ricerca indaga l'efficacia del Microsoft HoloLens2 nel fornire valutazioni quantitative dei movimenti dell'arto superiore, standardizzando la cinematica dei movimenti della mano durante le interazioni con oggetti fisici in un compito di pick-and-place. Sfruttando le capacità di tracciamento preciso di HoloLens2, questo studio fornisce analisi dettagliate dei movimenti di mano e occhio, facilitando una valutazione approfondita dei comportamenti motori.

Lo studio si concentra su persone affette da sclerosi multipla ed esamina tre categorie di movimenti: due nel piano frontale (movimenti verso l'alto e verso il basso) e uno nel piano trasversale. Gli obiettivi principali sono estrapolare, elaborare e conforntare i dati con quelli di soggetti sani per creare un prtoafoglio clinico dei pazienti testati, e comprendere come le traiettorie della mano siano influenzate quando si muovono contro o a favore di gravità mentre interagiscono con oggetti fisici, un aspetto essenziale delle attività della vita quotidiana e delle strategie di riabilitazione dell'arto superiore.

Sono state identificate features cinematiche chiave associate alla performance motoria di soggetti compromessi, affrontando l'attuale lacuna negli strumenti quantitativi necessari per monitorare il recupero nei processi riabilitativi. Sono state valutate metriche come la Smoothness, Efficiency e Accuracy, fondamentali per valutare la performance motoria

in individui con sclerosi multipla.

L'esplorazione dei pattern comuni nel comportamento dei pazienti con sclerosi multipla offre significativi spunti per migliorare la valutazione e la riabilitazione dell'arto superiore attraverso metodi e tecnologie innovative.

I risultati sperimentali hanno rivelato che le persone con sclerosi multipla mostrano prestazioni significativamente diverse rispetto agli individui sani, specialmente nei movimenti contro la gravità. Questa distinzione è stata evidente in diverse metriche cinematiche, tra cui Symmetry, Kurtosis, PTPV e TPE. Tuttavia, non tutte le metriche hanno mostrato differenze significative, evidenziando che ciascuna metrica fornisce una prospettiva unica sugli effetti della malattia. I risultati suggeriscono quindi che compiti complessi, come i movimenti verticali di pick-and-place, sono più propensi a rivelare le compromissioni motorie nei soggetti affetti da sclerosi multipla.

Questo studio sottolinea l'importanza di utilizzare questa innovativa tipologia di esercizi complessi e influenzati dalla gravità, per ottenere una comprensione completa dell'impatto della sclerosi multipla sul controllo motorio. Le differenze tra soggetti sani e compromessi erano più pronunciate nei movimenti contro la gravità, suggerendo che questi compiti potrebbero essere particolarmente utili per valutare e affrontare le compromissioni motorie associate alla malattia. Le caratteristiche uniche e le utilità specifiche di questi compiti forniscono una prospettiva più ampia sulle conseguenze della patologia, offrendo intuizioni preziose per lo sviluppo di strategie di riabilitazione più efficaci.

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“"Truth is not what you want it to be;
it is what it is,
and you must bend to its power
or live a lie."”
Miyamoto Musashi, Google by Google

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Acronyms

MS

multiple sclerosis

PwMS

people with multiple sclerosis

ADL

activities of daily living

CNS

central nervous system

MT

movement time

PTPV

percent time to peak velocity

PTPSD

percent time to peak standard deviation

NVP

number of velocity peaks

TPE

target position error

VR

Virtual Reality

AR

Augmented Reality

MR

Mixed Reality

Chapter 1

Introduction

Throughout development, the refinement of motor skills is crucial for enabling humans to interact with their environment and perform complex activities that require whole-body coordination. The musculoskeletal system, comprising bones, joints, and muscles, functions as a kinetic chain, where movement in one part affects the entire body [1]. In sports science, optimizing this kinetic chain is essential for enhancing athletic performance and reducing injury risks. Similarly, individuals with amputations or neurological disorders face significant disruptions in their kinetic and kinematic behaviors, affecting both fundamental and functional movements [2]. Impairments in upper-limb motor abilities can severely impact a person's independence and mental health.

The World Health Organization reports that multiple sclerosis (MS) affects approximately 2.8 million people worldwide, with about 1.2 million people living with MS in Europe alone. Annually, the incidence of new cases of MS is estimated to be around 2.5-5 per 100,000 people globally, which translates to tens of thousands of new cases each year [3]. Neurological patients typically undergo specialized treatments administered by physiotherapists, which vary in intensity based on recovery stages. For those with upper-limb impairments, full assistance is initially required to perform basic movements, transitioning to partial assistance as motor functions return, and eventually to home-based rehabilitation during the chronic stage.

The repetitive nature of these interventions has led to the development of various assistive technologies aimed at accelerating motor recovery and reducing the burden on clinicians. Integrating immersive technologies offers a promising patient-centric solution that surpasses the limitations of standard care. Research has highlighted the synergistic potential of introducing digital technologies in rehabilitation, emphasizing cost-effective, time-efficient, and repetitive exercises tailored for neurological patients [4]. The success of such approaches depends on the active involvement of therapists in the design process and the integration of advanced haptic and graphic systems, which enhance therapeutic effectiveness and patient engagement.

Despite advancements, rehabilitating everyday activities remains a challenge, leaving many patients with disabilities that significantly impact their daily lives. Current clinical trials and studies have struggled to differentiate between behavioral restitution and compensation, leading to an incomplete understanding of the relationship between movement quality recovery and upper-limb capacity restoration. This gap underscores the need for standardized protocols for quantitatively assessing upper-limb functional recovery [5].

1.1 Introduction to Multiple Sclerosis

Multiple sclerosis (MS) is the most common non-traumatic disabling disease affecting young adults globally. It is a complex, chronic illness characterized by immune-mediated attacks on the central nervous system, which includes the brain and spinal cord, leading to the demyelination of nerve fibers and subsequent neurodegeneration. This demyelination disrupts the normal conduction of electrical impulses along the nerves, leading to a variety of neurological symptoms and progressive disability. The exact cause of MS remains unclear, although it is believed to result from a combination of genetic predisposition and environmental factors such as low vitamin D levels, smoking, obesity, and Epstein-Barr virus infection [6].

1. **Pathophysiology**

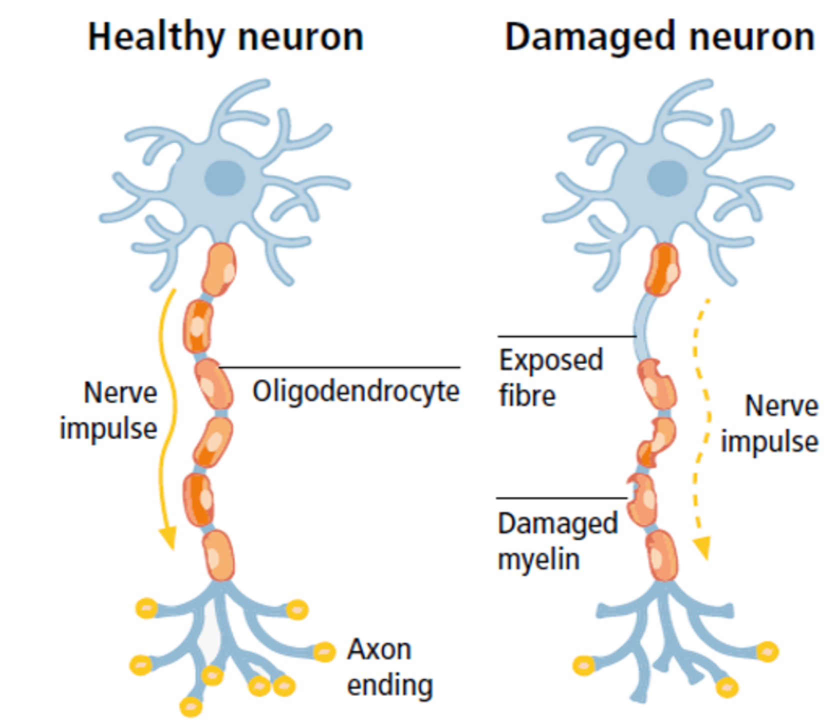

Figure 1.1: Comparison of Healthy and Damaged Neurons in Multiple Sclerosis. In the healthy neuron, nerve impulses travel smoothly along the axon insulated by intact myelin sheaths produced by oligodendrocytes. In contrast, the damaged neuron shows disrupted nerve impulses due to damaged myelin and exposed nerve fibers, which is typical in MS, leading to impaired neural communication.

MS is traditionally viewed as an autoimmune disease where the immune system mistakenly attacks the myelin sheath, a protective covering of nerve fibers. Inflammatory cells, including T-lymphocytes and B-lymphocytes, cross the blood-brain barrier and target myelin, leading to inflammation and demyelination [7, 6]. Recent studies suggest that B-cells play a significant role, especially in the formation of meningeal follicles that contribute to cortical pathology and disease progression.

Demyelination disrupts the transmission of nerve impulses, leading to neurological deficits. Axonal damage and neurodegeneration occur as the disease progresses, contributing to irreversible disability. Remyelination can occur, but it is often incomplete and declines with disease duration.

MS lesions, or plaques, are areas of demyelination typically found in the white matter of the Central Nervous System. These lesions can be detected using magnetic resonance imaging (MRI). Lesions can be "active" (inflammatory) or "inactive" (scarred). Active lesions are associated with acute relapses, while inactive lesions are indicative of chronic disease.

2. **Clinical Presentation**

   Relapsing-Remitting MS (RRMS) is characterized by episodes of neurological dysfunction (relapses) followed by periods of partial or complete recovery (remissions). Common initial symptoms include optic neuritis (inflammation of the optic nerve), sensory disturbances, and motor weakness. Secondary Progressive MS (SPMS) develops in some individuals after an initial relapsing-remitting course and is marked by a gradual worsening of neurological function over time, with or without relapses. Primary Progressive MS (PPMS) is characterized by a steady progression of neurological disability from the onset, without distinct relapses [6]. It typically presents with symptoms like progressive spastic paraparesis (muscle stiffness and weakness in the legs). Clinically Isolated Syndrome (CIS) is a first episode of neurological symptoms lasting at least 24 hours, caused by inflammation or demyelination in the CNS. Individuals with CIS may or may not go on to develop MS.

3. **Diagnostic Criteria**

   MRI is the most important tool for diagnosing MS, revealing characteristic lesions in the Central Nervous System [8]. Newer MRI techniques can detect subtle changes and monitor disease progression. Cerebrospinal fluid analysis can show the presence of oligoclonal bands, indicative of chronic inflammation in the CNS. Evoked potentials tests measure the electrical activity of the brain in response to stimuli, with abnormalities indicating demyelination.

4. **Disease-Modifying Therapies (DMTs)**

   Immunomodulatory treatments aim to reduce the frequency and severity of relapses and slow disease progression. Commonly used disease-modifying therapied include interferon-beta, glatiramer acetate, and newer oral medications like fingolimod and dimethyl fumarate. Monoclonal antibodies such as natalizumab, alemtuzumab, and ocrelizumab target specific components of the immune system to prevent attacks on the Central Nervous System [9]. These treatments have shown effectiveness in reducing relapses and delaying disability progression [6].

   Research is ongoing to develop more effective treatments with fewer side effects. Potential therapies include remyelination agents, neuroprotective drugs, and stem cell therapies.

5. **Symptom Management**

   Symptom-specific treatments are crucial for managing multiple sclerosis. Medications to manage symptoms such as spasticity (e.g., baclofen, tizanidine), pain (e.g., gabapentin, pregabalin), and bladder dysfunction (e.g., oxybutynin) are commonly used. For patients with cerebellar tremor treatment primarily involves invasive procedures such as Gamma Knife surgery, thalamotomy, or deep brain stimulation, tailored to individual needs [10]. Deep brain stimulation is the sole recourse for patients needing bilateral intervention. However, all treatment recommendations are supported by limited evidence. Additionally, tremors can sometimes resolve spontaneously following strategic multiple sclerosis lesion.

   Rehabilitation and supportive care play a significant role in maintaining mobility and function, with physical therapy, occupational therapy, and speech therapy being essential components [11]. Psychological support and counseling help manage the emotional and cognitive aspects of MS.

1.1.1 Impact of MS on Activities of Daily Living (ADL)

Multiple sclerosis is a chronic, progressive neurological disease that significantly impacts an individual's ability to perform activities of daily living (ADL). ADLs include basic self-care tasks such as eating, dressing, bathing, and more complex tasks like managing finances, driving, and maintaining a household. The impact of MS on these activities varies depending on the disease's progression and the specific symptoms experienced by the individual.

One of the primary symptoms is fatigue, which affects a majority of patients and can be debilitating. Fatigue is often described as overwhelming and not necessarily related to physical activity [12]. This can severely limit an individual's ability to carry out daily tasks, reducing their overall quality of life. For example, a person with multiple slcerosis may find it exhausting to perform simple tasks like brushing their teeth or preparing a meal, leading to increased dependence on others.

Motor dysfunction is another significant aspect of multiple sclerosis that affects activities of daily living as it can lead to muscle weakness, spasticity, and coordination problems, making movements difficult and often painful. Tasks that require fine motor skills, such as buttoning a shirt or writing, can become particularly challenging. Additionally, balance and gait issues common in such pathology increase the risk of falls, which can make walking, climbing stairs, and other mobility-related activities hazardous.

Cognitive impairments associated also play a crucial role in impacting activities of daily living. Many individuals affected by such disorder experience problems with memory, attention, and executive functions [3]. These cognitive issues can complicate planning and executing daily activities. For instance, a person with multiple sclerosis might struggle to remember steps in a recipe, manage medications, or keep track of appointments, necessitating additional support and adaptive strategies.

Sensory disturbances are prevalent and can include numbness, tingling, and pain. These sensory issues can interfere with the ability to feel and manipulate objects, further complicating daily tasks [7, 6]. For example, numbness in the hands can make it difficult to grasp utensils, turn doorknobs, or use a computer keyboard, impacting both personal and professional aspects of life.

Visual disturbances, including double vision, blurred vision, and loss of vision, can also affect activities of daily living [13]. These visual problems can make it challenging to read, drive, and navigate environments safely. Even with corrective lenses, the fluctuating nature of the disease symptoms can lead to inconsistent visual capabilities, requiring adaptive strategies and tools to manage daily activities effectively.

Depression and anxiety further exacerbate difficulties in carrying everyday tasks. The emotional burden of living with a chronic illness can reduce motivation and energy, impacting one's ability to engage in self-care and maintain social relationships. Psychological support and interventions are crucial in helping individuals with MS manage these emotional challenges and improve their overall functioning.

To conclude, multiple sclerosis affects activities of daily living through a complex interplay of physical, cognitive, sensory, and emotional symptoms. The impact is often multifaceted, requiring comprehensive management strategies that include medical treatment, rehabilitation, adaptive devices, and psychological support. Understanding the diverse ways such disorder influences daily life is essential for developing effective interventions that enhance independence and quality of life for individuals living with this condition.

1.1.2 Upper Limb Assessment in Neurological Disorders

Clinical assessments are among the most widely used tools for evaluating upper limb function. These assessments involve standardized tests and observational checklists that measure various aspects of motor performance. Notable clinical assessments include:

- **The Nine-Hole Peg Test (NHPT)**: As highlighted by the International Journal of Rehabilitation Research (1981) [14], the

NHPT is a standardized assessment tool widely used to measure fine motor coordination and dexterity of the upper limbs. The test involves timing the patient as they place nine pegs into nine holes on a pegboard and then remove them. (Figure 1.2) This process provides a quantitative measure of hand function, which is particularly useful for evaluating motor impairment in individuals with neurological disorders.

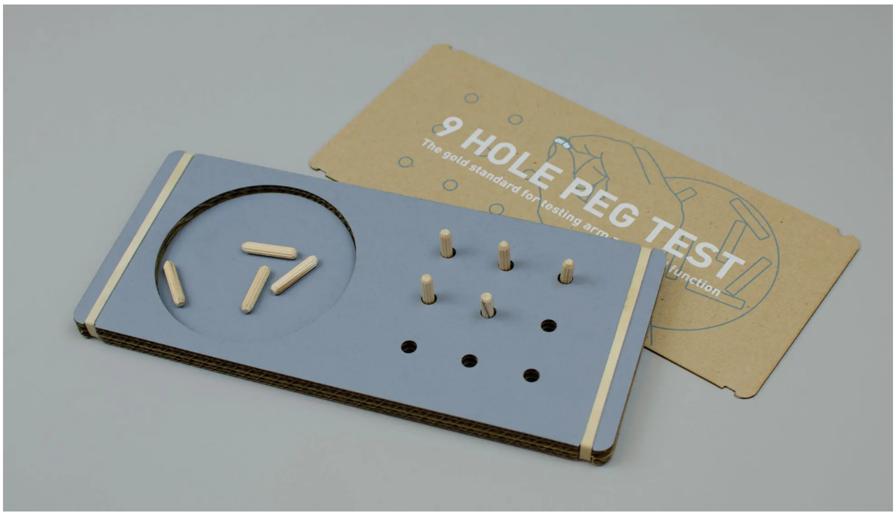

Figure 1.2: Nine-Hole Peg Test equipment

- **The Expanded Disability Status Scale (EDSS)**: This method is used to quantifiy the disability level in PwMS. It assesses a range of neurological functions, including muscle strength, coordination, speech, swallowing, sensory functions, and bowel and bladder control. The scale ranges from 0 to 10, with increments of 0.5. Lower scores (0 to 4.5) reflect minimal to moderate disability with retained ambulatory ability, while higher scores (5.0 to 9.5) indicate increasing levels of disability and reduced walking ability. (Figure 1.3) EDSS is widely used in clinical trials and by neurologists to monitor disease progression and evaluate the effectiveness of treatments [15].
- **The Fugl-Meyer Assessment (FMA)**: This comprehensive assessment tool measures motor recovery post-stroke. It includes

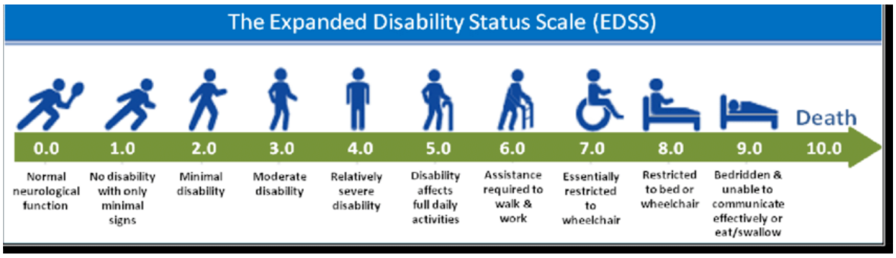

Figure 1.3: Expanded Disability Status Scale

subtests for upper limb motor function, coordination, and reflex activity, offering a detailed profile of motor impairment [14].

- **The Box and Block Test (BBT)**: It is a standardized assessment tool designed to measure manual dexterity, particularly in the context of upper limb function. During the test, the individual is asked to transfer as many small blocks as possible from one compartment of a box to another within a set time frame, typically one minute. (Figure 1.4) The number of blocks successfully transferred serves as a quantitative measure of hand dexterity and motor coordination. The BBT is particularly valued for its sensitivity in detecting changes in hand function over time, making it a valuable tool for assessing treatment outcomes and guiding rehabilitation strategies [16].

1.2 Virtual Reality in Rehabilitation

Upper-limb impairments can significantly impact an individual's ability to carry out daily tasks, reducing personal autonomy and affecting mental health. Proper treatment is necessary for individuals with neurological disorders to recover, as in the case of stroke survivors, or maintain function, as with multiple sclerosis, to sustain meaningful everyday activities.

Occupational therapy, often provided in clinical settings, aims to maximize functional recovery with the help of specialized therapists. Active patient participation is crucial for promoting recovery through

Figure 1.4: Box and Block Test equipment

neuroplasticity and ensuring lasting therapeutic benefits [17]. Providing appropriate feedback (such as visual, auditory, or haptic cues) can enhance patient engagement during rehabilitation. Incorporating immersive technologies can improve the overall experience for patients [18, 19].

