"A robotic device to assess and rehabilitate upper limb movements in cerebral palsy children and stroke adults"

Gilliaux, Maxime

Abstract

Cerebral palsy (CP) and stroke are major causes of permanent disabilities. These disabilities justify intensive interdisciplinary rehabilitation and regular assessments, which could be optimized using robotics. This PhD thesis investigated the clinical interest in robotic devices to assess and rehabilitate upper limb movements in CP children and stroke adults. This investigation was performed with the REAplan robot, which is an end-effector robotic device that moves the patient's upper limb in a horizontal plane using various assistance modes (i.e., active, active-passive, passive). The first part of this thesis investigated how a robotic device could quantitatively assess upper limb movements in both populations. A standardized protocol was developed to assess upper limb kinematics using the REAplan robot in CP children and stroke adults. The reproducibility, validity, responsiveness and reference standards of this protocol were established, and a short version of this protocol wa...

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A robotic device to assess and rehabilitate upper limb movements in cerebral palsy children and stroke adults

Robot-Assisted Therapy

Maxime GILLIAUX

Thesis submitted in fulfillment of the requirements for the degree of
“Docteur en sciences de la motricité”

Supervisors:
Prof. Christine Detrembleur
Prof. Gaëtan Stoquart

June 2015

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"Technology as destiny"[1,2].

JURY

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RESUME

L'infirmité motrice d'origine cérébrale (IMoC) et les accidents vasculaires cérébraux (AVC) sont les principales causes d'invalidités permanentes. Ces pathologies justifient une rééducation interdisciplinaire intensive et des évaluations régulières, pouvant être optimisées par la robotique. Cette thèse de doctorat a étudié l'intérêt clinique de dispositifs robotiques afin d'évaluer et de rééduquer les mouvements du membre supérieur chez les enfants IMoC et les adultes AVC. Cette investigation a été réalisée à l'aide du robot REAplan. REAplan est un dispositif robotique à effecteur distal permettant la mobilisation du membre supérieur dans le plan horizontal grâce à différents modes d'assistance (i.e., actif, activo-passif, passif). La première partie de cette thèse a investigué comment un dispositif robotique pouvait évaluer quantitativement les mouvements du membre supérieur au sein des deux populations. Un protocole standardisé a été développé afin d'évaluer la cinématique du membre supérieur chez les enfants et adultes cérébro-lésés, en utilisant le dispositif robotique REAplan. La reproductibilité, la validité, la sensibilité au changement et les normes de référence de ce protocole ont été établies. Une version courte de ce protocole a été créée afin de faciliter l'évaluation de la cinématique du membre supérieur en routine clinique. La deuxième partie de cette thèse a étudié comment un dispositif robotique pouvait efficacement rééduquer le membre supérieur chez les enfants IMoC. Un protocole standardisé de thérapie assistée par la robotique (TAR) a été développé en tenant compte des recommandations connues en rééducation neuro-pédiatrique. Ce protocole a été utilisé dans une étude randomisée contrôlée en simple aveugle afin d'évaluer l'efficacité de la TAR chez les enfants IMoC. Cette étude a montré que la combinaison d'une thérapie conventionnelle (TC) et de la TAR améliorait significativement la cinématique du membre supérieur et la dextérité manuelle des enfants IMoC par rapport à la TC seul. Cette thèse de doctorat a montré que les dispositifs robotiques pouvaient quantitativement évaluer et efficacement rééduquer les mouvements du membre supérieur chez les enfants et adultes cérébro-lésés. Cette recherche n'aurait pas été possible sans l'étroite collaboration entre ingénieurs, techniciens, cliniciens et chercheurs. Nous encourageons la continuation de telles collaborations afin de favoriser l'intégration de la technologie en rééducation.

Mots clés: accident vasculaire cérébrale - infirmité motrice d'origine cérébrale - robotique - biomécanique - rééducation

SUMMARY

Cerebral palsy (CP) and stroke are major causes of permanent disabilities. These disabilities justify intensive interdisciplinary rehabilitation and regular assessments, which could be optimized using robotics. This PhD thesis investigated the clinical interest in robotic devices to assess and rehabilitate upper limb movements in CP children and stroke adults. This investigation was performed with the REAplan robot, which is an end-effector robotic device that moves the patient's upper limb in a horizontal plane using various assistance modes (i.e., active, active-passive, passive). The first part of this thesis investigated how a robotic device could quantitatively assess upper limb movements in both populations. A standardized protocol was developed to assess upper limb kinematics using the REAplan robot in CP children and stroke adults. The reproducibility, validity, responsiveness and reference standards of this protocol were established, and a short version of this protocol was provided to facilitate the assessment of upper limb kinematics in routine clinical practice. The second part of this thesis investigated how a robotic device could efficiently rehabilitate upper limb movements in CP children. A standardized protocol for robot-assisted therapy (RAT) was first developed according to the current recommendations in CP neuro-rehabilitation. This protocol was used in a single-blind randomized controlled trial that assessed the efficacy of RAT in CP children. This trial showed that the combination of conventional therapy (CT) and RAT could significantly improve upper limb kinematics and manual dexterity in CP children compared with CT alone. Thus, robotic devices could quantitatively assess and efficiently rehabilitate upper limb movements in CP children and stroke adults. These findings would not have been possible without close collaboration between engineers, technicians, clinicians and researchers. Further similar collaborations should be encouraged to facilitate technological integration in rehabilitation.

Key words: stroke – cerebral palsy – robotics – biomechanics – rehabilitation

General introduction

General introduction

1. Context

Cerebral Palsy (CP) and stroke are major causes of long-term disabilities. CP, which affects two to four births per thousand worldwide[3–7], corresponds to "*a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, behaviour, by epilepsy and by secondary musculoskeletal problems*"[3–5]. Stroke, which affects one to four adults per thousand worldwide[8], corresponds to "*a disruption of the blood supply to the brain. This may result from either blockage (ischaemic stroke) or rupture of blood vessel (haemorrhagic stroke). The risk factors are high blood pressure, atrial fibrillation (a heart rhythm disorder), high blood cholesterol, tobacco use, unhealthy diet, physical inactivity, diabetes and advancing age*"[9]. One-third of stroke patients display permanent disabilities[9].

In both pathologies, the resulting brain damage can lead to abnormalities in motor control (e.g., hemi-/di-/quadriplegia), strength, tonus (e.g., spasticity, dystonia, hyperactivity of osteotendinous reflexes), and sensibility, which could be associated with ataxia, and to cognitive disorders (e.g., hemineglect, dyspraxia)[6,7,10]. These disabilities justify intensive interdisciplinary rehabilitation to (i) reduce patients' neurological impairments, (ii) improve their abilities in activities of daily living (ADLs) and social integration, and (iii) ultimately optimize their quality of life[4,10,11]. This rehabilitation should be associated with regular standardized assessments to monitor the patients' progress over time and to define or adapt their treatment[12,13].

These patients' rehabilitation and assessment could be optimized using robotics[14]. "*Robotics is the science and technology of the design of mechatronic systems capable of generating and controlling motion and force"(Paolo Dario, cited by Pignolo*[14]*).* This thesis focuses on the interests of upper limb robotics in CP children and stroke adults. Two families of robotic devices, end-effector and exoskeleton robots, are used in rehabilitation, both of which are illustrated in Figure 1 and described below. An end-effector robot generates and controls motions and forces of the upper limb via a unique interface linked to the subject (e.g., the hand)[14–16]. To the best of our knowledge, six upper limb end-effector robots have been involved in clinical studies: the MIT-Manus (USA, see Figure 1)[17], NeReBot (Italy)[18], Arm Guide (USA)[19,20], Gentle/S [21,22], ReoGo[23] and Braccio Di Ferro (Italy)[24]. An exoskeleton robot generates and controls motions and forces of different joints of the mobilized limb from a structure that is parallel to the limb[14–16]. To the best of our knowledge, seven upper limb exoskeletons have been involved in clinical studies: the Armin (Switzerland, see Figure 1)[15,25–27], Rupert (USA)[28], Reharob (Hungary)[29], L-Exos (Italy)[30], Hward (USA)[31], Hexorr[32] and Hand Mentor[33]. End-effectors have already been studied in CP and stroke populations[34,35], whereas exoskeletons have only been used in stroke patients.

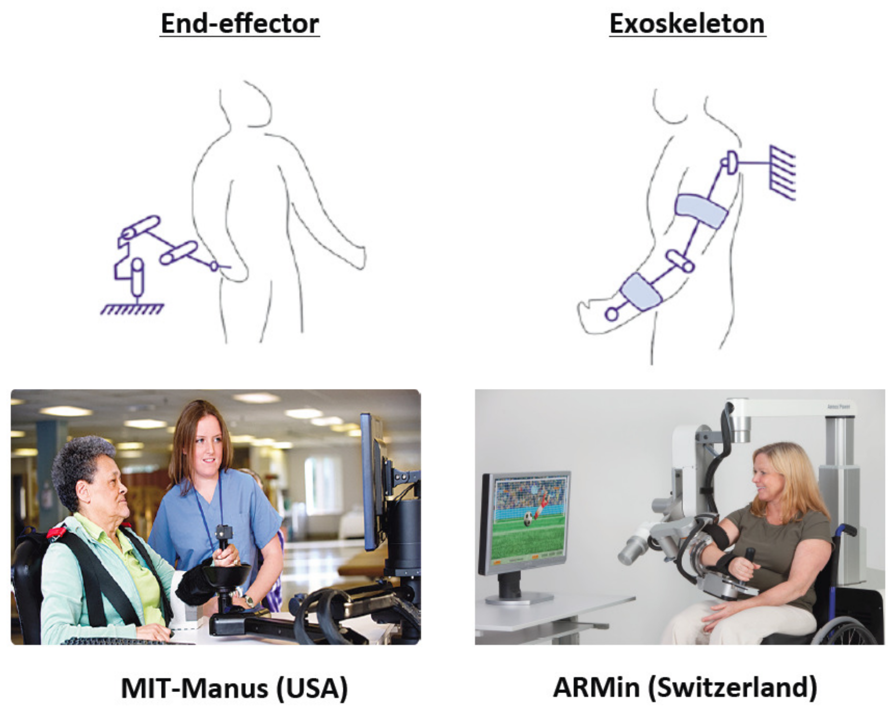

Figure 1: Illustrations and examples of end-effector and exoskeleton robots [Pictures adapted from[15,36,37]].

The REAplan robot, illustrated in Figure 2, was the only robot used in this PhD thesis[38]. REAplan is an end-effector robotic device that can mobilize a patient's upper limb by carrying the hand or the forearm along paths included in a horizontal plane. Like most rehabilitation robots, REAplan is fitted with force and position sensors. The force sensors measure the interaction force between the patient and the robot, which can determine a reference force using a force controller. The position sensors measure the kinematics of the patient's hand or forearm to determine the reference force based on the position and/or velocity and on specific exercises performed with the robot. This reference force is adapted for assessment (see first part of the thesis) and rehabilitation (see second part of the thesis) purposes. A screen and a speaker are installed in the robot to provide audiovisual feedbacks for patient performance.

Figure 2: View of the REAplan. 1: Planar end-effector robot; 2: visual interface for the subject; 3: physiotherapist's interface.

Conception of the REAplan robot resulted from a close collaboration between research engineers (Centre of Mechatronics from Université catholique de Louvain, Louvain-la-Neuve), clinicians (Cliniques universitaires Saint-Luc, Brussels), research clinicians (Institute of Neuroscience and Louvain Bionics from Université catholique de Louvain, Brussels). This collaboration, which began in 2006, enabled our team to develop three successive versions of REAplan, all of which were used in this thesis (Figure 3). Each version optimized REAplan to fulfill the needs of patients and clinicians in routine clinical practice.

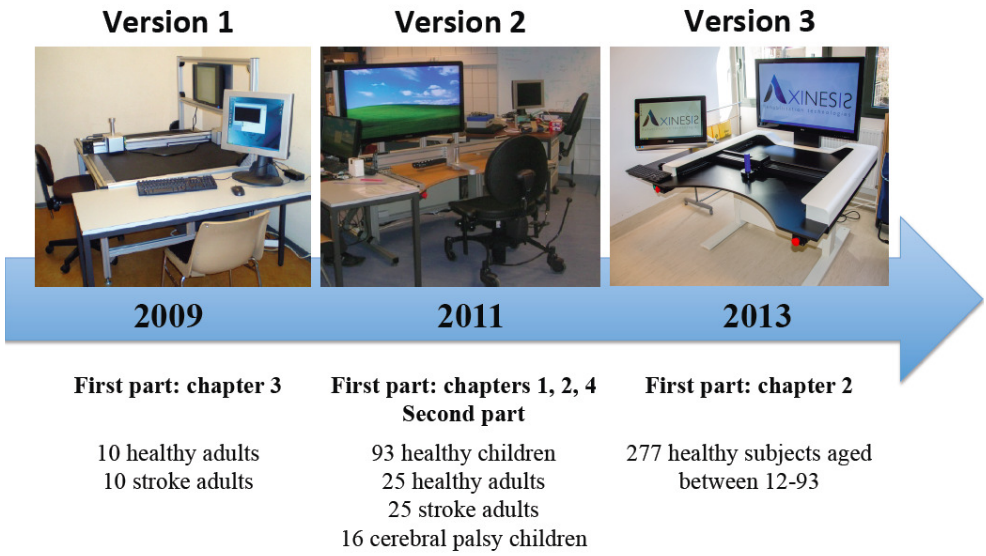

Figure 3: Illustration of the three successive versions of REAplan. For each version, the year of its development and the patients' number that were recruited in this PhD thesis are provided. The thesis part(s) and chapter(s) in which the corresponding version was used are listed.

2. Upper limb assessment

As described above, assessing patients' disabilities is important to monitor their progress over time and to define or adapt their treatment[4,10,12,13]. These assessments should be performed with standardized, norm-referenced, reproducible, valid, responsive and concise tools[12,13,39,40], which must consider the International Classification of Functioning, Disability, and Health (ICF) as recommended by the World Health Organization[11,41]. The ICF model, which is illustrated in Figure 4, considers the consequences of a disease (e.g., stroke) with three domains: (i) body functions (e.g., motor control of the hand) and structures (e.g., the muscle), (ii) activities (e.g., taking a cup of tea) and (iii) participation (e.g., having a drink with friends)[41]. These domains could be positively or negatively affected by environmental (e.g., family) and personal (e.g., motivation) factors[41]. For each domain, disabilities are defined by (i) impairments, (ii) activity limitations and (iii) participation restrictions[41].

