Locomotor Training in Subjects with Sensori-Motor Deficits: An Overview of the Robotic Gait Orthosis Lokomat

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ABSTRACT

It is known that improvement in walking function can be achieved in patients suffering a movement disorder after stroke or spinal cord injury by providing intensive locomotor training. Rehabilitation robots allow for a longer and more intensive training than that achieved by conventional therapies. Robot assisted treadmill training also offers the ability to provide objective feedback within one training session and to monitor functional improvements over time. This article provides an overview of the technical features and reports the clinical data available for one of these systems known as "Lokomat". First, background information is given for the neural mechanisms of gait recovery. The basic technical approach of the Lokomat system is then described. Furthermore, new features are introduced including cooperative control strategies, assessment tools and augmented feedback. These features may be capable of further enhancing training intensity and patient participation. Findings from clinical studies are presented covering the feasibility as well as efficacy of Lokomat assisted treadmill training.

Keywords: gait, locomotion; gait therapy, rehabilitation, rehabilitation robotics, assessment, biofeedback, robot-aided training, Lokomat

1. INTRODUCTION

Loss of the ability to walk represents a major disability for millions of individuals worldwide, and a major expense for health care and social support systems. More than 700'000 people in the U.S. suffer from a stroke each year; 60−75% of these individuals will live beyond one year after the incident, resulting in a stroke survivor population of about 3 million people [1]. Almost two-third of all stroke survivors have no functional walking ability and cannot walk without assistance in the acute phase following the incident [2]. On the other hand, for many of the 10.000 Americans who are affected by a traumatic spinal cord injury (SCI) per year, the most visible lingering disability is the lost or limited ability to walk [3]. One major goal in the rehabilitation of patients suffering from a movement disorder is retraining locomotor function. One approach frequently applied over the past 20 years for retraining of gait is locomotor training on a treadmill combined with partial body weight support [4−9].

A major limitation of manual-assisted, body weight supported treadmill therapy (BWSTT) is that a training session relies upon the ability and availability of physical therapists to appropriately assist the patient's leg movement through the gait cycle. Robotic devices can eliminate this problem through the use of a mechatronic system that automates the assistance of the leg movement [10, 11].

This article summarizes the neuroscientific rationale for robot-assisted therapy and presents the technological steps in the evolution of the design and development of Lokomat, an internationally well established robot for gait therapy. Findings from research studies will be presented covering feasibility and functional improvements in response to Lokomat assisted treadmill training in various motor disorders as well as studies aiming at understanding some of the basic mechanisms underlying behavioral recovery in response to Lokomat assisted training. In another (clinically focused) review to be published, we will detail the efficacy (i.e., therapeutic effect) of Lokomat assisted treadmill training for a number of pathologies.

2. NEURONAL BASIS UNDERLYING LOCOMOTOR TRAINING

Stroke and traumatic brain or spinal cord injury result in neurological disorders associated with impaired or total loss of locomotion. Patients show clinical symptoms of flaccid paresis or spasticity in one or both legs. Basic research studies in the animal model including the cat have shown that repetitive execution of the impaired movement (supported by any external help) can improve motor function of the affected limbs [4]. Research indicates that these improvements are based on neuroplasticity of the central nervous system at many levels and result in compensation for the loss of lesioned brain or spinal cord areas [12−14]. In spinal cord injury the supraspinal control over the neural circuitry in the spinal cord is impaired, while the spinal and supraspinal neural centers underlying locomotion remain intact. Evidence for the existence of a human spinal pattern generator is indicated by the observation of spontaneously occurring step-like movements [15] and myoclonus [16] as well as from late flexion reflexes [16] and from locomotor movements induced in body-weight supported paraplegic patients walking on a treadmill [5, 17]. Other studies have shown that a locomotor pattern may be induced and trained even in completely paraplegic patients when leg movements

were assisted externally and an appropriate afferent input to the spinal cord is provided [5, 17–20]. Nevertheless, the amplitude of leg muscle electromyographic (EMG) activity in these patients is small when compared with healthy subjects but increases during locomotor training sessions [5]. These studies provide indirect but sufficient evidence for the existence of a Central Pattern Generator (CPG) in human subjects. The spinal pattern generator and an appropriate proprioceptive feedback can be implemented in a training system to target neural circuits to induce plastic changes.