Virtual reality (VR) technologies have revolutionized the field of rehabilitation, offering innovative solutions to enhance patient engagement and improve therapeutic outcomes [4]. By creating immersive and interactive environments, VR can simulate real-life scenarios and activities that are both motivating and therapeutic. Below are described the different types of virtual reality—Virtual Reality (VR), Augmented Reality (AR), and Mixed Reality (MR)—and their applications in rehabilitation, particularly in the creation of customized exergames designed to meet individual patient needs [20].

Virtual Reality involves fully immersive environments where users are completely surrounded by a virtual world, typically experienced through head-mounted displays (HMDs) and sometimes complemented by additional sensory inputs such as haptic feedback. In rehabilitation, VR can be used to create controlled and safe environments for patients to practice movements and activities. For example, stroke patients can engage in virtual tasks that mimic daily activities, allowing them to practice and improve their motor skills in a risk-free setting.

Augmented Reality overlays digital information onto the real world, enhancing the user's perception of their surroundings without completely immersing them in a virtual environment. AR can be delivered through devices such as smartphones, tablets, or AR glasses. In rehabilitation, AR can provide real-time guidance and feedback during exercises. For instance, patients can see virtual prompts and corrections superimposed on their actual movements, helping them perform exercises more accurately and effectively.

Mixed Reality combines elements of both VR and AR, allowing for interaction between real and virtual objects. Devices like the Microsoft HoloLens 2 enable users to see and interact with holograms within their physical environment. In rehabilitation, MR can create highly interactive and engaging therapy sessions. Patients can manipulate virtual objects as part of their exercises, receiving immediate feedback on their performance. This blend of real and virtual worlds can make rehabilitation exercises more dynamic and adaptable to individual patient needs.

Using AR and MR instead of VR can be advantageous in rehabilitation, as they enable the development of games that improve hand-eye coordination better than traditional immersive or 2D applications. VR and AR technologies have been widely used in motor recovery, while MR applications have recently started to gain popularity [4]. These technologies allow for the creation of customized, interactive environments tailored to a patient's specific needs and leverage cameras and sensors for various biometric measurements, such as hand tracking and eye-tracking, and can sync with additional instruments to quantify user engagement. An example of such technology is Microsoft HoloLens2, which is well-suited for implementing daily living environments.

In fact patient engagement is a critical factor in the success of rehabilitation programs [21]. Traditional rehabilitation exercises can often be repetitive and monotonous, leading to decreased motivation and adherence. MR addresses this challenge by providing immersive and engaging experiences that can make rehabilitation more enjoyable. Patients are more likely to participate actively and consistently in their therapy when they find the activities enjoyable and stimulating.

In MR-based rehabilitation, patients can interact with virtual objects and projections and they can perform a wide range of activities, from simple exercises to complex, task-oriented scenarios. These virtual objects can be designed to provide immediate feedback, rewards, and progress tracking, which further enhances motivation and engagement. By making therapy sessions more interactive and enjoyable, MR can improve patient compliance and, ultimately, rehabilitation outcomes.

1.2.1 Upper Limb Assessment and Rehabilitation Using HoloLens2

Given the significant impact of MS on upper limb function, effective assessment and rehabilitation are crucial. The head-mounted mixed reality device HoloLens2, with its advanced hand-tracking capabilities and interactive mixed reality environment, offers a novel approach for both evaluating and enhancing upper limb function in PwMS [22]. The device can provide real-time feedback, engaging patients in immersive and motivating rehabilitation exercises. This technology can be applied in the rehabilitation field to improve motor skills, coordination, and overall upper limb function, thereby enhancing the ability of PwMS to perform ADLs more independently and effectively.

1.3 Biomechanical Kinematic Assessment

Biomechanical kinematic assessment involves the detailed analysis of movement mechanics, such as joint angles, velocities, and trajectories [23]. This analysis provides insights into the motor control strategies employed by individuals and helps in identifying abnormalities or improvements in motor function over time. Traditional methods of kinematic assessment include optical motion capture systems, which use cameras and reflective markers to track movements, and electromechanical systems, which utilize sensors attached to the body [24, 25].

These methods, while accurate, can be cumbersome and limited by the need for specialized equipment and controlled environments.

Kinematic analysis involves the study of motion without considering the forces that cause it. In the context of motor control, kinematic analysis provides a detailed understanding of how body segments move in space and time, which is essential for designing effective rehabilitation programs. This analysis concerns both hand and joint displacements in space, focusing on trajectories, velocities, and accelerations in both domains [26]. By examining these parameters, therapists can gain insights into the functional capabilities and limitations of patients, particularly those recovering from neurological injuries like stroke or managing conditions such as multiple sclerosis.

The brain forms a cognitive representation of the body and its interactions with the external environment, known as an internal model [27, 23]. This framework helps predict how the body will respond to actions, movements, and sensory inputs. Internal models can be both kinematic and dynamic, and they play a critical role in motor control and planning (Figure 1.5). Specifically:

- **Kinematic Internal Model**: A kinematic internal model involves the representation of the relationships between joint angles, body segments, and end-effector positions (such as the hand or foot). This model helps the CNS understand how changes in joint positions lead to changes in the position and orientation of the limbs and other parts of the body. In other words, it maps the spatial relationships between different body parts and the resulting motion in the environment, translating task space information, such as hand trajectory for the upper limb, to joint space.

- **Dynamic Internal Model**: A dynamic internal model involves the representation of the forces and torques involved in producing movement. This model helps the CNS predict the effects of muscle activations on limb movements and understand how external forces (e.g., gravity, friction) will affect movement, calculating the joint torques needed to perform a given task. It also includes information on how the body will react to different loads and perturbations.

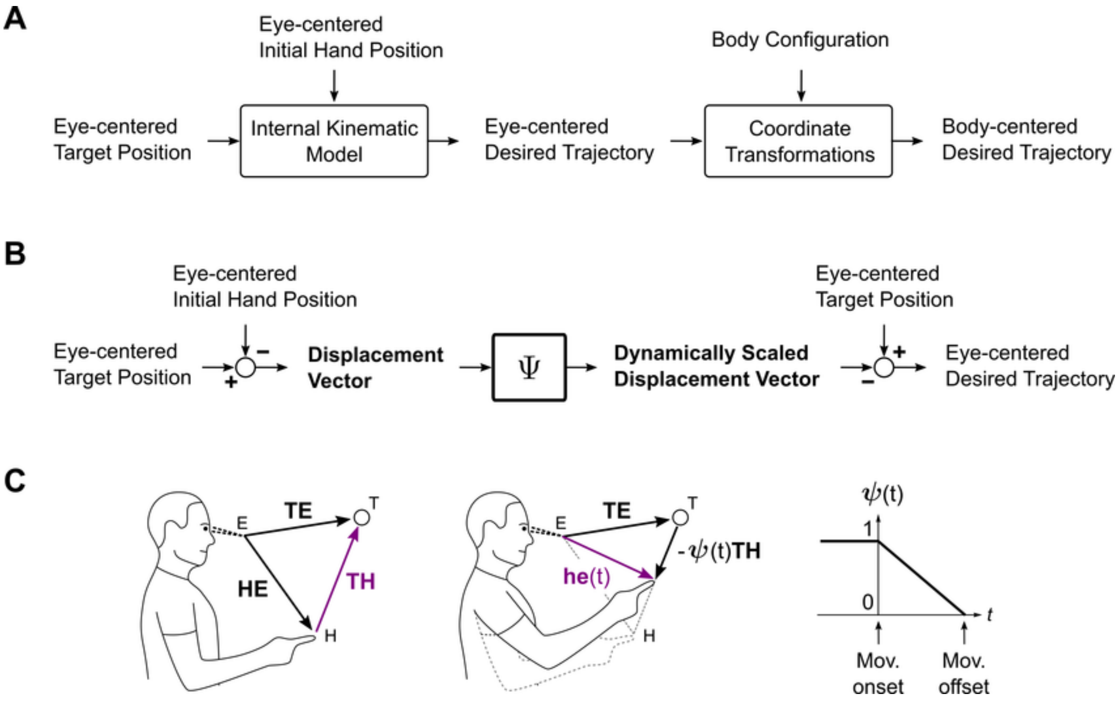

Figure 1.5: Sensorimotor transformations and the Internal Kinematic Model

However, motor planning introduces both kinematic and dynamic constraints on movement execution [28, 29]. The central nervous system takes into account the mechanical effects of gravity before executing a specific task. This is especially apparent in vertical tasks, where the execution path differs between upward and downward movements [30, 5].

Patients who lack proprioception lose this ability, resulting in abnormal reaching movements and hand trajectories, which limits motor learning abilities and independence in daily activities [2].

The studies of Papaxhantis et al. highlights that upward and downward movements involve different neurological processes within the CNS [31]. Therefore, rehabilitation should be tailored to address each type of movement. Properly quantifying postural patterns during movements against or with gravity can provide valuable insights for improving recovery in daily activities [32].

One other key aspect of kinematic analysis in motor control is the study of movement decomposition. Healthy individuals typically perform smooth and coordinated movements that involve well-integrated muscle activity. In contrast, individuals with motor impairments often exhibit fragmented or jerky movements, characterized by distinct submovements [33]. Submovements are small, discrete motion units that combine to produce a complex action. These can be observed as multiple, separate peaks in velocity profiles during a task that should ideally have a single, smooth peak.

Research by Rohrer et al. (2004) highlights that during recovery, submovements become larger, fewer, and more blended, indicating improvements in motor coordination and smoothness of movement. This change reflects the reorganization and adaptation of neural circuits involved in motor control as patients recover [34]. The ability to quantitatively measure these changes through kinematic analysis is crucial for assessing the effectiveness of rehabilitation interventions and guiding therapy adjustments.

1.4 State of Art of Motion Capture Techniques

The kinematic assessment of the upper limb is crucial in both clinical and research settings to understand movement patterns, diagnose disorders, and evaluate treatment outcomes [19]. Motion capture techniques have evolved significantly, providing detailed and accurate measurements of limb movements. This section discusses four prominent mocap techniques: Stereophotogrammetry, Inertial Motion Capture, Electromagnetic Motion Capture and head-mounted Visors for Augmented and Mixed Reality (AR/MR) [24].

1.4.1 Stereophotogrammetry

Stereophotogrammetry is a well-established motion capture technique that utilizes multiple cameras to capture three-dimensional movements.

Reflective markers are placed on key anatomical landmarks of the upper limb, and the cameras record the positions of these markers as the participant performs specific tasks. The primary components and advantages of this technique include:

- **High Precision and Accuracy**: Stereophotogrammetry systems, such as Vicon Nexus, provide sub-millimeter accuracy in capturing motion, making them ideal for detailed kinematic analysis.
- **Three-Dimensional Analysis**: The ability to capture 3D data allows for comprehensive analysis of complex movements, including joint angles, velocities, and accelerations.
- **Real-Time Feedback**: Advanced systems offer real-time tracking, which can be invaluable for both clinicians and researchers during interventions or experiments.

Despite its precision, stereophotogrammetry has some limitations. The setup requires a controlled environment with multiple cameras, which can be both time-consuming and expansive. Additionally, the need for reflective markers may restrict natural movement and comfort of the patient.

1.4.2 Inertial Motion Capture

Inertial motion capture uses inertial measurement units (IMUs), which include accelerometers (measure linear acceleration along three axes (X, Y, Z)), gyroscopes (measure rotational velocity around the same three axes), and sometimes magnetometers (measure the strength and direction of the magnetic field around the sensor, used to correct for drift in the gyroscope data, improving long-term accuracy), to track movement.

- **Wearable and Portable Sensors**: IMUs are placed on various body parts to capture the orientation and acceleration data. These systems offer high mobility and can be used in different environments without the need for external cameras.

- **Ease of Setup**: Setting up an IMC system is relatively straightforward. Users can quickly attach sensors to the body and start capturing data without extensive calibration.
- **Versatility**: These systems can be used in different settings, including outdoors and in constrained spaces, where optical systems might struggle.

However, IMC systems have some limitations. Inertial sensors are prone to drift over time, leading to inaccuracies in position data, particularly problematic in long-duration recordings. Magnetometers can be affected by external magnetic fields, which can distort the data. Accurate motion capture often requires sophisticated algorithms to fuse data from accelerometers, gyroscopes, and magnetometers to produce reliable outputs.

1.4.3 Electromagnetic Motion Capture

Electromagnetic Motion Capture (EMMC) systems use sensors that track their position and orientation relative to a known magnetic field.

- **Accuracy**: EMMC systems can provide high positional accuracy within the effective range of the transmitter.
- **No Line-of-Sight Requirement**: Unlike optical systems, EMMC does not require a direct line of sight between sensors and cameras, allowing for uninterrupted tracking even if parts of the body are obscured.
- **Real-Time Tracking**: These systems offer real-time data processing, which is beneficial for applications that require immediate feedback.

EMMC systems have their limitations. The effective range of electromagnetic systems is relatively small, typically within a few meters of the transmitter. Metallic objects and other electromagnetic sources can interfere with the system, causing inaccuracies. The setup requires careful placement of transmitters and consideration of environmental factors to minimize interference.

1.4.4 Head-Mounted Visors for Augmented and Mixed Reality

Recent advancements in augmented reality (AR) and mixed reality (MR) have introduced head-mounted visors as a novel tool for motion capture. Devices like the Microsoft HoloLens2 integrate AR/MR technology with motion tracking capabilities, providing several unique benefits:

- **Markerless Tracking**: Head-mounted visors use built-in sensors and cameras to track upper limb movements without the need for reflective markers, allowing for a more natural and comfortable user experience.
- **Enhanced Interaction**: AR/MR environments can overlay digital information onto the real world, facilitating interactive and immersive rehabilitation exercises or training scenarios.
- **Portability and Convenience**: These devices are often portable and easier to set up compared to traditional stereophotogrammetry systems, making them suitable for use in various settings, including clinics and patients' homes.

However, head-mounted visors also face challenges. The accuracy of motion capture might be lower than that of stereophotogrammetry, particularly for fine-grained movements. Furthermore, the reduced field of view can be disadvantageous for patient's engagement and battery life can limit extended use in clinical or research applications.

In conclusion, the kinematic assessment of the upper limb has greatly benefited from advances in motion capture technology. Stereophotogrammetry remains a gold standard for high-precision 3D motion analysis, while head-mounted visors for AR/MR offer innovative and user-friendly alternatives. Each method has its strengths and limitations, and the choice between them depends on the specific requirements of the assessment, the environment, and the desired balance between accuracy and convenience [25]. Future developments in these technologies promise to further enhance their applicability and integration into diverse fields such as rehabilitation, sports science, and robotics.

1.5 Aim of the thesis

Rehabilitation of upper-limb functionality is crucial for patients recovering from conditions such as stroke, traumatic injuries, and neurological disorders. Accurate assessment of progress and treatment outcomes is essential for guiding personalized therapy, yet current methods rely heavily on subjective clinical evaluations. Although motion capture systems provide more objective measurements, they often face limitations due to their high cost, bulkiness, and need for specialized operators.

In collaboration with the Italian Institute of Technology, this master thesis project explores the use of Microsoft HoloLens2, a mixed-reality head-mounted display, as an innovative alternative for assessing upper-limb functionality in rehabilitation settings. The research focuses on the potential of HoloLens2 to offer a portable, cost-effective solution by enabling quantitative hand and eye-tracking data acquisition through its advanced sensors.

HoloLens2's PICKapp application integrates holographic elements with physical objects to assess pick-and-place tasks, a critical aspect of upper-limb rehabilitation. By processing hand and eye-tracking signals, kinematic data metrics of clinical utility are extracted, providing insights into movement quality, coordination, accuracy and patient engagement.

This thesis addresses this gap focusing on the functional recovery of the upper limb in people with multiple sclerosis (PwMS), by developing a standardized protocol for assessing hand postural patterns during pick-and-place tasks. The research aims to derive clinically useful metrics from the upper limb kinematic data obtained from MS patients using the Microsoft HoloLens2 for mixed reality (MR) applications. The secondary objective is to enable clinicians to make meaningful comparisons between healthy subjects and MS patients, thereby facilitating a more nuanced understanding of upper-limb impairments. This comparative approach helps in identifying specific deficits and tailoring interventions more precisely. The integration of immersive technology, such as the Microsoft HoloLens2, not only enhances the assessment process but also offers potential therapeutic benefits. By developing these metrics and protocols, this thesis contributes to more effective and personalized rehabilitation strategies, ultimately aiming to improve the quality of life for individuals with multiple sclerosis.

The outcomes of this study aim to offer a more accessible and precise means of assessing patient progress. This could lead to improved therapy strategies, better patient care, and accelerated recovery outcomes.

Chapter 2

Materials and Methods

The study proposes using Microsoft HoloLens2, a mixed-reality head-mounted display, as an alternative to traditional motion capture systems for assessing upper-limb functionality in rehabilitation. HoloLens2 enables quantitative hand movement recording and enhances user engagement through the PICKapp application, which integrates holographic elements with physical objects for evaluating pick-and-place tasks. The accuracy of HoloLens2's hand-tracking was comparable to a motion capture system, with a cross-correlation above 0.95% and a root-mean-square error percentage below 10%. These findings suggest HoloLens2 is a portable, user-friendly, and cost-effective option for quantifying hand movements and could lead to personalized therapy applications [5].

2.1 Experimental Setup and Protocol

This section provides a comprehensive overview of the experimental setup and protocol employed in this study, detailing the methodologies and technologies used to assess upper limb motor control in participants with multiple sclerosis. By outlining the specific experimental conditions, the tools and devices utilized, and the procedural steps followed, this section aims to ensure the reproducibility and reliability of the study.

2.1.1 Participants

The research focused on investigating the performance of individuals diagnosed with multiple sclerosis (MS).

Subjects affected by multiple sclerosis were recruited according to Declaration of Helsinki and under ENACT01 protocol (229/2022) approved by the Ethical Committee of Liguria Region (Italy) on November 14th, 2022. Participants signed a written informed consent after being introduced to the objectives of the study. Subjects were characterised by different levels of disability both in the upper and lower limb (Table 2.1).

The group comprised 9 individuals, consisting of 4 males and 5 females, with an average age of 42 ± 11.8 years. The age range within this group varied from 29 to 64 years.

All participants were asked to performing a specific pick-and-place task. This task involved the action of picking up objects and then placing them in designated locations. The task was conducted utilizing the Microsoft HoloLens2 technology, which is designed for mixed reality (MR) applications.

Prior to participating in the study, all individuals provided written consent after being informed about the nature of the research. Moreover, the study adhered to ethical standards outlined in the Declaration of Helsinki.

In a previous study, healthy subjects were recruited to evaluate the accuracy of the HoloLens2 as a tracking device. The data collected from these participants were subsequently used to calculate various kinematic features. This initial assessment helped establish a baseline for understanding the tracking capabilities of HoloLens2 and ensured the reliability of the data used for further analysis in the current study.

In essence, the study aimed to compare the performance of individuals with MS and healthy counterparts in executing a specific task, all while ensuring ethical conduct and adherence to established guidelines.

2.1.2 Experimental Setup

For standardization of the pick-and-place task, a specialized library was developed. This library allowed for easy adjustment of the desk and shelf heights. During the experiment, the shelf was positioned at shoulder level and the table was set 40 cm below that (Figure 2.1). Transparent boxes, each measuring 10x8x9.5 cm and weighing 0.2 kg, were utilized as objects for the pick-and-place task, following the protocol established by prior research.