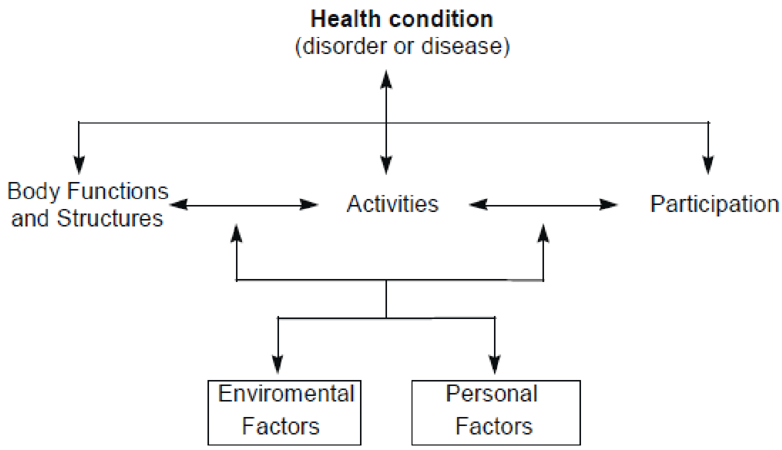

Figure 4: Illustration of the International Classification of Functioning, Disability and Health of the World Health Organization[41].

Recent systematic reviews have identified upper limb assessment tools for CP children[13,42–45] and stroke adults[12,46,47]; these tools are reported in Tables 1 and 2. Most of these tools describe upper limb impairments and abilities through performance observations (e.g., the *Quality of Upper Extremity Skills Test* for CP children[48] and the *Fugl Meyer Assessment* for stroke adults[49]) or questionnaires (e.g., the *Pediatric Evaluation of Disability Inventory* for CP children[50] and the *Stroke Impact Scale* for stroke adults[51]), which could be subjective. Moreover, most of the tools provide ordinal measures (e.g., scoring of the *Fugl Meyer Assessment*: 0 = no movement; 1 = partial movements; 2 = correct movements), which prevent the performance of parametric analyses.

Table 1: For each ICF domain, the recommended assessment tools of the upper limb in CP children are listed. Each tool is classified in function of its ability of providing ordinal or linear measures.

	Cerebral palsy children[13,42–45]	
	Ordinal measures	Linear measures
Body functions and structures	- House Scale (description of hand function)$^{\alpha}$ - Quality of Upper Extremity Skills Test (quality of upper limb movements) - Bruininks-Oseretsky Test of Motor Proficiency (gross and fine motor abilities) - Peabody Developmental Motor Scales (gross and fine motor abilities)	- Box and Block test (gross manual dexterity) - Kinematics
Activities	- Activities Scale for Kids$^{\beta}$ - Functional Independent Measure - Manual Ability Classification System$^{\alpha,\beta}$ - Melbourne Assessment of Unilateral Upper Limb Function$^{\alpha}$ - Pediatric Evaluation of Disability Inventory$^{\beta}$ - Shriners Hospitals for Children Upper Extremity Evaluation$^{\alpha}$ - Video Observations Aarts and Aarts$^{\alpha}$ - Revised Pediatric Motor Activity Log	- Abilhand-Kids$^{\alpha,\beta}$ - Assisting Hand Assessment$^{\alpha}$ - Jebsen-Taylor Hand Function Test
Participation & quality of life	- Children's Assessment of Participation and Enjoyment$^{\beta}$ - Child Health Questionnaire$^{\beta}$ - Cerebral Palsy Quality of Life Questionnaire for Children$^{\alpha,\beta}$ - Canadian Occupational Performance Measure$^{\beta}$ - Assessment of Life Habits$^{\beta}$ - Pediatric Quality of Life Inventory-Cerebral Palsy Module$^{\alpha,\beta}$	

For the impairment domain, the movement characteristics assessed with the tool are provided between brackets.

$^{\alpha}$ corresponds to specific tools, whereas the others are generic tools.

$^{\beta}$ corresponds to patient-reported questionnaires, whereas the others correspond to performance-based tool

Table 2: For each ICF domain, the recommended assessment tools of the upper limb in stroke adults are listed. Each tool is classified in function of its ability of providing ordinal or linear measures.

	Stroke adults[12,46,47,51–53]	
	Ordinal measures	Linear measures
Body functions and structures	- Modified Ashworth scale (spasticity) - Motor Status Score (motor control) - Medical Research Council (muscle strength) - Action Research Arm Test (motor control)	- Fugl Meyer Assessment (motor control)$^{\alpha}$ - Kinematics - Box and Block test (gross manual dexterity) - Nine-Hole Peg test (fine manual dexterity) - Purdue Peg Board Test (fine manual dexterity)
Activities	- Arm Motor Ability Test - Barthel Index - Functional Independent Measure - Motor Activity Log - Rivermead Motor Assessment - Motor Assessment Scale	- Abilhand$^{\alpha,\beta}$ - Wolf Motor Function test
Participation & quality of life	- Stroke Impact Scale$^{\alpha,\beta}$ - EuroQoL Quality of Life Scale$^{\beta}$ - Short Form 36 Healthy Survey$^{\alpha,\beta}$	- Stroke Impact Scale$^{\alpha,\beta}$

For the impairment domain, the movement characteristics assessed with the tool are provided between brackets.

$^{\alpha}$ corresponds to specific tools, whereas the others are generic tools.

$^{\beta}$ corresponds to patient-reported questionnaires, whereas the others correspond to performance-based tools.

To avoid the disadvantages of subjective and ordinal scales, previous reviews have recommended using kinematics to objectively and quantitatively assess upper limb movements in CP children[45] and stroke adults[12,39]. Upper limb kinematics, which assess the first domain of the ICF (body functions and structures), have primarily been assessed using optoelectric[54–58] or electrogoniometer[59] systems. Moreover, no consensus exists in the literature to determine the most relevant tasks and kinematic indices (for review, see tables 3 and 4). To the best of our knowledge, no study has provided a standardized, norm-referenced, reproducible, valid, responsive and concise protocol in CP children and stroke adults, by using a robotic device[12,45]. The development of such a protocol was recommended by Balasubramanian et al.[39] and appears to be feasible using sensors integrated into a robot[14,34,60,61].

Table 3: Listing of the main studies that assessed upper limb kinematics in CP children. All studies are classified in function of the material used for this assessment. For each study, the requested tasks and computed kinematic indices are provided.

	Cerebral palsy children	
Authors	Requested tasks	Computed indices
Robotic		
Krebs et al[61]	Multiple targets and drawing a circle	Targets: straightness, velocity, peak velocity, duration and smoothness Circle: Axe ratio (i.e., ability to draw circle)
Opto-electric		
Kreulen et al.[62]	Functional and simple tasks	Joint angles of trunk, shoulder and elbow
Chang et al.[56]	Multiple targets	Mean velocity, peak velocity, amplitude, smoothness, control strategy
Butler & Rose[63]	Reaching, grasping, transporting and releasing a cup	Paediatric upper limb motion index computed from eight joint angles of the trunk and arm
Coluccini et al.[57]	Reaching, grasping, transporting and releasing a block into a box	Joint angles of the head, trunk, shoulder, elbow and wrist Velocity/acceleration of the wrist
Reid et al.[64]	Four functional tasks	Joint angles of thorax, shoulder, elbow and wrist
Rönnqvist & Rösblad[65]	Reaching & grasping an object	Movement duration, straightness, peak velocity and smoothness
Mackey et al.[66]	Two functional tasks	Joint angles of trunk, shoulder and elbow
Ricken et al.[67]	Reaching and grasping a ball	Movement duration, peak velocity, joint angles of trunk, shoulder and elbow
Van Thiel & Steenbergen[68]	Multiple targets	Velocity, displacement, smoothness
Jaspers et al. 2011[69]	Three reaching tasks (forwards, upwards and sideways)	Movement duration, joint angles, peak velocity and straightness
Schneiberg et al.[70]	Reaching and grasping a wooden block	Joint angles of elbow and shoulder, straightness and smoothness
Butler et al.[71]	Reaching, grasping and Transporting a cup to the mouth	Joint angles of trunk, shoulder, elbow and wrist
Fitoussi et al.[72]	Two functional tasks	Joint angles of trunk, shoulder, elbow and wrist
Mackey et al.[73]	Two functional tasks	Joint angles of trunk, shoulder and elbow
Electro-goniometer		
Ramos et al.[74]	Multiple targets	Joint angle of elbow, velocity and peak velocity
Hurvitz et al.[59]	Reaching forward	Joint angle of elbow, velocity and peak velocity

Table 4: Listing of the main studies that assessed upper limb kinematics in stroke adults. All studies are classified in function of the material used for this assessment. For each study, the requested tasks and computed kinematic indices are provided.

	Stroke adults	
Authors	Requested tasks	Kinematic indices
Robotics		
Rohrer et al.[75]	Multiple targets	Five smoothness measures
Daly et al.[34]	One target	Accuracy and smoothness
Finley et al.[60]	Multiple targets	Straightness, mean velocity, peak velocity, smoothness and movement duration
Kahn et al. [19]	One target	Peak velocity and amplitude
Reinkensmeyer et al.[20]	One target	Peak velocity and amplitude
Ellis et al.[76]	Circular movements (clockwise and counter-clockwise)	Work area
Feng & Winters[77]	Drawing square and circle	Accuracy, straightness, mean velocity, variation of velocity, reaction time, smoothness
Bosecker et al.[78]	Multiple targets	Straightness, accuracy, movement duration, peak velocity, smoothness
Optoelectrics		
Wu et al.[79]	Reaching and pressing a desk bell	Reaction time, movement duration, total displacement, peak velocity, smoothness
Wagner et al.[54]	Reaching two targets at various velocity	Movement duration, peak velocity, reach extent, inter-joint coordination, smoothness, accuracy
Fridman et al.[80]	Reaching, grasping and transporting an object	Peak velocity, displayed distance and movement duration
Caimmi et al.[55]	Reaching and hand-to-mouth movements	Movement duration, smoothness, mean velocity and joint angles of elbow and shoulder
Bensmail et al.[81]	Multiple targets	Peak velocity, straightness, movement duration, smoothness
Murphy et al.[82]	Reaching, grasping, lifting a glass from the table and take a drink	Peak velocity, movement duration, movement strategy, smoothness
Electrogoniometers		
Kahn et al.[19]	Multiple targets	Amplitude, straightness and smoothness, coordination, joint angles of trunk, shoulder and elbow
Reinkensmeyer et al.[20]	Multiple targets	Accuracy
Rundquist et al.[83]	Elevation of upper extremity in frontal, sagittal and preferred planes of motion	Angles of glenohumeral and scapulothoracic joints
Combs et al.[84]	Multiple targets	Joint angles of trunk and elbow, movement duration, mean velocity, peak velocity and smoothness
Van Kordelaar et al.[85]	Reaching, Grasping and transporting a block	Movement duration, joint angles of trunk, elbow and hand

3. Upper limb rehabilitation

Upper limb disabilities have been rehabilitated in stroke adults and CP children using a large panel of interventions[86,87] that were either efficient or not efficient[88,89]. Systematic reviews[87,88] and meta-analyses[89–92] have highlighted the recommended interventions in both populations. For each population, the evidence-based recommendations of upper limb interventions and robot-assisted therapy (RAT) are summarized below, according to the ICF. For stroke adults, a recent Cochrane meta-analysis showed with a moderate level of evidence that transcranial direct current stimulation, constraint-induced movement therapy (CIMT), mental practice, sensory interventions (e.g., proprioceptive stimulations) and virtual reality could improve upper limb impairments in stroke patients[88]. Additionally, mirror therapy improved upper limb impairments in stroke patients and their abilities to perform ADL[88]. Finally, additional studies evaluated the usefulness of neurodevelopmental exercises (e.g., Bobath), repetitive transcranial magnetic stimulation, strength training and electrical stimulations[88]. For the robotic approach, many high quality randomized controlled trials (RCTs) were performed in stroke patients[17,18,25,34,93–98]. Two recent meta-analyses[91,92] and one systematic review[88] showed that upper limb RAT improved upper limb impairments and ADL abilities [88,91,92] in stroke patients but did not improve upper limb strength[92]. For CP children, one systematic review[87] and two meta-analyses[89,90] provided evidence-based upper limb intervention recommendations. These reviews provided strong evidence showing that (i) Botulinum toxin associated with conventional therapy (CT), (ii) intensive rehabilitation such as CIMT and (iii) goal-directed/functional exercises improved upper limb impairments and abilities to perform ADL in children[87,89,90]. Additionally, based on a moderate level of evidence, home programs (i.e., goal-oriented tasks performed in the home environment) and fitness training appear to improve activity and participation domains[87]. Finally, cranial osteopathy and neurodevelopmental exercises (e.g., Bobath concept) do not appearto be efficient in CP children[87]. For the robotic approach, no RCT has been performed yet but such studies should be performed to investigate RAT interests in CP children[4,87]. However, several preliminary studies have described the feasibility of upper limb RAT in CP children[22,35,61,99,100].

Previous studies have shown that RAT protocols have the potential to follow current recommendations in neuro-rehabilitation in CP children[22,35,61,99,100] and stroke adults[17,18,25,34,93–98]. These recommendations encourage the execution of repetitive and motivating movements[4,10,101], which should be assisted as needed and associated with feedbacks[16,102]. The primary interest in using robots is to allow patients to perform many movements in a limited period of time[17,96], which does not seem feasible with human therapists[103]. For example, previous studies have shown that CP children and stroke patients could perform 640 and 1060 movements, respectively, during 60-minute RAT sessions[17,35]. Additionally, the human/machine interface of a robot enables the patient to perform attractive exercises. For example, RAT has already been used for simple target tasks[17,34,61], video games[27], competitive or cooperative activities[104] and tasks that mimic ADL (e.g., reaching for a cup)[22] (cf. examples in Figure 5). Moreover, patients receive visual, auditory and sensory feedbacks while using robots[18,34,35,97,99], as recommended by Molier et al.[102].