Body un-loading and re-loading are considered to be of crucial importance to induce training effects upon the neurological locomotor centers because the afferent input from receptors signaling contact forces during the stance phase is essential for the activation of spinal locomotor centers [21]. Therefore, this cyclic loading is considered to be important for achieving training effects in cat, [22] and man [23, 24]. Because the available muscle force is not sufficient to support the body weight during walking, partial body weight unloading is necessary in order to allow for stable walking and locomotor training.

Recent findings demonstrated that following an acute, incomplete spinal cord injury in humans, an improvement of locomotor function was observed and was specifically attributed to the functional locomotor training [13, 25] in addition to the spontaneous recovery of spinal cord function that can occur over several months following spinal cord injury [26–29].

3. FROM MANUAL TO ROBOTIC GAIT TRAINING

Manually assisted BWSTT involves therapist assistance while the patient practices stepping movements on a motorized treadmill and with simultaneous unloading of a certain percentage of body weight. Manual assistance is provided as necessary (and as far as possible) to enable upright posture and to induce leg movements associated with adaptive physiological human gait. Over the last two decades, there has been growing evidence of support for the use of this technique in neurorehabilitation programs for stroke [30] and SCI subjects [8, 13, 20, 31]. Some studies showed stronger improvement in functional walking ability following BWSTT compared to conventional gait training [30, 32], whereas other groups did not report better functional outcome [8, 33, 34]. However, by using BWSTT, the support can be adjusted to the patient's stepping ability or to the severity of paresis.

Whereas evidence demonstrates improvement in locomotor function following manually assisted treadmill training, its practical implementation in the clinical setting is limited by the labor intensive nature of the method. Specifically, training sessions tend to be short because of the physical demands and time costs placed upon the therapists' resources. This resource constraint yields significant limitations upon access to the therapy, and ultimately, to the effectiveness of the therapeutic approach with patients. Particularly, in individuals with limb paralysis and/or a high degree of spasticity, appropriate manual assistance is difficult to provide; these patients require more than two therapists, which increases the already high cost and also limiting training time [36]. The success and promise of BWSTT and the limitations and resource constraints in the therapeutic environment have inspired the design and development of robotic devices to assist the rehabilitation of ambulation in patients following stroke or SCI.

The research team of the Spinal Cord Injury Center of the University Hospital Balgrist in Zurich, Switzerland, an interdisciplinary group of physicians, therapists, and engineers, began to work on a driven gait orthosis (DGO) in 1995 that would essentially replace the arduous physical labor of therapists in the administration of locomotor training [10]. The "Lokomat" (commercially available from Hocoma AG, Volketswil, Switzerland) consists of a computer-controlled robotic exoskeleton that moves the legs of the patient in an adjustable conjunction with a body-weight support system (Fig. 1a, b). Later on, other exoskeletal systems were developed including the "Autoambulator" by Healthsouth Inc. (USA), the "Lopes" by the University of Twente (Netherlands) [37] and the "ALEX" by the University of Delaware (USA) [38].

An alternative to exoskeletal systems are endeffector-based systems such as the commercially available Gait Trainer [11]. The Gait Trainer operates like a conventional elliptical trainer, where the subject's feet are strapped into two footplates moving the feet along a trajectory that is similar to a gait trajectory. Another Research group at the Los Amigos Research and Education Institute, Downey, California (USA) developed the "PAM" (Pelvic Assist Manipulator), which is a device that assists the pelvic motion during human gait training on a treadmill, and "POGO" (Pneumatically Operated Gait Orthosis), which moves the patient's legs with linear actuators attached to a frame placed around the subject [39].
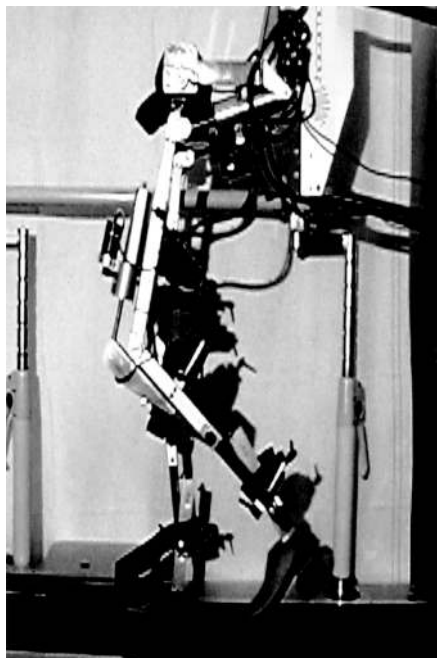

Figure 1a.   First clinical prototype of the Lokomat system (1999).