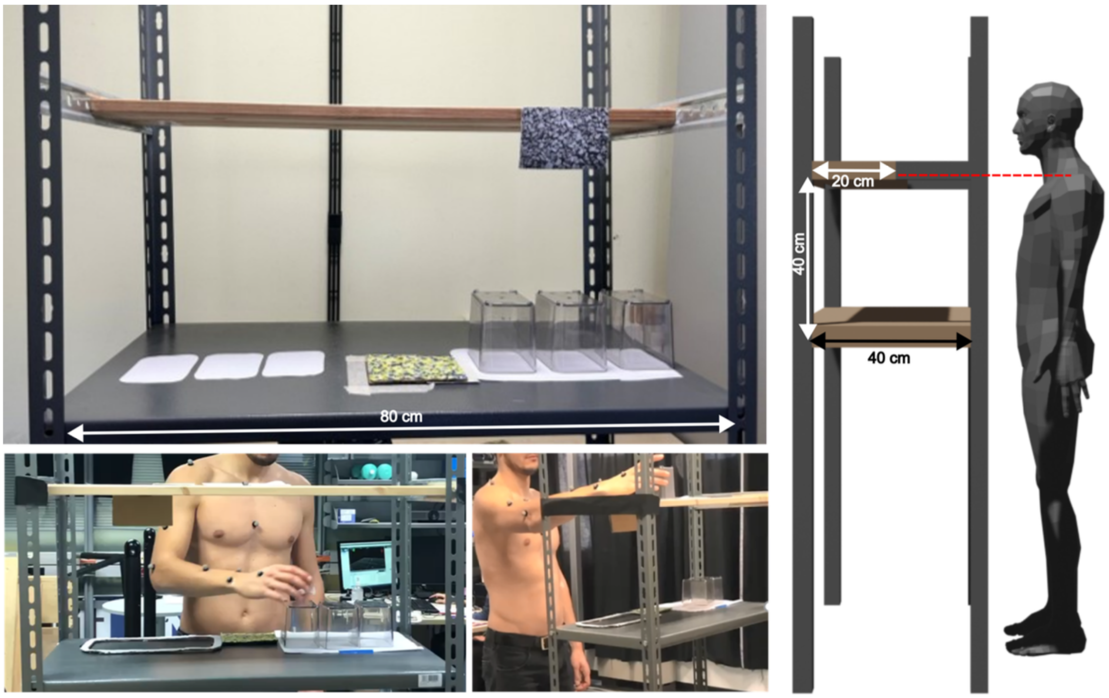

Figure 2.1: Experimental set-up

During the execution of the tasks, participants were required to wear the HoloLens 2 mixed reality headset.

2.1.3 Technologies

The HoloLens 2 is a state-of-the-art mixed reality (MR) device developed by Microsoft, designed to seamlessly blend the digital and physical worlds. This head-mounted display unit features a sophisticated combination of hardware and software to create an immersive, interactive experience that can be utilized in various fields, including rehabilitation, education, and industrial applications (Figure 2.2) [22].

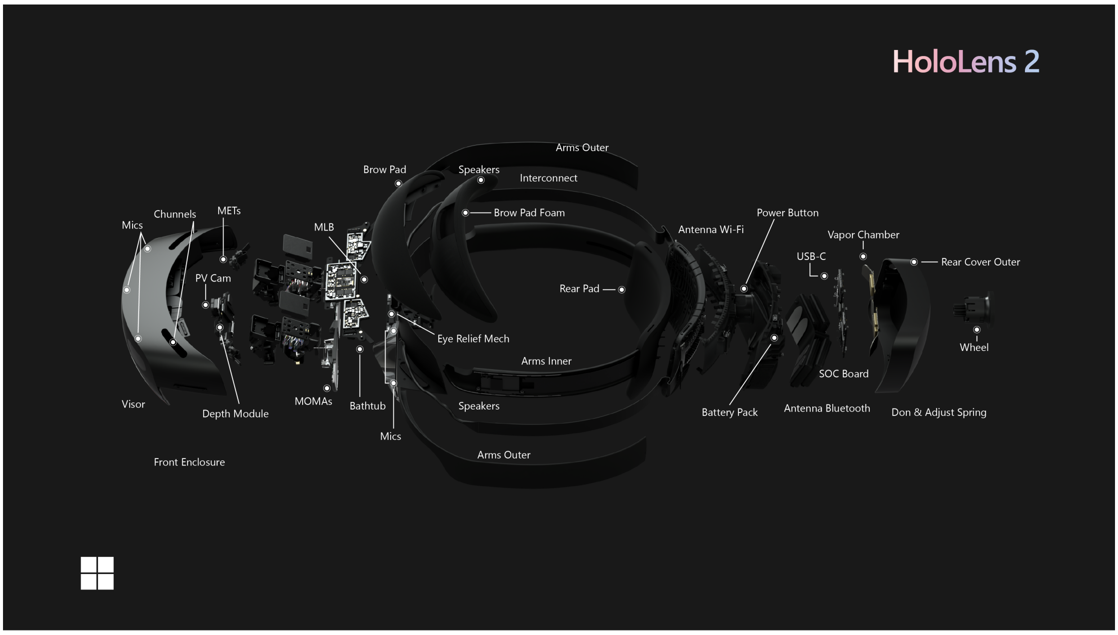

Figure 2.2: Hololens2 exploded view diagram

1. **Design and Ergonomics**: The HoloLens 2 is built with user comfort in mind, featuring a lightweight design that can be worn for extended periods without causing significant discomfort. The device includes an adjustable headband and a visor that flips up, allowing users to switch between the real and virtual worlds effortlessly. The ergonomic design ensures a secure and comfortable fit, accommodating a wide range of head sizes and shapes.

2. **Display and Optics**: At the core of the HoloLens 2's immersive experience are its advanced display and optics. The device features two high-resolution displays with a combined resolution of 2k per eye, offering a sharp and clear visual experience. The field of view is significantly larger compared to its predecessor, providing

a more expansive and immersive mixed reality environment. The holographic displays are rendered using laser-based waveguides, which deliver bright and vivid images that can be overlaid on the real world with precision.

3. **Sensors and Tracking**: The HoloLens 2 is equipped with an array of sensors that enable accurate tracking and interaction with the environment. These include:

   - **Inside-Out Tracking**: Using four visible light cameras, the device performs real-time environment mapping, allowing for precise spatial awareness and accurate hologram placement without the need for external markers.
   - **Eye Tracking**: The HoloLens 2 incorporates advanced eye-tracking sensors that monitor the user's gaze direction. This feature enhances interaction by allowing the device to respond to where the user is looking, providing intuitive control and improving the accuracy of holographic content manipulation.
   - **Hand Tracking**: The device features sophisticated hand-tracking capabilities through two depth sensors, enabling natural and intuitive interaction with virtual objects. Users can directly manipulate holograms using hand gestures, such as pinching, dragging, and tapping, making the experience more immersive and engaging.

4. **Computing Power**: The HoloLens 2 is powered by a custom-built Holographic Processing Unit (HPU) and a Qualcomm Snapdragon 850 Compute Platform. This combination delivers robust performance, capable of handling complex mixed reality applications smoothly. The device also includes 4 GB of LPDDR4 RAM and 64 GB of UFS 2.1 storage, providing ample resources for storing and running applications.

5. **Connectivity**: To support a wide range of applications, the HoloLens 2 offers comprehensive connectivity options, including Wi-Fi 802.11ac, Bluetooth 5.0, and a USB Type-C port. These

connectivity features enable seamless integration with other devices and networks, facilitating data transfer, streaming, and remote collaboration.

6. **User Interface and Interaction**: The HoloLens 2 is designed to provide a highly intuitive user interface. Interactions are facilitated through a combination of hand gestures, voice commands, and eye-tracking inputs. The integration of Microsoft's Cortana digital assistant further enhances the hands-free experience, allowing users to perform tasks and control applications using natural language commands.

The mixed reality (MR) environment was constructed using Unity 2021.2.16f1, with integration of both MRTK and PTC Vuforia extensions. This environment was then projected onto a Microsoft HoloLens2 device.

MRTK facilitated seamless interaction with virtual objects through its incorporated hand tracking algorithm. This algorithm had the capability to simultaneously detect both hands and calculate the position and orientation of various hand joints, including fingers, knuckles, palm, and wrist, at a sampling frequency of 50 Hz.

PTC Vuforia, an augmented reality (AR) software, enabled holographic interaction by leveraging different image recognition algorithms. Upon detection of specific image targets by the HoloLens2 camera, Vuforia anchored holograms to these targets, enhancing the AR experience [5].

The PICKApp application was developed to enhance the pick-and-place task. In this augmented environment, subjects could interact with physical objects while simultaneously seeing interactive holograms, such as targets and arrows, and receiving visual rewards like fireworks upon task completion [35].

After PICKApp was uploaded to the HoloLens 2 device a calibration phase was needed to ensure that the augmented cues aligned correctly with the physical objects. To define the working space, which included a desk and a shelf, the Vuforia extension for HoloLens2 was utilized [5]. When the camera recognized the Vuforia markers, a blue rectangle would appear at the base of one of the physical boxes, accompanied by an arrow indicating which box to pick up (Figure 2.3). Simultaneously, another blue rectangle and arrow would show where to place the object.

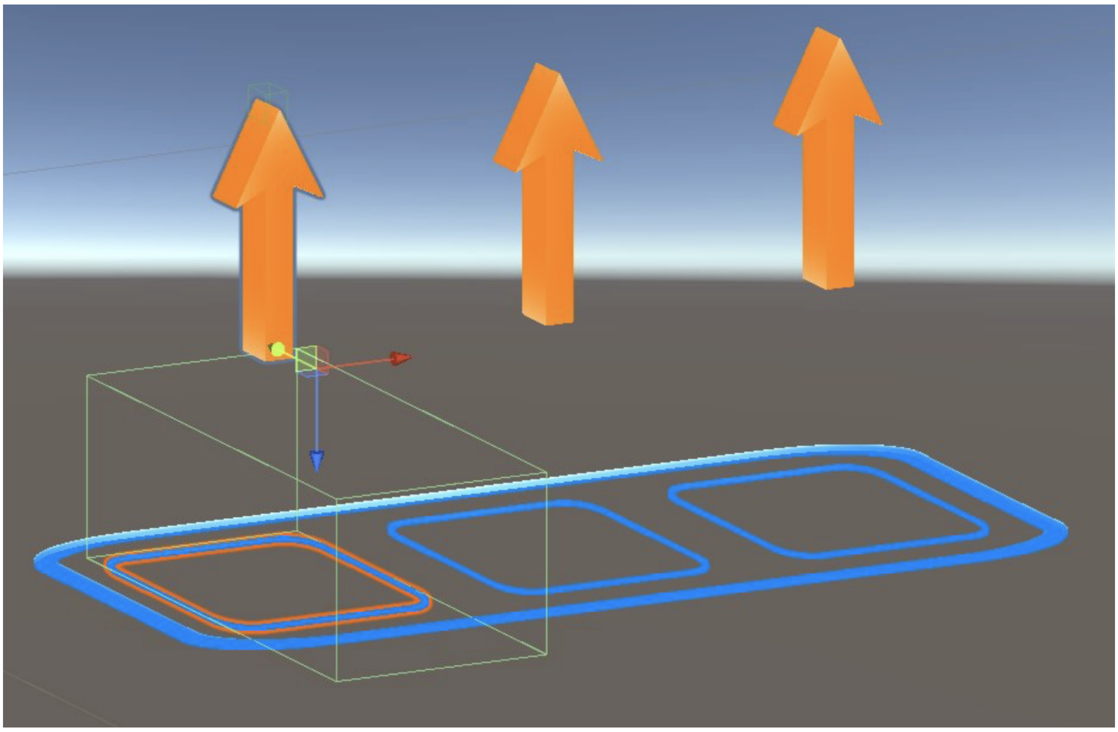

Figure 2.3: Representation of holographic shapes and cues

HoloLens2 was never shut down throughout the experiments of each subject, while it was powered off between participants. Each experimental session lasted 25 minutes circa, while the time interval between subjects was of at least 1 hour during which the device battery was recharged. The proposed MR environments were designed as assessment tools of upper-limb functional abilities. Pick-and-place was selected as a functional task performed during most of ADLs. To encourage physical objects interaction, the extended environment was enriched with visual cues while real objects were to be moved from one place to another. Rewards were unlocked when the object was correctly placed on mark.

Once the task was completed, fireworks and confetti were displayed to reward the user. The Unity Engine's collider components were used to detect when the box was picked up and placed on the target. Colliders in Unity define object boundaries and are involved in physics simulations in virtual worlds. A collider (C2) was assigned to the holographic targets, another collider (C1) was linked to the user's hand and tracked its position, and a third collider (C3) was attached to the starting position of the box. Interaction detection between C1 and C3 triggered a flag indicating the box had been picked up ("start collided"), while a collision between C2 and C1 indicated successful object placement ("end collided") (Figure 2.4). Data were logged according to the logic outlined in Algorithm 1.

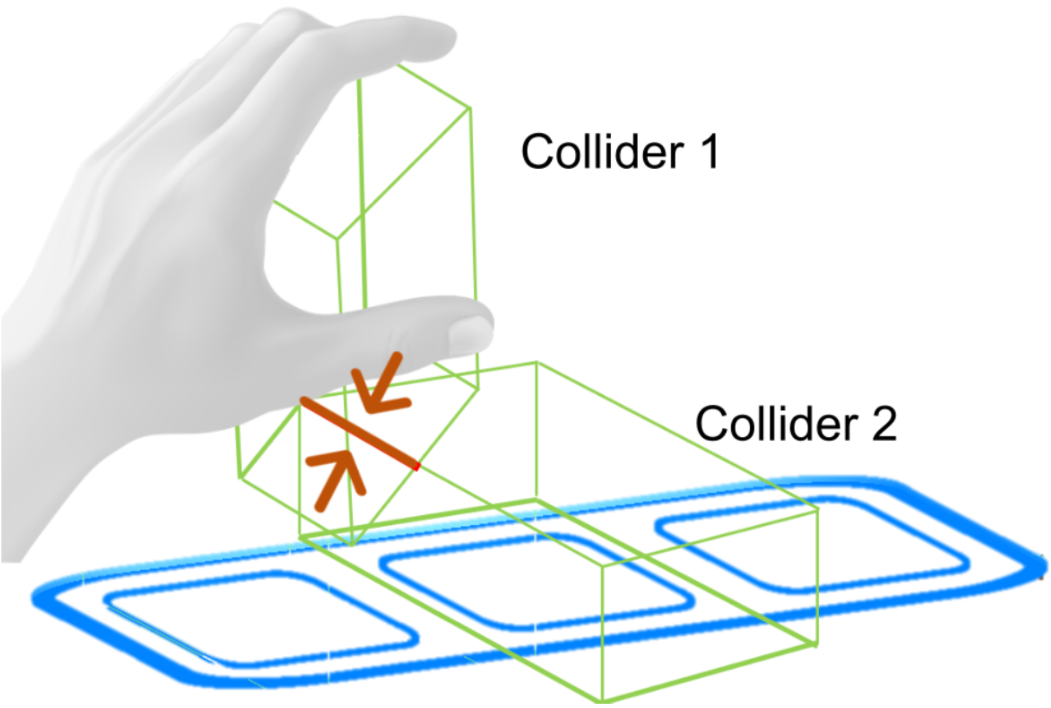

Figure 2.4: Representation of Unity colliders for PICKapp

Once all the movements were executed, a "Game Over" text appeared on screen. Through an Exit button it was possible to get back to the starting menu. The distance from which the user visualizes markers for the calibration can affect their recognition and placement in the space, thus leading to a mismatch in the actual position where clues are set

Algorithm 1 Pseudo-code for the creation of log files

```
Application starts
i = 0
while i < n_movements do
    Save HT and ET in logFile
    if Object(i).isPicked then
        Save trigger in logFile: Collider1
        if Object(i).isPlaced then
            Save trigger in logFile: Collider2
            i = i + 1
            Target(i) is loaded
        end if
    end if
end while
Application ends =0
```

with respect to the desired one. To minimize this issue, the application was developed such as the calibration needs to be performed exclusively once by the user. This choice was made to ensure that the user would visualize the clues always in the same position.

Medical Record of Recruited PwMS							
	Sex	Age	Side	EDSS	9-HPT	BBT	Tremor
S1	M	29	R	1	20.43	66	-
S2	F	38	R	1.5	15.53	71	-
S3	F	39	R	4.5	42.28	31	X
S4	M	39	R	2	25.30	49	-
S5	F	38	L	-	24.70	42	-
S6	M	34	R	3.5	23.50	52	-
S7	M	35	R	1	17.60	59	-
S8	F	63	L	6.5	66.34	33	X

Table 2.1: Clinical overview of subjects recruited

A visual feedback was added to PICKapp so that a warning is visualized when HoloLens2 fails at tracking the user's hand.

2.1.4 Experimental Protocol

Participants were instructed to complete nine pick-and-place movements in a predefined sequence (Figure 2.5):

- **M1, M2, M3**: from desk to shelf. These movements were performed upward, against gravity, thus will be referred as g^-.
- **M4, M5, M6**: from shelf to a new position on the desk. These movements were performed downward, propelled by gravity, thus will be referred as g^+.
- **M7, M8, M9**: from the desk back to their original position. These movements were performed with respect to the transversal plane, thus will be referred as g^0.

This sequence was repeated five times and no time or space constraint was imposed on subjects, who were asked to perform the movements in a relaxed and natural way. Targets were holographic squares matching the section of the boxes (Figure 2.6).

For each movement subjects were required to keep their arm on a resting position alongside the trunk, reach and grasp the box, move it onto target, and get back to the resting position. The primary objective of this study is to exclusively observe Cartesian trajectories of the hand while performing the pick-and-place movement.

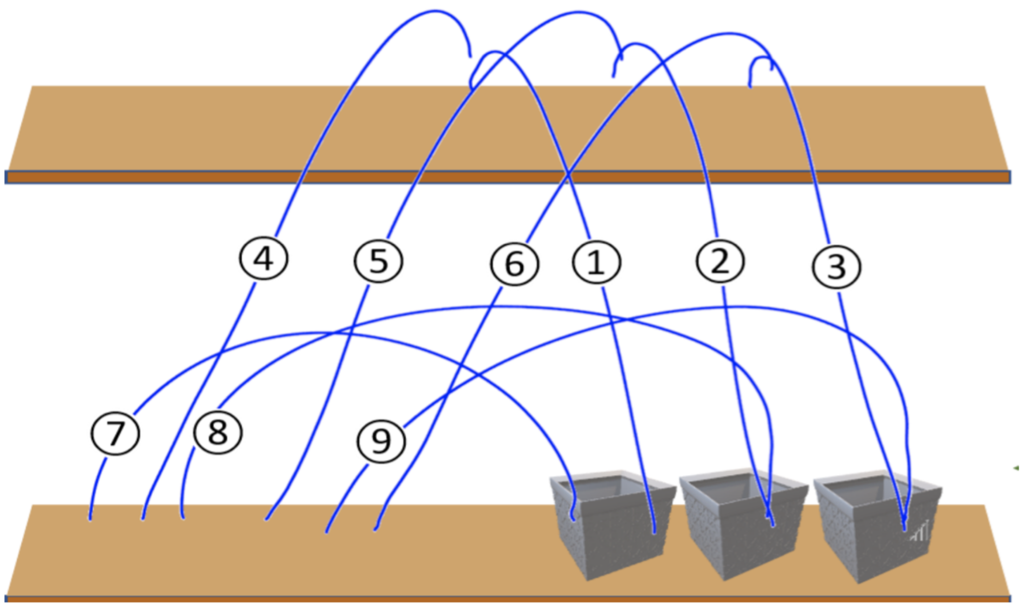

Figure 2.5: Schematic of movements. 9 pick-and-place movements were tested: M1, M2, M3 were performed against gravitational force, M4, M5, M6 in the same direction of the gravitational force, and M7, M8, M9 neutrally with respect to the gravitational force (Table 2.2).

After completing the exergame, participants were asked to fill out a 15-question multiple-choice questionnaire, aimed at assessing the level of engagement and stress induced by the rehabilitation activity. Additionally, data from the patients' medical records were collected, including the results of standard tests assessing the level of impairment

Gravity Condition	Movements	Label
Against	M1, M2, M3	g^-
Propelled	M4, M5, M6	g^+
Neutral	M7, M8, M9	g^0

Table 2.2: Labels for the proposed 9 pick-and-place movements. Movements performed in the same direction where clustered together and labeled under one name.

