

Chapter 2

Emerging Rehabilitation in Cerebral Palsy

**Stefan Lambrecht, Oiane Urrea, Svetlana Grosu
and Soraya Pérez Nombela**

Abstract Cerebral Palsy (CP) is the most frequent disability affecting children. Although the effects of CP are diverse this chapter focuses on the impaired motor control of children suffering from spastic diplegia, particularly in the lower limb. The chapter collects the most relevant techniques that are used or might be useful to overcome the current limitations existing in the diagnosis and rehabilitation of CP. Special emphasis is placed on the role that emerging technologies can play in this field. Knowing in advance the type and site of brain injury could assist the clinician in selecting the appropriate therapy. In this context, neuroimaging techniques are being recommended as an evaluation tool in children with CP; we describe a variety of imaging technologies such as Magnetic Resonance Imaging (MRI), Diffusion Tensor Imaging (DTI), etc. But creating new knowledge in itself is not enough; there must be a transfer from progress through research to advances in the clinical field. The classic therapeutic approach of CP thus hampers the optimal rehabilitation of the targeted component. Traditional therapies may be optimized if complemented with treatments. We try to collect a wide range of emerging technologies and provide some criteria to select the adequate technology based on the characteristics of the neurological injury. For example, exoskeleton based over-ground

S. Lambrecht (✉)
Bioengineering Group, Spanish National Research Council, Madrid, Spain
e-mail: s.lambrecht@csic.es

O. Urrea
Institute for Bioengineering of Catalonia, Barcelona, Spain
e-mail: ourra@ibecbarcelona.eu

S. Grosu
Department of Robotics & Multibody Mechanics, Vrije Universiteit Brussel, Brussels, Belgium
e-mail: sgrosu@vub.ac.be

S. P. Nombela
Biomechanics and Technical Aids Department, National Hospital, Toledo, Spain
e-mail: sperez@n@sescam.jccm.es

gait training is suggested to be more effective than treadmill-based gait training. So, we suggest a new point of view combining different technologies in order to provide the foundations of a rational design of the individual rehabilitation strategy.

Keywords Cerebral palsy · Robotics · Neurostimulation · Neuroimaging · Myoelectric signals

2.1 Introduction

The general objective of rehabilitation interventions is to restore previous functional levels or abilities. However, when children are involved, the target level cannot be limited to re-establish a prior-value. Pediatric rehabilitation implicitly involves a moving target, the maturing child with transitory emotional, behavioral, cognitive and motor abilities. Therefore the objective in pediatric rehabilitation is twofold, restore prior levels and facilitate the further development of these abilities (Alexander and Matthews 2009).

Among all disabilities affecting children, Cerebral Palsy (CP) is the most frequent and its incidence rate keeps rising, partly due to greater numbers of premature infants who are surviving and longer overall survival (Wilson-Costello et al. 2005). Despite the lack of consensus on a definition of CP, three elements are recurring: (i) brain lesion, (ii) onset at birth or early child years, and (iii) impaired motor control. A well-cited definition of CP defines CP as: “a group of disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, behavior, by epilepsy and by secondary musculoskeletal problems” (Bax et al. 2005). Currently there is no specific diagnostic protocol, nor is there a clear singular etiology and pathology. There is a need for knowledge and tools to facilitate a reliable and accurate prognosis of CP outcome.

CP results in different movement patterns including spastic, dyskinetic, hypotonic, ataxic, and mixed forms. The most common movement pattern is spastic, with a minority of cases being primarily dyskinetic, ataxic or hypotonic (Yeargin-Allsopp et al. 2008). The primary means of classifying in CP is done according to the anatomical distribution of motor complications. There are three categories, each occurring with fairly equal frequency: hemiparesis, diparesis, and quadriplegia. *Hemiparetic CP* affects only one side of the body and typically demonstrates greater impairments in the upper extremity. *Diparetic CP* primarily affects the lower limbs with very little or no impairment in the upper extremities. *Spastic quadriplegic CP* affects the entire body, including the axial as well as appendicular skeleton (Alexander and Matthews 2009). Given the wide variety of impairments related to CP we have decided to put the emphasis on the impaired motor control of children suffering from spastic diplegia, and gait rehabilitation in particular.

Advances in neuroscience, neurophysiology and neuroimaging techniques offer an important contribution to neurorehabilitation by generating knowledge on impaired motor control and providing guidance to set future clinical and research pathways. In CP the most common neurological abnormality is found in the white matter near the lateral ventricles, often termed periventricular leukomalacia (PVL). PVL abnormalities are present in up to 56 % of all CP patients, occurring mostly in premature infants (90 %) rather than in term infants (20 %), and arise as a result of intraventricular hemorrhage. Because the corticospinal tract fibers to the lower extremities are medial to those of the upper extremities in the periventricular white matter, children with PVL abnormalities typically have spastic diparesis (Korzeniewski et al. 2008).

In this chapter we will focus on the diagnosis and rehabilitation of the impaired gait and motor control of children with CP, and the role emerging technologies can play herein (Fig. 2.1). The main body of the chapter consists of a section highlighting the clinical needs in CP (Sect. 2.2), and a section dedicated to how technologies that are emerging in research or other clinical fields can alleviate (some of) those clinical needs (Sect. 2.3). The technologies discussed in this chapter were selected based on their promising potential in CP treatment, or demonstrated impact and effect in other neurorehabilitation areas, such as stroke management. The section on emerging technologies is further divided into four parts: Myoelectric signals (Sect. 2.3.1), Neuroimaging (Sect. 2.3.2), Neuro-stimulation (Sect. 2.3.3), and Rehabilitation robotics (Sect. 2.3.4).

2.2 Clinical Needs in Cerebral Palsy

Little is understood about the causes and mechanisms underlying CP. The few well established fundamentals have yet to find their way into clinical practice. As a consequence, the diagnosis and treatment of CP is largely based on empirical criteria. However, specialists in the field claim that children with CP may benefit from emerging technologies, both for diagnosis and rehabilitation. Their claim is supported by the positive impact demonstrated in an increasing number of studies. Furthermore, advances done in fields such as neuroimaging may help to shed light in the pathophysiology of CP or enable a more accurate diagnosis. Similarly, novel neuro-stimulation techniques or rehabilitation robotic devices are expected to significantly improve the outcome of rehabilitation. Despite the potential of emerging technologies to solve important clinical issues in CP, the technological transfer in this area is almost blocked. In this section we list some of the most relevant limitations found in the field of CP that could be mitigated with the use of appropriate technologies.

The research on CP is still far from giving a clear picture on the pathophysiology of the disease. The development of the human brain and how it is affected by different injury conditions such as hypoxia, trauma or encephalitis remains poorly understood. There are still manifestations of CP with a non-identifiable

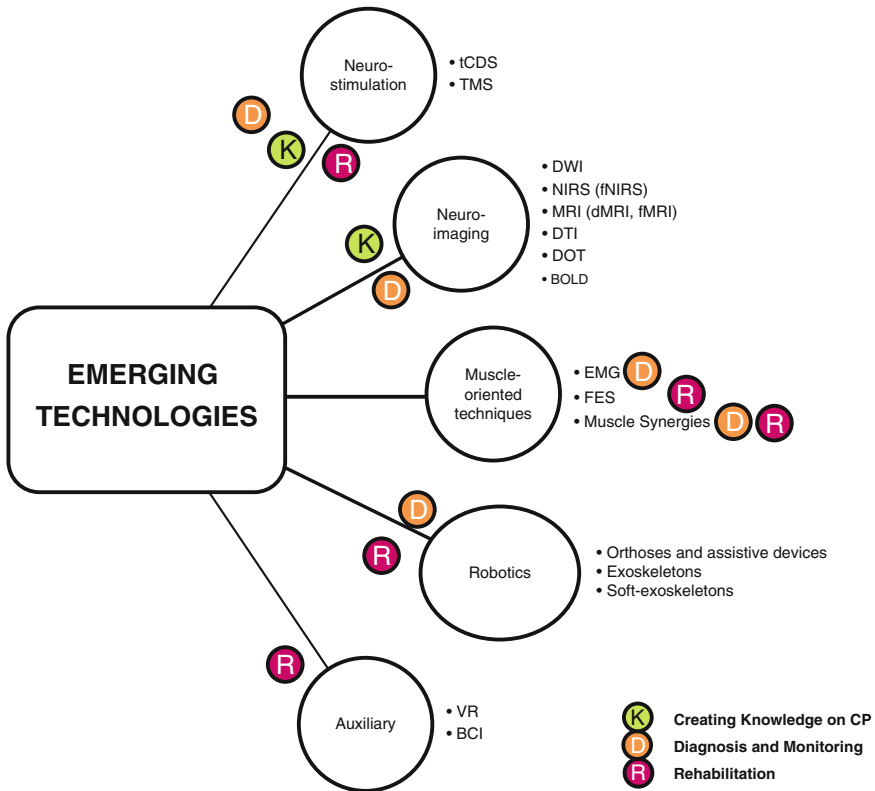


Fig. 2.1 The array of emerging technologies and their potential fields of impact related to cerebral palsy: rehabilitation, diagnosis, basic knowledge on physiopathology and motor control. *tDCS* transcranial direct current stimulation, *TMS* transcranial magnetic stimulation, *DWI* diffusion weighted imaging, *(f)NIRS* (functional)near-infrared spectroscopy, *MRI* magnetic resonance imaging, *DTI* diffusion tensor imaging, *DOT* diffusive optical imaging, *BOLD* blood oxygenation level dependent MRI, *EMG* electromyography, *FES* functional electrical stimulation, *VR* virtual reality, *BCI* brain-computer interface

neural cause. As a consequence, it is difficult to detect CP before motor symptoms appear. Therefore, in most cases rehabilitation starts relatively late (up to several years) after onset of injury. Interpreting the neural damage from the observable motor dysfunction alone is an almost impossible task. Some authors suggest that muscle synergy analysis may offer the clinician a better view of the neural structure underlying motor behaviors and how they change in motor deficits and rehabilitation (Safavynia et al. 2011). Such information could inform diagnostic tools and evidence based interventions specifically targeted to a patient's deficits.

