

Alma Mater Studiorum – Università di Bologna



PhD in Bioengineering (09/G2 - ING-INF/06)

XXV Cycle

TRAINING AND ASSESSMENT
OF PATIENTS WITH NEUROLOGICAL IMPAIRMENTS USING
VIRTUAL REALITY, AUGMENTED FEEDBACK, INERTIAL
SENSING AND LOW COST VIDEO TECHNOLOGY

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Thesis defense: 12th April 2013

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SUMMARY

Neurorehabilitation is an active process by which individuals affected by neurological impairments achieve a full recovery or, when this is not possible, realize their optimal physical, mental and social potential. The rehabilitation process can be considered successful when it improves daily activities of patients treated and, therefore, their quality of life. The essential components of an effective motor rehabilitation process include an expert multidisciplinary assessment, a realistic and goal-oriented programs and the evaluation of the patient's achievements through clinically appropriate, scientifically sound outcome measures. The main aim of this thesis was to develop quantitative methods and tools for the clinical treatment and assessment of patients with neurological impairments.

Conventional rehabilitation treatments typically require neurological patients to execute repetitive exercises over a long period, with consequences in their engagement and motivation. Virtual reality and augmented feedback are tools recently applied to motor rehabilitation, which have shown to involve patients, allowing repeatability and standardization of protocols. An augmented feedback tool based on the use of IMU for trunk control was developed and the evaluation of its usability is presented in this work.

Moreover, virtual reality allows individualizing the treatment according to the patient needs gradually adapting the difficulty level to the progress. A virtual reality-based application for gait rehabilitation was developed and tested in a 6-weeks training program on patients affected by multiple sclerosis. Usability, feasibility and acceptance of both system and training protocol were evaluated and the effectiveness of the treatment demonstrated.

Traditionally, the quantitative assessment of motor skills has been performed using motion capture systems. Unfortunately, their effective use in clinical practice is still limited by their cost, and the space, time and expertise required operating. Moreover, the application of markers on the body of patients may influence their natural movements. To overcome these limitations the use of inertial sensors has been introduced in the field. A methodology based on their use in assessing the arm swing in subjects affected by Parkinson's disease is

proposed and preliminary results show their ability in distinguishing healthy from pathological subjects.

Inertial sensors, which are small, accurate, flexible and portable, have the drawback to accumulate significant drift during long measurements. This particular issue has been analyzed in this work and findings suggest that drift and its consequences in determining gait parameters can be contained if the inertial unit is placed on the foot and accelerations are integrated starting from the mid stance phase of gait.

Finally, a validation of the Microsoft Kinect in tracking gait in a virtual reality-based training is presented. Preliminary results allow defining the range of use of the sensor for applications in rehabilitation.

SOMMARIO

La neuroriabilitazione è un processo attivo attraverso il quale gli individui affetti da patologie neurologiche mirano al conseguimento di un recupero completo o, quando ciò non è possibile, alla realizzazione del loro potenziale ottimale benessere fisico, mentale e sociale. Il processo di riabilitazione può essere considerato effettivo quando migliora le attività quotidiane dei pazienti trattati e, di conseguenza, la loro qualità di vita. Gli elementi essenziali di un processo di riabilitazione motoria efficace comprendono una valutazione clinica da parte di un team multidisciplinare, un programma riabilitativo realistico e orientato a pochi specifici obiettivi e la valutazione dei risultati conseguiti dal paziente attraverso l'intervento mediante misure scientifiche e clinicamente appropriate.

L'obiettivo principale di questa tesi è stato sviluppare metodi quantitativi e strumenti per l'intervento riabilitativo e la valutazione clinica di pazienti affetti da deficit neurologici.

I trattamenti riabilitativi convenzionali tipicamente richiedono a pazienti neurologici l'esecuzione di esercizi ripetitivi per un lungo periodo, andando a incidere negativamente sul loro impegno e sulla loro motivazione. La realtà virtuale e i feedback aumentati sono approcci recentemente adottati dalla riabilitazione motoria, in grado di coinvolgere i pazienti nel trattamento, permettendo la ripetibilità e la standardizzazione dei protocolli. In questo lavoro è stato sviluppato uno strumento basato sull'utilizzo di feedback aumentati e sensori inerziali per il controllo del tronco ed è stata presentata una valutazione sulla sua efficacia e usabilità.

Inoltre, la realtà virtuale permette individualizzare il trattamento in base alle esigenze del paziente, adeguando gradualmente il livello di difficoltà ai suoi progressi. Un'applicazione basata sulla realtà virtuale per la riabilitazione del cammino è stata sviluppata ed è stata poi testata su pazienti affetti da sclerosi multipla durante un programma riabilitativo di sei settimane. Sono state valutate l'usabilità, la fattibilità e l'accettazione sia del sistema sia del protocollo riabilitativo ed è stata dimostrata l'efficacia del trattamento.

Tradizionalmente, la valutazione quantitativa delle capacità motorie dei pazienti viene effettuata utilizzando sistemi di *motion capture*. Purtroppo, il loro uso nella pratica clinica è ancora limitato a causa del loro costo, dello spazio, del tempo e delle competenze necessari per il loro funzionamento. Inoltre, l'applicazione di marcatori sul corpo dei pazienti può influenzare il loro movimento naturale. Per superare queste limitazioni è stato introdotto in questo campo l'utilizzo di sensori inerziali. In questa tesi, viene proposta una metodologia basata sul loro uso nella valutazione dell'oscillazione delle braccia in soggetti affetti da morbo di Parkinson, e si mostra come essa sia in grado di distinguere tra soggetti sani e patologici.

I sensori inerziali, che sono piccoli, accurati, flessibili e portatili, presentano però l'inconveniente di accumulare *drift* rilevanti durante lunghe misurazioni. In questo lavoro è stato affrontato questo particolare problema e i risultati ottenuti suggeriscono che, se l'unità inerziale è posizionata sul piede e le accelerazioni sono integrate iniziando dalla fase di *mid stance* del cammino, il *drift* e le sue conseguenze nella determinazione dei parametri del cammino sono contenuti.

Infine, è stata presentata una validazione del Microsoft Kinect in un'applicazione per il *tracking* del cammino in ambiente virtuale. Risultati preliminari consentono di definire il campo di utilizzo del sensore per applicazioni in riabilitazione.

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1. Introduction

1.1. Rationale

The essential components of an effective motor rehabilitation program for subjects affected by neurological impairments include expert multidisciplinary assessment, realistic and goal-oriented interventions, and the evaluation of the impact of the rehabilitation through the use of clinically appropriate, scientifically sound outcome measures. Traditionally laboratory based motion capture systems have been used to assess the patient before and after the rehabilitative intervention. This approach usually requires the use of markers to be positioned on the patient's body surface. In some occasions, the presence of markers may represent a source of uneasiness and discomfort, influencing and interfering with the natural movements of the subject. Moreover, motion capture systems, which are generally very expensive, require expertise, space and a long time for set-up, further increasing the cost of the evaluation. All the above reasons help to explain the limited use of these systems in clinical practice, where the evaluations are mostly qualitative.

Rehabilitative interventions of neurological patients typically aim at recovering motor skills. It has been demonstrated that motor recovery is promoted by intensive skillful practice (Shumway-Cook, 2007) and increasing difficulty (Malouin, 2003). Therefore conventional physical therapies in clinical practice are often characterized by the regular and intense repetition of exercises over a long period, consequently limiting patients' engagement and motivation.

Recently, innovative technology and approaches have been proposed to overcome the above-mentioned limitations. The main goal of the project described in this thesis was to develop new quantitative rehabilitation methods and tools to be used in the clinical assessment and treatment of patients with neurological deficits.

1.2. Outline

The thesis is organized as follows.

Chapter 2 is an overview of the process of rehabilitation for people affected by neurological impairments.

Chapter 3 describes some of the limitations of conventional motor rehabilitation and proposes new methods and tools to overcome them.

Chapter 4 presents a study on the estimation of the stride length using an inertial measurement unit (IMU). The study evaluates the error associated with the zero velocity assumption in estimating stride length using several locations of the IMU on the foot and on the shank.

Chapter 5 presents a study focusing on a virtual reality (VR)-based system for gait training in subjects affected by multiple sclerosis (MS) using IMUs. The proposed system and training are explained in detail and their feasibility, acceptance and effectiveness are evaluated.

Chapter 6 presents a study on the measurement of the arm swing in Parkinson's disease (PD) patients using IMUs. The proposed methodology has been used both on patients and healthy subjects and preliminary results are presented.

Chapter 7 describes a tracking methodology based on the use of the Microsoft Kinect for the reproduction of gait in a VR application. The proposed methodology is validated using stereo-photogrammetry.

Chapter 8 describes an augmented feedback tool for trunk control based on the use of inertial sensing. Preliminary results on the usability of the tool on young healthy subjects are presented.

Chapter 9 summarizes advantages and limitations of the developed tools and the methods and suggests options for future research.

2. Rehabilitation in neurological impairments

2.1. Neurological impairments

The *World Health Organization* (WHO) defines impairment as any loss or abnormality in body structure or of a physiological or psychological function (World Health Organization, 2001). Specifically, all the disorders originating from structural, biochemical or bioelectrical abnormalities in the central and peripheral nervous system lead to neurological impairments. They may cause physical or mental problems, affecting an individual's speech, motor skills, vision, memory, muscle function or learning abilities. Not all neurological impairments are present from birth. A neurological impairment can be acquired as a result of some form of brain or spinal cord injury. Often, the results are very similar; the only difference is the way in which a given part of the brain becomes damaged. Because of its various forms, neurological impairment can be classified in many different ways.

Neurological disorders are diseases of the central and peripheral nervous system, which affect learning and behavioral abilities (World Health Organization, 2007).

Some of the more common neurological diseases (Hirtz, 2007) include multiple sclerosis (MS) and Parkinson's disease (PD), with a crude incidence rate, respectively, of 2.5 (with a range of 1.1–4) and 4.5–19 per 100,000 population per year, and a median estimated prevalence, respectively, of 30 (with a range of 5–80) and 100-200 per 100,000 (World Health Organization, 2007) (World Health Organization, 2008). MS and PD are considered neurodegenerative disorders (Trapp, 1999), (World Health Organization, 2001), (Gao, 2008) and will be particularly considered in the present thesis. Neurodegenerative diseases are defined as conditions characterized by progressive nervous system dysfunction. These disorders are often associated with atrophy of the affected central or peripheral structures of the nervous system.

MS is an inflammatory demyelinating condition of the central nervous system that is generally considered to be autoimmune in nature (World Health Organization, 2007). In

people with MS, the immune trigger is unknown, but the targets are myelinated central nervous system tracts. MS can lead to a wide variety of motor and cognitive symptoms, depending on the affected part of the body and on the severity.

Approximately 80% of individuals affected by MS initially present a form of this pathology called relapsing/remitting (Figure 1), which is characterized by unpredictable attacks, called relapses, during which new symptoms appear or those existing become more severe (Lidcombe, 2003). They can last for long periods (days or months) and are followed by a partial or total recovery, i.e., the remission.

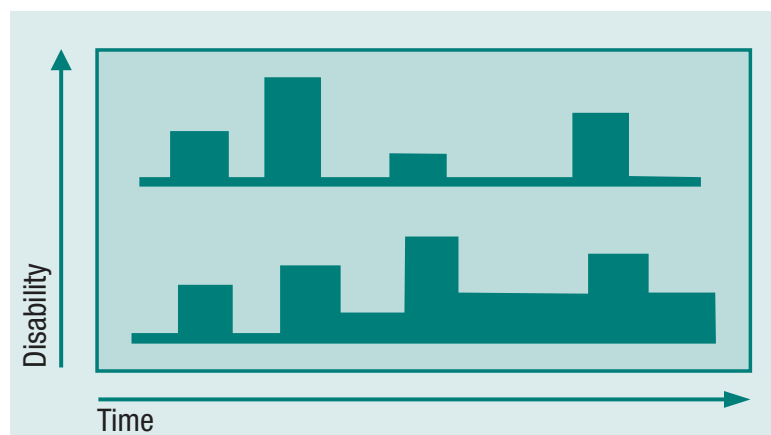


Figure 1 Example of two possible courses of MS in relapsing/remitting form.

The disease may appear clinically inactive for months or years, though a more frequent asymptomatic inflammatory activity is usually present. Over time, however, symptoms may become more severe with less complete recovery of function after each attack.

MS is usually accompanied by physical disability, complicated by fatigue, depression and possibly cognitive impairment and can lead to a functional decline. Typically disease onset is around 30 years of age, hence the loss in functional ability of patients with MS can be substantial and often prevents MS subjects from performing their customary roles.

PD is a chronic progressive neurodegenerative disorder of insidious onset (World Health Organization, 2007), (Gao, 2008). The motor symptoms become readily apparent and diagnosis is made based on cardinal predominate motor signs, however, non-motor features of the disease are increasingly recognized (Chaudhuri, 2006). PD is also associated with late-

onset motor symptoms, such as postural instability and falls, freezing of gait, speech and swallowing difficulties (Jankovic, 2008).

The pathophysiology of PD involves the progressive loss of dopamine-containing neurons of the pars compacta of the substantia nigra that lead to denervation of the nigrostriatal tract and a significant reduction of dopamine at the striatal level. The consequence of this denervation process is an imbalance in the striato-pallidal and pallido-thalamic output pathways, which is responsible for the major motor deficits (Albin, 1989).

Beyond motor and cognitive impairments, quality of life in PD also deteriorated significantly with increasing disease severity particularly in those aspects related to physical and social functioning (Schrag, 2001).

2.2. Neurological rehabilitation

2.2.1. The rehabilitation cycle

The WHO defines rehabilitation as an active process by which those affected by injury or disease achieve a full recovery or, when this is not possible, realize their optimal physical, mental and social potential and are integrated into their most appropriate environment (World Health Organization, 1981). Consequently, a rehabilitation process can be considered successful when it improves independence and quality of life of treated subjects, by maximizing their ability and participation.

The essential components of an effective rehabilitation include expert multidisciplinary assessment, realistic and goal-oriented programs and evaluation of impact on the patient's rehabilitation achievements through the use of clinically appropriate, scientifically sound outcome measures incorporating the patient's and the family's perspectives (European Multiple Sclerosis Platform and Rehabilitation in Multiple Sclerosis, 2004).

The rehabilitation process should be provided by a multidisciplinary team, usually including doctors, nurses, therapists, clinical neuropsychologists and social workers. The aim of the rehabilitation team is to treat impaired body structures to overcome diminished functions, while maximizing patients' activity and participation in their social setting and minimizing

the risk of further symptoms and disability, the patient's pain and the stress of the family and/or caregivers (Stucki, 2002).

The rehabilitation process, seen both from the guidance and from the service perspective, can be thought as an iterative process involving the following elements (Figure 2):

1. assessment of the nature of the patient's problems and needs;
2. assignment to an intervention program;
3. plan and implementation of the assigned intervention;
4. evaluation of the intervention.

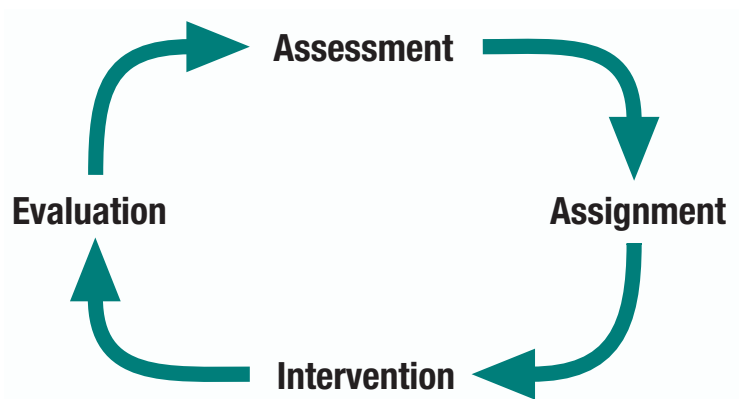


Figure 2 The rehab-cycle (Stucki, 2002), (World Health Organization, 2007)

ASSESSMENT

The assessment includes the identification of the impairments of patients, which contribute to the difficulties in function, the estimation of rehabilitation potential and prognosis and the definition of the goals of the intervention program. Since neurological subjects suffer from a combination of multiple impairments, it is crucial, to identify target problems, which may be treated and relieved in a reasonable amount of time. In this phase, information is collected through both standardized assessment and interviews.

The most commonly used measures of impairment in neurological patients include: a) the Motricity and the Ambulation Index for motor deficits; b) the Berg Balance test (Berg, 1995) and Timed Up and Go (Podsiadlo, 1991) for balance; c) the Beck Depression Index for depression (Lykouras, 1998); d) the Short Orientation Memory Concentration Test

(Katzman, 1983) and Mini Mental State Examination (Folstein, 1975) for brief cognitive screening e) the Frontal Assessment Battery (Dubois & Slachevsky, 2000), for neurological and cognitive features, and the Montreal Cognitive Assessment (Nasreddine, 2005) a cognitive screening tool. The two most widely used measures of disability are the Barthel Activities of Daily Living index (Collin, 1988) and the Functional Independence Measure (Dodds, 1993).

ASSIGNMENT

The assignment is the determination of a realistic intervention program, identifying and addressing it toward the factors with the greatest potential for improvement. The first aim of the assignment is to make the patient conscious about her/his disability and to stimulate her/him to have an active role on it. The second aim is to define the compensatory strategies for cognitive and behavioral deficits. The third aim consists in planning interventions aiming to generalize the compensatory strategies in the environment. Effective teamwork requires that all team members work towards common goals. Good rehabilitation practice should involve the patient (and the family, when appropriate) in the setting of meaningful, challenging and achievable short-term and long-term goals.

INTERVENTION

The task-oriented approach refers to the specification of the rehabilitative techniques, indicator measures and the target values to be achieved in a predefined time period. Practice of an impaired function usually involves repetition, starting with simple tasks and slowly increasing the level of difficulty (Malouin, 2003). An alternative approach is to use compensatory techniques, to help the patient to achieve the goal by different means. There has been a shift from exercising isolated impairments towards task-oriented therapy for activities of daily living (Horak, 1990).

EVALUATION

The evaluation refers to the assessment of goal achievement with respect to predefined treatment goals. In rehabilitation, the measurement of functioning and health is not only relevant to evaluate intervention outcomes, but the assessment and interventional

management as well. Thus these measures are examined much more closely both at the level of individual problems and at the level of instrumented scales.

Although all the phases of the cycle are present in the choice and implementation of a rehabilitation treatment, in this thesis, the focus will be prevalently on the stages of assessment and rehabilitation intervention, in the effort to make quantitative the outcome coming from them.

2.3. Rehabilitation methods

Rehabilitation should start as soon as possible after the diagnosis of a neurological impairment and should focus on the community rehabilitation perspective (World Health Organization, 2007). Neurological patients can present a wide number of complexities including physical functioning limitations, cognitive and communication impairments, behavioral problems, compromised basic daily living activities and psychosocial limitations. Consequently, intervention programs and services have been developed, showing to contribute effectively to the optimal functioning of people with neurological conditions. Here we will briefly discuss those aiming to treat motor and neuropsychological deficits.