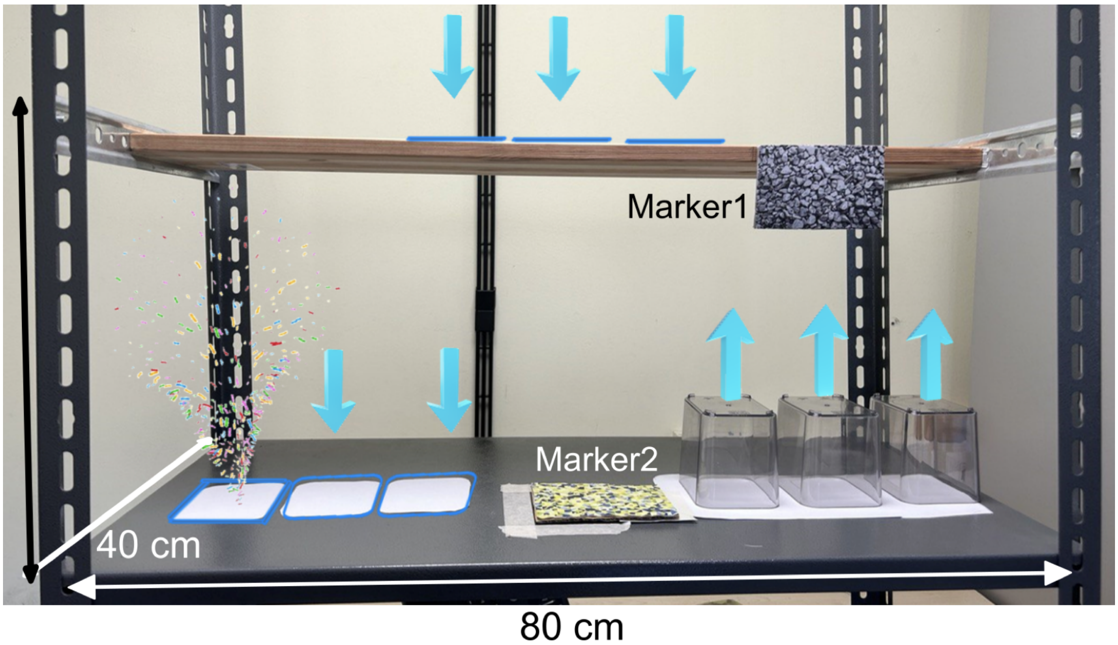

Figure 2.6: Experimental set-up. Characteristics of the library for pick-and-place applications. Holographic cues could be visualized on top of the real scene as arrows, squares, and rewards.

caused to the upper limb by the MS disease.

2.2 Preprocessing

The data processing stage of this study involved several steps to ensure the quality and usability of the kinematic data acquired from PwMS using the HoloLens2 mixed reality visor. The raw log file data from HoloLens2 were transferred to the MATLAB environment, where they underwent a series of transformations and interpolations to create a robust dataset for further analysis.

2.2.1 Data Transfer and Structured Dataset Creation

The preprocessing phase involves handling the hand and eye tracking data collected from the HoloLens 2 system. The HoloLens 2 operates with a sampling rate of 50 Hz, producing detailed log files that capture the raw data necessary for analysis.

The data were structured in hierarchical manner—first by subject, then by repetition, and finally by movement, allowing a systematically analysis of the performance metrics and the derivation of meaningful insights from the collected hand and eye tracking data. This structured approach is critical for the accurate assessment and evaluation of upper limb motor control in the study.

2.2.2 Handling Missing Values

HoloLens2 occasionally fails to detect the hand, resulting in "-100" values in the dataset. These erroneous values were replaced with "NaN" values (Not a Number) to signify missing data points. To maintain the integrity of the data, linear interpolation was performed to estimate these missing values.

Lastly, all the signals consisting of more than 25% "NaN" were discarded, ensuring that the interpolated data remained representative of the actual movements without introducing significant distortions.

2.2.3 Rototranslation and Filtering

A rototranslation was performed on the data to tranform the left-handed coordinate system of Hololens2 to a standard right-handed coordinate system.

The 3D positional data were processed to compute the absolute position using the formula:

$$\text{Absolute hand position} = \sqrt{X^2 + Y^2 + Z^2}$$

A 6-Hz cutoff fourth order low-pass Butterworth filter was applied to the trajectories to reduce noise. [36]

Similarly, the velocity of the hand movements was calculated using the formula:

$$\text{Absolute hand velocity} = \sqrt{V_x^2 + V_y^2 + V_z^2}$$

2.2.4 Automatic Movement Segmentation Algorithm

The focus of the "Automatic Movement Segmentation Algorithm" is to extract meaningful segments of the kinematic signals following the identification of true start and true end points of the movements. This step is crucial because the HoloLens 2 system is not capable of pinpointing the exact moments when the studied movement starts (i.e., when the subject grabs the box) and ends (i.e., when the box is placed down). Instead, the HoloLens 2 tracks the entire movement.

Specifically, the signals were trimmed to selectively extract the portions corresponding to the movement phase, excluding the "reach to grasp" and "return to resting position" segments. This selective extraction aimed to isolate the core movement phase for further analysis.

The first step of the segmentation process involves identifying the initial and final areas of each movement, represented by the "start collided" and "end collided" flags. These flags provide rough markers for the beginning and end of the movement window, respectively.

In the second step, velocity signals calculated for each movement are used to find the precise start and end points. Within the "start collided" window, the minimum velocity point is identified, which represents the moment when the hand stops to pick up the box. Similarly, within the "end collided" window, the minimum velocity point is identified to mark the moment when the hand stops to place the box in its final position, indicated by the holographic blue shape generated by HoloLens.

Once these minima are identified, the position and velocity signals are trimmed between these two points. To finalize the segmentation process, the Reaction Time Theory is applied: the signal is further cut between the two points at 5% of the peak velocity value. This operation ensures a more accurate delineation of the movement boundaries by excluding minor variations and noise around the true start and end points (Figure 2.7).

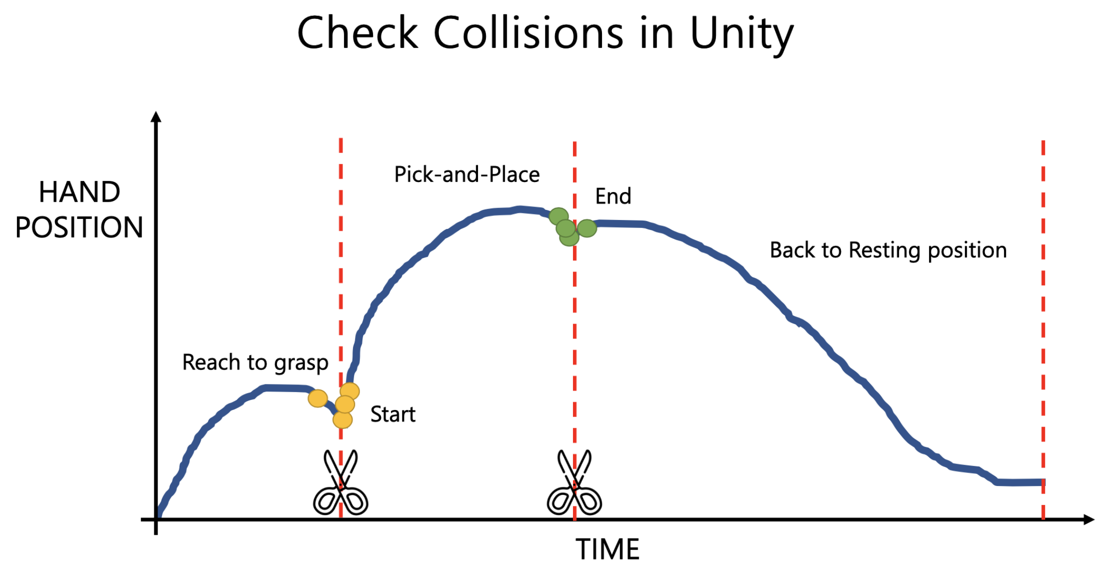

Figure 2.7: Hand movement tracked by HoloLens 2, with cluster points indicating start and end collided areas and dashed lines identified by the "Automatic Movement Segmentation Algorithm".

By implementing this segmentation algorithm, the preprocessing step effectively isolates the relevant portions of the movement, enabling a more precise and reliable analysis of the hand and eye tracking data collected from the HoloLens 2 system.

These pre-processing steps were designed to ensure that the kinematic data were robust, continuous, and accurately segmented. By enhancing the quality and precision of the data, it was possible to compute more reliable and clinically relevant metrics, which are pivotal for evaluating and monitoring upper-limb motor control in people affected by multiple sclerosis.

This comprehensive pre-processing approach lays a solid foundation for the subsequent analysis and interpretation of the rehabilitation data, ultimately contributing to the development of more effective and personalized therapeutic interventions for individuals with multiple sclerosis.

2.3 Data Processing

Once the relevant segments were extracted, they were stored in a new dataset, which was then utilized for computing the metrics of interest. Position and Velocity values were computed again, but this time only the 6-Hz cutoff fourth order low-pass Butterworth filter was applied to the trajectories, to preserve the main components of the velocity profile.

By focusing on the specific movement phase and excluding irrelevant segments, the analysis aimed to provide a more precise assessment of the motor control and coordination during upper-limb movements in subjects acquired.

The extracted dataset served as the basis for computing various kinematic metrics, that were instrumental in quantifying the quality and efficiency of movement execution and provided valuable insights into the motor performance of PwMS during rehabilitation exercises.

The utilization of the selectively extracted dataset ensured that the computed metrics accurately reflected the characteristics of the targeted movement phase, thereby enhancing the relevance and validity of the analysis. This approach allowed for a more nuanced understanding of the upper-limb motor control dynamics in PwMS and facilitated the identification of potential areas for intervention and improvement in rehabilitation strategies.

2.4 Metrics

This study selected several kinematic metrics related to hand displacements and velocities, focusing on smoothness, planning, efficiency, and accuracy [36, 5].

2.4.1 Smoothness

- **Spectral Arc Length (SPARC)**: SPARC is described as the Arch Length of the frequency spectrum obtained through a Fourier Transform of the velocity profile, and quantifies the spatial smoothness of a movement trajectory by analyzing the path taken by the limb during a task.

  This metric is inverted so that more negative numbers represent less smooth data. SPARC is considered a significant indicator of upper-limb impairments due to its reliability in measuring movement smoothness.

  $$\text{SPARC} = -\int_{f_{\min}}^{f_{\max}} \left| \mathcal{F}\left\{ \frac{dv(t)}{dt} \right\} \right|^2 dt$$

  Higher SPARC values indicate smoother, more controlled movements, while lower values suggest jerky or erratic motions, which are often seen in individuals with motor control impairments.

- **Number of Velocity Peaks (NVP)**: NVP represents the number of submovements needed to perform an action. Hand patterns reflecting several peaks in the speed curve indicate impaired smoothness, whereas a bell-shaped speed profile is typical of healthy behavior.

  This metric is used to quantify neurological recovery, as a decrease in the number of submovements suggests improved motor control.

  $$h_i \geq \frac{1}{2} \cdot h_{\max}$$

where $h_{\max}$ is the maximum peak height. Additionally, peaks were required to be separated from any preceding peak by a distance (di) of at least 10% of the total path length (L):

$$d_i \geq 0.1 \times L$$

NVP also provides insights into the motor control strategies used by individuals. Efficient movements typically have fewer velocity peaks, reflecting a more streamlined and coordinated motor execution.

2.4.2 Planning

- **Percent Time to Peak Velocity (PTPV)**: PTPV measures the fraction of the path at which maximum speed (Vmax) is detected.

  It provides insights into the timing and control strategy of the movement, reflecting the efficiency of the planning phase.

  $$\text{PTPV} = \frac{\text{Path length at } V_{\max}}{\text{Total path length}} \cdot 100$$

  A lower PTPV value typically indicates that peak velocity is reached early in the movement, which is characteristic of efficient, well-coordinated motions. Higher PTPV values suggest that peak velocity is reached later, which may indicate inefficient or compensatory movement strategies.

- **Percent Time to Peak Standard Deviation (PTPSD)**: PTPSD is defined as the fraction of the path at which hand displacements show maximum standard deviation, averaged over the x, y, and z dimensions.

  This metric indicates the consistency and variability of the movement across subjects and trials.

  $$\text{PTPSD} = \frac{\text{Path length at } \sigma_{\max}}{\text{Total path length}} \cdot 100$$

Lower PTPSD values indicate more consistent timing in reaching peak velocity, suggesting stable and reliable motor control. Higher PTPSD values indicate greater variability, which can be a sign of impaired motor control or difficulty in coordinating movements.

2.4.3 Efficiency

- **Movement Time (MT)**: MT is defined as the duration of the movement from the moment the object is picked to when it is placed on the target.

  It is widely associated with the overall efficiency of the movement.

  $$\mathrm{MT} = t_{\mathrm{end}} - t_{\mathrm{start}}$$

  Shorter movement times indicate more efficient and faster motor performance, while longer movement times suggest slower, potentially less efficient movements.

2.4.4 Accuracy

- **Target Position Error (TPE)**: Defined as the radius of the smallest sphere containing up to 95% of the final hand positions for each set of movements. Such marker could be useful in determining the level of impairment of neurological patients in accurately positioning an object on target (i.e., if the end-point falls inside or outside the spheres across repetitions) and check whether throughout the therapeutic journey the patient-specific sphere converges into healthy dimensions.

2.4.5 Morphology

- **Symmetry**: Symmetry is a measure of the similarity between the two halves of the movement. Symmetry can provide insights into the coordination and balance of movements. For patients undergoing rehabilitation, especially those recovering from conditions such as stroke or multiple sclerosis, symmetry is an important indicator of recovery progress.

$$\text{Symmetry} = \frac{\text{Duration of the Acceleration Phase}}{\text{Duration of the Deceleration Phase}}$$

Clinically, high symmetry in movements implies effective motor control and suggests that the patient's neuromuscular system is functioning well. Conversely, asymmetry in movements can indicate motor impairments or compensation strategies that might need further therapeutic intervention.

- **Kurtosis**: Kurtosis provides information about the distribution of velocity during the movement. High kurtosis indicates that the movement has more frequent extreme values (peaks), whereas low kurtosis suggests a more uniform distribution of velocities.

  From a clinical perspective, kurtosis can help in understanding the smoothness and control of a patient's movements. Higher kurtosis values may indicate abrupt or jerky movements, which are often characteristic of motor control issues or neurological disorders. Lower kurtosis values, on the other hand, suggest smoother and more controlled movements.

2.4.6 Hand-Eye Coorination

- **Pearson Coefficient**: The Pearson correlation coefficient, also known as Pearson's r, is a measure of the linear correlation between two variables X and Y. It quantifies the strength and direction of the linear relationship between the variables. The Pearson correlation coefficient is defined as the covariance of the two variables divided by the product of their standard deviations.

$$r = \frac{\text{cov}(\text{hand\_displacement}, \text{eye\_displacement})}{\text{std}(\text{hand\_displacement}) \cdot \text{std}(\text{eye\_displacement})}$$

This formula captures the degree to which the two absolute displacements are linearly related, with values ranging from -1 to 1.

$$1 \geq r \geq -1$$

From a clinical perspective, the correlation between eye and hand movements allows for the assessment of coordination between ocular and upper limb movements, which may be impaired in cases of cerebellar dysfunction. Correlation values approaching 1 indicate that eye movements accurately follow hand movements. Negative correlation values indicate an inverse relationship between eye and hand movements, while values approaching zero suggest a lack of synchronization between the two pathways, both indicative of non-physiological behavior.

2.5 Statistics

In this section, the statistical methods employed to analyze the data collected from the study participants are outlined. The analysis was performed in two key stages: first, to determine if the metrics extracted from the eight subjects with multiple sclerosis were statistically independent from each other; and second, to verify the statistical significance of the distributions of these metrics when compared to those of the healthy control group.

1. **Determining Independence of Metrics**
   To ascertain whether the metrics derived from the eight subjects were independent or if they could be grouped together for analysis, we employed the nonparametric Friedman's test. This test is particularly suited for detecting differences in treatments across multiple test attempts and is appropriate when the data does not necessarily adhere to a normal distribution [37]. By using Friedman's test, we assessed if the variances observed in the extracted metrics were consistent across the eight subjects. The outcome of

this test guided us in deciding whether to aggregate the data from all patients into a single dataset for comparison with the healthy control group or to conduct subject-by-subject comparisons.

2. **Assessing Statistical Significance**
   After establishing the independence of the metrics, we proceeded to evaluate the statistical significance of the metric distributions between the group of people with multiple sclerosis and the healthy group. For this analysis, we utilized the two-sided Wilcoxon rank-sum test, also known as the Mann-Whitney U test. This non-parametric test is used to compare two independent samples and determine if their population distributions differ significantly. The choice of the Wilcoxon rank-sum test was driven by its robustness in handling data that does not follow a normal distribution and its effectiveness in comparing small sample sizes [38].

   - **Single Subject Analysis**: When analyzing individual subjects, the Wilcoxon rank-sum test was applied to compare each subject's metrics directly with those of the healthy subjects.
   - **Grouped Data Analysis**: In cases where the Friedman's test indicated that the metrics from the subjects could be aggregated, the Wilcoxon rank-sum test was then used to compare the combined data of multiple sclerosis patients against the healthy control group.

These statistical methods ensured a rigorous examination of the data, allowing to draw meaningful conclusions about the differences in upper limb motor control between patients with multiple sclerosis and healthy individuals.

Chapter 3

Results

In this study, the kinematic profiles of hand position and velocity during various motor tasks were analyzed to quantify motor control performance in the acquired subjects (Figure 3.2, 3.3). The data were collected through the execution of a complex tasks designed to challenge different aspects of motor function, including smoothness, planning, efficiency, accuracy and morphology of the movement 3.1.

Performance	Metric	Abbreviation	Reference
Smoothness	Spectral Arc Length	SPARC	[39, 36, 40]
Smoothness	Number of Velocity Peaks	NVP	[39, 40]
Planning	Percent Time to Peak Velocity	PTPV	[39, 41, 42]
Planning	Percent Time to Peak Standard Deviation	PTPSD	[43]
Efficiency	Movement Time	MT	[39, 41, 43]
Accuracy	Target Position Error	TPE	[5]
Morphology	Symmetry	-	[44]
Morphology	Kurtosis	-	[44]

Table 3.1: Eight kinematic features were selected according to 5 different performance evaluations: smoothness, planning, efficiency, accuracy and morphology. Abbreviations are reported, as well as literature references, if present.

From position and velocity profiles, established metrics were computed and compared against metrics extrapolated from healthy subjects to provide a comprehensive assessment of motor control capabilities.

Following statistical tests and experimental observations (Figure 3.1), data from patients were consolidated into a single dataset. This decision was based on the finding that, for the vertical pick-and-place task, patients with and without tremor did not exhibit significant differences in terms of upper limb kinematics and metric values.

	G-	G+	G0
SPARC	0.940	0.750	0.094
NVP	0.190	0.470	0.066
PTPV	0.790	0.370	0.059
MT	0.127	0.320	0.180
SYMMETRY	0.730	0.710	0.180
KURTOSIS	0.710	0.830	0.410

Figure 3.1: Results of the non-parametric Friedman test for each metric across the three movements (g^{-}, g^{+}, g^{0}). Each cell in the table shows the p-value obtained from the Friedman test, indicating whether the differences observed in the metrics across subjects are statistically significant (statistically significant values were highlighted in red).