Figure 1b.   Current version of the Lokomat system with spinal cord injured patient (2007).

4. THE LOKOMAT SYSTEM

4.1. Orthosis Technology

Mechanical aspects: The Lokomat® is a bilaterally driven gait orthosis that is used in conjunction with a body-weight support system [10]. The Lokomat moves the patient legs through the gait cycle in the sagittal plane (Fig. 1b). The Lokomat's hip and knee joints are actuated by linear drives integrated into an exoskeletal structure. Passive foot lifters support ankle dorsiflexion during the swing phase. The leg motion can be controlled with highly repeatable predefined hip and knee joint trajectories on the basis of a conventional position control strategy. The orthosis is fixed to the rigid frame of the bodyweight support system via a parallelogram construction that allows passive vertical translations of the orthosis, while keeping the orientation of the robotic pelvis segment constant. The patient is fixed to the orthosis with straps around the waist, thighs and shanks.

The angular positions of each leg are measured by potentiometers attached to the lateral sides of the hip and knee joints of the orthosis. The hip and knee joint trajectories can be manually adjusted to the individual patient by changing amplitude and offsets. Knee and hip joint torques of the orthosis are measured by force sensors integrated into the orthosis in series with the linear drives. The signals may be used to determine the interaction torques between the patient and the device, which allows estimation of the voluntary muscle effort produced by the patient. This important information may be optimally used for various control strategies as well as for specific biofeedback and assessment functions.

The Lokomat geometry can be adjusted to the subject's individual anthropometry. The lengths of the thighs and shanks of the robot are adjustable via telescopic bars so

that the orthosis may be used by subjects with different femur lengths ranging between 35 and 47 cm. A new Lokomat was designed and developed in 2006 to accommodate pediatric patients with femur lengths between 21 and 35 cm (equivalent to body heights between approx. 1.00 m and 1.50 m). The width of the hip orthosis may also be adjusted by changing the distance between the two lower limbs. The fixation straps, available in different sizes, are used to safely and comfortably hold the patient's limb to the orthosis.

Drives: Ruthenberg and co-workers [40] reported the maximal hip torque during gait to be approximately 1 Nm per kilogram of body weight and an estimated average torque of approximately 35 Nm. In the Lokomat, hip and knee joints are actuated by custom-designed drives with a precision ball screw. The nut on the ball screw is driven by a toothed belt, which is in turn driven by a DC motor. The nominal mechanical power of the motors is 150 W. This yields an average torque of approximately 30 Nm and 50 Nm at the knee and hip, respectively. Maximum peak torques are 120 Nm and 200 Nm, respectively. This design has been demonstrated to be sufficient to move the legs against gravitational and inertial loads and, thus, to generate a functional gait pattern required in a clinical environment and suitable for most patients, even those with severe spasticity.

Safety: Whereas the mentioned peak torques are required in order to move the patient's joints in the presence of considerable interaction forces produced at the joints (e.g., due to spasticity) or between the patient's feet and treadmill (e.g., due to minor deviations of robot and treadmill speed), they can pose an inherent risk to the musculoskeletal system of the patient. In order to minimize this risk, various measures of safety were implemented into electronics, mechanics and software. The electronic and mechanical safety measures follow principles of medical device safety regulations and standards (e.g., galvanic insulation). Additionally, passive back-drivability and mechanical endstops avoid incidents that human joints get overstressed or blocked in case of actuator malfunction. The software safety measures manage proper operation of the device through control of nominal ranges of force sensors and also through the use of redundant position sensors. Software also checks plausibility of movement and stops the device as soon as the movement deviates too much from the known desired gait trajectory. Another important safety feature uses the static body weight support system, where the patient can be brought to a safe situation, when all drives have to be deactivated, e.g. when stumbling, or if spasticity causes the interaction forces to exceed the given threshold values. A wireless sensor system tracks the therapist's presence and prompts input from the therapist in order to ensure therapist's attention and to improve patient safety. Furthermore, several manual emergency stops enable the therapist (or patient) to cause a sudden stop of the movement whenever desired.