2.3.1. Motor deficits

The motor activity in neurological diseases acquires importance for the neuro-motor features of the movement that, although impaired, can be used to recondition and reach a new balance on coordinative pre-existing movement patterns. The physical exercise has shown to provide beneficial effects in neurodegenerative diseases like PD, (Bergen, 2002) but also in MS, where endurance exercises have been showed to make higher the threshold of the fatigue perceived by the patients (Gutierrez, 2005), contributing to improve their quality of life (Petajan, 1996), (Brown, 2005).

Rehabilitation in neurodegenerative disorders stands as its primary objective the improvement of the neuro-muscle-skeletal diseases, but also the enhancement of the global motor performance, with the consequent reduction of fall risk (Valobra, 2000). Therapeutic

approaches include stretching and strength training, rehabilitation of postural transitions, reeducation of postural instability and gait, and training to cognitive strategies.

One of the most common motor dysfunction encountered in the motor rehab of MS is muscle weakness, with onset in 90-100% of cases (Valobra, 2000). It is therefore important to maintain the level of physical performance for as long as possible, by a process that does not generate fatigue or changes in body temperature.

Postural instability is also a disorder consistently reported by MS patients, with onset in 23-82% of cases, (Valobra, 2000), and can be addressed with specific or non-specific rehabilitative approaches, which are based on intensive, repetitive tasks and augmented feedback. Specific treatments aim to learn patients of motor strategies pointing to improve their residual potential in postural control. Non-specific treatments include generic mobilization and stretching exercises, in order to maintain range and muscle elasticity, especially in the lower limbs.

Moreover, about the 55% of individuals with MS identify fatigue as one of the major symptoms affecting their mobility (Fisk, 1994). The exact origin of fatigue is unclear, although it could be sought in the association of weakness, spasticity, ataxia, depression, and heat (Jacobs, 1986).

Other common motor symptoms in MS are spasticity, paresis, stiffness, sensory impairments and fasciculation (Zuvich, 2009). Spasticity (onset 75% of cases) can become a problem as it often interferes with rehabilitation. After that the sources of nociceptive input have been identified and treated, the patient should be instructed to perform appropriate muscle stretching exercises aiming at expand the range of motion of the affected joints (Merritt, 1981). After, the facilitation of motor strength can be accomplished by using passive and active therapies, advancing to progressive resistance training. In active therapy the patient is encouraged to perform an exercise, while the therapist provide her/him a feedback about her/his performance, in order to avoid unnecessary muscle activity and to achieve selective control of specific muscles. Passive therapies include positioning patients on their side, sitting, or standing in a support frame, and stretching exercises.

Recurrent motor symptoms in PD, on which the rehabilitation has shown to be mostly effective, are bradykinesia, rest tremor, rigidity, and postural disturbances and, in late-onset, postural instability and falls and freezing of gait (Jankovic, 2008). The hypertonic muscles and bradykinesia aggravate the condition of the muscle-skeletal system, already altered by age (Valobra, 2000). Muscle stretching is definitely a basic treatment also in PD and the districts where it is prevalently needed are the flexor muscle groups of trunk and limbs. Stretching has the effect of lengthening the slow and progressive soft tissues and in presence of severe flexion contractures, where traditional stretching is not effective, prolonged statics stretching sessions could be required. This technique consists in maintaining tolerable postures for long periods, in order to act more markedly on shortened connective tissues. Joint mobilization is an imperative treatment modality for a disease that has immobility as the main effect. This method can be performed in passive mode, active-assisted or preferably active, depending on the degree of autonomy of the patient in the execution of exercises.

2.3.2. Reduced mobility and gait deficits

Neurological disorders, due to the characteristics of the disease, such as type, location, extension, stability or progressivity and age of onset, are characterized by an extreme variety of clinical manifestation, resulting in alterations of the motor control which cause, during walking, different changes in the kinematics of the upper and lower limbs and trunk. Regardless of the pathology, the ability of gait is modified in terms of:

- effectiveness: reduction in the rate of spontaneous and maximum sustainable speed;
- security: the need for assistance and / or supervision and / or direct assistance;
- efficiency: increase of energy cost;

with consequent limitations of autonomy and participation in social and working life.

The observational analysis and the global clinical segmental assessment allow defining the main problems of gait in terms of global imbalances, focal problems and coordination.

Reduced mobility is one of the most frequent impairment in MS patients and may be due to motor, sensory, balance and exploratory deficits. The aim of the rehabilitation project may be

restoration or maintenance of the residual skills, using also orthoses or assistive devices. Trunk stability represents a fundamental prerequisite for locomotor rehabilitation; therefore a preparation program to standing, performing exercises on the mat, usually precedes any gait treatment. Most of these activities aim at the reduction of the base support, the verticalization, the maintenance of postural stability, in both static and dynamic conditions. Once that a good alignment trunk-limbs is reached in the standing position, dynamic stability will be trained and obtained with destabilization-stabilization movements of the trunk. As soon as a suitable motor control in the upright position has been reached, it is possible to start to walk handling the bars, trying to reset the motor patterns of gait, coordinating the movement of the lower limbs with the pendular synkinesis of the arms.

Gait reduction plays an important role also in the rehabilitation of PD subjects (Valobra, 2000). The patient is trained to use the most correct gait pattern as possible, which is the more stable and the less energetically expensive. In PD, particular attention should be paid on direction changes, often usually carried out pivoting on a limb and causing instability. The patient should be instructed to change direction, particularly when turning back, touring enough largely to prevent the two legs stepping on each other. The path must be trained not only on smooth terrain such as gyms, but also on uneven surfaces. To make the rehabilitation treatment as effective as possible in real life, it is important to include also exercises upward and downward by a step, and training aiming at negotiating obstacles of different height and shape.

In treadmill (TM) training with partial body-weight support (BWS) the patient is secured into a harness hanging above a TM on which she/he walks. The use of TM finds in PD a beneficial application because it forces the subject to a rhythmic path. Indeed, this intervention has shown to improve gait in individuals affected by neurodegenerative disorders, such as PD (Mehrholz, 2010), (Miyai, 2002) and MS (Benedetti, 2009), (Pilutti, 2011)

For a further diagnostic-functional inspection, clinical examination can be extended to instrumental analysis, which is addressed to quantify:

- The dynamic neuromuscular pattern using dynamic electromyography;
- The global and segmental kinematic characteristics using optoelectronic systems;
- The global and segmental kinetic through force platforms and optoelectronic systems;
- The energy cost of ambulation through systems of measurement of oxygen consumption.

The three-dimensional optoelectronic analysis quantifies the spatial-temporal gait parameters, kinematics and kinetics segmental. The three main categories of problems can be scaled according to the deviation from normality data and are (Bowden, 2006):

- Reduced load acceptance;
- Reduced propulsion;
- Reduced load acceptance and reduced propulsion.

2.3.3. Neuropsychological deficits

Most neuropsychological interventions are related to the treatment or optimization of cognitive deficiencies including also emotional, behavioral and personality alterations, aiming at the best cognitive, neurobiological and social re-adaptation (Valobra, 2000).

Problems in memory and concentration are very common reported symptoms in neurodegenerative disorders and affect tasks such as decision-making, planning, sensory integration and dual tasking (Yogev-Seligmann, 2008). The memory is now considered as a function consisting of several components that work sequentially and integrally. We can distinguish between a short-term memory, perspective memory, which relates to knowledge skills that are implicitly acquired, and a long-term memory (Valobra, 2000). The rehabilitation intervention should take into consideration the specificity of patients and the level of their deficit, distinguishing subjects able to learn and apply new compensation strategies, from subjects able to acquire only implicit behaviors. According to literature of recent years, about half of MS patients are affected by memory disorders, as well as by attention, executive and visual-spatial functions (Rao, 1991). Disorders in long- and short-

term memory, saving the implicit memory, characterize these patients and are, with attention functions and speed processing, the first symptoms of the disease. Specifically, like in PD, the main cognitive affected areas include memory, executive functions and attention (Chiaravalloti, 2008), (Caballol, 2007).

Attention constitutes a phenomenon with more components including selectivity and intensity. The first dimension includes two separate processes: the focused attention, generally tested by asking to the subject to find a specific target stimulus among several distractors, and divided attention, assessed by dual task, where the individual must respond to two stimuli interfering with each other. The intensity does include the warning and physical alertness. The alert aims to implement a response following a warning signal, while the supervisory indicates the ability to maintain the appropriate response for a certain period of time. Batteries are standardized to highlight any shortfall depending on attention processes. The rehabilitation protocols can be gathered in two groups: the first one aims to recover the lost capacity, while the second aims to develop compensatory strategies.

Also neuropsychiatric and behavioral disorders are common in neurodegenerative disorders. Depression, for example, seriously affects the autonomy and quality of both individuals affected by MS (Arnett, 2008) and PD (Mayeux, 1984), (Taylor, 1986).

2.3.4. Dual task during walking

Performing two tasks simultaneously (dual tasking) is a frequent activity in everyday life, which requires divided attention. Indeed, when people attempt dual task, performance is generally impaired, characterized by more errors or longer reaction times than the same task performed without a concurrent task (Wu, 2008). The capacity to execute a second task (dual task performance) is highly advantageous during walking because it allows for communicating with people, transporting objects and monitoring the environment.

The effects of dual tasks on gait (dual task cost) have been studied in several populations, from healthy young and older adults to neurologic patients. In healthy adults, dual tasking has demonstrated to reduce the performance of the concurrent task and to decrease the gait

speed, highlighting how deficits in attention and executive functions are associated with fall risk, postural instability and impairments in daily life activities (Yogev-Seligmann, 2008). The dual task cost has been studied also in elderly people (Woollacott, 2002), showing an increase in the reaction times of the concurrent cognitive task or a decrease in gait speed (Chen, 1996), (Ebersbach, 1995), and an increased gait variability (Dubost, 2006). Age-related gait changes are more pronounced in people with cognitive impairments (Hausdorff, 1997), (Holtzer, 2006), (Lindenberger, 2000) and are accentuated under dual task condition. Lundin-Olsson et al. showed that the instability to maintain a conversation during walking constitutes a marker of future falls in older adults (Lundin-Olsson, 1997). Several studies have also demonstrated that dual tasking severely affected gait parameters in populations prone to falls, much more than in a healthy elderly people (Bloem, 2001), (Beauchet, 2005), (Toulotte, 2006), (Springer, 2006), (Verghese, 2002). Faulkner et al. observed that changes in performance while dual-tasking could be used to identify subjects at risk for recurrent falls (Faulkner, 2007). A recent study on a large sample of older adults found that the dual task cost of 18% or more predicted falls in individuals walking faster than a specific gait speed threshold (Yamada, 2011).

Typically, the dual task cost is larger in neurological patients than healthy age-matched controls (Sheridan, 2003). This has been largely investigated in PD patients and can be explained by their impairment in attention and in executive function processes (Dubois, 1996) and by their altered gait, typically characterized by slow gait speed, short strides, high double support time (Yogev, 2005) (Morris, 1994), (O'Shea, 2002), (Bond, 2000), (Camicioli, 1998), (Hausdorff, 2003), (Lewis, 2011), decreased symmetry and coordination between left and right steps (Plotnik, 2008), (Yogev, 2007), and increased stride-to-stride variability (Plotnik, 2011), (Yogev, 2005), (Hausdorff, 2003).

Contrarily to PD, the dual task cost during gait in MS has been poorly explored. In a recent case-control study (Hamilton, 2009) on MS subjects, walking and attention interaction have been investigated. Compared to healthy controls, MS subjects demonstrated slower speed and

elevated swing time variability in gait performance under cognitive dual task conditions. The authors suggested that fatigue and general cognitive ability contribute to this.

These results seem to be consistent with the differential dual-task decrements reported in another study on MS patients (D'Esposito, 1996), when compared to controls, during the execution of two cognitive tasks simultaneously. Different interpretations can explain these findings, including reduced working memory capacity, task demand, use of different strategies, confounding factors and a divided attention deficit. Moreover, another study (Sosnoff, 2011) investigated the effect of a cognitive task on gait performance in MS individuals with mild, moderate, and severe disability. The findings showed that, compared to patients with mild and moderate disability, the group with severe disability walked slower, with shorter steps, and spent a greater percentage of the gait cycle in double support.

The growing evidence that instability and falls increase during the performance of multiple tasks suggests the need of training balance and gait in dual task in neurological patients. Dual-task training involves the execution of the primary task (maintaining postural control or walking speed) while performing a secondary task, for example a cognitive challenge such as counting backwards, or a manual task such as carrying an item (Woollacott, 2002). Few studies have tried to specifically address this issue, and the findings have not always been consistent (You, 2009), (Yang, 2007), (Canning, 2008), (Silsupadol, 2009), (Schwenk, 2010), (Yogev-Seligmann, 2012), (Plummer-D'Amato, 2012). Still, promising results suggest that training improves dual task gait in older adults with balance impairment (Silsupadol, 2009), patients with dementia (Schwenk, 2010), post-stroke individuals (Yang, 2007), (Plummer-D'Amato, 2012) and PD subjects (Yogev-Seligmann, 2012), (Canning, 2008), suggesting that even among patients with neurodegenerative disease, intensive and repetitive practicing of DT while walking can lower dual-task costs.

3. Technological tools for designing new motor rehabilitation methods

The aim of the bioengineering research in motor rehabilitation is to develop new methods for the assessment of impaired patients and, simultaneously, on the basis of the responses gathered from them, to provide clinicians with tools to tailor or facilitate motor rehabilitative interventions (Bonato, 2010). These new approaches must be made with a view to overcoming current limitations in routine clinical practice, where qualitative scales and functional tests are still largely preferred, due to practical reasons, and where treatments are prevalently based on repetition. In this sense, the relevance recently gained by pervasive solutions and personalized interventions for healthcare among researchers and clinicians had a high impact on rehabilitation. New approaches have been primarily possible thanks to the recent progresses in several fields, such as telecommunications, electronics, computer science and real-time data analysis. In particular, a wide range of new technologies, including inertial sensors and low cost video technology, and tools, such as multi-sensory interfaces and virtual reality (VR) have been recently experimented, and in some case combined, opening new perspectives for relevant applications in motor rehabilitation. In this chapter we will introduce them, presenting their potential application in motor rehabilitation of neurological subject.

3.1. Measuring human movement in clinical practice: inertial sensing

The ability to measure human movement quantitatively represents an essential part of clinical assessment and evaluation, thus either allowing for a more complete diagnosis or determining the efficacy of motor rehabilitation interventions.

Motion capture systems, using instruments such as optical motion capture and force plates, are considered as the gold standard in the field of motion analysis for assessing joint kinematics and kinetics. For kinematics, optical motion capture system consists in tracking the position of markers attached to specific locations on the subject's body using a set of

cameras, and reconstructing their 3D position. Technology is either based on active or passive markers and uses the red and infrared light range. For kinetics measurements, the reference system used in laboratory setting is force platforms. They measure the ground reaction forces generated by a body standing on or moving across them. They can provide also accurate temporal parameters such as foot initial and terminal contact.

Measuring body movements in laboratory setting under controlled conditions allows getting precise, accurate and reliable measurements of the movement pattern of the subject, and add quantitative and objective figures to the clinical gait assessment. Nevertheless, motion capture systems present also several disadvantages, such as the costly equipment and the need of technical expertise to operate. Another drawback is represented by the confinement of such a system inside the laboratory setting, where the volume of measurement is limited. This aspect can strongly influence the natural behavior of the subjects and does not allow observing them in their everyday life. More importantly, the interpretation of the outcomes is not straightforward and requires further processing and analysis by clinical expertise. Consequently, the use of these devices in the routine clinical practice is limited and it is mostly used for research purpose. In order to overcome them, in the last two decades, new methods (e.g. markerless techniques (Deutscher, 2000) have been successfully implemented. Wearable technology overcomes the limitations of settings and cost, offering an inexpensive, and efficient manner of performing motion analysis in several health-related applications, outside the laboratory. Inertial wearable sensing, (Teng, 2008), (Bonato, 2010) may be used in in the motion analysis of neurological individuals (Bonato, 2009). These sensors, based on a technique for measuring the motion of an object without the need of an external reference, are named Inertial Measurement Units (IMUs) and are composed by different inertial sensor technologies, including accelerometers, gyroscopes and magnetometers. Gyroscopes provide a measurement of the angular velocity applied to the object and thus an estimation of the rotated angle and actual orientation if an initial reference is provided. Though they are usually based on the concept of measuring the Coriolis force, gyroscopes based on other operating principles also exist (electronic, microchip-packaged MEMS gyroscope devices,

solid-state ring lasers, fiber optic gyroscopes, and the extremely sensitive quantum gyroscope). They can be used for the measurement of the motion and posture of any human body segment (Ayrulu-Erdem & Barshan, 2011), (Catalfamo, Ghousayni, & Ewins, 2010), (Tuncel, Altun, & Barshan, 2009). Since gyroscopes have different sources of dynamic drift, the estimation of the orientation deteriorates with time. To correct these effects, accelerometers and magnetometers are added to the system through data fusion algorithms so that external references are provided for drift correction.

Accelerometers are inertial sensors measuring the linear acceleration along their sensitive axis. Their common operation principle is based on a mechanical sensing element consisting of a proof mass attached to a mechanical suspension system. According to Newton's second Law, under the influence of external accelerations the proof mass deflects from its neutral position and, using the physical changes in the displacement of the proof mass, the acceleration can be measured electrically. Three common types of accelerometers are available, namely, piezoelectric, piezoresistive, and differential capacitive accelerometers (Öberg, 2004), (Mathie, 2004).

Magnetometers are usually based on the magnetoresistive effect. If a magnetic field is applied, a Lorentz force proportional to it will deflect the current path, increasing the resistance. Since the resistance change is proportional to the tilt angle in relation to the magnetic field direction (Graham, 2004), magnetoresistive sensors can estimate changes in the orientation of a body segment in relation to the magnetic North or the vertical axis in the gait analysis (Dai, 1996), (O'Donovan, 2007), (Choi, 2008), providing information that cannot be determined by accelerometers or the integration of gyroscope signals. Accelerometers give a measure of the direction of the gravity vector, and magnetometers provide measurements of the direction of the Earth's magnetic field. With this technology, IMUs are able to accurately estimate their own orientation with respect to a fixed reference frame formed by gravity and the Earth's magnetic North vectors.

IMUs have great potential for measurement of human movement in rehabilitation. They can be used for kinematic measurements (Mayagoitia, 2002), (Luinje, 2005) in ambulatory

circumstances. Mathie et al. (Mathie, 2004) reviewed the accelerometer-based systems applied to human movement, distinguishing between monitoring of specific movements (e.g. gait, fall, sit-to-stand transfer etc.), assessment of physical activity and classification of movements. Godfrey et al. (Godfrey, 2008) compared all the techniques that have been used using accelerometers since the early 1990s to 2006 for human movement analysis. To obtain more information on human kinematics, gyroscopes and magnetoresistive sensors have been combined with accelerometers. Gyroscopes are usually used to measure the angular rate and the joints' range of motion (Tong, 1999), (Coley, 2005), (Miyazaki, 1997), while the magnetoresistive sensors provide an additional reference measure for body orientation. Recently, Altun et al. (Altun, 2010) compared the different techniques of classifying human activities using wearable inertial and magnetic sensors.