This lack of significant variation may be attributed to the nature of the task itself. The execution of a challenging task, such as moving a solid object along a complex trajectory, demands greater concentration and consequently necessitates more detailed planning and control of movement. This is in contrast to simpler, more traditional rehabilitative exercises, where differences between patients with varying levels of impairment might be more pronounced. By requiring such intense focus and precise motor planning, the vertical pick-and-place task likely levels the playing field, highlighting the fundamental motor control strategies shared among all patients, regardless of the presence of tremor.

Therefore, this type of task has its unique characteristics and specific utilities, as it provides a more comprehensive perspective on the consequences of the pathology during more complex activities. It appears that for such intricate tasks, the level of impairment of the patient has a relatively minor importance. This broader view is particularly valuable in understanding the overall impact of the disease on motor control and planning, offering insights that simpler rehabilitative exercises may not reveal.

In this results section the detailed findings from the analysis of the kinematic profiles are presented, providing insights into the specific motor control deficits in patients affected by multiple sclerosis and the potential for targeted rehabilitation strategies to improve motor function.

3.1 Kinematic Analysis

Participants were instructed to perform nine distinct movements (M1-M9) during a Motion Capture analysis (acquisition rate of 50 Hz). The task selected was the pick-and-place one: each subject was required to grab three boxes (10x8x9.5 cm, 0.2 kg) consecutively and move them onto different locations on a library, made of a table and a shelf.

Each sequence underwent three repetitions and no limitations on timing and paths were imposed. Indeed, subjects were asked to perform the movements in a relaxed and natural way. No Particular information was given about the task goals and aims to keep them as naive as possible.

It is important to note that the targets in the library were recreated on paper to match the rectangular shape of the boxes. This design choice restricted the orientation at which objects could be placed on the targets, thereby limiting wrist movements. This was intentionally done to promote movements in the glenohumeral and elbow joints. The recorded average standard deviation of wrist movements across subjects, repetitions, and tasks was 1.2° for flexion/extension, 8.4° for pronation/supination, and 4.4° for ulnar deviation.

3.1.1 Position and Velocity Profiles

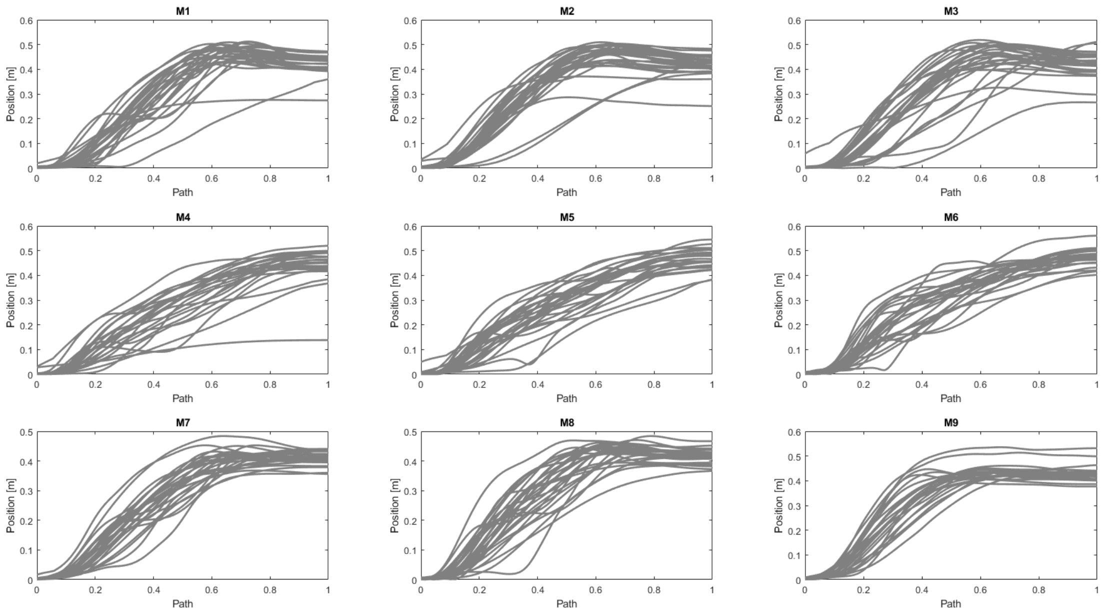

Figure 3.2: Representations of absolute hand positions across each subject, repetition, and movement. Each curve was normalized over their own duration. M1-M3 can be grouped as g^-, M4-M6 as g^+, and M7-M9 as g^0.

Figure 3.2 illustrates the progression of absolute hand displacements for each MS subject, repetition, and movement, normalized over their respective movement times

In healthy individuals the curves can be represented by 6th order polynomials, with an average root-mean-square-error (RMSE) of 3.3±1.9 mm [5]. Regardless of the movement direction, the curves exhibit a consistent pattern consisting of two distinct phases: an initial phase associated with hand motion and a subsequent plateau phase where hand displacements remain relatively constant concerning the path fraction. This second phase may indicate a corrective strategy for placing the object on the target. In contrast, for patients with multiple sclerosis, plateaus are not only present at the end of the movement as a corrective strategy phase, but also occur at intermediate points during the movement. This indicates that these subjects need to implement corrective strategies even during the intermediate phase.

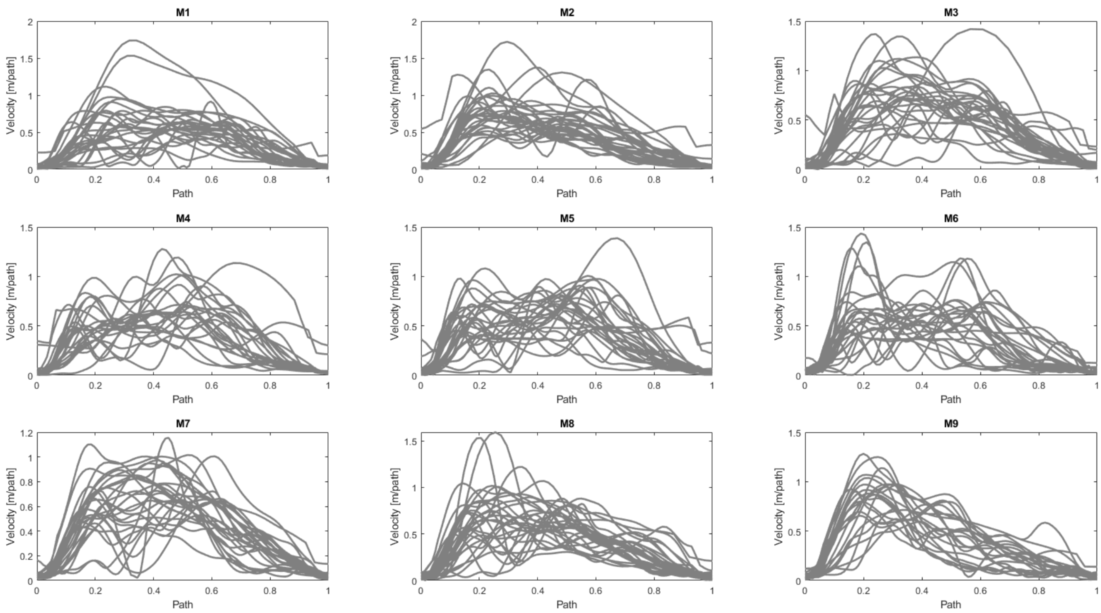

Figure 3.3: Representations of absolute hand velocity across each subject, repetition, and movement. Each curve was normalized over their own duration thus velocity is expressed as m/path. M1-M3 can be grouped as g^-, M4-M6 as g^+, and M7-M9 as g^0.

The figure 3.3 shows the absolute hand velocity profiles for each movement. Similarly, the trend is consistent across subjects and repetitions, with g^- and g^0 displaying overall similar behavior compared to g^+. Movements M1-M3 and M7-M9 feature an initially steeper slope followed by a more gradual descent. Conversely, M4-M6 appear qualitatively mirrored, indicating that when a local maximum is present, it is reached before the main peak, and vice versa for g^- and g^0.

The absolute hand velocity profiles of healthy subjects display asymmetrical bell-shaped trends for all movements [5]. The velocity profiles of patients with multiple sclerosis instead do not exhibit the classic asymmetrical bell-shaped curve observed in healthy subjects. Conversely, they tend to have multiple secondary peaks, both to the right and/or left of the primary peak.

It is easier to analyze the secondary peaks by observing graphs where the velocity profiles are aligned to their respective peak velocities (Figure 3.4).

Out of the total number of 87 curves for each direction-dependent movement, most display more than one peak (85% for g^-, 90% for g^+, and 61% for g^0). It is notable that both the g^- and g^+ sets exhibit a similar distribution of maximum peak counts across repetitions and subjects, as indicated by the Number of Velocity Peaks (NVP). However, the g^0 set shows a slight deviation from this pattern.

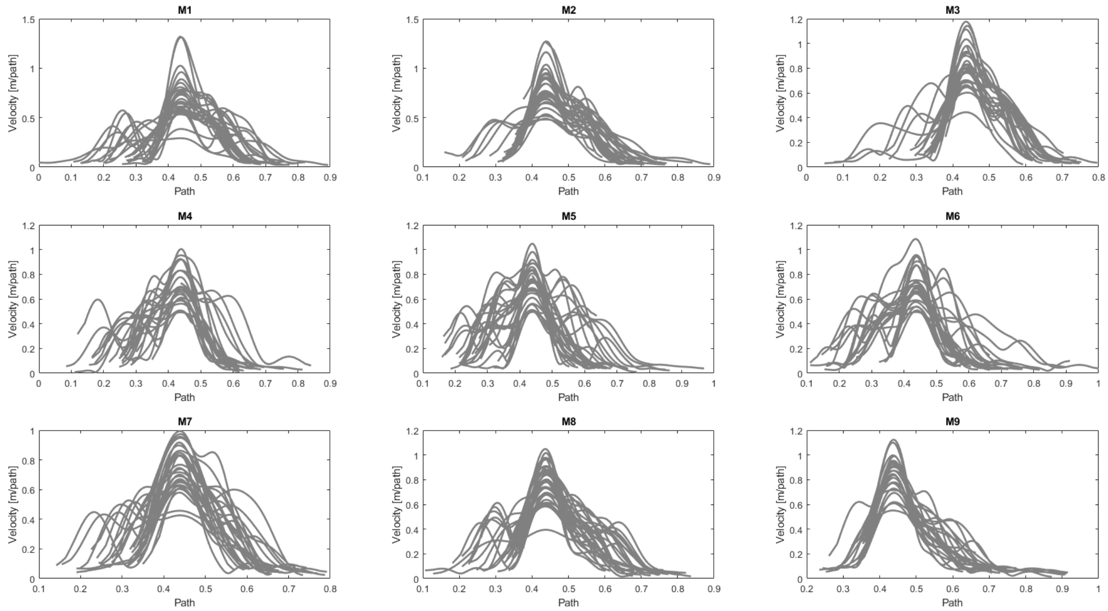

Figure 3.4: Representations of absolute hand velocity -aligned to their peak velocity- across each subject, repetition, and movement. Each curve was normalized over their own duration thus velocity is expressed as m/path. M1-M3 can be grouped as g^-, M4-M6 as g^+, and M7-M9 as g^0.

From the presented outlines 8 kinematic metrics were extrapolated (Table 3.1).

A qualitative observation of the absolute hand paths and speeds for movements against gravity, propelled by gravity, and neutral suggests a similarity between the g^- and g^0 conditions, with a noticeable difference when compared to g^+. This leads to the hypothesis that the selected kinematic features are influenced by the direction of movements relative to gravitational force (Table 2.2). Additionally, for pathological subjects, it is possible that only one of the three conditions is affected by the disease. This is because the hand paths in the three activities are different, which may also lead to differences in the neural pathways that guide muscle activation during movement.

3.1.2 Metrics

In the analysis of the extracted metrics, a notable pattern emerged: all metrics (SPARC, NVP, PTPV, MT, Symmetry), except for Kurtosis, exhibited parallelism between g^- and g^0 movements. This means that the values of these metrics were similar for movements against gravity (g^-) and transverse movements (g^0) (Figure 7, Figure 11). This finding is consistent with the study by Bucchieri et al., which also reported a strong similarity in the velocity profiles of healthy subjects for anti-gravity (g^-) and transverse (g^0) movements.

Furthermore, non-parametric Wilcoxon tests revealed that the distributions of the metrics for patients with multiple sclerosis significantly deviated from those of healthy subjects for the g^- and g^0 movements (Figure 3.7). This indicates a clear distinction in motor performance between the two groups for these types of movements. However, for the downward (g^+) movement, significant differences were observed only in the NVP (Number of Velocity Peaks) and MT (Movement Time) metrics.

These results underscore the complexity and the challenges patients face with anti-gravity and transverse movements. The similarities in the metrics for g^- and g^0 movements, as well as the significant deviations from healthy subject metrics, provide valuable insights into the specific motor control difficulties experienced by these patients. This parallelism suggests that rehabilitation strategies should perhaps focus more intensively on these movement types to better address the specific motor deficits in multiple sclerosis.

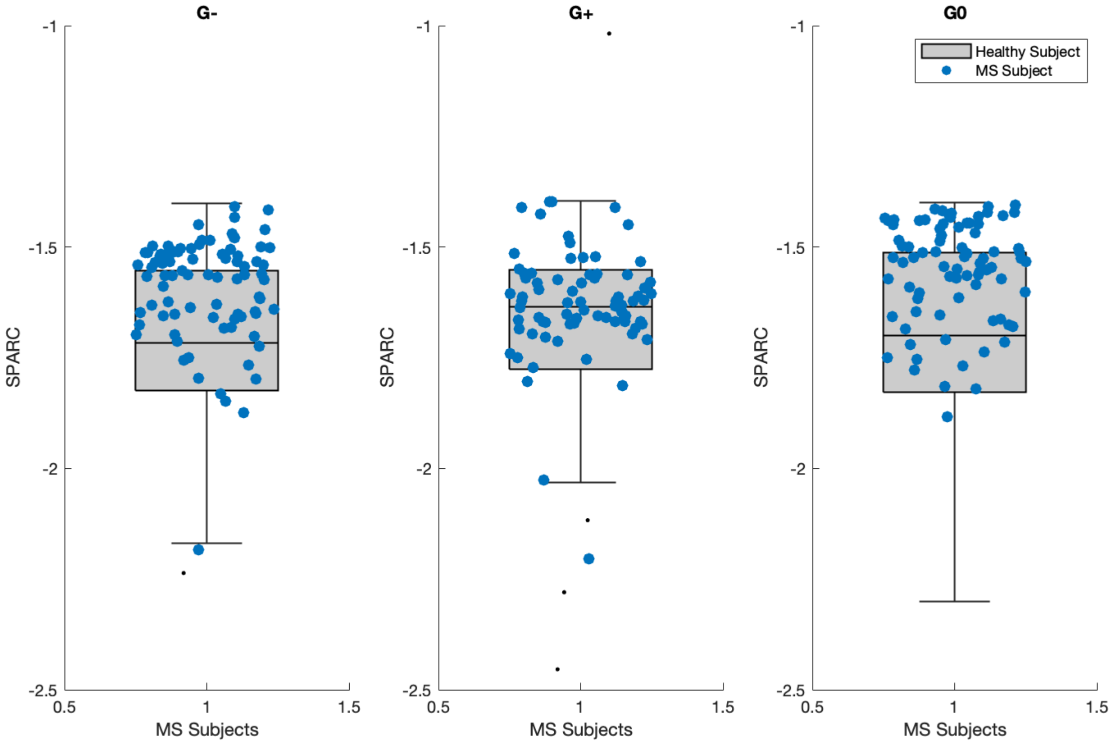

Figure 3.5: Box Charts of SPARC metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

3.1.3 Target Position Error

The Target Position Error metric (Figure 3.8) shows that for all patients, the radii of the spheres for movements against gravity (g^-, red) and with gravity (g^+, blu) are approximately equal. These radii are larger than those for the transverse movement (g^0, green).

For the transverse movement (g^0), the radii of the spheres are notably smaller compared to g^- and g^+ movements. However, there are patient-specific deviations, such as in the case of Subject 1. For this subject, the radius of the sphere associated with the g^- movement is larger than the g^+ and g^0 movements.

Patients suffering from tremor show even larger radii for their spheres, sometimes exceeding those of other patients by an order of magnitude.

These observations underline the importance of the TPE metric in assessing and monitoring the motor control abilities of patients

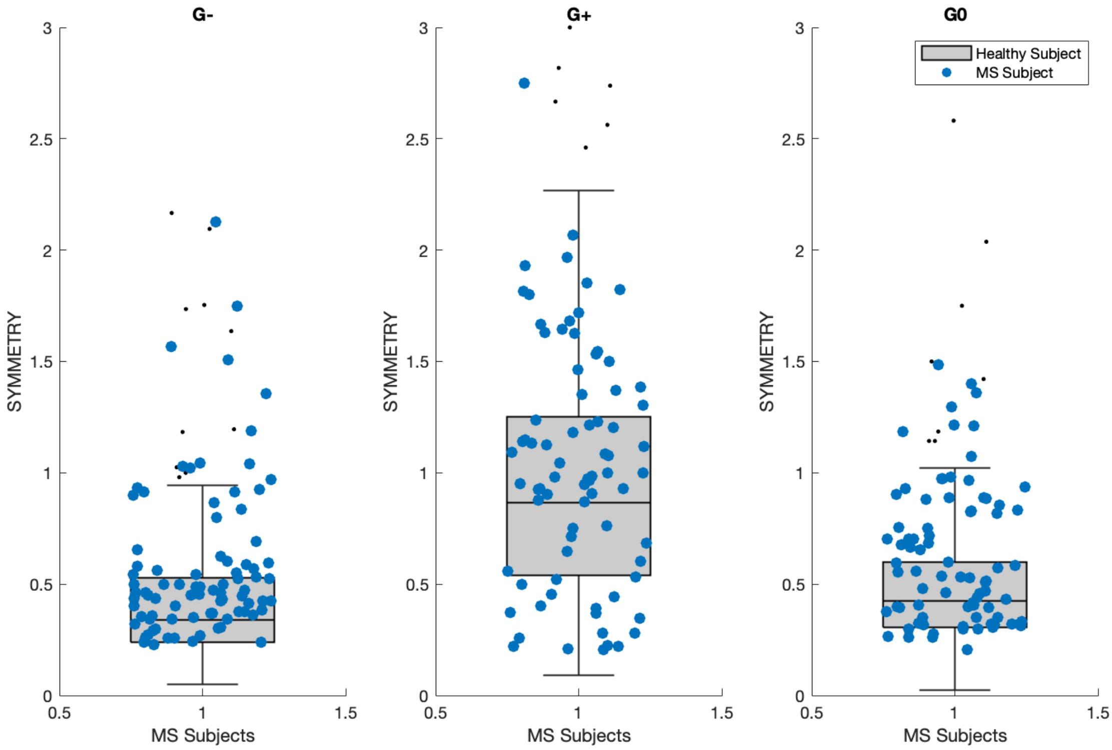

Figure 3.6: Box Charts of Symmetry metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

with neurological impairments. The data suggests that gravitational influence and the presence of tremor significantly affect the precision of hand movements, which is critical for designing effective therapeutic interventions.

3.2 Hand-Eye Coordination

In this section, the metrics of hand-eye coordination are evaluated. Unlike other metrics, the statistical analysis using Friedman's test for hand-eye coordination yielded statistically significant values across all three movement classes (g^-, g^+, and g^0), as shown in Figure 3.9. This result indicates that the data sets for each subject differ from the others in terms of their distribution, necessitating an individual analysis and comparison of each subject with healthy controls. Thus, in this section,

	G-	G+	G0
SPARC	1.5E-07	0.1565	3.3E-08
NVP	4.4E-07	1.0E-08	0.0008
PTPV	4.0E-06	0.2214	0.0016
MT	0.0037	0.0006	0.0155
SYMMETRY	2.0E-06	0.1473	0.0007
KURTOSIS	3.0E-09	0.6290	0.2840

Figure 3.7: This table shows the p-values from the non-parametric Wilcoxon test applied to kinematic metrics across subjects for the three movement classes: against gravity (g^-), with gravity (g^+), and transverse (g^0). Red colored cells indicate statistically significant values ($p < 0.05$).

the distinct patterns and deviations between each patient and healthy subjects will be explored.