Unfortunately, unlike in stroke, it is usually hard to detect the brain area that is affected in a patient with CP. Recent advances in neuroimaging could be of great value not only for delving into the physiopathology of CP but also for allowing the exact identification of the neural damage, beyond the symptomatic level

(Cioni et al. 1999). Emergent techniques such as Diffuse Tensor Imaging (DTI) are being used to shed light on the mechanisms underlying the disorder. This and related techniques may allow early diagnosis of CP, before motor dysfunctions can be observed. Given that during the first eight years of life the developing brain holds the capacity of rerouting and reorganizing damaged signal paths and neural patterns, prompt diagnosis offers tremendous potential in the treatment of CP. Therefore, the earlier the disorder can be diagnosed, the higher the potential success rate and more advanced the outcome of the therapy.

Different neurological injuries can lead to similar functional disabilities. Diagnosis based on the observable functional disability could thus result in patients with similar symptoms to be prescribed the same therapy. Furthermore, there are plenty of aspects of motor control, lower limb control in particular, that remain unsolved. The therapeutic possibilities of the rehabilitation depend to a great extent on the underlying causes of the disability, rather than on the disability itself. For example, an injury on the pyramidal system prevents the learning of new patterned movements. In this case, therapies promoting new movements are likely to fail. Thus, knowing in advance the type and site of injury could assist the clinician in selecting the appropriate therapy.

Enhanced knowledge and understanding of CP not only offers potential improved diagnosis and treatment, but would also assist in making more accurate predictions. A complete picture on the condition, including functional outcomes and the dysfunctions in the motor control generating those disabilities, would enable the creation of a theoretical framework. This framework can then be used to predict progress of functional impairment, impact of different therapies and their final outcome, and assist in the development of a specific therapy on a case-by-case basis to target the observed motor dysfunction.

Creating new knowledge in itself is not enough; there must be a transfer from progress through research to progress in the clinical field. Current knowledge about CP is not being used to its full potential in rehabilitation. For instance, it is known that injuries to the CNS cause three different types of motor impairment, each requiring a different therapy: (1) spasticity, (2) muscle weakness and (3) impaired motor coordination. Nevertheless, CP rehabilitation generally focuses on regaining motor coordination, whilst ignoring the other two. Based on this knowledge, a new therapy design could combine strategies to treat the three types of interacting motor impairments, in order to improve the overall motor function. The individual rehabilitation of each motor component could significantly improve the others. The classic therapeutic approach of CP thus hampers the optimal rehabilitation of the targeted component. Traditional therapies may be optimized if complemented with treatments for reducing spasticity or muscular weakness, by means of classical stretching exercises or more advanced techniques such as FES (Functional Electrical Stimulation). Of course, to do so more accurate measures of these conditions are desirable.

Functions of damaged brain areas can be taken over by other, non-affected, regions of the brain. This process is known as cortical reorganization and is based on the principle of brain plasticity (Merzenich et al. 1984; Calautti and Baron 2003).

This implies that motor control functions targeted by rehabilitation interventions can be affected by brain areas other than the primary site of injury.

Traditional therapeutic interventions follow a bottom-up paradigm. In gait retraining, the patient's limbs are moved along a fixed reference trajectory by the therapist, under the hypothesis that the generated movement pattern will be restored. Despite the relatively modest improvements obtained through this form of therapy it has been copied and adapted for use in combination with modern technology, such as exoskeletons and robotics. Hypothesizing that better effects could be achieved by increasing therapy intensity (movement repetition and movement time), and by canceling out imperfections in the execution of the reference pattern. However, this repetitive approach has not been found to stimulate cortical reorganization, nor is it in line with the current understanding of neurological mechanisms (Kollen et al. 2009).

Brain plasticity and cortical reorganization are thought to be strongly correlated with movement intention (efferent pathway) and appropriate proprioceptive feedback (afferent feedback). Therefore, it is important to target both pathways simultaneously during rehabilitation (Emken et al. 2009). By strictly focusing on the execution of the movement pattern, traditional approaches fail to meet these criteria. Recently an alternative approach is surging, based on the idea that the execution of the movement pattern should agree with the motion as intended or developed by the patient. This top-down approach is believed to result in the correct proprioception feedback for the brain, and is thus more closely linked with our current understanding from clinical and neuroscientific research.

In healthy populations EMG signals are an adequate measure to represent motion intention. However, in CP patients clinicians or researchers cannot rely solely on myoelectric control in order to describe intention. Incoherent, non-voluntary, rapidly changing, weak signals or spasms impede the reliable application of this metric. Therefore other techniques have to be used to measure intention in this population, such as: BCI, fNIRS, DTI, MRI and EEG

The amount of available technologies that have a potential positive impact on the rehabilitation of CP is continuously increasing. However, little of this potential is being realized. Clinicians lack clear guidelines on how to select and combine these technologies in order to increase the efficacy and efficiency of the treatment. Absence of these guidelines has rendered the inclusion of technology into rehabilitation strategies to not always be beneficial. Interference due to interaction between technologies can deteriorate the outcome of the therapy to the extent that the patient was better off prior to the introduction of one or several technologies. Incorporating technology into therapy does not automatically generate advantages or improvements for the patient. For instance, the introduction of virtual reality to enhance motivation in many cases did not result in an improved outcome of the therapy provided. It was not until coupled with a functional objective, such as a visual motor integration task, that inclusion of virtual reality resulted in superior outcomes. Selection of the adequate technology to be implemented into the therapy design should be based on the characteristics of the neurological injury, the observed functional impairments, and framed within a motor control improvement

strategy. For instance, exoskeleton-based over-ground gait training is suggested to be more effective than treadmill-based gait training. It is thought that afferent feedback is more naturally provided during the former, resulting in significant balance improvements. The choice of technology should be directed to create new motor skills, prompt specific muscle capabilities or activate specific physiological modules. Given the wide variety in underlying conditions and functional manifestations, personalized interventions are desirable.

Currently there is a wide range of treatments and therapies applied to patients with CP disability. This variety represents the diversity of clinical conditions that can be found despite similar functional disabilities. All therapies should accomplish a minimum set of care requirements and physical therapy goals: (1) to maximize level of independence, (2) to optimize mobility, (3) to prevent deformity, (4) to keep the pain under control, (5) to stimulate peer and social interactions.

In conclusion, emergent technologies may be of great value to solve important limitations present in the field of CP diagnosis and treatment. A solid framework is needed for the design of personalized interventions and to guide the clinician to select the most adequate technology on a case-by-case basis. This framework could provide the foundations of a rational design of the rehabilitation strategy. Thus, it should be continuously supported by the latest discoveries about the physiopathology of CP and allow tailoring of the rehabilitation strategy according to both, the motor impairment and neural damage of each patient.

2.3 Emergent Technologies

2.3.1 Muscle Oriented Techniques

From a clinical point of view, myoelectric signals provide valuable information to assess the neurophysiological state of the muscle. Such information can be very useful in a number of scenarios. The most obvious application is to use myoelectric signals as a tool to assist in making an accurate clinical diagnosis. But also, techniques such as electromyography (EMG) or muscle synergies may serve to monitor treatment outcome, or even to aid rehabilitation, as in the case of Functional Electrical Stimulation (FES) (see Fig. 2.1). The following sub-sections are dedicated to illustrate briefly each of these techniques.

2.3.1.1 Electromyography

Electromyography (EMG) records the electrical potential fired by skeletal muscles. As such, EMG allows a direct evaluation of muscle activity. EMG can be performed noninvasively, by placing the electrodes over the skin (surface, sEMG), or invasively, by introducing needle electrodes or a needle containing two fine-wire

electrodes straight into the muscle tissue (intramuscular EMG, iEMG). iEMG provides means to assess the activity of a few muscle fibers and their innervation. However, for certain applications, iEMG is considered to be too invasive. In contrast, despite its lower specificity, sEMG provides simple means to construct a general picture of the muscle activity. So, given its convenience of use, in the clinical practice surface EMG is preferred.

The electrode placement criteria are standardized by the recommendations of the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) protocol (van den Noort et al. 2010). It is remarkable that although sEMG represents one of the most accessible electrophysiological recordings, paradoxically, its interpretation is very complex and relies on advanced decomposition methods and the experience of the clinician. In addition, EMG signals can be large and highly variable, which precludes their clinical utility. However, in the last years intense work has been done in advanced signal processing techniques, so that nowadays it is possible to infer how muscles are neurally controlled or the state of the neuromuscular system from the decomposition of the EMG signal (Jiang et al. 2010). In this context EMG has been applied as a control signal in several devices and applications in neurorehabilitation (for more in-depth information on EMG, see [Chap. 14](#)).