Following Mathie's classification, IMUs can be used in rehabilitation to:

- a) Monitor specific movements, such gait (Tong, 1999), (Menz, 2003), (Sabatini, 2005), (Tao, 2012), sit-to-stand transfer (Najafi, 2002), falls (Williams, 1998), (Doughty, 2000), (Bourke, 2007), (Wu, 2008);
- b) Measure and assess human motion, for clinical assessment (Wade, 2010), (Parnandi, 2010), (Mancini, 2010), (Palmerini), (Mancini, 2012), for tracking purposes (Lee, 2003), (Zhu, 2004), (Foxlin, 2005), (Zhou, 2008), (Guo, 2009), (Hussain, 2012), and for treatment evaluation (Lorincz), (Jovanov, 2005);
- c) Detect and classify activities (Aminian, 1999), (Najafi, 2003), (Bao, 2004), (Ravi, 2005), (Parkka, 2006), (Preece, 2009), (Yang, 2010).

All these purposes are even more important for individuals affected by neurodegenerative disorders. An increasing interest toward inertial sensing has been recognized in measuring mobility or walking impairment in neurological populations (Pearson, 2004) including persons with MS (Weikert, 2010), (Snook, 2009). For example, quantitative measures coming from inertial units may assist clinicians in assessing gait (Salarian, 2004) and evaluating the above-mentioned turning difficulties of PD subjects, especially in home-based assessments (Boonstra, 2008), (Salarian, 2007). Zampieri et al. has showed that the Timed

Up and Go test, extensively used to assess balance and mobility in moderate-to-severe stage PD, measured with the sole stopwatch was not sensitive enough to detect abnormalities in early-to-mid stage PD and used inertial sensors to make the test more reliable (Zampieri, 2010).

In Chapter 0 an application based on the use of IMUs for motor assessment of PD patients is presented.

3.2. Virtual Reality in motor rehabilitation interventions

One of the main goals of motor rehabilitation is to increase the quantity and quality of patients' daily activities to improve their independent living. Essential for motor recovery is a task-oriented treatment characterized by intense skillful practice (Shumway-Cook, 2007) and increasing difficulty (Malouin, 2003). Consequently, physical therapies usually request patients to regularly execute movement patterns repetitively over an extended period, often limiting their engagement and motivation in rehabilitation. "Motivation is an important factor in rehabilitation and is frequently used as a determinant of rehabilitation out-come. In particular, active engagement towards a treatment/training intervention is usually equated with motivation, and passivity with lack of motivation" (Colombo, 2007). VR is a relatively recent approach in rehabilitation, which demands focus and attention, increasing patients' motivation, and provides them with a sense of achievement (Lange, 2011).

3.2.1. What is Virtual Reality

Coates in 1992 defined VR as "...electronic simulations of environments (...) enabling the end user to interact in realistic three-dimensional situations." (Coates, 1992). To date, VR refers to the use of interactive simulations created with computer hardware and software to present users with opportunities to engage themselves in environments reproducing the real world, (Weiss, 1998). Users interact with the environments, performing actions inside them and/or moving and manipulating virtual objects, in a way that attempts to "immerse" them within the simulation. Immersion is an important concept and relates to the extent to which the VR system succeeds in delivering an environment, which refocuses the user's sensations

from the real to a virtual world (Slater, 1999). A second key concept of VR is the sense of presence, which characterizes the user's interaction within the VR environment. Whereas immersion is an objective measure referring to the VR platform, it does not immediately correspond to the level of presence (which is subjective). VR environments may be delivered to the user via several technologies that differ in the extent to which they are able to "immerse". There is considerable evidence indicating that a high sense of presence may lead to deeper emotional response (Weiss, 2005), increased motivation and, in some cases, enhanced performance (Schuemie, 2001). To provide to the users augmented sensorial feedback (discussed in paragraph 3.2.4) about their performance, helps to achieve a stronger feeling of presence in the virtual world.

VR environments are usually experienced with the aid of special hardware and software for input (transfer of information from the user to the system) and output (transfer of information from the system to the user). The selection of appropriate hardware is important since may greatly influence the way users respond to a VR environment (Rand, 2005). The output to the user can be delivered by different modalities including visual, auditory, haptic, vestibular and olfactory stimuli. Visual information is commonly displayed by Head Mounted Displays (HMDs¹), projection systems or flat screens. Sophisticated VR systems employ more than specialized visual displays, such as audio and haptic² display, engaging the user in the VR environment. Other, less frequently used ways of making the virtual environment more life-like are by letting the user stand on a platform capable of perturbations and thereby providing vestibular stimuli such as the multisensory system CAREN (Motek, Amsterdam). Even less frequent is the provision of olfactory feedback to add odor to a virtual environment (Weiss, 2005).

¹ An HMD is composed of two small screens positioned at eye level within special goggles or a helmet. Thus users view the virtual environment in very close proximity. Advanced HMDs even provide stereoscopic 3D displays of the environment and usually are referred to as more immersive systems (Weiss P. K., 2005).

² Haptic feedback enables users to experience the sensation of touch, making the systems more immersive and closer to the real world experience (Weiss P. K., 2005).

Equally important to achieving a realistic experience within a virtual environment is the ability of the user to navigate and manipulate objects within it. Thus the user must be able to interact (directly or indirectly) with the environment via input technologies. One class of input technologies may be considered as direct methods since users behave in a natural way, and the system tracks their actions and responds accordingly. Generally, tracking (discussed in paragraph 3.2.3) is achieved by using special sensors (non-visual based systems) or by visual tracking (visual based systems). A second class consists of indirect ways for users to manipulate and navigate within a virtual environment. These include activation of computer keyboard keys, a mouse or a joystick or even virtual buttons appearing as part of the environment (Rand, 2005).

Beyond specialized hardware, application software is also necessary. In recent years, “off-the-shelf”, “ready-for-clinical-use” VR software has become commercially available. However, more frequently, special software development tools are required in order to design and code an interactive simulated environment that will achieve a desired rehabilitation goal. In many cases, innovative intervention ideas may entail customized programming to construct a virtual environment from scratch, using traditional programming languages (Weiss, 2005).

VR hardware, combined with virtual environments, provides engineers tools for designing rehabilitation interventions customized on patients. When creating a specific VR application for rehabilitation the clinician and technical team face the challenge of choosing and integrating the software and hardware. These decisions are made taking into account budget, physical space, mobility of the system, patient population, complexity of the task with respect to the patient population and the extent of immersion desired from the system. In Chapter 5 a VR application for motor rehabilitation is described in detail.

3.2.2. Virtual Neurorehabilitation

Virtual rehabilitation is the use of VR within rehabilitation (Burdea, 2002). It allows creating environments for assessing and rehabilitating patients, where controlled presentations of

stimuli, motion tracking and performance recording are possible (Rizzo & Kim, 2005).

The rationale for using VR in rehabilitation is based on a number of unique attributes of this technology (Riva, 1999), (Schultheis, 2001). These include the opportunity for active learning, which engages the participant in two or more cognitive and motor activities simultaneously (i.e., dual tasking). This involves and motivates the participant (Mantovani, 2003) and enhances motor learning through problem solving and decision-making. It has been shown that people with impairments seem able to both learn motor skills in VR and transfer the learnt abilities to their real life (Holden, 2005).

In addition, VR allows to objectively quantifying changes and measuring behavior in challenging but safe environments, while maintaining strict experimental control over stimulus delivery and measurement (Rizzo, 2002). VR also offers the possibility to individualize treatments and to standardize assessment and training protocols (Weiss, 2005). VR environments provide the opportunity for repeated learning trials and offer the capability of gradually increasing the complexity of tasks while decreasing the support and feedback provided by the therapist (Schultheis, 2001). Moreover, VR offers the opportunity to provide multi-sensory feedback simultaneously in order to broaden users' rehabilitation. The assumption is that, by displaying and augmenting the same information to different senses, it is possible to increase the amount of knowledge available to participants and consequently assist their performance. Finally, the automated nature of feedback delivery during a VR treatment enables a therapist to focus on the provision of maximum physical support when needed without reducing the complexity of the task.

Among the disadvantages, a factor that may limit the use of VR for patients is cybersickness, which refers to side effects experienced by some users during and following exposure to VR environments (Kennedy, 1997), (Kennedy, 1996). Effects noted while using some VR systems can include nausea, eye-strain and other ocular disturbances, postural instability, headaches and drowsiness. Effects noted up to 12 hours after using VR include disorientation, flashbacks and disturbances in hand-eye coordination and balance (Kennedy, 1997), (Stanney, 1998). Many of these effects appear to be caused by incongruities between

information received from different sensory modalities (Lewis C. a., 1998). Other factors that may influence the occurrence and severity of side effects include characteristics of the user and the display, the user's ability to control simulated motions and interactivity with the task via movement of the head, trunk or whole body (Lewis C. a., 1998).

VR has successfully been used in assessment and rehabilitation of in the neuropsychological and motor deficits in people affected by neurological impairments. Specifically, several studies have been used VR application aiming to train balance and posture, gait, upper and lower extremity function (Sveistrup, 2003). Bisson et al. measured attention demands and functional balance scores before and after a VR balance training programs with augmented biofeedback, demonstrating an improvement of functional balance in traumatic brain injury survivors (Bisson, 2007). VR-based motor training for lower limb has shown encouraging results in post-stroke populations (Laver, 2011), such as improvements in gait speed (Fung, 2006), (Yang, 2008), (Walker, 2010) and stride length (Jaffe DL, 2004), (Mirelman A., 2009), and in PD individuals (Mirelman A. M., 2011). For what concerns the virtual rehabilitation of the upper limb, the majority of the literature is addressed to post-stroke populations and has shown encouraging results (Levin, 2009) (Henderson, 2007), (Holden, 2005).

3.2.3. Motion tracking in virtual environments

In order to involve patients in the virtual motor rehabilitation treatment, it is necessary to immerse them into the simulation, reproducing their limbs movement in real-time inside the virtual environment. A good tracking of the head also contributes to enhance the sense of presence in the simulation, recording the head orientation and moving the virtual environment accordingly (Baillot, 2001).

Features that are usually required to a good real-time tracking are the high accuracy, low encumbrance, high robustness, low invasiveness (users should be unrestricted in their mobility) and minimum latency (Ribo, 2001).

The existing human limb tracking systems can be classified as non-vision based and vision-based systems. Non-vision based systems use inertial, mechanical and magnetic sensors to collect movement signals. Magnetic tracking systems do not require much space but they tend to have limited accuracy due to magnetic field distortions caused by large metal objects common to industrial environments. Inertial measurement systems can be used in many circumstances without limitations (i.e. illumination, temperature, or space, etc.) and show better performance in accuracy against mechanical sensors. With this sensor approach, such as used by Intersense (InterSense Inc., Billerica, MA, USA), InterTrax2, a three degrees of freedom, inertial orientation tracker used to track pitch, roll and yaw movements, the user wears a tracking device that transmits position and orientation data to the VR system. The main drawback of using inertial sensors is that accumulating errors (or drift) can become significant after a short period of time. This issue is discussed in detail in Chapter 4, while a tracking methodology for VR based on the use of IMUs is described in Chapter 5.

In vision-based systems, the user's motion is recorded by video cameras, where special software processes the video image, extracts the user's figure from the background in real-time, and identifies any motion of the body. Unfortunately this approach to human motion tracking often involves intensive computations, such as temporal differencing, background subtraction or occlusion handling (Sen, Leo, Tan, & and Tham, 2011).

The Microsoft Kinect for Windows is a low cost sensor belonging to the vision-based class since it exploits an infrared (IR) structured light to calculate the distances between the IR camera and points in the environment. It consists of three main components, such as IR laser emitter, an IR camera, constituting the depth sensor, and an RGB camera. The inventors describe the measurement of depth as a triangulation process (Freedman, 2010). The Kinect sensor captures depth and color images simultaneously at a frame rate of up to 30 fps. In Chapter 7 an application using the Microsoft Kinect for tracking gait and reproducing it in a VR environment is illustrated.

Remarkable improvements have been achieved by using hybrid tracking systems, which combine the strengths, eliminating the disadvantages, of complementary sensing systems

(e.g. optical and inertial tracking (You, 1999), optical and magnetic tracking (Auer, 1999) (Baltadjieva, 2006) (Behrman, 1998).

3.2.4. Augmented feedback

Reliable sensory information and correct integration of sensory information are necessary for motor control. In neurological impairments, and also as a natural consequence of ageing, this information may be inadequate and, consequently, the control results impaired (Dozza, 2007).

“Biofeedback can be defined as the use of instrumentation to make covert physiological processes more overt” (Huang, 2006). A sensory feedback, augmenting or substituting the sensory movement information, gives to neurodegenerative patients the opportunity to observe a physiological function otherwise not perceptible and regain the ability to better assess different physiological responses and possibly to learn self-control of those responses (Hilgard, 1975).

During the learning process of a motor skill, feedback is the positive or negative response that can inform the learner how well she/he performed the task. The term feedback can be divided in two classes: the inherent (or intrinsic) feedback and augmented (extrinsic) feedback. Inherent feedback is the sensory information that tells the learner how well the task was completed: a basketball player will understand that he/she made a mistake when the ball misses the hoop. In contrast, augmented feedback is information that supplements or “augments” the inherent feedback: for example, when a person is driving over the speed limit and a beep sound is generated by the car. Although the car did not do any harm, the beep gives augmented feedback to the driver in to increase safety (Schmidt, 2005).

The augmented feedback can assume a high number of independent dimensions: it can be concurrent or terminal, immediate or delayed, accumulated or distinct, verbal or non-verbal.

An important category of the augmented feedback is the knowledge of results (KR), which is defined terminal augmented feedback about the goal achieved and not about the movement itself. In experimental studies, KR usually refers to a score or, in any case, to information

provided over and above those sources of feedback that are naturally received when a response is made (Adams, Response feedback and learning, 1968).

Knowledge of performance (KP) refers, instead, to information about the quality or patterning of a movement. It may include information such as displacement, velocity or joint motion. KP tends to be distinct from intrinsic feedback and more useful in real-world tasks. It is a strategy often employed by rehabilitation practitioners (Winstein, 1991).

In the next chapters several applications of augmented feedback in virtual environments are described. In particular, in Chapter 8, a visual feedback tool for trunk control is presented.

4. Estimation of stride length using an IMU: a validation of the zero velocity assumption

This chapter was written on the basis of the published article “Estimation of stride length in level walking using an IMU attached to the foot: A validation of the zero velocity assumption during stance” (Peruzzi, Della Croce, Cereatti; Journal of Biomechanics 2011).

4.1. Introduction

Wearable IMUs, including accelerometers and gyroscopes, allow measuring and tracking human locomotion (Sabatini, 2005); (Yun X., 2007), along with the estimation of spatial parameters (such as the stride length), both outdoor indoor and in non-controlled environment and for prolonged periods of time. Once estimated the IMU orientation in the global reference frame (Sabatini, 2005); (Schepers, 2007), linear displacements can be obtained by double integrating the IMU linear coordinate acceleration in the global reference frame and by removing the gravitational contribution from the accelerometer signals. However, the described procedure is complicated by the next factors: (a) a drift commonly present when integrating the accelerometer and gyroscope signals introducing an error in the displacement estimations, which is nonlinearly related to the integration time (Djuric, 2000); (Thong, 2004); (b) the determination of the IMU orientation with respect to the global reference frame from gyroscopic and accelerometer data is not trivial (Woodman, 2007) and (c) in the integration of the coordinate accelerations an estimate of initial velocity needs to be provided.

Exploiting the cyclical nature of gait typically reduces the detrimental effects of the drift. This allows reduction of the interval of integration time to a single gait cycle but requires the identification in the cycle of an instant of known velocity to be used as initial velocity in the integration of the acceleration in the global reference frame.

Despite the fact that during stance in level walking the foot rolls from the outer edge to the inner edge (Rodgers, 1988) and the paths of movement of the forefoot and heel differ both in shape and time (Winter, 1984), the velocity of the sensor placed on the different foot and shank locations is often set to zero at the beginning of the integration interval (zero velocity assumption— (Veltink, 2003), (Sabatini, 2005), (Foxlin, 2005), (Yun X., 2007), (Schepers, 2007), (Ojeda, 2007), (Bamberg, 2008), (Feliz, 2009), (Li, 2010), (Mariani, 2010). In particular, the foot velocity has been assumed to be zero: (a) throughout the stance phase (Yun X., 2007), (b) during a portion of it (Sabatini, 2005), (Ojeda, 2007) or (c) only in a specific instant (Li, 2010).

While the zero velocity detection issue has been recently studied (Skog, 2010) and both drift reduction and IMU orientation determination have been extensively studied (Veltink, 2003), (Foxlin, 2005), (Sabatini, 2005), (Ouinge, 2005), in literature there is no study analyzing the validity of the zero velocity assumption.

4.2. Methods

This study aimed at determining the minimum velocity of progression of various points of the foot and shank during the stance phase of the gait cycle while walking at different speeds. Such an analysis allowed estimation of the magnitude of the errors in determining the stride length due to the zero velocity assumption. The analysis of other factors affecting the stride length estimate, such as accelerometer and gyroscope drifts and biases, IMU orientation errors and identification of the time epochs when the inertial sensors are not moving, was beyond the scope of this study.

Twenty subjects (9 females, age 35.9 ± 8 years, h 168 ± 9 cm), with no history of major injuries or gross lower limb musculoskeletal abnormalities, were enrolled.

Eight retro-reflective markers (14 mm) were placed on selected locations of the right foot and shank (Fig. 1), reproducing the IMU placements adopted in various studies (Sabatini, 2005), (Schepers, 2007), (Ojeda, 2007), (Li, 2010). Subjects were asked to walk at three different self-selected speeds (slow, comfortable and fast) wearing sneaker shoes.

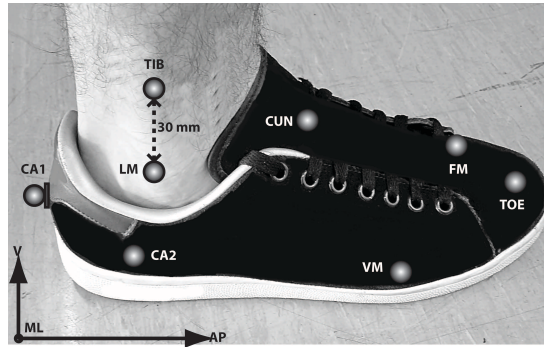


Figure 3 Marker locations for the right foot and shank and the global reference frame.

For three trials at each speed, marker positions were reconstructed using a stereophotogrammetric system (six-camera Vicon T20, 2Mpixel). The frame rate was set to 100 frames/s to preserve signal power (Antonsson, 1985). The measurement volume was a 1.5 m sided cube. The global reference frame was formed by a vertical axis (V), by an antero-posterior axis (AP) coincident with the direction of progression of gait and an axis perpendicular to the V and AP axes (Figure 3) The beginning and the end of the stance phase were identified, setting a threshold of 5 N to the vertical component of the ground reaction force measured with a 6-channel force platform (AMTI). For each trial, gait speed (s), gait cycle duration (T) and stride length (SL) were determined from marker positions. Trials were then reorganized in three equally populated groups ($slow_s$, $comf_s$, $fast_s$) based on the s values. The velocity of markers along AP (v) was estimated by applying a finite difference calculation of the relevant coordinates. At the times when the number of cameras used for reconstructing marker position changed due to loss/gain of marker visibility, abrupt artificial marker velocity changes were observed. To remove such outliers, for each marker, at any instant t_i , $v(t_i)$ was considered reliable only if both the differences $|v(t_i) - v(t_{i-1})|$ and $|v(t_{i+1}) - v(t_i)|$ were smaller than 0.005 m/s (0.015 m/s for the shank markers).