Regarding hand-eye coordination, a comparison with healthy subjects shows that the latter do not exhibit an extremely high correlation between hand and eye positions.

For patients, however, the metrics reveal values either very close to 1 or significantly below the average values of healthy subjects. This indicates a more variable and less predictable hand-eye coordination in patients, highlighting the distinct differences in motor control between the two groups.

The mean of the Hand-Eye Coordination distribution for patients S2, S5 show a statistically significant difference compared to the mean value of the healthy subjects for movement g^-.

The mean of the Hand-Eye Coordination distribution for patients

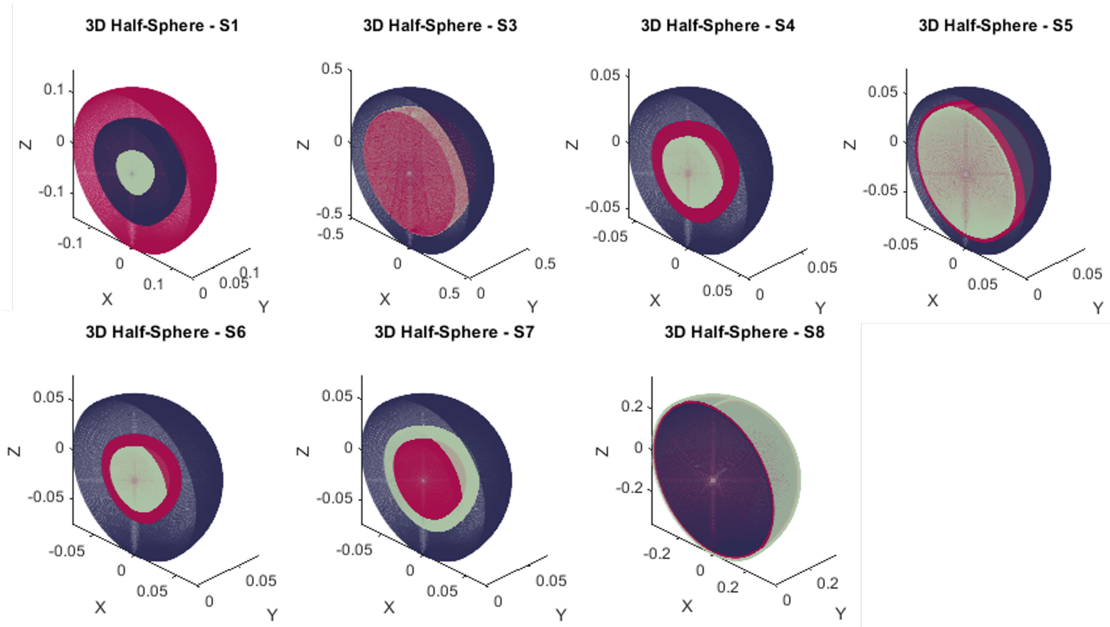

Figure 3.8: 3D view of Target Position Error (TPE) metric defined as the sphere whose radius contains up to 95% of hand end-points. Sphere related to g^- in pink, g^+ in violet and g^0 sphere in green.

	G-	G+	G0
HAND-EYE COORDINATION	0.0280	0.0290	0.0100

Figure 3.9: Results of the non-parametric Friedman test for hand-eye coordination across the three movements (g^-, g^+, g^0). Each cell in the table shows the p-value obtained from the Friedman test, indicating whether the differences observed in the metrics across subjects are statistically significant (statistically significant values were highlighted in red).

S4, S6, S7, S8 show a statistically significant difference compared to the mean value of the healthy subjects for movement g^+.

The mean of the Hand-Eye Coordination distribution for patients S1, S3, S5, S6, S7, S8 show a statistically significant difference compared to the mean value of the healthy subjects for movement g^0.

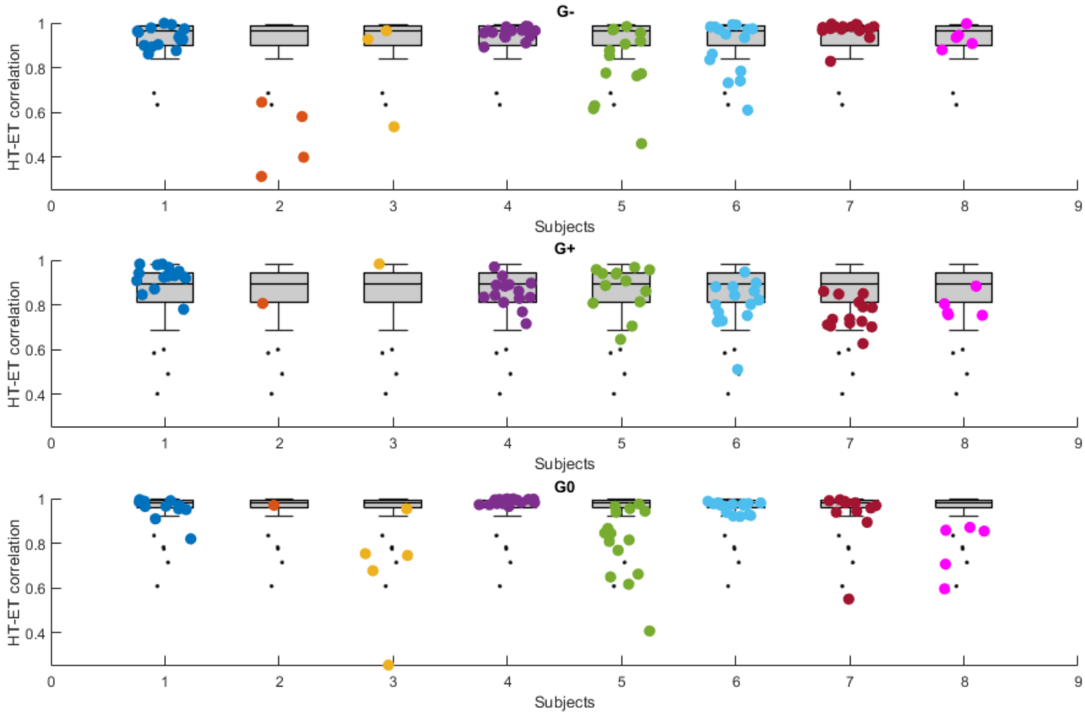

Figure 3.10: Distribution of Hand-Eye Correlation Coefficients. Box Charts of Hand-Eye Correlation Coefficients for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

Chapter 4

Discussion

Neurological disorders can severely impact upper limb function, hindering daily activities. Key tasks such as organizing, eating, and maintaining personal hygiene often require repetitive shoulder and elbow movements within the sagittal plane and involve handling various loads. Gravitational force plays a crucial role in the planning and execution of these movements.

This study presents an accessible setup to analyze postural patterns during functional tasks (Figure 2.1). Specifically, the pick-and-place movement is used as a simplified model of daily activities, providing a means to evaluate user performance in task completion.

The kinematic data collected during the execution of the task were processed to generate detailed position and velocity profiles for each participant. These profiles provide insights into the trajectory formation and movement strategies employed by individuals with MS. According to the foundational work by Abend, Bizzi, and Morasso (1982), natural limb movements typically involve the coordination of multiple joints, which the central nervous system manages to create smooth and efficient trajectories [26].

In people with multiple sclerosis motor control, defined as the ability to regulate and direct the mechanisms essential for movement, is fundamentally impaired due to the disruption of neural pathways responsible for coordinated muscular activity [6]. Shadmehr and Mussa-Ivaldi

(1994) [27] showed that the nervous system adapts to changes in dynamics through the formation of internal models, which are critical for the execution of smooth and coordinated movements. Similarly, Abend et al. (1982) [26] demonstrated that the brain utilizes a flexible control system to adaptively manage motor tasks, suggesting that variability in motor performance could reflect underlying neural adaptability or pathology.

Building on these observations, performing a more complex rehabilitative task, as opposed to a simple bi-dimensional movement on the horizontal plane, could reveal different behaviors, recruitment strategies, and control mechanisms, stemming from the adaptation to the pathological condition of multiple sclerosis. Furthermore, it is plausible that the consequences of the disease, from the perspective of kinematic analysis, manifest differently depending on the type of movement performed (g^-, g^+, g^0), as a result of the various control strategies and pathways underlying the execution of each of these complex movements.

In summary, the results suggest that the hypothesis regarding the impact of movement direction in relation to gravity on the selected metrics compared between healthy subjects and those suffering from multiple sclerosis is confirmed in g^- movement for every metric excluding TPE, which is analyzed separately. The hypothesis is proven in g^- movement for MT and NVP and finally in g^0 movement for PTPV, MT, SPARC and Symmetry.

4.1 Upper Limb Kinematics

This study centers on extracting kinematic features from hand and eye movement patterns captured by the HoloLens 2. We selected eight primary metrics to evaluate different characteristics of hand trajectories: Symmetry and Kurtosis for assessing morphology, Spectral Arc Length and Number of Velocity Peaks for analyzing smoothness, Movement Time for measuring efficiency, Percent Time to Peak Velocity for planning and Target Position Error for accuracy.

This thorough analysis aims to provide a comprehensive understanding of how these metrics can be utilized to assess upper limb motor control in individuals with multiple sclerosis, and how they compare to the performance of healthy subjects.

4.1.1 Smoothness

The shape of absolute hand velocity provides valuable insights into the smoothness of a performed movement and can be used as a marker for evaluating neurological disorders. One of the most established metrics for analyzing movement smoothness is the number of velocity peaks (NVP). According to numerous studies, patients with neurodegenerative diseases tend to exhibit more jagged velocity profiles with numerous secondary peaks due to the fragmentation or decomposition of movement into multiple submovements [34], unlike healthy subjects who typically show a smooth bell-shaped velocity profile with a single distinguishable peak. Significant deviations from the behavior of healthy subjects are observed specifically in movements against gravity (g^-) and with gravity (g^+). The increased NVP in g^- and g^+ movements reflects the greater difficulty these patients have in executing smooth, continuous movements against and with gravity, respectively. This suggests that tasks involving such movements might be more effective in revealing the extent of motor impairment in these patients.

Another perspective on movement smoothness is provided by the spectral arc length (SPARC) metric, which analyzes the frequency components of the movement. According to trends observed in studies by Bayle et al. [36], backward movements (g^+) exhibit lower SPARC values, indicating less smooth movements, compared to g^- and g^0. Moreover, The lower SPARC value for g^+ movements compared to the other two can be interpreted by the general observation that backward movements typically exhibit lower smoothness. This suggests that the movements most affected by the motor impairment due to the disease are those against gravity (g^-) and transverse movements (g^0), which are typically much smoother under normal conditions. Finally, comparison of SPARC data in the present study and data found in literature [36, 45] indicate that, overall, the proposed pick-and-place task leads to less smooth profiles than free reaching (either 3D or 2D). This might be due to the difference in the nature of the task and the additional interaction with physical objects.

4.1.2 Efficiency

The efficiency of movement is widely associated with the time taken to complete it, commonly referred to as Movement Time (MT). In this study, subjects were not constrained by any time restrictions, yet the task duration typically ranged between 1.5 and 2.5 seconds. Statistical analyses indicated that individuals with multiple sclerosis generally performed the task slower than the average of healthy subjects. A comparative analysis across the three different movement types revealed significant variability in task duration, especially for movements assisted by gravity (g^+), making it challenging to identify a clear central tendency.

4.1.3 Planning

The Percent Time to Peak Velocity (PTPV) provides insights into the movement strategy and planning, particularly how the central nervous system (CNS) plans and initiates motor tasks. In typical motor control, a smooth and well-planned movement is characterized by a PTPV value that reflects an initial rapid acceleration to peak velocity, followed by a more controlled deceleration phase. This pattern signifies efficient and coordinated motor planning. Healthy subjects generally exhibit PTPV values between 30% and 40%, indicating a quick approach to peak velocity followed by a steady deceleration. Patients with multiple sclerosis showed PTPV values ranging from 40% to 65%. These higher values suggest that multiple sclerosis patients take longer to reach their peak velocity and among the three movements analyzed in the pick-and-place task, the vertical movement against gravity (g^-) showed the most statistically significant difference compared to healthy subjects. This observation can be justified by the additional effort required to perform movements against gravity, which may exacerbate the motor control challenges faced by patients, together with the fact that multiple sclerosis often causes muscle weakness and fatigue, which can slow down the initial acceleration phase of the movement. It should be also taken into consideration that patients may adopt different movement strategies to compensate for their impairments, such as slower, more deliberate movements to maintain control and accuracy.

4.1.4 Morphology

Symmetry and Kurtosis are two important metrics in movement analysis. The symmetry metric is crucial for understanding the uniformity of the movement trajectory and refers to how evenly distributed the movement is around a central axis. In healthy subjects, symmetry values typically range between 0.35 and 0.75. This range indicates a balanced movement with a consistent pattern of acceleration and deceleration. In contrast, in the experiments conducted for this thesis, patients with multiple sclerosis exhibited symmetry values between 0.5 and 1.5. These higher values highlight a profound difference in morphology in comparison to the symmetric, bell-shaped, healthy velocity profile.

Among the three movements analyzed, the vertical movement against gravity (g^-) showed the most statistically significant difference in symmetry compared to healthy subjects. The transverse movement (g^0) also displayed notable differences. The increased asymmetry in these movements suggests that multiple sclerosis patients rely on compensatory mechanisms that disrupt the natural balance of movement, making their trajectories more asymmetrical.

Kurtosis measures the "tailedness" of the movement's velocity distribution. A high kurtosis value indicates that the movement has a sharp peak and heavy tails, meaning most of the movement is concentrated around a central velocity with occasional rapid changes. Lower kurtosis values suggest a more uniform distribution of velocities.

Healthy subjects typically exhibit kurtosis values between 1.5 and 3, indicating a well-distributed and controlled movement pattern. Patients showed kurtosis values between 1.3 and 2, particularly for the vertical movement against gravity (g^-). This reduction in kurtosis values is associated with less peaked and more variable movements, caused by the additional challenges posed by the complexity of the pick-and-place task, especially in vertical movements.

4.1.5 Accuracy

In examining accuracy, this study introduced a novel indicator, the Target Position Error (TPE), which assesses the precision in placing an object on a target. Unlike the other metrics discussed, TPE revealed a unique pattern, showing similarities between movements opposed by gravity (g^-) and neutral movements (g^0), as opposed to those assisted by gravity (g^+). Furthermore, TPE for vertical pick-and-place task was found to be the only metric with a significant statistical difference between subjects. Movements that exhibit the greatest accuracy through repetitions are neutral movements (g^0), this may be due to the underlying principles of hand-eye coordination. The retina's receptors provide critical feedback on the target's location relative to the limb, leading the CNS to create plans that depend significantly on seeing both the hand and the target simultaneously, along with motion impulses based on visual and proprioceptive feedback. Considering the experimental set-up (Figure 2.5), g^0 does not require large vertical head movements to visualize both the start and target position of the object, as well as the hand while moving it. This is not true for movements g^+, g^- thus explaining why TPE is higher in those two conditions.

The TPE metric indicated that for all patients, the sphere radii for movements against gravity (g^-, red) and with gravity (g^+, blue) were both larger than those for the transverse movement (g^0, green). This pattern suggests that achieving accuracy in hand positioning at the target is generally more difficult for movements influenced by gravity.

For the transverse movement (g^0), the sphere radii were noticeably smaller compared to g^- and g^+ movements, indicating better control and precision in movements unaffected by gravity. However, there were patient-specific variations. For example, Subject 1 exhibited a larger radius for the sphere associated with the g^- movement compared to g^+ and g^0 movements, indicating a higher level of imprecision in movements against gravity, suggesting significant impairment under this condition.

Patients with tremor showed even larger sphere radii, sometimes an order of magnitude greater than those of other patients. This significant increase highlights the severe impact of tremor on their ability to precisely position their hand on the target, further emphasizing the difficulties these individuals face in performing accurate movements.

In conclusion, the experiments conducted in this study revealed distinct differences in performance compared to healthy subjects, particularly in the movement against gravity (g^-), observations aligning with the conclusions drawn by Atkeson and colleagues [32] regarding the computation of reaching arm trajectories between distinct points in the vertical plane. However, this variation was not uniform across all the metrics analyzed. Each of these metrics provides a unique perspective on the impact of multiple sclerosis on motor control, suggesting that different aspects of motor impairment are highlighted depending on the metric used. The study design, particularly the division of the pick-and-place task into three movements, enables the extraction of additional data that cannot be obtained through standard clinical metrics such as the 9-Hole Peg Test, Box and Block Test, and Expanded Disability Status Scale. This structured approach allows for the identification of specific impairments that might be missed by these broader, qualitative clinical assessments. For instance, certain patients may exhibit high performance on the 9-HPT and BBT but still demonstrate significant precision issues in specific tasks like moving an object against gravity (g^-).

The findings suggest that more complex tasks, such as vertical pick-and-place activities, tend to expose motor impairments more effectively in movements against gravity (g^-) compared to other movements. This could be due to the increased difficulty of compensating for the effects of gravity, which places greater demands on the motor control system.

An alternative explanation is that the neural pathways responsible for controlling movements against gravity are more susceptible to the effects of multiple sclerosis and are less able to compensate for these effects compared to pathways involved in neutral or gravity-assisted movements. This insight emphasizes the need for targeted rehabilitation strategies that focus on improving motor control for a specific type of movement (movements against gravity, in this case) in people with multiple sclerosis.

The greater difficulty experienced by subjects in completing the task is confirmed by the fact that the average movement time (MT) is significantly higher compared to horizontal tasks performed by the same individuals using the same motion capture acquisition technologies. Additionally, the planning metric, PTPV, shows that for horizontal exercises, subjects reach maximum movement velocity in a relatively short time (about 30-40% of the movement), whereas in the vertical task, this value extends considerably. This indicates that the patient is forced to invest more energy in the planning phase, lengthening the acceleration phase and thereby reducing the overall speed.

Overall, these findings underscore the importance of selecting appropriate metrics for evaluating motor control in people with multiple sclerosis, as different metrics can reveal different aspects of motor impairment and highlight specific motor control problems that can not be addressed and revealed by classic clinical scales. Future research should continue to explore these differences and develop tailored rehabilitation approaches that address the specific challenges faced by patients in performing movements against gravity.

4.2 Hand-Eye Coordination

Regarding hand-eye coordination, a observation of healthy subjects demonstrates that they do not exhibit a very high correlation between hand and eye movements. This indicates their ability to perform more complex movements with less reliance on visual assistance, as the paths of their hands and gaze are not perfectly overlapping during the task. This suggests greater mastery and confidence in executing the movement.

For the patients, however, the metrics either approach very high values of correlation or fall well below the average values of healthy subjects. These two opposite cases can be explained by analyzing the patients' pathological conditions.

Subjects S3 and S8, who exhibit cerebellar tremor and associated visual problems, show lower correlation values and a significantly different mean from the distribution of healthy subjects. This can be explained by taking into account that patients with cerebellar tremor may struggle to synchronize visual input with motor output effectively. The tremor itself introduces unpredictable and erratic motion, making it difficult for the visual system to accurately predict and compensate for these movements. Indeed, while multiple sclerosis patients without cerebellar tremor may compensate for proprioceptive deficits by relying more on visual feedback, those with cerebellar tremor may find it challenging to utilize visual feedback effectively due to the continuous and involuntary oscillations.