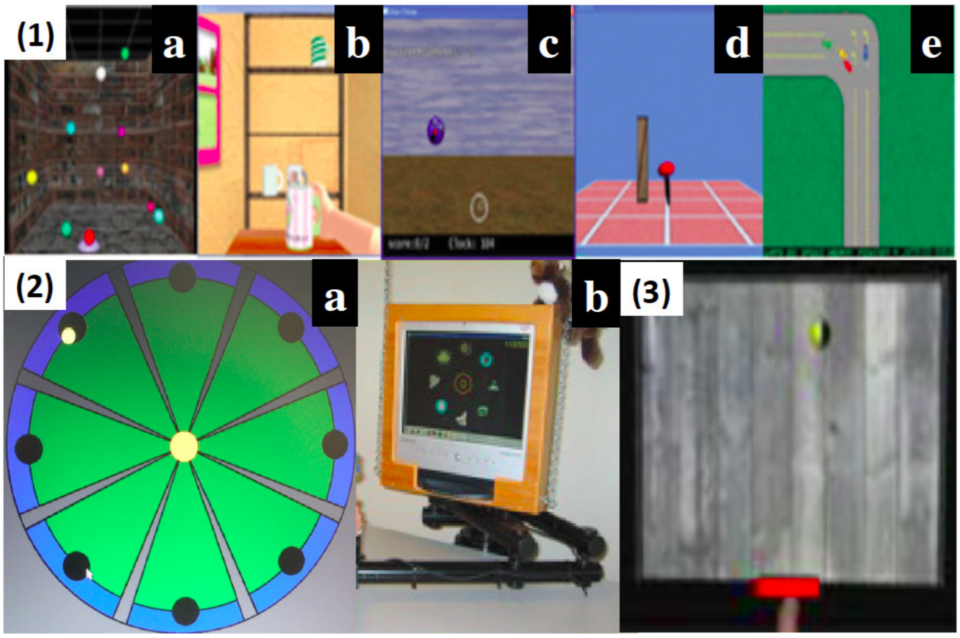

Figure 5: Illustrations of visual interfaces developed in (1a-e) Haptic Master®[22], (2a-b) MIT-Manus[34,61] and (3) Armin[27]**.** The exercises correspond to (1a, c, d and 2a, b) reaching targets, (1b) performing ADL, (1e) playing a car racing game or (3) moving a virtual handle (red in the picture) to catch a ball (yellow and black in the picture) that rolls down.

Finally, the robotic haptic interaction can provide objective assistance to the patients as needed[16,38,105]. This assistance is an advantage of robotics, in comparison to other treatment modalities[14] such as CIMT[79] or Hand-Arm Bimanual Intensive Therapy[106]. Indeed, the assistance of upper limb movements in patients with severe impairment is essential[16], especially in the acute stage of stroke rehabilitation[10]. Moreover, the adaptation of assistance level in function of patients' performances is relevant to progressively increase the difficulty of exercises in CP children and stroke adults[4,105]. Various methods have been developed to assist patients in function of their performances. Krebs et al.[105] implemented performance-based adaptive algorithms on the MIT-Manus robot (see Figure 1). These algorithms adapt the assistance provided to patients in function of velocity, time and electromyography variables. These algorithms assess the patients' ability to initiate movements and move towards the target. Moreover, the upper limb kinematics (straightness and accuracy) is also assessed during the patients' movements. All these measures enable the MIT-Manus robot to objectively increase or decrease the level of assistance in function of patients' performances[105]. Later on, Ronsse et al.[107] have developed an oscillator-based assistance. This approach is based on the synchronization between patients' movements and an adaptive oscillator. This synchronization continuously adapts the assistance provided to patients in function of their movements' characteristics (amplitude, frequency and offset). This approach has been initially developed for lower limb rehabilitation because it works only with rhythmic movements. However, the Ronsse's team is currently adapting these algorithms for upper limb purposes[108]. Beside assistance methods, haptic interaction could also be used to constraint patients by involving disturbing forces during their movements. For instance, Abdollahi et al.[109] asked patients to reach targets by using a robot, while the device applied an error augmenting force that pushed their upper limb away. We believe that this last assistance method should only be recommended in patients with mild to moderate impairments.

In addition to the potential of robotic devices to follow current neuro-recommendations, the technical properties of robotic devices could also complete the abilities of human therapists in neuro-rehabilitation. Pignolo[14] supported this hypothesis by listing both advantages, which are summarized below. On one hand, the mechatronic components of a robot (e.g., sensors, actuators, controllers) provide better reliability, reactivity, quantifiable measures, objectivity, memory storage and endurance than a human therapist during patient rehabilitation[14]. On the other hand, human therapists are distinguished from robots by their cognition, insight, and communication, as well as their precision in complex tasks such as ADL[14]. The association of a robot, which involves substantial movements, with a human therapist could enable one to re-allocate his or her time and energy to transferring the benefits of these repetitive movements (for example, improved motor control[92]) to ADL. Robotic devices should be used in complement and not in competition with human therapists[14]. Although this last suggestion seems obvious, most previous studies have investigated the interests of RAT at the only treatments, and not in combination with CT[17,25,35,61,93,94,96,99,100].

4. Purposes of the PhD thesis

The general introduction of this PhD thesis provided the backgrounds of upper limb assessment and rehabilitation in CP children and stroke adults.

Regarding the patients' assessment, we highlighted a lack of consensus for assessing upper limb kinematics in these patients. Moreover, no study has provided a standardized, norm-referenced, reproducible, valid, responsive and concise protocol in CP children and stroke adults, by using a robotic device[12,45]. Such a standardization is essential to reliably assess upper limb kinematics in clinical routine[12,39]. The first part of the thesis, which comprises four chapters, investigates how the REAplan robot could optimize the assessment of upper limb kinematics in both populations. The two first chapters present the age effects and reference standards of upper limb kinematics in healthy young children (chapter 1) and in healthy subjects throughout life (chapter 2) using the REAplan robot. The two last chapters present the standardization of a protocol to assess upper limb kinematics in adult stroke patients using the REAplan robot. This standardization was performed through preliminary (chapter 3) and validation (chapter 4) studies. The details about patient installation, tasks instructions, interpretations of kinematic indices and analyses of these kinematic indices are provided in Annexes 1 and 2, respectively, to make the reading of this part easier.

Regarding the patients' rehabilitation, we highlighted that no RCT has been performed yet to investigate RAT efficacy in CP children. Such investigation is essential to enhance evidences in rehabilitation[110]. The second part of the thesis investigates how the REAplan robot could efficiently rehabilitate the upper limb in CP children. This part presents a single-blind RCT that compares CT to a combination of RAT and CT. The assessment protocol of this trial included the kinematics protocol detailed in the first part of this thesis and considered the three ICF domains according to the current international recommendations[12,41]. In addition to this second part, a multi-center, single-blind RCT also began in May 2014 to investigate the efficacy of RAT in acute stroke patients. However, recruiting these patients took longer than recruiting CP children. Thus, the results of this study are not presented in this PhD thesis (*see* Discussion and perspectives).

Part 1
A robotic device to assess upper limb movements

Chapter 1

Age effects on upper limb kinematics assessed by the REAplan robot in healthy school-aged children

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1. Abstract

The use of kinematics is recommended to quantitatively evaluate upper limb movements. The aims of this study were to determine the age effects on upper limb kinematics and establish norms in healthy children. Ninety-three healthy children, aged 3 to 12 years, participated in this study. Twenty-eight kinematic indices were computed from 4 tasks. Each task was performed with the REAplan, a distal effector robotic device that allows upper limb displacements in the horizontal plane. Twenty-four of the 28 indices showed an improvement during childhood. Indeed, older children showed better upper limb movements. This study was the first to use a robotic device to show the age effects on upper limb kinematics and establish norms in healthy children.

Keywords: Robotics; Pediatrics; Kinematics; Outcome Assessment; Biomechanics; Reference Standards; Growth and Development

2. Introduction

Psychomotor development in children evolves with progressive improvements. Children display uncontrolled upper limb movements in the first months after birth, after which they develop reaching and grasping movements during the first year of life. Then, these motor abilities are transferred to activities of daily living (such as eating and dressing) in subsequent years[111]. However, motor development may be altered in children with cerebral palsy (CP). In particular, children with CP present impairments such as spasticity and muscle weakness that affect their ability to develop normal motor functions for performing activities of daily living[4].

The upper limb motor ability in children is typically described through observations, interviews, and standardized and non-standardized assessments[112,113]. The majority of these measures are subjective and use ordinal scales[13]. Several authors have recommended the use of kinematics to objectively and quantitatively assess upper limb movements in CP children to avoid the drawbacks of ordinal scales[45,56]. In addition, few studies have compared upper limb kinematics between healthy and CP children[57,63–65,74]. However, their small healthy children's sample (sample range: [5-11])[57,64,65,74] and their age criterion (age range in years: [5-18])[63] were not appropriate to create age groups and then, assess age effects in healthy children. Previous authors have also assessed the age effect of upper limb kinematics in healthy children; however, these studies did not include children younger than five years of age[114,115]. Until the age of five, these children significantly develop motor skills by improving quality of movements (e.g., subjective improvement of smoothness in upper limb movements) and manual abilities (e.g. to improve the hand coordination by stacking cubes and, later, threading beads)[111]. The motor development of these younger children could be better objectified with kinematics.

Upper limb kinematics in healthy children is mainly computed using optoelectric systems[57,63–65,114,115] or electrogoniometers[45,74]. However, no study performed to date has used a robotic device to quantitatively assess the age effect and establish norms of upper limb kinematics in healthy children. Robotic devices, such as the REAplan, have the advantage of quantitatively assessing upper limb movements and rehabilitating patients, which is not feasible with other assessment devices[39]. The REAplan is a planar end-effector robotic device that allows for mobilizations in a horizontal plane resulting from movements of the upper limbs[38]. We[116,117] provided a standardized protocol to compute several kinematic indices of movement from several tasks performed with this robot.

Few studies have established the construct validity of a kinematic protocol in healthy children[63,118]. Construct validity corresponds to the correlations between different assessment tools[12], and this measure can be used to assess relationships between kinematics and visual-motor control and dexterity in healthy children, which have not previously been studied.

In accordance with the above considerations, the aims of this study were to (1) assess the age effects and establish reference standards of upper limb kinematics and (2) study the construct validity of this tool in healthy children.

3. Materials and Methods

Subjects

Ninety-three healthy children recruited from a nursery and a primary school participated in this study (location: chapelle-aux-champs school, Brussels). The inclusion criteria consisted of an age between 3 and 12 years and adequate cognition skills for following instructions. These skills were verified by checking, during the training phase of each test, the correct application of instructions. The exclusion criterion was the presence of any disorder that could alter the movements of the tested upper extremity. The children were recruited in order to have a homogeneous number of subjects in each age group. The characteristics of the included children and the sample size of each age group are reported in Table 1. All of the subjects and their parents received an informative letter explaining the nature, the aim and the duration of the experiment. All of the parents provided informed consent. The ethics board of our Faculty of Medicine approved this study.

Table 1: Characteristics of the included children and sample size of each age group.

	Healthy Children (n=93)
Age *(yrs)*, mean (SD)	7.8 (2.7)
Gender *(male/female)*, n	41/52
Weight (kg), mean (SD)	28.6 (11.2)
Height (m), mean (SD)	1.3 (0.2)
BMI *(kg/m²)*, mean (SD)	16.2 (2.7)
Dominant arm *(right/left)*, n	83/10

Age (yrs)	3	4	5	6	7	8	9	10	11	12
Sample (n)	9	9	9	10	12	7	13	9	9	6

Abbreviations: BMI = Body Mass Index, SD = Standard Deviation

Hand dominance

The child was asked to pick up and throw a ball while the examiner observed which hand was used. This test was used to determine hand dominance.

Kinematic assessment

Apparatus

The robot used in the present study was the research prototype REAplan (Figure 1). This device is composed of a distal effector that is held in the subject's hand, which allows displacements in the horizontal plane resulting from various movements of the shoulder and elbow.

The REAplan is fitted with force and position sensors. The force sensors are intended to measure the interaction force between the child and the robot, which allows the determination of a reference force using a force controller. The position sensors measure the kinematics of the child's hand to determine the reference force on a positional basis and on the basis of the specific exercises performed with the robot. For this study, the only reference force used was a slightly viscous friction force to avoid the strange sensation of moving the hand on a frictionless surface. For the purposes of the study, the kinematic information provided by the position sensors was recorded during the exercise, which enabled us to analyze the data off-line (acquisition frequency 125 Hz). The planar robot is also equipped with a screen positioned in front of the subject. This screen displayed the tasks (Figure 2) and provided to the children a real time feedback of their movements.

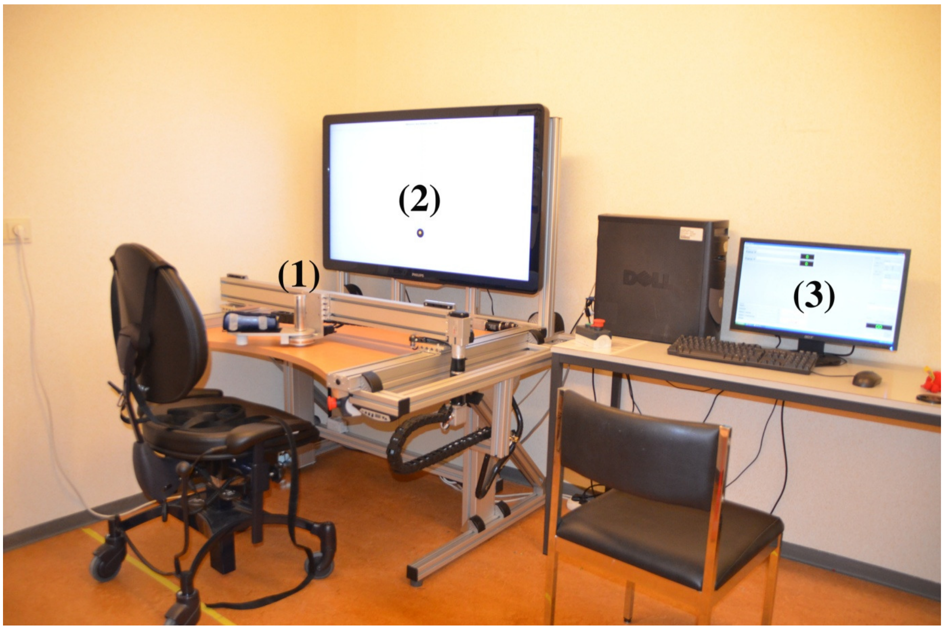

Figure 1: View of the REAplan. 1: planar end-effector robot; 2: visual interface for the subject; 3: physiotherapist's interface.