The accuracy of v estimates was assessed from the acquisition of a still marker positioned on the ground.

For each trial and each marker the minimum AP velocity during stance (v_{min}) and the relevant instant of occurrence, expressed as percentage of the stance phase ($SP_{\%v_{min}}$), were

determined. When v reached negative numbers, v_{min} was set to zero and the relevant $SP_{\%v_{min}}$ was set to the instant of zero crossing. For each walking speed group, the average of the v_{min} values (\bar{v}_{min}) and the average of the $SP_{\%v_{min}}$ values ($\overline{SP_{\%v_{min}}}$) along with their standard deviations (sd) were computed for all markers.

From noise-free coordinate acceleration data, SL can be determined by double integrating the AP coordinate acceleration $a(t)$ over T :

$$\int_{t=0}^T \int_{\tau=0}^t a(\tau) d\tau dt + v_b T;$$

where v_b is the AP velocity at the beginning of the integration interval. Under the zero velocity assumption, the stride length estimate (SL_0) is obtained when the integration interval begins at an instant when $v_b=0$. To quantify the influence of the zero velocity assumption on the SL estimation, v_b was set equal to the v_{min} value found for each trial, a stride length estimate (SL^*) was obtained and the stride length estimation error (e) was calculated as the difference between SL_0 and SL^* ($e \geq SL_0 - SL^* = -v_{min}T$).

The average percent error ($\bar{e}_{\%}$) was computed for each marker and for each walking speed group as follows:

$$\bar{e}_{\%} = \frac{1}{N} \sum_{j=1}^N \frac{-v_{min}T_j}{SL_j} \times 100 = \frac{1}{N} \sum_{j=1}^N \frac{e_j}{SL_j} \times 100,$$

where N represents the number of trials included in each walking speed group.

4.3. Results

The error in estimating the AP velocity of a still marker was lower than 0.002 m/s.

	Stride duration s	Stride Length mm	Gait speed mm/s
<i>slow_s</i>	1.3 (0.2)	1122 (118)	846 (106)
<i>comf_s</i>	1.1 (0.2)	1300 (165)	1164 (99)
<i>fast_s</i>	0.9 (0.2)	1324 (345)	1576 (192)

Table 1 Average and sd values of stride duration (T), stride length (SL) and gait speed (s) for each walking speed group (N=20).

Gait trials were reorganized in three equally populated groups (60 trials per group) based on the effective s value (*slow_s*, $s < 1$ m/s; *comf_s*, $1 < s < 1.33$ m/s; *fast_s*, $s > 1.33$ m/s).

Average values of gait speed, stride length and stride duration and relevant sd for each walking speed group are reported in Table 1.

Minimum velocity $\overline{v_{min}}$, percentage errors $\overline{e\%}$ and their sd are reported for each marker and for each walking speed group in Figure 4a and b, respectively. For each marker and for each walking speed group, $\overline{SP_{\%v_{min}}}$ values and sd are reported in Figure 5.

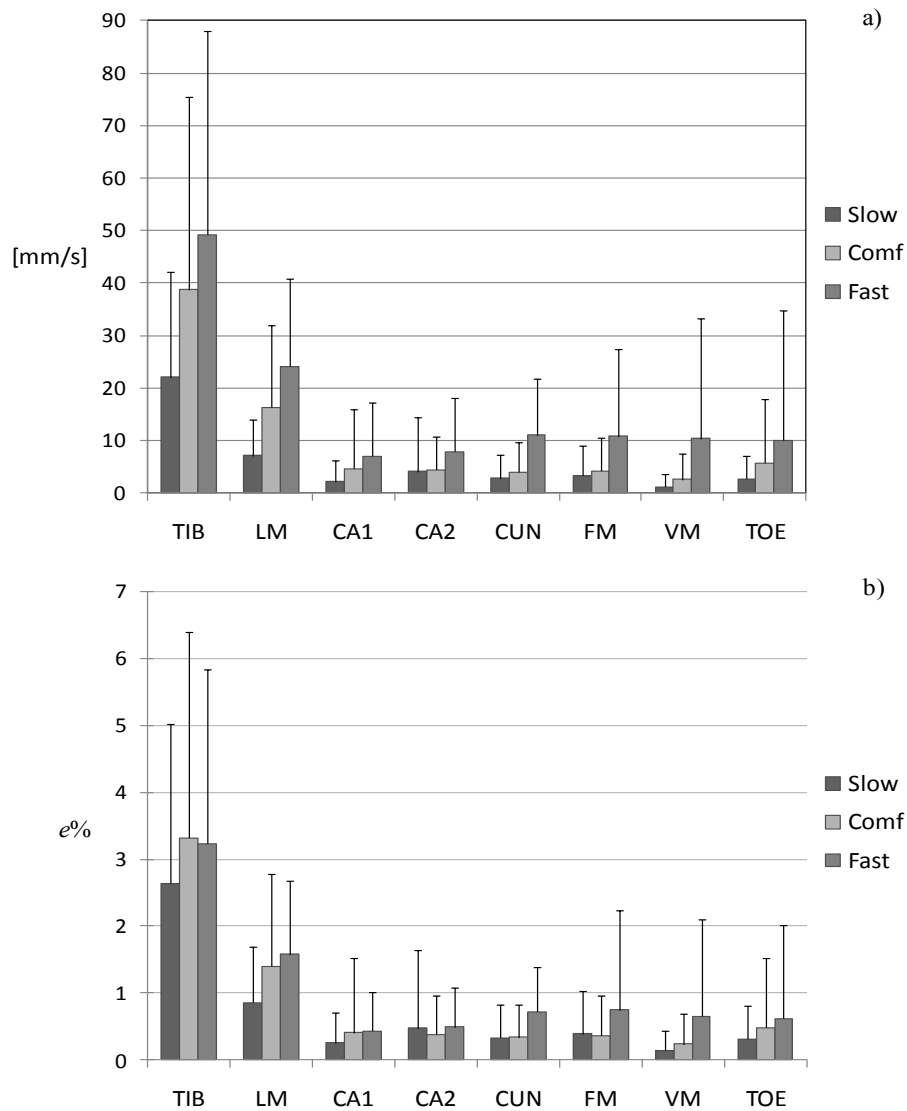


Figure 4 Average and sd of the minimum velocity v_{min} (a) and of the percent stride length error $e\%$ (b) for each marker location and speed group.

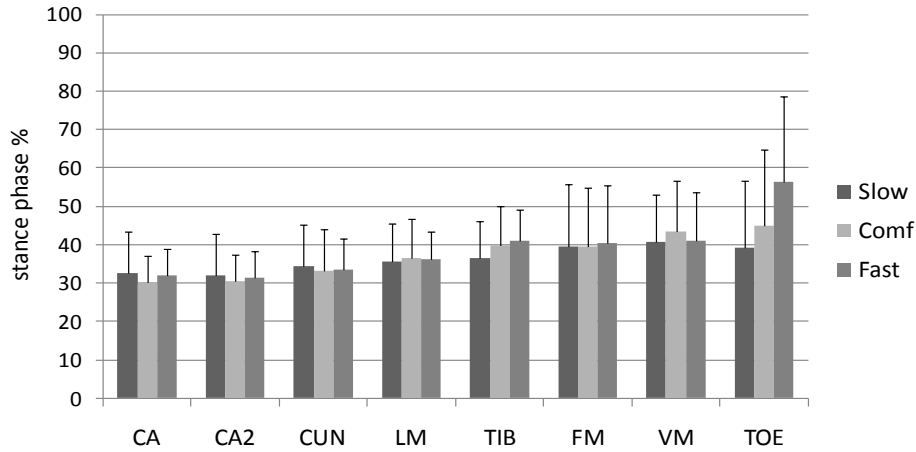


Figure 5 Average and sd of the instant of minimum velocity v_{min} , expressed as percentage of the stance phase $SP\%v_{min}$ for each marker location and speed group.

4.4. Discussion

To determine the stride length in level walking with an IMU positioned on the foot (or the shank) a double integration of the IMU's coordinate acceleration is needed and, consequently, a velocity value at the beginning of the integration interval must be specified.

In this context, velocities of foot and shank have been assumed, with no exception, to be equal to zero sometimes during the stance phase regardless of the sensor location and the gait speed. In this study, the validity of such assumption was tested by evaluating its isolated effects on stride length estimation for various IMU positions. Results showed, on average, that none of the tested points on foot and shank had zero velocity at any time during stance. However, the high *sd* values observed for some tested points indicate the high sensitivity of v_{min} to minor changes in foot contact mechanics. The minimum velocity of the foot points was always lower than that of the shank but still larger ($\overline{v_{min}} < 0.011$ m/s) than the estimate of velocity of a still marker ($v \leq 0.002$ m/s).

For foot points, the zero velocity assumption applied to drift-free coordinate acceleration data introduces an average stride length underestimation error up to -0.7%. For a shank point (0.03 m above the ankle joint) the $\overline{v_{min}}$ value resulted to be up to 0.049 m/s, causing stride length underestimation errors up to -3.3%. For all locations analyzed, $\overline{v_{min}}$ resulted to be

dependent on gait speed. These results are consistent with the representation of the foot during stance as a deformable rolling body for which an increase of the gait speed would presumably cause an increase of the angular velocity. Since none of the observed points were in contact with the ground during stance, their AP velocity is expected to increase as the gait speed increases.

Higher gait speeds resulted also in larger stride length values and lower stance durations. As a consequence, the increase of the stride length estimation error $\overline{e}_{\%}$ due to the increase of the minimum velocity was partially counterbalanced by the decrease of the stance duration and by the increase of the stride length.

The instant of occurrence of the minimum velocity ($\overline{SP_{\%v_{min}}}$) ranged between 31% (CA2) and 57% (TOE) of the stance phase duration and no dependency on gait speed was observed, except for the TOE point.

In conclusion, the results of the study suggest that if an IMU is positioned on the calcaneus (CA1) or on the lateral aspect of the rear foot (CA2) the influence of the error in estimating the stride length, associated with the zero velocity assumption, is minimized since during stance these points showed (a) a minimum velocity, (b) a limited dependency on gait speed and (c) a limited timing variability. Overall the assumption that the velocity of the IMU can be set to zero at some point during stance may be acceptable if the IMU is attached to the foot, whereas it may cause critical errors if it is attached to the shank.

5. Virtual reality and inertial sensing in motor training: application to multiple sclerosis

This chapter was written on the basis of a preliminary study of VR+TM training for MS patients. The results of the study have been divided in three articles. The first of them is “Feasibility and acceptance of a virtual reality, treadmill and wearable inertial sensors system for gait training of individuals with Multiple Sclerosis” (Peruzzi, Cereatti, Mirelman, Della Croce) and has been submitted to IEEE Transactions on Neural Systems and Rehabilitation. The second article is about the effectiveness of this kind of gait intervention on MS patients and will be submitted to the Journal of NeuroEngineering and Rehabilitation. The third article will be on the outcomes of motor and cognitive tests, whose choice and analysis has been performed by the clinicians who collaborate with my group. The methods and results will be reported for a complete overview of the study.

5.1. Introduction

Many of the common motor impairments of MS could lead to gait disturbances and difficulty in walking (Swinnen, 2012). About 85% of patients with MS develop gait problems (Armutlu, 2001). Individuals with MS frequently show, compared with the healthy controls, a greater variability in lower limb kinematics during gait, reduced stride length and walking speed, prolonged double limb support time (Crenshaw, 2006), (Martin, 2006). Approximately 75% of individuals with MS experiences mobility problems (Swingler, 1992), (Lord, 1998), such as a reduced walking ability (Thoumie, 2005). Moreover, about the 55% of individuals with MS identify fatigue, and, consequently, functional walking endurance, as one of the major symptoms affecting their mobility (Fisk, 1994). Additionally gait impairments can lead also to an increased risk of falling (Cattaneo, 2002). It is therefore important to develop effective rehabilitation interventions to address gait, balance and endurance in individuals with MS. As mentioned in paragraph 2.3.1, conventional therapeutic interventions for patients with MS usually include muscle-strengthening exercises, gait and balance control

techniques (O'Sullivan, 1988). Different studies have compared the effectiveness of task-oriented interventions to facilitation approaches to improve walking ability and balance in individuals with MS (Lord, 1998), (Wiles, 2001). Both methods have shown to improve functional mobility, walking speed and balance, demonstrating no significant differences in effectiveness between the two methods.

Locomotor training using a BWS and TM system is a task-oriented intervention that has shown to improve walking ability in individuals who have experienced neurological injuries such as spinal cord injury (Field-Fote, 2001), (Behrman, 2005), PD (Mehrholtz, 2010), stroke (Laufer, 2001), (Nilsson, 2001), (Sullivan, 2002) and MS (Swinnen, 2012). This training modality allows for repetitive training of locomotion throughout a complete gait cycle.

Although training of locomotion combined with the use of VR has shown promising results on neurological populations (Paragraph 3.2.2) to my knowledge, only a single-case study on MS has been found in literature. Fulk et al. of a BWS system and TM for training gait combined with a VR-based system for balance purpose (Fulk, 2005), suggesting that a rehabilitation intervention combining the use of TM and VR were appropriate to improve walking, balance, and endurance outcomes on an individual with MS.

Cognitive impairments are also common (43 - 65%) in MS (Rao, 1991), often associated with depression (Arnett, 2008). Specifically the main cognitive affected areas include memory, executive functions and attention (Chiaravalloti, 2008). In a recent case-control study (Hamilton F, 2009) in MS, interaction between walking and attention has been investigated. Compared to healthy controls, MS subjects demonstrated slower speed and elevated swing time variability in gait performance under a dual task condition. Since daily life is often characterized by walking with a concurrent cognitive task, a treatment of gait in MS should incorporate motor as well as cognitive training, in order to optimally enhance mobility in dual tasking and reduce fall risk, with a consequent improvement on quality of life. It is our hypothesis that a rehabilitation intervention combining TM training and VR will produce changes in gait and endurance of MS individuals.

Moreover, the success of a rehabilitation intervention relies on the patient's engagement, motivation and satisfaction (Lewis, 2011) (Jovanov, 2005). VR-based rehabilitation tools applied to upper extremity training of post-stroke patients have shown a high level of acceptance. Cameirão et al. (Cameirão, 2010) used a questionnaire to assess the usability and acceptance of a VR-based neurorehabilitation system for controlling two virtual limbs in individualized tracking tasks. They evaluated the enjoyment in performing the task, the understanding and ease of the task and the subjective performance. Similar questionnaires have been used to assess enjoyments and level of challenge during VR training as well as self-confidence and demonstrated high levels of satisfaction of these systems (Lewis, 2011), (Schwickert, 2011). Numerous studies underlined the importance of motivation and participation of patients involved in VR-based training. Zimmerli and colleagues (Zimmerli, 2009) showed that augmented feedback applications for gait training (a VR environment and a Lokomat - Hocoma, AG, Switzerland), increased the subject's motivation and activity level. In a second work they showed that the presence of a virtual opponent in a VR environment produced higher participation and enjoyment of children with gait impairment (Koenig, 2008), (Brütsch, 2010). In Girone et al., (Girone, 2000) subjects with ankle disorders responded favorably to a training combining a VR environment with an ankle rehabilitation device. Ease of use of the device and perception of limited fatigue during the training resulted in high acceptance and satisfaction (Deutsch, 2001), (Deutsch, 2005).

The first aim of this study was to build a VR system using wearable inertial sensors and a VR environment for gait training on TM. The second aim was to assess the acceptance and the feasibility of using the VR-based gait training approach, combining motor and cognitive aspects, for patients with MS. Finally, the last aim was demonstrate the efficacy of the 6-weeks gait intervention with TM and VR in patients with MS, evaluating possible gains over ground immediately after the end of the training period.

5.2. Methods

5.2.1. Experimental set-up

The following equipment was used to administer the proposed gait training program: a conventional TM, a BWS, three IMU (MTx Xsens, Enschede, The Netherlands) and a Head Mounted Display (HMD - Z800 Emagin, Bellevue, WA, USA) – or alternatively a large screen. The TM allowed controlling the patient's walking speed. Patients wore the harness to guarantee a safe experimental setup. The HMD was used to deliver the specifically designed VR environment. Two IMUs were attached to the patient shoes and the data recorded during the walking trails were used to generate in real time, the motion of a pair of shoes in the VR environment. An additional IMU was placed on the patient's head to monitor its rotation in the horizontal plane.

5.2.2. VR environment

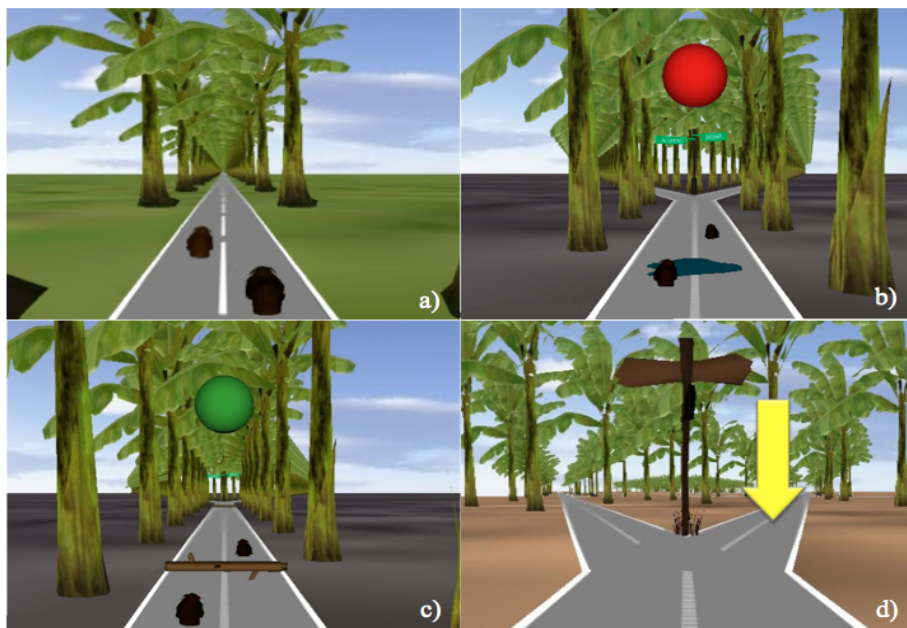


Figure 6 (a) A screen shot of the VR environment: a tree-lined road presenting obstacles and road bifurcations. The movement of the shoes reproduces in real time the patient's feet movement. (b) A positive visual feedback (green circle) is returned when the patient successfully passed an obstacle (a log) and (c) a negative visual feedback (red circle) is returned when the patient unsuccessfully negotiated an obstacle (a puddle). (d) A bifurcation as seen by the patient: the road sign shows two directions. The patient chooses a direction by turning her/his head towards it. The head rotation is captured by an IMU and a blinking arrow appears pointing at the selected direction just prior to the turn.

