Step into the future: mobility after spinal cord injury

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Step into the future: mobility after spinal cord injury

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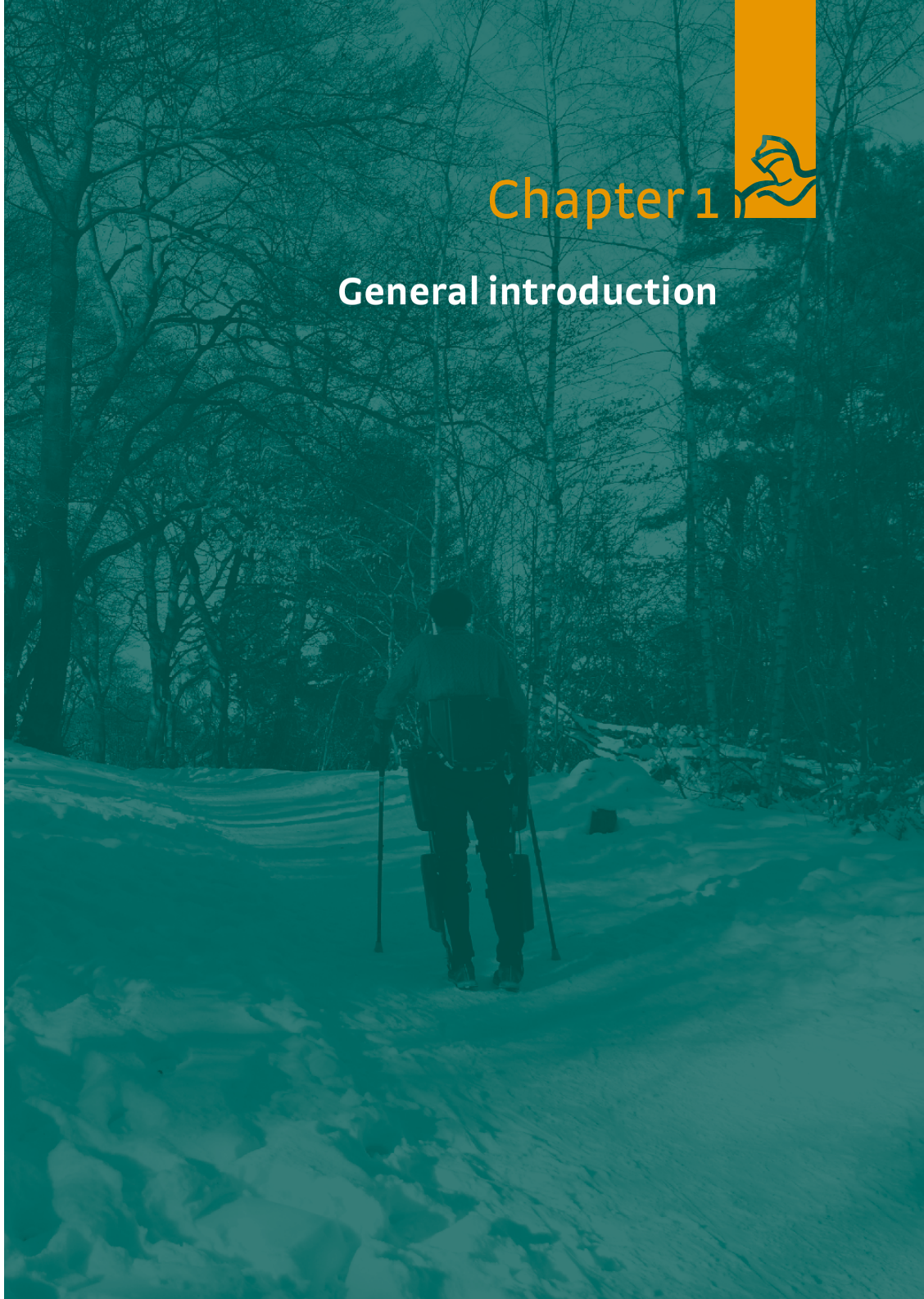
Table of contents



Chapter 1

General introduction

1

General introduction

Mobility can be defined as the capacity to get from one place to another which, for example, can be done by walking or by using means of transport. The degree of mobility determines to a large extent one's ability to participate in everyday activities.[1] Hence, it is not surprising that mobility is an important rehabilitation goals for people with a spinal cord injury (SCI). Depending on their functional recovery, different interventions can be offered to improve mobility in people with SCI. For instance, if a person is able to walk to some extent, one can try to improve his/her walking capacity with gait-specific training (i.e. stimulate functional recovery). If there is no chance of functional recovery, unassisted gait training is useless. In that case, assistive devices such as crutches and exoskeletons can be used to improve mobility. In this chapter, I will first address SCI in general as well as the rehabilitation after SCI. Subsequently, I will discuss various interventions aimed at improving mobility after SCI, including the two interventions covered in this thesis: 1) virtual reality based treadmill training for people with limited walking capacity following SCI; and 2) exoskeleton use for people without walking capacity due to SCI. This chapter will finish with an outline of the thesis.

Spinal cord injury

Spinal cord injury (SCI) is characterized by damage to the spinal cord that leads to (partial) loss of sensory, motor, and autonomic functions below the lesion level.[2] The incidence of SCI is approximately 180,000 cases per year worldwide[3] with 200 new cases per year in the Netherlands.[4] Demographically, the SCI population consists of more men than women (male-to-female ratio 3.8:1 worldwide[5] and 1.7:1 in the Netherlands[6]) and more adults than children.[7,8] Worldwide, up to 90% of SCIs are caused by trauma such as traffic accidents, falls, violence, and sports-related injuries.[8,9] In the Netherlands, slightly more than half (54.7%) of the people with SCI have non-traumatic causes, such as vascular disease, spinal degeneration, and tumors.[6] Over the last 20 years, an improved survival rate following SCI has been found.[10,11] The consequences of a SCI are related to the level and severity of the injury.

Level and severity of injury

In people with SCI, the formal lesion level is the lowest (i.e., most caudal) neurological level at which all sensory and motor functions are unaffected.[12] Generally, a higher lesion level corresponds with more impaired muscles. In people with a low (lumbar) lesion level mainly the leg muscles are impaired (i.e., paraplegia or paraparesis), whereas in people with a high (cervical) lesion level also the hand/arm and respiratory muscles are impaired (i.e., tetraplegia) (see Figure 1). The extent to which the muscles below the lesion level are affected depends on the damage to the spinal cord. Partial damage of the spinal cord leads to an incomplete loss of sensory and motor functions.[13] Frequently encountered deficits as a result of this incomplete SCI are muscle weakness, spasticity and impaired muscle coordination.[14] A complete interruption of the spinal cord leads to complete loss of sensation, control of movement, and autonomic functions. This type of complete SCI is characterized by paralysis of the muscles below the lesion level.[13] The distribution of incomplete and complete SCI is approximately 50/50%.[5]

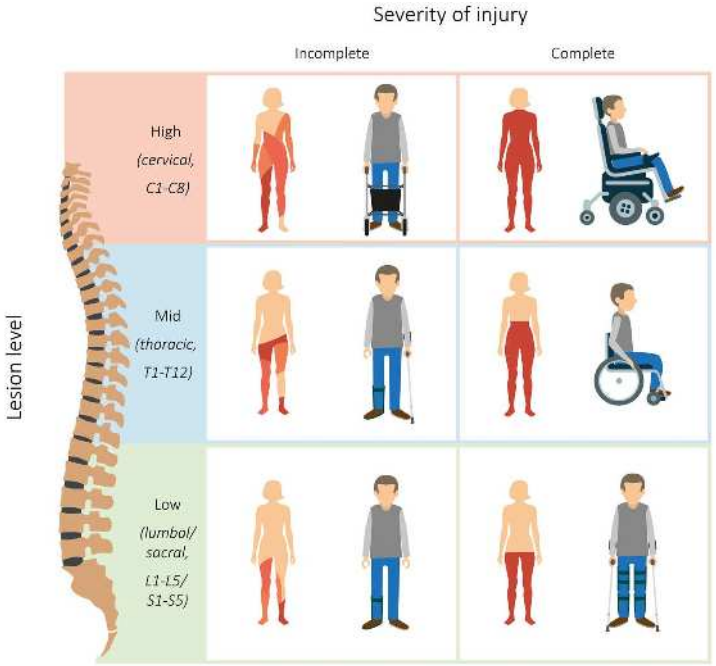


Figure 1. The consequences of the severity and level of spinal cord injury for muscle function and mobility for the moderately affected person in each lesion level. Colors in the human silhouette represent: unaffected function (beige), impaired motor and sensory function (red), impaired motor function (dark orange), impaired sensory function (light orange).

Classification of spinal cord injury

Classification of the severity and level of SCI most commonly takes place according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), often referred to as the ASIA-classification (American Spinal Injury Association).[12,15,16] In the ISNCSCI, the sensory and motor functions are assessed separately and the lesion level is identified. Sensory and motor functions are tested on both sides of the body, because damage can be asymmetrical. The formal neurological lesion level is the lowest level at which motor and sensory function is normal on both sides. Based on the sensory and motor functions in the most caudal segments (S4-5), the severity of injury is defined as complete (absence of voluntary anal contraction or sensation at S4-5) or incomplete (presence of voluntary anal contraction or sensation at S4-5).[12] The injury severity is graded with the ASIA Impairment Score (AIS), which ranges from AIS A (complete SCI) to AIS E (normal neurological function) (Table 1). An AIS A grade represents a motor and sensory complete SCI. An AIS B grade represents a motor complete but sensory incomplete SCI, whereas AIS C and D represent motor and sensory incomplete SCIs with varying levels of impaired motor function below the lesion level. The combination of the neurological lesion level and the AIS grade gives the final classification, e.g. traumatic paraplegia, level L1 AIS A.

Table 1. American Spinal Injury Association Impairment Scale.

A = Complete	No sensory or motor function is preserved in the sacral segments S4-5.
B = Sensory incomplete / motor complete	Sensory but not motor function is preserved below the lesion level and includes the sacral segments S4-5, and no motor function is preserved more than three levels below the motor level on either side of the body.
C = Motor incomplete	Motor function is preserved below the lesion level*, and more than half of the key muscle functions below the lesion level have a muscle grade <3.
D = Motor incomplete	Motor function is preserved below the lesion level*, and at least half of the key muscle functions below the lesion level have a muscle grade ≥3.
E = Normal	Motor and sensory function are normal.

* For a grade C and D, a person must have either (1) voluntary anal sphincter contraction or (2) sacral sensory sparing (at S4-5) with sparing of motor function more than three levels below the motor level for that side of the body.

Rehabilitation after spinal cord injury

Rehabilitation after SCI can be divided into three phases: acute, subacute, and chronic. There is no consensus about the exact time frame of these phases, but generally the acute and subacute phase correspond with the periods in which natural neurological recovery is still possible, whereas in the chronic phase the neurological recovery has plateaued.[15]

In the last decade, care in the acute phase has changed with the implementation of specialized Acute Spinal Cord Injury (ASCI)-Units (in Dutch: Acute Ruggenmergletsel Unit (ARU)). These ASCI units enabled very early (<24h) admission to specialized multidisciplinary care, which has shown to reduce hospital length of stay[17,18] and complication rates.[18] To diminish deconditioning and muscle atrophy, mobilization is an important aspect starting from the moment of hospitalization. As soon as the patient is medically stable they will be transferred to the rehabilitation department. In the (sub)acute phase after SCI, mobility exercises often start with (passive) turning and range of motion exercises.[19] In addition, upright position tolerance, bed mobility, and transfers from bed to wheelchair are trained early in the rehabilitation process to improve functional independence.[19] Because the majority of neurological recovery occurs during the first 6 to 9 months after SCI,[15] the treatment in the acute and subacute phases also focuses on promoting the conditions for optimal neurological recovery by treating loss of spinal stability, inflammation, disrupted hemodynamics, and autonomic dysregulation.[20] Besides the mobility and recovery aspects, rehabilitation encompasses other aspects, including independent self-care and psychosocial support.

Improvements in medical and surgical treatment have led to an improved life expectancy after SCI. Consequently, the group of people who are aging with SCI is growing. During a life time living with SCI, the occurrence of secondary health problems associated with SCI is common.[21,22] Examples of these problems are pressure ulcers, reduced cardiovascular function, spasticity, bladder and bowel disorders, osteoporosis, and (neuropathic) pain.[21,22] In addition, quality of life is reduced in people with SCI.[21] Care in the chronic phase after SCI focuses on prevention of secondary health problems and/or minimizing the burden of these problems.[23,24] For people with both an incomplete and complete SCI, attainment of independent mobility is the most important goal.[2] To improve mobility, rehabilitation focuses on exploiting compensatory mechanisms and use of assistive devices in all phases.[20]

Mobility after spinal cord injury

Prognosis of independent walking

Initial severity of the lesion is the most important predictor of walking capacity after SCI. People with an incomplete SCI have a more favourable prognosis in this respect than people with a complete SCI.[15] To distinguish independent walkers from dependent walkers or non-walkers, van Middendorp and colleagues developed a prediction rule for people with traumatic SCI.[25] Age, two motor scores (quadriceps and triceps surae), and two sensibility scores (L3 and L5 dermatome) gave an accurate early prognosis (<15 days after injury) of people's walking capacity (measured with the SCIM) one year post injury.[25] Lesion level was not found to be a (significant additional) predictor of walking capacity in people with traumatic SCI.[25] Also for people with incomplete SCI, lesion level does not affect walking capacity (FIM walking level <3 or ≥ 3) at rehabilitation discharge[26], although people with a higher lesion level require more lower extremity muscle strength than people with a lower lesion level.[27] In people with incomplete SCI, other factors that impact walking capacity are age,[28] time since injury onset,[29] spasticity,[30] and balance,[30] although their relative contributions are not known. In the chronic phase after SCI, mobility mainly depends on the severity of the injury.

Incomplete spinal cord injury

Most people with a chronic motor incomplete spinal cord injury (AIS C or D) are able to walk at least short distances.[31] However, the quality of their walking may be affected due to deficits inherent in incomplete SCI such as muscle weakness, spasticity and impaired muscle coordination.[14] If the muscles around the ankle joint are weakened, ankle foot orthoses (AFOs) are often prescribed to people with incomplete SCI to support these muscles, stabilize the ankle joints, and prevent toe drag.[32,33] Although the use of AFOs minimizes the risk of falls and enhances the ability to walk faster,[32,33] people with incomplete SCI often walk with a lower walking speed[34] and with an increased risk of falling compared to healthy elderly[35,36] due to impaired balance control. Even with the use of an assistive device, the incidence of falls is still high, ranging from 39 to 75%.[36,37] More than half of ambulatory people with incomplete SCI (64%) walk with assistive devices, such as a walker (45%), a cane (11%), or (two) crutches (8%).[38] The use of an assistive device has been associated with the speed and distance at which incomplete SCI people are able to walk. Those who do not rely on assistive devices are able to walk the longest distances[38,39] and at the highest speed[38], followed by those who use a single cane or crutch, and those who rely on a walker.[38,39] Walking speed and distance are important determinants for community ambulation.[38–40] A walking speed above 0.6m/s is needed to cross streets with traffic lights.[41] It is also the transition walking speed at which people with incomplete SCI tend to be able to walk in the community instead of using a wheelchair.[42] A minimum walking distance of approximately 300-350m is required for community walking tasks, such as walking from the car park to the grocery shop or visiting a healthcare practitioner.[40,43,44] More than half of the people with incomplete SCI are unable to meet these requirements for community walking.[38,39] Therefore, the independent walking capacity of people with incomplete SCI is often limited to certain conditions, such as indoors or over short distances, which can lead to problems with performing daily life activities and community participation.[45] Although the use of a wheelchair is another possibility for mobility, disadvantages such as access to buildings or getting under the kitchen bench to make a cup of coffee become evident.[46]

Complete spinal cord injury

Due to the paralyzed muscles, recovery of walking capacity in people with complete SCI is unlikely.[15,26] For mobility, most people with a chronic complete SCI (AIS A) have to rely on a wheelchair for a lifetime. The most commonly used wheelchair is a manual wheelchair,[47] which is lightweight (<14kg) and customizable (e.g., adjustable axle position).[48] For people with a high complete SCI, in which the upper limbs and trunk are also affected (i.e., tetraplegia), hand propulsion can be difficult. Therefore, people with a high complete SCI often use a powered wheelchair,[47,48] which is controlled with for example a joystick.[49]

As an alternative for the wheelchair, people with a low complete SCI (with the ability to control their hip flexors), can use (unpowered) knee-ankle-foot orthoses (KAFOs) to stand and walk. However, KAFO use puts a high load on the shoulders and arms and a high energy demand on the user.[50,51] KAFOs are therefore barely used in daily life. Thus, for daily mobility, the manual wheelchair is the most common mode of displacement for people with a low complete SCI, although some patients with a low complete SCI may have the capacity to walk with AFOs (ankle foot orthoses) with or without crutches.

Rehabilitation / training to improve mobility after spinal cord injury

In the (sub)acute phase after SCI, common exercises to improve mobility are aimed at upright sitting tolerance, bed mobility, and transfers from bed to wheelchair.[19] These exercises contribute to the overall goal of independent living and performing daily life activities. In order to maintain and further develop acquired skills, mobility exercises are continued in the chronic phase after SCI. Depending on the sensory, motor and autonomic functions a person with SCI is able to control, different aspects can be trained in the chronic phase. Furthermore, the appropriate rehabilitation treatment differs between incomplete and complete SCI, because the degree of preserved function differs between these groups. For instance, if a person with a chronic incomplete SCI is able to walk, one can aim to improve walking capacity (i.e. stimulate functional recovery). If there is no chance of functional recovery (i.e. chronic complete SCI), unassisted gait training is useless. In that case, alternative options, such as use of assistive devices, can be explored to improve mobility.

Incomplete spinal cord injury

Improvement of balance and walking capacity is one of the most important rehabilitation goals for patients with incomplete SCI.[52–54] A variety of rehabilitation interventions have been developed to improve walking after incomplete SCI.[55,56] These rehabilitation interventions include treadmill or overground walking training, either with or without body weight support. More recently, innovative rehabilitation methods, such as robot-assisted training and functional electrical stimulation have been developed.[56] Most of these interventions have been shown to improve walking capacity in the rehabilitation setting in terms of both speed and distance, without any intervention being superior to the others.[55] However, walking is an environment-dependent activity and most therapies refrain from training people to interact with and react to the environment, while challenging the person's balance capacity to individual limits.

With the use of virtual reality, environment-dependent activities can be simulated. Virtual reality is a technology in which users interact with and react to a simulated virtual environment (such as walking on a bridge, in a forest, or in a crowded place) (Figure 2). In recent years,

rehabilitation interventions using virtual reality have been introduced to train balance and walking capacity in people with incomplete SCI.[57] In these virtual environments, people have to shorten, lengthen and narrow their steps to changing environmental demands. They are not exposed to the actual danger of falling, due to a safety harness. In this way, patients are given the opportunity to train their balance and walking capacities by exploring their boundaries in a challenging and safe environment. Training in a virtual environment provides important prerequisites for rehabilitation, such as task repetition, feedback about performance, increased treatment time, motivation to endure practice, and confidence to perform rehabilitation exercises.[58,57] In addition, tasks involving obstacle avoidance and precision stepping can be performed in quick succession. In research, performing these tasks is often referred to as training 'gait adaptability'.[59–61] Gait adaptability is a key component for many tasks frequently encountered in daily life, such as stair walking or stepping over obstacles.[62,63] A prerequisite for gait adaptability is stability during walking, which implies that people have to maintain their balance while adapting a stable gait pattern to the environmental demands. Different adaptations can be made to enhance walking stability, such as walking slower[64,65], making wider steps[66,67], or taking shorter steps at a higher frequency (while maintaining a constant walking speed).[66,67] These adaptations can be explained as strategies to increase the safety margin (i.e., base of support or margin of stability) in which a person can keep his/her balance[66] and, thereby, decrease the risk of falls in the forward-backward or sideways direction.[68,69] Because in a virtual environment patients can train their walking stability, a positive effect of virtual-reality based walking training on walking mobility in daily life is expected.

Figure 2. Virtual reality based walking training on the Gait Real-time Analysis Interactive Lab (GRAIL).

Complete spinal cord injury

In people with chronic complete SCI there is no recovery of sensorimotor functions. Therefore, the options for improving walking capacity are limited. Although the inability to stand and walk is the most prominent aspect of complete SCI, a lifetime of predominant sitting is associated with multiple secondary health problems. Reducing the amount of sitting can be beneficial in preventing some of these secondary problems. To be able to stand and/or walk again, different technologies have been developed. Examples are the Lokomat, standing wheelchairs, and tilt tables. While these techniques are used during and after primary rehabilitation of complete SCI patients, the beneficial effects on secondary health problems are limited.[70] In addition, they do not help to improve (independent) walking capacity and can only be used in one place (i.e., stationary devices). A non-stationary option is the use of (unpowered) KAFOs in people with a low complete SCI. However, standing and walking with KAFOs puts a high energy demand on the user.[50,51] KAFOs are therefore barely used.

Another non-stationary option is the use of wearable exoskeletons in people with complete SCI. Wearable exoskeletons are external motorized orthoses that can facilitate the basic motions for ambulation (i.e., standing-up, sitting-down, standing, and walking). Advantages of wearable exoskeletons, in comparison to KAFOs, are that they are less tiring to use[71] and can be used by a larger population (i.e., also by people with thoracic levels of SCI). Examples of lower extremity exoskeleton are the exoskeletons from ReWalk™ Robotics (Figure 3), Ekso Bionics, and Parker Hannifin (Indego™). All these exoskeletons have actuators at the hip and knee joints, and ankle joints with a passive spring. They are donned and doffed in a sitting position by fastening the user's legs to the legs of the exoskeleton via straps. Adjustments in the upper leg, lower leg and hip region can be made to fit a user with a body height between 1.50 and 1.90m.[72] For balance support and control, the use of crutches or a walker is needed. Therefore, only people with unaffected arm and hand function (lesion level below T1) can safely use an exoskeleton.

In patients with complete SCI, an exoskeleton can be used as an exercise device (to promote physical health and well-being by reducing secondary health problems) and as an assistive device (to facilitate standing and walking capacity). Because of the possibility to stand and walk in an upright position, exoskeletons may have a beneficial effect on preventing secondary health problems, such as spasticity,[73,74] impaired bowel function,[75] and related loss of quality of life.[74] Before exoskeletons can be used as an assistive device, without physical assistance of a trainer, an intensive training period is needed.[76,77] Previous studies have shown that this training period is feasible and safe.[73,78] In addition, because exoskeleton use is not physically exhausting, some exoskeletons can be used regularly (at home).[79] Two exoskeletons have the legislatory clearance for use in the home and community environment (FDA ReWalk™, FDA Indego™). Media images suggest a future in which exoskeletons can be used to re-engage in everyday activities.[80] Moreover, the wish to make an exoskeleton a mobility device (i.e., replacement of a wheelchair) are evident from manufacturers' claims[72] and desired by potential users.[81] However, the applicability of exoskeletons in the home and community environment has to be confirmed. Furthermore, the limited walking speed, the heavy weight, and the need of a buddy are some expected challenges for community exoskeleton use.[80,82] Hence, although exoskeletons have been on the market for some time, they are still in the early phase of development. To evaluate the potential benefits of exoskeleton use, both in and outside the clinical setting, many areas need to be investigated.

Figure 3. Exoskeleton training with the ReWalk™ exoskeleton.

Outline of this thesis

The general aim of this thesis is to investigate two different interventions aimed at increasing mobility in people with chronic incomplete (**part 1**) and complete SCI (**part 2**).

The first part of this thesis studies whether a virtual-reality based treadmill training is effective in improving walking stability in people with limited walking capacity following an incomplete SCI. **Chapter 2** presents the test-retest reliability of six stability outcome measures during walking in healthy adults and rehabilitation patients including people with incomplete SCI. These measures are assessed in a 2-minute walking test during self-paced treadmill walking on the Gait Real-time Analysis Interactive Lab (GRAIL). In **chapter 3**, the same task and stability measures are used to assess the effect of a novel training method, i.e. an instrumented split-belt treadmill with a virtual reality environment (GRAIL) to improve mobility in people with incomplete SCI. In this study we evaluate the effect of GRAIL training on walking and dynamic balance in chronic ambulatory incomplete SCI patients.

The second part of this thesis focuses on improving mobility in people with complete SCI using an exoskeleton. More specifically, the feasibility of exoskeleton training for home and community use in people with complete SCI is investigated. In **chapter 4**, we describe the development and evaluation of an exoskeleton-skills-test to assess how people acquire such skills over a training period. Because exoskeleton skill acquisition is time consuming and diverse among people with complete SCI, we zoom in on factors that can predict exoskeleton skill acquisition (**chapter 5**). For this purpose, linear regression analyses is performed to examine nine potential predictors (personal and injury characteristics) of exoskeleton skill

performance. **Chapter 6** focuses on the risk of using an exoskeleton. In this chapter, two fractures related to exoskeleton use are described. Furthermore, advice is given for extra safety training and instructions. Besides the fact that the exoskeleton use improves standing and walking capacity, it may have beneficial health effects. Hence, the results of health questionnaires before and after exoskeleton training are presented in **Chapter 7**. The aim of this chapter is to assess the effect of exoskeleton use on quality of life and secondary health complications. The aim of **chapter 8** is to identify the potential of an exoskeleton for home and community use. Therefore, the amount, purpose and location of exoskeleton use is evaluated. In addition, this chapter evaluates participants' experiences using the exoskeleton at home and in the community. Due to the limited number of people who use an exoskeleton in daily life, the participants of **chapter 8** are re-approached to participate in an interview. The aim of this qualitative study (**chapter 9**) is to identify the needs and requirements for an optimal (future) exoskeleton aimed at home and community use. **Chapter 10** summarizes and discusses the work described in this thesis.

1

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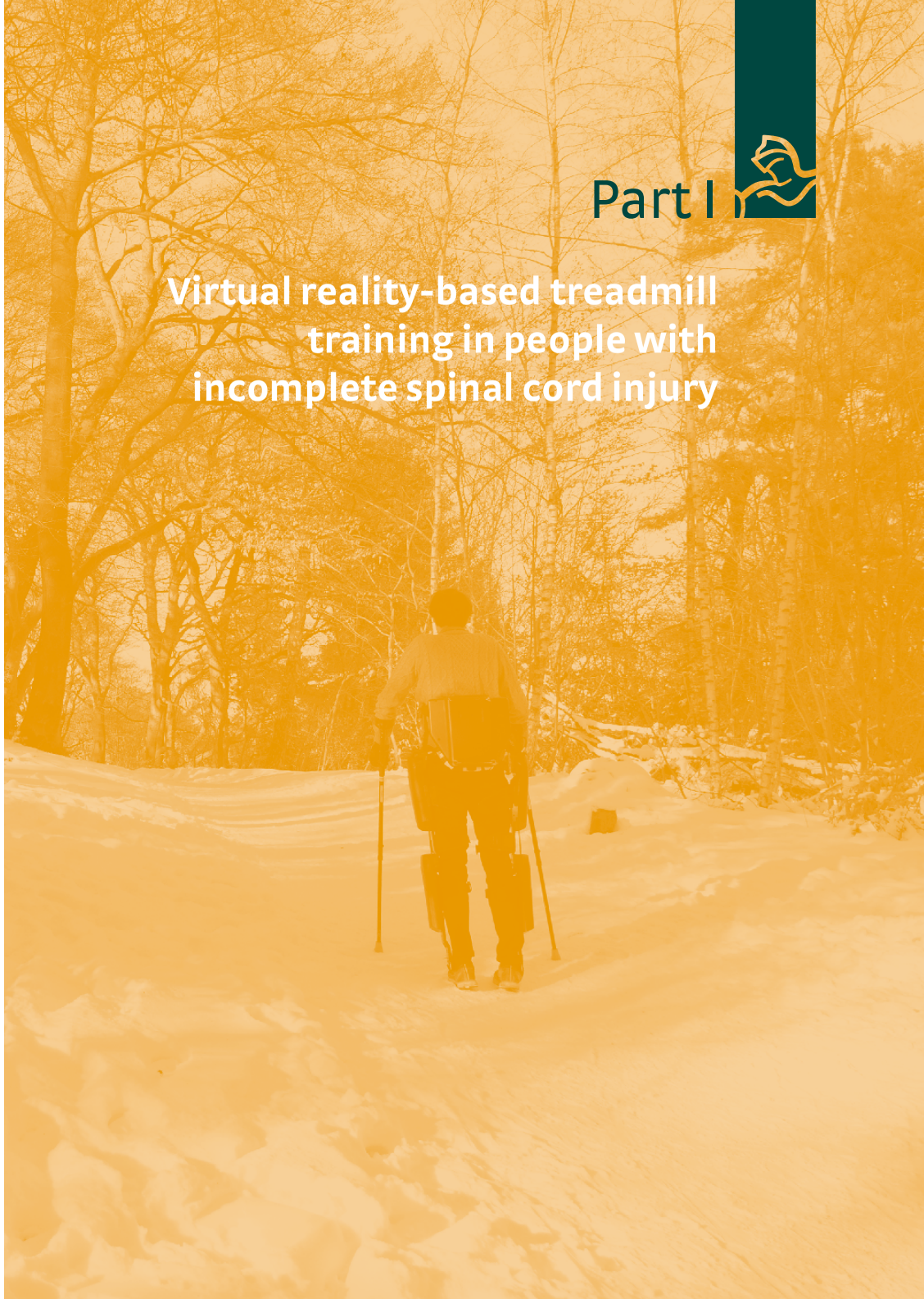
1

Part I

Virtual reality-based treadmill training in people with incomplete spinal cord injury



Chapter 2

Test-retest reliability of stability outcome measures during treadmill walking in patients with balance problems and healthy controls

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Abstract

Background

Improvement of balance control is an important rehabilitation goal for patients with motor and sensory impairments. To quantify balance control during walking, various stability outcome measures have described differences between healthy controls and patient groups with balance problems. To be useful for the evaluation of interventions or monitoring of individual patients, stability outcome measures need to be reliable.

Research question: What is the test-retest reliability of six stability outcome measures during gait?

Methods

Patients with balance problems (n=45) and healthy controls (n=20) performed two times a two-minute walk test (2MWT). The intraclass correlation coefficient (ICC) and Bland-Altman analysis (coefficient of repeatability; CR) were used to evaluate the test-retest reliability of six stability outcome measures: dynamic stability margin (DSM), margin of stability (MoS), distance between the extrapolated centre of mass (XCoM) and centre of pressure (CoP) in anterior-posterior (XCoM-CoP_{AP}) and medial-lateral (XCoM-CoPML) direction, and inclination angle between centre of mass (CoM) and CoP in anterior-posterior (CoM-$CoP_{AP\text{-}angle}$) and medial-lateral (CoM-$CoP_{ML\text{-}angle}$) direction. A two way mixed ANOVA was performed to reveal measurement- and group-effects.

Results

The ICCs of all stability outcome measures ranged between 0.51 and 0.97. Significant differences between the measurements were found for the DSM (p=0.017), XCoM-CoP_{AP} (p=0.008) and CoM-$CoP_{AP\text{-}angle}$ (p=0.001). Significant differences between controls and patients were found for all stability outcome measures (p< 0.01) except for the MoS (p=0.32). For the XCoM-CoP distances and CoM-$Co_{P\,angles}$, the CRs were smaller than the difference between patients and controls.

Significance

Based on the ICCs, the reliability of all stability outcome measures was moderate to excellent. Since the XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ showed no differences between the measurements and smaller CRs than the differences between patients and controls, the XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ seem the most promising stability outcome measures to evaluate interventions and monitor individual patients.

Keywords: Gait, balance control, stability, reliability, spinal cord injury, stroke

2

Introduction

Many patients with neurological and/or musculoskeletal disorders have difficulty maintaining their balance during standing and walking.[1,2] As a consequence, patients have a higher risk of falling, which can result in physical injuries, decreased social participation and reduced quality of life.[3,4] Because balance control plays an important role in performing daily activities,[5] improving balance control is an important rehabilitation goal.

In clinical practice, balance control has commonly been assessed and evaluated by clinical assessment tools like the Berg Balance Scale, Timed Up and Go and Activities-Specific Balance Confidence Scale.[6,7] These tools are easy to use, quick to perform and inexpensive.[7,8] However, most outcome measures of these clinical assessment tools are subjective, show ceiling effects and/or are not responsive to small changes.[7-9] Furthermore, these outcome measures do not reflect the underlying mechanisms of balance control.[7]

The biomechanically underlying mechanism of static balance control is the ability to stabilize the centre of mass (CoM) above the base of support (BoS).[10,11] However, in dynamic situations the CoM can be outside the BoS without losing balance. Therefore, the concept of the extrapolated centre of mass (XCoM) has been proposed for dynamic situations.[12] The XCoM is a state of the CoM taking into account both the instantaneous position and velocity of the CoM. Dynamic balance control is the ability to control the position of the XCoM with respect to the BoS. During walking the XCoM is not always within the BoS which is natural and necessary for forward progression.[12,13] To maintain balance during walking, the foot needs to be correctly placed to control the (X)CoM relative to the BoS.[5,14] Based on the control mechanism between the (X)CoM and foot placement (BoS and CoP), various stability outcome measure, like the dynamic stability margin (DMS),[15] margin of stability (MoS),[12] XCoM-CoP distance[13] and CoM-CoP inclination angles,[16] have been proposed in the literature. The DSM is based on the distance interaction between the XCoM and the front line of the BoS,[15] while the MoS[12] and XCoM-CoP distance[13] use the XCoM-CoP interaction to assess balance control. In addition, CoM-CoP inclination angles, defined as the angle between the line connecting the CoM and CoP and the vertical line passing through the CoP, are also used as an outcome measure for balance control during walking.[16] The above-mentioned stability outcome measures have been used to describe differences in balance control during walking between healthy controls and (patient) groups with balance problems. For example, the MoS of above-knee amputees was larger compared to healthy controls.[17] In elderly fallers the XCoM-CoP distance in the anterior-posterior distance (XCoM-CoPAP) and the anterior-posterior CoM-CoP inclination angle (CoM-$CoP_{AP\text{-}angle}$) were reduced,[13,16] whereas the medial-lateral CoM-CoP inclination angle (CoM-$CoP_{ML\text{-}angle}$) was larger compared to healthy elderly.[16] Furthermore, stroke patients with better balance control, represented by a higher Berg Balance Scale score (>45), reported larger DSM values than stroke patients with a lower Berg Balance Scale score (≤45).[15] These results illustrated that the above-mentioned stability outcome measures were able to distinguish between patients and controls, indicating construct validity.

In addition to validity, these stability outcome measurements should be reliable to be useful for the evaluation of interventions and monitoring of individual patients. However, the reliability of these stability outcome measures has not been evaluated yet. Therefore, the purpose of this study was to evaluate the test-retest reliability of six different stability

outcome measures (DSM, MoS, XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$) during gait in patients with balance problems and healthy controls.

2

Methods

Participants

Between May 2016 and November 2017, 56 patients and 22 healthy controls were recruited in the Sint Maartenskliniek Nijmegen. Patients were included if: 1) referred to GRAIL (Gait Real-time Analysis Interactive Lab) training for balance and gait training by a rehabilitation physician, 2) 18 years or older, and 3) could walk independently for two minutes without assistance at the beginning of their training period (Functional Ambulation Categories (FAC) ≥ 3). Patients were divided into three categories based on their diagnosis: spinal cord injury (SCI), stroke, and the diverse group with diagnoses including amputation, total knee prosthesis or other neurological disorders than SCI or stroke. The healthy controls were also 18 years or older and did not have any balance or gait problems and neurological or lower limb impairments.

All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee of Slotervaart Hospital and Reade (P1613/P1614) and by the internal review board of the Sint Maartenskliniek.

Experimental protocol

All participants performed twice a 2-minute walk test (2MWT) on an instrumented split-belt treadmill in the self-paced mode (GRAIL, Motek Medical BV, the Netherlands). The patients performed the 2MWT on two separate days within one week at the beginning of their training sessions. The healthy controls performed both 2MWTs on the same day with a minimum of four hours in between the measurements.

Twelve reflective markers were placed on the following anatomical landmarks of the lower leg: anterior superior iliac spine (ASIS) and posterior superior iliac spine (PSIS), femoral lateral epicondyle, lateral malleolus, metatarsal II and the calcaneus. Marker position was captured by an eight-camera motion capture system (VICON, Oxford, UK) with a sample frequency of 100 Hz. Force data were collected with two embedded force plates underneath each treadmill belt and sampled with 1000 Hz.

The speed of the treadmill was automatically controlled in the self-paced mode using the position of the pelvis.[18] The position of the pelvis was continuously compared to the zero line, located at the middle of the treadmill. Walking forward or backward relative to the zero line resulted in an acceleration or deceleration, respectively. The sensitivity of the self-paced mode (how fast the treadmill reacts at changes in position of the pelvis) was set at 1.0 or 1.5 (setting ranged between 1 and 5), while the maximum acceleration or deceleration was set at 0.25 m/s^2.

Prior to the measurements, participants performed multiple practice trials to familiarize themselves with walking on the GRAIL in the self-paced mode. During these trials, the participants practiced starting and stopping the treadmill, and controlling the speed of the treadmill to reach their steady state walking speed. On the first measurement day, participants

received at least three practice trials. During the first practice trial, starting and stopping the treadmill, and controlling the speed were practiced for 60 seconds. The other practice trials were focused on controlling the treadmill during the start-up phase to reach their steady state walking speed and lasted approximately 30 seconds. If participants were not able to control the speed of the treadmill after three trials, additional practice trials were performed until the participants were able to reach a comfortable walking speed within 20 seconds. On the second measurement day, one practice trial was performed for approximately 30-45 seconds. During the 2MWT measurements, participants were instructed to walk as far as possible at a comfortable walking speed in two minutes.[19] To assure safety, all participants wore a safety harness without providing any weight support.

2

Data analysis

Force plate data were filtered with a zero lag, second order low pass Butterworth filter with a cut-off frequency of 7 Hz. The position of the CoP was calculated using force plate data.[20] To obtain a continuous CoP signal, the CoP trajectory of each foot was weighted by the relative magnitude of the vertical component of the ground reaction force of the corresponding foot.[21]

The position data of the markers were low pass filtered with a zero lag, second order Butterworth filter with a 10 Hz cut-off frequency. The position of the CoM was estimated by the average of the four pelvis markers.[22] The XCoM was calculated according to Hof et al.: $XCoM = p_{CoM} + \frac{v_{CoM}}{\omega_0}$.[12] With pCoM representing the instantaneous position of the CoM, vCoM the instantaneous velocity of the CoM and ω_0= $\sqrt{g/l_0}$ in which g is the acceleration of gravity and lo the maximum height of the CoM.

Using the position data of the foot markers, heel strikes and toe offs were identified. Heel strikes were defined as the instant at which the velocity of the calcaneus marker started moving backwards, while toe offs were defined as the instant at which the velocity of the metatarsal II marker started moving forward. Steps were defined as the period from heel strike to contralateral heel strike, and strides were defined as the period from heel strike to ipsilateral heel strike. To remove the start-up phase, the first 20 seconds of the data were excluded for analysis. For each participant a constant number of 50 steps was used for analysis.

Figure 1

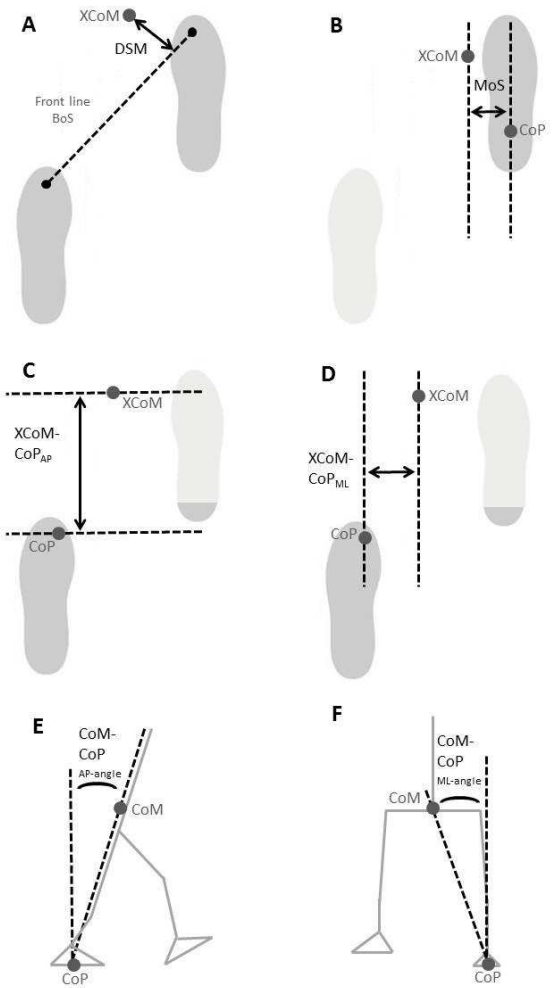

Figure 1. Stability outcome measures based on the position of the centre of mass (CoM), extrapolated centre of mass (XCoM), centre of pressure (CoP) and/or base of support (BoS). A – Dynamic stability margin (DSM); B – Margin of stability (MoS); C – Distance XCoM-CoP$_{AP}$; D – Distance XCoM-CoP$_{ML}$; E –CoM-CoP$_{AP\text{-}angle}$; and F – CoM-CoP$_{ML\text{-}angle}$. Darkened segments of the footprints represent foot contact.

Stability outcome measures

Six stability outcome measures based on the position of the (X)CoM relative to the foot placement (BoS and CoP) were determined. The DSM was calculated as the shortest distance from the XCoM to the front line of the BoS during double support.[15] Since the exact edge of the front line of the BoS was not available, the front line of the BoS was defined by a line through the metatarsal II markers of the left and right foot (Figure 1A). The MoS was defined as the shortest distance in the medial-lateral direction between the XCoM and CoP at the initial start of the single support phase of each step (Figure 1B).[12] The XCoM-CoP distance was defined as the shortest distance between the XCoM and CoP calculated at the instant of heel strike in the anterior-posterior direction (XCoM-CoP$_{AP}$) and in the medial-lateral direction (XCoM-CoP$_{ML}$) (Figure 1C-D).[13] The CoM-CoP inclination angle in the anterior-posterior (CoM-CoP$_{AP\text{-}angle}$) and medial-lateral direction (CoM-CoP$_{ML\text{-}angle}$), is defined as the angle between the line connecting the CoM and CoP and the vertical line passing through the CoP[16]. The peak inclination angle was defined as the difference between the minimal and maximal angle within one stride (Figure 1E-F). The stability outcome measures were calculated for each leg separately. If no difference between the legs were found, the results for the affected leg of the patients and left leg of the controls were reported. All data processing and analyses were performed using MATLAB R2009b (The MathWorks Inc, Natick, MA, USA).

Statistical analysis

Subject demographics between groups were compared with an ANOVA (α=0.05). Test-retest reliability for each stability outcome measure was estimated using the intraclass correlation coefficient (ICC (3,1)). ICCs were calculated for each patient group separately (SCI, stroke and diverse), all patients together, and the controls. In addition, Bland-Altman analyses were performed: limits of agreement were calculated to determine the coefficient of repeatability (CR)[23]. Differences in the six stability outcome measures and walking speed between the two measurement and the patient groups were assessed with a two way mixed model ANOVA (α=0.05), with measurement (1 and 2) as within factor and the groups (SCI, stroke, diverse and controls) as between factor. To indicate whether the stability outcome measures could be useful for monitoring individual patients, CRs were compared to the differences between patients and controls. The differences between the patient groups and the control group were determined and tested with post-hoc independent t-tests with Bonferroni correction (α=0.017). To establish an ICC of at least 0.6 with statistical significance (α=0.05 and β=0.80), we aimed to include at least 15 participants per subgroup[24].

Results

Participants

In total, 78 participants were included in this study. Data of ten patients and two healthy controls were incomplete due to technical reasons (e.g. no recording or incomplete marker data. One patient was excluded because he was not able to control self-paced walking. For data analysis, data of the remaining 45 patients and 20 healthy controls were used. One patient did not reach 50 steps during both measurements. For the analysis of this patient, we included 41 and 49 steps instead of 50 for measurement 1 and 2, respectively. Subject demographics are reported in Table 1. No significant differences in subject demographics, except for time post-injury, between the groups were found.

For walking speed a significant main effect for groups (p<0.001) and measurements (Δ=0.06, p<0.001) was found. Post-hoc testing revealed significant differences between the controls and all patient groups (SCI: Δ=0.60, p<0.001; stroke: Δ=0.80, p<0.001; diverse: Δ=0.62, p<0.001).