4.2. Body Weight Support System

Body-weight support systems enable patients with leg paresis to participate in functional gait-therapy, both on the treadmill and in over-ground walking [41]. A simple system consists of a harness worn by the patient, ropes and pulleys, and a counterweight used to partially unload the patient. However, these simple systems do not ideally accommodate the wide range of conditions a patient with sensori-motor deficits will encounter in gait therapy. The supporting vertical force varies mainly because of the effect of inertia that is induced by the vertical movements performed during gait [42]. A mechatronic
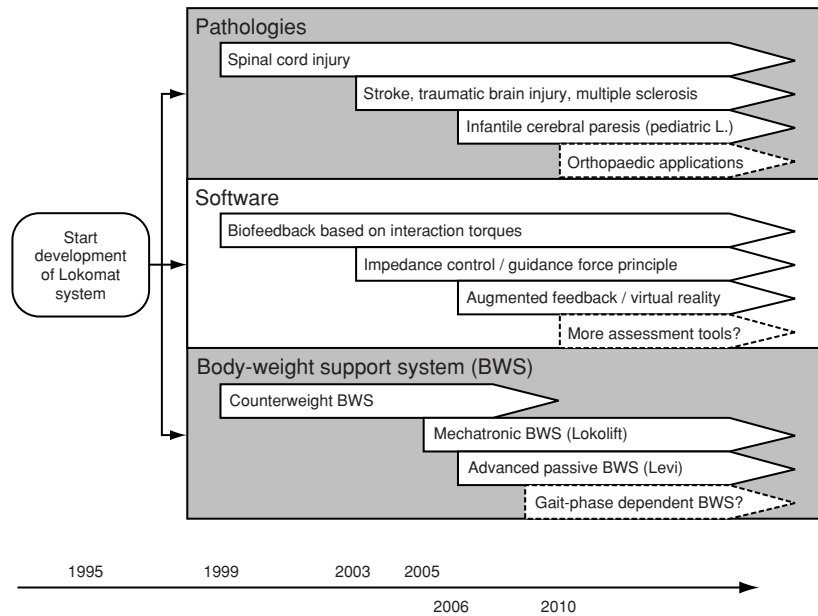
Figure 2.   Rough timeline and outlook of features of the Lokomat system.

body-weight support system called "Lokolift" has been developed to allow a more precise unloading during treadmill walking. The Lokolift combines the key principles of both passive elastic and active dynamic systems [42]. In this system, at unloading levels of up to 60 kg and walking speeds of up to 3.2 km/h, the mean unloading error was less than 1 kg and the maximum unloading error was less than 3 kg. This new system can perform changes of up to 20 kg in desired unloading within less than 100 ms. With this innovative feature, not only constant body weight support but also gait-cycle dependent or time variant changes of the desired force can be realized with a high degree of accuracy. More recently, a spring based (passive) system has been developed that allows similar results like the Lokolift system [43]. A chronological overview of the different developmental stages of Lokomat system is given in Fig. 2.

4.3. Control Strategies
In early clinical applications the Lokomat was only used in a position control mode, where the measured hip and knee joint angles are fed into a conventional PD controller that determines a reaction to the current error value (amplified by a factor P) and another reaction to the derivative error (amplified by a factor D) that is based upon the rate at which the error has been changing. In that original position control mode, the Lokomat does not systematically allow for deviation from the predefined gait pattern. However, rigid execution and repetition of the same pattern is not optimal for learning. In contrast, variability and the possibility to make errors are considered as essential components of

practice for motor learning. Bernstein's demand that training should be "repetition without repetition" [44] is considered to be a crucial requirement, and is also supported by recent advances in computational models describing motor learning [45]. More specifically, a recent study by Lewek et al. [46] demonstrated that intralimb coordination after stroke was improved by manual training, which enabled kinematic variability, but was not improved by position-controlled Lokomat training which reduced kinematic variability to a minimum.

In response to this important finding, "patient-cooperative" control strategies were developed that "recognize" the patient's movement intention and motor abilities by monitoring muscular efforts and adapt the robotic assistance to the patient's contribution, thus, giving the patient more movement freedom and variability than during position control [47, 48]. It is recommended that the control and feedback strategies should do the same as a qualified human therapist, i.e. they assist the patient's movement only as much as needed and inform the patient how to optimize voluntary muscle efforts and coordination in order to achieve and improve a particular movement.

The first step in incorporating a variable deviation from a predefined leg trajectory into the system, thus, giving the patient more freedom, may be achieved using an impedance control strategy. The deviation depends upon the patient's effort and behavior. An adjustable torque is applied at each joint depending on the deviation of the current joint position from the desired trajectory. This torque is usually defined as a zero order (stiffness), or higher order (usually first or second order) function of angular position and its derivatives. This torque is more generally called mechanical impedance [49]. Figure 3 depicts a block diagram of an impedance controller.