The software platform implementing the VR environment was based on Python (Python v2.4). The data extracted from the IMUs were streamed in real time into the VR environment at the sampling rate of 50 Hz. The VR environment was generated with the Vizard software (WorldViz, Santa Barbara, CA, USA).

The VR environment consisted in a tree-lined road presenting obstacles (puddles and logs). In addition, to evaluate decision-making, attention and problem solving, road bifurcations featuring street signs indicating both the pre-assigned destination and alternative destinations were included. As visual feedback, the subject could see her/his shoes while walking along the trial (Figure 6a).

While walking on the TM, when virtually approaching an obstacle, the patient was expected to negotiate the obstacle without colliding with it. This required motor abilities as well as cognitive function, specifically planning and information processing.

Environmental changes were also introduced as distracters in order to challenge divided attention. These included different modalities in the form of auditory (chirping birds, barking dogs, ambulance sirens, etc.) and visual stimuli (change in weather conditions or animals and vehicles crossing the walkway).

The VR environment had five levels of complexity. These were determined by the number of bifurcations, density of trees and road width. The trainer could set size, position and frequency of the obstacles in the walkway, according to the subject's needs. To promote motor learning, visual and auditory feedbacks were provided upon success or failure (Schultheis, 2001), (Fung, 2004), (Levin, 2010). A KR, expressed as the amount of passed obstacles, was shown on the display at the end of the training trial reflecting knowledge of results.

Gait replication

The identification of gait cycles was obtained from IMU pitch angle data: heel strikes and the toe off corresponded to IMU pitch angle minima and maxima values, respectively (Figure 7). The pitch angle data were used to reproduce the patient's shoes movement in the VR environment, which was made to move toward the patient's point of view depending on the

TM speed. The velocity of the patient's shoes in the VR environment during the swing phase v_{sw} was set under the assumption that when walking on a TM, the distance traversed during the stance phase Δs_{st} is equal to the distance traversed during swing Δs_{sw} :

$$v_{sw} = \frac{\Delta s_{sw}}{\Delta T_{sw}} \cong \frac{\Delta s_{st}}{\Delta T_{sw}} = \frac{v_{TM} \Delta T_{st}}{\bar{T} - \Delta T_{st}},$$

Where v_{TM} is the TM speed, ΔT_{sw} is the duration of the swing phase, which was assumed to be equal to the difference between the mean stride time \bar{T} (calculated over the previous 5 cycles) and the current stance phase time $\Delta T_{st} v_{TM}$.

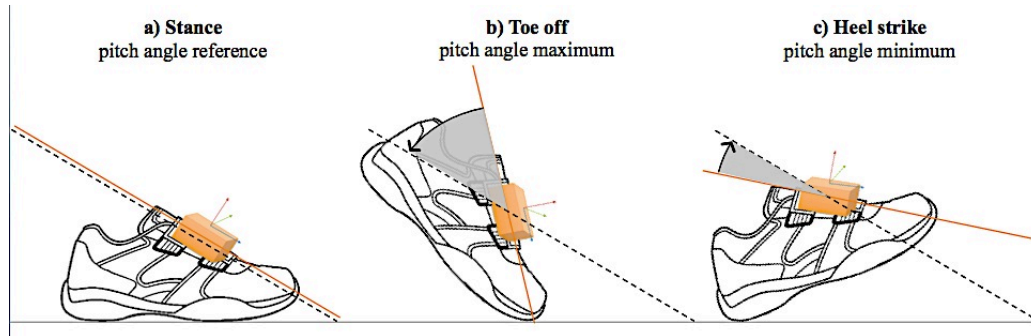


Figure 7 Gait cycles were identified from IMU pitch angle data: heel strikes and toe off instants corresponded to the instants of pitch angle minima and maxima, respectively. The gray solid line represents the longitudinal axis of the IMU, whereas the black dotted line represents the pitch angle reference of the IMU defined by the foot flat on the ground.

Therefore, to replicate gait in the VR, a shoe was made to move forward when a maximum pitch value was detected and backward when a minimum pitch value was detected, therefore traversing a forward distance equal to $v_{sw} \Delta T_{sw}$ during swing and a distance equal to $v_{TM} \Delta T_{st}$ during the stance phase. ΔT_{st} and ΔT_{sw} are defined as:

$$\begin{cases} \Delta T_{sw} = n_{sw} \times \Delta t \\ \Delta T_{st} = n_{st} \times \Delta t \end{cases}$$

Obstacles and bifurcations

Obstacles (puddles or logs) along the walkway appeared at variable intervals of time, while their number, size and orientation were adjusted by the trainer on a trial-by-trial basis. Patients had to raise their foot, when encountering a log, and lengthen their step, when encountering a puddle. In both cases the duration of the swing time was used as an indirect

measurement for discriminating successful tasks and an audio/visual feedback was generated (Figure 6b and c).

When in the proximity of a bifurcation, patients were instructed to express the chosen destination by turning their head accordingly. A blinking arrow pointing at the chosen direction, identified from the recording of the head mounted IMU, appeared just before encountering the bifurcation to allow a direction change if needed (Figure 6d).

If successful, a positive audio/visual feedback was provided immediately after the turn.

5.2.3. Study design and participants

This study used a repeated measures design (pre-training – Pre, post-training – Post, and follow-up at 4 weeks – F-Up), evaluating gait during single (ST) and dual task (DT) after a 6-week intervention using TM with VR in a single group of patients with MS.

Ten subjects affected by Relapsing Remitting type of MS according to McDonald et al.'s criteria (McDonald, 2001), were recruited from the Operative Unit of Neurology unit at the Sassari University Hospital and participated in this feasibility study (9 females, mean age: 44.3 ± 8.1 years). Patients had an Expanded Disability Status Scale - EDSS (Kurtzke, 1983) score between 3 and 6 and an Ambulation Index - AI (Rose, 2006), between 3 and 5. They had adequate cognitive ability to participate in the study (a Mini-Mental State Examination – MMSE (Folstein, 1975) - score of 24 or above), and had stable medical conditions with no relapses in the last 6 months prior to the study. Exclusion criteria included serious chronic medical illnesses (e.g., orthopedic, psychiatric or neurological) and severe visual deficits or depression. All participants provided an informed written consent prior to the beginning of the study.

5.2.4. Rehabilitation intervention

The VR environment required the participants to walk on a TM while processing multiple stimuli simultaneously and making decisions about obstacle negotiation. These decisions were made more difficult by a memory task, by distracters in the simulation to challenge the divided attention and by adjustment of the frequency and size of the virtual obstacles.

The intervention lasted six weeks (with two sessions per week for a total of 12 sessions). Training progression was based on an earlier study protocol of intensive progressive individualized TM training with VR in patients with PD (Mirelman, 2011). In both studies, participants walked on the TM with a safety harness that prevented falls but did not provide BWS. The subjects were required to lift their legs high enough and far enough to pass the virtual obstacles. Sessions consisted of three trials of ten minutes of walking followed by five minutes of rest, for a total time of about 45 minutes (30 minutes of training and 15 minutes of resting). The Borg Rating Scale of Perceived Exertion Scale – Borg Scale (Borg, 1982) was administered at the beginning and end of each session to assess and monitor the level of exertion and fatigue.

Week	Goal	Session	Speed	Difficulty level	Hand support	Distracters	Number of bifurcations		
1	Familiarization and adaptation	1	1.5/2.0 km/h	1	2	None	1		
		2	80%						
2	Increasing motor load	3	90%	2			None	2	
		4							
3	Increasing cognitive load	5	100%	3				None	3
		6							
4	Increasing both motor and cognitive load	7	110%	4		None			Easy
		8							
5	Improve balance	9		110%			4		None
		10							
6	Reach to the maximal potential	11	120%				5	None	
		12							

Table 2 Training progression milestones per week and setting ranges.

The VR training allows for an individual progression outline, which would fit each patient and their specific abilities and difficulties, and would be based on their performance during previous trials and sessions. In order to keep a standardized training program for all patients, general progression should be kept within the setting ranges framework and according to specific weekly goals (Table 2). The patient’s balance during training could be challenged by asking her/him to remove one or both hands from the handrail. The level of complexity of the VR environment was raised when the trainer considered the patient ready for a more intensive

cognitive task. During the first session the TM speed was set at low values in order to let people to familiarize with the training. In the second session TM speed was set at 20% lower than the patients over-ground walking speed (Brooks, 2003). In the following sessions, the TM speed was adjusted based on the fatigue, the balance and the VR complexity levels. Also orientation, size, frequency of appearance, and shape of the obstacles were manipulated according to individual needs, trying to follow the guidelines for training progression, which has been designed to achieve a success rate of 80% in clearing the obstacles to promote engagement and motor learning. Feedback was given to the participant in multiple ways including the scoring on the obstacle avoidance tasks and auditory and visual feedback about the motor and the cognitive performance.

5.2.5. Outcomes

- *Evaluation of the VR-based system-* The VR-based system, including hardware and VR environment, has been assessed in terms of usability (ease of use and safety of the system, accuracy of the user's task).
- *Evaluation of setup and administration of the gait training program-* The setup and the proposed training program were evaluated in terms of feasibility and acceptance.
 - Feasibility: a) number of patients completing the training program, b) number of unexpected events or accidents during the training, c) number of system crashes, d) number of uncompleted trials, e) TM speed progression associated to the fatigue, balance challenge and VR environment complexity levels.
- Acceptance: a questionnaire based on previous studies (Cameirão, 2010), (Chang, Chen, & Huang, 2011), (Zimmerli, 2009), (Girone, 2000), (Deutsch, 2001) was administered (Table 7). The questionnaire included aspects such as the ease and understanding of the task (statements 1-4), attitudes relating to the technology (statements 5-7), the subjective performance (statement 8-10) and enjoyment from the training (statements 11-14). Responses were recorded using a 5-point Likert scale with “strongly disagree”, rated as a 1, to “strongly agree”, rated as 5.

- *Gait analysis*- Patients were asked to walk over-ground in the gait analysis laboratory under two conditions: 1) comfortable speed (ST), 2) while serially subtracting 3 from a pre - defined number (DT). A stereo-photogrammetric system (six-camera Vicon T20, frame rate 100 frames/s), two force platforms (AMTI OR6-7, frame rate 1000 frames/s) and the Vicon Plug-in Gait marker set have been used to assess spatial temporal gait parameters, low limb joint kinematics and kinetics (dynamics).

	Parameter	Gait cycle phase
Kinematics	Ankle Flexion Angle Min deg	Double support
	Ankle Flexion Angle Max deg	Single support
	Ankle Flexion Angle Min deg	Swing
	Knee Flexion Angle Max deg	Double support
	Knee Flexion Angle Min deg	Stance
	Knee Flexion Angle Max deg	Swing
Dynamics	Hip Flexion Angle Max deg	Double support
	Hip Flexion Angle Min deg	Single support
	Ankle Moment Max Nm/Kg	Terminal Stance
	Hip Moment Min Nm/Kg	Terminal Stance
	Ankle Power Max W/Kg	Toe-Off
	Ankle Power Min W/Kg	Single Support
Spatial-temporal	Hip Power Max W/Kg	Swing
	Gait speed mean m/s	-
	Stride length mean m	-

Table 3 List of the analyzed parameters.

In Table 3 all the analyzed parameters have been reported. Three trials were evaluated for each condition. Since some of the patients exhibited bilateral impairments (Table 4), both data regarding the most and the less affected side has been reported.

- *Endurance*- The Six-minute walk test (6MWT) assessed endurance measured as the total distance walked in six minutes (Brooks, 2003). In this measure of walking endurance, subjects were instructed to cover as much distance as possible.
- *Disease severity of MS* - will be measured using EDSS.
- *Cognition*- Standardized cognitive tests will be used to assess executive function, visual processing and attention. These tests are: a) the Montreal Cognitive Assessment (MOCA)

to assess several cognitive domains (Nasreddine, 2005); b) the Trail Making Test³ (TMT) to evaluate visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning (Tombaugh, 2004) (Tombaugh, 2004); c) the Stroop Color-Word Test (STROOP)⁴ to measure selective attention, cognitive flexibility and processing speed, and it is used as a tool in the evaluation of executive functions (Howieson, 2004); d) frontal assessment battery (FAB), which includes simple tests of sequencing, behavioral inhibition, planning and frontal release signs, can be used as a screening test to elicit typical neurological and cognitive features (Dubois & Slachevsky, 2000); e) Serial Subtraction Dual Task (SSDT) performance. Subjects will be asked to walk while systematically subtracting three from a three-digit number. Performance in DT will be measured by the number of subtractions achieved (n°) and the number of mistakes made (err).

- *Dynamic Stability* - a) The Timed Up-and-Go (TUG) test to assess the ability to perform sequence movements of functional mobility (Podsiadlo, 1991). Patients are timed as they stand up from a standard chair, walk a distance of 3 meters at a normal pace, turn, walk back and sit down; b) The Four Square Step Test (FSST), a measure for dynamic balance involving stepping over low objects and movement in four directions under time constraints, has been used to assess overground obstacle negotiation and fall risk (Blennerhassett, 2008). The time to complete the test is used as performance metric.
- *Berg Balance Scale (BBS)* - To assess balance (Berg, 1995). It consists of 14 different balance tasks such as standing, reaching, bending, and transferring abilities, and has an overall score range from 0 (severely impaired) to 56 points (excellent). Although

³ The TMT includes two versions: in the TMT A the targets are numbers and the test taker needs to connect them in sequential order, while, in the TMT B, the subject alternates between numbers and letters (1, A, 2, B, etc.). The goal of the test is for the subject is to finish the part A and part B as quickly as possible; the time taken to complete the test is used as the primary performance metric.

⁴ The STROOP contains a word page (the names of colors printed in black ink), a color page (rows of X's printed in colored ink) and a word-color page (the words from the first page are printed in the colors from the second page). The subject's task is to look at each sheet and move down the columns, reading words or naming the ink colors as quickly as possible, within a given time limit (45 seconds). Three scores, as well as an interference score, are generated using the number of items completed on each page, with higher scores reflecting better performance and less interference on reading ability.

primarily used with geriatric clients and individuals with stroke, the BBS is a valid measure of balance for individuals with MS.

- *The Beck Depression Inventory (BDI)* - is widely used to assess emotional wellbeing (Beck, 1974)

5.2.6. Statistical analysis

Cognitive and motor (dynamic stability and balance) outcomes, DBI, endurance, spatial-temporal parameters, kinematics and dynamics of hip, knee and ankle were analyzed and descriptive statistics were calculated. Changes between Pre and Post and changes between Pre and F-Up were analyzed using the Wilcoxon Signed Ranks test with a significance level of 0.05. The EDSS measurements at Follow-Up were compared to those at baseline using the Wilcoxon Signed Ranks with a significance level of 0.05. All the statistical analyses were performed using SPSS (version 21).

5.3. Results

None of the subjects had a relapse within the period of enrollment. A summary of demographic and baseline gait characteristics of the study population is shown in Table 4.

Patient	Age	Gender	Disease Duration [years]	EDSS Pre	Ambulation index	Distance Pre [m]	Gait speed Pre [m/s]	MMSE	Clinical
P01	40	F	17	5	3	403	1.1	29	moderate cerebellar ataxia left hemiparesis
P02	60	F	17	5.5	4	270	0.8	30	moderate cerebellar and proprioceptive right ataxia very mild right hemiparesis antero-posterior bilateral knee instability
P03	38	F	5	3.5	3	249	0.7	28	mild cerebellar ataxia left hemiparesis
P04	43	F	5	4	3	321.8	0.9	29	mild proprioceptive ataxia right hemiparesis
P05	34	F	5	6	5	212	0.6	29	cerebellar and proprioceptive ataxia double hemiparesis left > right
P06	50	F	18	4	3	391.6	1.1	30	ataxia mild to moderate proprioceptive mild right hemiparesis
P07	42	F	11	6	4	187.6	0.5	27	proprioceptive ataxia double hemiparesis left>right very anxious depressive syndrome
P08	48	M	15	4.5	3	372	1.0	22	cerebellar and proprioceptive ataxia double hemiparesis left>right

Table 4 Participants characteristics.

Half of patients were bilaterally impaired (five of them have the left as the most affected side). Only one subject used an assistive device (crutches) for gait. During the study, participants did not receive concurrent physiotherapy. All subjects tolerated the training sessions well, and no incidences of falling occurred. In the initial training sessions, all patients walked clinging to the handrails with reduced TM speed, and were impaired in the negotiation of obstacles. However, during the training they learned to walk under multi modal conditions and to divide their attention within the VR environment. During the initial session, indeed, TM speed was 0.53 m/s and patients had a mean of 18% errors in negotiating the virtual obstacles (as a percent of the total obstacles in the session). In the last session, five of eight patients walked without their hand on the handrails, the TM speed was 0.81 m/s and the mean error percent increased to 67%. The mean value of the EDSS improved significantly from 4.8 in Pre to 4.3 in F-Up ($p = 0.04$).

5.3.1. Evaluation of the VR-based system

The VR- based rehabilitation system was built according to the requirements of the rehabilitation protocol and tested during a 6-weeks gait intervention with TM in patients with MS. No crashes and adverse events or complications occurred during the entire training period. The evaluation of the timing performance of the VR-system was also performed and the latency between the real movement and the virtual output in the environment was lower than 100 milliseconds. The speed inside the VR environment was constant and set equal to v_{TM} , while the subject inevitably moved on the TM in medio-lateral direction, introducing a variability that was not reported in the VR environment. Moreover, similar considerations regard gait, which was reproduced, as described in the methods section, according to maxima and minima pitch values. Finally, a consideration should be made on the unrealistic view of the subject of her/his shoes. Nevertheless, none of these discrepancies have been reported by subjects, who perceived the environment as plausible. Indeed, four of them became familiar with the VR environment after the first session, while the remaining, needed an extended acclimation time (two more sessions), probably due to the lack of experience in video gaming.

5.3.2. Evaluation of setup and administration of the gait training program

Feasibility

All patients completed the training, except for two who dropped out after the first session for personal reasons.

TM speed progression for all training sessions and for all patients is reported in Table 5. The table also reports the VR environment complexity levels and the training sessions carried out without using the handrails.