The application of EMG in children with CP offers a great range of possibilities. The most straightforward is the use of EMG to record the specific muscle activity during contraction. This procedure allows the accurate assessment of the motor dysfunction during diagnosis or along diverse therapy sessions to directly follow up the muscular outcome of the intervention. On the other side, EMG also provides means to evaluate the spasticity of the patient. Before any rehabilitation procedure is designed, it is crucial to determine the degree of muscle spasticity of the patient. Spasticity restricts the way in which motor rehabilitation is carried out to the point that in some cases Botulinum A toxin (BOTOX) injections are prescribed in order to decrease spasticity and improve motor function (see also [Chaps. 7 and 8](#)). BOTOX injections also decrease the pain produced by spasticity. In this scenario, EMG may facilitate the localization of the injection site. In more advanced designs, EMG may be used to record muscle response following, for example, stimulation of the motor cortex (For further details see Neurostimulation section).

2.3.1.2 Muscle Synergies

The production of voluntary movements relies critically on the functional integration of several motor cortical areas, such as the primary motor cortex, and the spinal circuitries. Muscle synergies are defined as the pattern of muscles co-activated to obey a given motor command. Each synergy involves different muscles, and different muscles can participate in more than one synergy. Increasing number of experimental demonstrations suggest that the motor system may coordinate muscle activations through a linear combination of muscle synergies (Cheung et al. 2009). Therefore, muscle synergies appear to play a key role to understand the motor control orchestrated by the brain.

Muscle synergies are identified by measuring with EMG the activity of all (or at least the main) muscles involved in a given movement. In a synergy, each muscle contributes in a different proportion to the overall activation pattern. On the fine motor control level, motor coordination and the performance of complex movements is achieved by combining different synergies (Ajiboye and Weir 2009). The use of muscle synergies, thus, may be of a great value to design motor control strategies for prosthetics, Functional Electrical Stimulation (FES) application or any other EMG-based technology by means of synergy pattern recognition and decoding. Most of these applications have been tested in stroke patients. Further studies are needed to establish and validate the clinical use of muscle synergies in children with CP.

In addition, the analysis of muscle synergies may offer the clinician a better view of the neural structure underlying motor behaviors and how this structure changes due to motor deficits or after rehabilitation. Consequently, muscle synergies are powerful candidates to inform diagnostic tools and design evidence-based interventions specifically targeted to patients' deficits (Safavynia et al. 2011).

2.3.1.3 Functional Electrical Stimulation

Functional Electrical Stimulation (FES) delivers small electrical currents on intact peripheral motor nerves innervating the muscle tissue to improve or restore the overall muscle activity. Electrically primed muscle contractions are coordinated to produce functionally useful movements such as writing, walking, standing or grasping. Different FES-based devices are commercially available for use on upper limbs, lower limbs, the bladder and bowel system, and the respiratory system (for an in-depth analysis on bladder and bowel neurorehabilitation, see Chap. 4). During gait rehabilitation, direct orthotic effect is achieved by applying FES on tibialis anterior (TA) either with or without gastrocnemius stimulation. On upper limb function, FES has been shown to increase muscle strength, extend the range of motion and improve the motor function in children with CP (Wright et al. 2012; van der Linden 2012). In the future, the optimized design of hybrid neuroprosthesis is postulated by combining FES-based muscle stimulations with the analysis of muscle synergies. The idea behind this design is to fire FES with the motor intention of the user and coordinate the electrical delivery patterns according to the activation of identified synergies. However, further studies are needed including randomized controlled trials to validate the use of FES in children with CP. An extensive description on FES-based applications can be found in Chap. 11.

2.3.2 Neuroimaging

Current measurements of motor deficits in individuals with CP are largely based on empirical criteria. This is partly due to the absence of techniques to assess the

CNS functions. Testing novel techniques for CP rehabilitation faces a major obstacle as the principal population to be targeted is constituted of developing children (Wittenberg 2009). Neuroimaging is an imaging technology that enables us to visualize neural activity and pathways in the brain. Recently, neuroimaging is being recommended as an evaluation tool in children with CP (Towsley et al. 2011). The patterns in the neuroimaging data of CP patients are correlated to neurological subtype, CP severity and other categorical variables such as functional motor scales (Towsley et al. 2011). Neurological subtype has been shown to be a powerful predictor of ambulatory functional status, both prior and post treatment (Shevell et al. 2009). Neuroimaging technology thus offers us a view to understanding the relationship between brain activity and motor function, as well as the pattern and severity of the brain injury underlying cerebral palsy (Shimony et al. 2008). Innovations in imaging enable early identification of injury, before motor deficits and other abnormalities are present. These advances have the potential to drive therapies to re-establish the cortical input to spinal motor centers, facilitate normal development, and avoid secondary injuries such as bone deformities (Kuřak et al. 2006). A variety of imaging technologies exists, each with its own strengths and weaknesses. Here we will specifically focus on neuroimaging technologies that, to the best of our knowledge, are or can be of value in CP rehabilitation or research: MRI, dMRI, DTI, DWI, BOLD fMRI, NIRS, fNIR (see Fig. 2.1).

A first distinction between the various technologies can be made with regard to their resolution. Current technologies suffer from a trade-off between temporal resolution (identify when an event occurs) and spatial resolution (where in the brain an event takes place). Technologies based on measuring electrical currents or magnetic fields provide high temporal resolution. On the other hand, techniques where blood flow is tracked offer great spatial resolution but are relatively slow.

Several technologies measure local changes in cerebral blood flow, often referred to as activations, which are related to neural activity (e.g. fMRI, NIRS) and enclosed in the term “neurovascular coupling” (Cabeza and Kingstone 2006; Leff et al. 2011). These methods result in high spatial accuracy. Within this group of technologies, there are methods that are more suited for focusing on specific areas (fNIRS, fMRI) and methods that enable the clinician to create a map of a bigger area (DOT, NIRS).

2.3.2.1 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has a high contrast resolution and is used to distinguish pathological from normal tissue. Strong magnetic fields and non-ionizing electromagnetic fields in the radio frequency range form the base of this technology. A typical MRI-examination consists of several sequences (up to 20), each providing a particular type of information about the patient’s tissues. A multitude of specialized MRI applications exist, each with their own strength. Compared to computed tomography (CT) MRI: offers a better tissue contrast resolution, is capable of generating images in multiple planes, and does not require ionizing radiation

(Accardo et al. 2004). Several advances have been made to improve the MRI image quality and the data subtracted from these images, for specific purposes. Standard MRIs are often applied in pediatric neurological examinations. However, the evaluation of conventional MRI sequences is relatively subjective when compared to other techniques such as Diffusion Tensor Imaging (DTI). The improvements in sensitivity and objectivity with DTI may present it as a more useful technique to detect small changes in developmental status in the future.

2.3.2.2 Diffusion Tensor Imaging

Diffusion MRI (dMRI) has become the standard for white matter disorders. Diffusion tensor imaging (DTI) is an MRI application that measures the diffusion of water molecules in biological tissues (Le Bihan et al. 1986). When applied to CP patients, DTI allows us to better understand the connectivity of white matter axons in the central nervous system. The models of brain connectivity created from this data can further be used to examine the connectivity of different regions in the brain (i.e. tractography), or to identify and study areas of neural degeneration (Miller et al. 2003). For example, current DTI applications are able to distinguish between acute ischemic changes and chronic ischemic changes in stroke patients; this may influence both the prognosis and design of rehabilitation interventions (Yang et al. 1999; Sotak 2002). DTI values have also been suggested to have a predictive value for evaluating hand function outcome in chronic stroke patients (Song et al. 2012). The relation between DTI results and clinical outcomes in stroke patients underlines the potential for DTI applications in CP (Mulcahey et al. 2012; Barakat et al. 2012; Rha et al. 2012). DTI metrics have also been shown to be sensitive to regional changes in the contralateral hemisphere, the role of which is still largely unknown in CP (Granziera et al. 2012). Furthermore, DTI results of the pyramidal tract in chronic stroke patients appear to be related to the residual motor function. Radlinska et al. reported that parameters of the pyramidal tract integrity obtained within the first weeks are highly correlated with residual motor function in the acute as well as in the chronic stage (Radlinska et al. 2010). DTI thus presents itself as a promising technique to improve diagnosis of CP and prediction of its outcome (Mulcahey et al. 2012).

2.3.2.3 Diffusion Weighted Imaging

Diffusion weighted imaging (DWI) is capable of detecting early changes in cellular function occurring in the lesion (Moseley et al. 1990; Utsunomiya 2011). DWI values are able to identify the extent of brain parenchymal injury. The severity of which has been reported to correlate with the patient's outcome (Utsunomiya 2011).

DWI currently is the most important diagnostic tool for evaluating pediatric stroke scenarios and has become an essential part of the diagnosis of the majority

of pediatric central nervous system disorders (Utsunomiya 2011). Its ability to make predictions about the patient's outcome, and the ability to rapidly diagnose acute neurological disorders result in an added value for the pediatric neurologist and neuroradiologist (Utsunomiya 2011).