The other patients, on the other hand, display higher correlation values. These subjects show mean distribution values that do not significantly differ from those of healthy individuals but are more concentrated in the upper area of the box chart, towards values closer to 1. This indicates less motor control in performing a more challenging rehabilitative task, which forces them to constantly monitor their hand position through vision. In fact, patients with multiple sclerosis may rely more on visual feedback to compensate for their impaired proprioception and motor control. Because of the demyelination and neuronal damage associated with multiple sclerosis, proprioceptive feedback (sensory information from muscles and joints) can be unreliable or delayed. Therefore, patients depend more heavily on visual cues to guide their movements. Also, performing a complex or unfamiliar task, like the proposed vertical pick-and-place exergame, may further enhance the reliance on visual feedback in MS patients. The increased difficulty level requires more frequent visual monitoring to ensure accurate and effective movement execution, leading to a higher correlation between hand and eye movements.

In conclusion, the experiments conducted in this study revealed distinct differences in performance compared to healthy subjects, particularly in the movement against gravity (g^{-}), observations aligning with the conclusions drawn by Atkeson and colleagues [32] regarding the computation of reaching arm trajectories between distinct points in the vertical plane. However, this variation was not uniform across all the metrics analyzed. Each of these metrics provides a unique perspective on the impact of multiple sclerosis on motor control, suggesting that different aspects of motor impairment are highlighted depending on the metric used. The study design, particularly the division of the pick-and-place task into three movements, enables the extraction of additional data that cannot be obtained through standard clinical metrics such as the 9-Hole Peg Test, Box and Block Test, and Expanded Disability Status Scale. This structured approach allows for the identification of specific impairments that might be missed by these broader, qualitative clinical assessments. For instance, certain patients may exhibit high performance on the 9-HPT and BBT but still demonstrate significant precision issues in specific tasks like moving an object against gravity (g^-).

The findings suggest that more complex tasks, such as vertical pick-and-place activities, tend to expose motor impairments more effectively in movements against gravity (g^-) compared to other movements. This could be due to the increased difficulty of compensating for the effects of gravity, which places greater demands on the motor control system.

An alternative explanation is that the neural pathways responsible for controlling movements against gravity are more susceptible to the effects of multiple sclerosis and are less able to compensate for these effects compared to pathways involved in neutral or gravity-assisted movements. This insight emphasizes the need for targeted rehabilitation strategies that focus on improving motor control for a specific type of movement (movements against gravity, in this case) in people with multiple sclerosis.

It is noteworthy that there are often parallels between the metric values for movements against gravity (g^-) and those for transverse movements (g^0). These two types of movements tend to show similar position and velocity profiles (Figure 3.3), distinguishing them from the movements with gravity (g^+). This similarity suggests that both g^- and g^0 movements share common motor control challenges and characteristics.

Overall, these findings underscore the importance of selecting appropriate metrics for evaluating motor control in people with multiple sclerosis, as different metrics can reveal different aspects of motor impairment and highlight specific motor control problems that can not be addressed and revealed by classic clinical scales. Future research should continue to explore these differences and develop tailored rehabilitation approaches that address the specific challenges faced by patients in performing movements against gravity.

Chapter 5

Conclusions

Building upon a novel and straightforward experimental setup for evaluating upper-limb functional recovery, this study aimed to characterize the kinematic strategies employed by people with multiple sclerosis during a pick-and-place task. Unlike the free-reaching tasks commonly explored in the literature, interacting with a load while performing movements can positively affect the functional performance recovery of neurologically impaired individuals. This study also integrates a contextualization with the state of the art in motor control strategies, focusing primarily on the impact of gravity on the three movements examined. This approach allows for a deeper understanding of how gravitational forces influence motor planning and execution, contributing valuable information to the field of upper-limb motor control and rehabilitation.

Focusing on upper-limb motor behavior in relation to motor control principles is crucial for discussing the applicability of research findings, informing rehabilitation strategies, and contributing to the ongoing advancement of knowledge in the field. Observations of healthy hand movements during the pick-and-place task have revealed the significant influence of varying gravity conditions on task performance [5]. Movements performed against or with gravity prompt different motor plans by the central nervous system, leading to noticeable distinctions in biomechanical behavior.

The findings of this study showed that for a vertical pick-and-place task with physical objects, patients with multiple sclerosis all exhibited similar behaviors with overlapping distributions among them, and that the kinematic metrics were statistically significant mainly when focusing on one gravity condition among subjects. Therefore, designing rehabilitation sessions for upper-limb impairments must consider these biomechanical differences during evaluations. However, not all metrics showed significant differences, highlighting that each metric provides a unique perspective on the effects of the disease. Finally, the results suggest that rehabilitative tasks requiring greater concentration and effort tend to make movement kinematics more comparable among subjects with different clinical profiles. This allows for the identification of patterns in the most critical movement classes. The increased difficulty of the vertical task is evidenced by significantly longer movement times compared to horizontal tasks performed under the same conditions. Furthermore, the PTPV metric indicates that subjects take a longer time to reach maximum velocity in vertical tasks, reflecting the increased energy required for planning and extended acceleration phases, which ultimately reduces overall movement speed.

This study also underscores the importance of using this novel type of complex, gravity-influenced tasks to gain a comprehensive understanding of the impact of multiple sclerosis on motor control. The differences between healthy and impaired subjects were most pronounced in movements against gravity, suggesting that these tasks could be particularly useful in assessing and addressing the motor impairments associated with the disease. The unique characteristics and specific utilities of these tasks provide a broader perspective on the consequences of the pathology, offering valuable insights for the development of more effective rehabilitation strategies.

Overall, this study characterized a standardized protocol of upper-limb functional movement for people with multiple sclerosis while interacting with a load and identified possible motor patterns that differ significantly form those of healthy subjects. The absolute hand positions and velocities demonstrated distinct behaviors for movements performed against or propelled by gravity, consistent with previous motor control studies. From this dataset, seven existing and one novel kinematic features were tested and compared with the state-of-the-art to assess the impact of gravity on impaired upper-limb functional movements, providing metrics useful in rehabilitation.

5.1 Future work

The limitations of this study include the recruitment of participants, making the proposed metrics match the reference age population of healthy subjects. Given that neurological impairments predominantly affect older individuals, future studies should include elderly, able-bodied participants to create a secondary, suitable kinematic dataset. Investigating any changes in the kinematic behavior of elderly subjects' hands is essential, as previous studies have highlighted differences in vertical movements among the elderly population. Additionally, while the acquired data reflect a balanced sex distribution, future research could explore potential differences in motor control strategies between female and male participants.

Several factors limit the investigational capabilities of this study, primarily stemming from the tracking capabilities of the HoloLens 2 device. Firstly, the HoloLens 2 has a sampling frequency that is half of what is offered by traditional motion capture systems like Vicon. This reduced sampling rate may affect the precision of the captured kinematic data.

Additionally, the field of view in which holograms are visible to the subject is restricted by the small size of the lenses. This limitation could hinder the subject's interaction with the holograms and potentially affect the naturalness and accuracy of their movements.

Moreover, the device is highly dependent on the initial calibration conditions and the surrounding environment. Any changes or inconsistencies in these factors can significantly impact the accuracy of the tracking and the overall reliability of the data collected.

Another limitation is the battery life of the HoloLens 2, which necessitates regular charging. This constraint prevents the device from being used for extended sessions, thereby limiting the duration of the study and the potential for long-term observations and analyses.

These limitations highlight the challenges of using the HoloLens 2 for detailed kinematic studies and suggest a need for further development and refinement of mixed-reality devices to enhance their applicability in rehabilitation and clinical research settings.

This appendix provides an extended collection of all the figures and graphs referenced throughout the thesis. This section serves as a comprehensive visual supplement to the main text, offering detailed illustrations of raw data plots and in-depth analyses of the metrics used in the study. Each figure and graph is presented with its full context and description, allowing for a clearer understanding of the experimental results and the methodologies employed. This extended visual representation ensures that all aspects of the research are thoroughly documented and accessible for detailed review and further study.

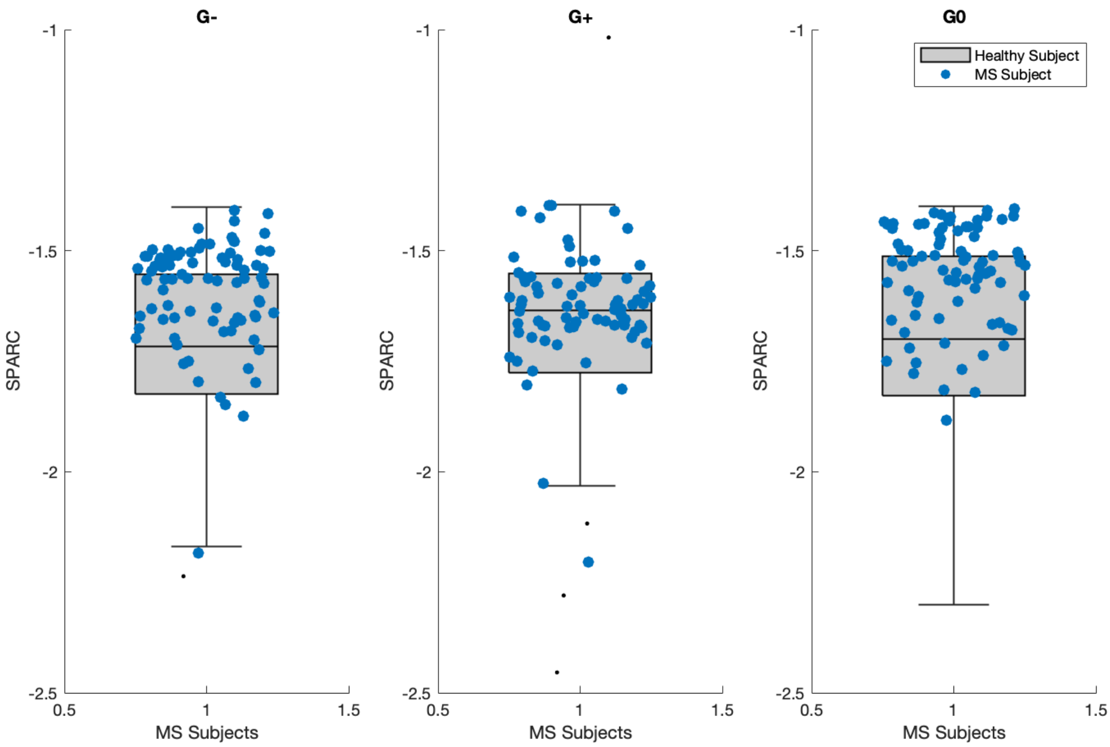

Figure 1: Box Charts of SPARC metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

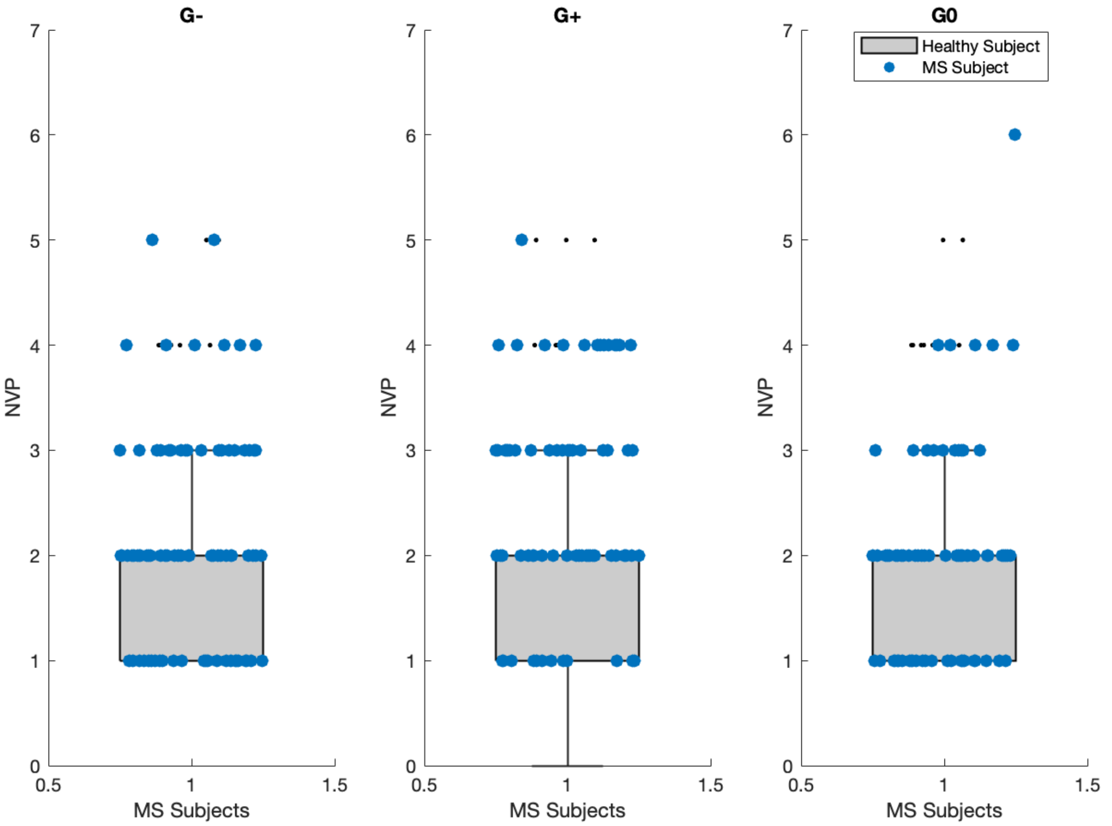

Figure 2: Box Charts of NVP metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

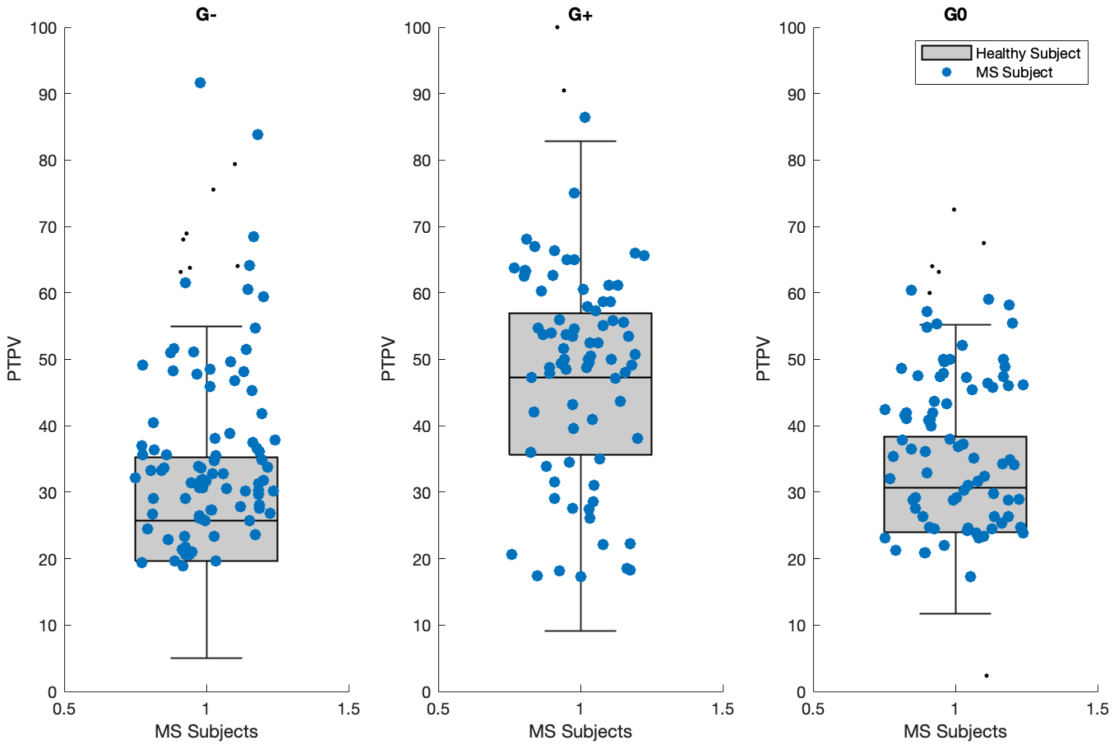

Figure 3: Box Charts of PTPV metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

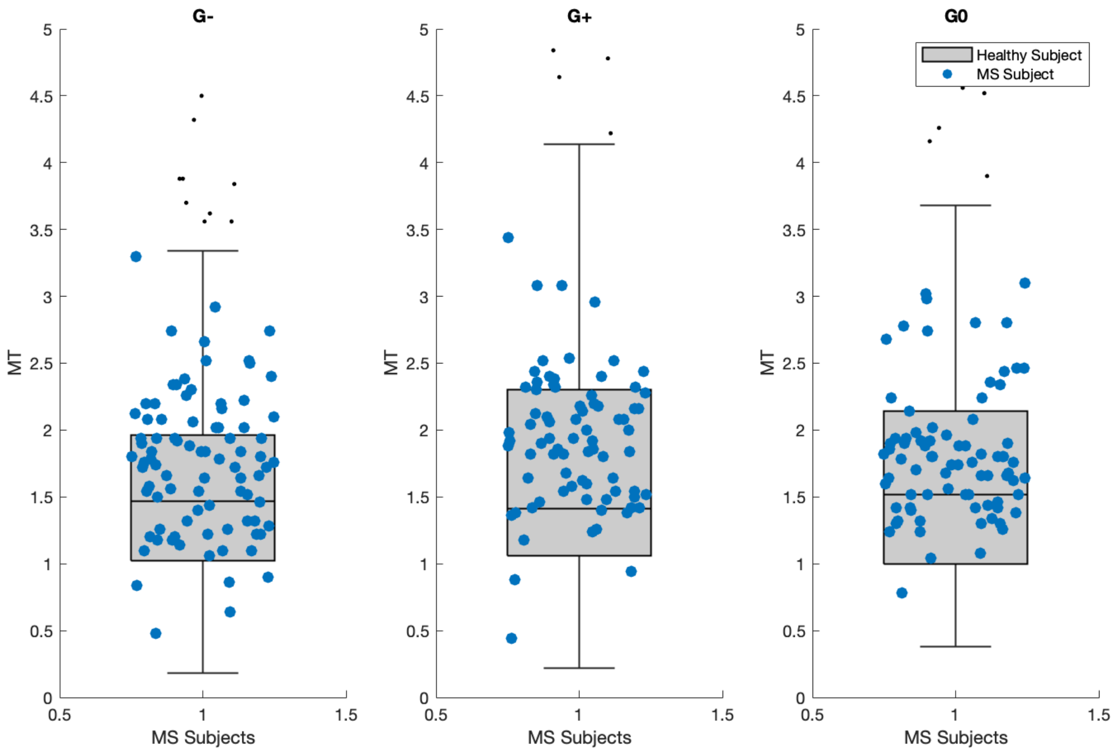

Figure 4: Box Charts of MT metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

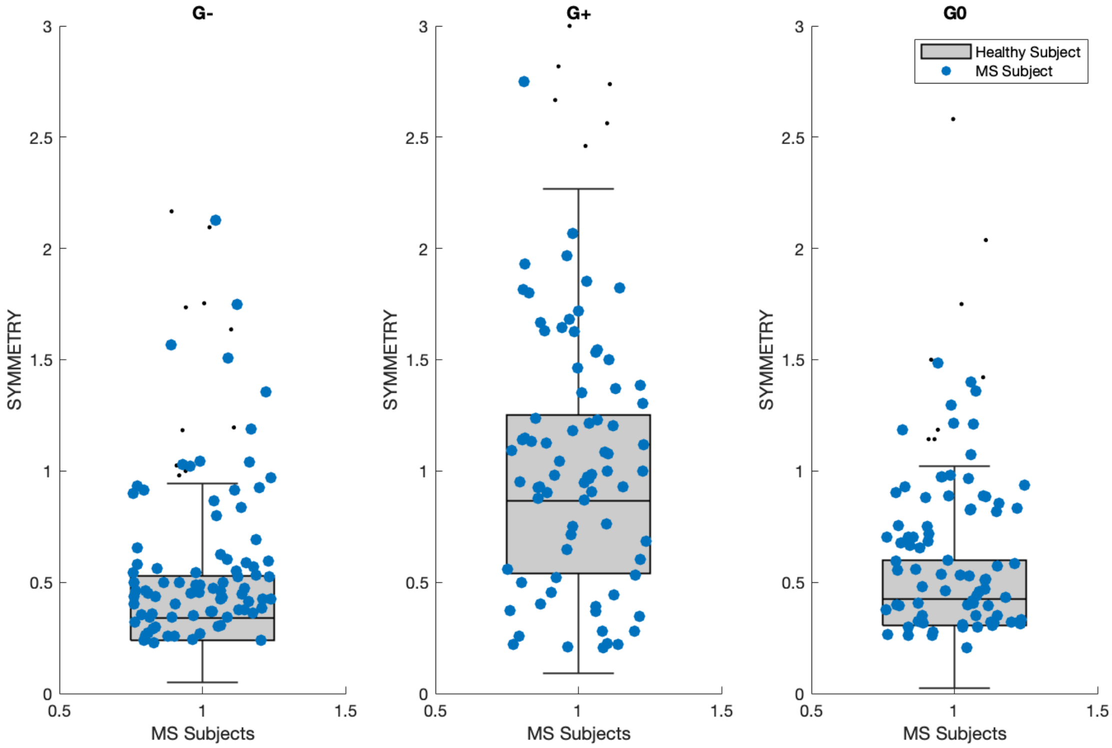

Figure 5: Box Charts of Symmetry metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