Table 1. Subject demographics.

	Patients			Controls	*p*
	SCI	Stroke	Diverse*		
N	15	15	15	20	
Gender (M/F)	11 / 4	7 / 8	9 / 6	8 / 12	0.195
Age (year)	57.7 ± 11.5	54.9 ± 15.6	58.8 ± 14.6	48.6 ± 17.7	0.232
Weight (kg)	84.1 ± 6.7	75.3 ± 19.6	82.8 ± 14.3	80.4 ± 15.3	0.379
Height (cm)	178.5 ± 7.3	171.1 ± 10.3	174.5 ± 10.3	177.2 ± 6.8	0.102
Post-injury (months)**	27.3 ± 26.9	10.7 ± 14.5	54.9 ± 72.1	-	0.034
Walking speed (m/s)**	0.93 ± 0.33	0.73 ± 0.29	0.91 ± 0.29	1.53 ± 0.28	<0.001

Values are displayed as mean ± SD. * The group diverse included the following diagnoses: brain tumour, contusion, amputation (n=2), total knee prosthesis (n=3), acquired brain injury, autosomal dominant cerebellar ataxia, neuropathic pain, Guillain-Barré syndrome, encephalomyelitis, brain trauma, hereditary spastic paraplegia, vestibular disorder and pain complaints of ankle and foot. ** Significant difference between the groups ($p<0.05$).

Test-retest reliability

The ICCs of all stability outcome measures for all groups are shown in Table 2 and ranged between 0.51 (MoS in the controls) and 0.97 (CoM-$CoP_{ML\text{-}angle}$ in the diverse patient group). Outcomes of measurement 1 and 2, mean differences and CR are presented in Table 3. The two way mixed ANONA revealed a significant main effect for groups for the DSM ($p<0.001$), XCoM-CoP_{AP} ($p<0.001$), XCoM-CoP_{ML} ($p=0.003$), CoM-$CoP_{AP\text{-}angle}$ ($p<0.001$) and CoM-$CoP_{ML\text{-}angle}$ ($p<0.001$). In addition, a significant main effect for measurements was found for the DSM ($p=0.017<0.001$), XCoM-CoP_{AP} ($p=0.008$) and the CoM-$CoP_{AP\text{-}angle}$ ($p=0.001$). Interaction effects between groups and measurements were not found for any of the stability outcome measures ($p>0.05$). Post-hoc tests revealed significant difference between the controls and all patients groups for the DSM, XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and the CoM-$CoP_{ML\text{-}angle}$ (all $p<0.001$).

Table 2. Intraclass Correlations Coefficients (ICC) for all stability outcome measures and all groups.

	Patients				Controls
	All	SCI	Stroke	Diverse	
DSM	0.77	0.79	0.83	0.70	0.60
MoS	0.92	0.89	0.81	0.95	0.51
XCoM-CoP_{AP}	0.88	0.94	0.83	0.83	0.93
XCoM-CoP_{ML}	0.84	0.86	0.84	0.84	0.80
CoM-$CoP_{AP\text{-}angle}$	0.88	0.95	0.82	0.83	0.87
CoM-$CoP_{ML\text{-}angle}$	0.94	0.92	0.89	0.97	0.88

SCI: spinal cord injury; DSM: dynamic stability margin; MoS: margin of stability; XCoM: extrapolate centre of mass; CoP: centre of pressure; CoM: centre of mass; AP: anterior-posterior; ML: medial-lateral.

Table 3. Measurement scores, mean differences and coefficient of repeatability (CR) of the (most) affected leg for patients and left leg for healthy controls.

			Measurement scores		Mean difference	
			Measurement 1 (mean ± SD)	Measurement 2 (mean ± SD)	Test 2 – Test 1 (mean ± SD)	CR
DSM (mm)*	Patients	All	20.9 ± 28.8	27.0 ± 28.8	6.1 ± 18.8	36.8
		SCI	22.8 ± 22.8	28.1 ± 20.4	5.3 ± 13.6	26.7
		Stroke	14.0 ± 32.3	18.5 ± 34.3	4.5 ± 19.6	38.4
		Diverse	26.0 ± 31.0	34.5 ± 29.5	8.5 ± 23.0	45.0
	Controls**		49.8 ± 20.6	54.1 ± 17.5	4.4 ± 17.0	33.2
MoS (mm)	Patients	All	28.7 ± 25.5	28.0 ± 21.6	-0.6 ± 9.7	19.1
		SCI	26.1 ± 22.8	27.4 ± 19.3	1.4 ± 10.2	19.9
		Stroke	35.3 ± 16.3	32.2 ± 13.8	-2.9 ± 9.2	17.9
		Diverse	24.7 ± 34.5	24.3 ± 29.5	-0.4 ± 10.0	19.7
	Controls		17.9 ± 13.1	21.4 ± 15.3	3.4 ± 14.1	27.6
XCoM-CoP_{AP} (mm)*	Patients	All	377.3 ± 154.9	398.5 ± 143.6	21.2 ± 71.2	139.5
		SCI	394.5 ± 158.5	413.7 ± 153.2	19.3 ± 50.2	98.4
		Stroke	317.9 ± 144.3	345.7 ± 125.1	27.8 ± 75.5	148.0
		Diverse	419.7 ± 153.2	436.2 ± 144.8	22.9 ± 65.0	172.1
	Controls**		684.9 ± 137.0	711.6 ± 158.0	26.7 ± 49.7	97.5
XCoM-CoP_{ML} (mm)	Patients	All	125.0 ± 26.6	124.6 ± 29.1	-0.3 ± 16.2	31.7
		SCI	125.8 ± 21.1	121.4 ± 25.9	-4.4 ± 12.4	24.3
		Stroke	128.7 ± 30.7	127.4 ± 31.8	-1.3 ± 18.3	35.9
		Diverse	120.5 ± 28.2	125.1 ± 31.1	4.6 ± 16.9	33.2
	Controls**		100.2 ± 19.3	94.2 ± 22.3	-6.0 ± 12.2	24.0
CoM-$CoP_{AP\text{-}angle}$ (°)*	Patients	All	13.9 ± 4.9	14.6 ± 4.5	0.7 ± 2.3	4.4
		SCI	14.0 ± 4.7	14.6 ± 4.9	0.5 ± 1.5	3.0
		Stroke	11.9 ± 4.1	12.9 ± 3.7	1.1 ± 2.3	4.4
		Diverse	15.9 ± 5.2	16.4 ± 4.4	0.5 ± 2.9	5.7
	Controls**		22.7 ± 4.2	24.2 ± 4.7	1.6 ± 1.8	3.6
CoM-$CoP_{ML\text{-}angle}$ (°)	Patients	All	11.5 ± 2.4	11.5 ± 2.5	0.00 ± 0.83	1.6
		SCI	11.3 ± 1.7	11.3 ± 1.7	0.02 ± 0.70	1.4
		Stroke	11.9 ± 1.9	11.8 ± 2.1	-0.06 ± 0.95	1.9
		Diverse	11.2 ± 3.4	11.2 ± 3.5	0.03 ± 0.87	1.7
	Controls**		8.4 ± 1.6	8.3 ± 1.5	-0.11 ± 0.77	1.5

SCI: spinal cord injury; DSM: dynamic stability margin; MoS: margin of stability; XCoM: extrapolate centre of mass; CoP: centre of pressure; CoM: centre of mass; AP: anterior-posterior; ML: medial-lateral; SD: standard deviation.
* Significant difference between test 1 and test 2 ($p<0.05$).
** Significant difference between patient groups and controls ($p<0.001$).

Discussion

This is the first study evaluating the test-retest reliability of the stability outcome measures, DSM, MoS, XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$, during treadmill walking in patients with balance problems and healthy controls. ICCs ranged between 0.51 and 0.97. Significant differences between measurements were found for the DSM, XCoM-CoP_{AP} and CoM-$CoP_{AP\text{-}angle}$. All stability outcome measures, except the MoS, showed significant differences between controls and patient groups, supporting the literature and indicating construct validity of these stability outcome measures.[13,15–17]

Based on the ICCs, a moderate to excellent test-retest reliability was found for all stability outcome measures in patients and controls on group level. The ICCs of the XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$ were good (ICC>0.80[25]) for all groups. These ICCs were comparable to the ICCs reported for spatiotemporal and kinematic parameters like step length, step width and knee flexion/extension (ICC>0.85) in healthy controls, stroke and SCI patients.[26–28] The ICCs of the DSM and MoS, ranging between 0.51 and 0.95, corresponded to the ICCs found for the kinematic and kinetic parameters ankle dorsi-plantar flexion and peak knee extension moment (0.65-0.79).[26] The ICCs of the healthy controls were in general lower than the ICCs of the patients which may be explained by the smaller between-subject variability in healthy controls (more homogenous group). Since the ICC is a relative measure depending on both the between-subject variability and test-retest variability, similar test-retest variability in combination with smaller between-subject variability resulted in lower ICC values.

Between the measurements, no significant differences were found for the MoS, XCoM-CoPML and CoM-CoPML-angle whereas DSM, XCoM-CoPAP, CoM-CoPAP-angle, and walking speed were significantly different. The increased walking speed suggests a learning effect, which has been found previously for walking tests like the six minute walk test.[29] When the walking speed increases, the XCoM will be situated more forward in the AP-direction. As a consequence, the distance between the XCoM and the BoS or CoP will increase, which results in larger values of the AP-direction based stability outcome measures (the DSM, XCoM-CoP_{AP}, CoM-$CoP_{AP\text{-}angle}$. Therefore, the increase in AP-direction based stability outcome measures in the second measurement seems to be related to the increase in walking speed. The systematic increase in walking speed, indicating a learning effect for the AP-direction based stability outcome measures, was probably caused by unfamiliarity with the treadmill and testing procedures on the first measurement day.[30] To reduce the learning effect, additional trials for practicing walking in the self-paced mode may be necessary.

To evaluate the reliability on an individual level, CRs of the stability outcome measures were used. The CR represents the difference between two repeated measures for 95% of pairs of measurements and sets the boundary of the minimal change that can be detected.[23] A weighted comparison between the six stability outcome measures is difficult since the CR is an absolute index in the same unit as the stability outcome measure. To be useful for monitoring of individual patients, the CR should be at least smaller than the differences between patients and controls. Therefore, we compared the CRs to the difference between the patients and controls. All stability outcome measures, except for the MoS, indicated significant lower balance control in patients compared to controls. The CRs of the XCoM-CoP distance and CoM-CoP angle in both AP- and ML-direction were smaller than the differences between patients and controls and may therefore useful for monitoring individual patients.

The XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ seem the most promising stability outcome measures for evaluation of interventions and monitoring of individual patients since these two stability outcome measures show high ICCs, no learning effects, independency of walking speed and smaller CRs compared to the differences between patients and controls. Further research should determine whether the stability outcome measures could be useful in clinical practice. The stability outcome measures should be able to distinguish between patients with different levels of balance control (i.e. fallers and non-fallers) and to detect improvements during and after interventions for improving balance control.

A limitation of this study is that test and retest for patients took place on separate days within one week. Disadvantage of this procedure is that subject conditions could differ between the days. However, performing two measurements on one day was not feasible in clinical practice since patients experience fatigue after exercise. Another limitation is the limited number of observations, especially in the subgroups, which affects the precision of the estimation of the CRs and confidence intervals. We recommend to confirm the CRs in a larger and independent sample.

Conclusion

The test-retest reliability of the DSM, MoS, XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$ for both patients and controls was moderate to excellent. No significant differences between measurements were found for the MoS, XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$, whereas a learning effect was found for the DSM, XCoM-CoP_{AP}, and CoM-$CoP_{AP\text{-}angle}$. All stability outcome measures, except for the MoS, showed significant differences between the controls and all patient groups. For the XCoM-CoP distance and CoM-CoP angle in both AP- and ML-direction, the CRs were smaller than the difference between patients and controls. Hence, the XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ seem the most promising stability outcome measures to evaluate interventions and monitor individual patients.

2

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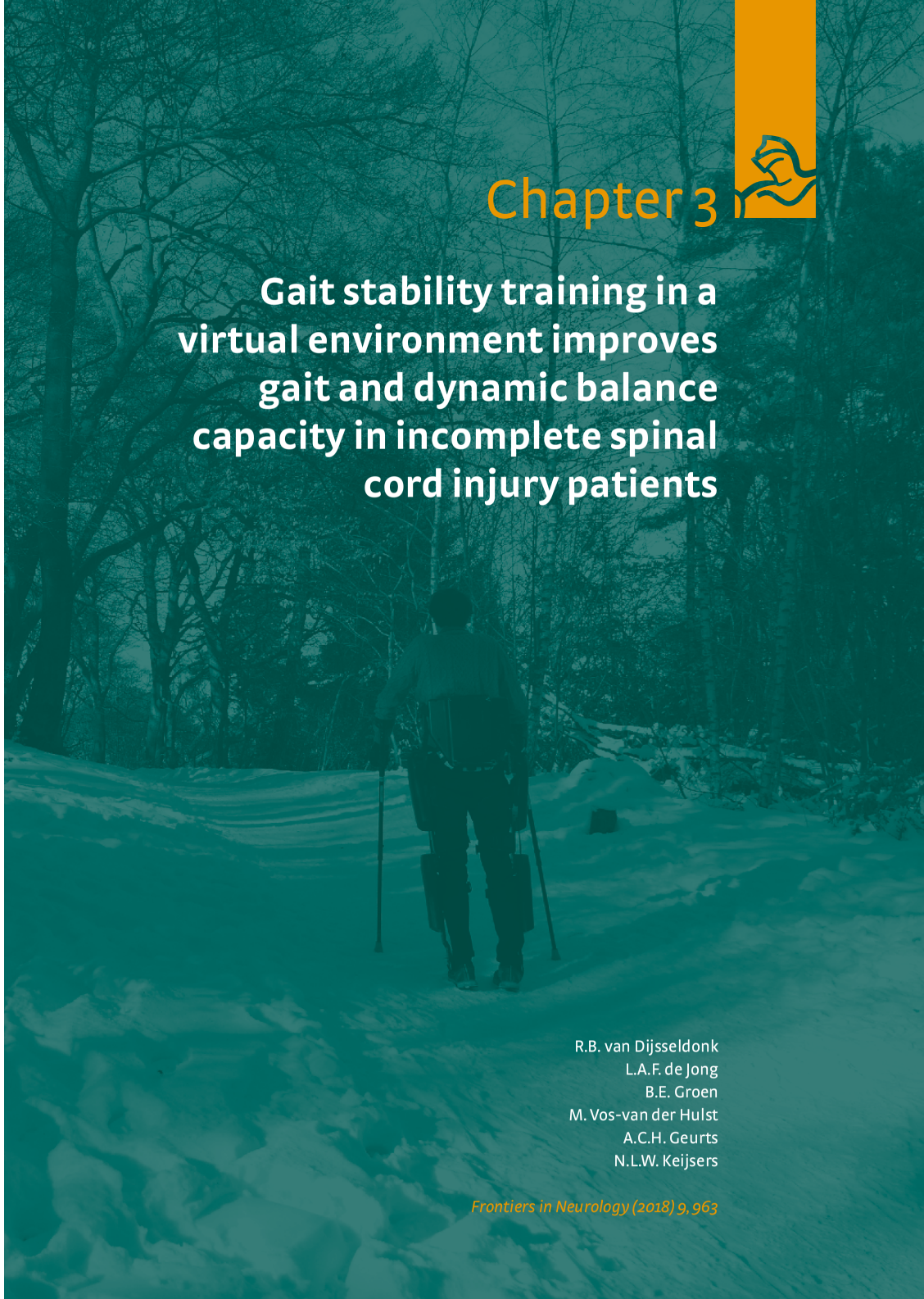
Chapter 3

Gait stability training in a virtual environment improves gait and dynamic balance capacity in incomplete spinal cord injury patients



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Abstract

Background

Many patients with incomplete spinal cord injury (iSCI) have impaired gait and balance capacity, which may impact daily functioning. Reduced walking speed and impaired gait stability are considered important underlying factors for reduced daily functioning. With conventional therapy, patients are limited in training gait stability, but this can be trained on a treadmill in a virtual environment, such as with the Gait Real-time Analysis Interactive Lab (GRAIL). Our objective was to evaluate the effect of 6-weeks GRAIL-training on gait and dynamic balance in ambulatory iSCI patients. In addition, the long-term effect was assessed.

Methods

Fifteen patients with chronic iSCI participated. The GRAIL-training consisted of 12 one-hour training sessions during a 6-week period. Patients performed 2-minute walking tests on the GRAIL in a self-paced mode at the 2nd, and 3rd (baseline measurements) and at the 12th training session. Ten patients performed an additional measurement after 6 months. The primary outcome was walking speed. Secondary outcomes were stride length, stride frequency, step width, and balance confidence. In addition, biomechanical gait stability measures based on the position of the center of mass (CoM) or the extrapolated center of mass (XCoM) relative to the center of pressure (CoP) or the base of support were derived: dynamic stability margin (DSM), XCoM-CoP distance in anterior-posterior (AP) and medial-lateral (ML) directions, and CoM-CoP inclination angles in AP and ML directions. The effect of GRAIL-training was tested with a one-way repeated measures ANOVA (α=0.05) and post-hoc paired samples t-tests (α=0.017).

Results

Walking speed was higher after GRAIL training (1.04m/s) compared to both baseline measurements (0.85m/s and 0.93m/s) (p<.001). Significant improvements were also found for stride length (p<.001) and stability measures in AP direction ($XCoM\text{-}CoP_{AP}$ (p<.001) and $CoM\text{-}CoP_{AP\text{-}angle}$ (p<.001)). Stride frequency (p=.27), step width (p=.19), and stability measures DSM (p=0.06), $XCoM\text{-}CoP_{ML}$ (p=.97) and $CoM\text{-}CoP_{ML\text{-}angle}$ (p=.69) did not improve. Balance confidence was increased after GRAIL training (p=.001). The effects were remained at 6 months.

Conclusion

Increased walking speed, stride length, AP gait stability , and balance confidence suggest that GRAIL-training improves gait and dynamic balance in patients with chronic iSCI. In contrast, stability measures in ML direction did not respond to GRAIL-training.

Keywords: Spinal cord injury, virtual reality, gait, balance, stability, ambulatory, rehabilitation, walking

Introduction

Approximately 60% of the patients with a spinal cord injury (SCI) suffer an incomplete lesion.[1] In the chronic phase of an incomplete SCI (iSCI) many patients will encounter deficits at and below the level of the lesion such as muscle weakness, spasticity and impaired muscle coordination.[2] These deficits can impact on functional ambulation[3] and social participation.[4] For functional ambulation, walking speed is considered one of the most important parameters[5]. Generally, iSCI patients walk at a low preferred walking speed [5] and with a deviant walking pattern.[2,6] One of the underlying causes of the reduced walking performance is impaired balance.[7,8] The high incidence of falls, ranging from 39% to 75%,[9,10] supports the impaired balance in ambulatory patients with iSCI.

Frequently, an important goal of rehabilitation is to improve balance and walking speed. Various interventions and training approaches aiming to improve walking performance in iSCI patients have been introduced and all approaches show some improvement without supremacy of one intervention over others.[11] Typical examples of balance and walking training are individual physical therapy and (body-weight-supported) treadmill training. However, these therapies are limited in training patients to react to environmental circumstances without challenging their balance capacity to individual limits.

In recent years, training in a virtual environment has been introduced in rehabilitation.[12,13] In these virtual environments, a simulation of challenging real life situations (such as walking in a forest) can be presented without exposing the user to the direct danger of falling. In this way, patients are given the opportunity to train their gait and balance capacities by exploring their boundaries in a challenging and safe environment.[14] Training in virtual environments will provide patients with important prerequisites for motor rehabilitation, such as repetitive practice, feedback about performance and motivation to endure practice[12]. In the virtual environment tasks involving precision stepping, obstacle avoidance and/or reacting to perturbations, often referred to as 'gait adaptability training', can be performed in quick succession. Such training is highly relevant to relearn daily activities such as walking on uneven surfaces or in crowded places, where people need to adapt their walking speed and walking pattern to environmental circumstances.[15–18] Previous research shows that gait adaptability training can improve functional ambulation by preventing falls[19] and improving gait stability in elderly, stroke patients, and patients with Parkinson's disease.[20–23] In iSCI patients training precision stepping has been shown to improve walking capacity measured with the spinal cord injury functional ambulation profile (SCI-FAP).[24] More recently, however, Fox and colleagues concluded that the efficacy of gait adaptability training on walking and balance function should be further investigated.[25]

Although walking speed is considered to be the most important characteristic of walking performance, balance capacity is a key element of functional ambulation as well.[7,8] Studies that focused on balance in iSCI patients often used the Berg Balance Scale as a primary outcome.[8,26,27] The Berg Balance Scale is easy to use, but it is known to have a ceiling effect[28] and assesses balance in rather static situations. Measuring gait stability is more complex and often requires additional equipment such as force plates and a motion capture system. Some virtual reality gait training devices, such as the GRAIL (Gait Real-time Analysis Interactive Lab), can be used as both a training and measurement device. The GRAIL consists of an instrumented dual

belt treadmill with two embedded force plates and an eight-camera VICON motion capture system (VICON, Oxford, United Kingdom). The self-paced mode of the GRAIL allows patients to vary the treadmill speed during walking, which induces a natural way of walking,[29] especially when a visual flow is presented in the virtual environment.[30] When reflective markers are adhered to the participants body, the marker data can be captured for objective offline movement analysis. In addition to walking speed, more complex biomechanical measures related to gait stability can be derived. Previous studies showed that these biomechanical gait stability measures were able to distinguish between elderly with and without balance problems,[31,32] between above-knee amputees and control subjects,[33] and between more and less affected stroke patients.[34] However, the responsiveness of the stability measures to gait training is unknown.

The main objective of this study was to evaluate the effect of six weeks GRAIL training on gait and dynamic balance capacity in ambulatory patients with chronic iSCI. In addition, the long-term effect was assessed six months after GRAIL training. Walking speed was used as a primary outcome, while other spatio-temporal parameters and gait stability measures were assessed as secondary outcome parameters. We hypothesised that GRAIL training will result in an improved walking speed and gait stability.

Material and Methods

Participants

Patients with iSCI who were referred to GRAIL training by a rehabilitation physician in the Sint Maartenskliniek between June 2016 and December 2017 were eligible to participate in this study. Eligible persons were adults in the chronic phase (>6 months) with an iSCI (American Spinal Injury Association Impairment Scale (AIS) C or D) who could walk independently for two minutes without assistance (Functional Ambulation Categories (FAC) ≥ 3). Patients were excluded if (i) they were not able to walk in the self-paced mode of the GRAIL without using the handrails, (ii) had other neurological or lower limb impairments in addition to the iSCI, (iii) had vision problems, or (iv) had walking and/or balance problems prior to the iSCI. The exclusion criteria (ii), (iii), and (iv) were checked by the researcher through questions. All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee of Arnhem-Nijmegen (2016-2474) and by the internal review board of the Sint Maartenskliniek.

Equipment

All training sessions and measurements were performed on the GRAIL at the Sint Maartenskliniek in Nijmegen (Figure 1). The GRAIL consisted of an instrumented dual belt treadmill with two embedded force plates and an eight-camera VICON motion capture system (VICON, Oxford, United Kingdom). The platform was able to move in several directions to generate mechanical perturbations. In front of the treadmill, virtual reality environments were projected on a 180° semi-cylindrical screen. Reflective markers were adhered to the patients to interact with the virtual environment and to capture kinematic data. The GRAIL system was controlled and the visual information was matched to the treadmill speed with the D-flow software (Motek Forcelink, Amsterdam, the Netherlands, version 3.22.1). To assure safety, patients wore a safety harness without body weight support.

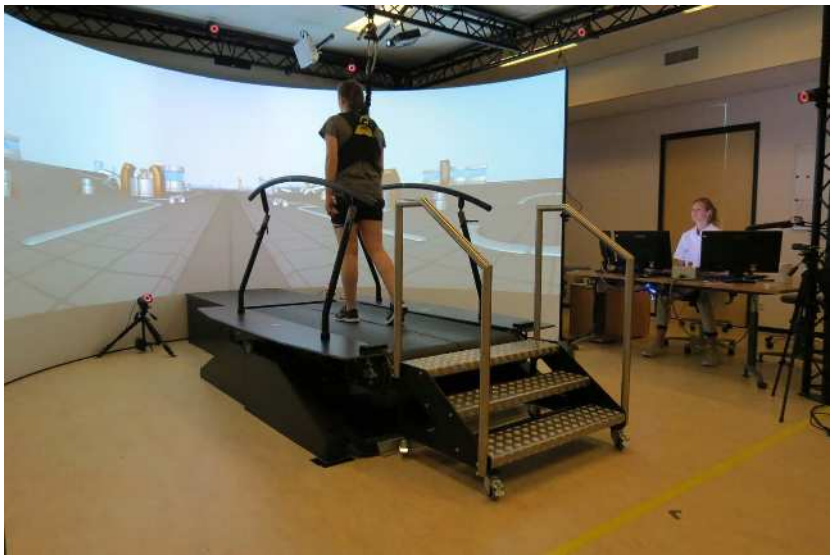

Figure 1. Gait Real-time Analysis Interactive Lab (GRAIL) at the Sint Maartenskliniek. Both persons have given their written and informed consent for publication of the picture.

Protocol

Intervention

The GRAIL training consisted of twelve one-hour training sessions spread over a six-week period. Per training session one physical therapist guided the training and a maximum of two physical therapists were responsible for all training sessions given to one patient. All physical therapists were certified GRAIL operators. Each training was individualized, as the physical therapist chose the training applications based on the specific rehabilitation goal and current level of the patient. For instance, patients who had problems maintaining their balance in stance typically performed applications in which they had to shift their weight, whereas patients with gait adaptability problems performed applications in which they had to perform precision stepping or obstacle avoidance. During the GRAIL training multiple applications were performed and after each training session the physical therapist documented the type and level of the performed applications. The applications were categorized in three themes; 'gait adaptability', 'walking+', 'balance in stance'(see Table 2). The first GRAIL training session was used for familiarization with the GRAIL system. From the second to the last training session, training intensity and complexity were gradually and individually increased.

Gait measurements

To evaluate the effect of GRAIL training on gait and balance, patients performed the 2-minute walking test (2MWT) at the 2nd, 3rd and last (12th) training sessions (baseline 1, baseline 2 and post measurement, respectively). For familiarization with the task, the 2nd baseline measurement (at the 3rd training session) was added to neutralize early learning (or task adaptation) effects.

To evaluate the long-term effect of GRAIL training on gait and balance, patients performed one additional 2MWT on the GRAIL six months after the last training session (follow-up). Patients performed the 2MWT in the self-paced mode on the GRAIL, which allowed them to walk at a self-selected speed. In the self-paced mode, the speed of the treadmill was automatically controlled using the anterior-posterior (AP) position of the pelvis markers and the AP midline of the treadmill. Walking forward or backward relative to the midline resulted in an acceleration or deceleration of the treadmill, respectively (Figure 2). Before measuring the 2MWT, patients received some explanation about the self-paced mode and performed a few practice trials to reach their preferred walking speed in a similar manner as in the study of Plotnik and colleagues.[30] During the 2MWT on the GRAIL, patients were instructed to walk as far as possible at a comfortable walking speed in two minutes. Patients received no feedback about their walking speed.

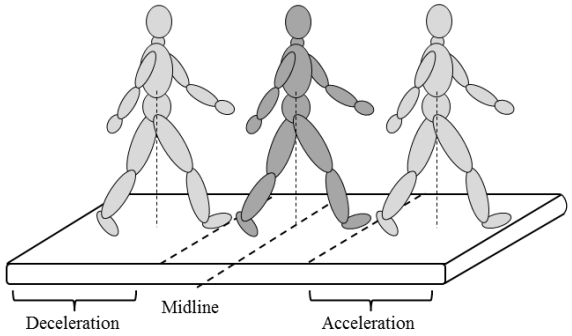

Figure 2. Self-paced mode on the GRAIL.

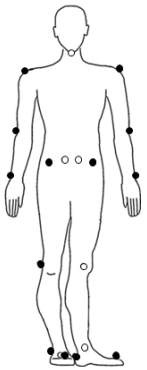

Figure 3. Placement of the reflective markers.

The self-paced mode was set at the lowest sensitivity value of 1.0 (setting ranged between 1 and 5). The maximum acceleration and deceleration of the treadmill was set at 0.25 m/s^2. Before the start of the 2MWT, nineteen reflective markers were adhered to the following anatomical landmarks: left and right acromion process, humeral lateral epicondyle, ulnar styloid process, anterior superior iliac spine (ASIS), posterior superior iliac spine (PSIS), femoral lateral epicondyle, lateral malleolus, metatarsal II, calcaneus and 7th cervical vertebra (Figure 3). The data of the reflective markers was sampled at a frequency of 100 Hz and the sample frequency of the force plates was 1000Hz. The data of the reflective markers were labeled using VICON Nexus 2.4 and analyzed using MATLAB R2017b. A zero lag second-order Butterworth filter with a cut-off frequency of 10Hz was used to filter the marker data. A cut-off frequency of 7Hz was used for the force data. Before the patients walked at their preferred walking speed, the treadmill had to accelerate. To remove the acceleration phase, the first 20 seconds of the 2MWT were removed before data analysis.

Spatiotemporal parameters

The primary outcome was walking speed defined as the average treadmill speed (m/s). Other spatiotemporal gait parameters (stride length, step width and stride frequency) were used as secondary outcome parameters. Stride length (cm) was determined as the average AP-distance between the heel markers at two consecutive heel strikes on the same side. Step width (cm) was determined as the average ML-distance between the heel markers at heel strike. Stride frequency (strides/s) was defined as the inverse of the interval between heel strikes of the same foot. Heel strikes were defined as the instant that the calcaneus marker started moving backwards.

Gait stability measures

The stability measures used in the current study were based on the position of the center of mass (CoM) or the extrapolated center of mass (XCoM) relative to the center of pressure (CoP) or the base of support (BoS), during a specific moment of the gait cycle (e.g. double support or heel strike). The position of the CoM depends on sex, body posture and direction of the limbs. In this study the CoM was calculated using nineteen reflective markers according to a method first described by Tisserand et al.[35] The XCoM takes the position and velocity of the CoM into account and is used to formulate requirements for gait stability.[36] To calculate the XCoM, the equation of Hof et al was used:[36,37]

$$XCoM = CoM' + \frac{vCoM}{\sqrt{\frac{g}{l}}}$$

CoM' represents the ground projection of the CoM, vCoM the velocity of the CoM, g = 9.81m/s^2, and l the maximum height of the CoM.[36,37] The CoP is the centroid of pressure distribution on the plantar surface of the foot and has been used to identify balance control during posture and gait.[38] The equation of Sloot et al was used to calculate the CoP for both force plates:[39]

$$CoP_{AP} = \frac{F_{AP} * CoP_V - M_{ML}}{F_V} \quad \& \quad CoP_{ML} = \frac{F_{ML} * CoP_V - M_{AP}}{F_V}$$

F represents the force in anterior-posterior (AP), medial-lateral (ML) and vertical (V) directions, M the moment of force, and CoPV the vertical distance between the surface of the treadmill belt and the force plates.[39] During the double support phase, the weighted average of the CoP in ML and AP directions was calculated based on the CoP of both force plates.

In this study the following five gait stability measures were calculated: the dynamic margin of stability (DSM),[34] the XCoM-CoP distance in AP and ML directions,[32,33] and the CoM-CoP inclination angles in AP and ML directions.[31] In general, better gait stability is characterized by a position of the XCoM far in front of the base of support in the AP direction, which suggests that patients are confident in walking at higher speeds with longer steps. In the ML direction, better gait stability is characterized by a position of the XCoM closer to the boundaries of the base of support, often accompanied by walking with a smaller step width. The DSM was calculated as the average of the shortest distance between the front line of the base of support (BoS) (i.e., the line between the two metatarsal II markers) and the XCoM during double support[34] (See Figure 4A for a visual representation). A large positive DSM represents better balance control than a

negative DSM (i.e., XCoM within the BoS) or smaller DSM. The distances between the XCoM and CoP were calculated at each heel strike in AP (Figure 4B) and ML directions (Figure 4C) separately.[32,33] A larger XCoM-CoP_{AP} distance and a smaller XCoM-CoP_{ML} distance reflect better balance control. The CoM-CoP inclination angles were calculated from the angle between the position of the CoM and the vertical line through the CoP.[31] The peak inclination angles were defined as the range between the maximum and minimum inclination angles in AP (Figure 4D) and ML directions (Figure 4E) of each gait cycle. A larger peak inclination angle in the AP direction and a smaller peak inclination angle in the ML direction represent better balance control.

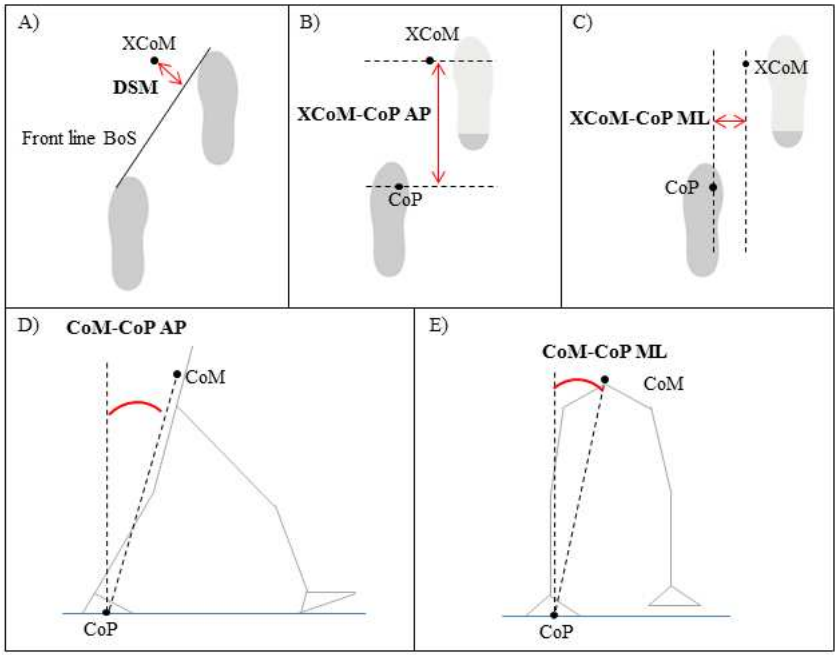

Figure 4. Gait stability measures based on the position of the center of mass (CoM), extrapolated center of mass (XCoM), center of pressure (CoP) and/or base of support (BoS) relative to each other; A) dynamic stability margin (DSM), B+C) XCoM-CoP distance in anterior-posterior (AP) and medial-lateral (ML) direction, D+E) CoM-CoP inclination angles in AP and ML direction.

Balance confidence assessment

Balance confidence was assessed with the activities specific balance confidence (ABC) (0 – 100) scale[40,41] at the second training session (before the first baseline measurement), at the last training session (after the post measurement) and at six months after the last training session (after the follow-up measurement).

Statistical analysis

Effect of GRAIL training

The spatiotemporal gait parameters (walking speed, stride length, step width and stride frequency) and gait stability measures (DSM, XCoM-CoP_{AP} distance, XCoM-CoP_{ML} distance, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$) were analyzed using descriptive statistics (mean and standard deviation). Differences in the spatiotemporal gait parameters and gait stability measures between the three measurements (baseline 1, baseline 2, and post measurement) were assessed with a one-way (factor Time) repeated measures ANOVA ($\alpha = 0.05$). If the assumption of sphericity was violated, the degrees of freedom were corrected using Greenhouse-Geisser correction and the Pillai's Trace value (V) was given. In the case of a significant effect of Time, paired samples t-tests with Bonferroni correction ($\alpha = 0.017$) were performed to determine which measurements were different from each other. In case the assumption of normality was violated, median and ranges were calculated and a non-parametric Friedman test ($\alpha = 0.05$) with Wilcoxon signed-rank post-hoc test ($\alpha = 0.017$) was performed. The effect of GRAIL training on balance confidence (the scores on the pre and post ABC-scale) was tested with paired samples t-test ($\alpha = 0.05$). F and t values were given when the repeated measures ANOVA and paired samples t-test were used, while XF2 and T were given for the non-parametric Friedman test and Wilcoxon signed-rank test.

Long-term effect of GRAIL training

The long-term effect of GRAIL training was evaluated by testing the differences in spatiotemporal gait parameters (walking speed, stride length, step width and stride frequency) and gait stability measures (DSM, XCoM-CoP_{AP} distance, XCoM-CoP_{ML} distance, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$) between the post and follow-up measurements as well as between the baseline 2 and follow-up measurements using paired samples t-tests ($\alpha = 0.05$). When the assumption of normality was violated, median and ranges were calculated and a non-parametric Wilcoxon signed-rank test ($\alpha = 0.05$) was performed. *t* values were given when the paired samples t-test was used, while *T* was given for the non-parametric equivalent, the Wilcoxon signed-rank test.

Results

Participants

In total 20 patients were assessed for eligibility in the study. Three patients were ineligible because they could not walk in the self-paced mode without using the handrails (exclusion criteria). One patient declined to participate. Sixteen patients were included in the study. One dropped out before completing the post measurement, resulting in fifteen patients who performed the baseline 1, baseline 2 and post measurements (Figure 5). An overview of the patient characteristics is given in Table 1.

Table 1. Patient characteristics

	Performed baseline 1, baseline 2 and post measurement (N = 15)	Completed follow-up (N = 10)
Sex (male / female)	11 / 4	9 / 1
Age (years), mean (SD)	59 (12)	59 (12)
Post-injury (months), mean (SD)	42 (48)	42 (46)
AIS* (C / D)	2 / 13	1 / 9
BMI**, mean (SD)	27 (2)	26 (2)
FAC*** (3 / 4 / 5)	1 / 6 / 8	1 / 4 / 5
More affected side (left/ right/ no difference)	7 / 3 / 5	5 / 1 / 4

* AIS = American Spinal Injury Association Impairment Scale
** BMI = Body-Mass Index
*** FAC = Functional Ambulatory Category

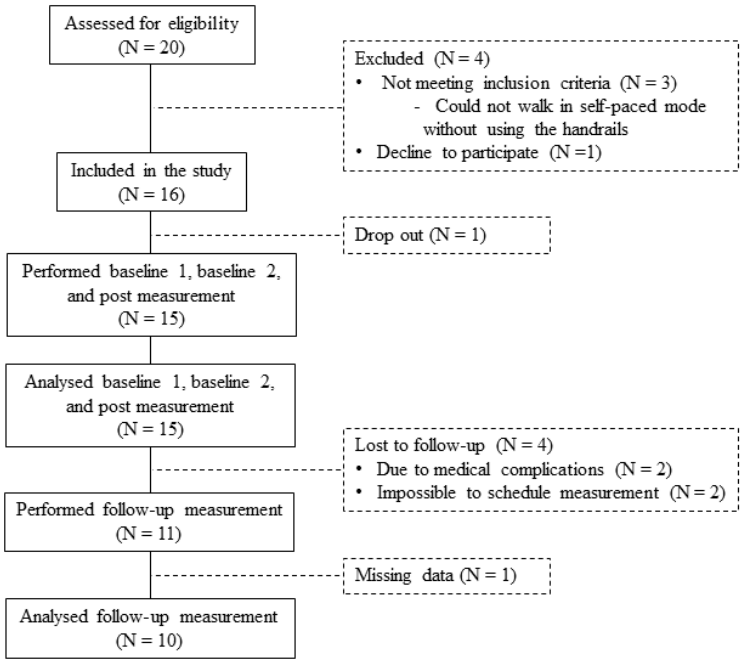

Figure 5. Flow diagram of patients in the study.

Content of GRAIL training

Two patients received nine and eight GRAIL training sessions instead of the scheduled 12 training sessions. These patients cancelled some training sessions at short notice, which made it impossible to reschedule the sessions within the training period. The other thirteen patients received 12 GRAIL training sessions. In total 30 different applications were performed during the GRAIL training. The themes of these applications were categorized in 'gait adaptability' (13 applications), 'walking+' (8 applications) and 'balance in stance' (9 applications). On average, patients performed 3.7±0.9 applications during one training session, of which 1.4±0.4 were gait adaptability applications, 1.3±0.4 walking+ applications, and 1.0±0.5 balance in stance applications. The most frequently practiced applications for gait adaptability were 'Microbes' (42%), for walking+ 'Perturbations' (23%) and for balance in stance 'Traffic jam' (42%). An explanation of the most frequently practiced applications per theme is depicted in Table 2.

Table 2. Most frequently performed applications on the GRAIL per theme.

Theme	Gait adaptability	Walking+	Balance in stance
Application	'Microbes'	'Perturbations'	'Traffic jam'
Virtual environment			
Task	Collecting as many green microbes by changing one's position on the treadmill during gait.	Walking on the treadmill and responding as quickly and accurately as possible to the perturbations.	Letting cars cross the road by lifting the feet in stance.
Training purpose	Accelerate and decelerate, change walking direction, adapt step length, avoid obstacles and perform foot clearance.	React to: sideward translation of the treadmill, treadmill pitch forward or backward, acceleration or deceleration of one treadmill belt.	Shift weight, perform foot clearance and initiate steps.

Effect of GRAIL training

Spatiotemporal parameters

The repeated measures ANOVA revealed significant Time effects of GRAIL training on walking speed ($F(2,28) = 18.53$, $p < .001$). Post-hoc analysis showed that the mean walking speed was significantly higher at post measurement (1.04±0.38m/s) compared to baseline 1 (0.85±0.41m/s, $p < .001$) and baseline 2 (0.93±0.37m/s, $p = .003$). There was a significant effect of GRAIL training on the stride length, $F(2,28) = 15.76$, $p < .001$. Stride length was significantly larger at the post measurement (112±31cm) compared to baseline 1 (94±39cm, $p < .001$) and baseline 2 (101±33cm, $p = .002$). Stride frequency ($V = .18$, $F(2,13) = 1.45$, $p = .27$) and step width ($F(2,28) = 1.76$, $p = .19$) were not significantly affected by GRAIL training. The spatiotemporal gait parameters at the three measurements are shown in Figure 6.

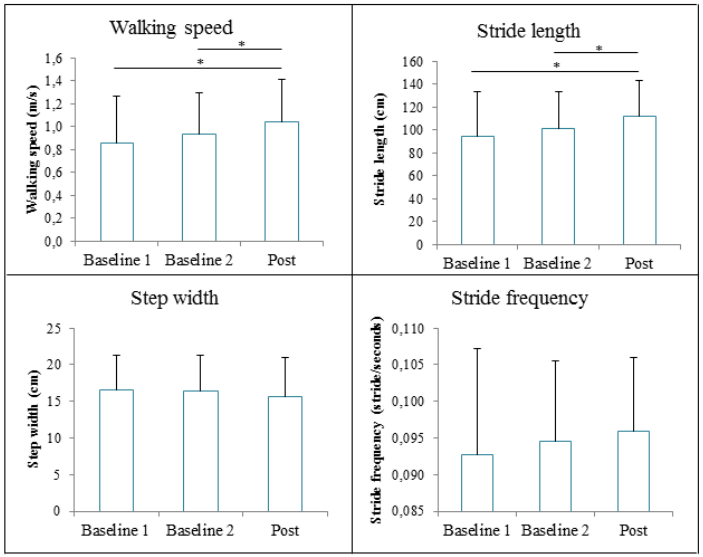

Figure 6. The spatiotemporal gait parameters (means and standard deviations) during the six weeks GRAIL training.

*Asterisk indicates a post-hoc significant difference (α = 0.017).

Gait stability measures

The repeated measures ANOVA revealed significant Time effects on XCoM-CoP_{AP} distance ($F(2,28)= 19.48$, $p<.001$) and CoM-$CoP_{AP\text{-}angle}$ ($F(2,28)= 15.90$, $p<.001$). The XCoM-CoP_{AP} distance was significantly higher at post measurement (491±175mm) compared to baseline 1 (404±195mm, $p<.001$) and baseline 2 (441±177mm, p=.003). The CoM-CoPAP-angle was significantly higher at post measurement (16.6±5.3°) compared to baseline 1 (14.1±5.5°, $p<.001$) and baseline 2 (14.7±4.8°, p=.003). The Time effect on the DSM nearly reached significance ($V=.36$, $F(2,13)= 3.64$, $p=.06$), whereas the XCoM-CoP_{ML} distance ($F(2,28)= 0.003$, $p=.97$) and CoM-$CoP_{ML\text{-}angle}$ ($F(2,28)= 0.38$, p=.69) were not significantly affected by GRAIL training. Figure 7 gives an overview of the gait stability measures across time.