2.3.2.4 Blood Oxygenation Level Dependent Functional MRI

Techniques such as DTI and Blood Oxygenation Level Dependent functional MRI (BOLD fMRI) can offer a view on the functional reorganization of the brain after injury. fMRI measures the signal changes in the cortical motor system that are due to changes in neural activity. However, it has been argued that DTI is more useful to evaluate white matter integrity with regard to interpreting motor deficits than fMRI (Qiu et al. 2011). The BOLD effect is based on the knowledge that increased neural activity creates a higher demand for oxygen in the active part of the brain. The vascular response to increase local oxygenation leads to a signal, detected by BOLD fMRI, which is thus related to neural activity. However, in the future cerebral blood volume (CBV) might prove to be a more useful metric due to an increased sensitivity when compared to BOLD fMRI or DTI. A limitation of CBV is the fact that a contrast agent has to be injected. The potential of CBV thus far been demonstrated in pre-clinical trials and awaits confirmation in clinical trials.

2.3.2.5 Near-Infrared Spectroscopy

A more portable solution to assess similar data is near-infrared spectroscopy (NIRS). NIR light is transmitted and absorbed differently depending on the underlying body tissue. NIRS uses this information to extract hemoglobin concentration changes. As stated earlier, increased neural activity is paired with an increase in oxygen demand. Similar to BOLD fMRI, NIRS tracks these changes in localized blood volume. Unlike fMRI which can be used to examine neural activation throughout the brain, NIRS activation radius does not reach beyond the cortical tissues. NIRS can thus not fully replace fMRI. However, the motor regions of the human cortex, the primary sensorimotor cortex (PSMC) and the premotor cortex (PMC) are proximal to scalp tissues and thus accessible by NIRS. The main advantage of NIRS is that it is portable, with wireless versions being available. NIRS can thus be used for data collection or research on freely moving subjects in a more realistic setting. This is especially useful in pediatric populations where the laboratory setting can be quite startling for the young patients. Current fNIR applications have managed to investigate cortical contributions during complex tasks such as walking (Miyai et al. 2001). Little is known on cortical recovery mechanisms, the large majority of suggestions reflect recruitment of pathways outside of the normal adult pattern of contralateral dominance in the projection to lower motor neurons from the PMC (Wittenberg 2009; Rossini et al. 1998).

Neuroimaging and other emerging fields present a huge potential but also come at a cost, they generate large and complex datasets that are seldom easy to interpret. In addition, the metrics deduced, what we are capable to measure, does not always fully agree with the knowledge that is sought after by the clinician. Models are capable of resolving both those issues, using the elaborate and complex data as an input and providing new clinically relevant data streams as output. These data streams consist in a prediction of measured and unmeasured variables (Smith 2011). To make future technological advances useful in the clinical field, attention should be paid to the representation and interpretation of technical data in a clinical format.

2.3.3 Neurostimulation

Neurostimulation intends to modulate the cortical activity by delivering electrical currents that are able to prime neurons. Similar to neuroimaging techniques, non-invasive neurostimulation methods provide means to track the cortical reorganization taking place during recovery. Stimulation has been shown to modulate the cortical excitability favorably when applied moments before starting the therapy session. Increased cortical excitement correlates to greater plasticity, while enhanced inhibition is associated with impaired plasticity (Johnston 2009). As a consequence, the advent of non-invasive neurostimulation tools have rocketed the interest in modifying cortical excitability to improve recovery from brain injuries. In hemi-paretic stroke patients, somato-sensory cortex stimulation has been shown to enhance the effects of training for functional hand tasks (Johnston 2009). Similarly, Eyre et al. evidenced the potential benefit of brain stimulation techniques such as Transcranial Magnetic Stimulation (TMS) or Deep Brain Stimulation (DBS) to correct the postnatal imbalance in cortical activity and thus reduce functional disability in children with CP (Eyre 2007). Although little work has been done in the field of CP, studies in other motor disorders such as stroke highlight the promising potential of neurostimulation as a rehabilitation instrument. Furthermore, the developing child's brain exhibits a greater intrinsic plasticity. Activity-dependent neuronal plasticity appears to play a role in the evolution of clinical signs of motor dysfunction in children with CP. So it is likely that children with CP may receive a greater therapeutic benefit from these emergent strategies than the effect observed in stroke patients. To achieve therapeutic success, taking full advantage of the brain's intrinsic plasticity mechanisms, a purposeful design of the intervention is required. In this section we highlight the most important stimulation techniques: TMS, DBS and transcranial Direct Current Stimulation (tDCS) (see Fig. 2.1).

2.3.3.1 Transcranial Magnetic Stimulation and Deep Brain Stimulation

Transcranial magnetic stimulation (TMS) is one of the principal non-invasive techniques used to investigate functionality and interconnections of the brain. TMS is claimed to be complementary to fMRI. The use of TMS in children with CP is well spread (Heinen et al. 1999; Pilato et al. 2009; Kesar et al. 2012). TMS is a comfortable and safe technique with well-established standard protocols (Rossini et al. 1994). TMS has been approved for pediatric application but is not recommended for children younger than 6-7 years, due to the high neural activation by evoking motor-evoked potentials (MEPs) (Wittenberg 2009). In fact, the number of studies assessing the safety and efficacy of TMS in children is reduced (D'Agati et al. 2010).

TMS generates rapidly changing magnetic field pulses to induce a weak electrical activity in focal brain areas (Hoyer and Celnik 2011). When the motor cortex receives sufficient current to produce the synchronic activation of upper and lower motor neurons, MEPs can be recorded on single or multiple muscles. Therefore, TMS allows an accurate mapping of muscle representation in the primary brain cortex and estimating of the speed/magnitude of the MEPs. From these maps, the size and location of muscles and movement cortical representations can be determined. These features can all be used to characterize characteristics (size, spreading,...) of CNS injuries (Milot and Cramer 2008). TMS-derived metrics thus relate to motor abnormalities. For example, there appears to be a relationship between the area of the motor cortex dedicated to a specific movement and the motor ability. Although the interpretation is complex, Liepert et al. associated larger motor maps with functional recovery after stroke rehabilitation (Liepert et al. 2000). In particular, TMS has been used in combination with MRI to perform early diagnosis of hand function in children with CP (Holmström et al. 2010). The time gained by incorporating TMS to standard diagnostic methods allows bringing forward the therapy and thus increases its rate of success.

TMS can also be used to enhance rehabilitation performance. TMS has potential as a therapeutic tool to balance the hemispheric excitability in the damaged brain. Therapeutic strategies can include the inhibition of the healthy hemisphere or enhancing the excitability in the injured hemisphere (Hoyer and Celnik 2011). Depending on the purpose, the TMS protocols differ in the frequency of the TMS pulses delivered. A decrease in the cortical excitability is achieved by applying low frequency trains (<10 Hz) of repetitive transcranial magnetic stimulation (rTMS). When aiming to facilitate the cortical excitability, high frequency (>10 Hz) stimulation of rTMS is required. Specific applications stimulating at low intensity but with very high frequency rTMS (>50 Hz) have also achieved modulation of the motor cortical excitability. The effect of rTMS lasts beyond the end of the stimulation. This novel form of rTMS is known as Theta Burst Stimulation (TBS) (Brunoni et al. 2008). The therapeutic potential of such techniques is very promising and exert long-lasting effects in motor recovery have been suggested. In Stroke patients, TMS has been used to safely improve motor performance (Hoyer and Celnik 2011).

TMS can also be applied in patients that are unable to control certain cortical zones. In many cases it is thought that this is due to neurons that cannot pass the excitatory threshold. TMS could be used to help these patients to recover to some extent the neural control of such zones by lowering the threshold. In other words, TMS-mediated brain priming prior to therapeutic intervention can facilitate the patients' ability to overpass the excitatory threshold and increase the success of the subsequent therapy. In addition, TMS has been used in combination with behavioral and neuroimaging studies, to develop models of functional connectivity between different brain regions and test theories of neural mechanisms that underlie stroke recovery (Hoyer and Celnik 2011).

Despite the promising potential of TMS for the treatment of CP, few studies have been published in the literature most of them being limited to treat spasticity (D'Agati et al. 2010; Benini and Shevell 2012; Valle et al. 2007). In all cases, a moderate to substantial improvement of spasticity has been reported, while non-adverse effects have been observed. However, the effects of TMS may be temporal. Therefore, repeated sessions may be required to ensure long-term effects (Holt and Mikati 2011).

2.3.3.2 Transcranial Direct Current Stimulation

As mentioned earlier, the manipulation of cortical excitability may have therapeutic benefits for patients with neurological impairments, and specifically for patients with CP (Vidailhet et al. 2009; Hayek et al. 2009). In rats, increased cortical excitability has been found to enhance brain plasticity (Holt and Mikati 2011). Transcranial direct current stimulation (tDCS) has been proposed as an alternative form of non-invasive neurostimulation to promote plasticity and modulate brain excitability. tDCS has been reported to lead to functional changes in discrete areas of the cerebral cortex by shifting membrane potential. In tDCS, low intensity currents (1–2 mA) are applied directly to the brain area of interest over a sustained period of time (5–30 min). tDCS is less focal than TMS, mainly due to the relatively large size of the electrodes used to deliver current over the scalp. However, tDCS unlike classical neurostimulation methods, does not produce muscle fasciculation that can be uncomfortable and often painful for the patient (Hayek et al. 2009). Thus, tDCS-based neurostimulation sessions are likely to be more tolerable, although it does not avoid classical side effects such as headache, dizziness, nausea or itching sensation (Nitsche et al. 2008).