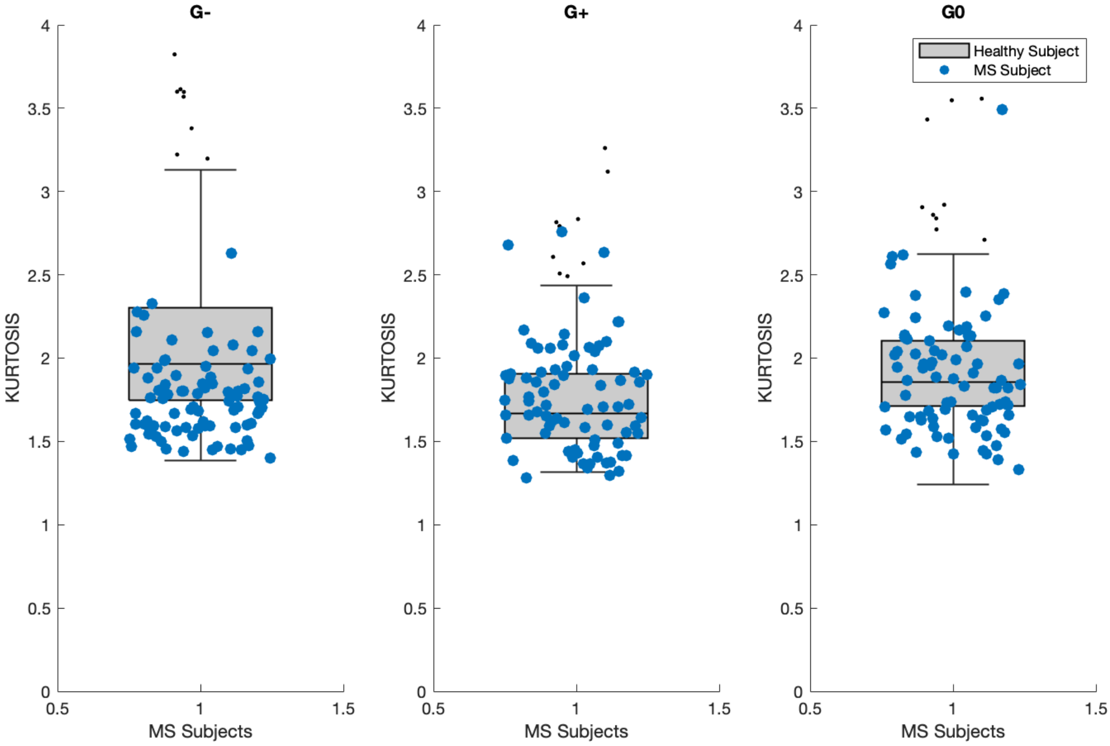

Figure 6: Box Charts of Kurtosis metric for Healthy Subjects with Overlaid Scatter Points for MS Subjects.

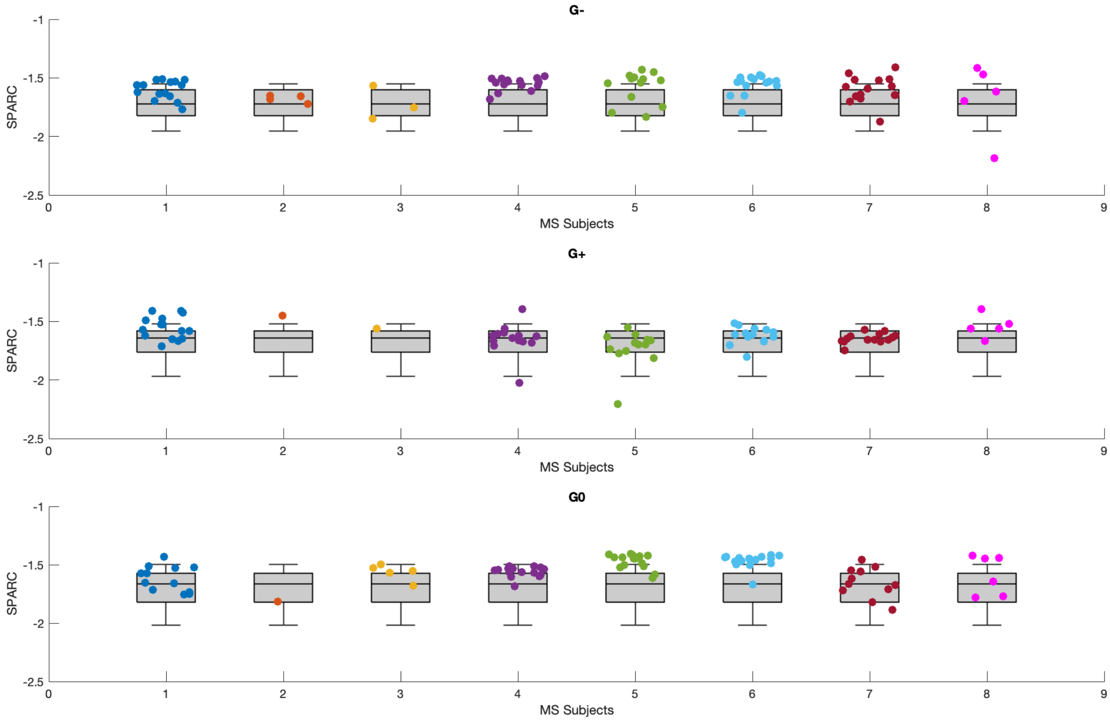

Figure 7: Box Charts of SPARC metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

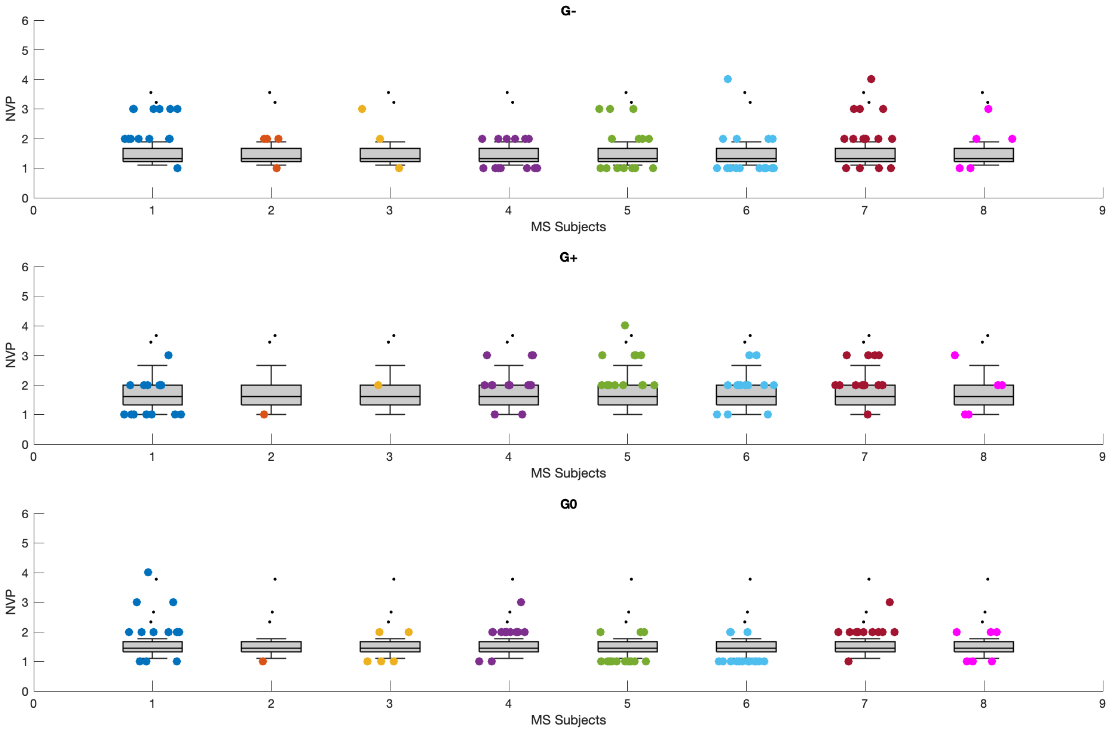

Figure 8: Box Charts of NVP metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

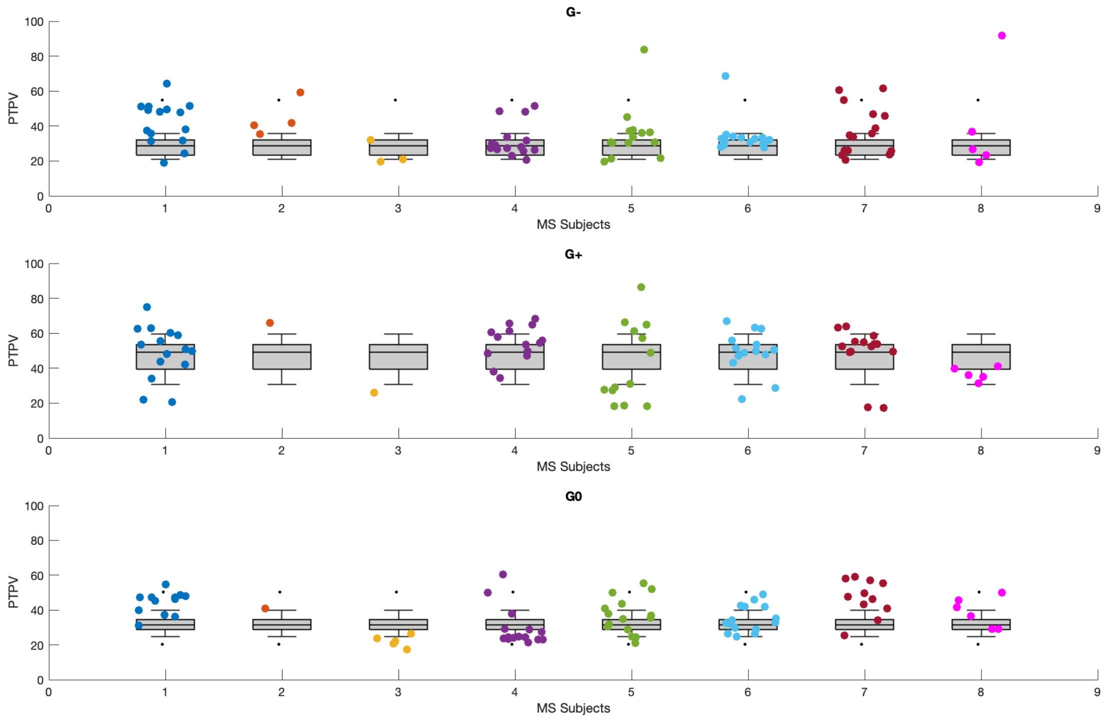

Figure 9: Box Charts of PTPV metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

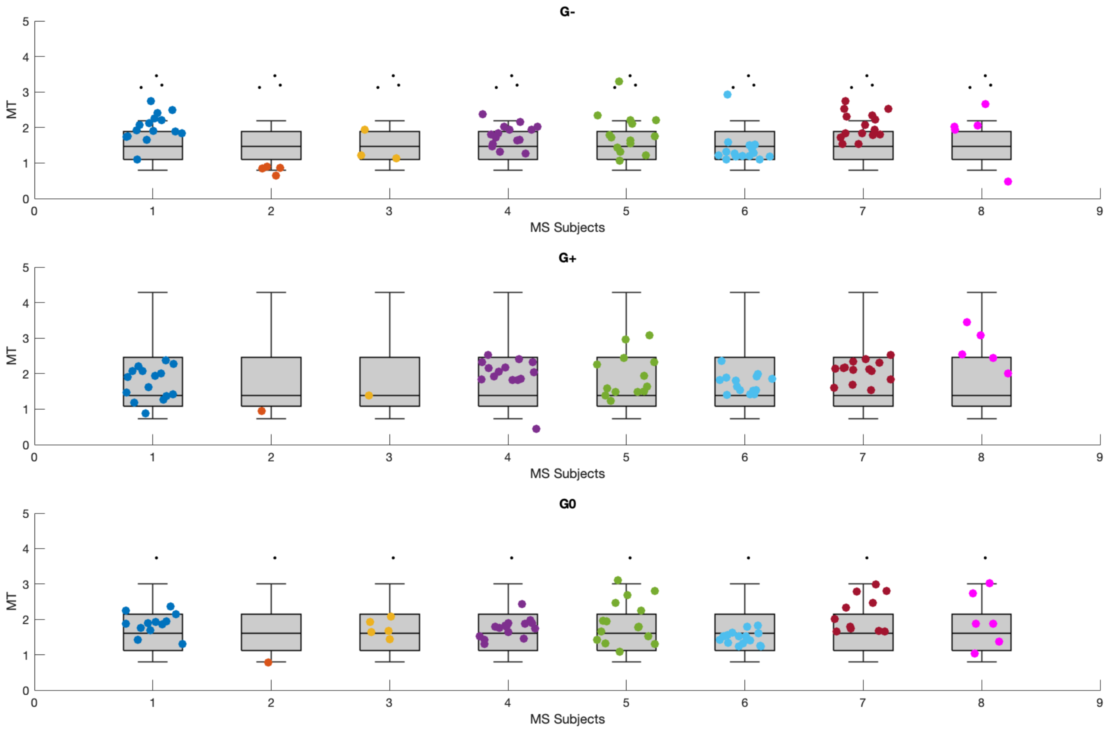

Figure 10: Box Charts of MT metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

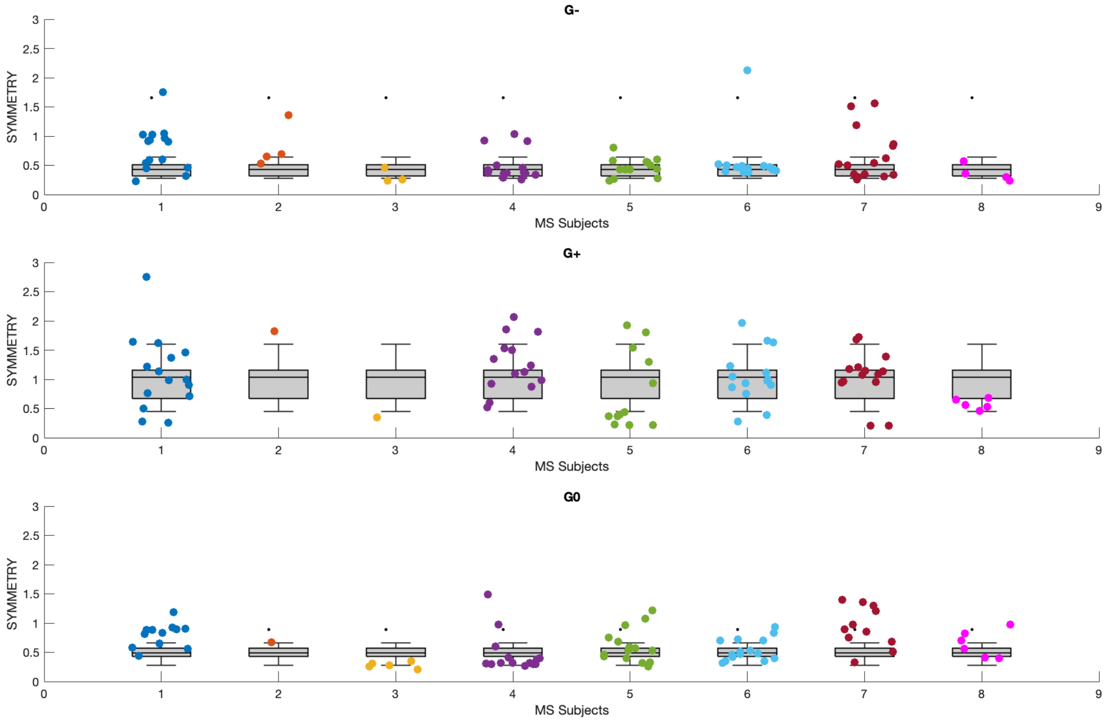

Figure 11: Box Charts of Symmetry metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

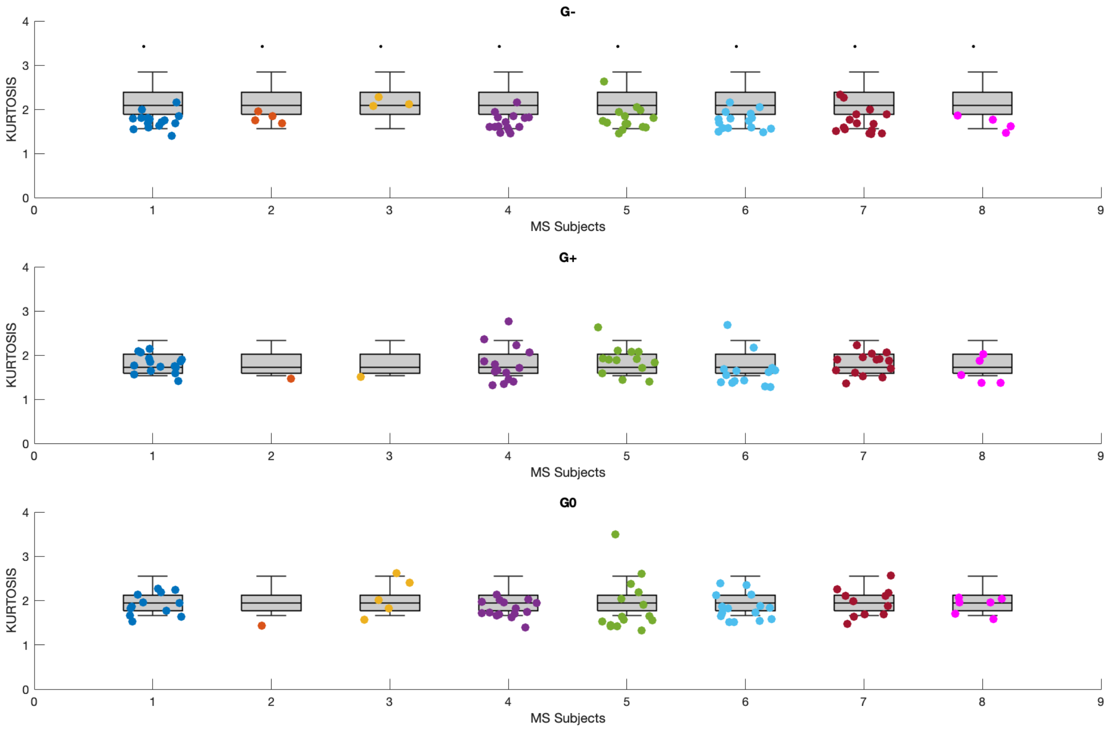

Figure 12: Box Charts of Kurtosis metric for Healthy Subjects with Overlaid Scatter Points for MS Subject-by-Subject.

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