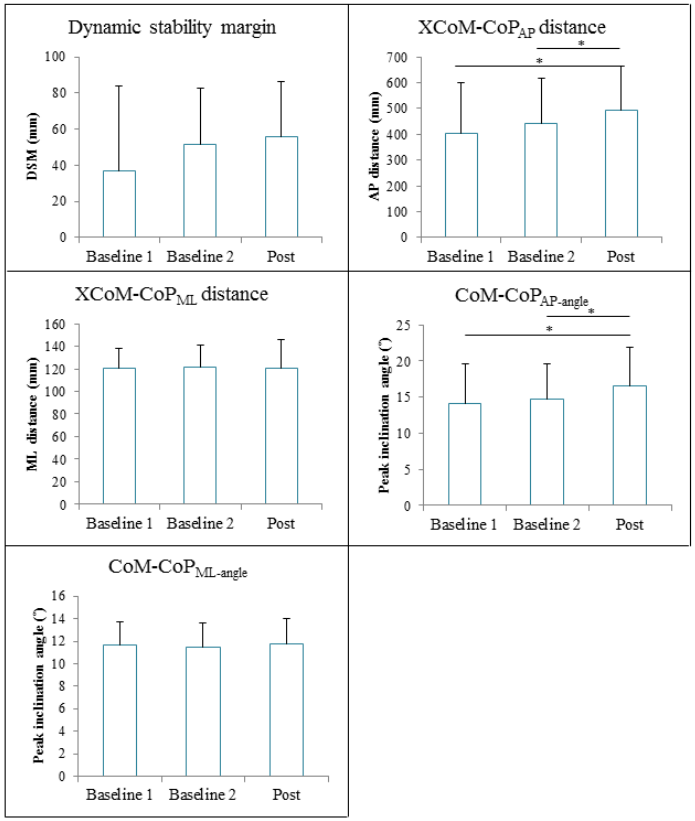

Figure 7. Gait stability (means and standard deviations) during six weeks GRAIL training. A visual representation of the gait stability measures is given in Figure 4.

*Asterisk indicates a post-hoc significant difference (α = 0.017).

Balance confidence

Patients' balance confidence significantly increased after GRAIL training (76±18), compared to baseline (69±18) ($t(13)= -4.55$, p=.001). The balance confidence scores before and after GRAIL training are shown in Figure 8.

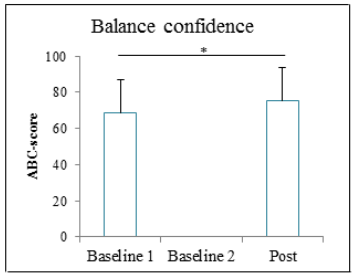

Figure 8. Activities specific balance confidence (ABC) score (means and standard deviations) before and after the six-weeks GRAIL training.
*Asterisk indicates a significant difference (α = 0.05).

Long-term effect of GRAIL training

The follow-up measurement was performed by 11 of the 15 patients (Figure 5). Two patients did not perform the follow-up measurement due to medical complications, which were not related to the GRAIL training. Two other patients were lost to follow-up, because it was impossible to schedule their measurements. As a result of a technical error during the follow-up measurement, the data of one additional patient was missing. Therefore, the results of ten patients were used for the analysis of the long-term effect of GRAIL training (see Table 1 for patient characteristics).

There was no significant difference in walking speed between post (median 1.13m/s) and follow-up (median 1.30m/s) measurement (T= 20.50, p=.48), nor was there a significant difference in stride length (T= 27, p=.96), step width ($t(9)$= 0.82, p=.43), or stride frequency ($t(9)$= -1.04, p= .33) between the post measurement and the follow-up measurement. The CoM-$CoP_{ML\text{-}angle}$ was significantly smaller in the follow-up (10.3±1.6°) compared to the post measurement (11.4±2.2°), ($t(9)$= 2.4, p=.04). The other gait stability measures (DSM, CoM-$CoP_{AP\text{-}angle}$ and XCoM-CoP_{AP} and XCoM-CoP_{ML} distances) and balance confidence score were not significantly different at the follow-up measurement compared to the post measurement. An overview of the spatiotemporal gait parameters, gait stability measures and balance confidence are shown in Table 3.

Walking speed (p=.03), stride length (p=.04) and CoM-$CoP_{AP\text{-}angle}$ (p=.03) were significantly higher in the follow-up measurement compared to at the baseline 2 measurement. The other outcome measures (step width, stride frequency, DSM, CoM-$CoP_{ML\text{-}angle}$ and XCoM-CoP_{AP} and XCoM-CoP_{ML} distances and balance confidence) were not significantly different at the follow-up measurement compared to the baseline 2 measurement (Table 3).

Table 3. The spatiotemporal gait parameters, gait stability measures and balance confidence in the baseline 2, post and follow-up measurement (N=10).
*Asterisk indicates a significant difference (α = 0.05) in the paired samples t-test (mean ± SD) or Wilcoxon signed-rank test (median [min–max]).

	Baseline 2 measurement (mean ± SD, median [min–max])	Post measurement (mean ± SD, median [min–max])	Follow-up measurement (mean ± SD, median [min–max])	*p* baseline 2 - follow-up	*p* post-follow-up
Walking speed (m/s)	0.89 [0.36–1.45]	1.13 [0.44–1.53]	1.30 [0.34–1.48]	.03*	.48
Stride length (cm)	103 [57–144]	118 [68–145]	128 [51–144]	.04*	.96
Step width (cm)	14.4 ± 4.7	13.7 ± 5.0	13.0 ± 4.4	.19	.43
Stride frequency (stride/s)	0.93 ± 0.13	0.96 ± 0.04	0.97 ± 0.05	.07	.33
DSM (mm)	54 ± 36	60 ± 32	57 ± 44	.70	.65
XCoM-CoP_{AP} (mm)	431 [161–718]	511 ± 170	525 ± 201 627 [158–696]	.07	.62
XCoM-CoP_{ML} (mm)	121 ± 23	118 ± 26	111 ± 22	.12	.15
CoM-$CoP_{AP\text{-}angle}$ (°)	15.1 ± 4.6	17.4 ± 5.0	17.7 ± 6.0	.03*	.77
CoM-$CoP_{ML\text{-}angle}$ (°)	10.9 ± 2.3	11.4 ± 2.2	10.3 ± 1.6	.23	.04*
ABC-score	70.3 ± 19.0	77.1 ± 19.3	74.5 ± 20.4	.13	.09

Discussion

The aim of the present study, was to assess the effects of six weeks GRAIL training on gait and dynamic balance capacities in chronic iSCI patients. Walking speed was increased after GRAIL training (1.04m/s) compared to baseline measurements (0.85m/s and 0.93m/s). Stride length was increased, but stride frequency and step width did not change. In addition, the stability measures in AP direction (XCoM-CoP_{AP} and CoM-$CoP_{AP\text{-}angle}$) were improved after GRAIL training, whereas stability measures in ML direction (XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$) or combining AP and ML directions (DSM) did not change. Patients' confidence in balance was increased after GRAIL training. At the six months follow-up measurement, improvements in walking speed, stride length and the stability measure CoM-$CoP_{AP\text{-}angle}$ remained increased compared to baseline.

In patients with iSCI, restoration of ambulation is considered the most important rehabilitation goal.[42] Typically interventions in these patients focus on improving locomotion.[43] For functional ambulation in daily life, walking speed is considered one of the most important parameters.[5] After GRAIL training, walking speed increased by 0.19m/s compared to baseline 1 and by 0.11m/s compared to baseline 2. Although previous studies in chronic iSCI patients used more gait training sessions (on average 45; range 24 - 58) due to a higher training frequency (on average 4 sessions/week; range 3 - 5), and a longer training duration (on average 12 weeks; range 8 - 16), these studies showed increases in walking speed ranging from 0.01 to 0.16 m/s.[24, 44–48] To our knowledge, only two interventions in chronic iSCI patients resulted in an increase in walking speed in the 0.11 to 0.19 m/s range (Kapadia et al., 2014; Alexeeva et al., 2011). These interventions consisted of 48 sessions of resistance training combined with aerobic training resulting in an increase of 0.13m/s[47] and 39 sessions of body-weight-supported treadmill training resulting in an increase of 0.16m/s.[44] Due to the higher number of training session, a

larger training effect can be expected. Despite the limited number of GRAIL training sessions in the present study, patients improved their walking speed significantly. This improvement exceeded the reported minimal clinically important difference (MCID) of 0.10m/s[49] in 10 out of 15 participants, reflecting clinical meaningful effects in these participants. Moreover, the effect on walking speed, stride length and the stability measure CoM-CoP$_{AP\text{-}angle}$ were still present six months after the last training session. Therefore, randomized controlled trials (or studies with a randomized cross-over design) are warranted to investigate the intervention effects of GRAIL training compared to other gait training interventions in patients with iSCI.

The increase in walking speed, accompanied by an increase in stride length but with a constant stride frequency, suggests that patients learned to take larger steps because they felt more confident after GRAIL training. Indeed, the statistically significant increase in balance confidence score supports the notion that patients felt more safe after the training. However, only one participants exceeded the reported minimal detectable change (MDC) of 14.87.[50] Therefore, the effect of GRAIL training on balance confidence seems to be relatively small. Nevertheless, the significant increase in balance confidence on a group level could be due to improved gait stability. In the current study, recently developed biomechanical stability measures were used to assess gait stability. In previous studies, these stability measures appeared to be significantly different between more and less impaired stroke patients,[34] above-knee amputees and healthy subjects,[33] and elderly with and without balance problems.[31,32] To our knowledge, this is the first study to assess these stability measures during gait in a pre- and post-intervention design. The gait stability in AP direction was significantly increased after six weeks GRAIL training. Because a high correlation between walking speed and AP gait stability can be expected and because we did not perform a post measurement in which patients walked at baseline speed, it cannot be definitively concluded whether patients walked faster after GRAIL training because of improved gait stability or vice versa. In the present study, the stability measures in the ML direction did not differ between the measurements. Future research should test the clinical value of gait stability measures in different directions in patients with iSCI.

Various factors could be responsible for the improved walking speed after GRAIL training. Firstly, patients performed tasks in a complex virtual environment, in which visual and auditory feedback were provided. Patients could make corrections and enhance their motor performance according to the feedback in real time (based on knowledge of performance) as well as at the end of the application (based on knowledge of results).[12] It is well accepted that feedback improves the rate of motor learning.[51] Feedback can be particularly beneficial in patients with iSCI in which internal feedback (such as from the proprioceptive system) is disturbed.[52] Secondly, different training environments can be quickly alternated during GRAIL training. According to Hedel and colleagues, in well-recovered iSCI patients, such as in the current study, rehabilitation programs should train adaptive locomotion in different environments.[52] Thirdly, GRAIL training can be personalized and the intensity and complexity of the applications can be gradually increased. We assume that the effects found in the current study are partly due to the personalization of the GRAIL training to the patients' individual goals. Therefore, it does not seen appropriate to standardize the GRAIL training for each patient.

Observed improvements could have been caused by a familiarization effect when walking on the GRAIL in the self-paced mode. To neutralize this effect, two baseline measurements were performed, one at the 2nd and the other at the 3rd GRAIL training sessions. Furthermore, a familiarization protocol with self-paced walking on the GRAIL, similar as in the study of Plotnik and colleagues[30], was performed before the first baseline measurement. In the study of Plotnik and colleagues, healthy participants reached their steady walking speed already after approximately 24m when visual flow was presented and reached a walking speed comparable with overground walking after merely 7.5 to 17.5m[30]. In the current study, an increase of 0.08m/s was seen between the baseline 1 and 2 measurements. This increase could be partly due to familiarization with self-paced walking on the GRAIL. Future research should investigate if familiarization with self-paced walking takes more time in patients with impaired gait stability than in healthy subjects. Important to note is that the self-paced walking was not practiced in the subsequent GRAIL training sessions. Nevertheless, patients further increased their walking speed significantly at the post-measurement compared to baseline 2 by 0.11m/s. Moreover, at six months follow-up, this beneficial effect was still present, suggesting a true effect of GRAIL training.

A limitation of the current study is that the follow-up measurement was completed by only ten patients and that we did not control co-interventions during the period after the GRAIL training. Another limitation is that we do not know how the effect of GRAIL training has affected gait and dynamic balance capacities during overground walking. Although previous studies concluded that self-paced treadmill walking induces natural gait[29] and that gait speed on a treadmill is comparable to overground walking[30], future research should investigate whether the effect of GRAIL training also extends to overground walking, walking in daily life, and to social participation in ambulatory iSCI patients.

Conclusion

The increased walking speed, stride length, AP gait stability, and balance confidence suggest that GRAIL training improves gait and dynamic balance capacity in patients with chronic iSCI.

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Part II

Wearable exoskeleton use in people with complete spinal cord injury

Chapter 4

A framework for measuring the progress in exoskeleton skills in people with complete spinal cord injury

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Abstract

Background
For safe application of exoskeletons in people with spinal cord injury at home or in the community, it is required to have completed an exoskeleton training in which users learn to perform basic and advanced skills. So far, a framework to test exoskeleton skills is lacking. The aim of this study was to develop and test the hierarchy and reliability of a framework for measuring the progress in the ability to perform basic and advanced skills.

Methods
Twelve participants with paraplegia were given twenty-four training sessions in eight weeks with the Rewalk-exoskeleton. During the 2nd, 4th and 6th training week the Intermediate-skills-test was performed consisting of twenty-seven skills, measured in an hierarchical order of difficulty, until two skills were not achieved. When participants could walk independently, the Final-skills-test, consisting of twenty skills, was performed in the last training session. Each skill was performed at least two times with a maximum of three attempts. As a reliability measure the consistency was used, which was the number of skills performed the same in the first two attempts relative to the total number.

Results
Ten participants completed the training program. Their number of achieved intermediate skills was significantly different between the measurements $X_F^2(2)=12.36$, $p=.001$. Post hoc analysis revealed a significant increase in the median achieved intermediate skills from 4 [1–7] at the first to 10.5 [5–26] at the third Intermediate-skills-test. The rate of participants who achieved the intermediate skills decreased and the coefficient of reproducibility was 0.98. Eight participants met the criteria to perform the Final-skills-test. Their median number of successfully performed final skills was 16.5 [13–20] and 17 [14–19] skills in the first and second time. The overall consistency of >70% was achieved in the Intermediate-skills-test (73%) and the Final-skills-test (81%). Eight out of twelve participants experienced skin damage during the training, in four participants this resulted in missed training sessions.

Conclusion
The framework proposed in this study measured the progress in performing basic and advanced exoskeleton skills during a training program. The hierarchical ordered skills-test could discriminate across participants' skill-level and the overall consistency was considered acceptable.

Keywords: Spinal cord injury, exoskeleton, paraplegia, ambulation, skills

Introduction

Worldwide the incidence of Spinal Cord Injury (SCI) is 180.000 cases per annum[1] of whom 50% have a complete lesion and become wheelchair-designated for their mobility.[2] A lifetime of sitting has been associated with an increased risk of multiple secondary complications, such as pressure ulcers, spasticity, and worsening of bladder and bowel dysfunction.[3,4] Exoskeletons (external active orthosis) make it possible for people with paraplegia to regain their standing and walking mobility by generating the basic motions for ambulation e.g. standing-up, sitting-down, standing and walking. Similar to other standing and robotic gait training devices,[5–7] exoskeletons have the potential to prevent secondary health complication.[8] The main benefit of exoskeletons compared to other robotic gait training devices (such as Lokomat®) is that exoskeletons can be used at home and in the community outside of a clinical setting.[9] However, several risks are identified with exoskeleton use such as falls, joint misalignment, skin damage, software malfunctions, electrical and fire hazard, and user errors.[10] So far, the chance and extent of the risks are not well understood.[10] Furthermore, manufacturers require an intensive training period before home and community use is allowed.

A prerequisite for safe and independent home and community exoskeleton use, is that users are able to perform basic and advanced exoskeleton skills. Previous research mainly focussed on the basic skills (sit-to-stand, stand-to-sit and walking) and has shown that basic skills can be learned in a 25 sessions-training program with varying levels of assistance.[11–13] The basic skills are highly relevant for use in a clinical setting, but for safe independent community use more advanced skills are required, including arresting gait on command, passing door thresholds, low curbs and ramps and controlling the input device[13,14]. The control of and interaction with the exoskeleton is diverse across the different exoskeletons available on the market. Moreover, some exoskeletons are more difficult or impossible to control dependent on the level and severity of the SCI of the user.[15] Several studies tested advanced skills in a limited number of motor complete SCI patients.[11–13,16,17] However, the advanced skills were not tested in a systematic way and for example Spungen and colleagues concluded that the skills could have been introduced earlier in the training program.[13] So far, a systematic framework to structure, test and evaluate exoskeleton skills during a training program is lacking. Therefore, the aim of this study is to develop a framework to measure the progress in the ability to perform exoskeleton skills. The proposed framework consists of exoskeleton skills arranged into a hierarchy so that the difficulty increased with each tested skill. If the exoskeleton skills formed a true hierarchy and a skill was not achieved, it can be assumed that the participant would not achieve all higher skills and would achieve all lower skills. Therefore, arranging the skills into a hierarchy would reduce the time and effort of the exoskeleton-skills-test.[18] Furthermore, it is essential that the exoskeleton-skill-tests in the framework are reliable. Accordingly, the skills had to be performed consistent to reduce the change of misjudging the participants' skill-level.

Before an advanced exoskeleton skill-level can be achieved, an intensive training program with multiple training sessions per week over a longer period of time is required. The risk factors associated with such an intensive training program are still not well understood.[10] However, it can be expected that such an intensive training program decreases the risk of falls, joint misalignment and user errors and increases the safety of exoskeleton home and community use. On the contrary, intensive exoskeleton use increases the risk of skin damage

and bruises. Previous research concluded that in hospital training with an exoskeleton was safe.[13,19–22] However, other studies disclosed mild to moderate skin damages in half of the participants (5 out of 10)[16] (4 out of 7).[12] Other reported complications were a fracture of the talus[23] and venous-lymphatic stasis in the lower limbs.[24] Hence, assessing the occurrence of complications such as skin damage, muscle or joint pain, incontinence problems, device related errors, fractures, venous-lymphatic stasis and falls during an exoskeleton training program is important for clinical recommendations.

In conclusion, the main objective of this study was to develop and test a framework for measuring the progress to perform basic and advanced exoskeleton skills in a group of individuals with motor complete SCI. The hierarchy and the reliability of the exoskeleton-skills-test in the framework was evaluated. As a secondary outcome, complications such as skin damage, muscle or joint pain and incontinence problems resulting from the intensive exoskeleton training program were assessed.

Material and Methods

Participants

People with paraplegia who gained knowledge about the exoskeleton technology throughout the media and who were interested in testing the potential of an exoskeleton contacted the rehabilitation centre of the Sint Maartenskliniek to participate in this study. Eligible persons were adult patients in the chronic phase (>6 months) with a motor complete SCI (American Spinal Injury Association Impairment Scale (AIS) A or B) between Thoracic 1 (Th1) and Lumbar 1 (L1). The exclusion criteria were physical factors that hamper proper functioning of the exoskeleton, such as severe spasticity (Modified Ashworth Scale > 3), taller than 1.90m or smaller than 1.60m, bodyweight above 100kg and restricted range of motion in the hip, knee or ankle joint. Other exclusion criteria were inability to control crutches, unable to make a transfer from a chair to a wheelchair without the use of external support, and patients with conditions that could interfere with the motor learning process (e.g. stroke). Potential subjects with an increased risk of adverse events such as patients with osteoporosis, fractures of the lower extremities in the last two years, balance disorders, neurogenic heterotopic ossification and pregnancy were also excluded. All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the medical ethics committee of Arnhem-Nijmegen (2016-2418) and the internal review committee of the Sint Maartenskliniek.

Procedure

All exoskeleton training sessions and measurements were performed in the sports hall at the rehabilitation centre. Prior to the start of the training a brief physical examination by a rehabilitation physician was performed, in which the in- and exclusion criteria of the study were checked. Participants were given twenty-four training sessions of 1.5-hour over an eight week period. Three physical therapists were trained by ReWalk™ Robotics to give the exoskeleton training. During each session at least two physical therapists were present to assure safety. The exoskeleton and the Lofstrand crutches were adjusted to the patients' body composition during the first training session. After each training the physical therapists notated the skills that were practiced. Participants kept a logbook during the entire study including any complications such as skin abrasions, muscle or joint pain, falls and incontinence problems. The logbook was filled out at least three times a week. To assess the progress in achieved skills the participants' skill-level was tested every two weeks during a training session. In total the skill-level was assessed four times during the study, three times with the Intermediate-skills-test and one time with the Final-skills-test.

Intermediate- and Final-skills-test

The Intermediate-skills-test was performed in training week 2, 4 and 6. The Intermediate-skills-test consisted of twenty-seven skills, which were measured separately of each other and were arranged into a hierarchy so that the difficulty increased with each skill. The intermediate skills were sorted into three categories; standing, walking, and advanced skills. Each subsequent category required more control of the user over the exoskeleton. Within each category the complexity of the skills also increased. In the standing skills the feet of the user remained roughly at the same place and participants learned to use their crutches, whereas there was displacement of the feet in the walking and advanced skills. In the walking skills, the increase of difficulty was related to the decrease in level of assistance and number of involuntary stops. In the advanced skills an additional task was performed while walking. The complexity of the task increased from walking turns with a decrease in number of involuntary stops to passing obstacles to passing obstacles that require raising or lowering of the centre of mass (walk up and down a martial arts mat). An overview of the twenty-seven skills of the Intermediate-skills-test is given in Table 1. Each intermediate skill was performed at least two times with a maximum of three attempts. An intermediate skill was considered achieved when the skill was performed independent without assistance of the exoskeleton trainer in at least two out of three attempts. The Intermediate-skills-test continued until two skills were not achieved. Participants were allowed to take rest between the various skills tested.

Table 1. Assessed exoskeleton skills in the Intermediate-skills-test

Category	Order	Intermediate skill
Standing skills	1	Weight shifting forward and backward and to the right and left
	2	Touching the wristband during standing
	3	Sit-to-stand
	4	Stand-to-sit
Walking skills	5	Walk 10m with assistance (with max. 2 stops)
	6	Stop with the preferred leg
	7	Stop with the not preferred leg
	8	Walk 10m without assistance (with max. 2 stops)
	9	Walk 10m without assistance (without stops)
Advanced skills	10	Arrest gait at command
	11	Walk a 90° curve to the right (with max. 1 stop)
	12	Walk a 90° curve to the right (without stops)
	13	Walk a 90° curve to the left (with max. 1 stop)
	14	Walk a 90° curve to the left (without stops)
	15	Walk a 180° curve (radius 1.8m) to the right (with max. 1 stop)
	16	Walk a 180° curve (radius 1.8m) to the right (without stops)
	17	Walk a 180° curve (radius 1.8m) to the left (with max. 1 stop)
	18	Walk a 180° curve (radius 1.8m) to the left (without stops)
	19	Arrest gait nearby a vaulting box (height 1.1m) and move a cone at chest height
	20	Pass a narrow passage (width 0.8m) (with max. 1 stop)
	21	Arrest gait nearby a door (width 0.8m), open the door away from you and enter (with max. 1 stop)
	22	Arrest gait nearby a door (width 0.8m), open the door towards you and enter (with max. 1 stop)
	23	Arrest gait near a chair (height 0.5m) and pivot turn to sit down
	24	Pass an upward and downward sloping doorstep (angle up 11.3˚and down 16.7˚, height 0.03m) (with max. 1 stop)
	25	Walk up a martial arts mat (height 0.04m) (with max. 1 stop)
	26	Walk down a martial arts mat (height 0.04m) (with max. 1 stop)
	27	Walk a slalom around 4 badminton poles (distance between poles 3.0m) (with max. 2 stops)

The Final-skills-test was performed during the last training week (week 8) in the final training session. A prerequisite for performing the Final-skills-test was that participants could control the remote control and walk without assistance of the exoskeleton trainer. The Final-skills-test consisted of a fixed set of twenty skills and was performed two times with a 5 minute break in between. In contrast to the Intermediate-skills-test, the tested exoskeleton skills were measured in sequence during the Final-skills-test, simulating daily life situations in which skills are rarely performed independent of each other. Moreover, performing skills in sequence made it more difficult to achieve a skill than performing skills independent from each other (e.g. arresting gait immediately after a sharp curve compared to arresting gait independent of the previous action).In the Final-skills-test the focus was on independent performance of skills

and the number of stops was not taken into account. Furthermore, the basic intermediate skills (e.g. weight shifting, touching the wristband, sit-to-stand and assisted walking) are required in performing most of the skills and were not tested separately. In order to assess the test in a sports hall with as little material as possible, the advanced intermediate skill of opening a door was not part of the Final-skills-test. To assure safety, the exoskeleton trainer walked behind the participant but did not intervene unless the participants lost their balance and could fall. The final skills were considered achieved when the participants performed the skills without assistance of the exoskeleton trainer. In Figure 1 a schematic representation of the Final-skills-test is given.

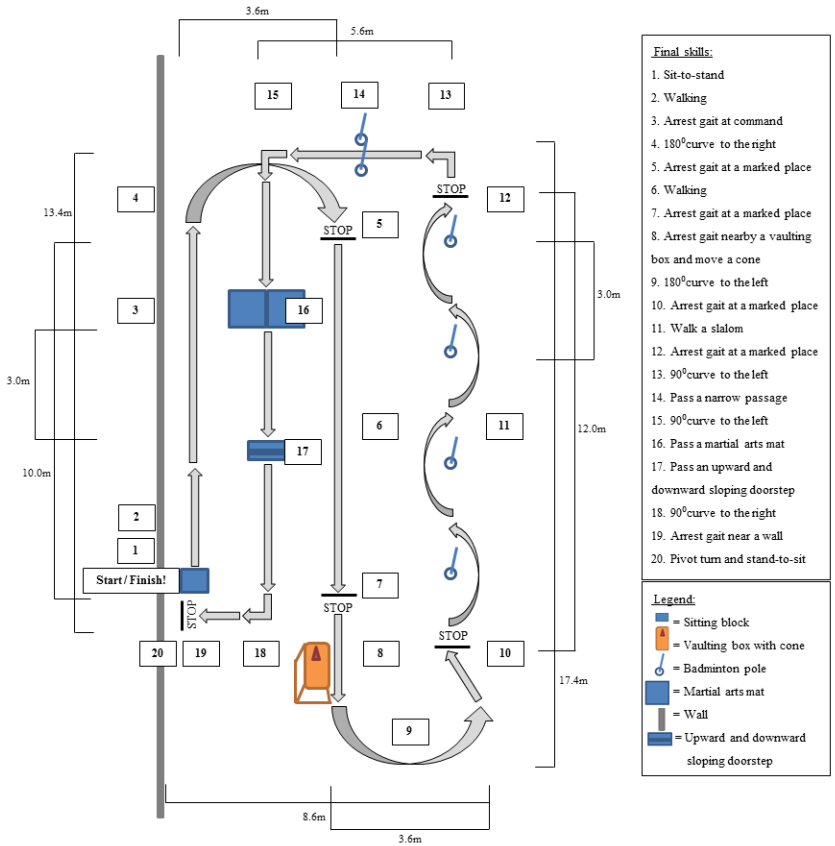

Figure 1. Schematic representation of the top view of the Final-skills-test. Arrows represent the walking direction.

Equipment

In this study two wearable robotic exoskeletons that enable powered hip and knee motion from ReWalk™ Robotics were used; (1) the ReWalk™ Rehabilitation System and (2) the ReWalk™ Personal 6.0. The exoskeleton systems provided user-initiated mobility through the integration of a wearable brace support, a computer-based control system and motion sensors. The exoskeleton systems have the Class II FDA clearance for both use in a rehabilitation setting as well as personal use. All participants started training with the ReWalk™ Rehabilitation System. Only participants who met de criteria to perform the Final-skills-test used the ReWalk™ Personal 6.0 system as well.

Data and statistical analysis

To assess if the proposed framework measured the ability to perform basic and advanced exoskeleton skills throughout an exoskeleton program, the skill-tests in the framework should measure progression in the number of achieved skills and show distinct skill-levels between participants. The skills should be arranged into a hierarchical order of difficulty. Moreover, the skills tested in the framework should be performed consistent. In addition, the relation between the Intermediate- and Final-skills-test was determined.

Achieved intermediate skills

The number of achieved skills was analysed using descriptive statistics (median and ranges). Differences in the number of achieved skills between the three Intermediate-skills-test was assessed with the non-parametric Friedman test (α=.05). In case of a significant Friedman test, Wilcoxon post-hoc test with Bonferroni correction (α=.017) was used to determine changes. The number of participants who showed the expected increase in number of achieved skills over the three intermediate measurements was determined. Each intermediate skill was also analysed separately for the number of times a skill was achieved.

Hierarchy of the skills

The hierarchy of the skills tested in the Intermediate-skills-test was analysed according to two measurements (1) the rate of participants achieving each intermediate skill and (2) the coefficient of reproducibility (Tyson & DeSouza, 2004[18]). Both tests are based on the theoretical expectation that the participants ability to achieve a skill would decrease as the difficulty of the task increased. For a more detailed description see Tyson and DeSouza (Tyson & DeSouza, 2004[18]). The coefficient of reproducibility was calculated with the formula described by Tyson and DeSouza: Coefficient of reproducibility = 1 – scaling errors / (number of skills x number of observations) (Tyson & DeSouza, 2004[18]). In which scaling errors is the number of participants who did not achieve the skills in the predetermined order. Since participants progressed during the training each intermediate skills measurement was considered as a separate observation in the analysis. A coefficient of reproducibility of at least 0.9 was considered acceptable (Guttman, 1944;[25] Tyson & DeSouza, 2004[18]).

Achieved final skills

The number of achieved final skills was analysed using descriptive statistics (median and ranges). Each final skill was also analysed separately for the number of times a skill was achieved. The correlation between the number of achieved skills in each skills-test was assessed with Kendall's rank correlation coefficient (Kendall's Tau).

Consistency

The consistency in the number of exoskeleton skills which were performed the same in the first two attempts (successful-successful or failure-failure) relative to the total number of performed skills was used as a reliability measure of the Intermediate-skills-test and the Final-skills-test. An overall consistency of >70% was considered reliable. Each intermediate skill and final skill was also analysed separately for the number of times a skill was tested, performed consistent and performed successful.

Complications

To assess the occurrence of complications during an exoskeleton training program both the physical therapists and participants filled out a logbook after each training session including any complications. The reported complications such as the number of skin damages, location of skin damages, incidence of reported muscle or joint pain, number of incontinence problems, device related errors, fractures, venous-lymphatic stasis and falls during the exoskeleton training program were analysed using descriptive statistics.

Results

Participants

Out of twelve participants ten (83%) completed the training program. Reasons for not completing the training program were inability to learn the basic skills of the exoskeleton (stopped after 7 training sessions and performed the first Intermediate-skills-test) and absence of perceived benefit (stopped after 2 training sessions and did not perform an Intermediate-skills-test). Eleven participants completed at least one Intermediate-skills-test, the data of these participants was used in the analysis of the hierarchy and consistency of the intermediate skills. Due to time constraints, one participant was not able to perform the skills a second time during the Final-skills-test. For this participant the set of final skills was repeated twice one week later. The data of the second Final-skills-test was only used for the consistency analysis whereas the first Final-skills-test was used for the analysis of the achieved skills after the training program. We do not expect that this had an impact on the outcome of the current study. An overview of the patient characteristics is given in Table 2.

Table 2. Patient characteristics

	Total (N=12)
Gender (male/female)	7 / 5
Age (years), median [range]	42 [24 – 56]
Level of SCI, median [range]	Thoracic 9 [4 – 11]
Post-injury (months), median [range]	75 [24 – 276]
AIS* (A/B)	11 / 1

* AIS = American Spinal Injury Association Impairment Scale

Achieved intermediate skills

The Friedman test revealed a significant difference between the number of achieved intermediate skills between the measurements (X_F^2 (2) =12.36, p=.001). Post hoc analysis revealed that the achieved intermediate skills significantly increased from a median of 4 [1 – 7] at Intermediate-skills-test one to 10.5 [5 – 26] at Intermediate-skills-test three. There was no significant difference in the number of achieved skills between Intermediate-skills-test one and two and between two and three. Figure 2 shows the achieved intermediate skills per participant. Five out of ten participants showed the expected increase in number of achieved skills over the three measurements.

Detailed post-hoc analysis revealed that five of the intermediate skills were achieved during all measurements (see completely green bars in Fig. 3). Three out of five intermediate walking skills, and two advanced skills were achieved in approximately half of the tested times, these skills are highlighted with an '#'-sign in Figure 3.

Hierarchy of skills

In general, the rate of participants who achieved the intermediate skills decreased. In three skills, the 'walk 10m without stops', '180° curve to the right without stops', and 'open door towards'-skill, the number of participants who achieved the skills was smaller than skills later in the hierarchical order (Fig. 4). The coefficient of reproducibility was 0.98 (number of scaling errors: 14, number of skills: 27 and number of observations: 31 (10 participants with 3 observations and 1 participant with 1 observations). The scaling errors occurred in 9 different skills (Intermediate-skill 3, 4, 6, 7, 9, 10, 12, 16 and 22) and in 8 out of 11 participants. Four scaling errors occurred in Intermediate-skills-test one, 3 in Intermediate-skills-test two, and 7 in Intermediate-skills-test three.

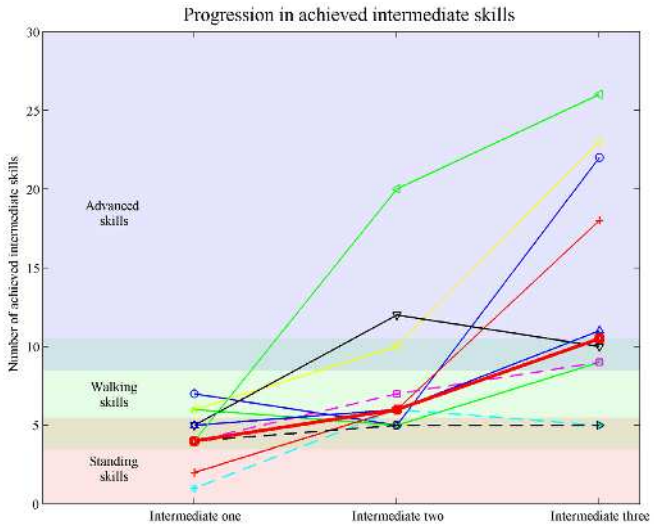

Figure 2. Achieved intermediate skills measured with the Intermediate-skills-test one, two and three. Each line represents a participants. Thick red line represents the median achieved intermediate skills. Dotted lines represent participants who did not perform the Final-skills-test.

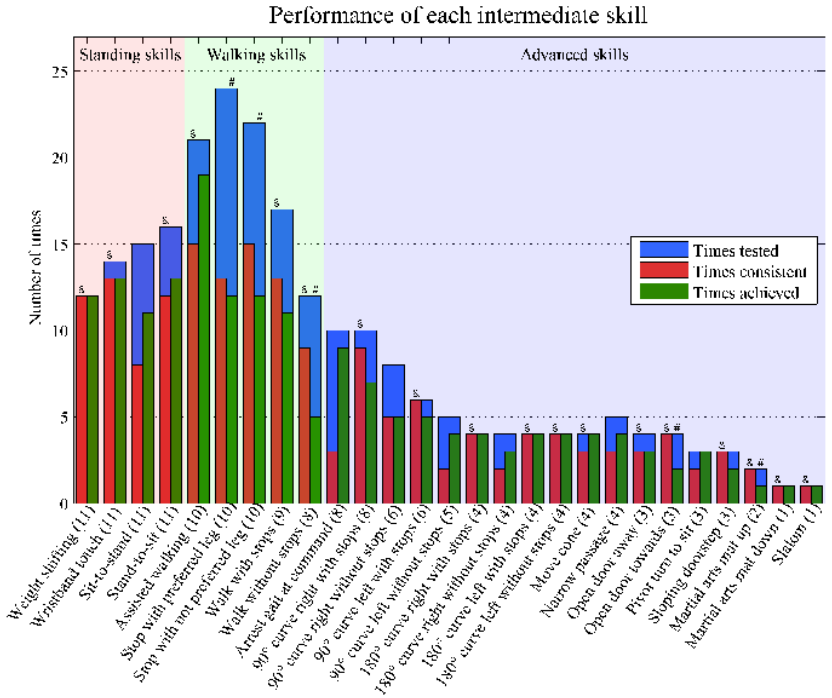

Figure 3. Times performed consistent and achieved of each separate intermediate skill. Numbers in brackets represent the number of tested participants.

Consistent = performed the same in the first two attempts (successful-successful or failure-failure)
Achieved = at least two out of three successful attempts
& = >70% performed consistent
# = achieved in approximately 50% of the times

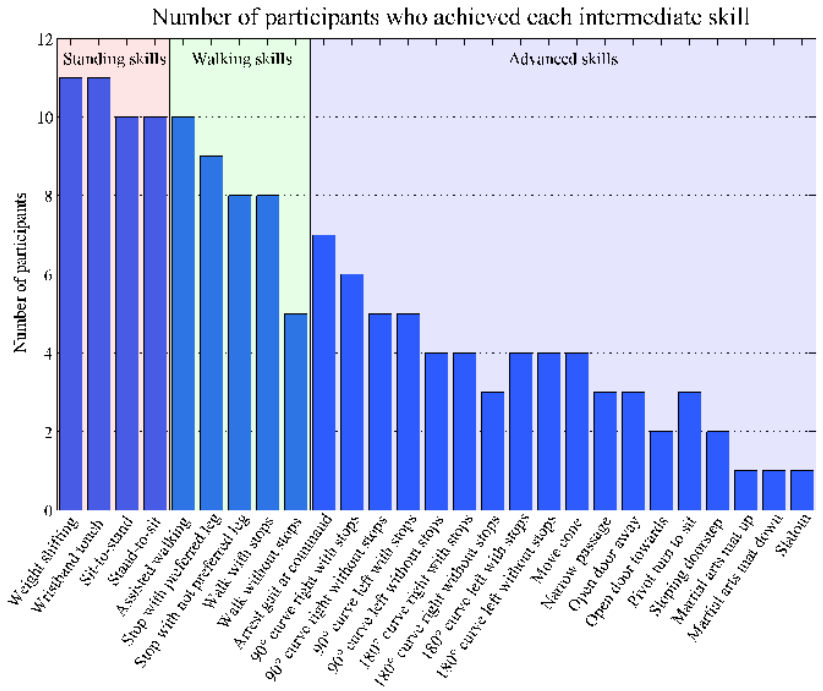

Figure 4. Rates of achievement of each intermediate skill.

Achieved final skills

Eight participants were able to walk without assistance between the 18th and 23th training session and therefore met the criteria to perform the Final-skills-test. The median number of successfully performed final skills in these participants was 16.5 [13 – 20] and 17 [14 – 19] skills in the first and second time. In the Final-skills-test, fifteen skills were at least one time achieved by all eight subjects (see Fig. 5). The martial arts mat was not achieved by half of the participants.

The number of achieved final skills in the first and the second time were significantly correlated (r_T =.75, p<.05) and not significantly different (z=-.71, p=.75, effect size=-.18). Table 3 revealed the correlation between the various skills-tests. The number of achieved skill in none of the Intermediate-skills-tests were significantly correlated with the achieved skills in any other skill-tests.

Table 3. Correlation (Kendall's tau) between all test moments. Digits in brackets represent the number of participants.

	Intermediate-skills-test 1	Intermediate-skills-test 2	Intermediate-skills-test 3	Final-skills-test 1	Final-skills-test 2
Intermediate-skills-test 1		-.15 (10)	.29 (10)	.08 (8)	.21 (8)
Intermediate-skills-test 2			.37 (10)	.00 (8)	-.13 (8)
Intermediate-skills-test 3				.15 (8)	.32 (8)
Final-skills-test 1					.75 (8)*

*. Correlation is significant at the .05 level

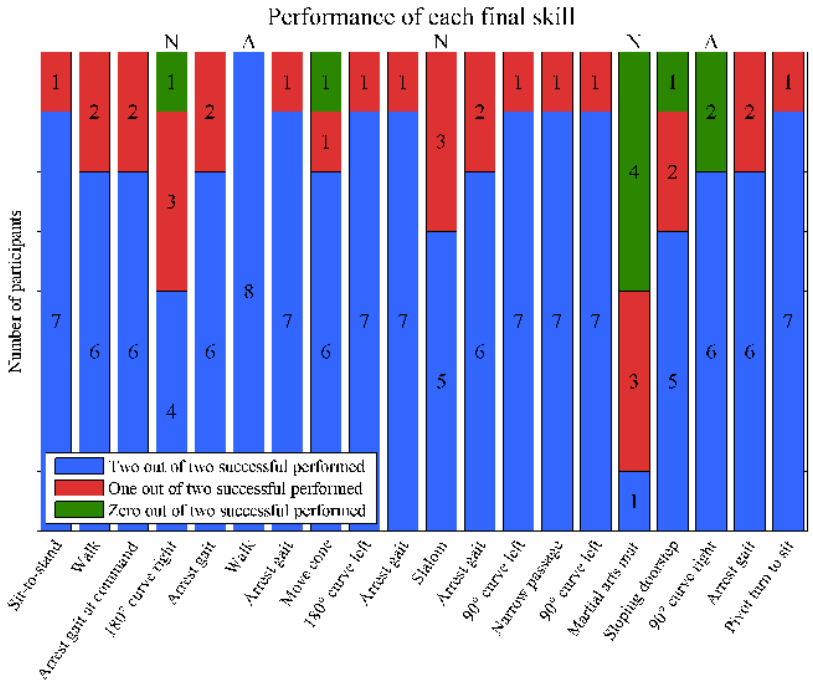

Figure 5. The number of consistent performances of each final skill. Green bars represent inconsistent performances in which one out of two attempt was successful performed. Blue and red bars represent consistent performances.

A = all performed consistent
N = <70% performed consistent

Consistency

Eleven participants performed in total 235 intermediate skills, of which 171 (73%) were performed the same in the first two attempts (successful-successful or failure-failure).

The number of participants who performed the skill, the number of times a skill was measured, the number of times a skill was performed consistent and the number of times a skill was achieved is shown for each intermediate skill in Figure 3. Eighteen skills were performed consistent in more than 70% of the times (highlighted with an '&'-sign in Fig. 3). Of these skills, ten skills were performed consistent during all Intermediate-skills-tests (see completely red bars in Fig. 3).

Eight participants performed all twenty final skills twice resulting in a total of 160 final skills. They performed 130 (81%) final skills the same in both attempts. The median number of inconsistent performed skills per participant was 2.5 [0 – 9]. An overview of the consistent and inconsistent performances of each final skill is depicted in Figure 5. Most skills were performed consistently by seven (9 skills) or six (6 skills) participants. Two skills were performed consistently by all participants (highlighted with an 'A'-sign in Fig. 5), whereas three skills were performed inconsistent by three participants (180° curve to the right, slalom and martial arts mat) (highlighted with an 'N'-sign in Fig. 5).

Complications

Eight out of twelve participants experienced device related skin damage at the feet (*n*= 3), knee (*n*= 5), thigh (*n*= 3), pelvic (*n*= 4) and/or trunk (*n*= 1) area. In four participants the skin damage resulted in at least one missed training session, which was rescheduled at the end of the training period. In case of skin damage, extra padding was added to prevent reoccurrence of the complication. As a result, most skin damage occurred in the early phase of the training program. Seven participants reported muscle or joint pain during the training program around the hands/wrists (*n*= 2), arms (*n*= 3), shoulders (*n*= 3), neck (*n*= 3), trunk (*n*= 1) and/or back (*n*= 3). None of the complications evolved into serious adverse events. During the entire study the incidence of device related errors was three times in 218 training sessions. No incontinence problems, fractures, venous-lymphatic stasis or falls were mentioned by the participants or physical therapists in the study.

Discussion

In the present study, a framework for measuring the ability to perform basic and advanced exoskeleton skills throughout an exoskeleton training program was developed and tested. Ten participants completed the training program and were tested during the 2^{nd,} 4th and 6th training week. They showed an increase in the achieved intermediate skills from 4 at the first to 10.5 at the third Intermediate-skills-test. The rate of participants who achieved the intermediate skills decreased and the coefficient of reproducibility was 0.98. In the last training week, eight participants successfully performed 16.5 and 17 skills in the Final-skills-test. An overall consistency of 73% in the Intermediate-skills-test and 81% in the Final-skills-test was achieved.