TM speed km/h	Session no.												
	1	2	3	4	5	6	7	8	9	10	11	12	
Patients no.	1	2.0	2.8	2.8	2.8	2.8	2.6	2.6	2.6	2.6	2.4	2.4	2.4
	2	2.0	2.0	2.1	2.3	2.6	2.6	2.6	2.7	2.8	2.8*	2.8*	2.8*
	3	2.0	2.0	2.0	2.1	3.0	3.0	3.0	3.3*	2.8*	3.0**	3.0**	3.0**
	4	2.0	2.5	2.6	2.9	3.8	3.8	2.8*	3.2**	3.3**	3.4**	3.4**	3.7**
	5	1.5	1.7	1.8	2.2	2.8	3.0	3.0	2.9	2.8*	2.8*	2.8*	2.3**
	6	2.0	3.1	3.1	3.1	3.4	3.4	3.4	3.6*	3.6*	3.0**	3.0**	3.1**
	7	2.0	1.5	1.7	1.8	2.5	2.6	2.7	2.8*	2.8*	2.8*	2.8*	2.8**
	8	2.0	2.0	2.3	2.5	2.9	2.9	3.2	3.5	3.0*	3.0*	3.0*	3.0*

COMPLEXITY LEVEL

1	2	3	4	5
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Table 5 Progression of the TM speed across the training sessions. The asterisks indicate trials in which patients took off one (*) or both () hands from the handrails. The gray tone of the cells indicates the complexity level. Bold numbers highlight the occasions when the trainer decided to lower the TM speed (when starting a higher level of complexity, or asking to remove hands from handrails or when fatigue increase was assessed as excessive).**

Table 6 reports the mean (and standard deviation) of the Borg Scale scores at the beginning of each training session (B_0) and their increments at the end of the training session ($DB=B_f-B_0$) averaged over patients. The percentage of uncompleted trials due to fatigue in each training session is also reported.

mean (std)	Session no.											
	1	2	3	4	5	6	7	8	9	10	11	12
B_0	8 (3)	8 (2)	8 (2)	8 (3)	8 (2)	9 (3)	8 (3)	8 (3)	9 (3)	9 (3)	8 (2)	9 (3)
ΔB	7 (3)	5 (2)	4 (2)	3 (2)	4 (3)	3 (2)	4 (3)	3 (3)	2 (2)	3 (3)	3 (2)	3 (3)
% incomplete	21	0	8	4	4	8	0	4	4	4	0	0

Table 6 Average and standard deviation over subjects of the Borg Scale score at the beginning of training sessions (B_0) and difference between Borg Scale scores at the end (B_f) and at the beginning of each training session ($DB = B_f - B_0$). In the last row of the table the percentage of the incomplete trials due to fatigue is reported for each training session.

Acceptance

Table 7 reports the results of the satisfaction questionnaire. The number of patients who provided the same score to each of the statements is reported in the last columns of the table.

Statement/Score	1	2	3	4	5
1. I had no trouble understanding what to do in the training	-	1	1	1	5
2. It was easy for me to learn how to move my feet and the head in the VR	1	-	3	1	3
3. It was easy for me to learn how to pass the obstacles	1	-	3	1	3
4. The visual and the audio feedbacks were helpful	-	-	-	-	8
5. Wearing the HMD was comfortable	-	-	-	3	5
6. Wearing the IMUs was comfortable	-	-	-	1	7
7. Wearing the harness was comfortable	-	-	-	1	7
8. The exercise was simple	3	2	3	-	-
9. The exercise was not tiring	1	2	1	2	2
10. I made few mistakes	-	-	3	3	2
11. I have noticed some improvements in my daily life performing the training	1	-	3	1	3
12. I enjoyed the training	1	-	-	1	6
13. Participating to the training was important for me	-	-	1	2	5
14. I would like to participate to the training again	1	-	1	1	5

Table 7 The administered questionnaire with the responses given by the patients. The questionnaire includes statements regarding the understanding of the task, the acceptance of the technology, the subjective performance and the enjoyment of the training. Patients' responses were recorded using a 5-point Likert scale from "strongly disagree", rated as a 1, to "strongly agree", rated as 5.

5.3.3. Gait analysis

Since a patient could not walk autonomously during the gait assessment, eight (N=8) subjects were considered in the analysis of the lower limb kinematics and spatial-temporal parameters, while seven (N=7) for the dynamics.

Gait in single task

Gait speed during usual walking increased by 10.9% immediately after the training (Pre: 0.77 ± 0.24 m/s, Post: 0.85 ± 0.25 m/s, $p = 0.12$) and 15.2% after one month (Pre: 0.77 ± 0.24 m/s, F-Up: 0.88 ± 0.23 m/s, $p = 0.07$). Stride length also increased in Post (Pre: 0.96 ± 0.19 m, Post: 1.04 ± 0.20 m, $p = 0.09$) improving up to 12.1% in F-Up (Pre: 0.96 ± 0.19 m, F-Up: 1.08 ± 0.16 m, $p = 0.03$). Kinematics and kinetics in ST have not shown significant changes

after the training, except to the minimum value of the knee flexion angle during the stance phase of the most affected side, which increased by about two degrees (Pre: 0.9 ± 3.5 deg, Post: 2.8 ± 4.8 deg, $p = 0.04$). For what concerns the less affected side, the maximum value of the ankle plantar-flexion angle during the swing phase increased (Pre: 8.1 ± 8.3 deg, Post: 15.3 ± 8.3 deg, $p = 0.02$) and the maximum value of the knee flexion angle during the mid stance significantly decreased in Post (Pre: 15.2 ± 6.9 deg, Post: 12.7 ± 5.2 deg, $p = 0.04$) and in F-Up (Pre: 15.2 ± 6.9 deg, F-Up: 11.6 ± 5.8 deg, $p = 0.05$). About the dynamics, the maximum value of the flexor hip moment (Pre: 0.62 ± 0.29 Nm/kg, Post: 0.87 ± 0.50 Nm/kg, $p = 0.13$) and power (Pre: 1.12 ± 0.65 W/kg, Post: 1.26 ± 0.72 W/kg, $p = 0.4$) showed a positive trend after the training in the most-affected side.

Gait in dual task

Gait speed during DT significantly increased (Pre: 0.65 ± 0.19 m/s, Post: 0.77 ± 0.24 m/s, $p = 0.04$) by 17.7% after training, reaching the 25.1% at F-Up (Pre: 0.65 ± 0.19 m/s, Post: 0.82 ± 0.21 m/s, $p = 0.01$). Stride length increased by 9.1% immediately after the intervention (Pre: 0.91 ± 0.15 m, Post: 1.00 ± 0.21 m, $p = 0.05$) improving up to 16.1% after one month (Pre: 0.91 ± 0.15 m, Post: 1.06 ± 0.10 m, $p = 0.01$). Also under this condition, the minimum value of the knee angle flexion during the stance phase increased in the most affected side (Pre: 0.4 ± 4.1 deg, Post: 3.62 ± 5.0 deg, $p = 0.03$). For what concerns the dynamics, the maximum values of the ankle moment (Pre: 1.20 ± 0.23 Nm/kg, Post: 1.28 ± 0.14 Nm/kg, $p = 0.4$, F-Up: 1.36 ± 0.16 Nm/kg, $p = 0.06$) and power increased in the most affected side (Pre: 1.25 ± 0.69 W/kg, Post: 1.90 ± 1.02 W/kg, $p = 0.03$, F-Up: 2.14 ± 0.76 W/kg, $p = 0.02$). A not significant positive trend has been also reported for the ankle moment (Pre: 1.26 ± 0.21 , Post: 1.30 ± 0.25 , F-Up: 1.32 ± 0.23 Nm/kg) and power (Pre: 1.47 ± 0.61 W/kg, Post: 2.01 ± 1.20 W/kg, $p = 0.18$, F-Up: 2.09 ± 1.01 W/kg, $p = 0.09$) in the less affected side. Also in DT condition, the maximum value of the flexor hip moment (Pre: 0.56 ± 0.26 Nm/kg, Post: 0.82 ± 0.48 Nm/kg, $p = 0.13$) and power (Pre: 0.78 ± 0.43 W/kg, Post: 1.02 ± 0.59 W/kg, $p = 0.18$) of the most-affected side showed a positive trend immediately after the training.

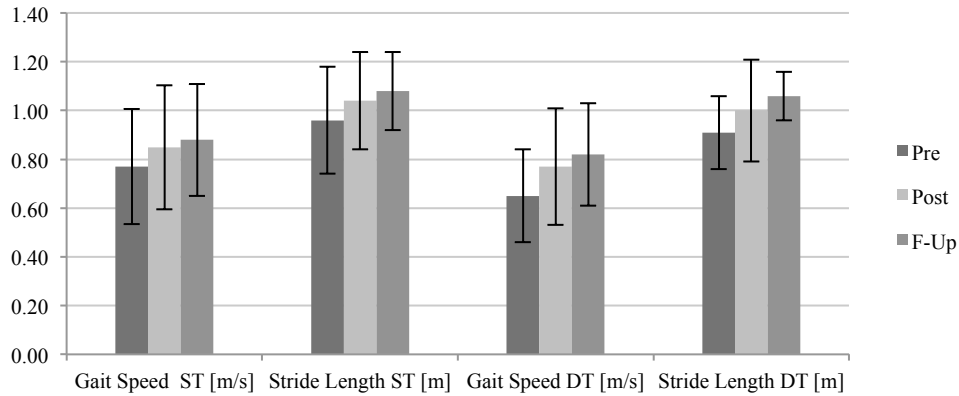


Figure 8 Effects of the TM+VR intervention on overground gait speed and stride length under ST and DT condition.

5.3.4. Endurance, balance and obstacle negotiation

Endurance, as measured by the distance walked during six minutes, improved after training by a mean of 8% in distance walked ($p = 0.12$), amounting to an increase of 23 m (Table 8), while gait speed during the 6MWT increased from 0.83 m/s to 0.90 m/s. In F-Up, the distance walked increased by 24%, amounting to an increase of 71 m ($p = 0.03$) and gait speed improved to 1.03 m/s.

Dynamic stability and functional mobility improved after the training, as assessed by the significant decrease of time in performing the TUG test (Post: 17%, $p = 0.05$; F-Up: 29%, $p = 0.02$). An additional significant improvement of balance, assessed by the BBS, was also observed (Post: 7%, $p=0.02$; F-Up: 15%, $p=0.02$).

Test	Pre	Post	p value (Pre-Post)	F-Up	p value (Pre-F-Up)
6MWT [m]	301 ± 83	324 ± 77	0.12	372 ± 67	0.03
TUG [s]	14 ± 5	12 ± 4	0.05	10 ± 3	0.02
FSST [s]	23 ± 10	18 ± 6	0.01	14 ± 4	0.01
BBS	41 ± 10	44 ± 12	0.02	47 ± 8	0.02

Table 8 Average and standard deviation of the motor tests results for each evaluation.

Obstacles negotiation, expressed by the FSST, revealed that time for executing the coordination task significantly decreased by a mean of 22% ($p = 0.01$) after the intervention and by the 37% after one month ($p = 0.01$).

5.3.5. Neuropsychological tests

For what concerns the cognitive sphere, the results (Table 9), in general, are not significant even if several trends may be observed. Indeed score in FAB and MOCA slightly increased. The time spent in performing the STROOP slightly decreased, as well as the mean number of errors and time spent in performing the TMT-B, while the time spent in performing the TMT-A increased. Patients made 36% fewer mistakes on the cognitive task in F-Up compared with values in Pre on the SSDT.

In addition, the training appeared to have a positive influence on psychosocial aspects such as the level of depression as assessed by the BDI.

Test	Pre		Post		p value	F-Up		p value
	Mean	Std	Mean	Std		Mean	Std	
TMT A [s]	80	30	85	33	0.14	96	71	0.53
TMT B [s]	142	111	138	63	0.74	129	49	0.89
FAB	15	2	15	2	0.34	16	2	0.09
MOCA	23	5	24	4	0.78	26	4	0.02
STROOP [s]	18	8	16	9	0.33	16	7	0.67
STROOP [err]	1	2	0	1	0.34	0	0	0.07
SSDT [n°]	14	7	15	7	0.33	17	3	0.21
SSDT [err]	2	1	2	2	0.52	1	1	0.39
BDI	20	14	19	12	0.57	13	8	0.18

Table 9 Average and standard deviation of the neuropsychological tests results for each evaluation.

5.4. DISCUSSION

The first aim of this study was to build a system and a VR environment so that they could be used to implement a rehabilitation protocol for gait on TM. The usability of both the system and the VR environment has been verified by their safe and intensive use, which lasted six weeks, with no adverse event. Secondly, although the discrepancies between real world and the VR environment, patients got familiar with it and had fun during the training, suggesting that the differences were negligible for our rehabilitation application.

Moreover, the evaluation of the experimental set up and administration of a novel VR based gait training program for patients with MS was conducted in this pilot study. The findings revealed that the patients tolerated the technology without major difficulties and demonstrated a high level of acceptance throughout the progression of the training program.

Eight of the nine patients were able to complete all training sessions without complications. The protocol allowed to effectively tune the TM speed based on: 1) the level of the VR environment complexity, 2) the amount of challenge of the patient's balance when asked to remove hands from handrails, and 3) the increase fatigue level after each training session. For all patients but one the trainer reduced the TM speed either when starting a higher level of complexity or at the same level of complexity. TM speed was generally kept constant or reduced when handrails were not being used. The average Borg Scale scores reported at the beginning of each session had limited variability across sessions (average B_0 between 8 and 9 and std between 2 and 3 – Table 6) signifying that, overall, training sessions begun at a similar level of fatigue. More importantly, the values of the average increments of the Borg Scale scores were almost constant across sessions (average varied between 2 and 5 except for the first session – Table 6) with a limited variability across subjects (ΔB std between 2 and 3 – Table 6), showing that an appropriate choice of the TM speed can also keep the fatigue increase at the end of the training session within a limited range. Moreover, the limited percentage of uncompleted trials due to fatigue in every training session (between 0 and 8% – Table 6), except for the first session, confirms that the tuning on TM speed and level of complexity was properly set. Both ΔB and the number of incomplete trials in the first session were higher than in the following sessions, suggesting that without reference to information regarding past sessions, the setting of the TM speed can result in excessive fatigue and higher number of incomplete trials.

The results obtained from the administration of the questionnaire revealed that the highest ratings were obtained for the usefulness of feedbacks and the acceptance of technology (Table 7). High ratings were also found for the ease and enjoyment from the use of the system and the training: all patients found the training easy to learn and most of them enjoyed it and would have liked to continue it. There was a high variability in the subjective responses relating to performance, highlighting the differences among patients in terms of task execution and perception of fatigue.

For what concerns the gait analysis, the results of this study showed that the six-week VR-based TM training was safe for the eight MS patients. They concluded the rehabilitation program without difficulties, enjoying every session and asking to continue the training after its end.

The main clinical findings demonstrate improved gait speed and stride length in ST condition between Pre and Post, as a result of the specific training (Figure 8). The intervention was directed at obstacle negotiation, which required the patients to take larger steps; hence the results demonstrate a specific training effect. The mechanism that allowed for this change probably lies in the kinematic analysis that demonstrated improved knee control during the mid stance in the most affected side. This in turn allowed for a more stable position that enabled a larger swing. Interestingly, most of the gains were maintained for one month, with some parameters even slightly improving from Post to F-Up. However, while taking into account the different starting values, the more impressive effects were reflected in the DT walk. The VR training is in fact a motor-cognitive DT training that implicitly improves gait. During the over ground DT evaluation, patients demonstrated improved spatial-temporal parameters (Figure 8) after training, and these changes are maintained and even improved in F-Up. These improvements were probably possible by increased moment and power generation in the ankle during push off that enabled the forward progression.

Moreover, the DT effect, measured as the difference in stride time duration between DT and ST, decreased from 0.15 seconds in Pre to 0.06 seconds in F-Up, demonstrating an improved ability of patients in dividing attention and coping with complex activities during gait. The fact that increased attention positively impacted on DT ability is confirmed also by the FSST (Table 8). In the present study, indeed, the serial subtraction executed by the patient during the evaluation of the intervention, as well as the task executed during the FSST, was not part of the training. Nevertheless after the VR-based TM training, patients walked faster under the DT condition, with longer strides compared with baseline and employed less time to execute the FSST, suggesting an ability to adapt the learned strategy to different tasks. Although, between-task transfer after VR-based TM training has been already shown in neurological

diseases, such as stroke (Jaffe, 2004) (Mirelman, 2009) and PD (Mirelman, 2011), this was not previously reported in patients with MS. Probably, the cognitive requirements characterizing the training in the VR environment allowed subjects to develop new movement strategies which are reflected in their natural motor behavior and that are maintained also after the end of the training.

This kind of intervention, as proved by the kinematics data, does not instruct to perform a specific walking pattern, but rather trains subjects to a more controlled gait also under DT conditions. Since mobility in everyday life frequently requires walking while performing simultaneous cognitive or motor tasks, this approach indirectly reduces the risk of falls of trained people and, consequently, positively impacts their quality of life.

Comparing the results of this study to those obtained by Mirelman et al. (Mirelman, 2011), the average overground speed gain during ST (0.11 m/s) and DT (0.17 m/s) are lower and less significant than those made by PD patients (ST: 0.12 m/s, DT: 0.21 m/s), but while in the current study the effective training time was 6 hours, in that case the training duration was 12 hours with a sample size of 20 instead of 8.

This pilot study has several limitations. Beyond the reduced sample size, the study design did not include a control group in order to unequivocally exclude the possibility that gains may have not been due to the training. The heterogeneity of the sample was another issue. Although the chosen criteria were very strict, a wide range of motor symptoms characterizes MS and, consequently, patients had different gait kinematics. Nonetheless, the results of the first study VR-based TM training applied to MS are quite promising and the more significant improvements during DT suggests that important gains were likely attributable to the VR and not to TM alone.

5.5. CONCLUSIONS

In this pilot study we evaluated the usability, feasibility and acceptance of a gait training setup including a TM and a VR environment created for gait training of patients with MS.

The results have shown a high level of feasibility and acceptance of the VR system and the gait training program.

This study is the first to examine the effects of TM with VR on the mobility of patients with MS. The results reported here are preliminary and the pilot study had a reduced and relatively homogeneous sample of people, therefore should be considered with caution. Nevertheless, the results indicate that intensive and progressive TM with VR training is viable for patients with MS and may positively affect complex gait conditions such as walking during dual tasking, endurance and obstacle negotiation. Larger scale, randomized controlled studies with long term follow-up are needed to confirm efficacy and retention of VR- based TM training on motor and cognitive aspects and quality of life of MS patients.

The training allowed for some flexibility (setting the TM speed and increasing level of complexity in the VR environment), which was shown to be highly important for providing tools for customizing sessions and engaging the patients whilst enhancing motivation and acceptance.

6. Inertial sensing in motor assessment: assessment of reduced arm swing in Parkinson's disease

This chapter was written on the basis of the work carried out in Tel Aviv, during my PhD period abroad, in the Laboratory for Gait and Neurodynamics of Ichilov Sourasky Medical Center. The preliminary results of the study have been published on several conference abstracts.

6.1. Introduction

PD is the second most common age-related, neurodegenerative disorder (Lewek, 2010). Tremor, rigidity, bradykinesia, and postural instability are hallmarks for the diagnosis of PD (Gelb, 1999), (Calne, 1992) with abnormal gait (e.g., short, shuffling steps, stooped posture, shorter stride length, reduced gait speed and arm swing (Morris, 1994). Although in PD reduced arm swing is the most frequently reported motor dysfunction (Nieuwboer, 1998) and it is associated with elevated fall risk (Wood, 2002), there have been only several studies aiming to quantify the arm swing of PD patients during walking. Most of them investigated shoulder kinematics in the sagittal plane using video-based (Knutsson, 1972), (Carpinella, 2007), (Zijlmans, 1996), (Behrman, 1998) or ultrasound-based systems (Roggendorf J, 2012). Since the total amount of arm swing during walking incorporates both elbow (Kuhtz-Buschbeck J. P., 2008) and trunk kinematics, it is important examining the trajectory of the end effector (e.g., wrist/hand) when quantifying arm swing. Lewek et al. defined the arm swing amplitude during walking as the distance traveled by the wrist in the anterior/posterior and medial/lateral directions with respect to the pelvis within a stride and measured it through a motion analysis system (Lewek, 2010). They demonstrated a significant difference in the asymmetry of arm swing amplitude between early PD and healthy control subjects.