Similar to TMS, tDCS can also enhance excitability via anodal polarization or decrease it via cathodal polarization (Song et al. 2011). Tests on healthy adults demonstrated that tDCS can increase cognitive performance on a variety of tasks, depending on the cortical area being stimulated (Chi and Snyder 2011). tDCS has been shown to be an effective treatment for migraines, depression or pain, but also constitutes an interesting tool for the modulation of motor cortex excitability (Nitsche and Paulus 2000). Nitsche et al. demonstrated that the application of tDCS can modulate the cortical excitability and influence spontaneous neural

activity influencing synaptic function (Nitsche et al. 2008). To the best of our knowledge, there are no studies done in children with CP using tDCS. It is important to highlight that tDCS is a technique that is just starting to be tested in the clinical field, so, protocols for safety and effectiveness have not been yet to be standardized, even for adults (Nitsche et al. 2008).

2.3.4 Assistive and Rehabilitation Robotics

Medical Robotics is a relatively new field that aims to augment the capabilities of either the clinician or the patient. It has been interpreted as technology for the recovery and functional compensation of missing motor skills and sensing, assuring safer environments and environments that promote regaining of movement. In the field of CP, two main branches of medical robotics are worth to be mentioned: Rehabilitation Robotics and Assistive Robotics. Rehabilitation robotics pursue the recovery or regaining of impaired motor function, while Assistive Robotics are intended to substitute or compensate missing motor and sensing skills. Rehabilitation systems differ from assistive devices. The former are designed to facilitate recovery by supporting therapy and monitoring the patient's progress, while robotic assistive devices and exoskeletons focus on providing dexterity, natural mobility, and sense of touch to missing or paralyzed limbs (Dellon and Matsuoka 2007).

Besides recovering the motor function and improving movement coordination, training with robotic devices may serve to accomplish secondary objectives within rehabilitation such as the so called “trick movements” or “compensation strategies”. In this case, the user learns new motion approaches to handle daily activities. Furthermore, the simple fact of promoting the movement of lower and upper limbs can prevent secondary complications such as muscle atrophy, osteoporosis, and spasticity (Riener et al. 2005).

An important aspect in robot-aided rehabilitation devices is the intrinsic interaction between the human and the robot (Pennycott et al. 2012). Currently, the field of rehabilitation robotics is progressively oriented to a human-centered approach in which robot performance is quantified by how the robot physically interacts with the patient. This interaction is mutual. In rehabilitation robotics a clinician or technician controls the robot by setting parameters that define the intervention. Whereas in assistive robotics devices, the robot is programmed to execute or assist in the execution of the preprogrammed tasks according to the motor limitations of the patient.

In comparison to the classical scale of performance, human-centered robot interaction implies a totally different set of requirements than what is used in industrial robotic systems. Unlike traditional robotics, the environment in which human—medical robot interactions take place is characterized by fast dynamics and prone to unexpected changes, adding difficulty to the design. Such requirements are safety, flexibility and mechanical compliance of the device, gentleness

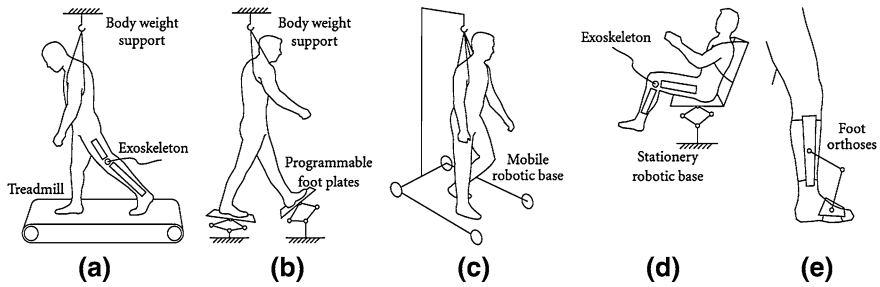


Fig. 2.2 The most common robotic systems used for lower limb rehabilitation; (a) treadmill gait trainers, (b) foot-plate based gait trainers, (c) over-ground gait trainers, (d) stationary gait and ankle trainers; (e) active foot orthoses (Díaz et al. 2011)

and adaptability towards the patient, ease of use, friendly user interface, humanoid-like appearance and behavior (Riener et al. 2006).

Robotic systems for lower-limb rehabilitation are generally classified according to the rehabilitation principle (Fig. 2.2) (Díaz et al. 2011). In the following sub-sections we will elaborate upon exoskeletons, orthoses and assistive devices. We will furthermore highlight a promising new type of robotic device “soft” exoskeletons; as well as a tool to augment efficacy of robot therapies, virtual reality and interactive games.

2.3.4.1 Exoskeletons

Partial body-weight supported therapy (PBWST) is an active, repetitive and task-specific approach used to facilitate execution of stepping and locomotion. The main objective of PBWST is to achieve a more normalized gait pattern. During classical PBWST, an overhead harness system supports the patient’s body weight, while the therapist manually guides the foot and leg movements. It has been observed that the use of this kind of robotic platforms considerably reduces the level of muscular loading undergone by patients during normal gait rehabilitation and minimizes energy consumption and fatigue (Hornby et al. 2005). Advanced configurations of body-weight supported therapy (BWST) allow the patient to do complete walking exercises while being suspended from a harness. These walking cycles can be carried out directly over-ground or assisted on a treadmill. There are evident benefits of BWS treadmill training, but the manually assisted movement training remains difficult for physical therapists. The labor-intensive task of the therapist consists of manually guiding the patient’s limbs into a gait pattern that progresses to a normal gait pattern. Therefore, the duration of the rehabilitation is usually defined by available man-hours and the fatigue of the therapist, and not so much by the needs of the patient. As a result, rehabilitation sessions are usually shorter than required to gain an optimal therapeutic outcome. In addition, the

movement repeatability of manually-assisted rehabilitation is poor and objective measures of patient's performance and progress are missed.

Nowadays, powered exoskeletons are integrated with treadmills or other kind of mobile platforms to solve this issue. Exoskeletons are mechatronic systems that wrap around the operator's limbs allowing the replication or enhancement of forces at body segments. In that case, the exoskeletons are externally linked to lower limbs of the patient, so that the patient is assisted to execute normal gait patterns and the therapist is released from the task of manually guiding walking. The use of exoskeletons doubles patient's benefit: longer rehabilitation sessions are achieved and the execution of gait normal patterns is more precise (Herr 2009). Furthermore, by using different types of sensors (cameras, microphones, accelerometers or inertial sensors...) and actuators, the motor performance of the user can be monitored and quantified.

Studies comparing over-ground walking with treadmill based therapies, as BWST, suggest that over-ground walking may be superior for gait training (Willoughby et al. 2010). The fact that treadmill exercise requires a higher control of propulsion and balance compared to over-ground walking may explain the additional benefits (Dodd and Foley 2007). Nevertheless, powered exoskeletons used in BWST therapy entail a number of issues such as energy consumption, duration of batteries, the actuation mechanisms or ensuring the portability of the device without affecting the natural movement of the patient that still need to be solved in order to spread the use of this technology.

Besides powered exoskeletons, passive exoskeletons can be also used in BWST. The main difference is that the energy needed for moving a passive exoskeleton is fully supplied by the user while in active exoskeletons a power source supplies at least part of it. However, the mechanical design of passive exoskeletons is often insufficient and demands considerable physical effort in comparison to active wearable robots.

There are two essential requirements that need to be fulfilled by any exoskeleton to achieve efficient restoration of normal gait: the joint stability and joint control. The behavior of the robot, and thus the prediction on treatment outcome, are influenced by the quality of these requirements. Therefore, a close study of the human neuro-physiology during walking such as muscle dynamics or central pattern generators is needed to further the development of rehabilitation prototypes. Currently, there is insufficient evidence to state that robot-assisted gait training improves walking function more than other motor training methodologies (Swinen et al. 2010). Based on the available data and compared with other walking rehabilitation therapies, assessing walking overground or on a treadmill with or without BWS, effectiveness is not greater with robot-assisted gait training than with other training modalities (Field-Fote et al. 2005). Although the effectiveness of robot-assisted training in children with CP was proven in a number of experiments (Borggraefe et al. 2010), performed clinical studies still show little evidence for a superior effectiveness of the robotic therapy.

2.3.4.2 “Soft” Exoskeletons

Rehabilitation robotics is in continuous progress and exoskeleton technology represents one of the most challenging areas. Advances in materials, mechanics, electronics, sensors, controls, artificial intelligence, communication, power sources and actuation must be integrated together. On top of that, safety must be a paramount issue since the fundamental criterion for an exoskeleton involves the inherent coupling between the human and the mechanical systems. It is therefore essential to design control systems that combine the positive attributes of conventional exoskeletons with a more compliant and safer interaction capacity.

Based on previous experience, we know that 2 h training is not sufficient to obtain significant improvements of motor control in patients with CP. However, nowadays it is still a challenge to design a rehabilitation exoskeleton that can be worn during the whole day so that it can be used in daily activities without needing the supervision of physiotherapists. Soft exoskeletons are postulated as the new generation of exoskeletons aiming at reaching such goal. Nowadays, only limited information regarding the design of “soft” wearable robots for rehabilitation purposes is available. However, the potential impact and numerous advantages of soft exoskeletons have recently been demonstrated. For example, Rocon et al. developed a soft exoskeleton to detect and suppress upper limb tremor (Gallego et al. 2011). Future advances will try to incorporate wearable “soft” robots into an overall network architecture to provide continuous monitoring of patients and build a complete health management system (Swinen et al. 2010).