Similar to other assistive technologies, such as prostheses and to a lesser extent wheelchairs, exoskeleton community use is preceded with a training program. Although the type and extent of the risks of exoskeletons are yet to be understood,[10] the risks associated with exoskeleton use seems higher than with prostheses or wheelchair. The advantage of a prostheses and a wheelchair is that it can be used independently for ambulation in an early phase. Therefore, clinical tests such as the timed up and go-test[26] or the mechanical efficiency[27] can be used to evaluate the progress in performance in using the assistive technologies. In contrast, most people are not able to perform basic ambulation skills at the start of an exoskeleton training program and multiple training sessions are needed before independent ambulation is possible. Assessing performance in using assistive technologies can also be done with standardized skills-tests. For wheeled mobility several skills-test, such as the wheelchair skills-test, are available.[28] Until now there were no standardized skills-test for exoskeleton performance. Several studies marked the training session in which a skill with an exoskeleton was performed with varying levels of trainer assistance.[11–13,16,17] However, in these studies the performed exoskeleton skills were kept up in a logbook and the independent achievement of skills was not tested on a regular bases. The main objective of this study was to develop a framework for measuring the ability to perform basic and advanced exoskeleton skills throughout an exoskeleton training program.

A framework to assess the progress of exoskeleton skills should consist of tests measuring achieved skills in a hierarchical order of difficulty. As a consequence participants should progress during an intensive exoskeleton training program. Although the Friedman test revealed a significant difference in the number of achieved skills between the Intermediate-skills-tests, these results should be interpreted with care because several tied ranks were observed and a small number of participants were included. Nevertheless, the number of achieved intermediate skills significantly increased from 4 at the first to 10.5 at the third Intermediate-skills-test. Furthermore, 9 and 7 out of 10 participants had an increase in the number of achieved skills between the first and second and the second and third Intermediate-skills-test, respectively. However, such an increase in number of achieved skills doesn't automatically indicate that the skills are in a correct order of difficulty. In the current study, two measures were used to assess the hierarchy. According to the coefficient of reproducibility (0.98) the intermediate skills were in the correct order of difficulty.[18,25] The rate of the number of participants achieving each skill revealed three skills (walk 10m without stops, 180° curve to the right without stops, and open door towards-skill) that were achieved by a larger number of participants in the subsequent skill. Detailed post hoc analysis revealed that only an unachieved 'walk 10m without stops'-skill was followed by achieved skills in more than two observations (five observations). Covering a distance of 10 meters without stops was the last basic skills before advanced skills were tested. The advanced skills consisted of an additional task during walking such as a sudden stop, curves or passing a doorstep, but a shorter distance of approximately 3 meters had to be covered. The length of the skill of walking a distance of 10 meters increased the chance of errors and not achieving the skill. Two other studies (Spungen en Platz) also recorded the moment the 10 meters walking skill was performed without assistance, four[13] and one[12] out of seven participants were able to perform the skill independent within 24 training sessions. Indicating the difficulty of walking 10 meters without assistance. In the current study each test session was scheduled in advance within a training session and an extra person was present during the skills-test. As a result, most participants were more stressed during the skills-test than during other training sessions.

An increased stress level could evoke more spasticity[29] causing involuntary stops, which particularly influenced the achievement of the '10m walking skill without stops'-skill. Because walking without stops is crucial in performing most advanced skills, we prefer to keep the proposed order of the skills. However, for future research we would advise to change the order of the Intermediate-skills for the 'walking curves' according to the preference of the patient.

In addition to assess the progression, the framework had to discriminate across participants. In all Intermediate-skills-tests, differences between participants were apparent. After two weeks of exoskeleton training participants were only able to perform basic skills, but varied between standing and walking skills. This was in line with the findings of Spungen and colleagues.[13] In the current study, all participants were able to perform all intermediate standing skills without assistance after four and six weeks of training, but differed in walking and advanced skills. In addition to differences across participants at the Intermediate-skills-tests, participants showed various learning curves. The low correlation between the three Intermediate-skills-tests (r_T between -.15 and .37) supports the various learning process across participants. In conclusion, the framework proposed in this study measured the progress in the ability to perform basic and advanced exoskeleton skills, had the skills in a hierarchical order of difficulty and could discriminate across participants.

A second important prerequisite of the framework is that the tested skills were reliable. An overall consistency of 73% in the Intermediate-skills-test and 81% in the Final-skills-test was achieved. Detailed analysis revealed several skills that had a consistency of less than 70% (See Fig. 3 and 5). Remarkable was a lower consistency for the same skills in the Intermediate-skill-test compared to the Final-skill-test or vice versa. A consistency below 70% in the Intermediate-skill-test whereas a consistency above 70% in the Final-skill-test was met for the skills: sit-to-stand, stopping with the preferred or not preferred leg, arresting gait at command, passing a narrow passage, and pivot-turn to sit. The lower consistency of the intermediate skills were possibly due to the learning process. During the Intermediate-skills-test participants had to perform skills they practiced only once or twice without assistance. As a result, the skill was sometimes successfully performed by chance instead of competence and therefore participants were unable to perform the skill consistent. Therefore, we recommend that a skill should be performed at least two times when tested. The skills 180° curve to the right, slalom and martial arts mat had a low consistency in the Final-skills-test whereas a high consistency was obtained in the Intermediate-skills-test. These skills were performed by only a minority of the participants during the Intermediate-skills-tests indicating that most participants were only in the last training sessions at a level that they could practice these advanced skills. Nevertheless, the majority of the tested skills were performed consistent in the Intermediate- and Final-skills-test. Therefore, considering a skill achieved after two out of three successful attempts seems a good assumption to evaluate the skill-level.

In order to achieve exoskeleton skills, participants received multiple training sessions per week over an eight week period. Such an intensive training program yields the potential of complications such as bruises and other skin damage. Most previous studies indicated that in hospital training with an exoskeleton was safe.[8,13,19–22] Although other studies disclosed mild to moderate skin damages in half of the participants (5 out of 10)[16] (4 out of 7),[12] the intensity (session per week) and duration of the training period in this study was similar to most previous studies.[8,12,13,16] In the current study, eight out of twelve participants experienced skin damage during the training program. In four cases this skin damage resulted in at least one missed training. Whereas all skin damages reported in the study of Benson and none of the skin damages reported by Platz led to discontinuation of the training.[12,16] Because of extra padding in the early phase of the training program, skin damage rarely occurred in the later phase. In addition, during the whole training program special care was taken to the correct joint alignment. Therefore, none of the patients had to reduce the training intensity in the later phase of the training program. Moreover, it suggests that special attention to joint alignment and padding during the training reduces the risk of skin damage.

In the current study, the ReWalk exoskeleton was used. Nowadays, there are multiple exoskeletons available on the market, which have their specific interaction with and control of the exoskeleton. As a consequence the hierarchical order of the skills in the framework might be slightly different between exoskeletons. The main difference between the current available exoskeletons for home and community is the control of initiation of gait, arresting of gait and involuntary stops. For example, to initiate gait, the ReWalk and Ekso require a forward and lateral shift of the trunk, the Indego exoskeleton requires a forward trunk excursion, and the Rex exoskeleton does not require any trunk movement.[15] Despite the differences in interaction with and control of the exoskeleton, all skills proposed in the current study are relevant and applicable to the current available exoskeletons. Standing and walking skills are presumed to be achieved before users can perform additional advanced skills, which are mostly performed during walking. The first eight advanced skills, require less interaction with the environment. Within these skills a distinction was made in the fluency of the performance (with or without stops). Therefore, we expect that the hierarchical order of the first eighteen intermediate skills can be applied to other exoskeletons. The hierarchical order of the last nine advanced skills might be slightly different across exoskeletons due to the difference in interaction with and control of the exoskeleton. However, achieving one of these skills indicates a highly advanced exoskeleton skill level.

The skills-tests proposed in this framework were based on independent performance of exoskeleton skills, but did not take the quality of the performance into consideration. For future research, the quality of how a skill is performed might be of interest in addition to if it is possible to perform a skill independent. Moreover, all exoskeleton skills in this study were assessed in a clinical setting and it remains unknown which skills are relevant and which skill-level is necessary for safe community use. Therefore, future research should focus on community use of an exoskeleton and its relation to the skill-level during the training period measured with the proposed framework.

Conclusion

The framework proposed in this study measured the progress in performing basic and advanced exoskeleton skills during a training program. The hierarchical ordered skills-test could discriminate across participants' skill-level. The overall consistency of the performed exoskeleton skills was considered acceptable.

4

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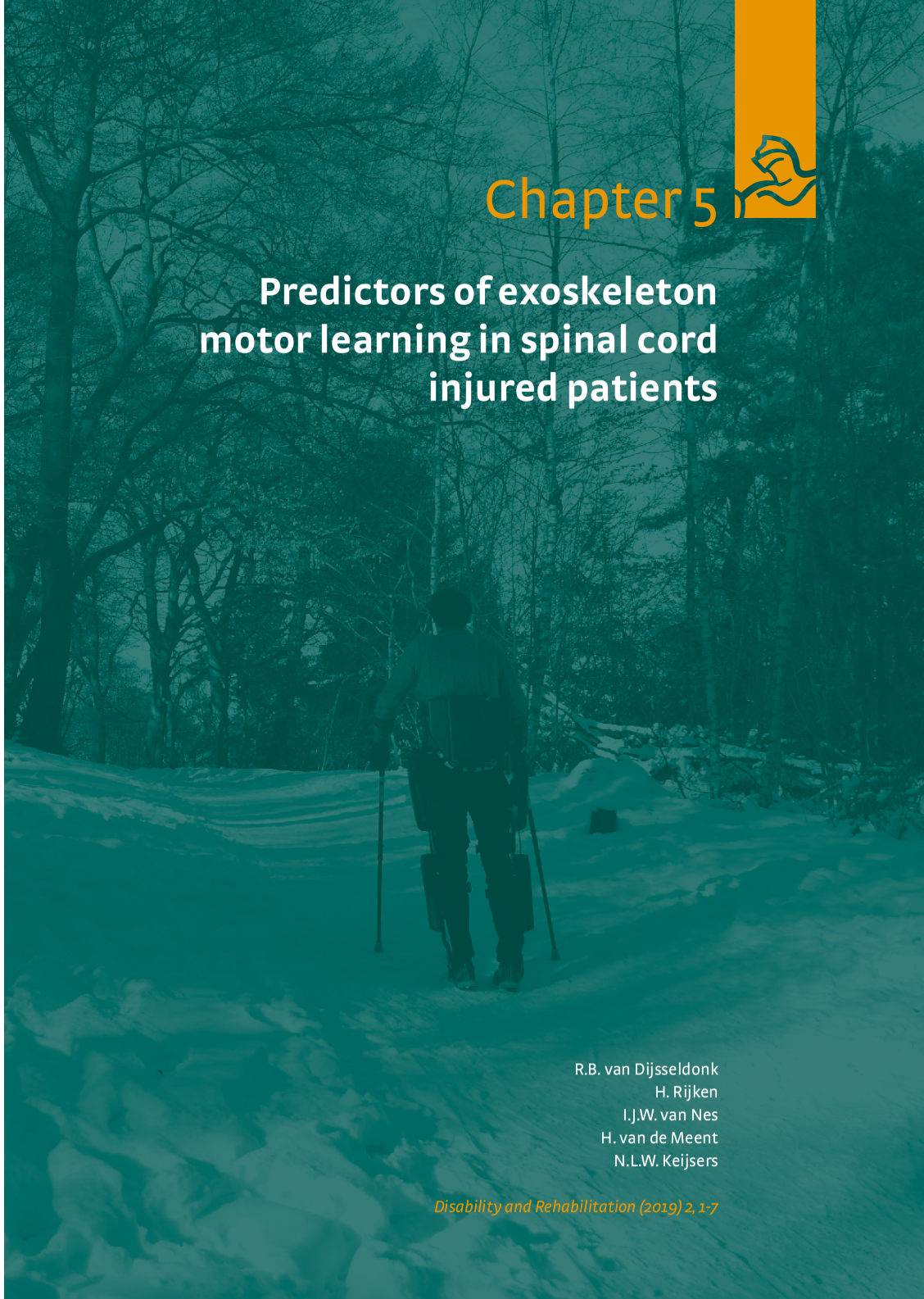

Chapter 5

Predictors of exoskeleton motor learning in spinal cord injured patients

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Abstract

Background
Learning to use an exoskeleton is time consuming and diverse between users. Knowledge about trainability of exoskeleton skills is relevant for planning and expectation management. The objective was to assess predictors of exoskeleton skill performance during and after exoskeleton training.

Methods
Twenty-four participants with a motor complete spinal cord injury were given 24 training sessions in 8 weeks. Nine potential predictors were identified; lesion level, age, gender, age at injury, time since injury, sport, active lifestyle, and anxiety. Univariate and multivariate linear regression analysis were performed to examine predictors of skill performance after 2, 4, 6 and 8 weeks.

Results
Twenty participants completed the training. Univariate analysis revealed that positive predictors were: low lesion level and more active lifestyle after 2 weeks, whereas low age at injury, low BMI, and more active lifestyle were positive predictors after 6 weeks. Multivariate regression model explained 65% of the performance after 2 weeks (predictors: lesion level, anxiety, active lifestyle) and 66% after 6 weeks (predictors: BMI, active lifestyle, age).

Conclusion
Lesion level was a predictor during the first 4 weeks, but did not influence participants' final skill level. BMI, age, and active lifestyle were predictors towards the end of the training period.

Keywords: Spinal cord injury, exoskeleton, motor learning, skill, predictor, performance

Introduction

The use of robotics for rehabilitation is a relatively new field, that received a lot of attention in the last decade.[1–3] In the '00, commercial available rehabilitation gait robotics, such as the Lokomat, were introduced in clinical setting. The Lokomat is mainly being used for restoration of gait in patients with spinal cord injury (SCI)[4] and stroke[5] and is always used in combination with a treadmill and body-weight support system. Although to a lesser extent, the Lokomat has also been used to prevent secondary health complications in SCI, such as pain and spasticity.[6] A disadvantage of such a gait robot is that it is mainly used in a clinical setting. In the last decade, wearable gait robots the so called exoskeletons have been introduced as an alternative.

Wearable exoskeletons can enable people with motor complete SCI to support their standing and walking ability outside the clinical setting. Because of the possibility to train in an upright position, exoskeletons may have a beneficial effect on preventing secondary health complications.[7,8] Previous studies have shown that the use of wearable exoskeletons in people with SCI is safe and feasible,[8,9] but an intensive training is required before users can safely and independent use an exoskeleton[10–13] outside the clinical setting. Although the majority of subjects with a complete SCI were able to walk independently with an exoskeleton, the number of training session required to reach this level of independent walking differed between participants ranging between 6 and 23 training sessions.[10]

The diversity between users raised the question: why do some users acquire more exoskeleton skills than others? Knowledge about trainability of exoskeleton skills during and after a training period is relevant for rehabilitation planning and expectation management. In learning to use other assistive devices, such as a manual wheelchair, relationships between personal and injury characteristics and wheelchair skill performance have been found.[14] For wheelchair skill training it was found that a lower lesion level, lower age, male gender, low body-mass index (BMI) and more time spent with endurance exercise were relevant predictors for wheelchair skill performance.[14,15] The same predictors may also be important for learning to perform exoskeleton skills. From sport psychology studies, it is known that motor performance is also influence by anxiety.[16,17] An increased level of anxiety overloads the attentional capacity, resulting in a decreased motor performance.[17] Finally, we expect that a shorter time since injury and a lower age at injury onset could influence exoskeleton skills learning.

The objective of this study was to evaluate the potential predictors for exoskeleton skill performance during and after an intensive training period in participants with motor complete SCI. The following personal and injury characteristics are hypothesized as potentially positive predictors for exoskeleton skill performance: low lesion level, low age, low BMI, male gender, large physical activity level, low anxiety level, short time since injury onset and a low age at injury onset.

Material and Methods

Participants

Patients with motor complete SCI who were interested in testing an exoskeleton contacted the Sint Maartenskliniek to participate in the study. Patients were first screened by telephone and secondly scheduled for a complete screening with the rehabilitation physician. Patients were eligible to enter the study if they were 18 years or older, at least 6 months since injury, and were classified as A or B on the American Spinal Injury Association (ASIA) impairment scale between Thoracic 1 (Th1) and Lumbar 1 (L1). Participants had to weigh less than 100kg and have a height between 1.60 and 1.90m for fitting in the ReWalk exoskeleton device. Exclusion criteria were: severe spasticity (Modified Ashworth Scale > 3); restricted range of motion in the hip, knee, or ankle joint; unable to control crutches; unable to make a transfer from a chair to a wheelchair without the use of external support; osteoporosis; fractures of the lower extremities in the last 2 years; pregnant or lactating; balance disorders; neurogenic heterotopic ossification; history of other conditions that could interfere with the motor learning process (e.g. stroke). All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee of Arnhem-Nijmegen (2016-2418) and by the internal review board of the Sint Maartenskliniek.

Device and training

The exoskeleton training sessions and measurements were performed in the sports hall at the Sint Maartenskliniek rehabilitation centre in Nijmegen. Participants were given twenty-four training sessions of 1.5-h over an 8 week period with a ReWalk exoskeleton. Two wearable exoskeletons were used in the study; the ReWalk™ Rehabilitation System and the ReWalk™ Personal 6.0. All participants started with the ReWalk™ Rehabilitation System and the first training session was used to adjust the exoskeleton to the patient's body composition. Per training session at least two physical therapist guided the training and a maximum of four physical therapists were involved in the training sessions. All four physical therapists were certified ReWalk trainers. Each training was individualized, as the physical therapists chose the specific goal based on the current level of the patient. The goal and practiced skills were notated by the physical therapist after each training session.

Measures

Performance of exoskeleton skills

The exoskeleton skills were measured with the Intermediate-skills-test and the Final-skills-test. The development and assessment of the skills-tests have been described earlier, and the reliability and ability to discriminate across participants' skill level was found to be good.[18] These skills-tests consisted of standardized tests in which the capacity to perform basic and advanced exoskeleton skills with varying levels of assistance were measured. Participants' skill-level was tested every 2 weeks (total of four times), the first three times with the Intermediate-skills-test and the last time with the Final-skills-test. The Intermediate-skills-test consists of 27 skills measured separately of each other in an ascending order of difficulty, until two skills were not achieved. The order of difficulty was from standing skills (e.g. weight shifting and sit-to-stand) to walking skills (e.g. walk 10m with and without assistance and arrest gait) to advanced skills (e.g. walk curves, passing a sloping doorstep and walk up and over a martial arts mat). Participants who could walk without assistance of the exoskeleton trainer between the 18th and 23th training session, performed the Final-skills-test in the last (24th) training session. The Final-skills-test consists of 20 skills measured in a fixed sequence and was performed twice with a 5-minute break in between. The Final-skill-test aimed to resemble daily life situations in which skills are often performed in sequence (e.g. make a curve after passing a doorstep). During all tests the physical therapist walked behind the participant to assure safety, but did not intervene unless necessary to prevent a fall.

Personal and injury characteristics

Nine potential predictors for exoskeleton skills performance were selected; neurological lesion level, age, gender, age at injury onset, time since injury, physical activity level (sport and active lifestyle), level of anxiety and BMI. Neurological lesion level was assessed by the rehabilitation physician and registered in the patient registration system prior to enrolment. Before the start of the exoskeleton training participants filled out their age, gender, age at injury onset, and time since injury on a form. In addition, participants filled out a questionnaire regarding their physical activity level and level of anxiety. Physical activity level was assessed through two questions; 1) Are you currently engaged in a sport? And if so, how many hours do you on average spend on it per week? (physical activity level: sport) 2) In addition to your sport, how many times a week do you usually perform a moderate to intensive physical activity that increases your heart rate or speeds up your breathing (e.g. leisurely hand biking) for at least 30 minutes? (physical activity level: active lifestyle). The former question addresses the Dutch physical activity guidelines, which is the minimum amount of physical activity required for a healthy and active lifestyle.[19] Level of anxiety was calculated from the 7-item anxiety subscale of the Dutch version of the Hospital Anxiety and Depression scale (HADS).[20] A higher anxiety sum score (range 0 – 21) represents more anxiety. During the first exoskeleton session participants height and weight were registered for adjustment of the exoskeleton. BMI was calculated as weight divided by the square of the height of the participant.

Data and statistical analysis

Only participants who performed all three measurement (Intermediate-skills-test 1, 2 and 3) were included in the analysis of the performance of the Intermediate-skills-tests. For the analysis of the Final-skills-test, only participants who met the criteria to perform the Final-skills-test were included. The outcome of the performance of the Final-skills-test was the average of the achieved final skills in both rounds.

Descriptive statistics were used to present the personal, injury characteristics and the number of achieved skills at the three Intermediate-skills-tests and the Final-skills-test. Univariate and multivariate linear regression analysis were performed to examine the personal and injury characteristics that can predict exoskeleton skill performance. The dependent variable was exoskeleton skill performance defined as the achieved basic and advanced skills at Intermediate-skills-test 1, 2, 3 and the Final-skills-test. The independent variables were the personal and injury characteristics (neurological lesion level, age at injury onset, time since injury onset, age, BMI, gender, sport, active lifestyle, and anxiety). All independent variables were univariately tested for their relationship with dependent variable (the achieved exoskeleton skills at the Intermediate-skills-tests and Final-skills-test). Independent variables were subsequently included in the multivariate analysis. A stepwise regression analysis was used to assess the predictors for the performance at Intermediate-skills-test 1, 2, 3, and the Final-skills-test. Variables with a p-value of F (probability of F) ≤.05 were entered in the stepwise regression analysis. Variables that were already in the equation and added less than

.10 (probability of F >.10) were removed from the regression equation. A Shapiro-Wilk test was performed to check if the residuals were normally distributed.

Results

Participants

Twenty-four participants were enrolled in the study and twenty (83%) completed the training program and performed all three Intermediate-skills-tests. At the end of the training program fifteen (75%) participants were able to walk without assistance of the physical therapist and therefore performed the Final-skills-test during the 24th training session. From one participant the data of the active lifestyle question was missing. This missing value was replaced with the mean of the active lifestyle questions of the other 19 participants in the stepwise multiple linear regression analysis. An overview of the personal and injury characteristics is given in table 1.

Table 1. Personal and injury characteristics

	Completed training program (N = 20)
Sex (male / female)	12 / 8
Age (years), mean (SD)	37 ± 10
Post-injury (years), mean (SD)	8 ± 8
Age at injury onset (years), mean (SD)	29 ± 10
Neurological level of SCI (Thoracic), mean (SD)	8 ± 3
AIS* (A/B)	19 / 1
BMI**, mean (SD)	23 ± 3
Sport (hours per week), mean (SD)	3 ± 2
Active lifestyle*** (times per week), mean (SD) †	5 ± 6
Anxiety (HADS**** sub score), mean (SD)	4 ± 3

*AIS, American Spinal Injury Association Impairment Scale **BMI, Body-Mass Index ***met the Dutch physical activity guidelines ****HADS, Hospital Anxiety and Depression Scale †N = 19

Intermediate-skills-test

The univariate linear regression between the independent variables and the achieved intermediate skills at Intermediate-skills-test 1, 2, and 3 is presented in figure 1. Various personal and injury characteristics were significantly correlated to exoskeleton skill performance at the Intermediate-skills-tests. A lower lesion level (R^2 =.35, p=.006) and a larger active lifestyle (R^2 =.22, p=.041) were associated with a higher exoskeleton skill performance at Intermediate-skills-test 1 (See figure 2). For Intermediate-skills-test 2 only the neurological level showed a significant correlation (R^2=.30, p=.012). For Intermediate skills-test 3, a higher exoskeleton skill performance was associated with a lower age at injury onset (R^2=.26, p=.023), lower age at enrolment (R^2=.26, p=.021), lower BMI (R^2=.26, p=.021), and a more active lifestyle (R^2=.22, p=.041).

Lesion level, anxiety and active lifestyle were included in the stepwise multiple linear regression analysis for the performance at Intermediate-skills-test 1. The model had a an explained variance (R^2) of 0.65 (F(3,16)=9.99, p=.001). Lesion level (ß=.59, p=.002), anxiety (ß=.45, p=.009), and active lifestyle (ß=.34, p=.040) significantly predicted performance at Intermediate-skills-test 1. For Intermediate-skills-test 2, no additional variable to lesion level (ß=.55, p=.012) was added in the stepwise regression analysis. The predictors of the performance at Intermediate-skills-test 3 were BMI (ß=-.36, p=.031), active lifestyle (ß=.51, p=.003), and age (ß=-47, p=.008). A significant regression equation was found (F(3,16)=10.23, p=.001), with an explained variance (R^2) of 0.66. Shapiro-Wilk test revealed that the distribution of the residuals from the regression analysis were normally distributed at all three Intermediate-skills-test (p=.224, p=.156, and p=.539). An overview of the outcome of the stepwise regression is presented in table 2.

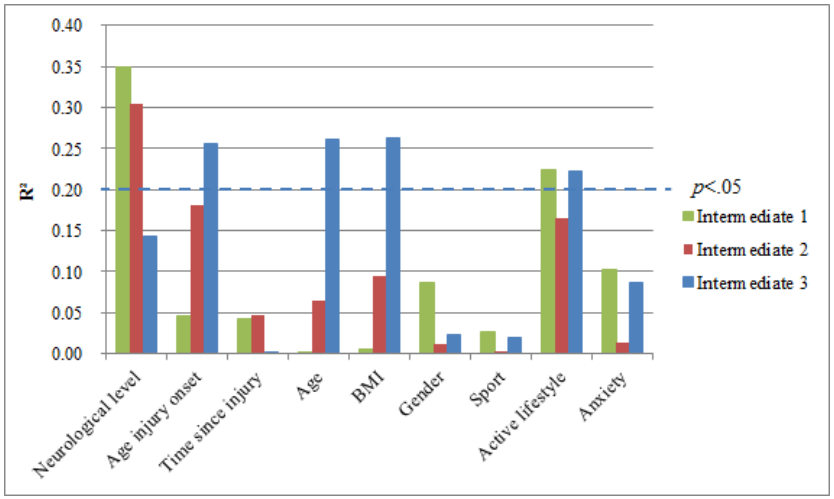

Figure 1. Explained variance (Pearson Correlation $(R)^2$) at Intermediate-skills-test 1, 2, and 3 for the 9 predictors. An R^2 above .20 is significant (p<.05), N=20.

Figure 2. Scatterplot for the predictors with a significant correlation with exoskeleton skill performance ($p < .05$) at Intermediate-skills-test 1, 2, and 3.

Table 2. Multiple forward stepwise regression.

	Variable 1	Variable 2	Variable 3	Model R^2	Model *p*-value	Formula
Intermediate-skills-test 1	Lesion level (ß=.59, *p*=.002)	Anxiety (ß=.45, *p*=.009)	Active lifestyle (ß=.34, *p*=.040)	0.65	.001	Performance = 1.20 (Lesion level) + 0.94 (Anxiety) + 0.45 (Active lifestyle) – 8.76
Intermediate-skills-test 2	Lesion level (ß=.55, *p*=.012)			0.30	.012	Performance = 1.12 (Lesion level) + 0.88
Intermediate-skills-test 3	BMI (ß=-.36, *p*=.031)	Active lifestyle (ß=.51, *p*=.003)	Age (ß=-.47, *p*=.008)	0.66	.001	Performance = -1.05 (BMI) + 0.84 (Active lifestyle) – 0.39 (Age) + 48.86

Final-skills-test

The univariate relationship between the independent variables and the achieved final skills is presented in figure 3. None of the independent variables were significantly related with the achieved final skills. In addition, no variables were entered in the stepwise regression analysis for performance at the Final-skills-test.

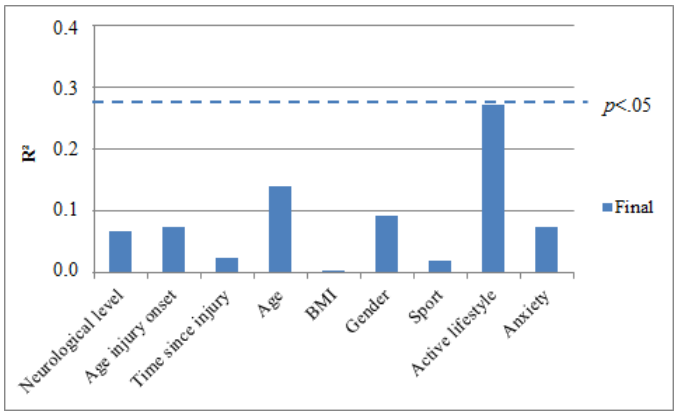

Figure 3. Explained variance (Pearson Correlation (R)²) of the average achieved final skills for the 9 predictors.

Discussion

The aim of the present study was to assess which personal and injury characteristics could predict exoskeleton skill performance during and after an 8 week intensive training program. After 2 weeks of training, lesion level, anxiety, and active lifestyle explained 65% of the skill performance. BMI, active lifestyle and age explained 66% of skill performance after 6 weeks of training. Active lifestyle appeared to be the most predictive variable for the exoskeleton skill level at the end of the 8 week training program.

Exoskeleton skill performance was measured at four moments during the training program. As a result, different predictive variables were identified at these moments. Moreover, some variables explained increasingly less during the training program, whereas other variables explained increasingly more indicating a change in the importance of personal and injury characteristics over the training period. The injury characteristic lesion level was the only variable that explained increasingly less during the training program (see figure 1). In the first 4 weeks, lesion level was the most important predictor (highest standardised beta coefficient at Intermediate-skills-test 1 (β=.59) and Intermediate-skills-test 2 (β=.55)), (see table 2). The relation between lesion level and functional outcomes has been previously described[21,22] and is often explained by the (im)possibility to (voluntary) control the trunk muscles involved in sitting and standing position (e.g. active core stability). Remarkably, lesion level was not a significant predictor of exoskeleton skill performance after 6 and 8 weeks, both in the univariate and in the multivariate analysis. Important to note with respect to core stability, is that 7 out of 10 participants with an impaired active core stability (lesion level above Th6) used a (plaster) corset during the exoskeleton use. These results suggest that an active core stability is beneficial for learning to perform exoskeleton skills in the first period of exoskeleton training, but has minimal influence on the skill level towards the end of the training period.

In contrast to lesion level, the more personal characteristics age, age at injury onset and BMI showed an increase in prediction of the exoskeleton skill performance over the training period. These variables had a significant explained variance after 6 weeks of training, a very low explained variance at 2 weeks and in between explained variance at 4 weeks (see figure 1). The importance of age and BMI was also supported by their inclusion in the multivariate regression model after 6 weeks of training. The most important predictors of exoskeleton skill performance at 6 weeks in the multivariate analysis were active lifestyle (β=.51), age (β=-.47) and to a lesser extent BMI (β=-.36) (see table 2). These variables were in accordance with learning to perform skills with other assistive technologies, such as manual wheelchairs. Age and BMI were found to be the best predictors of wheelchair skill performance after inpatient rehabilitation14 and physical capacity was highly correlated to wheelchair skill performance at the end of inpatient rehabilitation.[23] This supports the hypotheses that similar predictors are involved in learning to perform wheelchair skills and exoskeleton skills.

At the end of the training program, only participants who could walk independently performed the Final-skills-test and were included in the analysis. The Final-skills-test is part of a bigger study and was designed to assess whether participants were skilled enough to use the exoskeleton safe in their home environment. Therefore, only a subgroup of more skilled participants (e.g. who could walk independent) performed the Final-skills-test. As a consequence, a smaller and homogenous group with respect to injury and personal characteristics were used in the multivariate analysis. Furthermore, the distribution of the mean achieved final skills was small, ranging between 13,5 and 19,5 final skills of which half of the participants achieved at least 19 out of 20 final skills. Therefore, the explained variance at the Final-skills-test by the injury and personal characteristics was low.

Active lifestyle was the only significant or nearly significant predictor of exoskeleton skills in all three Intermediate-skills-tests and the Final-skills-test. This variable should be addressed carefully, because one participant had an extremely active lifestyle (score of 21 times per week) and was already very skilled after 2 weeks of training (achieved all 27 intermediate skills). This participant can be seen as outlier with a high influence in the regression analysis. One additional participants achieved 26 out of 27 intermediate skills after 2 weeks of training. Both highly skilled participants had used a Reciprocating Gait Orthosis (RGO, such as the ARGO walker) and indicated that they experienced benefits from this. There are similarities between RGO and exoskeleton use, such as balance in stance, anterior-posterior weight shifting and sometimes the use of crutches. Therefore, former experience with a RGO is likely an important predictor, but this was not registered in this study.

Two crucial steps can be identified in the learning process of independent exoskeleton use. Firstly, weight shifting in stance and standing up are important exoskeleton skills that can be seen as prerequisites for walking. Independent weight shifting and sit-to-stand was achieved by 85% and 60% of the participants after 2 weeks of training, and 95% and 90%

after 4 weeks of training. The second important step in the learning process is independent walking. When independent walking was achieved, most participants were able to achieve several advanced exoskeleton skills within two weeks. Independent walking was achieved by 15 participants at the end of training program. Compared to other studies with the same number of total training sessions (14% (1 out of 7)[12] or 57% (4 out of 7)[13]), we found a higher percentage of 75% people who were able to walk independently with the exoskeleton. Despite this higher percentage, still five participants were unable to walk independently after 24 sessions. Due to the fixed training period in this study, we do not know how many additional training sessions these participants would have needed to achieve the skill independent walking. In addition to independent walking, donning the exoskeleton is an important skill for independent use. Independent donning was possible by 40% of the participants after 2 weeks of training, and 55% after 4 and 6 weeks of training. During the Final-skills-test, 87% of the participants were able to don the exoskeleton independently. The participants who did not achieve the donning skill required assistance with putting on the shoes. The remaining part of donning the exoskeleton, such as fixating the straps around the thigh and trunk, could be done independently by all 20 participants.

With 24 participants enrolled, this is the exoskeleton study with the largest sample size investigating the independent use of an exoskeleton. Despite that, the sample size of 24 is small for multivariate regression analysis limiting the number of predictors that could be tested. Other characteristics may also have been of interest to predict exoskeleton skill performance, such as previous experience with other technologies, balance capacity and general motor competence. While walking with a (ReWalk) exoskeleton, the user has to shift the body weight continuously to allow for a good swing foot clearance challenging the users balance capacity. Although there are suitable measures to assess balance capacity (e.g. ability to control someone's centre of mass while seated or during stance[24]), outcome measures to assess general motor competence in people with SCI are lacking. Lesion level can be seen as an exploratory measure of participants functioning, but might not be sufficient to describe the participants general motor competence. Because the important predictors for wheelchair and exoskeleton skills performance show similarities, a wheelchair skills test may be a good alternative for measuring general motor competence in chronic SCI patients. Also measures related to motor learning capacity, such as the variability in performance of motor tasks, might be related to the learning rate of new motor skills.[25,26] Future research should investigate the influence of other potential predictors of exoskeleton skills performance, such as experience with other technologies, balance capacity, general motor competence and motor learning capacity.

Conclusion

Knowledge about predictors of exoskeleton skill performance is relevant for potential user and can be used by the rehabilitation specialist during patient counselling. Lesion level appeared to be an important predictor during the first 4 weeks of training, but did not influence participants' final skill level. BMI, age, and active lifestyle were predictors of exoskeleton skill performance towards the end of the training period.

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Chapter 6

Case report: Description of two fractures during the use of a powered exoskeleton

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Abstract

Introduction
Powered robotic exoskeletons are a promising solution to enable standing and walking in patients with spinal cord injury (SCI). Although training and walking with an exoskeleton in motor complete SCI patients is considered safe, the risks of unexpected (technical) adverse events and the risk of fractures are not fully understood. This article reports the occurrence of two different cases of bone fracture during exoskeleton usage. Furthermore, advice is given for extra safety training and instructions.

Case presentation
The first case concerns a 47-year-old woman with T12 AIS A SCI. Her exoskeleton shut down unexpectedly probably causing a misalignment of the joints of her lower extremities relative to the joints of the exoskeleton, which resulted in a fracture of her left tibia. The second case involves a 39-year-old man with L1 AIS B SCI. An unexpected fracture of the right distal tibia occurred without a specific prior (traumatic) incident.

Discussion
Exoskeleton training instructors, SCI patients and their buddies should be instructed how to handle emergency situations. Furthermore, they should be aware of the risk of stress fractures of the lower extremities. Proper alignment of the exoskeleton relative to the body is of utmost importance to reduce fracture risk. In the case of swelling and discoloring of the skin, radiographic examination should be performed in order to exclude any fracture.

Introduction

New technological developments, like a powered robotic exoskeleton, make it possible for people with motor complete spinal cord injury (SCI) to independently stand, walk and climb stairs. Nowadays, multiple commercial exoskeletons are available and some of these exoskeletons are certified for use outside a clinical setting. In general, the of training programs in a clinical setting with an exoskeleton are considered feasible.[1–4] The use of these powered exoskeletons in real-world settings has also shown to be safe.[2] However, literature about adverse events involving a powered exoskeleton is scarce. The adverse events that have been described are fractures and skin aberrations.[2,4–6] Two incidents of bone fractures with exoskeleton use have been reported in the literature.[4,5] A meta-analysis by Miller et al.2 based on one single reported event, determined an incidence of bone fracture at any time during the training program of 3.4%.

Our institute has offered the ReWalk™ in-hospital training program since 2015, as it was the only CE and FDA approved exoskeleton for both in-hospital and home use.[7] The program consists of three 1.5 hours training sessions a week for 8 weeks . These training sessions are under the supervision of at least two physiotherapists, who are certified exoskeleton instructors. When the participants are able to use the exoskeleton independently and safe and have sufficient exoskeleton skills, the participants are enabled to use the exoskeleton in their homes for an additional 2 weeks.[7] In case of home-use, a 'buddy' is instructed by the therapists to guide a patient walking in an exoskeleton and the participants are taught to always be accompanied by this instructed buddy.

This article reports two cases of bone fractures during exoskeleton usage: one during home use and one during an in-hospital training session. Subsequently, advice is given for additional training and instructions regarding safety procedures to prevent these adverse events.

Case presentation

Case 1
The first case concerns a 47-year-old woman with a traumatic T12 AIS A SCI since 2004. She did not have spasticity or contractures in the joints of her lower extremities. She completed the training program successfully along with two weeks of exoskeleton use at home. After completing the training program and still being enthusiastic about the exoskeleton, ReWalk allowed her to use the exoskeleton on several occasions such as demonstrations, presentations and occasionally at home. When walking with the exoskeleton, she was always assisted by her buddy.

During at home usage, while walking outside, she lost her balance. Her buddy grasped the exoskeleton to help her restore her balance and accidentally pressed the power button of the exoskeleton. As a consequence of the sudden loss of power (i.e. in the case of a major system failure or turning the exoskeleton off while in standing position), the ReWalk™ exoskeleton ran the 'graceful collapse' algorithm and gently lowered the woman to the floor.

While she was on the floor, the woman was guided by her buddy to the sitting position and she gave the command to stand up again with her remote-control input device. While standing up, she heard a snapping sound in her left calf and the system stopped unexpectedly halfway and began to collapse again to the sitting position. With help of her buddy, she detached herself from the exoskeleton and sat in her wheelchair. She noticed a hematoma on her left knee and back along with unnatural mobility of her left knee.

Radiographic examination revealed severe osteopenic bone with a comminuted intra-articular fracture of the left tibial plateau. The orthopedic surgeon performed closed reduction followed by treatment with plaster cast for 8 weeks. This was complicated by pressure ulcers on her heel. Full consolidation of bone was established not until nine months after trauma. After healing of the bone she returned to walking with her exoskeleton without problems.

Evaluation of the exoskeleton by the manufacturer, did not reveal any deficits in the hard- or software of the exoskeleton. Our hypothesis for the bone fracture, is that the position of her left lower extremity was misaligned relative to the joints of the exoskeleton due to the graceful collapse (Fig.1). It is likely that the subsequent standing up motion caused relatively excessive torsion forces on her lower extremities due to this misalignment, resulting in a comminuted intra-articular fracture of the left tibial plateau.

After the incident, a Dual Energy X-ray Absorptiometry (DEXA)-scan was performed which showed a T-score of her left hip of -2.7 and of her right hip of -2.7, indicating osteoporosis. Treatment with additional calcium, vitamin D and bisphosphonate was started.

Figure 1. Example of misalignment of the hip joint relative to the exoskeleton

Case 2

The second case concerns a 39-year-old man with L1 AIS B traumatic SCI since 2000. He started exoskeleton training at the beginning of 2018. He did not have spasticity or contractures in the joints of his legs. During his fifth in-hospital training session he noticed some swelling and experienced slight pain at his right ankle. No incidents had occurred during the training session or at a former training session. The pain subsided the day after the fifth session. Two

days later he again noticed an increase of the swelling and a bluish-red discoloration of the skin. An emergency physician considered this to be an infection and prescribed antibiotics. After the weekend, he visited his own physician and radiography revealed a fracture of the distal tibia at the tibial plafond with damage of the subchondral bone. The cause of trauma was discussed in a multidisciplinary team meeting with the physiatrist, orthopedic surgeon and physiotherapists. No incident or specific movement that could have caused the fracture was noticed or recalled.

A DEXA-scan was performed and revealed a T-score of his left hip of -1.2 and of his spine (L4) of 1.2, indicating no osteoporosis or osteopenia of these specific bones. However, the conventional radiography showed a relative osteoporotic distal tibia and the individual received the advice to start with vitamin D.

Discussion

Although training with an exoskeleton has generally been shown to be safe[2], the present cases show that there is always a risk of unexpected serious adverse events. A meta-analysis by Miller et al. [2] reported a 3.4% incidence of bone fracture in exoskeleton-assisted walking. This low incidence rate was based on a single reported bone fracture in one study in the literature. The two additional cases reported in the current study and a case reported by Gagnon and colleagues4 suggest that the 3.4% incidence might be an underestimation.

Loss of bone mass coupled with excessive torque of the exoskeleton on the lower extremities during exoskeleton-assisted walking and the potential risk of misalignment, are associated with a higher risk of bone fractures.[8] We have described two cases of bone fractures related to exoskeleton use, one at home use after a successful in-hospital training and one during an in-hospital training period.

In the first case, the woman and her buddy completed the training program successfully and were very experienced in using the exoskeleton. However, they were not trained well enough in reacting to situations in which the exoskeleton would shut down unexpectedly. During an unexpected shut down, the ReWalk™ exoskeleton will run a 'graceful collapse' algorithm that gently lowers the user to the floor. The first case made us realize that both the individual with the SCI and their buddy need extra instructions on how to react in such an emergency situation. Ever since this incident, we have extended our exoskeleton training protocol with extra training and instructions regarding safety procedures in case of unexpected software problems or in the case the exoskeleton is accidentally switched off. A storyboard after accidental shut down of the exoskeleton is shown in Figure 2; and the instructions are available in the supplementary video.

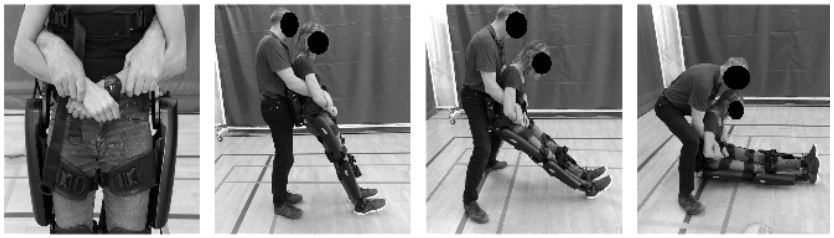

Figure 2. Storyboard of the training instructions after accidental shut down of the exoskeleton

After accidently switching off an exoskeleton the individual should switch the exoskeleton back on as fast as possible, resulting in a lock of the ReWalk™ exoskeleton in its current position. Second, the buddy must stabilize the standing position of the user and press the power button again (switch off) to initiate the 'graceful collapse' algorithm, guiding the user to the floor or to a nearby chair, if present. Lastly, when the user is in a stable position, the user is assisted out of the exoskeleton and is instructed not to use the device until further inspection.

One of the main causes for a fracture of the lower extremities during exoskeleton use, is misalignment of the joints of the exoskeleton relative to the joints of the lower extremities, especially in osteopenic or osteoporotic bones. In our first case, the hip joints of the exoskeleton were misaligned relative to the users own hip joints after the 'graceful collapse' motion (Fig.1). The subsequent standing up motion caused excessive torsion forces on her legs, resulting in the fracture of her left tibial plateau. Proper alignment of the exoskeleton relative to the body is, therefore, of the utmost importance. Alignment should be checked before and after the sit-to-stand transition and always after a graceful collapse motion.