The impedance controller was initially tested in several healthy subjects with no known neurological deficits and also in several subjects with incomplete paraplegia [48]. In the impedance control mode, angular deviations increased with increasing robot compliance (decreasing impedance) as the robot applied a smaller force to guide the human legs along a given trajectory. Inappropriate muscle activation produced by high muscle tone, spasms, or reflexes, can affect the movement and may yield a physiologically incorrect gait pattern,
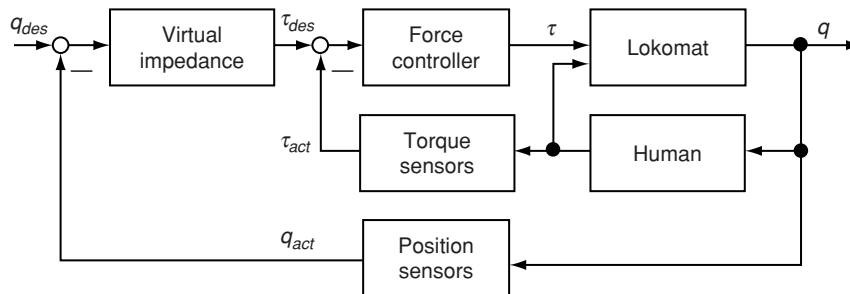

Figure 3. Example of an impedance control architecture for the compliance of rehabilitation robot [43]. Symbols: q is the vector of generalized positions or joint angles; τ is the vector of generalized joint torques; index "*des*" refers to the desired reference signal; index "*act*" refers to the actual, measured signal.

depending on the magnitude of the impedance chosen. In contrast, several subjects who used the system with the impedance controller stated that the gentle behavior of the robot feels good and comfortable (personal experience of subjects told to the authors).

The disadvantage of a standard impedance controller is that the patient needs sufficient voluntary effort to move along a physiologically correct trajectory, which limits the range of application to patients with only mild lesions. In addition, the underlying gait trajectory allows no flexibility in time, i.e., leg position can deviate only orthogonally but not tangentially to the given trajectory.

Therefore, the features of the impedance controller have been extended into a novel "path controller" [47] in which the time-dependent walking trajectories are converted to walking paths with user determined free timing. In this manner, the controller enables the impedance along the path to vary in order to obtain satisfactory movement particularly at critical phases of gait (e.g., before heel contact) [47]. This is comparable to fixing the patient's feet to soft rails, thus limiting the accessible domain of foot positions calculated as functions of hip and knee angles. The patients are free to move along these "virtual rails". In order to supplement these *corrective* actions of the Lokomat, a *supportive* force field of adjustable magnitude can be added. Depending on the actual position of the patient's legs, the supportive forces act in the direction of the desired path. The support is derived from the desired angular velocities of the predefined trajectory at the current path location. Supportive forces make it possible to move along the path with reduced effort. Compared to the impedance controller, the path controller gives the patient more freedom in timing, while he/she can still be guided through critical phases of the gait, providing a safe and variable repetitive gait therapy.

The reference trajectory has been recorded from healthy subjects [10] and is used as set point for the impedance controller. The treadmill speed is selected by the therapist. A dynamic set point generation algorithm is used to minimize the Euclidean distance between the reference trajectory and the actual trajectory. An adjustable zero band of a predefined width creates a virtual tunnel around the reference trajectory. The width of the zero band has been designed heuristically based upon the evidence and experience from pre-trials. The width was computed to permit larger spatial variation during late swing and early stance phase to account for the large variability of knee flexion at heel strike. Additionally, the reference trajectory has been adapted to a less pronounced loading response and more knee flexion during swing phase so that the desired zero band spreads symmetrically around the reference. In this way, a common tunnel was obtained that could accommodate all subjects, and enable additional variability and support. Within the tunnel, the controller is in so called "free run" mode; i.e., the output of the impedance is zero, and gravity and friction torques of the robot are compensated. Therefore, subjects can move freely and with their own timing as long as they stay within the tunnel. Leg postures outside the tunnel are corrected by the impedance controller. The spring constant of the virtual impedance is chosen as a function of the distance to the tunnel wall. These measurements were experimentally determined such that the wall of the tunnel felt comfortably soft to the subjects. We have implemented a nonlinear stiffness function to allow for a compromise between soft contact with the wall and strong corrections for larger deviations. An additional damping constant was determined as a function of the stiffness such that the system is critically damped.