2.3.4.3 Assistive Devices and Orthoses

Orthoses should be considered as an important tool in locomotion rehabilitation for CP patients. Orthoses are used to support, align, prevent, or correct deformities of the limbs and are designed with one of two main goals: either to affect the body structure or to assist locomotion. In case of children with CP, orthoses are frequently designed to achieve both of these aims.

Upper extremity orthoses have proved to be effective in achieving some task specific goals as they can improve grasping and increase the range of motion to perform a given activity (Yonclas et al. 2006). Braces are indicated to stretch muscles that are over-flexed. Back braces are of special interest in children with CP as they might help straightening the back of children having trouble to sit down or even, to correct the spine developing a deformity. Hand splints and soft body jackets are also used to give support and comfort to individual particularities of patients.

Lower limb orthoses may improve gait efficiency by restoring clearance of the foot from the ground during swing phase, appropriate prepositioning of the limb at the end of swing phase and achieving an adequate step length. Orthoses may reduce energy expenditure by decreasing the need for compensatory gait deviations to achieve locomotion. In the case of lower extremity orthoses, the foot-to-ground contact is normalized by correcting foot and/or ankle alignment.

Precisely, Ankle Foot Orthoses (AFOs) are the most frequently prescribed devices for children with CP (Brehm et al. 2008). The general role of the AFOs is to limit unwanted ankle movement, primarily ankle plantar flexion but indirectly knee and hip function are also positively affected. As a result, AFOs manage abnormal plantar flexion, prevent contractures and improve gait. Children with spastic CP often acquire a dynamic equinus deformity, preventing them from putting their heel flat and as such attain a stable base for stance or walking. Assuming the ankle can be placed in a neutral position at rest; such deviation can be corrected by one or several AFO constructions, depending on the capabilities and particularities of the patient. However, it is important to underline that in patients with spasticity the AFOs can prevent or delay the development of a deformity, but not overcome pre-existing abnormalities.

To date, the studies examining the efficacy of orthoses for walking children with CP have included small numbers of children. The evidence to support specific orthotic interventions for children with CP remains to be demonstrated using more robust research methods.

2.3.4.4 Virtual Reality and Interactive Gaming

Current bottom-up motor learning theories state that improved motor performance and postural control is achieved by repetitive motor practice. This type of training requires high levels of attention and motivation that might be difficult to achieve in children (Brütsch et al. 2011; Banz et al. 2008). In addition, active participation is an important prerequisite for motor learning and for improved motor and functional outcomes. However, children with CP tend to be less participative than typically developing children (Mitchell et al. 2012).

In this context, the use of Virtual Reality (VR) and Interactive Gaming is becoming a key component of modern rehabilitation systems to assist traditional therapeutic approaches. VR serves both to provide augmented feedback on the motor performance of the patient, and to enhance motivation and attention through the implementation of attractive and challenging games. That way, the accomplishment of intensive and prolonged practice can be facilitated in children. Some authors report that games could hold the children's attention for sessions of 60 min (Qiu et al. 2009). However, other studies describe that children lost their interest in the game after 15 min (Brütsch et al. 2011). Nevertheless, even in that latter case authors emphasized that all children declared they enjoyed playing the games during the sessions. In addition, it seems that patients undergoing VR-based rehabilitation present a more active participation (Brütsch et al. 2011). However, the scope of these results is limited. Further research might be needed to reveal whether participation rates are correlated to the improvement of functional outcomes.

VR offers a number of desirable characteristics for rehabilitation such as the possibility to design patient-centered strategies by tailoring the game to the age and patient's disability level. The therapist can adapt the practice intensity in each

session to the progress made by the children. The competitive nature of most children makes the sense of self-efficacy provided by the augmented online feedback a successful incentive to enhance their involvement with the therapy. It appears that challenging VR environments promote the creativeness of children. Several studies report that the use of VR in children with CP improved their self-image and motivation towards the rehabilitation (Brütsch et al. 2011).

It has been hypothesized that VR might accelerate the recovery process by targeting specific brain networks. In particular, You et al. found measurable changes in cortical reorganization in the lower extremity of stroke patients after rehabilitation via fMRI (You et al. 2005).

VR usually links the patient's motor outcome during rehabilitation with actions in the virtual world. A high percentage of children with CP present severe functional and motor disabilities usually characterized by slow speed and disturbed motor control. This obstructs them from participating in daily activities done by their peers. In that sense, the effectiveness of VR should be emphasized as it allows children to participate in more activities (Brütsch et al. 2011; Parsons et al. 2009).

Despite the promising potential of VR and Interactive Gaming in motor rehabilitation, their contribution to improve motor function and performance is still unclear. Several studies show improvement in walking function and speed after rehabilitation with VR (Mirelman et al. 2010; Patriitti et al. 2010) while others report insignificant or no improvement at all (Brütsch et al. 2011). In particular, the review by Mitchell et al. exposes the little research done in this field in patients with CP (Mitchell et al. 2012). In fact, the incorporation of VR to traditional therapies for children with CP may be less encouraging. One of the main limitations found is the relatively large motor function needed for utilizing this kind of systems. The use of adaptive robotic systems together with VR is a possible strategy to overcome that issue. In addition, the load of sensory stimulation should be carefully considered specially when dealing with patients with cognitive impairments. Another approach is to use a filter approach for standard or customized interfaces. One such example is ENLAZA, an inertial sensor based interface that enables children with CP to play games on the computer and independently conduct an electrical powered vehicle. The core of ENLAZA is a Kalman filter that takes out the non-voluntary components of movement and derives the intended direction for the cursor or car (Raya et al. 2012). In general, virtual environments are recommended to be as simple as possible while keeping the ability of capturing the attention of the users. In a more advanced approach, the complexity of the virtual environment is personalized according to the processing ability of the patient (Wolbrecht et al. 2008). The relation between the ability of processing sensory cues and the ability to keep attention hasn't been investigated yet in children with CP (Qiu et al. 2009), so further studies might be required to establish methods to determine the proper volume of sensory stimulation needed by each patient.

2.4 Conclusion

A lot of promising techniques and technologies are emerging that have the potential to reveal how motor control is organized in the human brain and body. Additionally they could provide insight into the cortical reorganization that takes place upon and after cerebral injury. This knowledge should be used to personalize therapies, not only to the individual patient's motor outcomes but also to the source of their disparities. We have tried to summarize technologies that are being developed or used in related fields (e.g. Stroke rehabilitation) and that show great potential for application in CP rehabilitation. To take full advantage of this potential, researchers and clinicians should actively engage in transferring knowledge and developments from the technical field to the clinical scenario.

Acknowledgments This chapter was partially based on a presentation titled “*Can children with cerebral palsy learn how to walk from a robot?*” presented by Dr. Paolo Bonato at the Summer School on Neurorehabilitation 2012 in Zaragoza, Spain. The authors would like to thank Dr. Bonato for the insights and comments provided over several discussion sessions following said presentation. Furthermore we would like to thank Dr. Diego Torricelli for his constructive feedback throughout the revision process of this chapter.

References

- Accardo J, Kammann H, Hoon AH (2004) Neuroimaging in cerebral palsy. *J Pediatr* 145(2 Suppl):S19–S27
- Ajiboye AB, Weir RF (2009) Muscle synergies as a predictive framework for the EMG patterns of new hand postures. *J Neural Eng* 6(3):036004
- Alexander MA, Matthews DJ (2009) Pediatric rehabilitation: principles and practice. Demos Medical Publishing
- Banz R, Bolliger M, Colombo G, Dietz V, Lünenburger L (2008) Computerized visual feedback: an adjunct to robotic-assisted gait training. *Phys Ther* 88(10):1135–1145
- Barakat N, Mohamed FB, Hunter LN, Shah P, Faro SH, Samdani AF, Finsterbusch J, Betz R, Gaughan J, Mulcahey MJ (2012) Diffusion tensor imaging of the normal pediatric spinal cord using an inner field of view echo-planar imaging sequence. *Am J Neuro Radiol* 33(6):1127–1133
- Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, Jacobsson B, Damiano D (2005) Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol* 47(8):571–576
- Benini R, Shevell MI (2012) Updates in the treatment of spasticity associated with cerebral palsy. *Curr Treat Opt Neurol* 14(6):650–659
- Borggraefe I, Schaefer JS, Klaber M, Dabrowski E, Ammann-Reiffer C, Knecht B, Berweck S, Heinen F, Meyer-Heim A (2010) Robotic-assisted treadmill therapy improves walking and standing performance in children and adolescents with cerebral palsy. *Eur J Paediatr Neurol*: Off J Eur Paediatr Neurol Soc 14(6):496–502
- Brehm M-A, Harlaar J, Schwartz M (2008) Effect of ankle-foot orthoses on walking efficiency and gait in children with cerebral palsy. *J Rehabil Med: Off J UEMS Eur Board Phys Rehabil Med* 40(7):529–534
- Brunoni AR, Boggio PS, Fregni F (2008) Can the ‘yin and yang’ BDNF hypothesis be used to predict the effects of rTMS treatment in neuropsychiatry? *Med Hypotheses* 71(2):279–282