Loss of bone mass and osteoporosis are common secondary complications associated with SCI with increased risk of bone fractures.[9] In the first case, excessive torsion forces on the osteoporotic bones of the lower extremities resulted in the fracture of the tibial plateau. In the second case the bone fracture occurred during one of the training sessions. The participant was the 18th patient that was trained in our rehabilitation center. The training sessions are always given by the same three ReWalk™ certified physiotherapists, who had given more than 600 hours of training sessions, indicating they were very experienced. Neither the participant, nor the physiotherapists noticed an incident during or after the training session. Furthermore, no misalignment of the exoskeleton was recalled by the physiotherapists. To our knowledge, the only logical explanation of the second case was axial compression of the relatively dense talus on the osteoporotic distal tibia, resulting in a fracture of the distal tibia. It is important to be aware of complications as a result of relatively osteoporotic or osteopenic bones of the lower extremities. Gagnon et al.[4] reported an individual with bilateral type 1 non-displaced fractures of the calcaneus after two familiarization sessions and the first training session with the EKSO™ robotic exoskeleton. Benson et al.[5] reported an individual with a hairline fracture of the talus seen on magnetic resonance imaging (MRI). They reported that, apart from a temporarily swollen ankle noticed the morning following the fourth training session, no other signs and symptoms were present. Similar to our second case, uncertainties about the specific cause of the fracture existed in the studies of Gagnon et al. and Benson et al. The limited clinical symptoms reported by Benson et al. show many similarities with our second case. Therefore, we recommend to checking the lower extremities after each training session. In the case of swelling or discoloring of the skin, X-ray examination should be performed to exclude fracture. In case of persistent symptoms, repeat the X-ray or other additional examination (like MRI) should be performed because stress fractures are not always present at first examination.

Some studies involving powered exoskeletons screen for osteoporosis to define objective exclusion criteria.[2,6] However, criteria differ between studies and the association between fracture risk at specific levels of bone mass density is still unknown.[6] Therefore, cut-off points with respect to bone mass density or a threshold of exclusion for exoskeleton usage, are difficult to define. After the incidents in our hospital, Rewalk advised to perform a DEXA-scan before commencing a training program of each individual patient. ReWalk recommends a T-score of > -3.5. In our cases, both patients had T-scores above -3.5 (-2.7 and -1.2 respectively), but still sustained fractures of the lower extremities.

Conclusion

Although training and walking with an exoskeleton in motor complete SCI patients is considered safe, one should always be aware of risks of unexpected (technical) adverse events and the risk of fractures. It is important to incorporate specific instructions regarding safety procedures for unexpected situations in a exoskeleton training program to prevent adverse events. The higher risk of (stress) fractures, especially in the case of osteopenic or osteoporotic bones, should be always considered. Maintaining proper alignment of the exoskeleton relative to the body is of the utmost importance and regular checks are necessary. Powered robotic exoskeletons are a promising solution to enable standing and walking in patients with SCI; however we strongly recommend training users in a multidisciplinary setting including experienced physiotherapists, a physiatrist and a researcher so as to gain more experience in the possibilities of these great innovations.

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Chapter 7

Improvement of quality of life after 2-month exoskeleton training in patients with chronic spinal cord injury

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Abstract

Objective
To examine changes in quality of life (QoL) after an eight-week period of robotic exoskeleton training in a homogeneous group of patients with chronic complete spinal cord injury (SCI).

Design
Prospective study.

Setting
Rehabilitation center.

Participants
Patients with a chronic (>6 months) motor complete SCI (T1-L1).

Intervention
Twenty-four training sessions with the ReWalk™ exoskeleton over an eight-week period.

Main outcome measure
QoL, assessed with the sum score of the Short Form-36 with Walk Wheel modification (SF-36ww). Secondary outcome measures were the eight SF-36ww subdomains, satisfaction with bladder and bowel management, lower extremity joint passive range of motion (pROM), and lower extremity spasticity.

Results
Twenty-one participants completed the training. QoL significantly improved after the training period (average SF-36 sum score 571 ± 133) compared to baseline (621 ± 90) ($t(20)=-2.5$, $p=.02$). Improvements were seen on the SF-36ww subdomains for pain ($p=.003$), social functioning ($p=.03$), mental health ($p=.02$), and general health perception ($p=.01$). Satisfaction with bladder management (range 1-5) improved from median 3 at baseline to 4 after exoskeleton training (p=0.01). No changes in satisfaction with bowel management ($p=.11$), pROM (hip-extension ($p=.49$), knee-extension ($p=.36$) and ankle dorsiflexion ($p=.69$)), or spasticity ($p=.94$) were found.

Conclusion
Even in patients with chronic motor complete SCI and a relatively high level of QoL at baseline, a short-term exoskeleton training improved their QoL, pain and satisfaction with bladder management; findings that warrant further controlled studies in this specific SCI population.

Keywords: Spinal cord injury, powered exoskeleton, quality of life, health state

Introduction

Despite advances in the acute medical care for patients with spinal cord injury (SCI), full recovery of mobility after complete SCI is uncommon.[1] Of the approximately 450 new cases each year in the Netherlands,[2] a majority will remain (at least substantially) dependent on a wheelchair. This wheelchair dependence coincides with a sedentary lifestyle, which has a significant impact on one's daily life activities, social participation and quality of life (QoL).[3–8] Moreover, patients with complete SCI are predisposed to multiple secondary health complications. A lifetime of sitting has been associated with an increased risk of osteoporosis, cardiovascular disease, pressure ulcers, bladder and bowel malfunctioning, infections, joint contractures and (increased) spasticity.[9–17] These secondary health complications are related to a lower general health state, poorer QoL and a lower life expectancy compared to the general population.[18] They typically lead to high levels of healthcare utilization and health care costs.[8] Hence, reducing the occurrence and effects of secondary health complications is an important target in the lifelong care for people living with SCI.

Technological developments such as powered exoskeletons give patients with complete SCI the possibility to stand, walk and even climb stairs.[19–26] In comparison with other orthotic devices, such as hip-knee-ankle-foot orthoses (HKAFO) and a reciprocating gait orthosis (RGO), powered exoskeletons are less metabolically demanding and allow a higher walking speed.[20,23,27–30] Moreover, gait training with a powered exoskeleton in people with complete SCI may contribute to a reduction of secondary health complications, in particular those that are caused by loss of the standing and walking capacity.[20,31–35] Previous studies have reported improved bladder and bowel function,[20] enhanced ankle dorsiflexion and hip extension,[34] reduced spasticity,[24,25,31,36] and less severe (neuropathic) pain.[36] However, evidence for these health benefits of powered exoskeletons is still low due to small-sized studies (sample sizes 5 to 12).[22,37] In addition, inclusion of mixed research populations (often combinations of paraplegia and tetraplegia as well as complete and incomplete injuries with different times since injury) hamper the interpretation of results for specific populations, such as patients with a chronic complete SCI.[32]

In addition to the health benefits, the evidence of improving QoL with exoskeleton training is low, especially in people with chronic complete SCI. The group of Baunsgaard et al. found positive effects on QoL, but 41% of their participants had some walking capacity outside the exoskeleton and 48% were recently injured.[32] In contrast, Juszczak and colleagues did not find an effect on QoL in a similar heterogeneous group of SCI patients.[38] Because changes in QoL are more likely to be expected in people with a recent injury or people with the prospect of functional recovery (i.e., people with an incomplete SCI), a positive effect of exoskeleton training on QoL in people without spontaneous functional recovery (i.e., chronic complete SCI) is less likely. Hence, for future developments in exoskeletons, it is important to know if short-term exoskeleton training can improve the QoL of patient with chronic complete SCI.

Therefore, the primary aim of this study was to examine the potential beneficial effects of short-term training with an exoskeleton on QoL in a homogeneous group of patients with chronic motor complete SCI. The secondary aim was to examine the effects of this training on satisfaction with bladder and bowel management, lower extremity joint passive range of motion (pROM), and lower extremity spasticity.

Material and Methods

Participants and training program

This study is part of a larger study to investigate the home and community use of a powered exoskeleton by people with complete SCI.[39] People with complete SCI who were known at the rehabilitation center of the Sint Maartenskliniek and who were interested to participate were enrolled. The in- and exclusion criteria are presented in table 1.

The training program consisted of 24 sessions with the ReWalk exoskeleton (ReWalk™ Rehabilitation System and the ReWalk™ Personal 6.0) of 1.5 hour each, distributed over an eight-week period. The study was approved by the medical ethics committee of the region Arnhem-Nijmegen (nr. 2016-2418) and the internal review board of the Sint Maartenskliniek. All participants signed informed consent forms in accordance with the Declaration of Helsinki.

Table 1. In- and exclusion criteria

Inclusion criteria	Exclusion criteria
• SCI classification AIS* A or B • Level of SCI between T1 and L1 • Age ≥ 18 years • Injury onset > 6 months • Body height sufficient to fit into the ReWalk device: >1.60 m and <1.90 m • Body weight less than 100 kg • Able to make a transfer from a chair to wheelchair independently • Good upper extremity function (capacity to use crutches)	• Skin integrity problems/pressure ulcers on surfaces that would contact the ReWalk device • Heterotopic ossifications • Pregnancy • Fractures of the lower extremities in the past 2 years • Medical history of spontaneous bone fractures • Insufficient mastery of the Dutch language • Other interfering neurological conditions (e.g. stroke or multiple sclerosis) • Severe lower extremity spasticity (Modified Ashworth Scale > 3) • Limited passive range of motion at the hip or knee joints on either body side (hip flexion / extension less than 90-0-0°, knee flexion / extension less than 90-5-0°, ankle dorsiflexion less than 0° with extended knee) • Insufficient time to train

* AIS, American Spinal Injury Association [ASIA] Impairment Scale. T= Thoracic, L= Lumbar

Procedure

Patients were first screened by telephone, after which an appointment was scheduled with a rehabilitation physician, experienced with SCI, for a complete check of the in- and exclusion criteria (See Table 1).

At the start of the study the following **demographic parameters** were registered: sex (male, female), age (years), time since SCI (years), SCI-classification (AIS A or B), level of SCI, and level of anxiety and depression (Hospital Anxiety and Depression Scale (HADS)).[40] The HADS score ranges between 0 and 21 points, and higher scores indicate higher levels of anxiety and depressed mood.

Prior to the first and the last session of the eight-week clinical training period, the participants filled out questionnaires concerning QoL, and satisfaction with bladder and bowel function. In addition, the lower extremity passive joint mobility and level of spasticity were assessed by a physical therapist who had ample experience with SCI patients.

Questionnaires and physical measurements

QoL was assessed with the Short Form-36 with Walk Wheel modification (SF-36ww).[41] In addition to the total SF-36 score (sum score range: 0- 800),[45] eight subdomains of health were considered: physical functioning, physical role limitation, emotional role limitation, bodily pain, general health, vitality, social functioning, and mental health (subdomain scores range: 0-100). A higher score indicates a more favorable health state. Reliability and validity have been established as good to excellent in populations with SCI.[42–45]

Satisfaction with bladder and bowel function was assessed with parts of the Neurogenic Bladder Symptom Score (NBSS)[46,47] and the Neurogenic Bowel Dysfunction Score (NBDS).[48] General satisfaction with bladder and bowel management was scored on a 5-point ordinal scale, ranging from 1 (extremely dissatisfied) to 5 (extremely satisfied). In addition, we assessed the reported number of urinary incontinences per week, time used for bowel management per week, and number of fecal incontinences.

pROM was measured by the physiotherapist using goniometry. Bilateral joint movements at the hips, knees and ankles were assessed and rounded to 5 degrees. A mean score of the bilateral hip extension, knee extension and ankle dorsiflexion was calculated.

Spasticity was assessed bilaterally with the Modified Ashworth Scale (MAS)[49] for the following muscles: hip flexors and extensors, knee flexors and extensors, and ankle dorsiflexors and plantar flexors (12 muscle groups in total). As a measure of overall spasticity, the MAS sum score of all 12 muscle groups was calculated (0-60 scale), which is a similar approach as used by Baunsgaard et al.[32]

Data and statistical analysis

Descriptive statistics (mean ± standard deviation or median [range]) were calculated for the demographic parameters: sex, age, time since injury, level of injury, SCI-classification, and HADS score. All numeric outcome variables were assessed for normality with the Kolmogorov-Smirnov test. Paired t-tests (normally distributed parameters) or Wilcoxon-signed rank test (not normally distributed parameters) were utilized to compare changes in SF-36ww sum score, SF-36 subdomains, satisfaction with bladder and bowel management, pROM score, and MAS sum score. The α-level was always set at 0.05.

Results

Demographic and clinical parameters

Twenty-one out of 25 participants completed the training program. Reasons for not completing the program were inability to learn the basic exoskeleton skills (1 participant), development of hematoma in the sacral area (n=1), fracture of the distal tibia (n=1), and musculoskeletal shoulder pain (n=1).

The data of these four participants were not included in the statistical analysis. An overview of the baseline characteristics of the 21 included patients is given in Table 2.

Table 2. Clinical and demographical characteristics of participants

	Total (N = 21)
Sex (M/F)	13/8
Age (years), median [range]	36 [24-57]
Level of SCI, median [range]	Thoracic 6 [T3-L1]
Time since injury (years), median [range]	5.4 [0.8-27]
AIS* (A/B)	20/1
HADS**, median [range]	7 [1-18]

*AIS= American Spinal Injury Association (ASIA) Impairment Scale. ** HADS= Hospital Anxiety and Depression Scale.

Table 3. Changes in health outcome measures before (pre) and after (post) exoskeleton training.

		Pre score (mean ± SD or median [range])	Post score (mean ± SD or median [range])	Statistics (paired *t*-test or Wilcoxon signed-rank (*Z*))
Health state	SF-36ww* sum score	571 ± 133	621 ± 90	$t(20) = -2.5$, $p=.02$
	Bodily pain	63 ± 22	75 ± 16	$t(20) = -3.4$, $p=.003$
	Social functioning	88 [25 – 100]	88 [63 – 100]	$Z = -2.1$, $p=.03$
	Mental health	84 [52 – 96]	84 [60 – 100]	$Z = -2.3$, $p=.02$
	General health perception	62 ± 17	70 ± 20	$t(20) = -2.7$, $p=.01$
	Physical functioning	67 ± 27	67 ± 25	$t(20) = -0.1$, $p=.91$
	Physical role limitation	100 [0 – 100]	100 [0 – 100]	$Z = -1.1$, $p=.27$
	Emotional role limitation	100 [0 – 100]	100 [0 – 100]	$Z = -0.3$, $p=.76$
	Vitality	68 ± 16	70 ± 19	$t(20) = -0.5$, $p=.59$
Bladder & bowel	Bladder management satisfaction	3 [1 – 5]	4 [1 – 5]	$Z = -2.5$, $p=.01$
	Urinary incontinence (/week)	0 [0 – 63]	0 [0 – 35]	$Z = -0.2$, $p=.83$
	Bowel management satisfaction	4 [1 – 5]	4 [3 – 5]	$Z = -1.6$, $p=.11$
	Bowel time	115 ± 75	102 ± 65	$t(20) = 1.3$, $p=.21$
	Fecal incontinence	0 [0 – 1]	0 [0 – 1]	$Z = -1.4$, $p=.15$
pROM** & spasticity	Hip extension† (°)	16 ± 10	18 ± 9	$t(18) = -0.7$, $p=.49$
	Ankle dorsiflexion† (°)	10 [0 – 20]	10 [3 – 20]	$Z = -0.4$, $p=.69$
	Knee extension† (°)	5 [0 – 10]	5 [0 – 10]	$Z = -0.9$, $p=.36$
	MAS*** sum score†	4 [0 – 48]	5 [0 – 26]	$Z = -0.1$, $p=.94$

*SF-36ww= short form 36 with walk-wheel modification. **pROM = passive Range of Motion. ***MAS= Modified Ashworth Scale. † N=19

Quality of life

SF-36ww sum score significantly improved after the exoskeleton training period (mean=621, SD=90) compared to baseline (mean=571, SD=133) ($t(20) = -2.5$, $p=.02$) (table 3). Significant improvements were also seen on the subdomains for bodily pain, social functioning, mental health, and general health perception. No significant changes on the other four SF-36ww subdomains were found (table 3).

Bladder and bowel management

General satisfaction with bladder management improved from median 3 ('neutral') at baseline to 4 ('mostly satisfied') ($Z=-2.5$, $p=.01$) after the exoskeleton training (see table 3). No significant change in the number of urinary incontinence incidents per week was found. Likewise, no change in satisfaction with bowel management, time used for bowel management, or the number of fecal incontinence incidents was seen.

Passive range of motion and spasticity

No significant changes in lower extremity pROM scores or MAS sum score (N=19) were found after the exoskeleton training (see table 3).

Discussion

In the current study, the significant increase in SF-36ww sum score indicates an improvement of QoL after a short-term training period of eight weeks in chronic complete SCI patients. Four of the eight SF-36ww subdomains significantly improved: bodily pain, social functioning, mental health and general health. In addition, an improved satisfaction with bladder management was found. There was no improvement in satisfaction with bowel management, lower extremity pROM or spasticity.

In contrast to previous studies assessing the health effects of exoskeleton training,[20,22,32,33,35] we included a homogeneous group of 21 people with chronic complete SCI. The advantage of including only chronic complete SCI patients is that the chance of spontaneous functional recovery is negligible. Hence, the health effects found in the current study are most likely attributable to the training with the powered exoskeleton.

The improvement in QoL could be the result of several factors. Detailed analysis revealed that there were differences in the crucial contributors to the improvement of QoL between individuals. For example, one participant mainly reported pain reduction, whereas another specifically showed an increase in social functioning. The effect size for pain reduction was largest, in contrast to the study of Baunsgaard et al. who found no significant pain reduction.[32] Importantly, it has been argued that pain reduction is crucial for QoL improvement in people with chronic SCI.[50] Some participants specifically improved on the domains of general health, social functioning and mental health, which may be directly related to the training as an activity in itself. During the training sessions, participants learned to perform a new activity with the attention and guidance from dedicated physical therapists. This new experience of interaction at eye level during the training sessions may have improved their perceived QoL.

Similar to other studies, we found a significant improvement of satisfaction with bladder management,[22,32] while no participant reported worsening of bladder function satisfaction. In contrast to our study, several other studies reported a positive change in bowel management (less incontinence and constipation) as well as decreased time and assistance required for bowel management.[20,31,38,51] We had expected this result as well, because in healthy individuals regular walking activity can stimulate bowel movement and prevent constipation.[52,53] Our discrepant finding may be explained by a more homogeneous and more severely affected (complete SCI) group, by the relatively short training period, or by the fact that the initial satisfaction with bowel management was already high pre-training (median of 4 on a 1 to 5 scale) allowing little room for improvement.

The fact that we did not find effects of the exoskeleton training on lower extremity pROM or spasticity may be explained by our stringent exclusion criteria with regard to limited pROM at the ankles, knees and hips, and the presence of spasticity.

Limitations

The eight-week training period in the current study was relatively short to find other improvements in secondary health complications e.g. regarding satisfaction with bowel management. Previous studies have emphasized a variety of possible benefits of exoskeleton use on secondary health complications and reduction of costs associated with SCI.[8] Future studies should therefore implement a longer training period and include additional measures, e.g. regarding bone density, skin problems, and cardiopulmonary status, to assess a broader effect of exoskeleton training on secondary health complications in complete SCI patients. Longer training periods could be attained if people would have their own exoskeleton that they could use in the home environment. Secondary health benefits would even be more likely if people with chronic complete SCI would be able to use an exoskeleton as an assistive and/or exercise device in daily life.[20,54]

The relative short period of exoskeleton use was also the reason why we did not assess any cardiovascular risk factors, e.g., lipid profile, blood pressure or glucose. Nevertheless, such metabolic parameters would be relevant to assess in future studies with a longer period of training or home use.

Four patients were not able to finish the training period due to an inability to learn the basic exoskeleton skills (1 participant) or the occurrence of complications (n=3). We therefore advise to concentrate the training of powered exoskeletons in people with complete SCI to specialized rehabilitation centers with ample experience and knowledge of this technology and population to minimize the number of complications.

Conclusion

This study has shown that a short-term (eight-week) training program with a powered exoskeleton improves the QoL and satisfaction with bladder management in a group of 21 patients with a chronic complete SCI. These findings warrant larger, controlled studies in this specific SCI subpopulation.

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Chapter 8

Exoskeleton home and community use in people with complete spinal cord injury

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Abstract

A consequence of a complete spinal cord injury (SCI) is the loss of gait capacity. Wearable exoskeletons for the lower extremity enable household and community ambulation in people with SCI. This study assessed the amount, purpose, and location of exoskeleton use in the home and community environment, without any restrictions. The number of steps taken was read from the exoskeleton software. Participants kept a daily logbook, and completed two user experience questionnaires (Quebec User Evaluation of Satisfaction with assistive Technology (D-QUEST) and System Usability Scale (SUS)). Fourteen people with a complete SCI used the ReWalk exoskeleton a median of 9 (range [1–15]) out of 16 ([12–21]) days, in which participants took a median of 3226 ([330–28882]) steps. The exoskeleton was mostly used for exercise purposes (74%) and social interaction (20%). The main location of use was outdoors (48%). Overall, participants were satisfied with the exoskeleton (D-QUEST 3.7±0.4) and its usability (SUS 72.5 [52.5–95.0]). Participants with complete SCI report satisfaction with the exoskeleton for exercise and social interaction in the home and community, but report limitations as an assistive device during daily life.

Keywords: Spinal cord injury, exoskeleton, home and community use, personal use, user experience

Introduction

The incidence of spinal cord injury (SCI) is approximately 180,000 cases per year worldwide.[1] Half of the people with SCI have a complete lesion,[2] which has a huge impact on their daily lives.[3] For mobility, a manual wheelchair is the most common option. Over the last decade, an alternative locomotion option for people with SCI was introduced: a wearable exoskeleton. With an external active orthosis and supported by two crutches, the basic motions for ambulation (i.e., standing-up, sitting-down, standing, and walking) can be initiated and controlled.

Until now, exoskeletons are mostly used in clinical settings, which has been shown to be feasible and safe for a broad range of patients with SCI.[4,5] As a gait retraining device, the exoskeleton is used to improve ambulatory capacity in patients with some residual leg motor function or in those for whom functional recovery is still possible (i.e., incomplete SCI). The potential of an exoskeleton for gait restoration was demonstrated by improving unassisted gait speed and walking distance after exoskeleton training.[6] Furthermore, two non-walkers with an incomplete SCI became walkers after exoskeleton training.[4,7] Hence, for people with incomplete SCI, 'therapeutic' exoskeleton use has the potential to improve ambulatory capacity independent of the exoskeleton.

In patients without (the potential for) ambulatory capacity (i.e., complete SCI), who are wheelchair users for their mobility, an exoskeleton can be used as an assistive device in order to walk. However, exoskeleton use as an assistive device without physical assistance from a trainer requires an intensive training period.[7–9] In our previous study, we have shown that more than half of the participants with a complete SCI could use an exoskeleton independent of assistance under supervision of a buddy after 24 training sessions.[9] Moreover, most of these participants were able to perform multiple advanced skills during independent walking (e.g. walking up and over a sloping doorstep) and standing (e.g. moving a cone at chest height),[9,10] which strengthens the idea of exoskeleton home use during some daily activities. Another advantage of exoskeleton use are the potential health benefits.[11,12] Because of the possibility to stand and walk in an upright position, exoskeletons may help to prevent secondary health complications, such as spasticity,[11,12] impaired bowel function,[13] and related loss of quality of life [11]. From this perspective, exoskeletons are used as an exercise device to promote physical health and well-being by reducing secondary health complications. However, to actually reduce secondary health complications, the frequency and intensity of exoskeleton use are critical. The intensity of walking with an exoskeleton is similar to regular physical activities performed at a moderate intensity,[14,15] which is known to yield health benefits.[12] In contrast to the use of conventional knee-ankle-foot-orthoses, the use of exoskeletons is not physically exhausting,[16,17] which is why they can be used more regularly.[14] This strengthens the idea of continued exoskeleton use at home and/or in the community.[18]

To date, one study described a gym-based setting for exoskeleton use.[19] To our knowledge, no other studies have been described for the use of exoskeletons outside the clinical setting. Instead of in the actual home and community environment, exoskeleton use was investigated in a gym-based setting. Four participants with SCI were interviewed and reported that gym-based exoskeleton use had a positive impact on their lives and enhanced their perceived wellbeing and sense of community integration.[19] Yet, daily life entails much more than

just the usage in a gym-based setting. According to Fritz et al.,[20] home and community use entails engaging in age normative and meaningful activities such as meeting friends at a pub, attending a graduation ceremony, performing one's job, or going on holiday 20. In addition to these social activities, home and community use also entails household chores such as cooking or doing the laundry. The question thus remains whether exoskeletons are already applicable in these settings.[21] Up to now, the applicability and effectiveness of exoskeletons in the community have not been demonstrated. Some expected challenges for community exoskeleton use are the limited gait speed, the heavy weight during transport, and the need of a buddy.[18,22] Only when users had an exoskeleton at their disposal in the community, the full range of problematic scenarios and safety concerns become apparent.[20] Such information is an important step for further exoskeleton development. Hence, the main objective of the present study was to assess the amount, purpose, and location of exoskeleton use in the home and community environment by people with complete SCI. Users' experiences and health related effects during this period were studied as well.

Material and Methods

Participants

People with complete SCI who gained knowledge about the existence and availability of an exoskeleton through the media and who were interested in testing the potential of such an exoskeleton contacted the rehabilitation center of the Sint Maartenskliniek to participate in this study. The eligibility criteria have been described previously 10. Adults in the chronic phase (>6 months) after a motor complete SCI (American Spinal Injury Association Impairment Scale (AIS) A or B) between the levels Thoracic 1 (Th1) and Lumbar 1 (L1) were eligible. Persons with physical characteristics that would hamper proper functioning of the exoskeleton, such as severe spasticity (Modified Ashworth Scale > 3), body height more than 1.90m or less than 1.60m, body weight above 100kg, or restricted range of motion at any hip, knee or ankle joint were excluded. Other exclusion criteria were inability to control crutches, inability to make a transfer from a regular chair to a wheelchair without the use of external support, and any co-morbidity or condition that could interfere with motor learning (e.g. stroke). Subjects with an increased risk of adverse events, such as those with osteoporosis, fractures of the lower extremities during the previous two years, balance disorders, neurogenic heterotopic ossification, or pregnancy, were also excluded. The increased risk of adverse events was checked by the rehabilitation physician through questions. From participant 7 onwards, osteoporosis was tested with a dual energy x-ray absorptiometry (DEXA)-scan at the hip. Before participants were allowed to use the exoskeleton at home or in the community, the following criteria had to be met:

1) Participants had to complete an 8-week exoskeleton training and achieve a skill level for safe home and community use (i.e. at least 17 final skills in the previously described Final-skills-test[10]).
2) Participants were required to have a buddy who received instructions about guiding the participant during multiple skills, including donning and doffing, sit-to-stand, and walking. In addition, a device related error was simulated so that both the participant and the buddy practiced trouble shooting via a graceful collapse (see van Herpen et al. for a more detailed description of the trouble shooting protocol[23]). This protocol was added to the current study from participant 7 onward, after the occurrence of a bone fracture as described in two case reports.[23]

All participants gave written informed consent in accordance with the Declaration of Helsinki. All research activities were carried out in accordance with the guidelines and regulations of the Medical Research involving Human Subjects Act (WMO) and the Netherlands Code of Conduct for Research Integrity. The study was approved by the medical ethics committee of Arnhem-Nijmegen (2016-2418) and the internal review board of the Sint Maartenskliniek.

Equipment

The ReWalk Personal 6.0, a wearable robotic exoskeleton from ReWalk Robotics that enables powered hip and knee motion, was used. The exoskeleton provided user-initiated mobility through the integration of a wearable brace support, a computer-based control system, and motion sensors. The ReWalk Personal 6.0 has a Class II FDA clearance for use both in a clinical setting and in the home and community environment.[24]

Protocol

Participants had no restrictions regarding the amount, purpose, or at which location they used the exoskeleton. For safety reasons, they were instructed not to use the exoskeleton without supervision of their buddy. The period of home and community use was at least two weeks with a maximum of three weeks per participant. The return date was agreed in advance, depending on the schedules of both the participant and the physical therapist. Before and after a period of home and community use, the number of steps taken was read from the exoskeleton software and notated. During the period of home and community use, participants filled in a logbook each day. If participants did not use the exoskeleton on a specific day, a short reason was given, while the other sections of the logbook were left blank. If participants did use the exoskeleton, the complete logbook was filled in (see Fig 1). The logbook included questions regarding the performed activities with the exoskeleton, the amount of use, and skin integrity. Comments related to the overall experience with the exoskeleton and/or health related effects could be registered in the blank sections of the logbook. After the first week, the primary researcher (RD) called the participants by phone to check whether the logbook was filled in correctly and to monitor if they had experienced any problems. When the exoskeleton was returned to the clinic, the logbook was handed in and two user experience questionnaires were completed by the participants: (1) the Dutch version of the Quebec User Evaluation of Satisfaction with assistive Technology scale (D-QUEST 1 – 5 scale)[25] and (2) the System Usability Scale (SUS 0 – 100 scale).[26]

Date:.....7-7-'17..... Day:.....1.....

Describe the activities in which you have used the exoskeleton today. If you did not use the exoskeleton today, state the reason why (you do not need to fill out the rest of the logbook).
First, inside the house put on the exoskeleton to show it to friends. Then we walked around the house with a group of 10 people. Walked a slalom and made many turns. It was a wonderful feeling to walk with a group of friends. I really enjoyed it today.

How long have you used the exoskeleton today? Approximately ..... 45 .....minutes

What was the total covered distance with the exoskeleton today? Approximately ..... 265 .....meters

What is the longest consecutive distance you have walked with the exoskeleton today? If you have paused for more than 1 minute, this does not count as one consecutive distance ..... 60 .....meters

How often have you put the exoskeleton on today ..... one .....time(s). **Give an indication of the amount of time you had the exoskeleton on each time.** Multiple answers are possible 1. ..... 45 .....minutes 2. .....minutes 3. .....minutes

Have you noticed any bruises or other injuries during the 'self-check' today? ☐No ☒Yes, describe what and where.....

Tick the boxes with the activities for which you have used the exoskeleton today. Multiple answers are possible.

☒ Take a short walk in the house	☒ Take a walk outside	☐ Open a door
☐ Small household tasks (such as making tea)	☐ Walk up a slope	☒ Walk up a sidewalk
☐ Large household tasks (such as handing the laundry)	☐ Walk down a slope	☒ Walk down a sidewalk
☒ Social events (such as a party or go to the bar)	☐ Other inside, namely.....	☐ Other outside, namely.....

Other remarks: After the use, no more spasm for the rest of the day. When bright sunlight shines on the remote control watch, it's hard to read it. I had to guess if I selected the correct mode.

Figure 1. Example of the logbook during the period of home and community use.

Outcome measures

Exoskeleton use

Exoskeleton home and community use was assessed as (1) the amount of use, (2) the purpose of use, and (3) the location of use. The primary outcomes for exoskeleton use were the total number of steps taken, total number of days of usage, and total number of sessions. The total number of steps was extracted from the exoskeleton software (i.e. difference in total number of steps between the start and the end of the period of home and community use). The total days of usage and total number of sessions were obtained from the logbook (i.e. a completed page in the logbook indicated that they used the exoskeleton that day and multiple sessions on a day were written down). In addition, the amount of use per day (i.e. minutes of active time, total distance covered, and maximal distance covered without rest) was estimated by the participants and extracted from the logbook. Per session, the purpose and location of use were derived from the logbook and divided into various categories for the analysis. The five categories for purpose of use were: (1) individual exercise, (2) participation/social event, (3) exercise and social event, (4) explore indoor usability, and (5) other. The definitions of these purpose categories are described in Table 1. Location of use was divided into four categories: (1) outdoor use, (2) in home use, (3) indoor use at location (e.g. local fitness hall or indoor parking lot) and (4) mixture of use at the same day (i.e. indoor/home and outdoor). The percentage per category was calculated as the number of session per category divided by the total number of sessions. Reasons for non-use were extracted from the logbook.

Table 1. Definitions of the categories for purpose of exoskeleton use.

	Total distance walked		Presence of other people than the buddy	
	< 100m	≥100m	Yes	No
Individual exercise		X		X
Participation / social event	X		X	
Exercise and social event		X	X	
Explore indoor usability*	X			X
Other				

* location is at home

Exoskeleton experience

The exoskeleton experience was assessed as the satisfaction, importance, and usability of different aspects of the exoskeleton. In addition, other experiences with the exoskeleton (e.g. fall or device error) that were recorded in the logbook were evaluated. Satisfaction was derived from the 12-item D-QUEST questionnaire[25] and divided into satisfaction with the assistive device (8 items), satisfaction with the service (4 items), and overall satisfaction (average). The satisfaction (sub)scores ranged between 1 and 5, with a higher score indicating greater satisfaction. Item analysis of satisfaction scores was performed, in which an item score of 1, 2 or 3 was considered dissatisfied.[27] In addition, the importance of each item was analysed by calculating how frequent a particular item was indicated by the participants as one of the three most important items. Usability was derived from the 10-item SUS questionnaire[26] and evaluated as the overall usability and at item level. Each SUS item was scored from 0 (low usability) to 4 (high usability). The overall SUS score was calculated by multiplying the sum of the item scores by 2.5 and ranged between 0 and 100,[26] with a higher score indicating better usability. A mean SUS item score below 3 was considered low usability.

Health related effects

If participants reported health related effects in the logbook, these effects were categorised into positive (e.g. less neuropathic pain or improved mental health) and negative (e.g. increased pain or spasticity) effects. All negative effects were analysed regarding whether they resulted in non-use of the exoskeleton.

Statistical analysis

The distribution of the data was tested for normality using a Shapiro-Wilk test. All outcome measures were analysed with descriptive statistics (mean and standard deviations). In case the assumption of normality was violated, median and ranges were calculated. The distribution of the amount, purpose, and location of exoskeleton use was reported using percentages (for grouped results) and frequencies (for individual results). In addition, frequency analysis of the user experiences and health related effects were reported.

Results

Exoskeleton use

Fourteen participants had the exoskeleton at their disposal for home and community use. An overview of the participant characteristics is given in Table 2. Median exoskeleton use was 9 (range 1 – 15) out of 16 (range 12 – 21) days, in which participants performed a median of 9.5 (range 1 – 19) sessions and took a median of 3226 (range 330 – 28882) steps. An overview of the amount of exoskeleton use per participant is given in Table 3. Per day, the estimated median active time was 46 (range 19 – 84) minutes, during which the median estimated total distance covered was 243 (range 22 – 1367) meters and the median estimated maximal distance covered without rest was 120 (range 12 – 1125) meters (Table 3). The subject-reported primary purpose of exoskeleton use was for individual exercise (90 out of 121 sessions, 74% of all sessions) (Fig 2). Other purposes of exoskeleton use were a combination of exercise and social event (14%, 17 sessions), participation/social event (6%, 7 sessions), explore indoor usability (4%, 5 sessions), or other (2%, 2 sessions). The location of exoskeleton use was mostly outdoors (58 out of 121 sessions, 48% of all sessions) (Fig 3). The remaining location of exoskeleton use was 27% (33 sessions) indoors (e.g. gym or indoor parking lot), 19% (23 sessions) combination of indoors and outdoors, and 6% (7 sessions) at home. The following factors were mentioned as reasons for non-use of the exoskeleton: weather conditions (i.e. storm (participant I) and snowstorm (participant M)), becoming a father (participant J), dependence on buddy availability (participant K), and not meeting expectations (participant L),.

Table 2. Participant characteristics.

	Total (N=14)
Sex (male / female)	7 / 7
Age (years), median [min - max]	29 [24 – 49]
Time post injury (years), median [min - max]	6.25 [0.75 – 27]
Neurological level of SCI (thoracic), median [min - max]	Th9 [Th4 – L1]
Classification of SCI level (low (Th7–12) / high (Th1–6))	8 / 6
AIS* (A / B)	13 / 1

* AIS = American Spinal Injury Association Impairment Scale

Table 3. Amount of exoskeleton use during the period of home and community use.

Participant	Number of days at home	Primary: Total exoskeleton use			Secondary: Estimated exoskeleton usage per day (average)		
		Days of usage (%)	Number of sessions	Number of steps	Active time (minutes)	Total distance covered (m)	Distance covered without rest (m)
A	20	15 (71%)	19	3065	59	245	95
B	17	15 (88%)	15	11562	50	296	162
C	18	12 (67%)	12	4358	38	199	58
D	17	11 (65%)	12	7044	79	318	80
E	18	9 (50%)	11	3276	48	344	200
F	15	10 (67%)	10	28882	81	1367	1125
G	15	10 (67%)	10	5098	19	207	132
H	15	9 (60%)	9	3184	53	258	120
I	15	7 (47%)	7	10333	64	727	590
J	15	5 (33%)	5	367	21	22	12
K	17	5 (29%)	5	572	84	240	120
L	17	3 (18%)	3	655	42	183	45
M	15	2 (13%)	2	768	28	220	210
N	12	1 (8%)	1	330	40	150	75
Median [min-max]	16 [12 – 21]	9 (55%) [1-15] (8-88%)	9.5 [1 – 19]	3230 [330 – 28882]	49 [19 – 84]	243 [22 – 1367]	120 [12 – 1125]

Figure 2. Purpose of exoskeleton use during the period of home and community use.

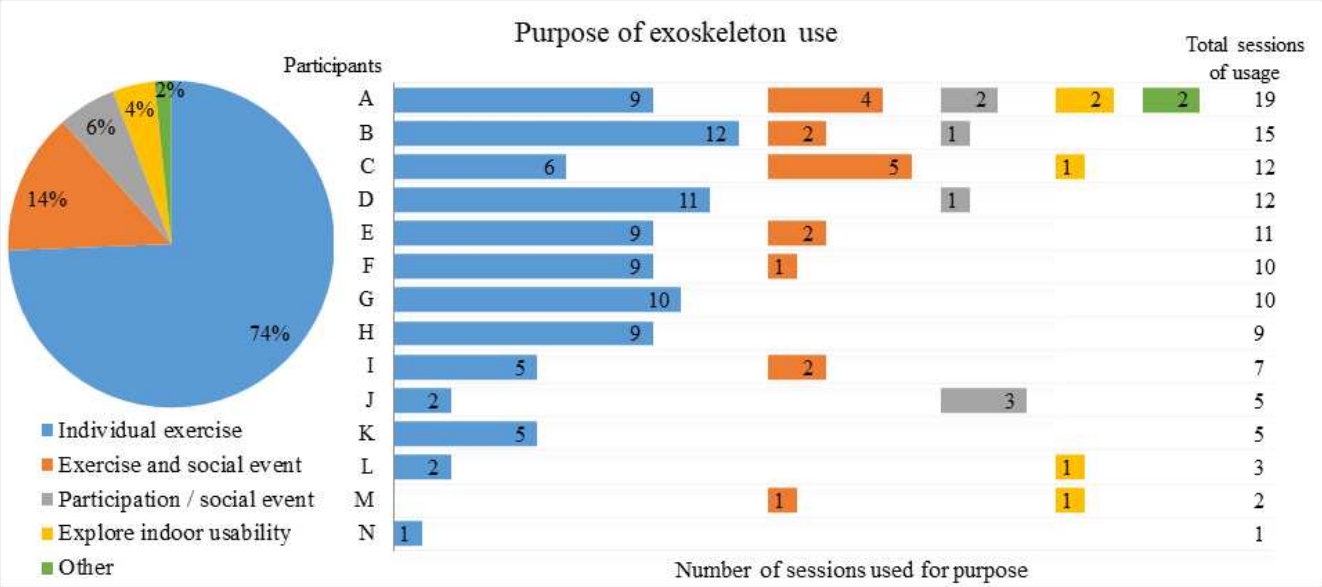
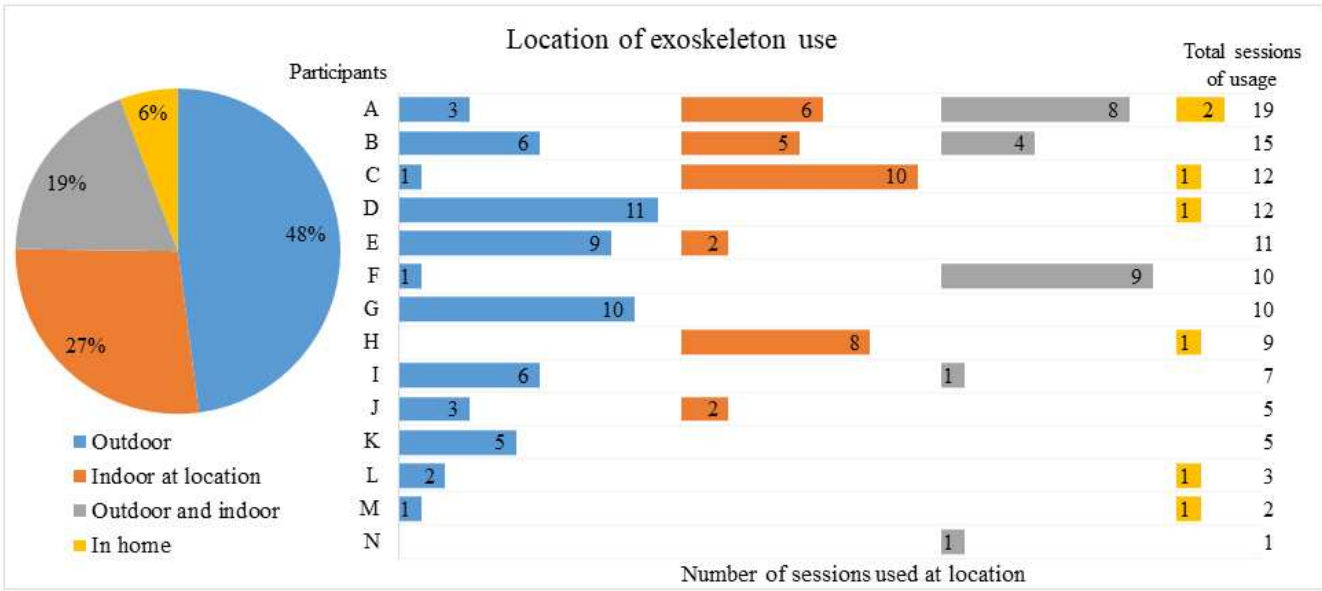


Figure 3. Location of exoskeleton use during the period of home and community use.



Exoskeleton experience

The average satisfaction with the exoskeleton was rated as 3.7±0.4 (D-QUEST total), 3.5±0.4 (subscale assistive device), and 4.2±0.5 (subscale service). An overview of the item analysis of satisfaction and importance is shown in Fig 4. 'Weight', 'Effectiveness', 'Ease of use', and 'Safety' were most frequently scored as dissatisfied (D-QUEST item score ≤ 3) and – at the same time – indicated as important. The usability of the exoskeleton was rated with a median of 72.5 [52.5 – 95.0]. Two SUS items had a mean SUS score below 3, indicating low usability ('I needed to learn a lot of things before I could get going with this system (2.1±1.5)' and 'I found the various functions in this system were well integrated (2.3±0.8)'). Other experiences that participants recorded in the logbook were one fall and one device error (participant B). These incidences did not lead to health complications. Regarding the device error, the exoskeleton use was interrupted for three days until the error was resolved.

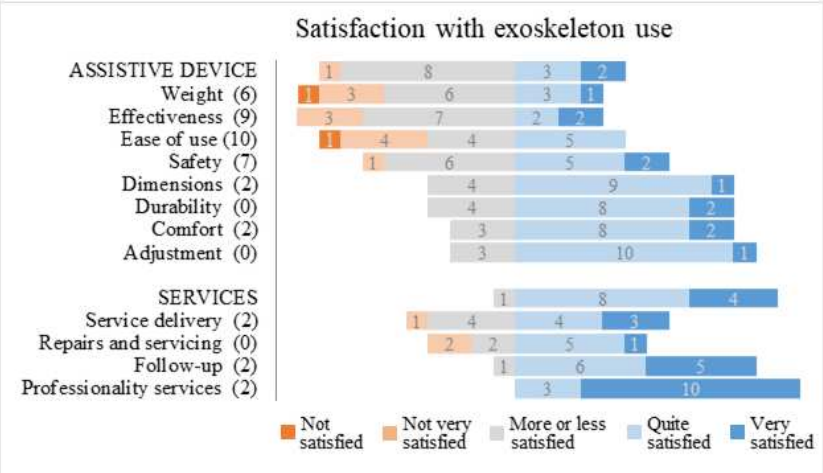


Figure 4. Distribution of the satisfaction scores on the items of the Quebec User Evaluation of Satisfaction with Assistive Technology (D-QUEST).

A satisfaction score of 'more or less satisfied' or less (D-QUEST ≤ 3) was considered dissatisfied. The numbers in brackets represent how frequent an item was indicated within the top 3 most important items of the D-QUEST by the participants.