Adjustable supportive torques can be superimposed to the controller output. To determine the direction of support, a torque vector is calculated by differentiating the reference trajectory with respect to the relative position in the gait cycle. Thus, the direction of the torque vector is tangential to the movement path in joint space. The supportive torques not only are important in helping a patient to overcome weaknesses, but also reduce the effect of the uncompensated inertia of the robot. More details and data regarding the path controller may be found in [47].

4.4. Assessment Tools

Using robotic devices in locomotor training can have more advantages than just supporting the movement and, thus, increasing the intensity of training. Data recorded by the position and force transducers can also be used to assess the clinical state of the patients throughout the therapy. The following clinical measures can be assessed by Lokomat:

Mechanical Stiffness: Spasticity is an alteration in muscle activation with increased tone and reflexes. It is a common side effect of neurological disorders and injuries affecting the upper motor neuron, e.g., brain or spinal cord injuries. Formally, spasticity is usually considered as "a motor disorder characterized by a velocity-dependent increase of tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexitability of stretch reflexes" [50]. It appears as an increased joint resistance during passive movements. Recently, Sanger et al. [51] introduced a more functional rather than physiological definition describing spasticity as "a velocity-dependent resistance of a muscle to stretch". Most commonly, spasticity is evaluated by the Ashworth Test [52] or Modified Ashworth Test [53]. In both tests, an examiner moves the limb of the patients while the patient tries to remain passive. The examiner rates the encountered mechanical resistance to passive movement on a scale between 0 and 4. However, such an evaluation is subject to variable factors, such as the speed of the movement applied during the examination and the experience of the examiner and inter-rater variability.

The mechanical resistance can also be measured with the Lokomat [54, 55] which is capable of simultaneously recording joint movement and torques. The actuation principle allows for assessment of the hip and knee flexion and extension movements in the sagittal plane. The stiffness measurement can be performed immediately before and following the usual robotic movement training without changing the setup. To measure the mechanical stiffness with the Lokomat, the subject is lifted from the treadmill by the attached body-weight support system so that the feet can move freely without touching the ground. The Lokomat then performs controlled flexion and extension movements of each of the four actuated joints subsequently at different velocities. The joint angular trajectories are squared sinusoidal functions of time replicating the movements applied by an examiner performing a manual Ashworth Test. Measured joint torques and joint angles are used to calculate the elastic stiffness as slopes of the linear regression of the torque-position plots. As the recorded torques also include passive physical effects of the Lokomat and the human leg, the measured torque is offline-compensated for inertial, gravitational, Coriolis and frictional effects obtained from an identified segmental model of the orthosis including the human leg. Patient data comparisons with manual assessments of spasticity based on the Modified

Ashworth Scale demonstrated that higher stiffness values measured by Lokomat corresponded with higher ratings of spasticity [54, 55]. Assessment of spasticity is still in an experimental status and needs further validation in future studies.

Voluntary force: For some patients, maximum voluntary force is a measure of limiting factor for walking. In order to assess the maximum voluntary force in the Lokomat [54], the examiner instructs the patient to generate force in each joint, first in flexion and then in extension directions. The force is generated against the Lokomat, which is position-controlled to a predefined static posture, thus providing a quasi-isometric measurement condition. Simultaneously, the joint moments are measured by the built-in force transducers and displayed to the patient and the therapist. The maximum moments for flexion and extension are used as outcome variables. An improved version standardizes the computerized sequence and instructions and uses a time-windowed calculation for the output values [56]. It was shown that this measurement method has a high inter- and intra-tester reliability and can be used to assess the strength of the lower extremities [56].

Range of motion: In a manner similar to conventional clinical range of motion assessments, the therapist moves the leg of the patient until the passive torque produced by the patient's joint reaches a certain threshold that is qualitatively predefined by the therapist based on his or her expertise. As the patient's legs are attached to the device with the anatomical and technical joint axes in alignment with each other, and the recorded joint angles correspond with the patient's joint angles, the passive range of motion is determined by the maximum and minimum joint angles measured. This parameter can be used for further assessments and training. The Lokomat measures the joint range of motion within values typical for human gait and may represent only a fraction of the patient's physiological range. This test provides important additional measures of the patient relevant to the gait and further conditions making contractures and other joint limitations (e.g., due to shortened tendons) quantifiable. These measures are directly relevant to activities of daily living.