- Brütsch K, Koenig A, Zimmerli L, Mérillat-Koencke S, Riener R, Jäncke L, van Hedel HJA, Meyer-Heim A (2011) Virtual reality for enhancement of robot-assisted gait training in children with central gait disorders. *J Rehabil Med: Off J UEMS Eur Board of Phys Rehabil Med* 43(6):493–499
- Cabeza R, Kingstone A (2006) *Handbook of functional neuroimaging of cognition*, 2nd edn. MIT Press, Cambridge
- Calautti C, Baron J-C (2003) Functional neuroimaging studies of motor recovery after stroke in adults: a review. *Stroke J of Cereb Circ* 34(6):1553–1566
- Cheung VCK, Piron L, Agostini M, Silvoni S, Turolla A, Bizzi E (2009) Stability of muscle synergies for voluntary actions after cortical stroke in humans. *Proc Natl Acad Sci USA* 106(46):19563–19568
- Chi RP, Snyder AW (2011) Facilitate insight by non-invasive brain stimulation. *PLoS One* 6(2):e16655
- Cioni G, Sales B, Paolicelli PB, Petacchi E, Scusa MF, Canapicchi R (1999) MRI and clinical characteristics of children with hemiplegic cerebral palsy. *Neuropediatrics* 30(5):249–255
- D'Agati D, Bloch Y, Levkovitz Y, Reti I (2010) rTMS for adolescents: safety and efficacy considerations. *Psychiatr Res* 177(3):280–285
- Dellon B, Matsuoka Y (2007) Prosthetics, exoskeletons, and rehabilitation [grand challenges of robotics]. *IEEE Robot Autom Mag* 14(1):30–34
- Díaz I, Gil JJ, Sánchez E (2011) Lower-limb robotic rehabilitation: literature review and challenges. *J Robot* 2011:1–11
- Dodd KJ, Foley S (2007) Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial. *Dev Med Child Neurol* 49(2):101–105
- Emken JL, Bobrow JE, Reinkensmeyer DJ (2009) Robotic movement training as an optimization problem: designing a controller that assists only as needed. In: 9th international conference on rehabilitation robotics, 2005. ICORR 2005, vol 6, pp 307–312
- Eyre JA (2007) Corticospinal tract development and its plasticity after perinatal injury. *Neurosci Biobehav Rev* 31(8):1136–1149
- Field-Fote EC, Lindley SD, Sherman AL (2005) Locomotor training approaches for individuals with spinal cord injury: a preliminary report of walking-related outcomes. *J Neurolog Phys Ther* 29(3):127–137
- Gallego JA, Rocon E, Ibanez J, Dideriksen JL, Koutsou AD, Paradiso R, Popovic MB, Beldalois JM, Gianfelici F, Farina D, Popovic DB, Manto M, D'Alessio T, Pons JL (2011) A soft wearable robot for tremor assessment and suppression. In: 2011 IEEE international conference on robotics and automation, pp 2249–2254
- Granziera C, Ay H, Koniak SP, Krueger G, Sorensen AG (2012) Diffusion tensor imaging shows structural remodeling of stroke mirror region: results from a pilot study. *Eur Neurol* 67(6):370–376
- Hayek SM, Jasper JF, Deer TR, Narouze SN (2009) Occipital neurostimulation-induced muscle spasms: implications for lead placement. *Pain Phys* 12(5):867–876
- Heinen F, Kirschner J, Fietzek U, Glocker FX, Mall V, Korinthenberg R (1999) Absence of transcallosal inhibition in adolescents with diplegic cerebral palsy. *Muscle Nerve* 22(2):255–257
- Herr H (2009) Exoskeletons and orthoses: classification, design challenges and future directions. *J Neuroeng Rehabil* 6:21
- Holmström L, Vollmer B, Tedroff K, Islam M, Persson JKE, Kits A, Forssberg H, Eliasson A-C (2010) Hand function in relation to brain lesions and corticomotor-projection pattern in children with unilateral cerebral palsy. *Dev Med Child Neurol* 52(2):145–152
- Holt RL, Mikati MA (2011) Care for child development: basic science rationale and effects of interventions. *Pediatr Neurol* 44(4):239–253
- Hornby TG, Zemon DH, Campbell D (2005) Robotic-assisted, body-weight-supported treadmill training in individuals following motor incomplete spinal cord injury. *Phys Ther* 85(1):52–66

- Hoyer EH, Celnik PA (2011) Understanding and enhancing motor recovery after stroke using transcranial magnetic stimulation. *Restor Neurol Neurosci* 29(6):395–409
- Jiang N, Falla D, D'Avella A, Graimann B, Farina D (2010) Myoelectric control in neurorehabilitation. *Crit Rev Biomed Eng* 38(4):381–391
- Johnston MV (2009) Plasticity in the developing brain: implications for rehabilitation. *Dev Disabil Res Rev* 15(2):94–101
- Kesar TM, Sawaki L, Burdette JH, Cabrera MN, Kolaski K, Smith BP, O'Shea TM, Koman LA, Wittenberg GF (2012) Motor cortical functional geometry in cerebral palsy and its relationship to disability. *Clin Neurophysiol: Off J Int Fed Clin Neurophysiol* 123(7):1383–1390
- Kollen BJ, Lennon S, Lyons B, Wheatley-Smith L, Scheper M, Buurke JH, Halfens J, Geurts ACH, Kwakkel G (2009) The effectiveness of the Bobath concept in stroke rehabilitation: what is the evidence? *Stroke J Cereb Circ* 40(4):e89–e97
- Korzeniewski SJ, Birbeck G, DeLano MC, Potchen MJ, Paneth N (2008) A systematic review of neuroimaging for cerebral palsy. *J Child Neurol* 23(2):216–227
- Kulak W, Sobaniec W, Kuzia J-S, Boćkowski L (2006) Neurophysiologic and neuroimaging studies of brain plasticity in children with spastic cerebral palsy. *Exp Neurol* 198(1):4–11
- Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M (1986) MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology* 161(2):401–407
- Leff DR, Orihuela-Espina F, Elwell CE, Athanasiou T, Delpy DT, Darzi AW, Yang G-Z (2011) Assessment of the cerebral cortex during motor task behaviours in adults: a systematic review of functional near infrared spectroscopy (fNIRS) studies. *NeuroImage* 54(4):2922–2936
- Liepert J, Bauder H, Miltner WHR, Taub E, Weiller C (2000) Treatment-induced cortical reorganization after stroke in humans. *Stroke* 31(6):1210–1216
- Merzenich MM, Nelson RJ, Stryker MP, Cynader MS, Schoppmann A, Zook JM (1984) Somatosensory cortical map changes following digit amputation in adult monkeys. *J Comp Neurol* 224(4):591–605
- Miller J, McKinstry R, Mukherjee P, Philip J, Neil J (2003) Pictorial essay: diffusion tensor imaging of normal brain maturation. A guide to structural development and myelination. *AJR* 180:851–859
- Milot M-H, Cramer SC (2008) Biomarkers of recovery after stroke. *Curr Opin Neurol* 21(6):654–659
- Mirelman A, Patrissi BL, Bonato P, Deutsch JE (2010) Effects of virtual reality training on gait biomechanics of individuals post-stroke. *Gait Posture* 31(4):433–437
- Mitchell L, Ziviani J, Oftedal S, Boyd R (2012) The effect of virtual reality interventions on physical activity in children and adolescents with early brain injuries including cerebral palsy. *Dev Med Child Neurol* 54(7):667–671
- Miyai I, Tanabe HC, Sase I, Eda H, Oda I, Konishi I, Tsunazawa Y, Suzuki T, Yanagida T, Kubota K (2001) Cortical mapping of gait in humans: a near-infrared spectroscopic topography study. *NeuroImage* 14(5):1186–1192
- Moseley ME, Cohen Y, Mintorovitch J, Chileuitt L, Shimizu H, Kucharczyk J, Wendland MF, Weinstein PR (1990) Early detection of regional cerebral ischemia in cats: comparison of diffusion- and T2-weighted MRI and spectroscopy. *Magn Reson Med: Off J Soc Magn Reson Med/Soc Magn Reson Med* 14(2):330–346
- Mulcahey MJ, Samdani A, Gaughan J, Barakat N, Faro S, Betz RR, Finsterbusch J, Mohamed FB (2012) Diffusion tensor imaging in pediatric spinal cord injury: preliminary examination of reliability and clinical correlation. *Spine* 37(13):E797–E803
- Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol* 527(Pt 3, no. 2000):633–639
- Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, Antal A, Paulus W, Hummel F, Boggio PS, Fregni F, Pascual-Leone A (2008) Transcranial direct current stimulation: state of the art 2008. *Brain Stimul* 1(3):206–223