Health related effects

Five patients reported positive health related effects in four domains: effects on social and mental health (n=5), decreased spasticity (n=3), reduced neuropathic pain (n=1), and increased range of motion of the hip and back (n=1). Five participants reported negative health related effects, among which muscle or joint pain (n=4), skin damage (n=2), increased spasticity (n=1), and fecal incontinence problems (n=1). In two participants who reported shoulder pain, exoskeleton use was stopped for one day (participant H) and during the remaining period (participant N), respectively.

Discussion

This study assessed the amount, purpose, and location of exoskeleton use in the home and community environment in people in the chronic phase of motor complete SCI. In addition, users' experiences and health related effects during the home and community use were studied. Fourteen people with a complete SCI used the exoskeleton 9 out of 16 days. The exoskeleton was mostly used for exercise purposes and social interaction. In half of the sessions the location of use was outdoors. Overall, participants were satisfied with the exoskeleton and its usability.

There was a large variation in the amount of exoskeleton use between the participants. The days of usage ranged from 1 to 15, during which 330 to 28882 steps were taken. The low amount of use in some participants could be attributed to exoskeleton related factors (i.e. shoulder complaints, not meeting expectations, and dependence on buddy availability) or external factors (i.e. snowstorm and becoming a father). In contrast, more than half of the participants used the exoskeleton at least one out of two days. Because of the novelty of the exoskeleton and the relatively short time period of exoskeleton availability, participants probably optimally exploited the possibilities. Thus, although our results are likely representive for short term home and community use, they may be an overestimation with regard to long term exoskeleton use.

Based on the purpose and location of use, the potential of a wearable exoskeleton can be identified. The expected potential of an exoskeleton has previously been addressed in a qualitative study by Manns and colleagues.[28] They found that some participants expected the best potential for outdoor exoskeleton ambulation, whereas others expected better potential for functional indoor use during daily life activities (e.g. cooking while standing).[28] Yet, only when participants have an exoskeleton at their disposal in the home and community setting, the full potential of an exoskeleton can be truly assessed. In the current study, all participants used the exoskeleton for exercise purposes and two thirds of the participants used it for social interaction, either with or without exercise. For exercise and social interaction purposes, the exoskeleton was used at locations with large, open, and smooth surfaces, either outdoors or indoors. In contrast, the exoskeleton was barely used at home. Indoor usability at home was explored by only four participants (and repeated once by merely one participant). The current findings support the general thought that an exoskeleton has a high potential to be used as an exercise device and for social interaction at eye-level, but a low potential as an assistive device for supporting daily activities.[18,20]

Despite the shortcomings of the investigated exoskeleton as an assistive device during daily life activities, participants were generally satisfied with its use. Based on conversations with the participants, we assume that participants evaluated their overall satisfaction of the exoskeleton with respect to the current use and their expected applications. Most participants used it as an exercise device and for social interactions and indicated the following aspects of improvement in order of importance: ease of use, effectiveness, safety, and weight. Ease of use has also been rated as most important for manual wheelchair[29,30] and walker use.[29] One difference between wheelchair / walker use and exoskeleton use is, the requirement of a buddy during exoskeleton use, thus potentially limiting the individual's independence. Ten of the participants reported that the buddy was a hindrance, as has been reported in

other studies.[18,22] The buddy requirement presumably influenced the other three aspects of improvement (effectiveness, safety, and weight) as well. The comments related to 'satisfaction with effectiveness' (e.g. the degree to which the device meets one's needs) reflected participants' desire for independent functional use. The participants also commented that they felt most safe with the buddy constantly guarding them during use and that because of the weight (~27kg) of the device, a buddy was needed for transporting the device in and out of their cars. Since detailed information regarding transportation was not investigated in the current study, future studies should investigate the implications and issues regarding transport. Nevertheless, participants also emphasized that there are no other devices that enable similar options for exercise or social interaction in an upright position. Therefore, the overall satisfaction with the exoskeleton and its usability was considered as good, although less need for a buddy and improved transportability is desired. For these reasons, it is important to investigate how the exoskeleton can be further improved with respect to the applications that users have in mind.

For application at home and in the community, two exoskeletons are currently FDA and CE approved (ReWalk and Indego[24,31]). The main difference between these exoskeletons is that the Indego exoskeleton is modular and weighs less, [1] which facilitates transportation. Despite this difference in modularity, both exoskeletons require the use of upper extremity support (i.e. crutches) for balance, are only allowed to be used with a trained buddy, and have the same three options for mobility (sit, stand, and walk[24,31]). Although in the current study the ReWalk exoskeleton was investigated, we expect similar findings for other currently commercially available exoskeletons that rely on upper extremity points of contact with crutches for balance.

In the current study, participants with a low (Th7–12, n=8) and high (Th1–6, n=6) complete SCI who could control crutches were included, reflecting a large range of the complete SCI population. However, selection bias is likely, because only people with a complete SCI who were interested in exoskeleton use and who could commit to the exoskeleton training protocol participated. Furthermore, only participants who achieved a skill level for safe home and community use (i.e. at least 17 final skills in the previously described Final-skills-test[10]) were included. Therefore, the results should be interpreted with caution and are not generalizable to the whole SCI population.

In conclusion, the exoskeleton investigated in this study (ReWalk) has a good potential to be used as an exercise device in the home and community environment. For this purpose, participants with a motor complete SCI were satisfied with its use, but wished for technological improvements to reduce the need for a buddy and to improve the overall transportability of the device. In addition, the exoskeleton enables social interaction at eye-level. Therefore, the use of an exoskeleton has the potential to contribute to the physical and mental health in people with complete SCI. As an assistive device during daily life activities, the exoskeleton has many limitations. Further exoskeleton development should, thus, look at other (more functional) applications that are important to their potential users.

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Chapter 9

Needs and wishes for the future exoskeleton: an interview study among people with spinal cord injury with community-based exoskeleton experience

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Abstract

Background

Exoskeleton use by people with complete spinal cord injury (SCI) in daily life is still a challenge. To optimize its daily life use, a better understanding of the purpose of use and the accompanying improvements are needed. The perspective of experienced exoskeleton users provides an important contribution to the improvement of future exoskeletons.

Methods

Face-to-face semi-structured interviews were held with 13 people with SCI, who were experienced exoskeleton users. Interviews were audio-taped, transcribed and analysed thematically.

Results

Participants expressed three future purposes of exoskeleton use: for daily activities, exercise, and social interaction. Exoskeleton use during daily activities was the ultimate goal. Therefore, the future exoskeleton should be: *easy to use*, *small and lightweight*, *tailor made*, *safe*, *comfortable*, *less distinctive*, *durable*, and *affordable*. Improving the ease of use was relevant for all purposes, for all participants. The other suggestions for improvement varied depending on the purpose of use and the participant.

Conclusion

Increasingly more advanced improvements to future exoskeletons are needed to transition from an exercise purpose, to social interaction, and ultimately use during daily activities. In the current study, detailed suggestions for improvements from experienced exoskeleton users have been made. Only when multiple of these suggestions are adjusted, can the exoskeleton be used to its full potential.

Keywords: Spinal cord injury, exoskeleton, user experience

Introduction

Spinal cord injury (SCI) is characterized by damage of the spinal cord that leads to (partial) loss of sensory, motor and autonomic functions below the lesion.[1] A complete SCI is characterized by paralysis of the muscles below the lesion level and, thus, recovery of walking capacity is unlikely, resulting in a lifetime reliance on a wheelchair.[2,3] Further, people with SCI are also at risk for the occurrence of secondary health complications, such as bladder and bowel disorders, pressure ulcers, spasticity and pain,[4,5] which are associated with a lower quality of life.[5] Recently, wearable exoskeletons (such as the ReWalk™, Ekso™, and Indego® exoskeleton) have appeared on the consumer market.[6] In the clinical setting, wearable exoskeletons are mainly used for training purposes and to enhance health benefits in people with complete SCI. The health benefits include less spasticity,[7,8] improved bowel function,[9] and improved overall quality of life.[7] However, to preserve these health benefits, regular exoskeleton use is necessary. One approach to facilitate regular exoskeleton use is to ensure that wearable exoskeleton can be used at home and in the community.

Little is known about the use and experienced benefits of exoskeleton use in the community. To our knowledge, two studies investigated community exoskeleton use, namely in a community-based gym[10] or in and around home.[11] In both studies, the exoskeleton was mainly used for exercise purposes.[10,11] Participants also emphasized the usefulness of an exoskeleton for social interaction.[10,11] The exoskeleton was rarely used to facilitate functional mobility during daily activities.[11] Study participants reported physical and psychosocial benefits after using the exoskeleton for approximately ten weeks[11] or one year.[10] They experienced less spasticity, less pain, better wound healing, improved bowel function, and improved mental wellbeing and increased energy to (socially) interact at eye-level.[10,11] Although there seem to be physical and psychosocial benefits for exoskeleton users, it is unclear which barriers exoskeleton users experience in the home and community setting.

A few studies examined possible barriers and/or improvements of an exoskeleton in order to optimize its use. Reported areas of improvement were safety,[12–15] ease of use (including the need of a buddy,[12–14] need of upper extremity support,[13,16] walking speed,[12,14,15] donning,[12–15] transportability,[13,16] and energy demand[14]), costs,[14, 15] and comfort.[15] However, these suggested improvements are from researchers and individuals with no exoskeleton use experience.[12–16] The needs and wishes for the future exoskeleton from the perspective of people with SCI with community-based exoskeleton experience are still unclear. In addition, the various barriers people with SCI may experience when using the exoskeleton may vary depending on the purpose of its use (e.g., the need of a buddy might be a barrier for functional daily use, but not for social interaction at an eye-level).

To optimize the use of exoskeletons in daily life by people with complete SCI, a better understanding of the purpose of use and accompanying improvements from the perspective of exoskeleton users are needed. The perspective of experienced users provides an important contribution to the improvement of future exoskeletons. These insights can inform future exoskeletons designs, and ultimately, can help to optimize community-based exoskeleton use. Therefore, the main research questions of this qualitative study were (1) for which purpose(s) would (potential) exoskeleton users like to use the exoskeleton in the future and (2) which improvements are needed to the current exoskeleton to facilitate these desired purpose(s) of use?

Methods

A qualitative study design involving in-depth semi-structured interviews with thematic analysis was chosen to address the research questions. All participants gave written informed consent in accordance with the Declaration of Helsinki. The medical ethics committee of Arnhem-Nijmegen determined that this study met the requirements for exemption from the Medical Ethics Committee review under the Dutch Medical Research Involving Human Subjects (2019-5637). The study was approved by the internal review board of the Sint Maartenskliniek.

Participants and recruitment

Adult people in the chronic phase (>6 months) after a motor complete SCI (American Spinal Injury Association Impairment Scale (AIS) A or B) who used a wearable exoskeleton both in the clinical setting and community-setting, and had proficiency in the Dutch language were eligible. Eligible people who participated in our previous exoskeleton study (2016-2418[11]) and who gave consent to be contacted for a follow-up study were approached. In addition, people in the Netherlands who purchased their own exoskeleton were contacted to participate. To our knowledge, this was the entire population of Dutch people with complete SCI who used an exoskeleton in the home and in the community setting. Potential participants were first approached via an e-mail containing the information letter. If they had no objections, they were contacted by telephone after one week of reflection and, if they wanted to participate, to schedule an interview appointment.

Data collection

Single face-to-face interviews were held at the participant's home or at the rehabilitation clinic, according to the preference of the participant. The interview guide consisted of semi-structured open-end questions (Figure 1). Interviews were conducted by the first author (PhD candidate), with whom all participants were familiar from the previous study[11] and who received training to perform interviews. No other participants or researchers were present during the interview. As a sensitizer, each interview started with a short videoclip (+/- 1 minute) of the participant's final clinical training session with the exoskeleton before two-weeks of community use as part of the previous study.[11,17] Each interview was audio-recorded and transcribed verbatim for data analysis. During and after each interview, field notes were made. To ensure complete and transparent reporting, the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist was used.[18]

Question 1:	*Could you describe the first day you used the exoskeleton at home or outside the clinic?*
Question 2:	*Could you describe the last time you used the exoskeleton at home or outside the clinic?*
Question 3:	*Suppose you would use the exoskeleton every day, for example like putting in your contact lenses every morning or wearing your glasses, what should the exoskeleton look like to you?*
Question 4:	*For which activities would you like to use that exoskeleton? What would the purpose of the exoskeleton use be?*
Question 5:	*Which changes to the current exoskeleton are needed for that purpose?*
Question 6:	*Looking back at the exoskeleton you used, what do you think are the most important changes that are needed?*

Figure 1. A short version of the interview guide.

Data analysis

Data collection and data analysis was alternated and repetitively reflected on by two researchers (RvD and JV). Analysis of the data was done in an iterative process using thematic analysis. Transcripts were coded by the first author and discussed with the second author until consensus was reached. Initial open coding was performed by the first author, with labelling segments of the transcript close to the phrasing of the participant. Thereafter, codes were refined throughout the analysis and categorized into themes (axial coding). The core themes were based upon concepts extracted from literature.[11,13,15,19] Memos were written and used during the analysis to help the researchers keep track of and reflect upon decisions made. To help interpret the findings, the field notes (from during and after the interview) were used. Data saturation was assumed if no new axial codes emerged from the analysis of the last two interviews. The final results (selective coding) were discussed with the first, second, and last author and adjusted if necessary, until consensus was reached. The software program ATLAS.ti was used to code the data and write the memos.

Results

Thirteen out of the sixteen contacted people participated in the study. Reasons for not participating were self-reported lack of sufficient community-based exoskeleton experience (n=1), and limited time to participate (n=2). A summary of the characteristics of the thirteen participants is given in Table 1. To ensure confidentiality, codes ($P1^{gender(age)}$, $P2^{gender(age)}$ etc) were used instead of the participant's names when indicating from whom a quote originated. All participants were experienced exoskeleton users, who completed a clinical training period of approximately eight weeks (+/- 24 training sessions). They all used the ReWalk™ exoskeleton in the home and community setting, the amount of community use ranged from three to more than 100 days). Three participants had purchased their own ReWalk™ exoskeleton through crowdfunding and, thus, had much more community exoskeleton experience. In addition, six participants also had experience with another exoskeleton: the Indego® exoskeleton in a clinical setting (n=4, +/- 3 years ago) and/or a research exoskeleton (i.e., March or Symbitron) in a lab setting (n=4, +/- 1.5 years ago). The time between the last community-based exoskeleton use and the interview ranged between one day and four years (median of two years). The duration of the interviews varied between 30 and 90 minutes.

Table 1. Participant characteristics.

	Total (N=13)
Sex (male / female)	7 / 6
Age (years), median [min - max]	33 [25 – 52]
Time post injury (years), median [min - max]	8 [2 – 28]
Neurological level of SCI (thoracic), median [min - max]	Th9 [Th4 – L1]
Classification of SCI level (low (Th7–12) / high (Th1–6))	7 / 6
AIS* (A / B)	12 / 1

* AIS = American Spinal Injury Association Impairment Scale, Th = Thoracic, L = Lumbar

Purpose of exoskeleton use

Three future purposes of exoskeleton use were mentioned in the interviews, namely for daily activities, exercise, and social interaction. Table 2 provides an overview of the purposes of use with exemplary citations. The use during daily activities and for exercise was addressed in the interviews of all participants. Most participants wanted to use the future exoskeleton during daily life activities in which they now used the wheelchair, such as grocery shopping or driving a car. One person even expressed that he wanted to do all activities that he was able to before the SCI, such as walking on the beach or running up the stairs. Participants also mentioned that they were interested in using the exoskeleton as an exercise device to stay fit and to stimulate health benefits. Furthermore, the use of the exoskeleton for social interaction (e.g., go to the pub or join in a group chat at a party with bar tables) was mentioned in almost all interviews. Some participants emphasized that for exercise and social interaction you do not need to purchase your own exoskeleton, but could share an exoskeleton with others as well.

Table 2. Purposes of exoskeleton use with exemplary citations.

Daily activities
"As it is now, I would use the Rewalk for what I call physio sports. However, you would want to use it to do the things you used to be able to do, like getting up, driving a car, you'd put it on in the morning and keep it on all day. Possibly using it in combination with a wheelchair. It'd be nice though if you didn't need your wheelchair at all." P10[female(52)]
"Ultimately, I'd like to be able to, for example, go for a walk on the beach with my daughters, or take them to an amusement park, and go on rides you actually have to go up steps for. Or at least that you can do things that you can't do right now because of that [wheel]chair." P3[male(29)]
"Well, what I envision is a kind of exoskeleton that I can put on like a pair of trousers and that I can wear sitting in my wheelchair. So that, whenever I want to, I can get up or climb a flight of stairs, or whatever. [...]. When I think of that, of what would be possible, a whole new world opens up." P11[male(37)]
Exercise
"The purpose of walking? Well, for me it's pushing back the boundaries. Each time, I try to walk further with it. That's great. First just a short distance, and then each time go a bit farther. Yeah, the goal is to push back the boundaries and see how far you can walk with a suit [=exoskeleton] like this." P9[male(49)]
"But I'd like to use it in a rehabilitation centre, for example, to be able to walk. Preferably together with others, so you can learn from each other. For the health benefits, you know. I wouldn't use it so much for practical things, but more to improve my health, and not have to sit in my chair all day. That I can walk. That there's pressure on my joints. So that you can keep walking. That's why I think it's useful... to improve your health. I'd really like to use it for that." P2[female(44)]
"Also for health reasons, of course. Having walked for about three and a half months I felt even fitter. Just bladder and bowel goes easier and, when you walk and move your hips a few times a week, it [your body] feels more comfortable, that sounds a bit weird, but yes that's what happens." P4[female(49)]

Social interaction
"So that you can join in. For instance, I hate parties where they have standing tables. It'd be great to be able to just stand at a table like that. And with a bar stool nearby for support if necessary or to rest a bit, so that basically you don't stand out from the crowd. Yes, I think that's something that would make this kind of suit [=exoskeleton] very useful." P7[female(30)]
"I didn't want to think about that for a very long time. I told myself that it wasn't really important to me. But it's true that people really like to look at you at eye level. And they suddenly notice you again and say, hey, wow, I haven't seen you standing up like this before." P5[female(49)]

Motives for exoskeleton use

In addition to the purposes of future exoskeleton use, three motives for exoskeleton use were clearly described in the interviews, namely societal importance, preserving autonomy, and fun. A few participants mentioned that for them, a motivation for exoskeleton use was the societal importance for further development.

> P5[female(49)]: *"I think it's something that's still in its infancy, that needs to be developed further. [...]. I think we should all do our bit to make that happen [...] it may actually be something that will be covered by health insurance in the future. Mainly for people who've recently suffered a spinal cord injury, I should think."*

The use of the exoskeleton was frequently compared to wheelchair use, which is something this population uses on a daily basis. For example, some participants stressed that they are completely autonomous with their wheelchair, and that this level of independence is something they also wanted to pursue with the future exoskeleton, especially during daily activities.

> P2[female(44)]: *"Independence. I think that's the biggest one. I'm now too dependent on someone else or on devices, for safety, weight, all the things I can't do myself, over which I've no control now. Yes, independence. Not needing help with anything. That's it basically."*

Contrary to wheelchair use, the motive for exoskeleton use was sometimes referred to as 'for fun', in which fun was an end in itself.

> P7[female(30)]: *"Well.. it has to be fun. That it becomes less therapeutic. Sure, it will never be exactly the walking you were used to [before the injury], but I do think that it's very close, that you can just go for a nice stroll around the block."*

Improvements of exoskeleton

To optimize the future exoskeleton, different improvements were suggested. Experienced exoskeleton users mentioned that their future exoskeleton is easy to use, small and lightweight, tailor made, safe, comfortable, less distinctive, durable, and affordable (figure 2). The most inner circle (i.e., easy to use) of figure 2 represents the desired improvement that was relevant for all purposes of use, for all participants. The circles further to the edge, represent improvements that are more person-dependent or dependent on the purpose of use. In the next sections, the different suggestions for improvement will be discussed.

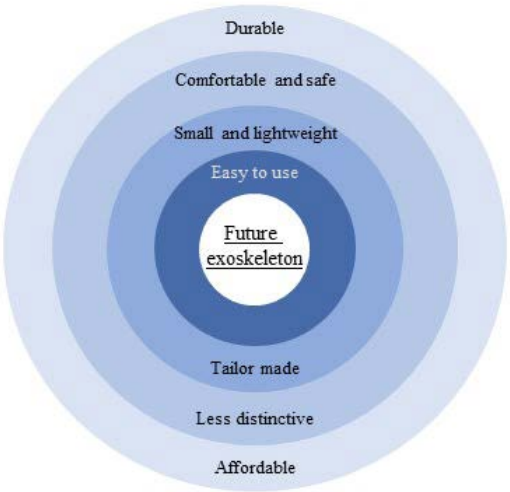

Figure 2. Exoskeleton improvements. Darker shades circles are relevant for all purposes of use and for all participants, whereas lighter shades circles are more person-dependent and dependent of the purpose of use.

First circle: Easy to use

Regardless for which purpose the future exoskeleton will be used, all participants mentioned that the future exoskeleton should be easier to use. Therefore, participants advised to improve the remote-control watch, balance, step and speed adjustments, and donning and doffing of the exoskeleton. Improvements to the remote-control watch were mentioned most frequently, for instance improving readability in sunlight and/or changing control options. Suggested control options were via speech or via touch (e.g., touching the thigh to walk and touching the bottom to sit down). Some participants suggested to relocate the control to the crutches, as long as the crutches are needed for balance support. This crutch-control would preferably include a small screen on which different speeds, step heights and step frequencies could be selected. In addition, participants mentioned that keeping balance with the exoskeleton (especially in stance) required much physical and mental effort. To be able to focus on other things, such as a conversation or use of kitchen utensils, balance improvements in the future exoskeleton were desired.

> P11$^{male(37)}$: *"What's essential in that suit [=exoskeleton]? What can still be improved? Well, first of all, the balance. Not having to use crutches anymore is the most important thing. […] That you don't constantly need to keep your balance; the suit should do that for you. That's what I think is crucial. Suppose I could walk the way I am doing now, but could keep my balance without needing crutches. That would immediately be a real functional improvement."*

Step and speed adjustments were desired so that the exoskeleton could be used more broadly.

> P9$^{male(49)}$: *"It should have gears, like in a car. Or let's take a bike as an example. Let's say you have one, two, three positions and that the third position is the highest gear. This gear allows you to, for example, take a big step, or increase your pace. That works perfectly for outdoors. Position two would then be something just in between. And position one would reduce the length of your steps and their frequency. Then I think it could be used functionally in a home situation indoors."*

In addition, some participants expressed the wish don and doff the exoskeleton, without needing several preparations: P10$^{female(52)}$: *"You also have to bring something [a stool] on which you put it [the exoskeleton], to be able to don it there."* and P6$^{female(29)}$ *"I don't want to spend more time putting it on than that I'm actually using it."*

Second circle: Small, lightweight, and tailor made

The improvements in the second circle were mostly related to transporting the exoskeleton and adjusting the hardware to the body of the user. Participants agreed that they could not lift and transport the exoskeleton (in a convenient way) by themselves, due to the weight and the physical dimensions.

> P8$^{male(28)}$: *"But maybe it will make a difference when carrying it to and from the car. If I can move it myself, for example, in three sections instead of one big awkward lump for which I would need someone else to help me. […] It wouldn't be so heavy then. Maybe it'll save some space. That would make me independent. I'd be very happy, even if it did take me five minutes longer to put it on."*

In addition, participants mentioned that, especially due to the crutches, you need a lot of space. Therefore, some participants noted that their (wheelchair friendly) house was too cramped for exoskeleton use. A minority of the participants expressed the desire for an exoskeleton that is exactly tailored to their body, but can also be adjusted to different people, in case you want to share an exoskeleton.

> P7$^{female(30)}$: *"Normally you have enough space but now it feels mega small, because with that suit [=exoskeleton] and those crutches you're a bit like a big robot stomping around the house. It's not very pleasant. I hope that in the future they'll be able to develop suits that are as compact as possible, so that you can easily use [them] at home. It would be really great if I could do more things standing or walking."*

Third circle: Safe, comfortable, and less distinctive

Opinions on improving safety were diverse. Some participants considered the safety of the exoskeleton as very important and even something that – if not guaranteed – would lead to disuse, while others felt that using the exoskeleton was safe and the risks were similar to other activities.

> P5$^{female(49)}$: *"Improvements that would make me use it regularly to move about? Well, most certainly an emergency stop. […] Suppose getting up doesn't go well… if you could just press something in your crutches if things start to go wrong, and you'd be able to get back in the right position and slowly lower it, so that you go back to base [the sitting position], if I had had those options I think it would have been less scary for me."*

P4[female(49)]: *"In the end there is one thing you don't want and that is falling."*

P9[male(49)]: *"Yes, you can fall, but you can also fall over in your wheelchair, you know. There's no danger of that. Zero, nil, nothing! It may happen that your crutch slips when you're walking somewhere and that it bounces a bit, but so what? If I go handcycling, another road users may not see me and I may get hit by a car, but that's a risk I'm willing to take."*

Participants who desired an exoskeleton that could be worn all day, mentioned that it should be comfortable to wear and that, for example, a battery on your back would be inconvenient in order to sit comfortably (anywhere).

P11[male(37)]: *"It's just a hassle with that thing. You're completely constricted, even when sitting. You can't really move well in it. So I could sit in the pub in it, but I wouldn't feel very relaxed."*

Although most participants focused more on the functionality of the exoskeleton, some participants expressed the wish to make the exoskeleton's appearance as close to normal as possible, so that they don't attract (extra) attention in public situations (e.g., less visible and less noisy).

P1[male(27)]: *"That it [the walking pattern] looks natural. So that people don't think you're some kind of robot. I think you could easily do this with the latest software."*

Fourth circle: Affordable and durable

Most participants indicated that the current exoskeletons are too expensive, especially with respect to what it is currently capable of. Therefore, almost all participants focused on improvements to its functionality. However, a minority mentioned that not all improvements were necessary and one participant pointed out that the exoskeleton should have fewer functionalities, so that it could be marketed cheaper and become accessible to a larger group.

P1[male(27)]: *"I think you first need to focus on affordability and, of course, functionality, particularly if you want to stimulate further development. After all, it's a very specific target group."*

In addition, only a few participants mentioned improvements about the durability of the exoskeleton.

P13[male(25)]: *"Then [to be able to walk in the rain] you need to make it waterproof. So, for example, the bearings need to be well sealed, and you need to use corrosion-resistant material. Like mobile phones. All mobile phones are water resistant nowadays... So that means a backpack... but that will all drive up the price."*

Discussion

In this qualitative study, experienced exoskeleton users expressed three future purposes of exoskeleton use: for exercise, social interaction, and daily activities. Using the current exoskeleton for exercise is already possible[11,20,21] and only a few improvements to make it easier to use were desired for this purpose. To facilitate social interaction, besides easier to use, the exoskeleton should also be small and lightweight, tailored to the person, and for some people less distinctive. For the ultimate purpose of future exoskeleton use, namely during daily activities, the most improvements were needed.

The extent of improvements needed for daily activities varied between participants, possibly reflecting participants who kept their answers closer to nowadays reality (i.e., feasible with the current technological knowledge) and participants who were willing/dared to describe their ultimate future exoskeleton ('the sky is the limit'). For instance, improvements to the comfort level varied from improving seating comfort in a (wheel)chair, to a level where the exoskeleton never has to be taken off again (i.e., a lifetime of 24/7 use, including wearing it in bed and while showering). Although participants who described the 'sky-is-the-limit' exoskeleton may have given unrealistic answers from a designer's perspective, there is great value in these answers because they provide insight into what is ultimately pursued. Exoskeleton use during daily activities was often discussed in the context of participants current, wheelchair-bound, execution of daily activities. Contrary to wheelchair use, the motive for exoskeleton use was also referred to as 'for fun'. Something that will rarely be stated about the wheelchair, which was only considered an assistive device.

Although we (partly) found similar areas of improvement as previous studies, the relevance and content of these areas of improvement sometimes differed. A previous survey study concluded that safety, affordability, ease of use, and comfort were considered the most important areas of improvement.[15] The relevance of improving the ease of use was supported by our findings (i.e., inner circle in figure 2). However, the other areas of improvement were more purpose and person dependent, suggesting that they were considered less relevant. Especially for safety, the relatively low relevance of improvement was not expected from both a clinical and a design perspective. In addition, the content within an area of improvement sometimes differed with previous findings. For example, the current study revealed specific improvements to the remote control watch (e.g., readability), to make the exoskeleton easier to use, instead of the earlier reported improvements to the comprehensive concept of 'ease of use' of the exoskeleton.[15] In addition, being able to adjust the speed (i.e., accelerate and decelerate) while using the exoskeleton in various situations was desired, instead of maximizing the speed of the exoskeleton itself.[12,14,15] Also a reduction in the number of preparations needed before exoskeleton use (e.g., placing the exoskeleton on a stool) was desired, whereas, once these preparations were made, donning and doffing the exoskeleton was not an issue. These detailed, yet very important, improvements have hardly been discussed in previous studies.

The discrepancy compared to previous studies could be attributed to the distinct enrolled (patient) populations. The suggested improvements in previous studies are from researchers and individuals who have not used the exoskeleton.[12–16] Only people with exoskeleton experience (outside the clinical setting) will be able to mention detailed, yet very important, improvements for home and community use (such as to the remote control watch). In addition,

all participants involved in this study can be seen as 'early adopters', meaning that they were already willing to use these not (yet) fully developed exoskeletons. However, it is important to keep in mind that the (needs and) requirements of these early adopters, may differ from the ultimate target group of the exoskeleton (i.e., the general SCI population). Nevertheless, also in these early adopters, multiple improvements were mentioned before the technology will become mainstream for a larger population.

Strengths and limitations

A strength of the current study is that almost the entire population of Dutch people with a complete SCI who used an exoskeleton in the home and in the community setting were interviewed and that data saturation was met. However, the community exoskeleton use was relatively long ago for some participants, which could have led to recall bias. To recall memories, and, thus, minimize the recall bias, a video of the participants own ReWalk™ exoskeleton use was shown prior to the interview. Although participants in the current study were particularly experienced with the ReWalk™ exoskeleton, we expect that the purposes of use, areas of improvement and, to a large extent, the relevance of the improvements are generalisable to other wearable exoskeletons that rely on upper extremity support. Caution apply to the remote control watch and the 'small and lightweight'-suggestion is advised, because these aspects differ between the most commonly used exoskeletons (i.e. ReWalk™, Indego®, and Ekso bionics™).[22–24]

Conclusion

Experienced exoskeleton users expressed three future purposes of exoskeleton use: for daily activities, exercise, and social interaction. Increasingly more advanced improvements of future exoskeletons are needed to transition from an exercise purpose, to social interaction, and ultimately use during daily activities. In the current study, detailed suggestions for improvements from experienced exoskeleton users have been made. Only when multiple of these suggestions are adjusted, the exoskeleton can be used to its full potential.

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9

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Chapter 10

Summary and general discussion

The general aim of this thesis was to investigate two interventions aimed at increasing mobility in people with incomplete spinal cord injury (part 1, virtual reality-based gait stability training) and complete spinal cord injury (SCI) (part 2, exoskeleton training). Specifically, the first part of this thesis studied whether virtual reality-based treadmill training would be effective in improving gait stability in people with limited walking capacity following an incomplete SCI. In the second part of this thesis, the feasibility of exoskeleton training for home and community use in people with complete SCI was investigated from several perspectives. In this chapter the main findings will be highlighted. Subsequently, theoretical and methodological considerations and the clinical implications will be discussed. This chapter will end with directions for future research and the overall conclusion.

Summary

Part 1 – Improving mobility in people with incomplete SCI using virtual reality-based treadmill training

In the first part of this thesis, a virtual reality-based walking training to improve gait stability in people with incomplete SCI was evaluated. In **chapter 2** we assessed the test-retest reliability of six stability outcome measures during self-paced treadmill walking in a virtual environment. In this study, both healthy adults and patients with incomplete SCI participated. We found that all six stability outcome measures had moderate to excellent reliability. The stability outcome measures in the medial-lateral (ML) direction (XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$) were considered the most promising measures to evaluate interventions and monitor individual patients.

In **chapter 3** we evaluated the effect of virtual reality-based walking training in chronic ambulatory incomplete SCI patients using spatiotemporal walking parameters, balance confidence, and the stability measures as described in **chapter 2**. The intervention consisted of 12 one-hour training sessions on a treadmill in a virtual environment (GRAIL). Participants had to react to or interact with the virtual environment by changing their walking pattern or shifting their weight during stance. People with chronic incomplete SCI increased their walking speed, stride length, anterior-posterior (AP) gait stability, and balance confidence following the intervention. The effects were retained after 6 months. These results suggest that virtual reality-based walking training improves walking and dynamic balance in people with chronic incomplete SCI. However, the stability measures in ML direction, which were considered the most promising measures to evaluate interventions (**chapter 2**), did not respond to the training.

Based on the results of chapters 2 and 3, we conclude that virtual reality-based treadmill training is effective in improving forward gait stability in people with limited walking capacity following an incomplete SCI.

Part 2 – Improving mobility in people with a complete SCI using a wearable exoskeleton

Improving mobility in people with complete SCI using an exoskeleton was the main topic in the second part of this thesis. First, we developed a framework to assess how people with a complete SCI learn to use an exoskeleton (**chapter 4**). The framework proposed in this study consisted of an Intermediate-skills-test and a Final-skills-test. During the 2nd, 4th, and 6th training week the

Intermediate-skills-test, consisting of skills in a hierarchical order of difficulty, was performed. When participants could walk independently, the Final-skills-test, which simulated skills needed during daily life situations, was performed in the last training session (week 8). With the Intermediate-skills-test, the progress in performing basic and advanced exoskeleton skills during a training program was measured. In addition, the Intermediate-skills-test included tasks in a hierarchical order of difficulty and could discriminate across participants' skill-level. As a reliability measure, the consistency of performing exoskeleton skills was used. The overall consistency of both the Intermediate-skills-test and the Final-skills-test was considered acceptable. In addition, learning to use an exoskeleton appeared to be time consuming and exoskeleton skill acquisition was diverse between participants.

The diversity between users raised the question: why do some users acquire more exoskeleton skills than others? In **chapter 5** we addressed this question by identifying the personal and injury characteristics that predict exoskeleton skill performance during and after an exoskeleton training period. Multiple regression analysis was performed to examine the predictive value of nine personal and injury characteristics (lesion level, age, body mass index (BMI), sex, sports participation, active lifestyle, anxiety level, time since injury onset, and age at injury onset) on exoskeleton skill performance measured with the Intermediate-skills-tests and the Final-skills-test (developed and tested in **chapter 4**). Lesion level appeared to be an important predictor during the first 4 weeks of training, but did not influence participants' final skill level. BMI, age, and active lifestyle were predictors of exoskeleton skill performance toward the end of the training period. None of the personal and injury characteristics were significantly related with the achieved skills at the end of the training period.

Although training and walking with an exoskeleton in motor complete SCI patients is considered safe, one should always be aware of risks of unexpected (technical) adverse events and the risk of fractures. **Chapter 6** reports the occurrence of two different cases of bone fracture related to exoskeleton usage. One case was most likely caused by misalignment of the joints of the exoskeleton relative to the joints of the lower extremities after an accidental shut down of the exoskeleton during walking. The cause of the other case remained unclear. Precaution measures to prevent adverse events, such as a bone mass density examination before training and regular alignment checks during the training, were given. In addition, specific training instructions were given both to the patient and his buddy on how to react to accidental shut down of the exoskeleton.

Despite the risk of fractures during exoskeleton use as described in **chapter 6**, the possibility to train in an upright position is expected to contribute to the maintenance and possible improvement of health in people with a complete SCI. The effects of eight weeks of exoskeleton training on quality of life and secondary health complications was evaluated in **chapter 7**. Health questionnaires revealed that short-term exoskeleton training in motor complete SCI patients improved their quality of life, pain, and satisfaction with bladder management. No changes in bowel function, range of motion and spasticity were found.

After a training period, participants were allowed to use an exoskeleton outside the clinical setting if 1) they achieved a skill level to perform daily life situations (measured with the Final-skills-test of chapter 4); and 2) they received specific safety instructions (described in **chapter 6**). Only when exoskeletons are used in the home and community, the applicability

in these settings can be assessed, which is important information for further exoskeleton development. The aim of **chapter 8** was to assess actual exoskeleton use in the home and community. The period of home and community use was at least two weeks during which participants kept a logbook. Participants had no restrictions regarding the amount, purpose, or at which location they used the exoskeleton. For safety reasons, they were instructed not to use the exoskeleton without supervision of their buddy. The amount of exoskeleton use was diverse between participants. Logbook data revealed that the exoskeleton was mostly used for exercise purposes and social interaction. In half of the sessions the location of use was outdoors. Participants reported satisfaction with the exoskeleton for exercise and social interaction in the home and community, but mentioned serious limitations regarding the use as an assistive device during daily life.

Exoskeletons have been developed based on what is currently technologically possible, which determines to a large extent what exoskeletons are used for. To optimize the use of exoskeletons in daily life by people with complete SCI, a better understanding of the desired purpose of use and related improvements of the exoskeleton are needed. Hence, incorporating the perspective of experienced exoskeleton users in the development of exoskeletons is important. Therefore, the participants from **chapter 8** were re-approached to participate in a qualitative (interview) study (**chapter 9**). Participants mentioned three future purposes of exoskeleton use; for 'daily activities', 'exercise', and 'social interaction'. Exoskeleton use during daily activities was the ultimate goal. Therefore, the future exoskeleton should be; 'easy to use', 'small and lightweight', 'tailor made', 'safe', 'comfortable', 'less distinctive', 'durable', and 'affordable'. Improving the ease of use was relevant for all purposes, for all participants. These other suggestions for improvement varied depending on the purpose of use and the participant.

Based on the results of chapter 4 to 9, we conclude that learning to use an exoskeleton is time consuming and that the amount of training needed for exoskeleton skill acquisition differs strongly from person to person. Of the 25 enrolled people, 21 people completed the training program. After the exoskeleton training program, 14 people achieved a safe skill-level for home and community use. During the period of home and community use, the exoskeleton was mainly used outdoors for exercise purposes. Participants noted that the training sufficiently prepared them for this home and community use, but exoskeleton improvements would be needed for use during daily activities. Overall, we conclude that eight weeks of intensive exoskeleton training is feasible for home and community use in people with complete SCI.

General discussion

Technology acceptance

For the implementation and use of technology in rehabilitation, it is important that the technology is accepted by the users. There are several models that are intended to understand the degree of technology acceptance by a group of people by means of revealing the potentialities and limitations of a specific technology. The most well-known models are: the Theory of reasoned action (TRA), Theory of planned behaviour (TPB), Unified theory of acceptance and use of technology (UTAUT), and the technology acceptance model (TAM). There is not one model fully suitable for the rehabilitation technologies (GRAIL and

exoskeleton) described in this thesis. The TAM,[1,3] developed by Davis[1] and later refined by Venkatesh and Davis[3], is one of the most commonly used models for explaining and predicting use of technology. The TAM describes the 'perceived usefulness' and the 'perceived ease of use' as the main factors influencing 'attitude towards using' a technology and, therefore, the 'actual system use' (see Figure 1).[3] The TAM was originally developed to explain computer usage behaviour in a workplace setting,[1] and is still most widely used to explain the use of information systems (e.g., Word, Excel, Powerpoint, etc[2]). Similar factors are involved in the acceptance of rehabilitation technology in a clinical, social or domestic environment. With the term 'perceived usefulness' Davis referred to 'the degree to which an individual believes that using a particular system would enhance his or her job performance', and with 'perceived ease of use' the 'degree to which a person believes that using a particular system would be free of effort'.[1] Ease of use was also mentioned as the most important factor for the exoskeleton technology (chapter 8). Hence, the TAM seems to be the most suitable model to describe the acceptance of technologies in a rehabilitation setting.

For user acceptance it is important to consider who 'the user' is. The definition of a user differs between the virtual reality-based gait stability training system (GRAIL) and the exoskeleton intervention and depends on the phase of the training. For the GRAIL, the physical therapist is the primary user. The patient can also be considered as a user, but in a more dependent position. In the initial (clinical training) phase with the exoskeleton, the physical therapist can also be considered as the primary user. However, the role of the physical therapist decreases when the patient gains exoskeleton skills. When the patient is able to walk with the exoskeleton without assistance of a physical therapist, the patient becomes the primary user. For the two technologies described in the this thesis, the acceptance by the user is of great importance. However, the two technologies are in different stages of acceptance and in different stages of development. The GRAIL is in a later (i.e., more accepted and developed) stage of technology acceptance, whereas the exoskeleton is in an early stage of acceptance. In the next section, I will first explain the technology acceptance of the GRAIL on the basis of the TAM. In addition, I will discuss the clinical implication of the GRAIL and directions for future studies. Subsequently, I will discuss the exoskeleton acceptance, its clinical implications and future directions for studies with the exoskeleton.

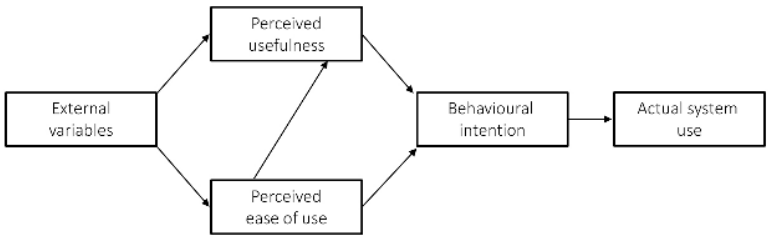

Figure 1. The Technology Acceptance Model (TAM) (Venkatesh & Davis 19963, p453).

Virtual reality-based treadmill training on the GRAIL

Technology acceptance

As argued above, the TAM indicates that for technology acceptance the perceived usefulness and perceived ease of use are important. A rehabilitation method that is often perceived as useful is mimicking daily life situations during walking training in people with incomplete SCI. This is an example of task-specific training, in which there is continuous interaction with the environment. To realize such a training situation during conventional rehabilitation therapy, physical therapists need to make use of objects one has to step over, such as a cube or a line. A disadvantage of using physical objects is the lack of safety, i.e. the danger of falling. Moreover, the physical therapist often has to physically support the patient, or stay very close to the patient, which impedes his/her ability to observe the patient. During GRAIL training, elimination of the fall hazard can be guaranteed by using a safety harness, while the mimics of a daily life situation can still be offered. As a result, a GRAIL system will be easily accepted by its users: both the physical therapist and the patient. The physical therapist operates the GRAIL system via the computer. Subsequently, the patient performs the exercises that are chosen by the therapist and provided via the GRAIL system. In a study about GRAIL system use in stroke survivors, physical therapists perceived benefits for improving balance and walking.[4] Stroke survivors also positively evaluated the GRAIL intervention and enjoyed the training sessions.[4] Moreover, it was indicated that the enjoyment of virtual reality-based treatment may lead to increased motivation for therapy adherence.[5,7] This confirms that the usefulness of the GRAIL is accepted by both physical therapists and patients with stroke. However, the perceived usefulness of the GRAIL by patients with other neurological diseases, including people with incomplete SCI, has not yet been evaluated.

The second important factor in technology acceptance, according to the TAM, is the perceived ease of use, which seems to be high for the GRAIL system as well. Firstly, the therapist is relieved from physical effort, as virtual objects are projected onto the screen and treadmill. Secondly, the therapist does not have to physically support the patient due to the safety harness. The GRAIL system rather requires a different, more technical, working method than most physical therapists are used to, which could limit the perceived ease of use at first instance. Therefore, to make sure that physical therapists become proficient with the GRAIL system, they have to complete a two-day course. This course can be seen as an external variable in the TAM and contributes to the effortless ability to offer all the adjustments and potentialities of the GRAIL system to patients. GRAIL system use can also be seen as a challenge and an extension of the treatment possibilities for physical therapists, which makes their profession more interesting. In addition, as with many other technologies, regular use of the GRAIL system is important, so that the physical therapist does not lose the acquired technical skills.

The GRAIL and comparable CAREN systems have now been introduced both in rehabilitation centres and in (university) hospitals. At the end of 2020, there are already 82 GRAIL and comparable CAREN systems installed worldwide, which emphasizes the acceptance of this technology. In the Netherlands, seven rehabilitation centres (Sint Maartenskliniek, UMCG/ Beatrixoord, RMC Groot Klimmendaal, Amsterdam UMC, Revant, Maastricht UMC+, and MRC Aardenburg) use the GRAIL or CAREN system for treatment purposes. It is interesting that, although the effectiveness of virtual reality-based treadmill training in patients with neurological diseases has not yet been established by randomized-controlled trials, the technology is already being widely used and perceived as useful.