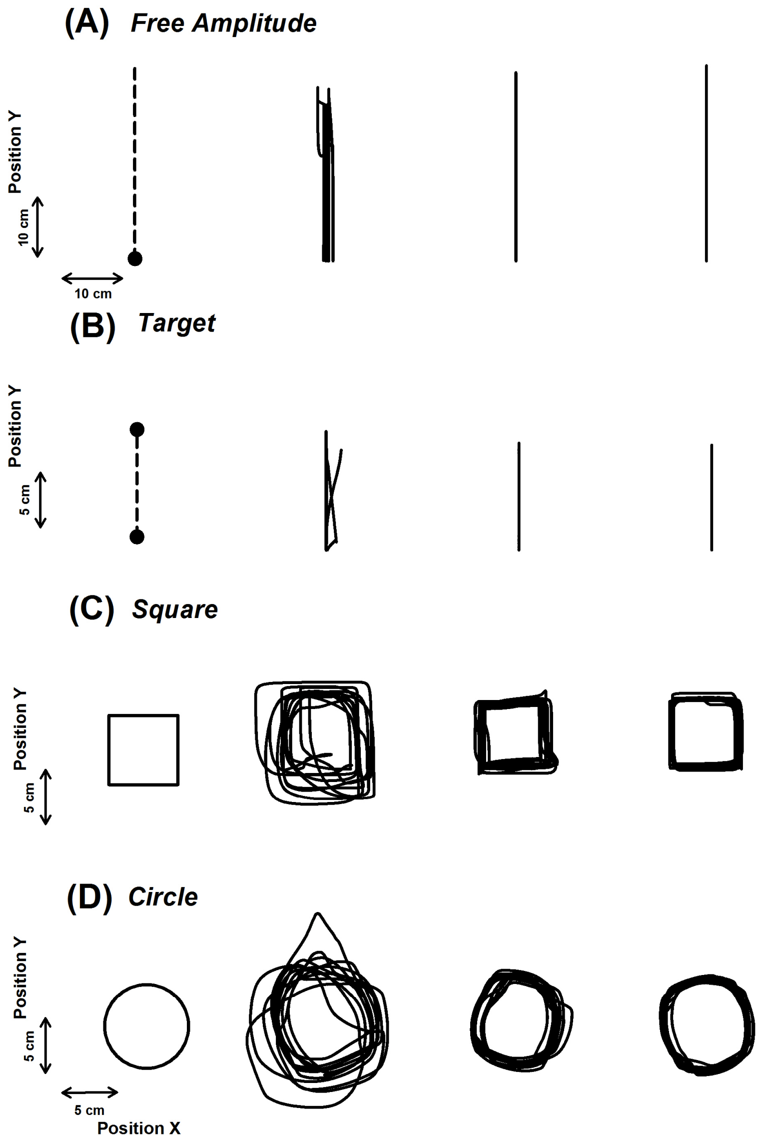

Figure 2: For each task (A, B, C, D), illustrations of the requested task presented on the visual interface (*first column*) and the tasks performed by children aged 4 years (second column), 8 years (*third column*) and 12 years (*fourth column*) are shown.

Placement of subjects
All of the subjects were placed in an ergonomic and standardized sitting position (Figure 3). The start position of the end-effector was centered and placed 13 cm in

front of the subject. The angle between each subject's hip and trunk was maintained at 120° to limit lumbar constraints. The children's feet were kept flat on a footrest for stability, and the trunk was secured with webbing to minimize movement compensations at this level.

Figure 3: Illustration of the ergonomic and standardized sitting position of a child aged five years.

Tasks

We[116] provided a standardized protocol to quantitatively assess active movements of the upper limb in stroke patients. This protocol consists of the performance of 4 different tasks with the REAplan. These tasks, which are illustrated in Figure 2 and are described below, were performed with the dominant arm and at spontaneous velocities.

For the Free Amplitude task, the subject had to reach straight out in front of them as far as possible and brought the arm back to the starting. For the Target task, the subject made movements in the most precise and direct manner toward a specific target placed a distance of 10 cm from the starting point in front of the subject. This target was placed closer than that in previous studies evaluating kinematics in adults to avoid amplitude limits in smaller children.[75,116] After performing this task, the robot brought the subject's arm back to the starting position. For the Square and

Circle tasks, the subject had to draw 2 geometrical shapes: a square with 6-cm sides and a circle with a 4-cm radius. Each shape was centered in front of the subject. These shapes were drawn clockwise with the right upper limb or counter-clockwise with the left limb. This last instruction enabled children to perform inward movements whatever the upper limb used. To summarize this protocol, the subjects performed rhythmic (i.e., Free Amplitude and Circle tasks) and discrete (i.e., Target and Square tasks) movements. The experiment started with a ten-minute training phase to limit learning bias. For the data-acquisition phase, the order of the tasks was randomly assigned. Each task was performed 10 consecutive times, and the rest period between each task was 1 minute.

Kinematic analysis

For each task, the elapsed time of the end-effector position was recorded by the robot. These variables were analyzed for each task using a specific customized program in a LabWindows/CVI (8.5) environment.

For the Free Amplitude task, the computed indices included the amplitude, velocity, straightness (ratio between the amplitude and path length covered by the subject; ratios closer to 1 indicate more rectilinear paths) and smoothness (ratio between the mean and peak velocity; ratios closer to 0 indicate less smooth movements)[75]. For the Target task, the amplitude index was replaced by a target inaccuracy index (distance between the target position and the end position achieved by the child; higher scores indicate more inaccurate movements). For the Square and Circle tasks, we computed the shape inaccuracy (distances mean between reference shape and shape drawn by the child; higher scores indicate more inaccurate movements)[116], velocity and smoothness indices. Each index in this protocol was computed from the 10 cycles of movement and was averaged. The coefficient of variation (CV), calculated from the subjects' 10 cycles of movement, was computed for each index.

Bruininks-Oseretsky test of motor proficiency (BOTMP)

Fine and gross motor skills were assessed with the Bruininks-Oseretsky test of motor proficiency (BOTMP), which is a standardized, validated, and reliable tool used in clinical and school practice settings for subjects between the ages of 4 and 21 years[113,119]. For this study, because we focused on the upper limbs, only 2 of the 8 subtests of the BOTMP were assessed: the Visual-Motor Control subtest and the Upper-Limb Velocity and Dexterity subtest. For the Visual-Motor Control subtest, a score ranging from 0 to 24 was obtained, with higher scores indicating better visual motor control. For the Upper-Limb Velocity and Dexterity subtest, a score ranging from 0 to 72 was obtained, with higher scores indicating better upper limb dexterity.

Session organization

For each investigation, two physiotherapists simultaneously assessed two children. The experiment started with the hand dominance test. After that, one child firstly performed the BOTMP and then, the kinematic assessment; the other child firstly performed the kinematic assessment and then, the BOTMP. For each pair of children, this order was randomized by lottery.

Statistical analysis

Age effect and reference standards for upper limb kinematics in children

For each kinematic index, a dynamic exponential curve (2 parameters) was fitted with the results of the 93 children using SigmaPlot 11.0 software (WPCubed GmbH, Munich, Germany). The equation for this curve provided the corresponding kinematic results for a specific age.

A correlation coefficient (r) related to each dynamic exponential curve was used to quantify the age effect. For each kinematic index, an age effect was considered if the $|r|$ was > 0.30, corresponding to a moderate to excellent correlation[12].

Construct validity

Correlations between each kinematic index and the score of each BOTMP subtest were performed with a Spearman correlation test using SigmaStat 3.5 software (WPCubed GmbH, Munich, Germany). A correlation was considered excellent, moderate or poor if the $|r|$ was >0.60, 0.30-0.60 or <0.30, respectively[12].

4. Results

All of the results are presented in Table 2 and illustrated in Figures 2, 4, 5 and 6.

Age effect and reference standards for upper limb kinematics in children

For each kinematic index, an equation corresponding to the reference standards of the upper limb kinematics in children is provided in Table 2. For each kinematic index, the age effect is illustrated in Figures 4 and 5 and is described below.

For the Free Amplitude task, all of the indices showed an age effect ($|r|$ range: [0.34; 0.85]). Indeed, the youngest children's movements were not as large, rectilinear, smooth, or fast compared to those of the older children. The youngest children also presented greater variability in amplitude, linearity, smoothness and velocity for the 10 cycles of movement (Table 2) (Figure 4).

For the Target task, 6 of 8 indices showed an age effect (│r│range: [0.30; 0.56]). Indeed, the youngest children's movements were less rectilinear and smooth than those of the older children. Moreover, the youngest children presented greater variability in inaccuracy, linearity, smoothness and velocity for the 10 cycles of movement. The target inaccuracy and velocity indices did not show any age effects (r = -0.23 and 0.05) (Table 2) (Figure 4).

For the Circle and Square tasks, 5 of 6 indices showed an age effect (│r│range: [0.30; 0.68]). Indeed, the youngest children's movements were less accurate and smooth than those of the older children. Moreover, the youngest children presented greater variability in inaccuracy, smoothness and velocity for the 10 cycles of movement. The velocity index (of both tasks) did not show any age effect (r = 0.05 and 0.10) (Table 2) (Figure 5).

Construct validity

Construct validity was calculated to examine the correlations between each kinematic index and the Visual-Motor Control and Upper Limb Velocity and Dexterity subtests of the BOTMP. For both subtests, the results of the 93 children are illustrated in Figure 6.

Sixteen of twenty-eight indices showed moderate to excellent correlations for both subtests (│r│ range: [0.41; 0.62]) (Table 2). The $CV_{velocity}$ (Free Amplitude task) and shape inaccuracy (Square task) indices showed moderate correlations with the Visual-Motor Control subtest (r = -0.30 and -0.35, respectively); however, there were no correlations with the Velocity and Dexterity subtest (r = -0.28 and -0.25, respectively) (Table 2). The other indices showed insignificant correlations (p>0.05) or poor correlations (p<0.05; │r│<0.3) with both subtests (Table 2).

Table 2: The coefficients (a and b) and the standard deviation (SD) of the equation corresponding to the child's kinematic result as a function of age for each kinematic index; the results of the age effect for each kinematic index; and the results of the Spearman's correlation test for each kinematic index and each BOTMP subtest.

				Coefficient correlation (r)		
	a	b	SD	*Age Effect*	*Visual-Motor Control (/24)*	*Velocity and Dexterity (/72)*
Free amplitude						
Amplitude (cm)	30.0	0.36	1.6	**0.85***	**0.50**	**0.58**
$CV_{amplitude}$ *(%)*	14.8	0.18	2.1	**-0.65***	**-0.56**	**-0.55**
Straightness	1.0	1.18	0.01	**0.57***	**0.25**	**0.26**
$CV_{straightness}$ *(%)*	6.5	0.25	1.1	**-0.52***	**-0.26**	**-0.25**
Velocity (cm/s)	15.1	0.26	4.6	**0.34***	**0.29**	**0.27**
$CV_{velocity}$ *(%)*	26.5	0.07	5.8	**-0.42***	**-0.30**	**-0.28**
Smoothness	0.64	0.28	0.07	**0.69***	**0.56**	**0.60**
$CV_{smoothness}$ *(%)*	25.6	0.09	4.5	**-0.55***	**-0.48**	**-0.42**
Target						
Target inaccuracy (cm)	1.1	0.03	0.3	**-0.23**	-0.12	-0.08
$CV_{target\ inaccuracy}$ *(%)*	79.0	0.09	16.3	**-0.52***	**-0.49**	**-0.56**
Straightness	1.0	1.18	0.01	**0.34***	**0.24**	**0.26**
$CV_{straightness}$ *(%)*	4.8	0.18	2.0	**-0.30***	**-0.22**	-0.19
Velocity (cm/s)	5.6	0.77	1.7	0.05	0.00	0.01
$CV_{velocity}$ *(%)*	49.8	0.10	9.6	**-0.56***	**-0.59**	**-0.62**
Smoothness	0.51	0.50	0.04	**0.48***	**0.53**	**0.49**
$CV_{smoothness}$ *(%)*	38.3	0.15	8.7	**-0.51***	**-0.52**	**-0.50**
Square						
Shape inaccuracy (cm)	1.4	0.01	0.13	**-0.30***	**-0.35**	**-0.25**
$CV_{shape\ inaccuracy}$ *(%)*	27.0	0.01	4.9	**-0.55***	**-0.53**	**-0.45**
Velocity (cm/s)	5.7	0.69	2.1	0.05	0.05	0.09
$CV_{velocity}$ *(%)*	37.1	0.12	5.0	**-0.68***	**-0.57**	**-0.55**
Smoothness	0.56	0.31	0.07	**0.58***	**0.41**	**0.54**
$CV_{smoothness}$ *(%)*	23.6	0.07	3.7	**-0.56***	**-0.43**	**-0.44**
Circle						
Shape inaccuracy (cm)	2.7	0.16	0.53	**-0.54***	**-0.56**	**-0.54**
$CV_{shape\ inaccuracy}$ *(%)*	51.5	0.07	9.1	**-0.51***	**-0.42**	**-0.45**
Velocity (cm/s)	7.9	0.51	4.0	0.10	-0.05	-0.02
$CV_{velocity}$ *(%)*	29.2	0.07	5.4	**-0.52***	**-0.46**	**-0.47**
Smoothness	0.65	0.39	0.11	**0.40***	0.21	**0.24**
$CV_{smoothness}$ *(%)*	20.85	0.07	3.9	**-0.49***	**-0.42**	**-0.45**

The underlined indices are related to the equation: $F=a.(1-e^{(-b.yrs)})$. For the other indices: $F= a.e^{(-b.yrs)}$.