- Parsons TD, Rizzo AA, Rogers S, York P (2009) Virtual reality in paediatric rehabilitation: a review. *Dev Neurorehabil* 12(4):224–238
- Patritti BL, Sicari M, Deming LC, Romaguera F (2010) The role of augmented feedback in pediatric robotic-assisted gait training : a case series. *Technol Disabil* 22:215–227
- Pennycott A, Wyss D, Vallery H, Klamroth-Marganska V, Riener R (2012) Towards more effective robotic gait training for stroke rehabilitation: a review. *J Neuroeng Rehabil* 9:65
- Pilato F, Dileone M, Capone F, Profice P, Caulo M, Battaglia D, Ranieri F, Oliviero A, Florio L, Graziano A, Di Rocco C, Massimi L, Di Lazzaro V (2009) Unaffected motor cortex remodeling after hemispherectomy in an epileptic cerebral palsy patient. A TMS and fMRI study. *Epilepsy Res* 85(2–3):243–251
- Qiu Q, Ramirez DA, Saleh S, Fluet GG, Parikh HD, Kelly D, Adamovich SV (2009) The New Jersey Institute of Technology Robot-Assisted Virtual Rehabilitation (NJIT-RAVR) system for children with cerebral palsy: a feasibility study. *J Neuroeng Rehabil* 6:40. doi:[10.1186/1743-0003-6-40](https://doi.org/10.1186/1743-0003-6-40)
- Qiu M, Darling WG, Morecraft RJ, Ni CC, Rajendra J, Butler AJ (2011) White matter integrity is a stronger predictor of motor function than BOLD response in patients with stroke. *Neurorehabil Neural Repair* 25(3):275–284
- Radlinska B, Ghinani S, Leppert IR, Minuk J, Pike GB, Thiel A (2010) Diffusion tensor imaging, permanent pyramidal tract damage, and outcome in subcortical stroke. *Neurology* 75(12):1048–1054
- Raya R, Rocon E, Ceres R, Pajaro M (2012) A mobile robot controlled by an adaptive inertial interface for children with physical and cognitive disorders. In: 2012 IEEE international conference on technologies for practical robot applications (TePRA), pp 151–156
- Rha D, Chang WH, Kim J, Sim EG, Park ES (2012) Comparing quantitative tractography metrics of motor and sensory pathways in children with periventricular leukomalacia and different levels of gross motor function. *Neuroradiology* 54(6):615–621
- Riener R, Frey M, Bernhardt M, Nef T, Colombo G (2005) Human-centered rehabilitation robotics. In: 9th international conference on rehabilitation robotics. ICORR 2005, pp 319–322
- Riener R, Lünenburger L, Colombo G (2006) Human-centered robotics applied to gait training and assessment. *J Rehabil Res Dev* 43(5):679
- Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, Dimitrijević MR, Hallett M, Katayama Y, Lücking CH (1994) Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalogr Clin Neurophysiol* 91(2):79–92
- Rossini PM, Caltagirone C, Castriota-Scanderbeg A, Cicinelli P, Del Gratta C, Demartin M, Pizzella V, Traversa R, Romani GL (1998) Hand motor cortical area reorganization in stroke: a study with fMRI, MEG and TCS maps. *NeuroReport* 9(9):2141–2146
- Safavynia SA, Torres-Oviedo G, Ting LH (2011) Muscle Synergies: implications for clinical evaluation and rehabilitation of movement. *Topics Spinal cord Inj Rehabil* 17(1):16–24
- Shevell MI, Dagenais L, Hall N (2009) The relationship of cerebral palsy subtype and functional motor impairment: a population-based study. *Dev Med Child Neurol* 51(11):872–877
- Shimony JS, Lawrence R, Neil JJ, Inder TE (2008) Imaging for diagnosis and treatment of cerebral palsy. *Clin Obstet Gynecol* 51(4):787–799
- Smith M (2011) Shedding light on the adult brain: a review of the clinical applications of near-infrared spectroscopy. *Philos Trans Ser A, Math Phys Eng Sci* 369(1955):4452–4469
- Song S, Sandrini M, Cohen LG (2011) Modifying somatosensory processing with non-invasive brain stimulation. *Restor Neurol Neurosci* 29(6):427–437
- Song F, Zhang F, Yin D-Z, Hu Y-S, Fan M-X, Ni H-H, Nan X-L, Cui X, Zhou C-X, Huang C-S, Zhao Q, Ma L-H, Xu Y-M, Xia Q-J (2012) Diffusion tensor imaging for predicting hand motor outcome in chronic stroke patients. *J Int Med Res* 40(1):126–133
- Sotak CH (2002) The role of diffusion tensor imaging in the evaluation of ischemic brain injury—a review. *NMR Biomed* 15(7–8):561–569

- Swinnen E, Duerinck S, Baeyens J-P, Meeusen R, Kerckhofs E (2010) Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. *J Rehabil Med: Off J UEMS Eur Board Phys Rehabil Med* 42(6):520–526
- Towsley K, Shevell MI, Dagenais L (2011) Population-based study of neuroimaging findings in children with cerebral palsy. *Eur J Paediatr Neurol; Off J Eur Paediatr Neurol Soc* 15(1):29–35
- Utsunomiya H (2011) Diffusion MRI abnormalities in pediatric neurological disorders. *Brain Dev* 33(3):235–242
- Valle AC, Dionisio K, Pitskel NB, Pascual-Leone A, Orsati F, Ferreira MJL, Boggio PS, Lima MC, Rigonatti SP, Fregni F (2007) Low and high frequency repetitive transcranial magnetic stimulation for the treatment of spasticity. *Dev Med Child Neurol* 49(7):534–538
- van den Noort JC, Scholtes VA, Becher JG, Harlaar J (2010) Evaluation of the catch in spasticity assessment in children with cerebral palsy. *Arch Phys Med Rehabil* 91(4):615–623
- van der Linden M (2012) Functional electrical stimulation in children and adolescents with cerebral palsy. *Dev Med Child Neurol* 54(11):972
- Vidalhet M, Yelnik J, Lagrange C, Fraix V, Grabli D, Thobois S, Burbaud P, Welter M-L, Xie-Brustolin J, Braga M-CC, Ardouin C, Czernecki V, Klinger H, Chabardes S, Seigneuret E, Mertens P, Cuny E, Navarro S, Cornu P, Benabid A-L, Le Bas J-F, Dormont D, Hermier M, Dujardin K, Blond S, Krystkowiak P, Destée A, Bardinet E, Agid Y, Krack P, Broussolle E, Pollak P (2009) Bilateral pallidal deep brain stimulation for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study. *Lancet Neurol* 8(8):709–717
- Willoughby KL, Dodd KJ, Shields N, Foley S (2010) Efficacy of partial body weight-supported treadmill training compared with overground walking practice for children with cerebral palsy: a randomized controlled trial. *Arch Phys Med Rehabil* 91(3):333–339
- Wilson-Costello D, Friedman H, Minich N, Fanaroff AA, Hack M (2005) Improved survival rates with increased neurodevelopmental disability for extremely low birth weight infants in the 1990s. *Pediatrics* 115(4):997–1003
- Wittenberg GF (2009) Motor mapping in cerebral palsy. *Dev Med Child Neurol* 51(suppl 4):134–139
- Wolbrecht ET, Chan V, Reinkensmeyer DJ, Bobrow JE (2008) Optimizing compliant, model-based robotic assistance to promote neurorehabilitation. *IEEE Trans Neural Syst Rehabil Eng: Publ IEEE Eng Med Biol Soc* 16(3):286–297
- Wright PA, Durham S, Ewins DJ, Swain ID (2012) Neuromuscular electrical stimulation for children with cerebral palsy: a review. *Arch Dis Child* 97(4):364–371
- Yang Q, Tress BM, Barber PA, Desmond PM, Darby DG, Gerraty RP, Li T, Davis SM (1999) Serial study of apparent diffusion coefficient and anisotropy in patients with acute stroke. *Stroke; J Cereb Circ* 30(11):2382–2390
- Yeargin-Allsopp M, Van Naarden Braun K, Doernberg NS, Benedict RE, Kirby RS, Durkin MS (2008) Prevalence of cerebral palsy in 8-year-old children in three areas of the United States in 2002: a multisite collaboration. *Pediatrics* 121(3):547–554
- Yonclas PP, Nadler RR, Moran ME, Kepler KL, Napolitano E (2006) Orthotics and assistive devices in the treatment of upper and lower limb osteoarthritis: an update. *Am J Phys Med Rehabil/Assoc Acad Physiatr* 85(11 Suppl):S82–S97
- You SH, Jang SH, Kim Y-H, Hallett M, Ahn SH, Kwon Y-H, Kim JH, Lee MY (2005) Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke: an experimenter-blind randomized study. *Stroke; J Cereb Circ* 36(6):1166–1171

Author Biographies

Stefan Lambrecht is a PhD Candidate (2011-) at the Bioengineering Group (GBIO) of the Spanish National Research Council (CSIC). His research focuses on the development of a wearable (quasi) real-time neuromusculoskeletal analysis system for the upper extremity. Specific topics of interest are: wearable sensors, personalization of multi-body models, biomechanics, hybrid EMG-/kinematics-driven models and neurorehabilitation.

Oiane Urrea Biotechnologist and PhD student in Biomedical Engineering. She works on neurorehabilitation, motor recovery strategies, interactive gaming and brain plasticity in collaboration with the groups of Robotics and Biomedical Signal Processing and Interpretation in the Institute for Bioengineering of Catalonia (IBEC).

Svetlana Grosu PhD student at Vrije Universiteit Brussel, Department of Robotics & Multibody Mechanics. In framework of the cognitive gait rehabilitation robot project (CORBYS), the main topics of her study interest are represented by rehabilitation robotics, human-robot interaction, motion data processing, 3D modeling and dynamic simulations

Soraya Pérez Nombela Physical Therapist in the Biomechanics and Technical Aids Department of National Hospital for Spinal Cord Injury, Toledo, Spain. Scientific interests are movement analysis, muscle synergies and neurorehabilitation

Emerging Therapies in Neurorehabilitation

Pons, J.L.; Torricelli, D. (Eds.)

2014, X, 345 p., Hardcover

ISBN: 978-3-642-38555-1