Preliminary efficacy

Besides that a training intervention should be perceived as useful and ease to administer, the effectiveness of an intervention in daily clinical practice is important. The results from chapter 3 suggested that a short period of virtual reality-based walking training on the GRAIL in people with incomplete SCI may improve walking speed, balance confidence, and dynamic stability in the line of progression, whereas it did not result in improved step width or more stability in the frontal plane during walking. Hence, we can conclude that GRAIL training in people with incomplete SCI has shown some preliminary efficacy that should be further substantiated by larger and well-controlled clinical trials.

For evaluation of walking training interventions, assessment of walking capacity and dynamic balance is important. In general, walking speed is an excellent indicator of basic walking capacity. Indeed, reduced walking speed has found to be indicative of reduced overall health status, functional dependence, fall risk, cognitive decline, risk of hospital admission and mortality in a wide range of populations.[5] Other frequently used measures for walking capacity are spatiotemporal parameters, such as step length and step width. Decreased step length and increased step width have been observed in elderly, especially in people with increased fall risk.[6,7] These changes in spatiotemporal characteristics can be regarded as compensation strategies for reduced dynamic stability.[8,9] Several complex tasks, such as precision stepping, withstanding balance perturbations and obstacle avoidance have been used to assess dynamic stability, but their application in outcome assessment is complicated by the fact that these tasks are also the ones trained in many walking interventions, including the GRAIL, and – thus – cannot be used to prove more generalized skill acquisition. Hence, other outcome measures for dynamic stability have been based on a biomechanical approach, in which parameters based on the position of the centre of mass (CoM) or extrapolated CoM (XCoM) relative to the centre of pressure (CoP) or base of support (BoS) are used. Generally, these parameters measure gait stability in either the anteroposterior (AP) and/or mediolateral (ML) direction. In chapter 2, we found that ML stability measures (i.e., XCoM-CoP_{ML}, CoM-$CoP_{MLangle}$) were reliable and promising to assess gait stability. However, in chapter 3, we did not find a significant change in these outcome measures over time, suggesting that they might be poorly responsive to training. The stability measures that also took the AP direction into account (XCoM-CoP_{AP}, CoM-$CoP_{APangle}$, and dynamic stability margin (DSM)) appeared to be more responsive to training, but strongly correlated with walking speed. Moreover, the AP stability measures were significantly different between test and retest within a one-week interval (chapter 2), whereas such a fast effect of training on gait stability is probably unlikely. Therefore, for the time being, we do not yet suggest to use complex, biomechanical stability measures to assess gait stability, but to rely on walking speed and (other) spatiotemporal parameters for the evaluation of walking training interventions.

Clinical implications and future directions

Although the results from chapter 3 revealed that a short period of virtual reality-based training on the GRAIL in people with incomplete SCI is promising in improving walking capacity and dynamic stability, we do not know the effect size of GRAIL training compared to other walking interventions. For this purpose, randomized controlled trials (RCTs) are warranted. To our knowledge, there are no RCTs on this topic yet. Recently, a RCT has been initiated that aims to assess whether GRAIL training will lead to a better walking performance than endurance / strength training (control intervention) in people with chronic incomplete SCI (Netherlands Trial Registry (NTR) registration number NL7964). The hypothesis is tested that the task specificity, task repetition, variability of practice, and feedback about performance – inherent in the GRAIL training – will result in a larger effect on walking performance than endurance / strength training. This study is ongoing and its results are expected to be available at the end of 2021.

Apart from the direct effects – assessed immediately after a training period – it is important that treatment effects are retained in the long term. In chapter 3, we found a sustained effect of GRAIL training on walking speed, stride length and gait stability in the AP direction after 6 months follow-up. In contrast, the immediate positive effect of GRAIL training on balance confidence was not retained at 6 months. Balance confidence is considered an important factor influencing physical activity in multiple patient populations, including diabetes,[10] knee osteoarthritis,[11] stroke,[12] and spinal cord injury.[13,14] For example, people with incomplete SCI who have fear of falling reported that this fear limited their ability to be physically active and engage in social activities.[13,14] Therefore, it is important to pay attention to balance confidence as a unique outcome of rehabilitation interventions.

So-called 'booster sessions' have the potential to enhance long-term maintenance of treatment effects.[15] Booster sessions are based on periodic follow-up appointments several weeks or months after a supervised intervention, and meant to work as a 'refresher'. In neurorehabilitation, booster sessions are often used after behavioural or cognitive interventions, such as promoting exercise maintenance[16] or coping with pain and anxiety,[17] but may just as well be strong reinforcers of motor skill training. When considering booster sessions, their frequency, timing, and modality (e.g., physical sessions vs online/telephone sessions) are important.[18] In case of the GRAIL intervention, the use of booster sessions might be especially interesting for retaining balance confidence. Because the GRAIL training effect on balance confidence was not retained at follow-up, a booster session should preferably be given within six months after the intervention. Such a booster session should ideally be given on the GRAIL system itself, because it gives the patient the opportunity to explore the boundaries of his/her balance and walking capacities within a safe environment. Especially people with limited balance confidence can (re)discover in this way how much more they are capable of than they initially expected. Besides the possibility of booster sessions, frequent (daily) exercises seem to be important.[16] One approach to facilitate frequent and task specific exercises is with home-based interventions. Commercially available serious gaming systems such as the Nintendo Wii fit™ or YouKicker® are meant for home use and may help to maintain beneficial effects on walking, balance, and lower extremity motor function,[19–21] but more studies are needed to assess whether home-based serious gaming interventions could enhance long-term maintenance of GRAIL treatment effects.

To ensure that patients benefit from the GRAIL intervention in the long term, it is also important that the intervention is effective in improving functional mobility in the home and community environment. Afterall, patients start an intervention to attain a specific rehabilitation goal, which is generally related to preferred daily life activities. The results from chapter 3 indicate that GRAIL training is effective in improving walking and dynamic balance, when measured and trained on the GRAIL system. However, it is unknown whether these effects also extend to overground walking, performance of daily activities and social participation. The above mentioned recently started RCT (NTR NL7964) aims to answer this question and to assess

10

whether GRAIL training or endurance / strength training (control intervention) is superior in improving overground walking, performance of daily activities and social participation. In addition, the patient's perspective on the interventions is investigated. Because – during GRAIL training – patients train to adapt their walking pattern to challenging (virtual) real life situations, it is hypothesized that this training will positively influence patients' capacity to perform daily physical activities such as walking over a carpet, up and down stairs, and over and around obstacles. In addition, it is expected that GRAIL training will increase the motivation of people with SCI to exercise, optimizing therapy adherence.[57]

Wearable exoskeletons

Technology acceptance

In contrast to the GRAIL system, the acceptance and use of exoskeleton technology by people with complete SCI and their physical therapists is less evident. The TAM learns us that various external variables can influence the perceived usefulness and perceived ease of use. Examples of such external variables are system characteristics and the required training before actual use is possible.[3] Globally, the system characteristics are similar for the commercially available wearable exoskeletons, but there is some variation concerning, for instance, the option to adjust the guidance force, the modularity of the exoskeleton, and the need of additional devices. These small variations influence applicability of the technology and its ease of use. Adjusting the guidance force of the walking pattern to the user's needs (e.g., Ekso bionics™ and Indego®), for example, enables the possibility to train and improve the walking capacity of people who have a prospect of functional recovery. In addition, ease of transport is improved with a modular exoskeleton (e.g., Indego™), and ease of use is better when no additional devices are needed to maintain balance (e.g., REX® and ATALANTE™). Only two exoskeletons (ReWalk™ and Indego®) are currently FDA and CE approved for use outside the clinical setting. Besides the fact that some system characteristics (e.g., guidance force and CE/FDA approval) determine the intended exoskeleton use, the intended exoskeleton use itself will also determine the technology acceptance. Four types of intended use can be distinguished for exoskeletons, namely: gait re-training, exercise training, social interaction, and functional assistive use (Figure 2). While the purpose of gait re-training is suitable for people with a prospect of functional recovery (i.e., those with incomplete spinal cord injury), the other three purposes may apply to users with the prospect of no or limited functional recovery. In the section below, I will discuss the four types of intended use separately. In addition, the factor related to the required training before actual use is possible, differs for the purpose gait re-training compared with the other three purposes. For the purposes exercise training, social interaction and functional assistive use a (clinical) training period is required before these goals can be pursued ('exoskeleton pre-training'). From this perspective, exoskeleton acceptance during the training period will be separately discussed below.

Gait re-training

The use of a wearable exoskeleton for gait re-training originates from rehabilitation interventions with robot-assisted gait trainers, such as the Lokomat™. These robot-assisted gait trainers can be seen as stationary exoskeletons, which are mostly used in combination with a treadmill and sometimes body-weight support. Such robot-assisted gait re-training has been widely used since the late 1990s. A review concluded that robot-assisted gait training leads to improvements in walking distance, strength, speed and balance in people with incomplete SCI.[22] Therefore, robotic gait trainers can be considered as clinically accepted for gait rehabilitation in people with incomplete SCI.

More recently, in addition to robot-assisted gait training, wearable exoskeletons are used for gait re-training in people with incomplete SCI. An important requirement for such exoskeletons to be useful is that guidance of the walking pattern can be adjusted. The observed improvements in walking capacity seem to indicate the efficacy of exoskeleton-based gait re-training. Indeed, several studies have shown that people with incomplete SCI can improve their walking speed and walking distance through exoskeleton training.[23–26] More importantly for gait re-training, is that these improvements can be transferred to walking without an exoskeleton, such as improvements in walking speed,[24,27] walking distance,[24] balance,[27] Timed-Up and Go (TUG),[27] and overall walking capacity (measured with the WISCI II).[24] Baunsgaard and colleagues concluded that, for people with independent walking capacity, the improvements in TUG and Berg Balance Scale (BBS) primarily reflect gains in balance,[27] which may be the underlying factor for improved walking capacity after exoskeleton training.

Exoskeleton use for gait re-training is also considered to be easy, safe and practical in a clinical setting.[23,26–28] Most rehabilitation centres focusing on people with SCI already have experience with technical gait training devices, which allows similar devices to be easily implemented. However, exoskeleton use is not completely free of implementation problems, because exoskeletons can only be used by people within a specific height and weight range.[29] In addition, they are quite expensive.[30] Nevertheless, wearable exoskeletons are already widely used as a gait re-training devices which, on top of the observed gains in walking capacity, indicates their acceptance by rehabilitation centres and professionals.

Exoskeleton (pre-)training

People without the prospect of functional recovery can use an exoskeleton for exercise training, social interaction and/or as a device to assist in functional activities. However, an intensive training period is required before people with SCI have learned to use an exoskeleton safely without assistance from a physical therapist. Such training has been shown to be feasible and safe.[27,31] In our study, the majority of the participants (15 out of 21) were able to learn walking with an exoskeleton without assistance, but the number of training session required to reach this level of unassisted walking differed between participants, ranging from 6 to 23 training sessions (chapter 5). Because there was a large variation amongst participants, the external factor 'required training' is likely to have influenced the perceived ease of use positively in some users and negatively in others. Indeed, participants who were able to walk without assistance within the training period were more likely to perceive the training period as 'easy'.

Exercise training

SCI patients without the prospect of functional recovery can use the exoskeleton as an exercise device. So far, the perceived usefulness of the exoskeleton as an exercise device in people with complete SCI seems to be high. They primarily use the exoskeleton to remain physically active and to pursue health benefits. Indeed, the results of a survey among 481 stakeholders support the high perceived usefulness of an exoskeleton for enhancing health benefits.[30] The health effects of exoskeleton use have been investigated in several studies. Overall, improvements

10

in bladder and bowel function,[31,32] spasticity,[31,33] (neuropathic) pain severity,[33,34] and joint mobility were found.[35] In our own study we found similar health benefits (chapter 7). Apart from these benefits, intensive exoskeleton use increases the risk of skin damage[23,36] or even fractures.[23,37] The results described in chapter 4 and 6 confirm the importance of monitoring such risks. Nevertheless, there are no other devices than exoskeletons available that can give a similar 'full body exercise experience' in an upright position to people with a complete SCI. The need to conceptualize the exoskeleton as an exercise device (rather than a mobility device) was highlighted by users.[38] The (perceived) health benefits in combination with the unique 'full body exercise experience' contribute to a high perceived usefulness of exoskeletons for exercise purposes by the users.

While the perceived usefulness of an exoskeleton as an exercise device is high, its ease of use for exercise purposes could be improved. The use of an exoskeleton for exercise in a clinical setting by people with complete SCI is considered safe and feasible,[37,39] and requires not much cognitive40 or physical[40] effort. This might suggest a high ease of use. However, users also mentioned the desire to apply the exoskeleton as an exercise device outside the clinical setting. Afterall, having to travel each time to a specialized clinic for exercise is a considerable barrier. In order to optimize the ease of use for exercising outside the clinical setting, improvements related to the control/input device, balance, step and speed adjustments, and donning and doffing of the exoskeleton were mentioned by the users (chapter 9). Although various improvements were desired to increase the ease of use, the perceived usefulness for exercise was still high.

The actual use of exoskeletons reflects best how well the technology has been accepted by its users. In chapter 8 we looked at the actual system use for different purposes. When people were free to choose for which purpose they would use the current exoskeleton, we found that they used it by far the most for exercising (74%) (chapter 8). This finding confirms that the exoskeleton has already been accepted by the users for exercise purposes.

Social interaction

Another intended use of exoskeletons for people with complete SCI who have no prospect of functional recovery is for social interaction. The perceived usefulness of an exoskeleton for social interaction has already been emphasized in a study by Cahill.[38] Users reported the importance of upright communication at eye-level, which was facilitated by exoskeleton use. In addition, after exoskeleton use within a gym-based community setting, participants reported psychosocial benefits, such as improved mental wellbeing and increased energy to socially interact at eye-level.[38] Thus, the perceived usefulness of exoskeletons for social interaction is considered good. However, similar as for exercise purposes, their ease of use should be improved. For one-time use, the benefits of interaction at eye-level seem to outweigh the limited ease of use. However, for repeated use to improve social interaction, this seems to be different. Firstly, controlling and maintaining balance in the exoskeleton takes effort, which makes it more difficult to focus attention to other activities, such as conversating. This applies to conversation while standing, but also to conversation during more challenging activities such as walking. Secondly, conversation during walking is hampered by the difference in walking speed between the user wearing the exoskeleton and the able-bodied interlocutor. Although maintaining balance and dividing attention over different activities improves with training, the speed of the current exoskeletons remains a limiting factor[41,42] during social interaction while walking. The current exoskeletons have an average walking speed of 0.26m/s (range 0.03-0.71m/s),[43] whereas healthy abled-bodied persons have a preferred walking speed between 1.0-1.5 m/s.[44] Moreover, a walking speed of 0.6m/s or higher is commonly seen as sufficient to replace a wheelchair for daily mobility.[45] Thirdly, the ease of use of walking with an exoskeleton in a crowded place (e.g., a bar, pub, or party) is low for several reasons, such as limited space, danger that people run into the user, and that the user will (unintentionally) stand out. Thus, to interact at eye-level, for instance while standing, the exoskeleton is perceived as useful, but its usefulness during more challenging activities, such as having a conversation while walking or while walking in a crowded place, seems to be much lower.

Although users mentioned that the ease of use for social interaction during walking could be improved (chapter 9), the actual system use reported in chapter 8 indicated that the exoskeleton was more often used for social interaction *in combination with* walking (14%) than without walking (6%). We believe that these results do not contradict each other, but rather reflect the high technology acceptance of the exoskeleton for exercise purposes as described above. After this primary category of actual use, social interaction (20%) was the second largest category. This finding reflects the willingness of users to accept the exoskeleton as a device to facilitate social interaction at eye-level. When considered from the perspective of friends and family, they too experience the exoskeleton as valuable, for instance to interact with the user in an upright position again and to talk to each other while standing and walking.

Functional assistive use

The final type of intended exoskeleton use for people with complete SCI who have no prospect of functional recovery is to improve their daily life functioning. This type of intended use refers to an exoskeleton as an assistive mobility device with the ultimate goal of replacing a wheelchair during activities of daily life. Manufacturers promote the possibility of using the current exoskeletons as a functional device through media images, marketing materials, and by spreading visions such as "to deliver mobility to wheelchair users through advanced robotics; where those that have lost their mobility can stand, walk and live active lives in their community". If the exoskeleton would be able to fully replace the wheelchair, its usefulness would be undisputable. However, the currently available exoskeletons are not nearly there to replacing modern, lightweight wheelchairs. With the current exoskeletons some functional mobility gains can be realized compared to what is possible with a wheelchair. For instance, the possibility to select different operating modes, such as standing, walking or stair climbing, gives the user a choice how to perform certain tasks (e.g., seated or standing) and allows him/her access to specific activities (e.g., entering a building with external steps or stairs). However, all commercially available exoskeletons have only a limited number of such functionalities, namely sitting, standing, walking, and (in some cases) stair walking.

In addition to the limited number of functionalities, the usefulness of exoskeletons in daily life is hampered by limited ease of use. To diminish practical barriers, multiple areas of improvement have been addressed in the literature, such as the need of a buddy,[42,46] need of upper extremity support,[46,47] transportability,[46,47] donning,[42,46] comfort,[30] weight,[47] battery life,[46] walking speed,[42] and safety.[30,42] Only when a large number of these areas will be improved, exoskeletons will become truly useful as functional devices in daily life.

Although the desire of users to improve exoskeletons for functional purposes was evident (chapter 9), the actual system use, described in chapter 8, showed that the exoskeleton was rarely used as a functional device during daily activities. Hence, the usefulness of currently available wearable exoskeletons is still low and not even near the functional level required to replace a wheelchair.

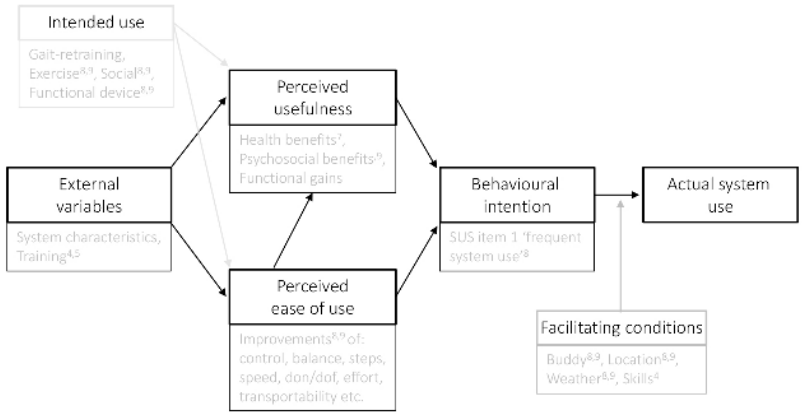

Figure 2. Exoskeleton acceptance based on the final version of the Technology Acceptance Model (TAM) (Venkatesh & Davis 1996[3], p453).

Thick black outline: original factors from the TAM. Dark grey outline: added factor from Thompson 1991[48] (facilitating conditions). Light grey outline: exoskeleton specific addition based on the work in this thesis. Numbers in superscript represent the chapters of this thesis in which these aspects have been addressed.

Preliminary efficacy

For people with a complete SCI, current exoskeletons have the highest user acceptance regarding exercise training and social interaction, whereas the lowest user acceptance was found for functional use as an assistive device. Nonetheless, the degree of user acceptance does not directly result in perceived efficacy or actual system use, which is primarily determined by the users' behavioural intentions and greatly influenced by facilitating conditions, such as availability of a buddy and environmental factors.

The behavioural intention of people with complete SCI was measured with the statement "I think I would like to use this system frequently" in the SUS questionnaire (chapter 8). This statement had to be answered after completing the clinical training period and the period of home use. Hence, the intentions might have been adjusted based on the experiences gained. Slightly more than half of the users (8 out of 14) indicated the intention to frequently use the exoskeleton. The other users were not certain (n=3) or did not have the intention to use the exoskeleton frequently (n=3). We expect that through technological improvements, the ease of use will become greater and the behavioural intention will increase. However, even if all

users would have indicated the intention to frequently use the system, this would still not automatically result in actual system use.

Between behavioural intention and actual system use, Thompson introduced the factor "facilitating conditions" (see Figure 2).[48] With the term facilitating conditions Thompson referred to "objective factors in the environment that observers agree make an act easy to accomplish".[48] In case of the current exoskeletons, examples of such facilitating conditions are low purchase costs, buddy availability, location suitability, good weather conditions and, to some extent, the user's skill level. The fact that the purchase costs of an exoskeleton are around €85,000/$70,000 keeps people from buying and using this device.[30] A buddy living in the user's house or neighbourhood and/or the possibility to use the exoskeleton at both indoor and outdoor locations will make it easier to actually use the exoskeleton. Some facilitating conditions can even be seen as prerequisites for actual exoskeleton use. For example, even if someone has a strong intention to use the exoskeleton, without the availability of a buddy the safety of exoskeleton use may be seriously compromised. The user's skill acquisition and beliefs in his/her own capacities can also be seen as facilitating conditions. Indeed, a more skilled user will have less difficulty with exoskeleton use at a challenging location (e.g., in a crowd or on uneven surfaces) than a less skilled user.

Clinical implications and future directions

Combining exoskeleton (pre)training in a clinical setting with independent use in the home and community environment could be an opportunity for future rehabilitation developments. For example, an exoskeleton might be stored at a local physical therapy practice or community gym to exercise at this location while, at the same time, users might sign up for a 'rental' period to use the exoskeleton at home. This 'shared device' option has the advantage that the healthcare costs remain low and that the exoskeleton can be used for different purposes according to individual needs. A safety prerequisite would be that an individual training program has been completed aimed at home and community use. Such a program should preferably be delivered in a multidisciplinary setting, including the involvement of a physiatrist (for adequate response in case of complications) and experienced physical therapists (for efficient training and monitoring). In this way, a basic skill level can be achieved and the exoskeleton can be used safely under supervision of (less experienced) buddies in the community. To our knowledge, the possibility of sharing an exoskeleton for combined purposes has not yet been put into practice, but it would be an interesting option to explore in the near future. In addition, shared exoskeleton use might make some of the previously mentioned improvements (e.g., less distinctive and more affordable) less urgent, although improvements would still be beneficial to increase the ease of use.

Recent exoskeleton studies, including the studies reported in this thesis, have provided a lot of knowledge about the current state of exoskeleton use in people with complete SCI and its possibilities for the future. Wearable exoskeletons have only been on the market for a relatively short time. In the next decade, many new improvements are expected that can then be tested in gradually larger groups of people, as the number of experienced users will be growing. One of the important areas of expected improvement is balance. Similar to walking in people with incomplete SCI, balance is a very important aspect of exoskeleton use. In most wearable exoskeletons, users need upper extremity support (e.g., from crutches or a walker)[46,47] to maintain their balance and to control the exoskeleton. However, for an exoskeleton to become a functional device in the home and community environment, it is important that the user's

hand(s) are free, so that he/she can manipulate and carry objects while standing and walking. When the exoskeleton itself might be able to support balance control, the need of crutches might be reduced. Another technological improvement would be the introduction of more intuitive control devices. In the interviews, users emphasized that as long as the crutches are needed to maintain balance, they would want the input device to be in the crutch as well. This input device would preferably include a small screen on which different (gait) modes can be selected. Eventually, however, people want to control the exoskeleton without needing the crutches. Options for this are control of the exoskeleton via speech or touch (e.g., touching the thigh to initiate walking and touching the bottom to initiate sitting down). A final important area of functional improvement is improving feedback of performance to the nervous system of the user. Different types of artificial feedback (e.g., auditory via earphones or visual via google glasses) of different aspects of exoskeleton use (e.g., weight distribution, foot clearance, safety) were suggested by the users during the interviews (chapter 9). It is likely that improved feedback of performance will accelerate skill acquisition and/or improve the ease of use. Indeed, in people with lower limb amputation[49,50] or with severe vestibular deficits,[51,52] artificial performance feedback has shown to improve balance and mobility. In people with complete SCI performance feedback has not been investigated. Recently a study started, that aims to assess whether (vibrotactile) feedback of weight shifting and step initiation to experienced exoskeleton users with a complete SCI will improve exoskeleton performance (NTR NL9107). The results of this study are expected in 2021/2020. Improvements in the balance, the control device, and the feedback of performance, are all developed as part of the research program Wearable Robotics, by the Dutch Research Council (NWO). These developments all aim to contribute to the overall goal: shifting the role of the users from a 'passenger' to a person who is in control ('pilot'). Only when (experienced) users can test such new developments, the true benefits of these developments can be assessed.

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Chapter 11

Samenvatting in het Nederlands

Dit proefschrift richt zich op het verbeteren van de mobiliteit bij mensen met een dwarslaesie. Mobiliteit kan hierbij worden gedefinieerd als het vermogen om van de ene plaats naar de andere te komen, hetgeen bijvoorbeeld te voet of met een rolstoel kan worden gedaan. Iemands mobiliteit heeft grote invloed op zijn/haar vermogen om deel te nemen aan dagelijkse activiteiten. Het is dan ook niet verwonderlijk dat het verbeteren van mobiliteit een belangrijk revalidatiedoel is voor mensen met een dwarslaesie. Afhankelijk van de prognose kunnen verschillende interventies worden aangeboden om de mobiliteit te verbeteren. Als een persoon tot op zekere hoogte in staat is om te lopen, is het zinvol om te proberen het loopvermogen te verbeteren middels loop-specifieke training (d.w.z. het stimuleren van functioneel herstel). Echter, is looptraining niet zinvol als de beenfunctie zo beperkt is dat lopen niet meer mogelijk is en er geen kans is op herstel. In dat geval kan een exoskelet gebruikt worden om de mobiliteit te verbeteren.

Het algemene doel van dit proefschrift was om twee interventies te onderzoeken die gericht zijn op het verbeteren van de mobiliteit bij mensen met een dwarslaesie. De eerste interventie bestaat uit een loopbandtraining in een virtuele omgeving voor mensen met een beperkt loopvermogen na een incomplete dwarslaesie. Dit wordt beschreven in de hoofdstukken 2 en 3 (deel 1). De tweede interventie betreft het exoskeletgebruik voor mensen zonder loopvermogen als gevolg van een complete dwarslaesie, beschreven in de hoofdstukken 4 tot en met 9 (deel 2).

Deel 1 - Verbetering van de mobiliteit van mensen met een incomplete dwarslaesie met behulp van een op virtuele realiteit gebaseerde loopbandtraining

In het eerste deel van dit proefschrift werd een loopbandtraining in een virtuele omgeving geëvalueerd. Deze interventie werd gegeven in een trainingsopstelling die bekend staat als Gait Realtime Analysis Interactive Lab (GRAIL). Tijdens de GRAIL interventie bevindt iemand zich op een loopband in een virtuele trainingsomgeving bestaand uit een 180 graden gebogen scherm waarop videobeelden worden geprojecteerd (zie foto rechts). Er wordt gebruik gemaakt van computergames waarbij iemand in een interactieve omgeving moet reageren op de geprojecteerde gebeurtenissen. Via camera's kan de computer detecteren waar de persoon zich op de loopband bevindt en hoe bewegingen worden uitgevoerd. De loopband is een belangrijk onderdeel van de GRAIL. Deze kan zijwaarts bewegen en in hellingposities worden gebracht. Hierdoor kan het lopen worden verstoord om zo de stabiliteit te beoordelen en te trainen. Om de veiligheid te garanderen wordt een harnas gedragen, waardoor een eventuele val opgevangen kan worden.

In **hoofdstuk 2** beoordeelden we de test-hertest betrouwbaarheid van zes uitkomstmaten voor de stabiliteit tijdens het lopen op de GRAIL. Aan dit onderzoek namen zowel gezonde volwassenen als mensen met een incomplete dwarslaesie deel. We vonden dat de zes stabiliteitsmaten een matige tot uitstekende betrouwbaarheid hadden. De stabiliteitsmaten in de zijwaartse richting (XCoM-CoP_{ML} en CoM-$CoP_{ML\text{-}angle}$) werden als de meest veelbelovend beschouwd om interventies te evalueren en individuele vooruitgang te monitoren.

In **hoofdstuk 3** evalueerden we het effect van een interventie bestaande uit loopbandtrainingen in een virtuele omgeving op het loopvermogen van mensen met een chronische (>6 maanden) incomplete dwarslaesie. Er werd gekeken of deze specifieke loopbandtraining leidde tot verbeteringen in spatiotemporele loopparameters (zoals loopsnelheid en staplengte), vertrouwen in balans, en de in hoofdstuk 2 beschreven stabiliteitsmaten. De interventie bestond uit 12 loopbandtrainingen op de GRAIL van een uur, gedurende zes weken. Tijdens de training voerden de deelnemers verschillende opdrachten uit, zoals het lopen over een wiebelende virtuele hangbrug terwijl ze vogels moesten ontwijken, of het besturen van een virtuele boot door het verplaatsen van het lichaamsgewicht. Deelnemers moesten dus interacteren met de virtuele omgeving door hun looppatroon te veranderen of hun houding aan te passen. Na de interventie bleken loopsnelheid, staplengte, voorwaartse loopstabiliteit en vertrouwen in balans van de mensen met een incomplete dwarslaesie verbeterd. Bovendien waren deze effecten zes maanden later nog altijd aanwezig. De resultaten van dit onderzoek laten zien dan de interventie veelbelovend is voor het verbeteren van lopen en balans bij mensen met een chronische incomplete dwarslaesie. De stabiliteitsmaten in de zijwaartse richting, die als de meest veelbelovend voor de evaluatie van interventies werden beschouwd (hoofdstuk 2), veranderden echter niet als gevolg van de training.

Loopbandtraining in een virtuele omgeving

- Loopstabiliteit kan betrouwbaar worden gemeten in een virtuele omgeving.
- Loopbandtraining in een virtuele omgeving kan de balans en loopvaardigheid verbeteren bij mensen met een incomplete dwarslaesie; zij krijgen meer vertrouwen in hun balans, lopen sneller, maken grotere passen en tonen een betere voorwaartse loopstabiliteit.
- Deze effecten beklijven tot een half jaar later na de looptraining.

Deel 2 - Verbetering van de mobiliteit van mensen met een complete dwarslaesie met behulp van een exoskelet

Over het algemeen zijn mensen met een complete dwarslaesie voor hun dagelijkse mobiliteit afhankelijk van een rolstoel. In het tweede deel van dit proefschrift stond een andere mogelijkheid om de mobiliteit van mensen met een complete dwarslaesie te verbeteren centraal, namelijk met het gebruik van een exoskelet. Een exoskelet is een robotpak dat aan de buitenkant van de benen geplaatst is. In het heup- en kniescharnier van het exoskelet zit een aandrijvingsmechanisme. Het exoskelet kan op maat worden gemaakt en wordt zittend aangedaan door gespjes om de benen te klikken. Vervolgens kan men het exoskelet gebruiken door op een bijbehorend horloge de acties te selecteren van zitten, staan of lopen. Tijdens het staan en lopen houden mensen zich met behulp van krukken in balans. Daarom kunnen alleen

mensen met een goede hand- en armfunctie het exoskelet gebruiken. Sommige commerciële exoskeletten mogen zowel in de kliniek als thuis worden gebruikt. Voor de veiligheid wordt het exoskelet altijd in het bijzijn van een 'buddy' gebruikt.

Eerst hebben we een kader ontwikkeld om te kunnen beoordelen hoe mensen met een complete dwarslaesie gebruik leren maken van een exoskelet, beschreven in **hoofdstuk 4**. Het in dit onderzoek ontwikkelde kader bestond uit tussentijdse vaardigheidstesten ('Intermediate-skills-test') en een eindvaardigheidstest ('Final-skills-test'). Tijdens de 2e, 4e, en 6e trainingsweek werd de tussentijdse vaardigheidstest uitgevoerd. Deze tussentijdse vaardigheidstest bestaat uit 27 vaardigheden, die worden gemeten in een oplopende volgorde van moeilijkheid. Eerst worden eenvoudigere vaardigheden gemeten, zoals het verplaatsen van je gewicht in stand, gevolgd door steeds moeilijkere vaardigheden, zoals het lopen van bochten en het nemen van kleine opstapjes. Zodra de deelnemers zonder hulp van de 'buddy' konden lopen, werd in de laatste training (week 8) de eindvaardigheidstest uitgevoerd. In deze eindvaardigheidstest worden vaardigheden gesimuleerd die nodig zijn in situaties uit het dagelijks leven, zoals het passeren van een deur. Belangrijk is dat met deze vaardigheidstesten onderscheid kan worden gemeten tussen vaardigheidsniveaus. Met de tussentijdse vaardigheidstest werd de individuele vooruitgang tijdens de trainingsperiode en de verschillen tussen deelnemers in vaardigheidsniveau gemeten. Hierbij vonden we grote verschillen tussen de deelnemers wat betreft de snelheid waarmee de exoskeletvaardigheden verworven werden, alsook in het uiteindelijke vaardigheidsniveau.

De diversiteit tussen de deelnemers deed de vraag rijzen: waarom verwerven sommige deelnemers meer en sneller exoskeletvaardigheden dan anderen? In **hoofdstuk 5** hebben we deze vraag onderzocht door te kijken of we met persoons- en dwarslaesiespecifieke kenmerken de verworven exoskeletvaardigheden tijdens en na een trainingsperiode konden voorspellen. Negen persoons- en dwarslaesiespecifieke kenmerken werden in dit onderzoek meegenomen, namelijk: letselniveau, leeftijd, body mass index (BMI), geslacht, sportdeelname, actieve levensstijl, mate van angst, tijd sinds het ontstaan van de dwarslaesie, en leeftijd bij het ontstaan van de dwarslaesie. Met behulp van een meervoudige regressieanalyse werd de voorspellende waarde van de negen kenmerken voor de verworven exoskeletvaardigheden onderzocht. Deze verworven vaardigheden werden gemeten met de Intermediate-skills-testen en de Final-skills-test (ontwikkeld en getest in hoofdstuk 4). Het letselniveau bleek een belangrijke voorspeller te zijn tijdens de eerste 4 weken van de trainingsperiode, maar had geen invloed op het uiteindelijke vaardigheidsniveau van de deelnemers. Een lage BMI, lage leeftijd en een actieve levensstijl bleken voorspellers van een hoog vaardigheidsniveau tegen het einde van de trainingsperiode. Geen van de persoons- en dwarslaesiespecifieke kenmerken had een significant verband met het uiteindelijke vaardigheidsniveau.

Hoewel het trainen en lopen met een exoskelet bij mensen met een motorisch complete dwarslaesie als veilig wordt beschouwd, hebben we helaas botbreuken geconstateerd. In **hoofdstuk 6** rapporteren we twee verschillende botbreuken die verband houden met het gebruik van een exoskelet. Eén botbreuk werd waarschijnlijk veroorzaakt door een verkeerde uitlijning van de scharnieren van het exoskelet ten opzichte van de beengewrichten van de gebruiker. Dit gebeurde nadat het exoskelet per ongeluk werd uitgeschakeld tijdens het lopen. De oorzaak van de botbreuk van de andere persoon bleef onduidelijk. Er werden voorzorgsmaatregelen genomen om zulke ongewenste voorvallen te voorkomen, zoals

een botdichtheidsonderzoek voorafgaande aan de trainingsperiode en regelmatige uitlijningscontroles tijdens de training. Daarnaast werden specifieke trainingsinstructies gegeven aan zowel de gebruiker als zijn/haar buddy over hoe te reageren bij het per ongeluk uitschakelen van het exoskelet.

Ondanks dat het belangrijk is om bewust te zijn van de risico's van exoskeletgebruik, verwachten we dat de mogelijkheid om in een rechtopstaande houding te trainen bijdraagt aan het onderhouden en verbeteren van de gezondheid van mensen met een complete dwarslaesie. De effecten van acht weken exoskelettraining op de kwaliteit van leven en dwarslaesiespecifieke gezondheidsproblemen werden in **hoofdstuk 7** geëvalueerd. Uit gezondheidsvragenlijsten bleek dat kortdurende exoskelettraining bij mensen met een motorisch complete dwarslaesie de kwaliteit van leven, de pijn en de tevredenheid met de beheersing van de blaas verbeterde. Er werden geen veranderingen in beheersing van de stoelgang, het bewegingsbereik van de gewrichten of de mate van spasticiteit gevonden.

Training met een exoskelet
- Een exoskelet leren gebruiken vergt veel training en tijd.
- Hoeveel training er nodig is verschilt sterk van persoon tot persoon.
- Een gezond gewicht, een lage leeftijd en een actieve levensstijl zijn voordelig voor het leren gebruiken van een exoskelet.
- Om de veiligheid van exoskeletgebruik te waarborgen zijn goede instructies, begeleiding en controles nodig.
- Het staan en lopen in een exoskelet leidt tot gezondheidsvoordelen, zoals verbeteringen in kwaliteit van leven, pijn, en tevredenheid met de blaasbeheersing.

Na de trainingsperiode mochten de deelnemers het exoskelet buiten de klinische setting gebruiken als:
1. zij een vaardigheidsniveau hadden bereikt dat noodzakelijk is voor het uitvoeren van dagelijkse situaties (gemeten met de Final-skills-test van hoofdstuk 4), en
2. zij specifieke veiligheidsinstructies hadden ontvangen (beschreven in hoofdstuk 6).

Alleen als het exoskelet daadwerkelijk thuis en in de woonomgeving wordt gebruikt, kan de toepasbaarheid in deze setting worden beoordeeld. Dit levert belangrijke informatie op voor de verdere ontwikkeling van het exoskelet. Het doel van **hoofdstuk 8** was het evalueren van het daadwerkelijk gebruik van het exoskelet, zowel thuis als in de woonomgeving. De periode van thuisgebruik was ten minste twee weken, waarin de deelnemers een logboek bijhielden. Er waren geen beperkingen met betrekking tot de hoeveelheid gebruik, het doel of de locatie waar ze het exoskelet konden gebruiken. Om veiligheidsredenen werd hun geïnstrueerd om het exoskelet niet zonder toezicht van hun buddy te gebruiken. De hoeveelheid exoskeletgebruik was uiteenlopend tussen de deelnemers. Uit de logboekgegevens bleek dat het exoskelet vooral werd gebruikt voor training/lichaamsbeweging en sociale interactie. Tijdens de helft van de sessies was de gebruikslocatie buitenshuis. De deelnemers gaven aan tevreden te zijn over het exoskelet voor training/lichaamsbeweging en sociale interactie in de thuis- en woonomgeving, maar noemden serieuze beperkingen met betrekking tot het gebruik van het exoskelet als hulpmiddel in het dagelijks leven.

Exoskeletten zijn ontwikkeld op basis van wat op dit moment technologisch mogelijk is, hetgeen voor een groot deel bepaalt waarvoor ze kunnen worden gebruikt. Om het gebruik van exoskeletten in het dagelijks leven door mensen met een complete dwarslaesie te optimaliseren, is meer inzicht in de wensen van de gebruikers nodig; in het bijzonder voor welke doelen men het toekomstig exoskelet wil gebruiken en welke daarmee samenhangende verbeteringen van het exoskelet nodig zijn. Het is essentieel om het perspectief van ervaren exoskeletgebruikers te integreren in de verdere exoskeletontwikkeling. Om die reden werden de deelnemers uit hoofdstuk 8 opnieuw benaderd om deel te nemen aan een kwalitatief (interview)onderzoek, beschreven in **hoofdstuk 9**. De deelnemers noemden drie doelen waarvoor ze het toekomstige exoskelet zouden willen gebruiken: voor 'dagelijkse activiteiten', 'training en lichaamsbeweging' en 'sociale interactie'. Exoskeletgebruik tijdens dagelijkse activiteiten was het ultieme doel. Daarvoor moet het toekomstige exoskelet volgens ervaren gebruikers 'gemakkelijk te gebruiken', 'klein en licht', 'op maat gemaakt', 'veilig', 'comfortabel', 'minder opvallend, 'duurzaam', en 'betaalbaar' zijn. Het verbeteren van het gebruiksgemak was relevant voor alle gebruiksdoelen en voor alle deelnemers. Andere suggesties voor verbetering varieerden afhankelijk van het doel en de deelnemer.

Thuisgebruik van een exoskelet
- Het exoskelet wordt nu nog vooral buitenshuis gebruikt voor trainingsdoeleinden.
- Andere mensen 'recht in de ogen' kijken blijkt een welkom effect van exoskeletgebruik.
- Het verbeteren van het gebruiksgemak is voor dagelijkse toepassing noodzakelijk.
- Het toekomstige exoskelet moet klein en licht, op maat gemaakt, veilig, comfortabel, minder opvallend, duurzaam en betaalbaar zijn.
- Voor optimaal gebruik moeten meerdere van deze aspecten worden aangepast/ verbeterd.
- Exoskeletgebruik in het dagelijkse leven is het ultieme doel van de meeste mensen.

Conclusies

Mensen met een chronische incomplete dwarslaesie kunnen functionele winst boeken middels loopbandtraining in een virtuele omgeving. Allereerst zorgt dergelijke loopbandtraining voor een verbetering van hun loopvermogen en loopstabiliteit. Na de training liepen deelnemers sneller, maakten zij grotere stappen en verbeterden zij in voorwaartse loopstabiliteit. Of dit ook tot een verbeterde mobiliteit in het dagelijks leven leidt is nog onduidelijk. Voor het gevoel van de deelnemers had de loopbandtraining een algeheel positief effect, waarbij zij meer vertrouwen kregen in hun balans tijdens dagelijkse activiteiten. Deze effecten waren een half jaar later nog altijd aanwezig.

Door exoskeletgebruik hebben mensen met een chronische complete dwarslaesie ook perspectief op verticale mobiliteit, in dit geval het vermogen om te staan en te lopen. Hiermee zorgt het voor verbetering in kwaliteit van leven, pijn en tevredenheid met de blaasbeheersing. Het lopen met een exoskelet is in de beginfase uitdagend en vermoeiend, en wordt daarom als een soort training dan wel vorm van lichaamsbeweging gezien. Tijdens het thuisgebruik daagden mensen met een complete dwarslaesie zichzelf uit om steeds verder en langer te lopen. Ook werd het exoskelet regelmatig in sociale situaties gebruikt. Andere mensen 'recht in de ogen' kijken bleek eveneens een welkom effect van het exoskelet. Onder andere

op het gebied van gebruiksgemak is er echter nog veel winst te behalen, zodat het exoskelet toepasbaar wordt voor het ultieme doel van de meeste mensen: gebruik ten behoeve van mobiliteit in het dagelijks leven.

Afscheidsbrief gericht aan het exoskelet

Geschreven door één van de deelnemers aan het exoskelet onderzoek

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Nou, daar ga je dan maatje...