* correspond to indices with age effects ($|r| > 0.3$)

Indices with a significant correlation ($p < 0.05$) are shown in bold

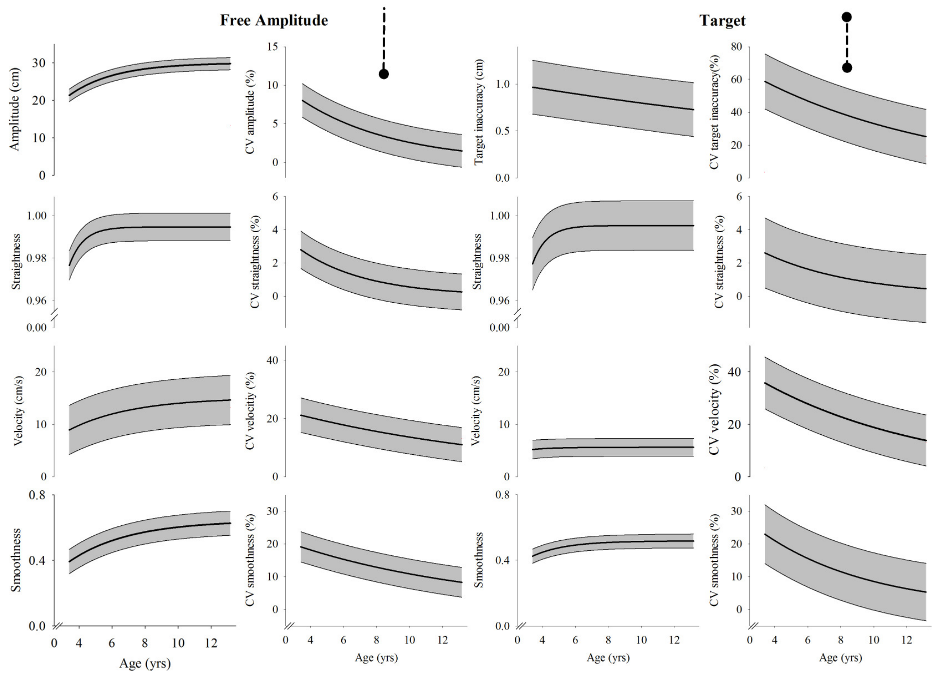

Figure 4: For each index of the Free Amplitude and Target tasks, illustrations of the reference standards of healthy children (corresponding to the black line ± SD [Grey area]) are shown as a function of age.

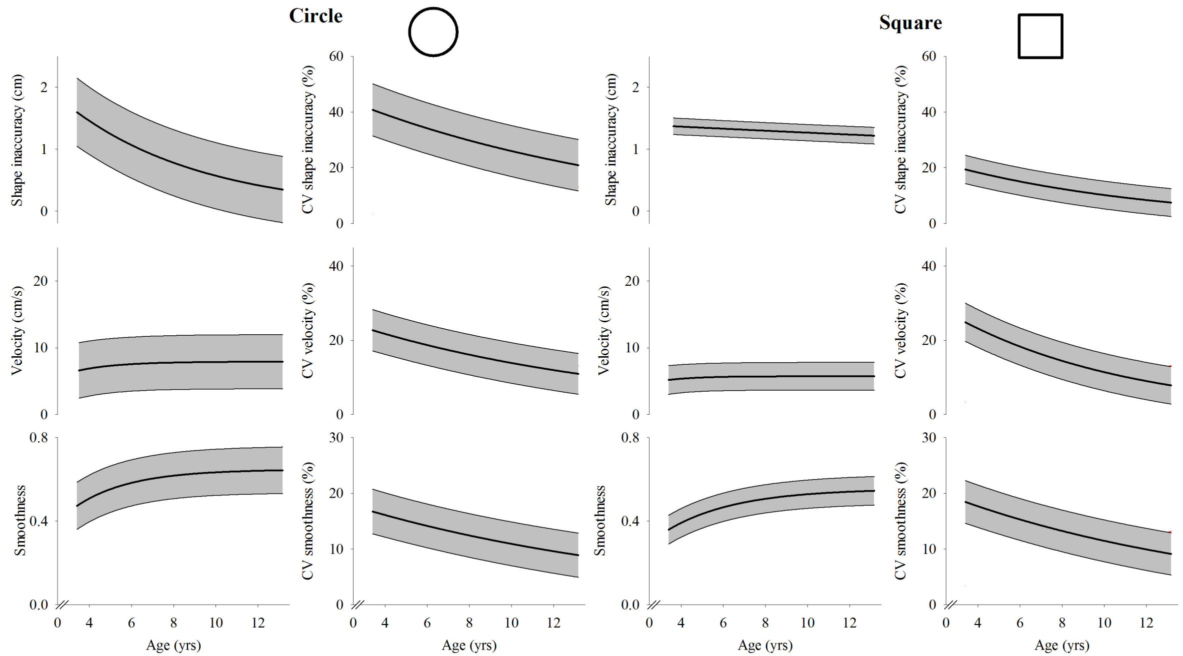

Figure 5: For each index of the Circle and Square tasks, illustrations of the reference standards of healthy children (corresponding to the black line ± SD [Grey area]) are shown as a function of age.

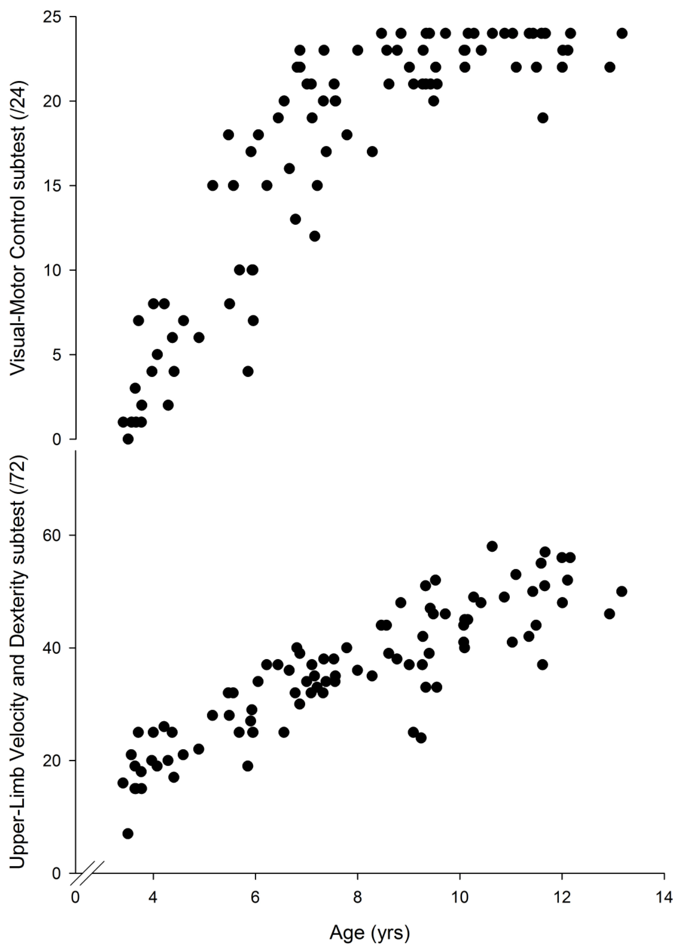

Figure 6: For each subtest of the BOTMP and as a function of age, the results of the 93 healthy children are shown (1 dot corresponds to 1 child's result).

5. Discussion

The aim of this study was to assess age effects and establish reference standards of upper limb kinematics in healthy children aged 3 to 12 years. These data enabled us to analyze the relationships between kinematics and visual-motor control and upper limb velocity and dexterity, as assessed with the Bruininks-Oseretsky test of motor proficiency.

Age effect and reference standards of kinematic indices obtained with a robot

For all of the tasks of the kinematic protocol, nearly all of the indices demonstrated an age effect in healthy children. However, some indices (e.g., the amplitude, straightness, and smoothness indices for the Free Amplitude and Target tasks [Figure 4] and the smoothness index for the Circle and Square tasks [Figure 5]) appeared to show an improvement of upper limb kinematics until the age of 8 years, after which time the indices showed a steady state. These results are in agreement with those of Olivier et al.[114], who showed changes of the upper limb kinematics in children between 5 and 8 years of age and no change in children between 8 and 11 years of age. Other indices (e.g., $CV_{velocity}$ and $CV_{smoothness}$ for all tasks [Figure 4 and 5]) seemed to show an improvement until the age of 12 years but they did not demonstrate a steady state. These results are in agreement with those of Petuskey et al.[115], who showed a significant improvement in upper limb displacement in subjects aged 5 to 18 years. Finally, for 3 of 4 tasks, the upper limb velocity of movement was identical for children aged 3 to 12 years. These results may be explained by one of our instructions, which instructed the children to perform movements at spontaneous velocities.

One can argue that the greater variability observed in younger children could be related to a training effect. We believe that the ten minute-training were adequate for all participants, even the younger ones, for two reasons. Firstly, the training effect was assessed through ten consecutive cycles of movement in the nine children aged three years old. For each index, each cycle of movement was analyzed separately, and the data submitted to a one-way repeated measures analysis of variance. No training effect was found for the different tasks (p-value > 0.05). Secondly, for the same tasks and ten minute-training, it was showed (i) no

training effect in adult stroke patients[116] and (ii) reproducible results in children with cerebral palsy (age range, in years: [5-18])[120] and adult stroke patients[116].
This study improves the current understanding of upper limb kinematics in children in 4 ways. First, development in children is often described through descriptive observations (e.g., older children show better movements)[111]. This study showed that descriptive observations could be quantified with kinematics. Second, this study followed the current recommendations by presenting, using a robot, reference standards of kinematic indices[39]. Third, previous studies assessed age effects and established reference standards by computing traditional kinematic indices, such as the range of motion and velocity[114,115]. In contrast, this study was the first to propose a protocol with detailed kinematic indices (i.e., inaccuracy, smoothness, straightness and reproducibility) to analyze the quality of children's upper limb movements. Fourth, contrary to previous studies[63,114,115], this study assessed upper limb kinematics in healthy children younger than 5 years of age, for whom motor skills are less developed than in older children[111].

Relationship between upper limb kinematics and upper limb visual-motor control, velocity and dexterity

In addition to the kinematic analyses computed with the REAplan, the children also performed 2 parts of the BOTMP. This assessment allowed us to analyze the correlations between each subtest and each kinematic index. The results obtained led to the establishment of construct validity for a kinematic protocol in children, as recommended by Sivan et al.[12]. The kinematic analysis, assessed with the REAplan, was then used to measure the Visual-Motor Control and the Upper-Limb Velocity and Dexterity in children aged 3 to 12 years. However, most correlations were moderate ($|r|<0.6$) because our protocol also assessed other aspects of the movements, such as the submovements[75], which could not be measured using classical psychomotor scales. These results are in accordance with those of Gilliaux et al.[116], who showed correlations in stroke patients between kinematic indices, assessed with the REAplan, and upper limb motor control and gross manual dexterity, assessed using the Upper Limb Sub-Score of the Fugl-Meyer Assessment[49] and the Box and Block test[121].

Correlations between the kinematic and psychomotor tests could have implications for therapists. Thus, it is important to identify disorders of the upper limb visual-motor and dexterity abilities to understand functional problems that children demonstrate at home, at school and during play. Between 5-6% of school-aged children show a developmental coordination disorder[122], which is a neuro-developmental condition that affects motor coordination and renders everyday tasks such as dressing, eating and playing more difficult[123]. Kinematics may represent a new objective, quantitative tool to detect and assess these conditions. Additionally, kinematics allows for the comparisons of supposed healthy children to clear standards, which could enable psychomotor therapists to detect delays in motor development and follow the evolution of development over time.

Limitations and perspectives

Our study sample was limited to children with a maximum age of 12 years, and upper-limb kinematics may continue to change after 12 years of age[115]. Thus, further studies are necessary to evaluate the evolution of kinematic indices beyond 12 years of age and to define the age limit of maturity for those indices. It could also be interesting to examine whether there is an optimal age for kinematics and whether there is deterioration with age.

Kinematic indices have been computed for patients in different studies[12,56,116,117,120]. Researchers or clinicians could use this norm-referenced protocol to (1) objectify impairments in CP children and (2) provide a sensitive way to assess changes in response to intervention, such as robotic-assisted therapy[100,120], or following injections of upper limb botulinum toxin[72,73].

The REAplan conception allows end-effector movements in 2 spatial dimensions (2D). Despite these horizontal plane movements, the shoulder and elbow movements involve displacements in 3D. Further studies could apply this protocol to an exoskeleton robotic device[124] or an optical tracking system[63], which assess upper limb movements in 3D.

6. Conclusions

This study was the first to use a robotic device to assess the effect of age and establish reference standards for upper limb kinematics in healthy children aged 3 to 12 years old. This study also showed correlations between kinematics and visual motor control and upper-limb velocity and dexterity. This research has contributed to enhance the assessment of upper limb kinematics in children. These results could be used to routinely evaluate the performance of a child at a specific age and assess the child's progress over time. Moreover, the use of a robotic device enables accurate, objective and sensitive assessments and is especially appropriate for body function measurements in children.

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Chapter 2

Age effects on upper limb kinematics assessed by the REAplan robot in healthy subjects aged 3 to 93 years

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1. Abstract

Kinematics is recommended for the quantitative assessment of upper limb movements. The aims of this study were to determine the age effects on upper limb kinematics and establish reference standards in healthy subjects. Three hundred and seventy healthy subjects, aged 3 to 93 years, participated in the study. They performed two unidirectional and two geometrical tasks ten consecutive times with the REAplan, a distal effector robotic device that allows upper limb displacements in the horizontal plane. Twenty-eight kinematic indices were computed for the four tasks. For the four tasks, nineteen of the computed kinematic indices showed an age effect. Seventeen indices (the inaccuracy, velocity and smoothness indices and the reproducibility of the inaccuracy, velocity and smoothness) improved in young subjects aged 3 to 30 years, showed stabilization in adults aged 30 to 60 years and declined in elderly subjects aged 60 to 93 years. Additionally, for both geometrical tasks, the velocity index exhibited a decrease throughout life. This study is the first to assess age effects on upper limb kinematics and establish reference standards in subjects aged 3 to 93 years.

Keywords: Robotics; Pediatrics; Adult; Aged; Kinematics; Outcome Assessment; Healthy Volunteers; Biomechanics; Reference Standards; Growth and Development; Ageing

2. Introduction

Motor abilities in healthy subjects evolve during their lives. Children display uncontrolled upper limb movements in the first months after birth, after which they develop reaching and grasping movements in the first year of life. These abilities are transferred to activities of daily living (ADLs) (such as eating and dressing) in subsequent years[111]. Subsequently, young adults maintain or improve these abilities by performing physical activities[125]. Finally, a decrease in physical performance and functional abilities is considered to appear progressively in the elderly[126–128]. However, this evolution throughout life has not yet been proven based on objective and quantitative measures.

Indeed, the upper limb motor ability of subjects, regardless of their age, is typically described through observations, interviews, and standardized and non-standardized assessments[112,113,128]. The majority of these measures are subjective and employ ordinal scales[112,113,128]. Several authors have recommended the use of kinematics to objectively and quantitatively assess upper limb movements in subjects to avoid the drawbacks of ordinal scales[12,39,45,116,117,129].