Wearable inertial sensors are relatively inexpensive and easier to implement in a clinical setting than video-based motion analysis and, therefore, ideal to assess the human motion of PD patients. Indeed, the same group (Huang, 2012), recently, attached accelerometers to each

forearm and collected angular accelerations, demonstrating that PD subjects have reduced bilateral coordination of arm swing during walking. Zampieri et al. (Zampieri, 2010) reported asymmetries in peak arm swing velocity, measured using wearable sensors, during the TUG test.

The main objective of this study was to explore how inertial sensors could be used to quantify arm swing movements during gait and to develop tools for analyzing the trials to be easily used by clinicians. The second aim of the study was to quantify arm swing amplitude during normal over-ground walking in patients with PD using wearable sensors and to compare it to the movement observed in healthy controls.

6.2. Methods

Eleven patients with PD (PDG - 7 females, 56.6 ± 8.0 years, mean disease duration 3.5 ± 2.0 years, Hoehn and Yahr Scale: II-III) and thirteen healthy controls (CTRG - 9 females, 52.1 ± 9.5) participated in this study. They were recruited from the Movement Disorders Unit at Tel Aviv Sourasky Medical Center in Israel. Two synchronized IMUs (Xsens, MTx, Enschede) were placed on the wrists of the subjects. Patients walked at their self-selected comfortable speed for one minute in a well-lit 25-meter corridor. Orientation data was extracted from sensors and processed by a custom-made algorithm in MatLab (see Appendix) to calculate parameters of arm swing, such as the range of motion and the asymmetry, of selected trials. Comparisons were made between left and right arms, affected and less affected arms and results were compared to data collected from a healthy control group.

6.3. Preliminary results

As reported in Figure 9a, arm swing range was significantly lower in the PD group ($p=0.03$). Figure 9b illustrates that, in the CTRG, there is a tendency for greater arm swing range of the dominant arm than the non-dominant arm ($p=0.08$), while PDG demonstrated (Figure 9c) a significantly higher degree of left-right asymmetry ($p=0.04$). Peak amplitude was moderately correlated to disease duration ($r=0.61$, $p=0.05$).

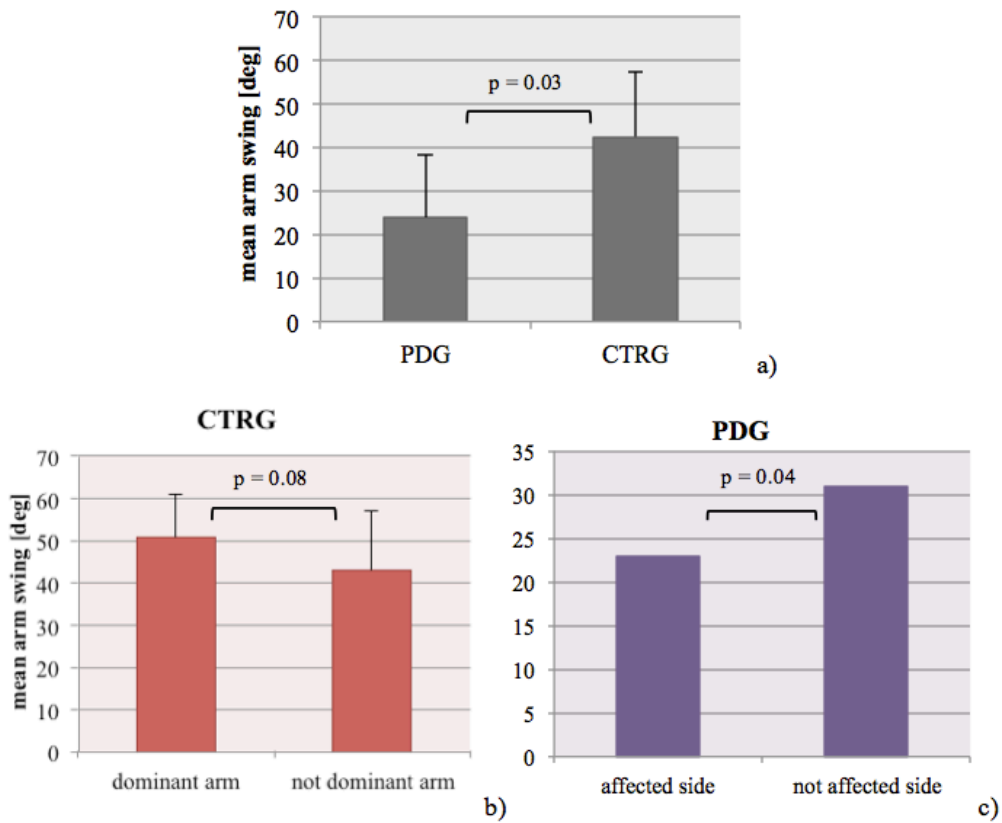


Figure 9 a) Comparison of the armswing amplitude of PDG and CTRG; b) arm swing range in CTRG; c) swing asymmetry in PDG between affected and not affected side arm.

6.4. Conclusions

In this study it was demonstrated that an automated algorithm based on data from wearable sensors is able to meaningfully quantify arm swing amplitude and asymmetry. In patients with PD this feature distinguishes between the more affected and less disease affected arms. Additional studies are needed to more fully evaluate clinical utility and the potential of this new approach.

7. Low cost video technology for tracking in virtual reality applications: the Microsoft Kinect

VR-based exercises have the potential to revolutionize therapy for people with neurological impairments and older adults at risk of falls. However, to immerse these individuals in VR it is necessary to reproduce their movements in real-time within the virtual environment. Current tracking systems are based on optical, electromagnetic, mechanical, and inertial measurements. Usually in motor rehabilitation, the immersion in virtual environments is obtained through expensive optical systems, which are difficult to use, time and space requiring.

In the past years, low cost depth sensing cameras have also become commercially available, including the widely publicized Microsoft Kinect, which allows detecting human movement and pose without the use of markers or handheld devices (Lange, 2011).

The Microsoft Kinect is a motion sensing input device, using an RGB camera combined with an infrared-based 3D depth sensor, which comprises actively emitted structured infrared (IR) light and a single IR sensitive camera to estimate distance between the sensor and the environment. The Kinect sensor captures depth and color images simultaneously at a frame rate of up to 30 fps. The 3D depth accuracy of the Kinect camera has been evaluated, showing an accuracy of depth reconstruction in the order of 1-4 cm in the range of 0.5-5 m (Khoshelham, 2012).

Amongst its advantages, Kinect is inexpensive, easy to set up, and can be used in both home and clinical environments (Chang, 2012). Though the Kinect was originally designed for interactive entertainment, the features of the device, such as the easy interfacing with a variety of operating systems and measurement of the performance, have soon interested researchers from the rehabilitation field. Indeed, several studies have soon recognized the advantages of using an inexpensive depth camera, such as the Microsoft Kinect, for rehabilitation and assessment of body function. Actually, a system to calculate the kinematics of 20 joints of human body in real time mode has been recently proposed (Warade, 2012). A

further study (Suma, 2011) tried to address the problem of skeletal tracking of a human body using the Microsoft Kinect device. The authors, using a bottom up approach, developed a skeleton toolkit that allows a programmer to add full-body control to games and VR application.

The same group implemented an interactive game-based rehabilitation tool, based on the Kinect, for training balance in adults after neurological injury (Lange, 2011).

Change et al. (Chang, 2011) developed a Kinect-based system to involve students with motor impairments in rehabilitation training. The system, based on upper limb tracking and gesture recognition, has been also evaluated in terms of effectiveness by the same authors.

Zhang and colleagues proposed a flexible motion tracking approach that can be used with a combination of Kinect devices, demonstrating its robustness and accuracy, and a significantly better performance in the presence of occlusions than current state-of-the-art implementations of single-sensor trackers (Zhang, 2012). Based on the Microsoft Kinect, non real-time applications providing accurate and robust tracking have been also implemented (Oikonomidis, 2011).

The Microsoft Kinect has been used successfully also for tracking applications of other clinical fields, including medical imaging (Noonan, 2011), robotics (Bimbo, 2012), (Loconsole, 2012) and home monitoring (Stone, 2011), (Satyavolu S., 2012)

7.1. Kinect-based gait tracking for VR clinical applications

In this study, a new, low cost motion tracking methodology, based on the use of the Microsoft Kinect is proposed and evaluated against optoelectronic technology. Several attempt have been already done in this direction. Dutta captured four cubes in a static position with the Microsoft Kinect and the multi-camera based system, to avoid the synchronization issue (Dutta, 2012). The 3D coordinates of the centers of the target cubes have been then compared through the RMS, indicating that the accuracy of that Kinect motion capture system would be at least an order of magnitude less than that of a optoelectronic system. In a recent work, Chang et al. validated the motion tracking capability

of the Kinect with respect to a multi-camera based system on three different motor tasks (Chang, 2012). They compared the trajectories and measured the relative latency between the outputs of the two systems, concluding that Microsoft Kinect is a promising VR neurological rehabilitation tool both for clinical settings and home environments. In another study, Clark et al, assessed the validity of the anatomical landmarks collected using of the Kinect against a multi-camera 3D motion analysis system (Clark, 2012) during three standing postural control assessment tests. Specifically, they assessed the anatomical landmark displacements calculated by the two systems, confirming the potential for the Kinect to be used in clinical screening programs for a wide range of patient populations.

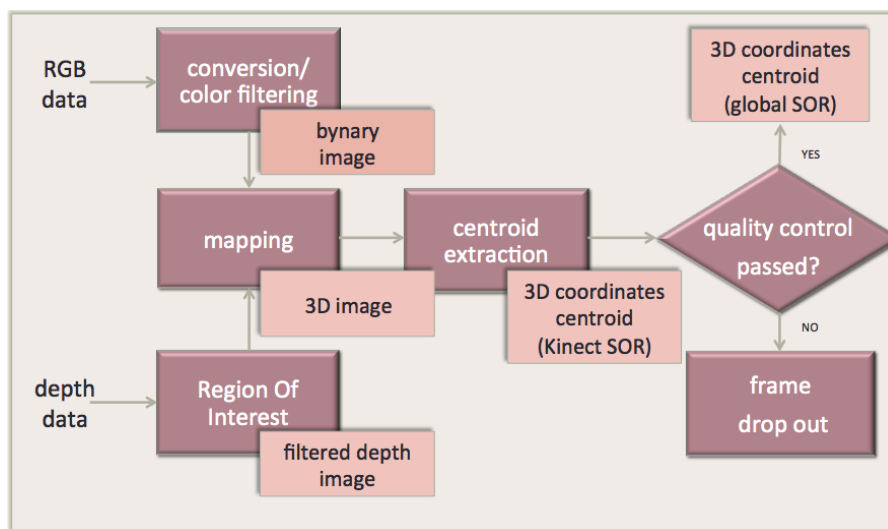


Figure 10 A representation of a new methodology based on the use of Kinect for tracking gait in a VR environment

Since in our VR application we were interested in gait, we decided to track the feet. Considering that the accuracy of the Microsoft Kinect decreases with the distance from the sensor and that the Skeleton Tracker needs to see the head of the subject, we would need a large room, therefore losing in tracking accuracy. For these reason, it has been decided to implement a new methodology (INATION, London, UK), which did not consider the upper part of the body, but focusing on feet. The methodology is synthetically illustrated in Figure 10 and it is currently used in a multi-modal rehabilitation intervention, centered around the use of TM and VR, which aims to enhance mobility and reduce fall risk in a large sample of

PD and Mild Cognitive Impairment patients and elderly fallers [V-TIME - EU funded research project (European Union, 2012)].

7.1.1. Methods

A healthy subject (male, 35 years old) walked on a TM at 0.3-0.4 m/s, in six different ways: a) foot-dragging walk (Drag), b) asymmetric gait (Asym), c) avoiding vertical obstacles (Vert), d) with minimum clearance (Minclear), e) short steps (Short) f) normal gait (Normal). A Kinect for Windows® (Microsoft, USA)⁵ was placed 1m above the ground, and 0.95m frontally from the TM, so that it had an unobstructed view of the TM surface. A 6-camera (2MPixel) optoelectronic system (Vicon, UK) was used as gold standard.

Two green patches were placed on each shoe as markers for the Kinect: the smaller one (5x3.5 cm²) was placed on the anterior part of the shoe and the second (8x3.3 mm²) on the tarsus (Figure 11). Four retro-reflective markers (14 mm diameter) were placed on each shoe on the patches extremities.



Figure 11 Retro reflective markers and green patches locations on the foot. The yellow circles indicate the position of the centroids (RDP, RPP, LDP, LPP).

The Kinect captured the raw RGB and depth data at 30Hz, while the Vicon system captured at 100Hz. The two systems were synchronized. A standard color filter was used to isolate the green patches on the shoes, and then the 3D trajectories of the centroid of the patches were extracted and compared to those of the mid-point of the optical markers placed at the side of the patches (RDP, RPP, LDP, LPP – Figure 11). The comparison was carried out through estimation of the Root Mean Square Deviation (RMSD).

⁵ <http://www.microsoft.com/en-us/kinectforwindows/>

7.1.2. Preliminary results

The RMSD between the optical markers mid-point and the patches centroid is reported for each gait pattern and for each component (Table 10): vertical (V), medio-lateral (ML) and antero-posterior (AP).

RMSD mm	Gait																	
	Drag			Asim			Vert			Minclear			Short			Normal		
Marker	AP	V	ML	AP	V	ML	AP	V	ML	AP	V	ML	AP	V	ML	AP	V	M
RDP	11	2	2	14	4	3	14	2	2	15	2	2	14	3	2	13	3	2
RPP	11	2	1	12	3	2	14	4	6	15	3	1	13	4	2	14	5	2
LDP	11	3	2	20	3	3	13	5	2	16	2	2	10	3	2	14	4	2
LPP	12	4	3	15	6	3	13	3	4	16	3	3	10	4	2	15	5	2

Table 10 The RMSD between the optical markers mid-point and the patches centroid for each gait pattern and for each component

7.1.3. Discussion

The preliminary results of the study showed a limited RMSD, between 2 and 6 mm, along the V and ML directions, while the reconstruction of the centroid of the green patches along the AP direction was about 3 to 5 times less accurate with an RMSD value from 10 to 20 mm. This appears to be consistent with previous studies (Khoshelham, 2011), (Khoshelham, 2012), which have shown that the random error of depth measurements increases with the square of the distance from the sensor, reaching 4 cm at its maximum range. Moreover, Khoshelham and Elberink (Khoshelham, 2012) indicated also that the depth resolution decreases quadratically with increasing distance from the sensor, specifying that the point spacing in the depth direction (along the optical axis of the sensor) is as large as 7 cm at the maximum range of 5 meters. Moreover, among their final and general indications about the use of the Kinect for mapping applications, the authors also suggest to acquire data within 1–3 m distance to the sensor, because at larger distances the quality of the data would be degraded by the noise and by the low resolution of the depth measurements.

The research leading to these results has received funding from the European Union - Seventh Framework Programme (FP7-HEALTH-2011) under grant agreement n°278169 (V-TIME).

8. Augmented biofeedback: a tool for trunk motor control

Feedback has been defined as any sensory information that is available to an individual during or after the execution of a movement (Schmidt, 2008).

Augmented (extrinsic) feedback is sensory information about a movement provided in addition to intrinsic feedback, which is delivered through the sensory systems within the body. The external source may be a therapist or a device such as a biofeedback system. Traditionally the role of augmented sensory feedback in learning of motor skills has been considered satisfying, motivational, or informational in nature (Adams, 2001.). Augmented sensory feedback has been shown to facilitate muscle activation during the early stages of learning (Kim, 1997), (Mulder T., 1984), (Henry, 2007). The impact of feedback on motor learning varies as a function of the frequency, delay, and precision with which information is provided (Winstein, 1991).

Augmented feedback has been used in the past as a training tool that enables people to learn how to change physiological activity or behavior for the purposes of improving performance (Henry, 2007). There are two main goals for feedback motor training. One is to allow the central nervous system to re-establish appropriate sensory-motor loops under volitional control that may have been damaged by injury, disease, or surgery; the second goal is to assist in the development of greater cognitive awareness and control of a physiological process that has been previously considered “involuntary” or beyond the consciousness (Kenneth R., 1981).

8.1. Augmented feedback in neurological impairments

Augmented feedback training of balance, posture and motor control has shown to be effective in people affected by neurological impairments, such as peripheral neuropathy (Wu, 1997), vestibular loss (Tyler, 2003), (Kentala, 2003), (Dozza, 2007), stroke (Van Vliet, 2006), (Dursun, 1996), (Langhorne, 2009), (Stanton, 2011) traumatic brain injury (Guercio, 1997), (Wong, 1997), cerebral palsy (Talbot, 1981), (Nash, 1989), (Metherall, 1996), (Wooldridge,

1976), incomplete spinal cord injury (Kohlmeyer, 1996), (Brucker, 1996) and PD (Verschueren, 1997), (Mirelman, et al., 2011), (Marchese, 2000).

A systematic review on augmented feedback in motor recovery in subjects with neurological disorders found that extrinsic feedback was commonly provided in the form of biofeedback, kinetic feedback and kinematic feedback (Van Vliet, 2006). While biofeedback concerns physiological processes, both kinetic and kinematic feedback is related to movement variables measured during task performance: kinetic feedback variables may be related to force and torque, while kinematic feedback variables are usually derivatives of distance and time (e.g., displacement, velocity, movement time, trajectory straightness). Kinematic and kinetic feedback can be provided in relation to either the outcome of the movement or the movement pattern itself (Levin, 2010).

Moreover, the effects of biofeedback-assisted performance of balance and motor tasks have been explored using a variety of sensory feedbacks including visual, auditory and tactile modality (Dozza, 2005), (Dozza, 2007), (Verhoeff, 2009), (Vuillerme, 2007), (Wall & Kentala, 2005), (Dursun, 1996). Adamovich et al. (Adamovich, et al., 2004) developed a multi-feedback system for VR hand rehabilitation improving performance in patients with neurological impairments.

8.2. Inertial-based visual feedback tool for trunk control

Numerous tools aiming to improve trunk posture and control are based on inertial sensing: Wall et al., combining accelerometers and gyroscopes, developed a wearable vibrotactile feedback device based on trunk-tilt improved balance performance in healthy (Wall, 2001) and vestibular (Kentala, 2003) subjects. A system consisting of three inertial sensors and estimating the spinal curvature changes during trunk movements was shown to improve the subject's posture when feedback signals were provided (Huang, 2006). Using the inertial sensors of a smartphone, Franco et al., developed an integrated auditory-biofeedback tool estimating the 3-D orientation of the user's trunk during bipedal stance to improve balance (Franco, 2012).