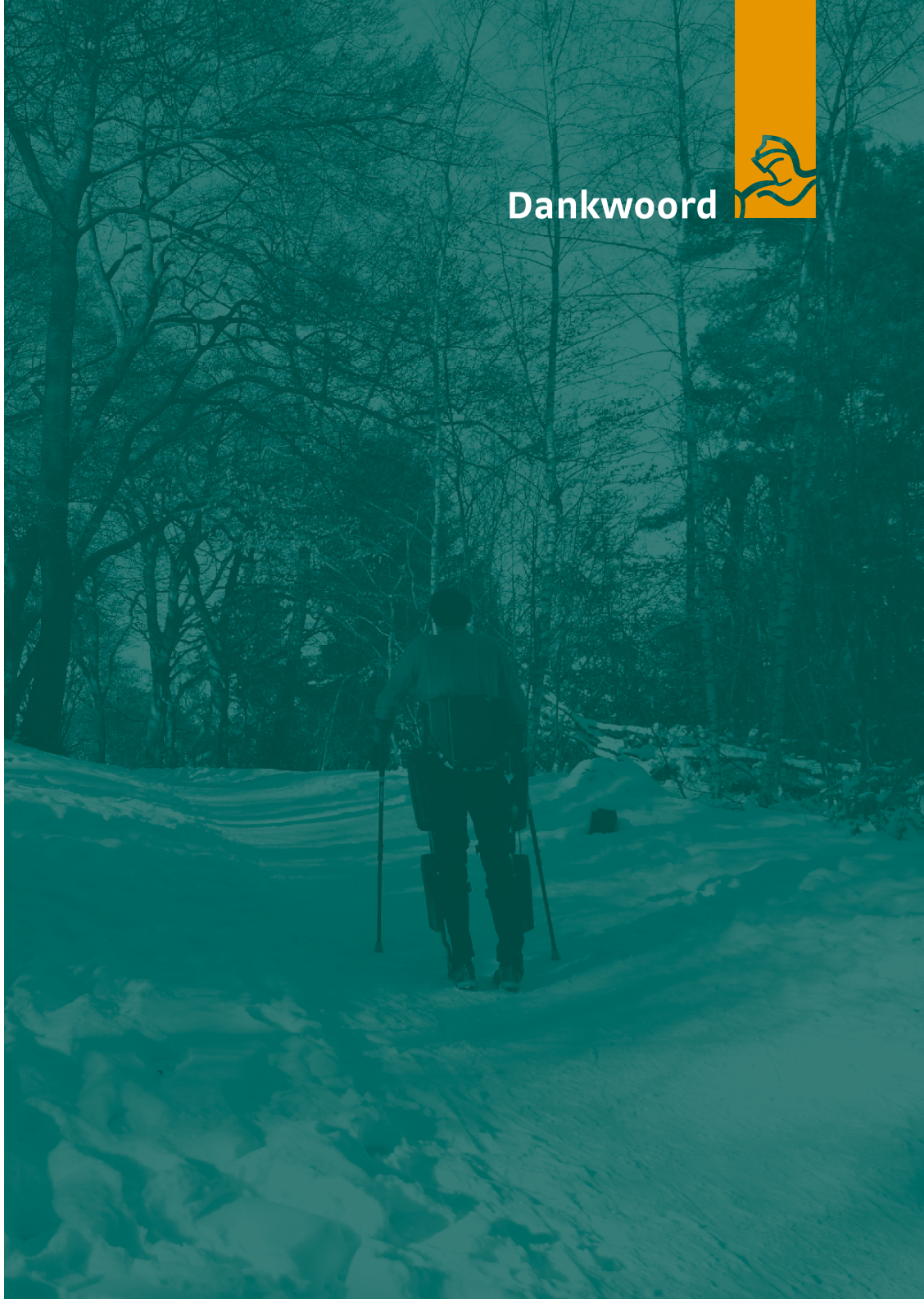
Na bijna drie maanden intensief trainen in de Sint Maartenskliniek, mocht je twee weken bij mij komen logeren. Wat waren wij een team ♥ Zo nu en dan ging het er best wel pittig aan toe, want ik wilde niet altijd even goed naar je luisteren. Jij daarentegen was een tikkeltje dominant, maar met een beetje geduld en wat handigheid verliep onze vriendschap toch wel volgens plan. Gelukkig mocht jij mijn vriend J. ook meteen vanaf de kennismaking, hij deed zijn uiterste best om ons twee ons ding te laten doen. Op het begin was dat even wennen, maar goed we hebben hem beiden het vertrouwen gegeven. Wat was ie zorgzaam hè? Dat is ie nou altijd, daarmee mag ik echt van geluk spreken.

Ik had je graag aan nog meer familie en vrienden willen voorstellen, maar hé jij maakte mij wel héél moe en soms had ik het te druk met andere dingen, waardoor ik je niet iedere dag genoeg aandacht kon geven. Weet wel dat ik een super tijd met je heb gehad. Ik heb mogen ervaren wat voor mogelijkheden er zijn zonder die rolstoel. Valse hoop heb je me zeker niet gegeven, maar ik ben wel tot een besluit gekomen. Schrik niet, maar ik kan je even een paar jaar niet zien. Er moet wat gebeuren...

Ze zeggen wel eens dat een goede vriendschap onbetaalbaar is, in dit geval is dat zeker zo. Vergoedingen en verdere ontwikkelingen zijn er echt nodig om jou weer in mijn armen, of beter gezegd om mijn benen te sluiten. Ik blijf je volgen en zal je daarom absoluut niet vergeten! Jij gaat komende jaren anderen weer heel blij (en ja ook héél moe) maken met de vrijheid, fitheid en gelijkheid die je ze kan geven. Want daar ben je namelijk echt heel goed in.

Bedankt voor de fijne tijd en tot ooit, maatje!

Dankwoord



Dankwoord

In de afgelopen vijf jaar hebben veel mensen een waardevolle bijdrage geleverd aan de totstandkoming van dit werk. Daarvoor wil ik iedereen persoonlijk hartelijk bedanken.

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Behalve deelnemers is een goede begeleiding ook essentieel geweest voor de totstandkoming van dit proefschrift. Noël, ontzettend bedankt voor jouw fijne begeleiding! Hoewel we het over sommige inhoudelijke punten nooit eens zullen worden, heb je me in mijn denkwijze meer gekneed/gevormd dan ik eigenlijk toe zou willen geven. Dank dat je het me hebt volgehouden als ik toch wel erg koppig was en me de vrijheid hebt gegeven om hier en daar mijn eigen draai aan de projecten te geven. Naast dat je een goede leidinggevende bent, ben ik ook blij je als persoon te hebben mogen leren kennen. Niet veel mensen kunnen op zo'n natuurlijke wijze wisselen tussen rol als leidinggevende en persoon waarmee je je weekend doorspreekt of een gezellige stadswandeling maakt tijdens een congres.

Dan natuurlijk mijn (ex)-roomies van Wo.07; Lise, Cheriel, Wieneke, Eline, Koen en Michiel. Wat is er allemaal wel niet in Wo.07 besproken. Alles werd er gedeeld: lief, leed, frustraties, recepten, thee SOPs, weekend verhalen en nog veel meer. Meestal kon je vooraan in de gang al horen hoe de bezetting op de kamer was. Wat hebben wij samen veel lol gehad, of dat nu in Wo.07, bij café Jos, op de zomerfeesten, of bij een van de dinertjes/borrels bij één van ons thuis was. Ik kon me geen leukere roomies wensen en ben jullie heel erg dankbare voor alle mooie momenten, waardoor het maar al te leuk was om steeds die berg op te fietsen (of ja, na mijn eerste kop koffie kon ik ervan genieten)! Lise en Cheriel, met jullie heb ik de meeste tijd en verhalen gedeeld. Dank voor alle, meer dan welkome, afleiding die jullie hebben geboden, onder andere met behulp van nutteloze kantoorartikelen, maffe uitdrukkingen en schitterende foto's. Dat jullie mij vandaag ook als paranimfen willen ondersteunen vind ik helemaal super! Wieneke, het was heel leuk om met jou (en je concentratie verhogende bubbling-muziek) even de kamer te mogen delen. Gelukkig hebben we ook genoeg koffie-bijklets-momentjes kunnen plannen nadat we uit elkaar zijn gezet. Eline en Koen, met jullie heb ik vanwege covid een stuk korter dan gepland de kamer gedeeld. Desondanks hebben jullie een blijvende indruk achter gelaten, mijn receptenboek uitgebreid, en mij kennis laten maken met de wereld van foto-editing en VR-games. Ook hebben jullie laten zien dat een beroep als onderzoeker prima kan worden gecombineerd met die van een jongleur.

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Daarnaast heb ik vanaf het begin af aan het voorrecht gehad om met een aantal ervaren rotten in het dwarslaesie-vak te mogen werken. Hennie, Jacques, Cebrail en later ook Patrick. Hennie, dank dat je altijd tijd maakte voor een (soms niet zo) kort vraagje, je (vaderlijk) advies, en natuurlijk jouw 'geen idee of het lukt, dus laten we het uitproberen'-mentaliteit. Cebrail, ik ken maar weinig mensen die zo lief zijn voor de mensen om zich heen. Dank dat je me hebt laten zien om overal en in iedereen altijd het positieve te zien. Jacques, dank voor je geintjes, *down-to-earth* mentaliteit en dat je me regelmatig hebt geholpen om knopen door te hakken. Patrick, wat fijn dat je (ook) de exoskelettrainingen op je wou nemen toen we je nodig hadden. Je bent een ontzettend fijne aanwinst voor het exoskeletteam en ik weet zeker dat ons researchteam nog regelmatig bij je zal aankloppen voor advies. Jullie enthousiasme, slap geouwehoer, maar ook kritische kijk op de researchplannen heeft mij enorm veel gebracht. Door jullie verschillende meningen en opvattingen kon ik met jullie allen goed sparren over mijn vraagstukken en de praktische kant erachter. Het gaf mij altijd een enorme boost als ik weer eens bij een exoskelettraining was komen binnen vallen. Ik vind het erg jammer dat we elkaar in het laatste jaar maar erg weinig hebben gezien, maar dat doet niet af van jullie enorme bijdrage aan dit proefschrift!

Aan de dataverzameling van de GRAIL-onderzoeken hebben meerdere GRAIL operators bijgedragen. Annelein, Ellen, Esther, Fanny, Hennie, Henrike, Liesbeth en Patrick heel erg bedankt voor jullie medewerking. Bart en Lise jullie wil ik ook nog heel erg bedanken voor het maken van de testapplicaties en het meedenken met de protocollen. Zonder jullie technische ondersteuning waren deze onderzoeken nooit van de grond gekomen. Patrick, Ellen en Hennie wil ik daarnaast nog in het bijzonder bedanken voor het meedenken met de vervolgstappen voor het onderzoek. Zonder jullie was het niet gelukt om er een klinisch relevante vraag van te maken, die wetenschappelijk goed in elkaar zit, maar ook nog praktisch uitvoerbaar blijft. Al moet voor het praktisch uitvoerbaar maken ook zeker onze top planner Rik worden bedankt. Ik weet niet hoe je het steeds voor elkaar krijgt om deze onmogelijke puzzel steeds kloppend te krijgen, maar daarvoor ben ik je erg dankbaar. Eline, dat jij dit onderzoek verder vorm gaat geven vind ik heel fijn. Ik weet zeker dat je dit tot een mooi resultaat gaat brengen, in samenwerking met Marije, Juha, Hiltje en Ayman.

Een artikel schrijf je nooit alleen. Zonder de input van alle mede-auteurs waren de artikelen die tot dit proefschrift hebben geleid niet tot dit niveau gekomen. Brenda, Frank, Hennie, Henk, Jan Willem, Joke, Lysanne en Marije nogmaals dank voor alle hulp bij het schrijfwerk. Een aantal van de mede-auteurs wil ik nog persoonlijk bedanken. Brenda, dank voor jouw altijd kritisch blik en dat je steeds feilloos de 'compromissen' die Noël en ik hadden gesloten eruit wist te pikken en te verbeteren. Lysanne, duizend maal dank voor het schrijven van het Matlab-script! Hennie en Marije, dank dat jullie ervoor zorgden dat de klinische vraagstelling niet uit het oog werd verloren. Marije, wat is het fijn dat je als arts, maar zeker ook als persoon, zo betrokken bent bij de onderzoeken. Frank, heel erg bedankt voor de tijd die je hebt gestoken in het netjes invoeren van de vragenlijstdata. En Joke, ontzettend bedankt dat je me met zoveel enthousiasme hebt geholpen met het doorzetten van het interview onderzoek en het ordenen van de wirwar aan codes.

Ook wil ik alle (andere) collega's van de afdeling research bedanken. Ik denk met veel plezier terug aan alle cake-van-de-week momenten, kerstdiners, bingo's, challenges, borrels en researchlunches in het W-gebouw.

Meerdere stagiaires hebben mij de afgelopen jaren geholpen. Jeske, Sanne B, Sanne J, Anne, Lysanne en Kim, behalve dat jullie (hopelijk) iets van mij geleerd hebben, heb ik ook veel van jullie geleerd. Dank voor jullie kritische houding en goede inzet! Lysanne, dat jij nadat je stage bij mij had gelopen (of ik bij jou, dat is een kwestie van perspectief...) onze research afdeling bent komen ondersteunen was helemaal super. Dat we niet op dezelfde kamer terecht zijn gekomen is denk ik heel verstandig geweest voor onze productiviteit. Gelukkig zijn er genoeg borrelmomentjes geweest waarbij we wel lol hebben kunnen trappen.

Uiteraard wil ik ook de rest van mijn promotieteam bedanken. Ilse, heel wat presentaties hebben we samen gehouden door het hele land. Zonder jouw bijdrage was het exoskeletonderzoek niet van de grond af gekomen of had het zoveel publiciteit gekregen, en daarvoor ben ik je enorm dankbaar. Ondanks je drukke agenda wist je altijd tijd te maken wanneer nodig en jouw drive om dwarslaesie (onderzoek) op de kaart te zetten is inspirerend. Sander, jij hebt de artikelen écht tot een hoger niveau getild en daarvoor wil ik je ontzettend bedanken. Wat kan ik nog veel van jou leren over zinsopbouw, grammatica en het op papier krijgen van mijn gedachtenspinsels. Dank dat je steeds zo snel tijd vrij wist te maken om mijn stukken van feedback te voorzien.

Collega-onderzoekers van het Radboudumc, ook jullie wil ik heel erg bedanken. Dank voor het sparren over de verschillende onderzoeken. De gezamenlijke *journal* clubs en de *lab meetings* hebben ervoor gezorgd dat ik een andere kijk heb gekregen op verschillende onderzoeksmethodes, terminologie, en documentatie.

Beste leden van de manuscriptcommissie, prof. dr. T.J.J. Maal, prof. dr. ir. H. van der Kooij en prof. dr. M.W.M. Post, bedankt voor jullie bereidheid om het manuscript te beoordelen en zitting te nemen in de oppositie.

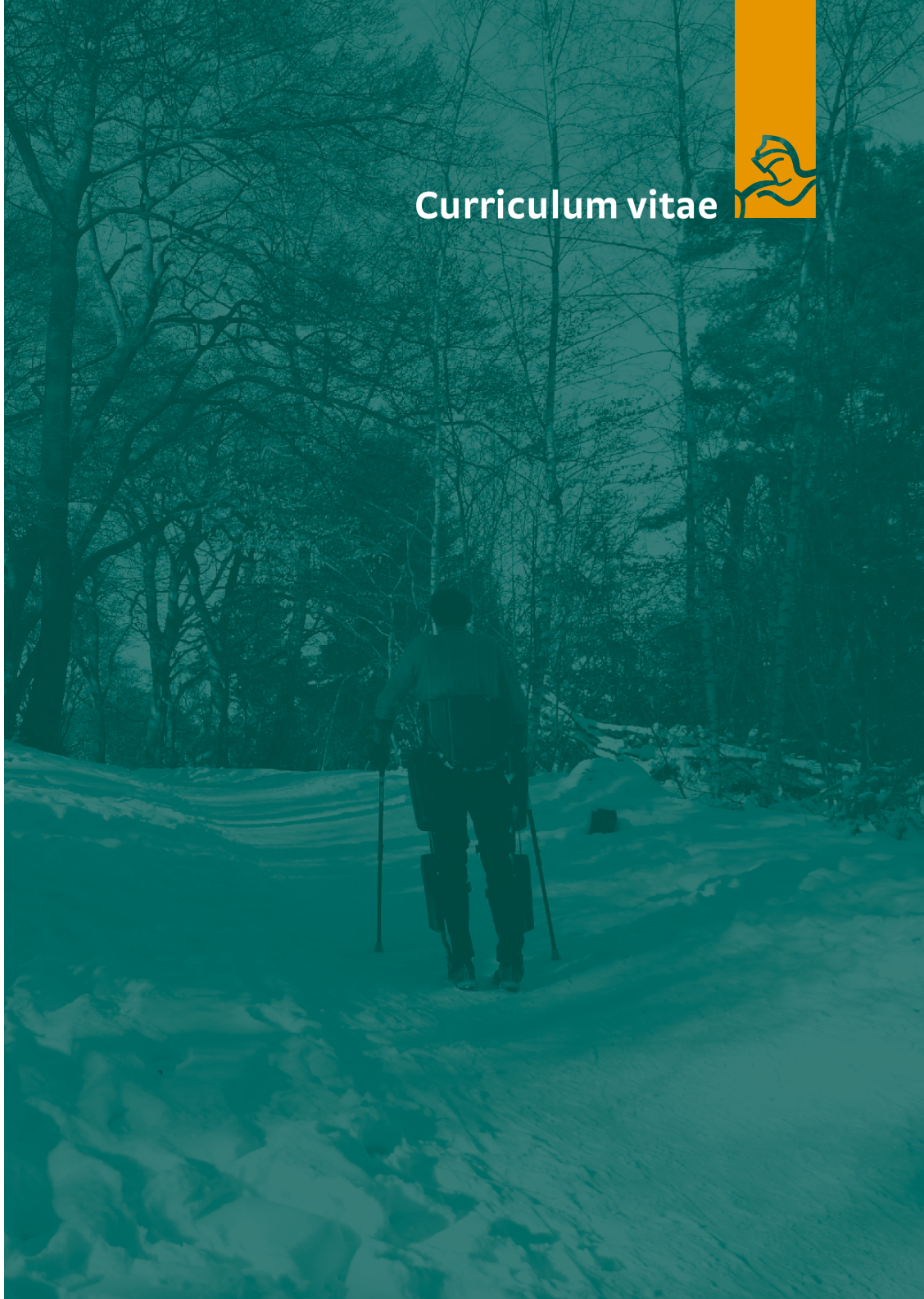
Special thanks to NWO-TTW for funding the studies that have led to this thesis and which gave me the opportunity to collaborate with all the colleagues from the Wearable Robotics team. With pleasure I look back at the conferences and the monthly telco's. But with even more please I recall the fanaticism that came with the wheelchair basketball and the pub quiz during our social event weekend in Nijmegen.

Lieve vrienden, dank dat jullie me laten zien wat echt belangrijk is in het leven; samen lachen en tijd doorbrengen met de mensen waar je van houdt. Samen hebben we al heel veel herinneringen gemaakt met weekendjes weg, wijnproeverijen, escape rooms, etentjes, wandelingen, basketbaltoernooitjes en nog veel meer. Het is super fijn om een groep mensen om je heen te hebben waarvan je weet dat ze altijd voor je klaar zullen staan. Of het nu de broodnodige afleiding is wanneer 'zoals gepland alles anders loopt dan verwacht' of wanneer het de hoogste tijd is om eens onder je steen vandaan te kruipen. Zoals ze het in Brabant zo mooi kunnen verwoorden: 'Da ge bedankt zijt, da witte!'

Ook wil ik graag mijn familie en schoonfamilie bedanken. Jullie hebben misschien niet letterlijk bijgedragen aan de totstandkoming van dit proefschrift, maar de onvoorwaardelijke steun van mijn familie en de voetjes terug in de klei/modder-mentaliteit van mijn schoonfamilie hebben mij tot dit punt gebracht. Adriaan en Maaike, wat ben ik blij met een broer en schoonzus als jullie! Jullie eindeloze energie, enthousiasme en tikkeltje ADHD werkt aanstekelijk en zorgt

ervoor dat ik steeds weer een blijer mens ben als ik weer bij jullie ben geweest. Dat ik binnenkort getuige ben op jullie bruiloft vind ik een ontzettend grote eer. Lieve pap en mam, bedankt voor álles: jullie onvoorwaardelijke steun, trots om alles wat ik doe, en soms een duwtje in de rug om 'Miss Twijfel' een keuze te laten maken wanneer het nodig is. Ik weet dat jullie er altijd voor mij zullen zijn. Bedankt voor alles wat jullie voor mij hebben gedaan, tofste gezin ever!

Tot slot, lieve Rob, Robbie, Robertus. Ondertussen zijn we bijna 13 jaar samen en wat hebben wij samen al veel mee gemaakt! Dank dat je er altijd voor mij bent, me aan het lachen maakt, mijn gekke ideeën steunt, me soms tempert en me stoom laat afblazen als ik niet meer weet wat ik met mijn energie aan moet. Ik kan niet wachten om met jou het volgende avontuur te beleven, want samen kunnen wij de wereld aan. Love you!



Curriculum vitae

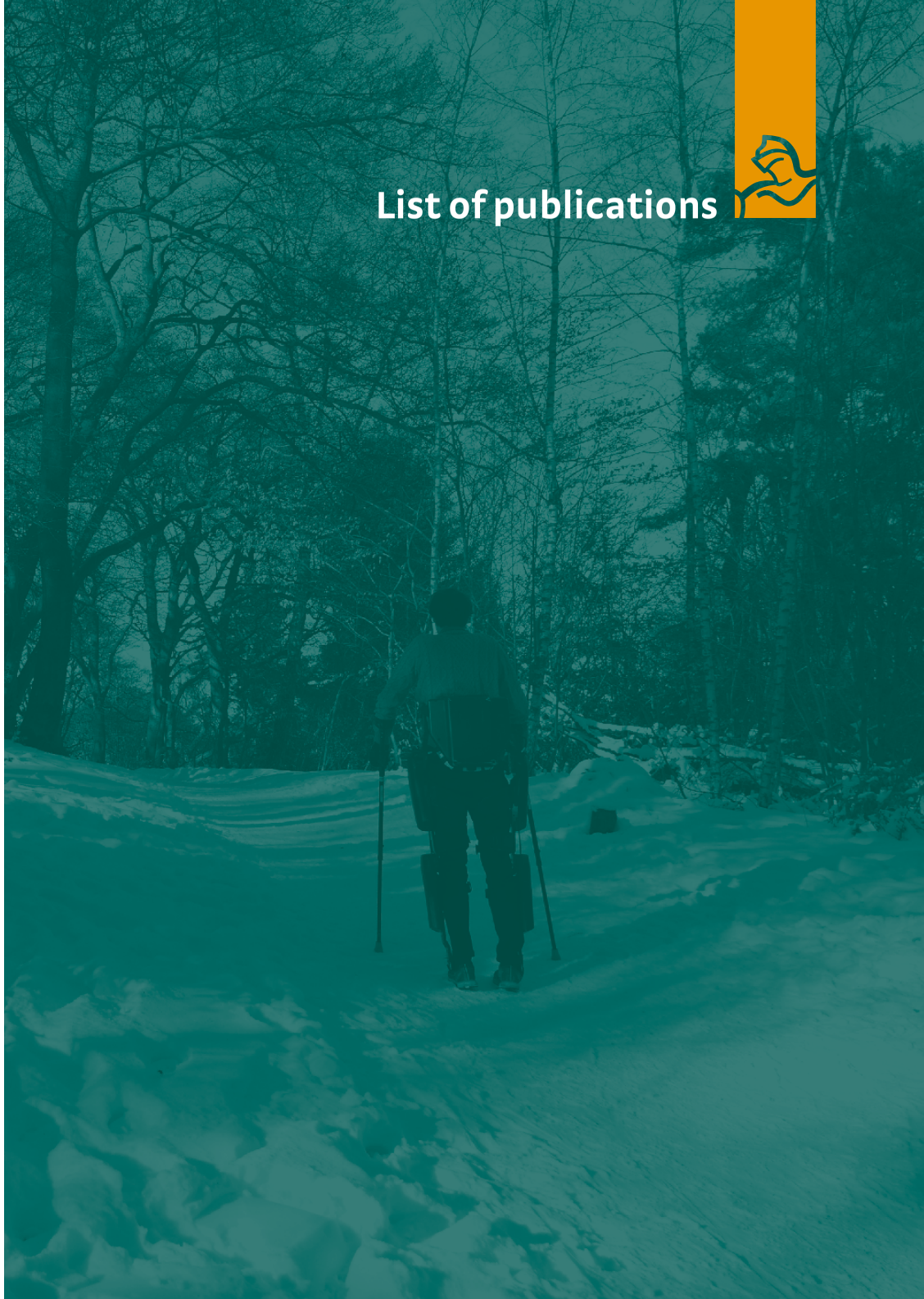
Curriculum vitae

Rosanne van Dijsseldonk was born in München on April 26th, 1991. After graduating from high school (HAVO, Pius-x College, Bladel) in 2008, she started to study Sports and Movement Education at the Fontys Sporthogeschool in Tilburg. She received her bachelor of education in 2014 and started the study Human Movement Sciences at the Vrije Universiteit Amsterdam that same year. Rosanne performed her research internship at Motek, where she studied the effect of treadmill walking in a virtual reality environment on motor learning. In her practical internship at InnoSportlab 's Hertogenbosch, she developed a protocol to measure the rehabilitation process after a anterior cruciate ligament reconstruction. She also measured the intensity of premier league basketball training sessions. During her master Human Movement Sciences, Rosanne became interested in rehabilitation programs, in particular in people with spinal cord injury.

Following her graduation in 2015, Rosanne started as a junior researcher at the Sint Maartenskliniek, in Nijmegen. In 2018 she started her PhD trajectory, which was a collaboration between the department of rehabilitation at the Radboud University Medical Center and the department of research at the Sint Maartenskliniek. In this trajectory she was supervised by Prof. dr. Sander Geurts, Dr. Noël Keijsers and Dr. Ilse van Nes. Rosanne's PhD was part of the Wearable Robotics project in which she closely collaborated with academic, industrial, and clinical partners. The various research projects about innovations aimed at improving mobility in people with spinal cord injury have led to this thesis. At the end of her PhD, Rosanne received a Short Term Scientific Mission (STSM) grant.

Rosanne is currently living in Rosmalen together with her partner Rob. She plans to continue to work in the field of spinal cord injury.

List of publications



List of publications

This thesis

R.B. van Dijsseldonk, I.J.W. van Nes, A.C.H. Geurts, N.L.W. Keijsers (2020) Exoskeleton home and community use in people with complete spinal cord injury. Scientific reports. doi: 10.1038/s41598-020-72397-6

F.H.M. van Herpen, **R.B. van Dijsseldonk**, H. Rijken, N.L.W. Keijsers, J.W.K. Louwerens, I.J.W. van Nes (2019) Case report: Description of two fractures during the use of a powered exoskeleton. Spinal cord series and cases. doi: 10.1038/s41394-019-0244-2

L.A.F. de Jong, **R.B. van Dijsseldonk**, N.L.W. Keijsers, B.E. Groen (2019) Test-retest reliability of stability outcome measures during treadmill walking in patients with balance problems and healthy controls. Gait & posture. doi: 10.1016/j.gaitpost.2019.10.033

R.B. van Dijsseldonk, H. Rijken, I.J.W. van Nes, H. van de Meent, N.L.W. Keijsers (2019) Predictors of exoskeleton motor learning in spinal cord injured patients. Disability & Rehabilitation. doi: 10.1080/09638288.2019.1689578

R.B. van Dijsseldonk, L.A.F. de Jong, B.E. Groen, M. Vos-van der Hulst, A.C.H. Geurts, N.L.W. Keijsers (2018) Gait Stability Training in a Virtual Environment Improves Gait and Dynamic Balance Capacity in
Incomplete Spinal Cord Injury Patients. Frontiers in Neurology. doi: 10.3389/fneur.2018.00963

R.B. van Dijsseldonk, H. Rijken, I.J.W. van Nes, H. van de Meent, N.L.W. Keijsers (2017) A Framework for Measuring the Progress in Exoskeleton Skills in People with Complete Spinal Cord Injury. Frontiers in Neuroscience. doi: 10.3389/fnins.2017.00699

Other publications

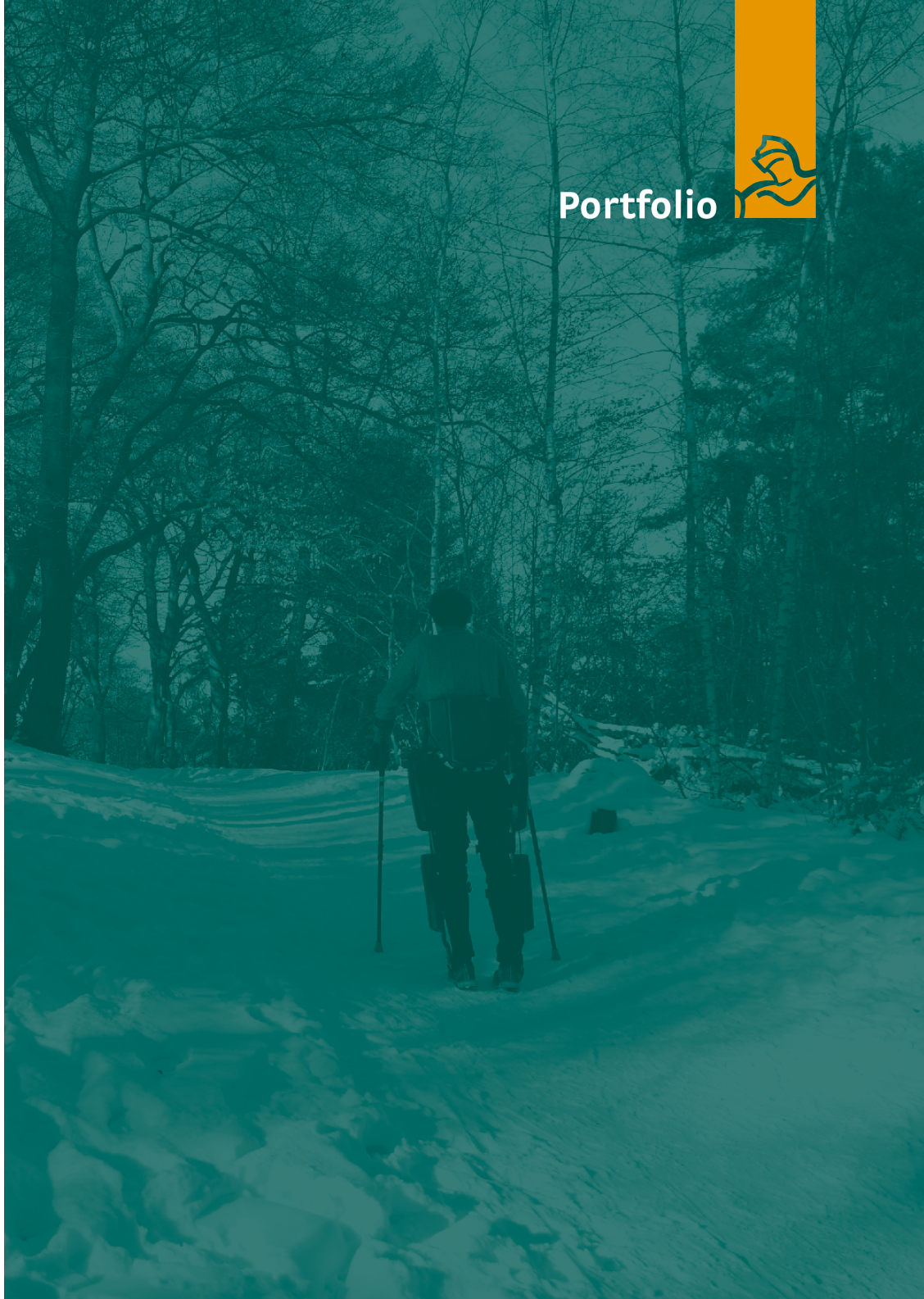
R.B. van Dijsseldonk, I.J.W. van Nes, N.L.W. Keijsers (2021) Thuisgebruik van het exoskelet. Dwarslaesie Magazine.

K. van der Kooij, **R.B. van Dijsseldonk**, M. van Veen, F. Steenbrink, C. de Weerd, K.E. Overvliet (2019) Gamification as a Sustainable Source of Enjoyment During Balance and Gait Exercises. Frontiers in Psychology. doi: 10.3389/fpsyg.2019.00294

R.B. van Dijsseldonk, L.A.F. de Jong, B.E. Groen, M. Vos-van der Hulst, N.L.W. Keijsers (2019) Loop en balanstraining bij incomplete dwarslaesie. Dwarslaesie Magazine.

R.B. van Dijsseldonk, I.J.W. van Nes, H. Rijken, H. van de Meent, N.L.W. Keijsers (2019) RehabMove 2018: A framework of exoskeleton-skill-tests in patients with complete spinal cord injury. Zenodo. doi: 10.5281/zenodo.2593417

H. Muijzer-Witteveen, N. Sibum, **R.B. van Dijsseldonk**, N.L.W. Keijsers, E.H.F. van Asseldonk (2018) Questionnaire results of user experiences with wearable exoskeletons and their preferences for sensory feedback. Journal of NeuroEngineering and Rehabilitation. doi: 10.1186/s12984-018-0445-0



Portfolio

Portfolio

Oral presentations at international conferences

Nov. 2019 — 58th International Spinal Cord Society (ISCoS) Annual Scientific Meeting, Nice, France
Title: *Feasibility and functional use of exoskeleton in complete SCI - results of use at home*

Sep. 2019 — 16th congress of the Nordic Spinal Cord Society (NoSCoS), Copenhagen, Denmark
Title: *Exoskeleton skill acquisition and home use*

Dec. 2018 — 6th RehabMove congress, Groningen, the Netherlands
Title: *Do high and low spinal cord injured subjects learn exoskeleton skills differently?*

May. 2018 — IMDI CoRE NeuroControl congress, Soesterberg, the Netherlands
Title: *Training and home-use of an exoskeleton*

Nov. 2017 — Dutch Congress of Rehabilitation Medicine 2017 (DCRM), Maastricht, the Netherlands
Title: *A framework for measuring the progress in exoskeleton skills in people with complete spinal cord injury*

Nov. 2017 — Dutch Congress of Rehabilitation Medicine 2017 (DCRM), Maastricht, the Netherlands
Title: *Virtual reality training to improve gait stability in patients with chronic incomplete spinal cord injury: useful or useless?*

May. 2017 — 3rd congress on NeuroRehabilitation and Neural Repair, Maastricht, the Netherlands
Title: *Wearable exoskeleton for patients with complete spinal cord injury: training and home-use*

Nov. 2016 — Dutch Congress of Rehabilitation Medicine 2016 (DCRM), Maastricht, the Netherlands
Title: *The exoskeleton used as an orthosis: experiences and results from the Sint Maartenskliniek*

Poster presentations at international conferences

July 2019 — International Society of Posture & Gait Research congress 2019 (ISPGR), Edinburgh, Scotland
Title: *Predictors of exoskeleton skill performance in people with spinal cord injury*

Dec. 2018 — 6th RehabMove congress, Groningen, the Netherlands
Title: *Gait stability training in a virtual environment in incomplete spinal cord injury patients*

Oct. 2017 — 56th International Spinal Cord Society (ISCoS) Annual Scientific Meeting, Dublin, Ireland
Title: *A framework for measuring the progress in achieved exoskeleton skills in people with motor complete SCI*

Oct. 2017 — 56th International Spinal Cord Society (ISCoS) Annual Scientific Meeting, Dublin, Ireland
Title: *Wearable exoskeleton for patients with motor complete spinal cord injury: training and home-use*

Oct. 2017 56th International Spinal Cord Society (ISCoS) Annual Scientific Meeting, Dublin, Ireland
Title: *Virtual reality training to improve gait stability in patients with chronic incomplete spinal cord injury: useful or useless?*

Award

Jan. 2021 Short Term Scientific Mission (STSM) of COST Action Wearable Robotics

Courses

	Year	ECTS
• BROK & hercertificering	2017	1.5
• Presenteren eigen onderzoek	2017	1.5
• Masterclass patiëntenparticipatie	2017	0.2
• Effective writing strategies	2017	3.0
• GRAIL operator level 1 (Motek)	2018	1.3
• Mindfulness	2018	2.0
• Scientific integrity	2018	0.3
• Digital tools for scholary information	2018	0.2
• Achieving your goals	2018	1.5
• Perfecting your academic writing skills	2018	1.5
• Presenteren in 1 dag (Spies & Spreken)	2018	1.5
• Kwalitatieve analyse (Evers Research & training)	2019	0.7
• Design and illustration	2019	1.0
• Qualitative research methods and analysis	2020	3.0

Supervision

• Supervision of master students biomedical sciences, research internship (2 times)	2016, 2019
• Supervision of bachelor students biomedical sciences, research internship (3 times)	2016, 2017, 2020
• Supervision of master student biomedical sciences, literature internship	2018

Conferences and symposiums

• ONVZ health insurance*, Nijmegen	2019
• KNMG avondsymposium*, Zwolle	2019
• XoSoft symposium, Amsterdam	2019
• GRAIL symposium, Arnhem	2019
• To walk again symposium, Herentals, Belgium	2018
• Wearable robotics symposium, Enschede	2018
• Refereeravond Dwarslaesie*, Nijmegen	2017
• NVDG symposium*, Wijk aan Zee	2017
• HAL symposium, Bochum, Germany	2017
• Achmea symposium – letselschade voor de toekomst*, Zeist	2016
• Symposium Saxion Hogescholen*, Enschede	2016
• NVDG symposium*, Hoensbroek	2016
• Design presentation MARCH I – IV, Delft	2016 – 2020

*Indicate oral presentation

Lectures, seminars, and workshops

• Exoskeleton demonstrations (House of delegates (2016), Achmea (2018), Doctors Nepal (2018), Heliomare (2018), Minor neurorevalidatie (2018), UTwente (2018, 2019), Student meets patient (2018, 2019), ONVZ (2019), LEC symposium (2019))	2016 – 2019
• Indego exoskeleton demonstration and testing (2 times)	2017
• Research lunch Sint Maartenskliniek & Lablunch Sint Maartenskliniek	2016 – 2020
• Journal club Radboudumc and Sint Maartenskliniek & Labmeeting Radboudumc	2018 – 2019
• Research content meeting (ReCoMe) Sint Maartenskliniek	2019 – 2020

Other activities

• Review scientific publication (2 times) - Disability and Rehabilitation & Neurorehabilitation and Neural repair	2018, 2019
• Organize a two-day PhD retreat TTW, Nijmegen	2019
• Organize user focus group (TUDelft), Nijmegen	2019
• Organize mini-symposium Sunnaas rehabilitation hospital (Norway), Nijmegen	2019

Research data management

Research data management

General information about the data collection

This research followed the applicable laws and ethical guidelines. Research Data Management was conducted according to the FAIR principles. The paragraphs below specify in detail how this was achieved.

Ethics

This thesis is based on the results of human studies, which were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was provided by all participants. The medical ethics committee on Research Involving Human Subjects region Arnhem-Nijmegen has given approval to conduct the studies described in chapters 4, 5, 7, and 8 (dossier number 2016-2418). The other studies met the requirements for exemption from medical ethics committee review, which was determined by the medical ethics committee on Research Involving Human Subjects region Arnhem-Nijmegen (chapter 3 - dossier number 2016-2474, and chapter 9 - dossier number 2019-5637) or the medical ethics committee of Slotervaart-Reade (chapter 2 - dossier number P1613/P1614). The studies described in chapter 3, 5, 7, 8, and 9 in this thesis are part of the research program Wearable Robotics with project number P16-05, which is financed by the Dutch Research Council (NWO). The studies described in chapter 2, 4, and 6 did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

FAIR principles

Findable: Data were stored on the server of the research department at the Sint Maartenskliniek. The paper CRF files were stored at the research department (room W0.07) and will be transferred to the department's archive after publication of the study. Data sets and documentation to describe the data sets can be found on the department's server at V:\research_reva_studies\725_GRAILdwarslaesie, V:\research_reva_studies\0697_Rewalk, V:\research_reva_studies\875_Future_exoskeleton, and Y:\research_archief.

Accessible: All data will be available on reasonable request by contacting the staff secretary of the research department at the Sint Maartenskliniek (secretariaat.research@maartenskliniek.nl) or the corresponding author.

Interoperable: Documentation was added to the data sets to make the data interpretable. The documentation contains links to publications, references to the location of the data sets and description of the data sets. The data were stored in the following file formats: .xlsx (Microsoft Office Excel), .sav (IBM SPSS statistics), .mat (MATLAB, Mathworks, USA), and .atlproj (ATLAS.ti). Data from chapter 2 and 3 were converged to MATLAB and Microsoft Excel for analyses. Data from chapter 4, 5, 7, and 8 were converged to Microsoft Excel and IBM SPSS for analyses. Data from chapter 9 was analysed using ATLAS.ti. No existing data standards were used such as vocabularies, ontologies or thesauri.

Reusable: The data will be saved for 15 years after termination of the study concerned. Using these patient data in future research is only possible after a renewed permission by the patients as recorded in their informed consents.

Privacy

The privacy of the participants in this thesis has been warranted using encrypted and unique individual subject codes. The encryption key was stored separately from the research data and was only accessible to members of the project who needed access to it because of their role within the project.

Donders Graduate School for Cognitive Neuroscience

For a successful research Institute, it is vital to train the next generation of young scientists. To achieve this goal, the Donders Institute for Brain, Cognition and Behaviour established the Donders Graduate School for Cognitive Neuroscience (DGCN), which was officially recognised as a national graduate school in 2009. The Graduate School covers training at both Master's and PhD level and provides an excellent educational context fully aligned with the research programme of the Donders Institute.

The school successfully attracts highly talented national and international students in biology, physics, psycholinguistics, psychology, behavioral science, medicine and related disciplines. Selective admission and assessment centers guarantee the enrolment of the best and most motivated students.

The DGCN tracks the career of PhD graduates carefully. More than 50% of PhD alumni show a continuation in academia with postdoc positions at top institutes worldwide, e.g. Stanford University, University of Oxford, University of Cambridge, UCL London, MPI Leipzig, Hanyang University in South Korea, NTNU Norway, University of Illinois, North Western University, Northeastern University in Boston, ETH Zürich, University of Vienna etc.. Positions outside academia spread among the following sectors: specialists in a medical environment, mainly in genetics, geriatrics, psychiatry and neurology. Specialists in a psychological environment, e.g. as specialist in neuropsychology, psychological diagnostics or therapy. Positions in higher education as coordinators or lecturers. A smaller percentage enters business as research consultants, analysts or head of research and development. Fewer graduates stay in a research environment as lab coordinators, technical support or policy advisors. Upcoming possibilities are positions in the IT sector and management position in pharmaceutical industry. In general, the PhDs graduates almost invariably continue with high-quality positions that play an important role in our knowledge economy.

For more information on the DGCN as well as past and upcoming defenses please visit:
http://www.ru.nl/donders/graduate-school/phd/

Theses Sint Maartenskliniek

Theses Sint Maartenskliniek

Pelle, T. (2021). *Beating osteoarthritis by e-self management in knee or hip osteoarthritis.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Van Heuckelum, M (2020). *Novel approaches to improve medication adherence in rheumatoid arthritis.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Mathijssen, E. (2020). *The voice of patients with rheumatoid arthritis.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Bakker, S. (2019). *Regional anesthesia and total knee arthroplasty. Anesthetic and pharmacological considerations.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Claassen, A. (2019). *Strategies for patient education in rheumatic diseases.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Fenten, M. (2019). *Optimizing locoregional anesthesia in fast track orthopaedic surgery.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Minten, M. (2019). *On the role of inflammation and the value of low dose radiation therapy in osteoarthritis.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Verhoef, L. (2019). *Effective and efficient use of bDMARDs in rheumatoid arthritis.* Radboud University Nijmegen, Nijmegen. The Netherlands.

Bekker, C. (2018). *Sustainable use of medication. Medication waste and feasibility of redispensing.* Utrecht University, Utrecht. The Netherlands.

Bikker, I.(2018). *Organizing timely treatment in multi-disciplinary care.* University of Twente, The Netherlands.

Bouman, C. (2018). *Dose optimisation of biologic DMARDs in rheumatoid arthritis: long-term effects and possible predictors.* Radboud University Nijmegen, The Netherlands.

Mahler, E. (2018). *Contributors to the management of osteoarthritis.* Utrecht University, The Netherlands.

Tweehuysen, L. (2018). *Optimising biological treatment in inflammatory rheumatic diseases. Predicting, tapering and transitioning.* Radboud University Nijmegen, Nijmegen, The Netherlands.

Geerdink, Y. (2017). *Getting a grip on hand use in unilateral cerebral palsy.* Radboud University, Nijmegen, The Netherlands.

Remijn, L. (2017). *Mastication in children with cerebral palsy.* Radboud University, Nijmegen, The Netherlands.

Selten, E. (2017). *Beliefs underlying treatment choices in osteoarthritis.* Radboud University, Nijmegen, The Netherlands.

Van Hooff, M. (2017). *Towards a paradigm shift in chronic low back pain? Identification of patient profiles to guide treatment.* VU University Amsterdam, Amsterdam, The Netherlands.

Lesuis, N. (2016). *Quality of care in rheumatology. Translating evidence into practice.* Radboud University, Nijmegen, The Netherlands.

Luites, J. (2016). *Innovations in femoral tunnel positioning for anatomical ACL reconstruction.* Radboud University, Nijmegen, The Netherlands.

Pakvis, D. (2016). *Survival, primary stability and bone remodeling assessment of cementless sockets. An appraisal of Wolff's law in the acetabulum.* Radboud University, Nijmegen, The Netherlands.

Schoenmakers, K. (2016). *Prolongation of regional anesthesia. Determinants of peripheral nerve block duration.* Radboud University, Nijmegen, The Netherlands.

Altmann, V. (2015). *Impact of trunk impairment on activity limitation with a focus on wheelchair rugby.* Leuven University, Leuven, Belgium.

Bevers, K. (2015). *Pathophysiologic and prognostic value of ultrasonography in knee osteoarthritis.* Utrecht University, Utrecht, The Netherlands.

Cuperus, N. (2015). *Strategies to improve non-pharmacological care in generalized osteoarthritis.* Radboud University, Nijmegen, The Netherlands.

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