The evolution of subjects' upper limb kinematics across various ages has been investigated in healthy subjects. Previous studies have demonstrated the effects of age on upper limb kinematics in children aged from 3 to 18 years[115,129]. Olivier et al.[114] showed progress in upper limb kinematics over time by comparing children (age range in years: [6-11]) and young adults (mean age in years: 38). Finally, some studies have objectified the ageing of upper limb kinematics by comparing young adults (age range in years: [20-23]) and the elderly (age range in years: [70-80])[130,131]. However, the sample sizes and age criteria employed in these studies were limited and did not allow the authors to (i) quantify the evolution of upper limb kinematics throughout life or (ii) determine an age limit of maturity for upper limb kinematics. The development of children, the age limit for maturity among subjects and ageing might be objectified with upper limb kinematics, which has never been studied.

The present study investigated the evolution of upper limb kinematics throughout life. Even though the motor development of subjects during their lives has been well described[111,125–127], this study aimed to quantify this evolution and to establish reference standards for upper limb kinematics in healthy subjects aged 3 to 93 years.

The present study is linked with a previous study[129] assessing the age effects on upper limb kinematics in ninety-three healthy children aged three to twelve years using the REAplan. The REAplan is an end-effector robotic device that can mobilize a subject's upper limb by carrying the hand or the forearm along paths included in a horizontal plane[38]. The results showed that twenty-four of the twenty-eight computed kinematic indices improved during childhood (older children exhibited better upper limb movements).

3. Materials and Methods

Subjects

Three hundred and seventy healthy subjects participated in this study. These subjects were recruited from a nursery, a primary school (*chapelle-aux-champs* school, Brussels), a high school (*Lycée Martin V*, Louvain-la-Neuve), a university (Université catholique de Louvain, Brussels and Louvain-la-Neuve) and a nursing home (*Le Point du Jour, Bierges*). The inclusion criteria consisted of an age greater than 3 years and adequate cognition skills for following instructions. These skills were verified by checking the correct application of instructions in all subjects and a score greater than 24/30 on the Mini Mental State Examination in elderly individuals older than 75 years. The exclusion criterion was the presence of any disorder that could alter the movements of the tested upper limb. The participants were recruited to obtain a homogeneous sample in each age group. The characteristics of the included subjects and the sample size of each age group are reported in Table 1. All of the participants and the children's parents received an informative letter explaining the nature, aim and duration of the experiment, and all of these individuals provided informed consent. The ethics board of our Faculty of Medicine approved this study.

Hand dominance

The following test was used to determine hand dominance in children less than 13 years: each child was asked to pick up and throw a ball while the examiner observed which hand was used. For the older subjects, the dominant hand corresponded to the hand mainly used in ADL, such as writing

Table 1: Characteristics of the subjects and sample size of each age group.

	Healthy subjects (n=370)								
Age range (*yrs*)	3-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-93
Sample (n)	78	70	55	46	29	21	19	18	34
Age *(yrs)*, mean (SD)	7.0 (2.2)	14.5 (2.5)	25.0 (2.9)	35.8 (3.0)	45.1 (2.9)	55.5 (2.7)	65.2 (2.3)	75.3 (3.0)	86.9 (4.0)
Gender *(male/female)*, n	32/46	29/41	34/21	28/18	12/17	7/14	8/11	9/9	10/24
Weight (*kg*), mean (SD)	25.3 (8.1)	54.0 (11.9)	68.6 (12.0)	71.8 (15.3)	71.3 (18.4)	68.5 (12.1)	68.3 (12.0)	61.9 (8.5)	60.6 (13.4)
Height (*m*), mean (SD)	1.24 (0.2)	1.66 (0.11)	1.75 (0.09)	1.74 (0.10)	1.71 (0.11)	1.72 (0.07)	1.69 (0.09)	1.66 (0.07)	1.63 (0.11)
BMI *(kg/m^2)*, mean (SD)	15.8 (2.3)	19.4 (2.5)	22.3 (2.9)	23.4 (3.8)	24.7 (6.3)	23.3 (3.0)	23.7 (2.3)	22.4 (2.5)	22.7 (2.3)
Dominant arm *(right/left)*,n	73/5	63/7	49/6	38/8	28/1	21/0	17/2	18/0	31/3

Abbreviations: BMI = body mass index, SD = standard deviation

Kinematic assessment

All participants were subjected to the protocol described in the previous chapter[129]. Twenty-eight kinematic indices were computed from two unidirectional tasks (i.e., reaching a target and performing a back-and-forth movement) and two geometrical tasks (i.e., drawing a circle and a square). These tasks, which are illustrated in Figure 1, were performed ten consecutive times with the dominant arm at spontaneous velocities using REAplan. The REAplan is a distal effector robotic device that allows for upper limb displacements in the horizontal plane (Figure 2). The upper limb movements were performed without assistance from the robot[129]. For each task, the elapsed time of the end-effector position was recorded by the robot (acquisition frequency 125 Hz). Each kinematic index (i.e., amplitude, inaccuracy, straightness, velocity and smoothness [assessed using the speed metric index[75]]) evaluated in this protocol was computed from these ten cycles of movement and was then averaged. A coefficient of variation (CV), calculated from the subjects' ten cycles of movement, was computed for each index.

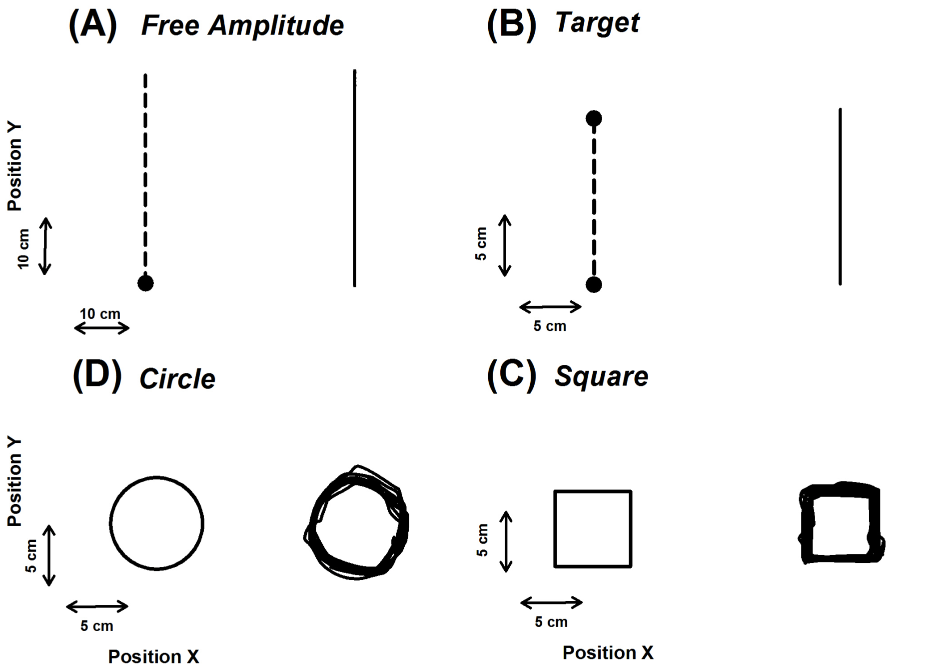

Figure 1: For each task (A, B, C, D), illustrations of the requested task presented on the visual interface (first column) and the ten cycles of movement performed by a subject aged 40 years (second column) are shown.

Figure 2: View of the REAplan. 1: planar end-effector robot; 2: visual interface for the subject; 3: physiotherapist's interface.

Statistical analysis

Age effects for upper limb kinematics

For each kinematic index, a polynomial quadratic curve was fitted based on the results for the three hundred and seventy subjects using SigmaPlot 11.0 software (WPCubed GmbH, Munich, Germany). A correlation coefficient (r) related to each polynomial quadratic curve was used to quantify the age effects. For each kinematic index, an age effect was considered to occur if the r coefficient was ≥ 0.30, corresponding to a moderate (r range [0.30-0.60]) to excellent (r > 0.60) correlation[12,129].

Reference standards for upper limb kinematics

Reference standards were established as a function of the age effect results. For each index that was significantly influenced by age ($r \geq 0.30$), the reference standard corresponded to the equation for the polynomial quadratic curve (i.e., $F = a.yrs^2 + b.yrs + c$) providing the corresponding kinematic results for a specific age. In addition, a second equation of a polynomial quadratic curve (i.e., $F = a.yrs^2 + b.yrs + c$) was computed to provide the variation of these kinematic results (i.e., standard deviation [SD]) for a specific age. For each index that was not influenced by age ($r < 0.30$), the reference standard corresponded to the average and SD of the results for the three hundred and seventy subjects.

Principal component analysis

The correlations between the kinematic indices, tasks and subjects' age were investigated. A principal component analysis (PCA) was performed using StatView 5.0 software (SAS Institute, Cary, NC, USA) with the following model:

$$Y = PX,$$

where X is the original subjects' kinematic results and age of subjects. X corresponds to the m x n matrix, where m = 29 (kinematic indices and age) and n = 370 (subjects number). Y corresponds to the new results, resulting from of the orthogonal linear transformation P (using Varimax transformation). Thus, Y corresponds to a new m x n matrix, where m = 4 (principal components) and n = 29 (kinematic indices and age). The eigenvalues magnitude and variance proportions of each principal component are computed. The Bartlett's Chi Square of this PCA was also calculated. Finally, for each principal component, we highlighted the correlated variables with a factor loading ≥ 0.60, corresponding to an excellent correlation[12].

4. Results

All of the results are presented in Tables 2 and 3 and illustrated in Figures 3, 4 and 5. For the Free Amplitude task, the greater subjects did not reach as far as they could because their movements were halted by the robot's mechanical stop. Hence, the amplitude and $CV_{amplitude}$ indices were removed from the analyses.

Age effects and reference standards for upper limb kinematics

For each kinematic index, the age effects and reference standards are illustrated in Figures 4 and 5 and are described below.

For the Free Amplitude task, four of the six indices showed an age effect (r range [0.40-0.54]). Indeed, the velocity and smoothness indices exhibited an increase from 3 to 30 years, a steady-state between 30 and 60 years and a decrease from 60 to 93 years. Moreover, the velocity and smoothness results were more reproducible during the ten cycles of movements in young adults (age range in years = [30-60]) than in children (< 30 years) and older adults (> 60 years). The two other indices did not show any age effect (r = 0.25 and 0.28) (Table 2; Figure 4).

For the Target task, three of the eight indices showed an age effect (r range: [0.30-0.57]). Indeed, the target inaccuracy index exhibited a steady state from 3 to 40 years and a decrease from 40 to 93 years. The velocity index showed an increase from 3 to 30 years, a steady-state between 30 and 60 years and a decrease from 60 to 93 years. Moreover, the velocity results were more reproducible during the ten cycles of movements in older adults (> 60 years) than in younger subjects (< 60 years). The five other indices did not exhibit any age effect (r range: [0.07-0.22]) (Table 2; Figure 4).

For both geometrical tasks, all of the indices showed an age effect (r range: [0.30-0.70]). Indeed, the shape inaccuracy index exhibited a decrease from 3 to 30 years, a steady-state between 30 and 60 years and a decrease from 60 to 93 years. Furthermore, the velocity index decreased throughout life, and the smoothness index showed an increase from 3 to 30 years, a steady-state between 30 and 50 years and a decrease from 50 to 93 years. Finally, the inaccuracy, velocity and smoothness results were more reproducible during the ten cycles of movements in adults (age range in years: [30-60]) than in young subjects (< 30 years) and older adults (> 60 years) (Table 2; Figure 5).

The coefficients of the equations (F= a.yrs^2 + b.yrs + c) are provided for each kinematic index that was influenced by age (Table 2). For each kinematic index that was not influenced by age, the reference standards corresponded to the mean of results and SD for the three hundred and seventy subjects (Table 2).

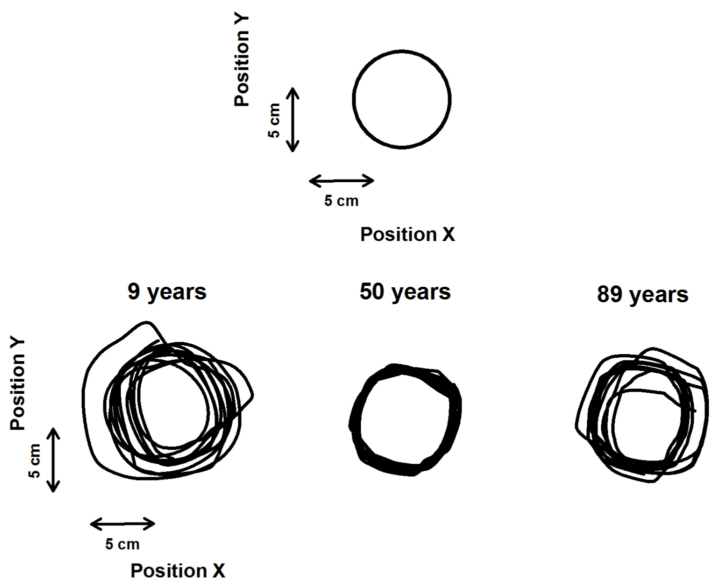

Figure 3: Example of the evolution of upper limb kinematics throughout life. For the Circle task, an illustration of the requested Circle task (upper graph) presented on the visual interface and the Circle task performed (lower graphs) by a child (first column), an adult (second column) and an elderly subject (third column) are shown.

Table 2: Results regarding age effects for each kinematic index; for each kinematic index showing an age effect, the coefficients (a, b and c) of the equation corresponding to the subjects' kinematic results (Mean) and the 2 standard deviation (2SD) as a function of age ($F= a.yrs^2 + b.yrs + c$) are presented; for each kinematic index without an age effect, the mean and the 2SD corresponding to the subjects' kinematic results are presented regardless of their age.