4.5. Biofeedback

Compared to manual treadmill therapy, robotic gait retraining changes the nature of the physical interaction between the therapist and the patient. Therefore, it is important to incorporate the features into the Lokomat system to assess the patient's contribution and performance during training and to provide necessary feedback and instructions derived from precise measurements taken by the system. The patient may have deficits in sensory perception and cognition interfering with his/her ability to objectively assess movement performance, and making it difficult to engage the patient and to encourage active participation in the movement and training. With the new feature of Lokomat, the technology of biofeedback has a potential to challenge and engage the patient in order to increase the benefit on motor recovery and neurological rehabilitation [57, 58].

The built-in force transducers can estimate the muscular efforts contributed by the patient's knee and hip joints. Incorporating this information into an audiovisual display can simulate the "feedback" the therapist usually gives to the patient during manual training where the therapist estimates the patient's activity based on the effort required to guide the patient's legs.

The goal of the biofeedback function is to derive and display performance values that quantify the patient's activity in relation to the target gait function such that the patient can improve muscle activity towards a more functional gait pattern. An early implementation of a force-biofeedback strategy for the Lokomat has been described [48, 59, 60].

In order to obtain relevant biofeedback values, the gait cycle is divided into stance phase and swing phase. For each phase, weighted averages of the forces are calculated at each joint independently, thus yielding two values per stride per joint. Eight biofeedback values are available for each gait cycle from all four joints of the two lower limbs. Because of the bilateral symmetry, four weighting functions are required for the averaging procedure (hip stance, hip swing, knee stance, knee swing). The weighting functions were selected heuristically to provide positive biofeedback values when the patient performs therapeutically reasonable activities (e.g., active weight bearing during stance, sufficient foot clearance during swing, active hip flexion during swing, active knee flexion during early swing, knee extension during late swing). The graphical display of these values has been positively rated by the patients and leads to an increased instantaneous activity by the patients [61, 62]. However, there is no direct clinical evidence showing that this training with computerized feedback leads to better rehabilitation outcomes or faster recovery compared with Lokomat training without feedback.

To further increase patient's engagement and motivation, virtual reality and computer game techniques may be used to provide virtual environments that encourage active participation during training (Fig. 4). A first feasibility study showed that the

Figure 4.   Walking through a virtual environment. Lokomat in combination with a
                 virtual reality system.

majority of subjects could navigate through a virtual environment by appropriately controlling and increasing their activity of left and right legs while walking through a virtual underground scenario [63].

5. CLINICAL SIGNIFICANCE OF THE LOKOMAT SYSTEM

Recent research studies investigated the feasibility as well as functional improvements in response to Lokomat assisted treadmill training [10, 25, 64–77]. However, so far, it is still difficult to draw a general conclusion due to the small numbers of participants enrolled in the studies and heterogeneous selection criteria (e.g., acute and chronic patients, different pathologies of different severities) involved [35]. Furthermore, Lokomat training was rather variable in terms of training onset, duration, specific training parameters (e.g., walking speed, levels of body-weight support and guidance force) as well as the amount and type of conventional physiotherapy which the patients received in parallel to the Lokomat therapy. Nevertheless, today, it is commonly accepted that Lokomat training can be integrated into the normal therapy program and has proven to be feasible for treatment of a number of different pathologies such as spinal cord injury [10, 25, 70, 78], stroke [68, 69, 71, 73, 76, 77], multiple sclerosis [64, 72] and cerebral palsy [65–67, 74, 75]. Beneficial effects of Lokomat-assisted training were quite diverse, ranging from gains in gait velocity, walking endurance, to improvements in numerous walking tests [25, 64, 66, 70, 72–75, 77]. Some of these functional improvements were associated with changes in gait parameters [64] leading to a better gait quality [71, 79] as well as better voluntary control [80]. Besides locomotor benefits, a positive influence on abnormal reflex function [66, 73], respiration [81] as well as cardiovascular response [82, 83] have been reported.

Recently, a number of studies aiming to directly compare the efficacy of robot-assisted treadmill training with conventional training therapies were reported [68, 69, 71, 73, 76, 77, 84]. It became apparent that patients, especially those with severe locomotor deficits, benefited from Lokomat assisted treadmill training [71, 73, 76] while manually assisted gait training or additional therapies including balance and strength training are more suitable for patients who are able to walk [68, 69]. This is reasonable as manually assisted treadmill training has proven to be rather difficult in acute and subacute patients with severe lesions due to their reduced ability to support their body weight, their deficits in movement control, and the high physical demands on the therapists. The Lokomat was designed to assist leg movements specifically in severely dysfunctional subjects by allowing longer training periods with a high number of repetitions leading to a better outcome [85]. Increases in muscle mass and a loss of fat mass associated with cardiovascular training [71] as well as significantly increased oxygen consumption in response to changes in body weight support [86] demonstrate that walking in the Lokomat does represent an active movement task as described earlier [24].