In particular, feedback signals based on the distance from a specific target (error detection / error correction) have shown to facilitate learning processes (Magill, 2003). Several recent studies have developed and assessed feedback systems for motion guidance that use a control signal proportional to the error between the target and subject. In Sergi et al. (Sergi, 2008) and Kapur et al. (Kapur, 2010) the kinesthetic guidance systems is obtained employing magnetic motion tracking technologies and provide tactile feedback allowing patients to feel limb configuration errors continuously. Lieberman and Breazeal (Lieberman, 2007), using an optoelectronic system, developed a real-time wearable vibrotactile feedback suit to facilitate upper limb motor learning. The feedback, representing the difference, in terms of joint angles, between the target and the subject's motion, contributed to decrease the error and accelerated motor task-learning rate. Also inertial sensors have been widely used for tracking body segments in applications for motion guidance. A mobile virtual trainer, developed by Lee et al., is able to map the trainee's movements and return both instructions and real-time feedbacks based on inertial sensors data (Lee, 2011). Redd et al. developed a multisensory (visual, audible, or vibrotactile) feedback system for correcting gait information (Redd, 2011).

Chiari et al. developed a portable auditory feedback based-system that, encoding the signals provided by an accelerometer on the trunk into a stereo sound, improved balance (Chiari, 2005). Based on the latter study, we designed and implemented a real-time visual biofeedback tool.

The aim of the present work was to provide a preliminary evaluation of the usability and effectiveness of a real-time visual biofeedback (VBF) tool to assist the execution of specific motor tasks. The tool is designed to possibly become a component of a home-based rehabilitation system, relying on ICT systems aiming at providing real-time feedbacks for rehabilitation of PD patients [CuPiD FP7/2007-2013 - EU funded research project (European Union, 2011)].

8.2.1. Methods

The hardware of the developed tool is composed by an IMU (MTx Xsens, Enschede, The Netherlands) recording inertial signals and a PC providing visual feedback.

The IMU featuring a 3-axis accelerometer, a 3-axis gyroscope and a 3-axis magnetometer, was placed on the trainee's lower back (approximately on L5). Trunk inclination on the sagittal plane, computed on the device through an embedded Kalman filter, was recorded.

The Graphical User Interface (GUI) providing the feedback has been implemented using a Python-based commercial software (Vizard 3.0, WorldViz, Santa Barbara, CA, USA).

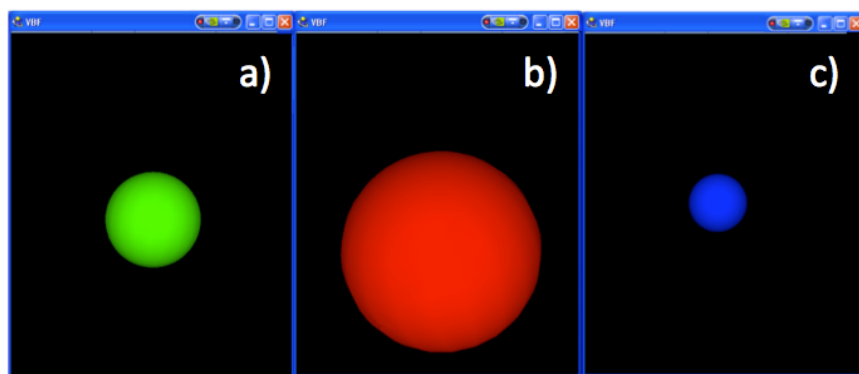


Figure 12 The VBF is a sphere that is: a) green, if the subject is in the *Target Zone*, red b) and blue c) if trunk inclination exceeds respectively backward or forward.

The GUI guides the trainee in executing specific motor tasks, by providing a real-time visual feedback (Figure 12) of the difference (*err*) between a computer generated reference orientation (*Ref*) and the measured trunk orientation. If *err* is within a specific range (*Target Zone*), the sphere is green and the cursor is centred on the antero-posterior direction; if *err* increases, the sphere moves on the antero-posterior direction toward the *Limit Zones* getting red (excessive backward trunk inclination) or blue (excessive forward trunk inclination). The raising of the sphere indicates the subject when to lift from the chair.

Amplitudes of the *Target Zone* and of the *Limit Zones* are subject-specific and are based on a simple initial calibration phase (Chiari, 2005), (Nicolai, 2010).

The effectiveness and usability of the tool was evaluated in a preliminary experimental session, during which eight healthy subjects (5 males, 25-35 years) were asked to perform three types of exercises (Figure 13), lasting 20 seconds each, for five times:

- Sit-to-stand without VBF (S2S - VBF);
- Trunk flexion (range 2°-20°) by sitting with VBF, as preparatory act to raise (PrepS2S + VBF);
- Sit-to-stand (in the range of flexion of the trunk 8°- 16°) with VBF (S2S + VBF)

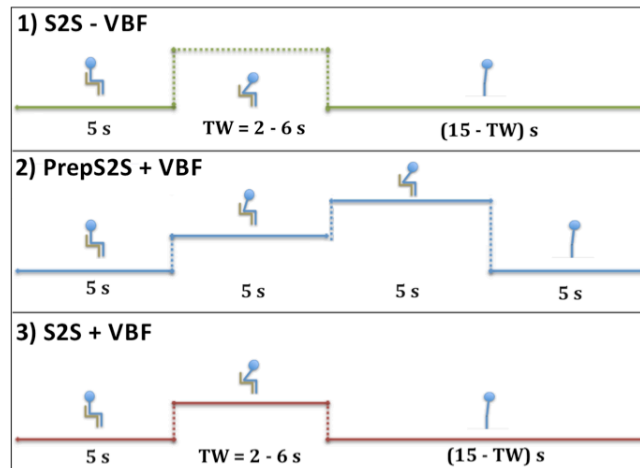


Figure 13 Representation of the Ref during the phases of three motor exercises. The time window (TW), in which the subject is asked to perform the movement, varies from 2 to 6 seconds for task 1 and 3.

For every task, subjects were instructed, to try to follow the *Ref*, maintaining the slider cursor within the *Target Zone*. Before recording the trials, subjects performed a practice trial.

8.2.2. Preliminary results

All subjects were able to move the trunk reaching the *Target Zone* and keep it for the time required. The residence time in Target Zone for each motor task (Target Time Zone) is shown in Figure 14. Contrary to what happens in S2S - VBF, subjects in PrepS2S + VBF and in S2S +VBF are able to achieve and maintain the desired inclination of the trunk. The permanence in the target zone is greater in S2S + VBF compared to S2S - VBF and, generally, increases with the increase of TW, showing the effectiveness of the instrument VBF.

In this preliminary study, the effectiveness of a new tool based on the use of augmented visual biofeedback to assist motor tasks, such as sit-to-stand, in real time has been evaluated. The results showed the intuitiveness and ease of use of the VBF and its flexibility, resulting from the ability to adjust the time window TW and the amplitude of the target zone. The

instrument VBF therefore allows you to customize the motion exercises according to the residual capabilities of the patient and to the movement to train. In the future we intend to apply the tool VBF to pathological populations, in particular in subjects coming from a long-term bed rest in which the motor control of the trunk is usually compromised. Additionally, the control of the trunk in the medio-lateral direction will be added.

Acknowledgement

The research leading to these results has received funding from the European Union - Seventh Framework Programme (FP7/2007-2013) under grant agreement n°288516 (CuPiD project).

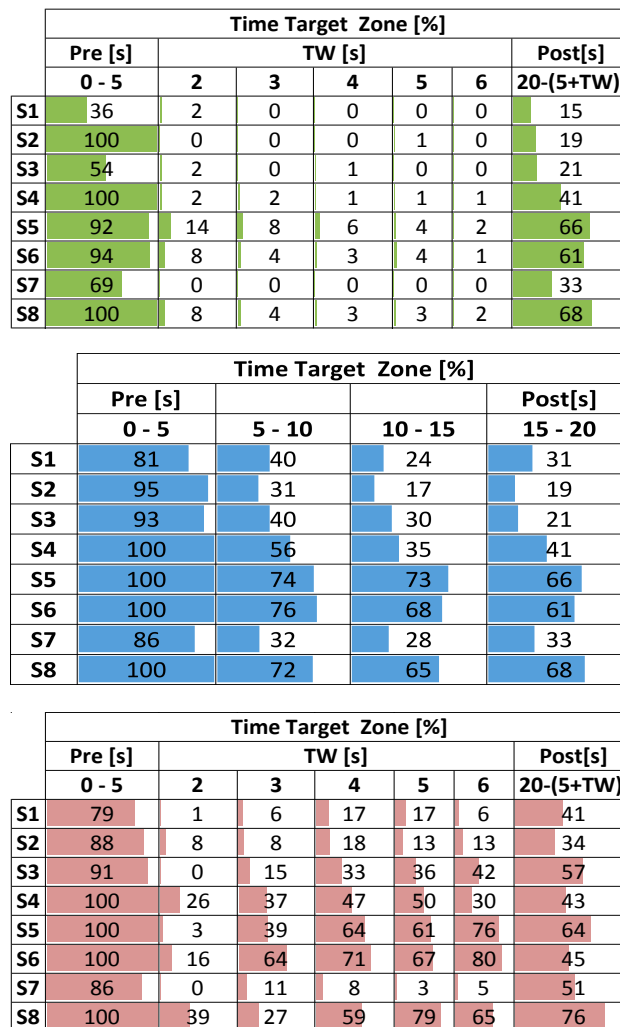


Figure 14 Values of Time Target Zone for each motor task: a) S2S - VBF b) PrepS2S VBF + c) + S2S VBF. In b) has been showed the average of the Target Time Zone in the four phases of the year (Pre, I, II, Post). In a) and c) the averages are reported only for the pre-and post phases, while the phase of execution of the movement the Time Target Zone is estimated to vary from TW.

9. Conclusions

The tools and methods presented in this thesis are all based on new technologies, such as miniature inertial sensors and low-cost video systems, and have, as primary aim, the inclusion of a quantitative approach in the rehabilitation cycle that takes place in the clinical practice. A methodology based on the use of IMUs for the estimation of the arm swing in PD patients was proposed and applied in a pilot study. More needs to be done to elevate the method at the level of a clinical tool.

The use of VR and augmented feedback in rehabilitation aims at overcoming the lack of engagement and motivation of patients involved in conventional physical therapies, while controlling the specifics of the training administered. The preliminary results about the usability and flexibility of a newly developed augmented feedback tool for trunk control based on the use of IMUs are presented. The tool will be adapted to be used in training the motor control of the trunk in neurologic patients after a period of bed rest.

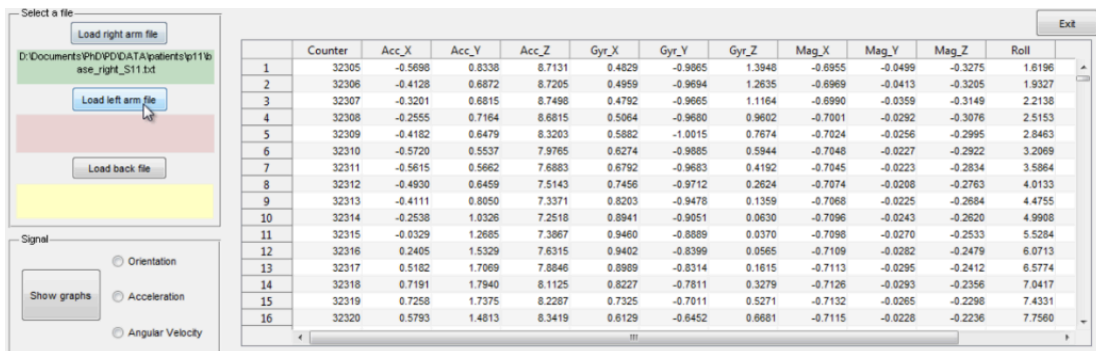
VR allows the rehabilitation in dual task (motor and cognitive task at the same time, typical of daily life), crucial in neurological impairments, and the transfer of the acquired skills to the real life. In this work we have shown how a VR-based intervention is effective in gait rehabilitation of MS patients, especially in dual task. Nevertheless, to ascribe these gains solely to the VR-based training, it is necessary to include a control group in the study.

Finally, two tracking systems for immersive environments have been explored in this work. We have used both non vision-based systems, such as inertial sensors, and low cost video technologies, such as the Microsoft Kinect. Inertial sensors are small, accurate, flexible, portable, but show a drift during extended measurements. This particular issue has been analyzed in this work and solutions proposed. Vision-based systems, like the Kinect®, are low-cost, flexible, easy to set up, but less accurate than non vision-based systems. Nevertheless, the preliminary results of a validation study show a limited error within three meters from the sensor, therefore acceptable for tracking in VR rehabilitation. In the near future, a more complete validation analysis will be carried out.

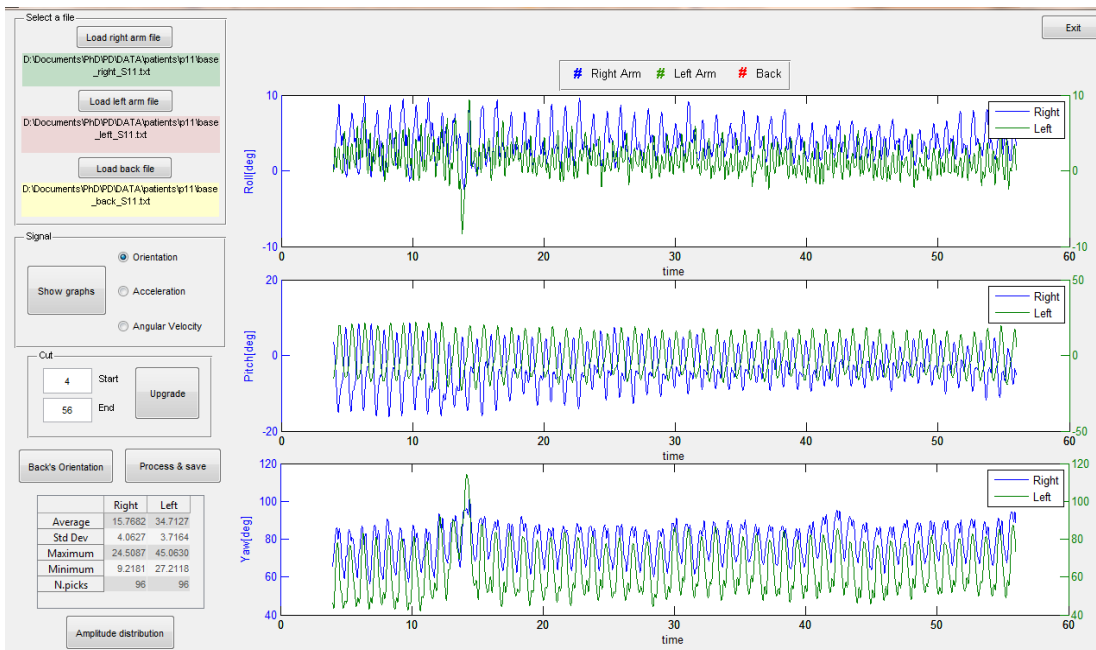
Appendix

I. Armswing GUI

- Once the file Armswing.fig has been opened, the GUI will be displayed on the screen.
- In the “Select a file” panel, load the right arm file and its name will be displayed in the string below while the data contained in it will appear in a table on the right side. Load also the left arm file and, eventually, the back file.



- When all the files loaded are displayed in the strings, push the button “Show graphs” in the panel “Signal” and you will see the orientation graphs of the two arms in the right side of the GUI.



- If you want to see also acceleration and angular velocity graphs you can switch them in the panel “Signal”.

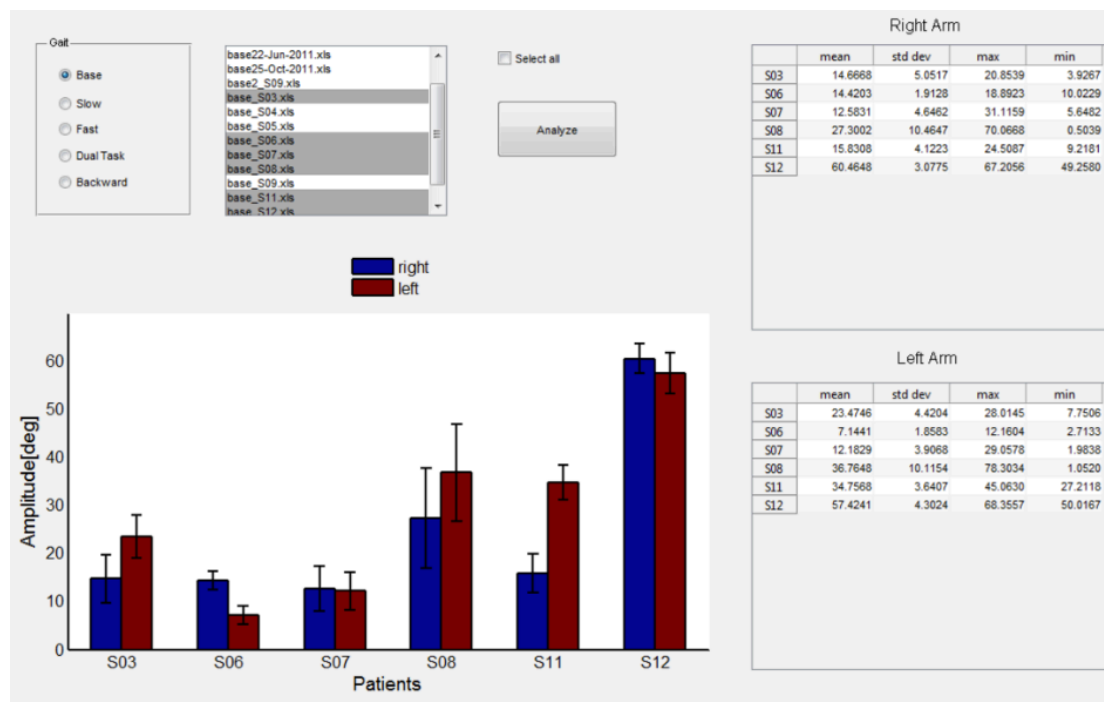
- In the “Cut” panel you can cut your signal, writing the time of the start and of the end and pushing the button “Upgrade”.
- If you also chose a back file you can also see the “Back’s orientation” button in order to display also the back’s graphs.
- Pushing the “Process and Save” button you will display the “Amplitude Table” and saving data in an excel file that you will find in the folder of the patient analyzed. The Amplitude data contains the average and the standard deviation of the ROM for every arm, the max and min values and the number of peaks.
- If the number of picks (N.picks) of the two arms (last row) is the same, the “Amplitude distribution” button will appear below. After pushed it, the amplitude distribution graph will be showed.

	Right	Left
Average	15.8308	34.7568
Std Dev	4.1223	3.6407
Maximum	24.5087	45.0630
Minimum	9.2181	27.2118
N.picks	104	104

- Once the analysis was accomplished, push the “Exit” button to close the window.
- You will find the excel file in the folder called as the patient’s name of the analyzed trial.

II. Trials Analysis GUI

- Once the file TrialsAnalysis.fig has been opened, the GUI will be displayed on the screen.
- In the “Gait” panel, choose the gait modality to analyze and all the trials will appear in the list box on the right.
- You can decide to analyze all the data displayed (“Select all”) or to choose only some of them. Once the file has been chosen push the “Analysis button”.
- A histogram will show you the mean values and relative standard deviations of the range of amplitude of both arms for the chosen subjects. On the right a table containing the processed data will appear. Everything will be saved in an excel file.



- Once the analysis was accomplished, push the “Exit” button to close the window.
- You will find the excel file in the folder called as the chosen gait modality.

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