	Age effect	Mean	Kinematic result in a function of age			2SD	2SD in a function of age		
			a	b	c		a	b	c
Free Amplitude									
Straightness	0.25	1.00				0.02			
$CV_{straightness}$ *(%)*	0.28	0.7				1.8			
Velocity (cm/s)	0.50*		-0.005	0.369	12.1		-0.004	0.300	8.1
$CV_{velocity}$ *(%)*	0.41*		0.004	-0.303	16.1		0.001	-0.026	9.6
Smoothness	0.40*		-4.4 E-05	0.003	0.54		3.4 E-05	-0.002	0.13
$CV_{smoothness}$ *(%)*	0.54*		0.004	-0.387	14.9		0.001	-0.109	8.6
Target									
Target inaccuracy (cm)	0.30*		-5.4 E-05	2.0 E-04	1.0		-2.7 E-05	0.001	0.7
$CV_{target\ inaccuracy}$ *(%)*	0.07	46.6				42.6			
Straightness	0.11	0.98				0.1			
$CV_{straightness}$ *(%)*	0.09	2.3				11.4			
Velocity (cm/s)	0.57*		-0.005	0.408	6.5		-0.003	0.180	5.4
$CV_{velocity}$ *(%)*	0.46*		0.002	-0.340	27.0		0.002	-0.278	19.5
Smoothness	0.08	0.48				0.12			
$CV_{smoothness}$ *(%)*	0.22	16.2				23.2			
Circle									
Shape inaccuracy (cm)	0.34*		1.0 E-04	-0.012	0.88		2.0 E-04	-0.022	0.7
$CV_{shape\ inaccuracy}$ *(%)*	0.52*		0.005	-0.578	32.4		0.002	-0.224	18.4
Velocity (cm/s)	0.50*		2.0 E-04	-0.078	8.3		0.001	-0.142	8.3
$CV_{velocity}$ *(%)*	0.49*		0.005	-0.416	17.8		0.003	-0.173	10.5
Smoothness	0.62*		-8.4 E-05	0.005	0.59		1.1 E-05	-0.001	0.20
$CV_{smoothness}$ *(%)*	0.44*		0.003	-0.234	13.5		0.001	-0.097	7.9
Square									
Shape inaccuracy (cm)	0.30*		8.3 E-05	-0.008	0.67		2.0 E-04	-0.018	0.5
$CV_{shape\ inaccuracy}$ *(%)*	0.51*		0.004	-0.462	33.4		0.002	-0.239	18.6
Velocity (cm/s)	0.58*		-3.0 E-04	-0.024	6.3		2.2 E-05	-0.038	4.5
$CV_{velocity}$ *(%)*	0.40*		0.003	-0.282	14.8		0.003	-0.205	10.1
Smoothness	0.70*		-7.8 E-05	0.005	0.49		8.5 E-06	-2.0 E-04	0.11
$CV_{smoothness}$ *(%)*	0.44*		0.003	-0.212	13.7		9.0 E-04	-0.039	7.0

* indicates indices with age effects ($p<0.001$; $r \geq 0.3$)

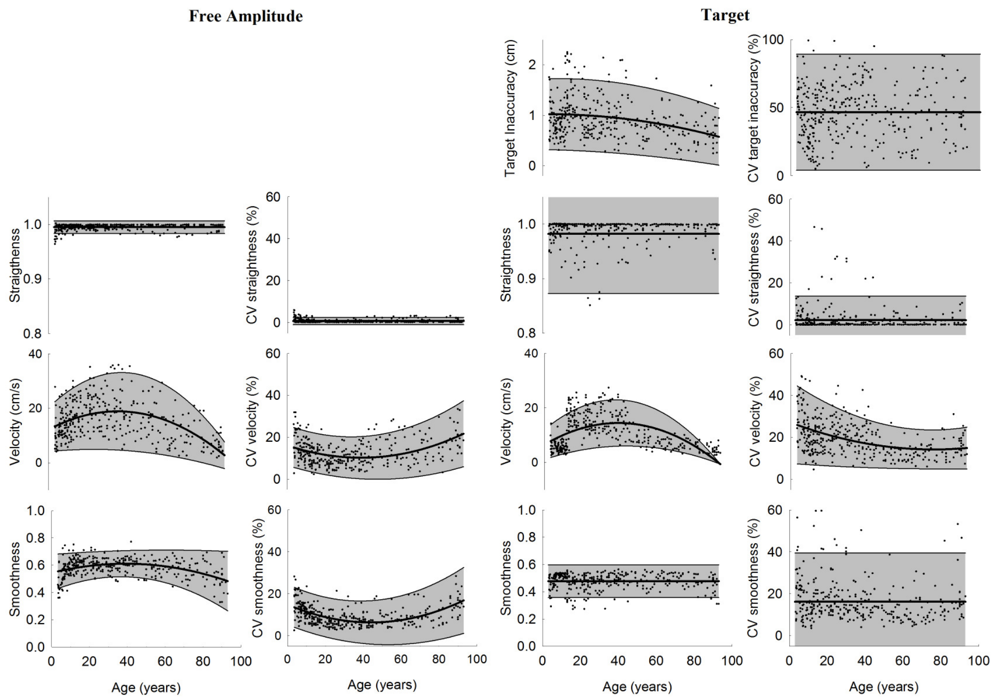

Figure 4: For each index assessed in the Free Amplitude and Target tasks, illustrations of the reference standards for healthy subjects (corresponding to the black line ± 2 SD [Grey area]; 1 point corresponds to 1 subject's result) are shown as a function of age.

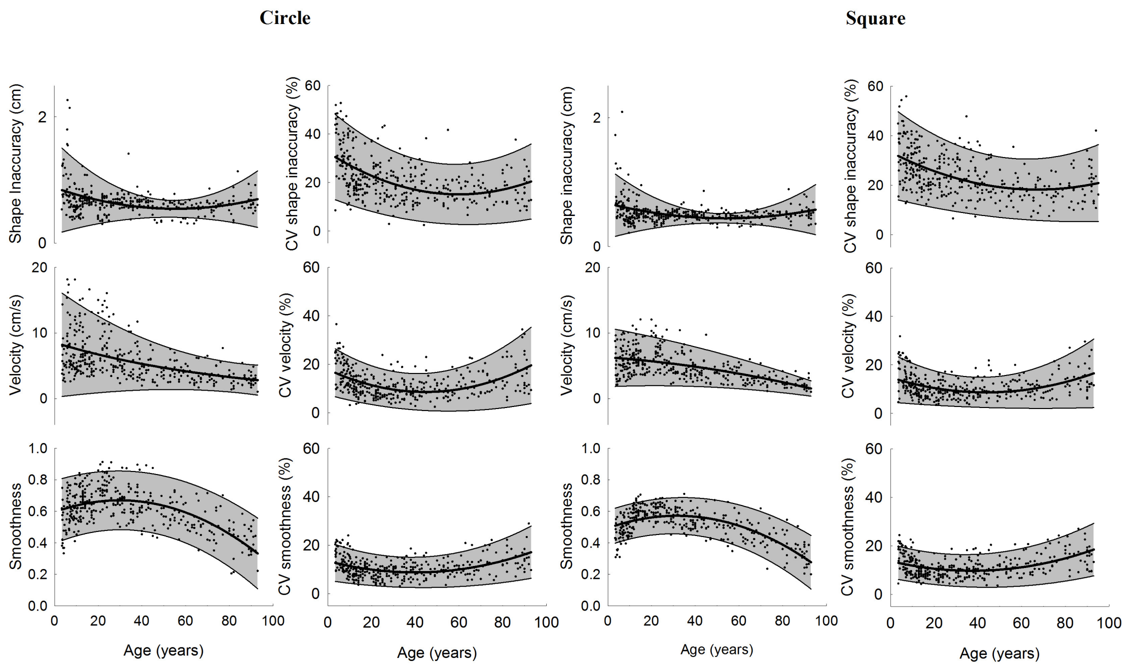

Figure 5: For each index assessed in the Circle and Square tasks, illustrations of the reference standards for healthy subjects (corresponding to the black line ± 2 SD [Grey area]; 1 point corresponds to 1 subject's result) are shown as a function of age.

Principal component analysis

As indicated above, the amplitude and $CV_{amplitude}$ data were removed from the analyzed matrix [X] of the PCA. The Bartlett's Chi Square was equal to 4639.6 (p-value < 0.001). The new matrix [Y] resulting from the PCA is presented in Table 3. The factor loading of each kinematic index, the variance proportions and the eigenvalues magnitude are provided for the four principal components (Table 3).

The two first principal components showed that subjects' age and kinematic indices computed from the Circle, Square and Target tasks were correlated as follows (Table 3):

- The smoothness and $CV_{smoothness}$ indices (both geometrical tasks), the velocity index (Target task) loaded on the first principal component ($|r|$ range: [0.65-0.80]).
- The velocity index (both geometrical tasks), $CV_{shape\ inaccuracy}$ (Circle task), and age loaded on the second principal component ($|r|$ range: [0.66-0.79]).

The two last principal components showed that the kinematic indices computed from the Free Amplitude and Target tasks were correlated as followed (Table 3):

- The straightness, $CV_{straightness}$, smoothness and $CV_{smoothness}$ indices (Target task) loaded on the third principal component ($|r|$ range: [0.73-0.84]).
- The straightness, $CV_{straightness}$ and $CV_{smoothness}$ indices (Free Amplitude task) loaded on the fourth principal component ($|r|$ range: [0.68-0.80]).

Table 3: Factor loadings of the principal component analysis for the three hundred and seventy subjects for age and twenty-six kinematic indices.

	PC 1 (factor loading)	PC 2 (factor loading)	PC 3 (factor loading)	PC 4 (factor loading)
Age (yrs)	-0.37	**-0.66**	0.04	-0.16
Free Amplitude				
Straightness	0.11	-0.16	0.00	**-0.80**
$CV_{straightness}$ (%)	-0.18	0.18	-0.04	**0.78**
Velocity (cm/s)	0.47	0.33	0.22	-0.32
$CV_{velocity}$ (%)	-0.52	-0.07	-0.03	0.41
Smoothness	0.39	0.11	-0.12	-0.42
$CV_{smoothness}$ (%)	-0.39	0.04	-0.01	**0.68**
Target				
Target inaccuracy (cm)	0.53	0.02	0.09	0.32
$CV_{target\ inaccuracy}$ (%)	-0.13	0.12	0.35	-0.36
Straightness	-0.10	-0.03	**-0.84**	0.04
$CV_{straightness}$ (%)	0.07	0.05	**0.83**	-0.05
Velocity (cm/s)	**0.66**	0.06	0.27	-0.14
$CV_{velocity}$ (%)	0.13	0.48	0.40	0.22
Smoothness	-0.01	-0.01	**-0.73**	0.01
$CV_{smoothness}$ (%)	0.09	0.03	**0.83**	0.06
Circle				
Shape inaccuracy (cm)	-0.19	0.58	0.10	-0.06
$CV_{shape\ inaccuracy}$ (%)	-0.16	**0.75**	0.03	0.10
Velocity (cm/s)	0.35	**0.79**	-0.02	-0.09
$CV_{velocity}$ (%)	-0.59	0.26	0.04	0.21
Smoothness	**0.69**	0.55	0.00	-0.17
$CV_{smoothness}$ (%)	**-0.68**	-0.08	0.09	0.15
Square				
Shape inaccuracy (cm)	-0.17	0.48	0.09	0.02
$CV_{shape\ inaccuracy}$ (%)	0.07	0.58	-0.02	0.07
Velocity (cm/s)	0.49	**0.75**	0.01	-0.03
$CV_{velocity}$ (%)	-0.53	0.30	0.00	0.18
Smoothness	**0.80**	0.31	0.05	-0.12
$CV_{smoothness}$ (%)	**-0.65**	0.04	-0.11	0.06
Variance proportions, %	23	14	11	6
Eigenvalue magnitude	6.2	3.9	2.9	1.7

Abbreviations: PC: principal component; CV: coefficient of variation.

For each principal component, the correlated indices (factor loading ≥ 0.60) are shown in bold.

5. Discussion

The aims of this study were to assess the age effects and establish reference standards for upper limb kinematics in three hundred and seventy healthy subjects aged between 3 and 93 years. The correlations between the subjects' kinematic results and their age were also investigated based on PCA.

Age effects and reference standards for upper limb kinematics

For all of the tasks assessed in this study, two third of the computed kinematic indices showed an age effect. Upper limb kinematics improved in young subjects aged from 3 to 30 years, were stable in adults aged between 30 and 60 years and declined in elderly subjects aged from 60 to 93 years. These results were consistent with previous studies that have shown maturation of upper limb movements in children aged from 3 to 18 years[115,129] and significant ageing in the elderly[130,131]. Indeed, older children's movements (> 8 years) were larger[115,129], smoother, and more linear, accurate and reproducible[129] than younger children's movements (< 8 years). Moreover, the movements of elderly individuals (age mean ± SD in years: [75.3 ± 4.0]) were slower and less smooth than the movements of young adults (age mean ± SD in years: [22.1 ± 0.1])[130]. Surprisingly, the velocity index for both geometrical tasks decreased throughout life. The velocity of the upper limb movements may have been influenced by the "spontaneous velocities" instruction. This instruction was essential to allow the subjects to perform natural movements. However, the maximum velocity abilities of the upper limbs were not assessed[20]. Thus, further experiments could specifically assess the evolution of the maximum velocity abilities of the upper limb in healthy subjects throughout life.

The current study completes our biomechanical understanding of upper limb ability throughout life. This study is in accordance with the findings of Mathiowetz et al.[132,133], who quantified the evolution of manual dexterity in 1,099 healthy subjects aged between 6 and 94 years using the box and block test. These authors showed that manual dexterity improved from 6 to 24 years of age and progressively declined from 25 to 94 years of age. However, although human development throughout life has been well characterized[111,125–127], the current work and that of Mathiowetz et al.[132,133] are the only studies to quantify this evolution using upper limb kinematics[39] and manual dexterity[132,133].

Finally, researchers and clinicians could use this norm-referenced protocol to assess upper limb kinematics in patients. Previous studies have quantified the kinematic alterations of the upper limbs in children with cerebral palsy[58,120], young adults with multiple sclerosis[134,135] and older adults with stroke[12,39,116] or Parkinson disorders[136,137]. Hence, this norm-referenced protocol could characterize various disorders regardless of the patient age. Then, our protocol could be computed to monitor the evolution of upper limb kinematics in patients during rehabilitation, for example, when employing robot-assisted therapy[34,60,61,120], constraint-induced movement therapy[79] and botulinum toxin[72,73,80]. Finally, a robot is an assessment tool but also a rehabilitation tool. Kinematic analyses computed during robot-assisted therapy could enable the device to adapt the level of assistance provided to the patients in real time[120].

Principal component analysis

The correlations between kinematic indices computed from four tasks and the subjects' age were investigated through PCA to limit redundancy within this protocol. In this section, the tasks and indices that should be included in each assessment of upper limb kinematics performed in healthy subjects or patients are discussed.