In contrast, patients with the ability to walk probably require a gait training that is more intensive than currently being provided by robot assisted treadmill training. Therefore, future technical requirements include the ability for the Lokomat to extend gait control beyond the two-dimensional gait pattern that prevents training of coordination and balance. Some studies have reported higher inconsistencies in

intra-limb coordination [46] as well as significantly lower EMG activity in response to robot-assisted therapy than therapist-assisted walking [83]. However, gait quality was improved by locomotor training in individuals with SCI regardless of training approach [79]. These results illustrate the importance of further minimizing robotic guidance force in order to increase patient's participation and to enable training balance which requires robotic devices with sophisticated control strategies and additional degrees of freedom [46]. Furthermore, large multicenter clinical trials are required to ascertain appropriate patient selection for optimal treatment programs and intensity.

Future clinical and basic research is needed to investigate a wide range of important topics including but not limited to optimal training paradigms, duration, protocols, parameters for objective metrics and best combination with conventional therapies using the Lokomat as a diagnostic tool and prognostic indicator. In the future, the Lokomat might further help to investigate the rehabilitation of lower limb dysfunction and the underlying mechanisms of recovery. A number of research groups have already begun using the Lokomat as a diagnostic and experimental tool collecting and analyzing data to get a better understanding of the mechanisms, which lead to functional improvements such as the provision of appropriate afferent input [19]. Another study was able to demonstrate supraspinal plasticity as well as increased activation of the cerebellum in response to Lokomat-assisted treadmill training [78]. The Lokomat has further been employed to investigate the effect of treadmill training on corticospinal excitability [87, 88] reflex modulation [19, 89], muscle activation pattern in incomplete and complete SCI patients [24, 83] on spinal neuronal function in chronic complete SCI [90] and changes in cardiovascular, metabolic as well as autonomic responses [82, 91, 92]. In the future, close collaborations between clinical and basic research will aim to improve robot functions and individual training protocols in order to achieve the best functional outcome for patients.

6. CONCLUSION

Robotic rehabilitation devices become increasingly important and popular in clinical and rehabilitation environments to facilitate prolonged duration of training, increased number of repetitions of movements, improved patient safety and less strenuous operation by therapists. Novel sensor, display and control technologies made possible the improvement of the function, usability and accessibility of the robots by increasing patient participation and improving performance assessment. Improved and standardized assessment tools provided by robots can be an important prerequisite for the intra and inter-subject comparison that the researcher and the therapist require to evaluate the rehabilitation process of individual patients and entire patient groups. Furthermore, rehabilitation robots offer an open platform for the implementation of advanced technologies, which will provide new forms of training for patients with movement disorders. With the use of different cooperative control strategies and particular virtual reality technologies, patients can be encouraged not only to increase engagement during gait training but also to improve their motivation to participate in the therapy sessions.

CONFLICT OF INTEREST

LL, IM and GC are employees of Hocoma AG, Volketswil, Switzerland, manufacturer of Lokomat. However, Hocoma as a company was not involved in planning, writing, finalizing, or approving publication of this paper. In their previous employments, LL, IM and GC were all affiliated with research institutes at the University of Zurich and ETH Zurich, both in Switzerland. Their contributions to this article were based upon their independent scientific motivation and their scientific backgrounds. In addition, their contributions to this article resulted from the long-term scientific collaborations and research partnerships among ETH Zurich, University Hospital Balgrist, and Hocoma.
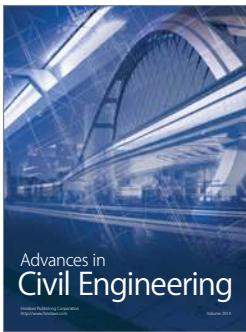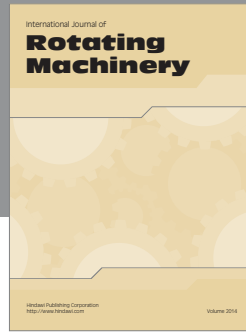
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