Both unidirectional tasks should be included in each kinematic assessment of the upper limbs, as recommended by Gilliaux et al.[116]. Indeed, both unidirectional tasks assessed separate movement characteristics because these tasks were uncorrelated between them and with geometrical tasks (Table 3). Moreover, both tasks assess rhythmic (i.e., Free Amplitude) and discrete (i.e., Target) movements, which involve different neuronal mechanisms[138]. In addition to the two unidirectional tasks, one of the geometrical tasks should be included in each assessment for two reasons. First, the two geometrical tasks were correlated with each other but were not correlated with the two unidirectional tasks (Table 3). Second, assessing only one geometrical task could allow a less time-consuming assessment to be performed and limit the exhaustion of patients with severe impairments. Finally, some kinematic indices were correlated with each other (see Table 3) and should not be included in the same assessment. In summary, a comprehensive assessment of upper limb kinematics should include both unidirectional tasks and one geometrical task. For each task, only one index highlighted in Table 3 should be computed. These recommendations could enable clinicians and researchers to *(i)* avoid results redundancy and *(ii)* facilitate the monitoring of healthy subjects' evolution over time and patients' progress during therapy.

6. Conclusions

This study was the first to assess the effect of age and establish reference standards for upper limb kinematics in healthy subjects aged 3 to 93 years. Researchers and clinicians could use this norm-reference protocol to (i) quantitatively and objectively assess upper limb movements in subjects, regardless of their age and pathology, and (ii) monitor healthy subjects' evolution over time and patients' progress during therapy. A robotic device is a rehabilitation tool but also an assessment tool. Robotic assessment of upper limb kinematics could improve accuracy, objectivity and sensitivity in routine assessments performed in clinical and research settings.

Acknowledgements

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Chapter 3

A robotic device as a sensitive quantitative tool to assess upper limb impairments in stroke patients: a preliminary prospective cohort study.

Maxime Gilliaux, Thierry Lejeune, Christine Detrembleur, Julien Sapin, Bruno Dehez, and Gaëtan Stoquart.

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1. Abstract

Objective: To compare kinematic indices in age-matched healthy subjects and stroke patients, by evaluating various tasks performed with a robotic device, and provide an objective and standardized protocol to assess upper limb impairments in stroke patients.
Design: A prospective cohort study. Subjects: Age-matched healthy subjects (n=10) and stroke patients (n=10). Methods: Various kinematic indices were analyzed from three randomly assigned tasks performed by the affected arm in stroke patients and the dominant arm in healthy subjects. These tasks, composed of large amplitude, targeted and geometrical movements, were standardized and performed with the REAplan robotic device. Results: For large-amplitude movements, the stroke patients' path lengths were less constant in amplitude, less rectilinear and less smooth than healthy subjects ($p<0.001$). For the targeted movements, the stroke patients' path lengths were less rectilinear than the healthy subjects ($p<0.001$). For the geometrical movements, the stroke patients had greater difficulty drawing the requested shapes compared with the healthy subjects ($p<0.01$).
Conclusion: Our study proposes an objective and standardized protocol to assess stroke patients' upper limbs with any robotic device. We suggest that further randomized controlled trials could use this quantitative tool to assess the efficacy of treatments as robot-assisted therapy.

Keywords: robotics, outcome assessment, biomechanics, stroke, upper extremity.

2. Introduction

Fifteen million people throughout the world suffer from cerebral vascular accidents each year[9] and one third of these individuals display permanent neurological impairments[9]. An intensive and prolonged multidisciplinary rehabilitation has been shown to reduce the neurological impairments and improve patients' activities and participation[139,140].

To evaluate the active movements of stroke patients' upper limbs before and after rehabilitation as robotic-assisted therapy (RAT)[14,92,141–143], some authors have recommended the use of kinematic measures to quantitatively and objectively assess upper limbs[12,142] while avoiding the disadvantages of ordinal and qualitative scales[12].

Kinematic indices could be obtained with a distal effector robotic system used in RAT[12,19,20,34,60,75,144]. Some of these indices have been studied in stroke patients[12,19,20,34,60,75,144], primarily in trials evaluating RAT efficacy[12,19,20,34,60]. Although various indices have been described, such as target inaccuracy[34], amplitude of movement[19,20], straightness[19,60,144], velocity of movement[19,20,60], peak velocity of movement[60] and smoothness[34,60,75,144], no consensus about the choice of these kinematic indices has been clearly described in the literature.

Kinematic indices have been computed from various tasks, such as pointing at one[34] or multiple targets[60,75,144], moving as far as possible in various directions[19,20], and carrying out geometrical movements[144]. Although several studies used the fastest velocity of displacement possible[19,20], other studies did not take the velocity of displacement into account[34,60,144]. In addition, some tasks have been performed without any constraints, where as others have been performed by applying assistance or constraints to the subjects[76,77]. Furthermore, kinematic assessments have been performed in two (2D[34,60,75,76,144]) or three spatial dimensions (3D[19,20,77]). No study has clearly demonstrated which movements or instructions are the most relevant.

The sensitivity of kinematic indices and specific tasks to detect impairments has only been studied by comparing patients who received RAT with patients who did not receive RAT[19,34] Interestingly, no study has compared kinematic indices between age-matched healthy subjects and stroke patients using a distal effector without any assistance or constraint.

According to all the previous considerations, the present study aimed to use various tasks performed with REAplan to compare kinematic indices in age-matched healthy subjects and stroke patients. REAplan corresponds to a distal effector robotic device that allows displacements of the upper limb in the horizontal plane. This comparison could provide a synthetic, specific, objective and standardized protocol that includes the most relevant tasks and indices to assess upper limb impairment in stroke patients.

3. Materials and Methods

Subjects

Twenty subjects participated in our study. Our cohort consisted of healthy subjects (control group; n=10) and stroke patients (stroke group; n=10), and the characteristics of patients and healthy subjects are described in Table 1. Patient inclusion criteria were an antecedent of ischemic and hemorrhagic stroke (no restriction of localization), a minimal strength of muscles with a Medical Research Council[145] score above 2/5 in proximal muscles (shoulder abduction, elbow flexion and elbow extension) to ensure that they were able to move the robot's distal effector and the comprehension of instructions. The exclusion criterion was the presence of any other significant orthopedic or neurological antecedent that could alter active or passive movements of the upper limbs. In healthy subjects, the only exclusion criterion was the presence of a significant orthopedic or neurological antecedent that could alter active or passive movements of the upper limbs. Both groups were matched for age and body mass index. Descriptions of patients' neurological impairments (Stroke Impairment Assessment Set[146]) and activity limitations (ABILHAND[147]) are also presented in Table 1. Every subject volunteered and freely participated in the study, which was approved by the local Ethics Board of the Faculty of Medicine.

Table 1. Characteristics of control (healthy subjects) and stroke groups.

	Control (n=10)	Stroke (n=10)
Gender (male/female)	6/4	7/3
Age (years)	68.6 (8.7)	71.6 (10.4)
BMI (kg/m^2)	26.8 (5.0)	24.2 (2.2)
Dominant arm (right/left)	9/1	10/0
Affected arm (right/left)	N/A	4/6
Post-stroke time (months)	N/A	2.7 (1.8)
SIAS (…/76)	N/A	63 [57-67]
ABILHAND (logits)	N/A	0.46 (1.58)

Mean (SD); Median [Q1-Q3]. Abbreviations: BMI = Body Mass Index; SIAS = Stroke Impairment Assessment Set; N/A= Not Applicable. For the age and BMI, there is no significant difference between groups ($p>0.05$).

Apparatus

The robot used in the present study was the research prototype REAplan[38], which is illustrated in Figure 1. The REAplan is composed of a distal effector that is held by the patient's hand, which allows displacements in the horizontal plane resulting from various movements of the shoulder and elbow. If the patient had a hand weakness, the hand was attached from an orthosis to the distal effector. In the present study, the subjects only performed movements with REAplan in the active mode. The active mode means that the subjects performed movements without any help from the robot. In addition, the mass and viscosity of the robotic device were at minimal levels to enable subjects to perform unconstrained movements. Moreover, the robot was provided with incremental position sensors (Maxon Motor®) to record distal effector trajectory in X and Y planes as a function of time (acquisition frequency: 40 Hz). Then, assessments were only made in 2D conditions because of the REAplan conception.

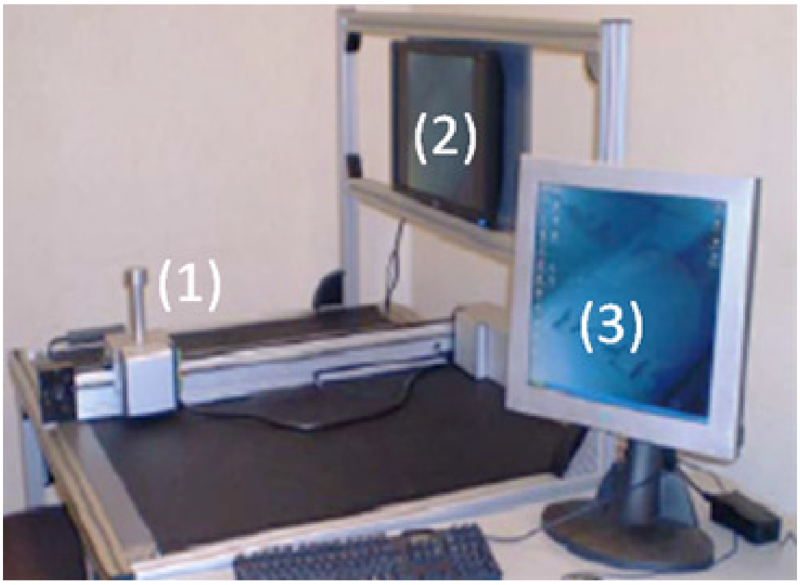

Figure 1: View of the "REAplan" robot.1, 2 and 3 correspond to the distal effector, visual interface of the subject and the physiotherapist's interface, respectively.

Placement of subjects

All the subjects were placed in an ergonomic and standardized sitting position. The angle between each subject's hip and trunk was maintained at 120° to limit lumbar constraints. The subjects' feet were on a footrest to stabilize them, and the trunk was secured to minimize movement compensations at this level. In addition the distal effector was strictly centred in front of the subject.

Tasks

All 20 subjects performed three kinds of tasks with REAplan at spontaneous velocities. The tasks, which are illustrated in Figure 2, were presented to subjects via the subject's visual interface (Figure 1). Movements were performed by the affected arm in stroke patients and the dominant arm in healthy subjects.

For the first two tasks, the subjects had to perform large-amplitude movements and targeted movements. For the large-amplitude movements, the subjects went back and forth as far as they could in an indicated direction. For the targeted movements, the subjects made movements in the most precise and direct manner toward a specific target placed at a distance of 14 cm, similar to the method used by Daly et al.[34]. Both tasks were performed in three directions: homolateral (on the side of the moving arm), contralateral (on the opposite side) and straight (in front of the subject). These directions enabled us to evaluate different movements of the shoulder and elbow and determine whether a specific direction was more relevant than another.

For the third task, the subjects had to draw two kinds of geometrical shapes: a square that was 25 cm long on each side, and a circle that had a 12.5-cm radius.

The experiment started with a training phase, which took approximately 20 min. The training phase, which was not recorded, was used to limit learning bias. In the acquisition phase, the order of execution was randomly assigned, and each task was performed 5 consecutive times (corresponding to 5 consecutive cycles of movement). The rest between each task lasted 5 minutes. The subjects' results were recorded in the acquisition phase.

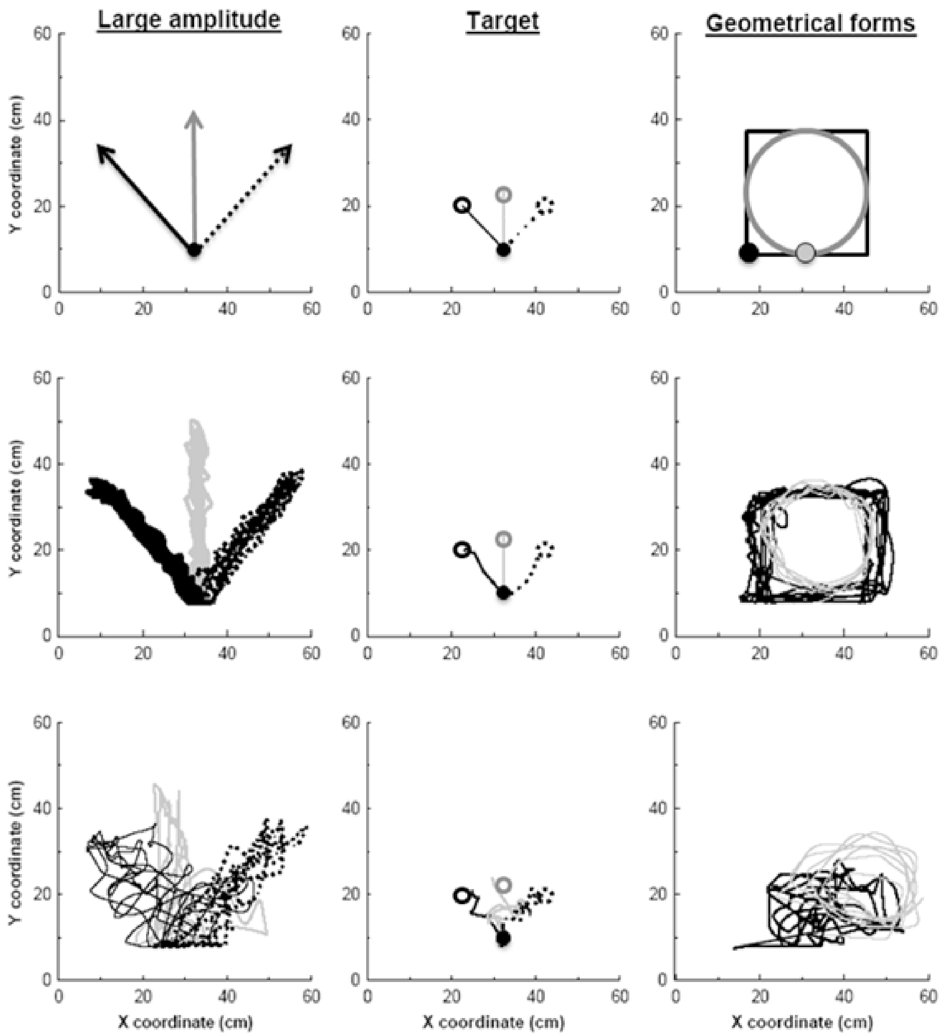

Figure 2: Illustration of the instructions presented on the visual interface (upper graphs) and the tasks performed by a healthy subject (middle graphs) and a patient (lower graphs). For large amplitude and geometrical movements, 5 goings and comings are presented (middle and lower graphs) for each movement (i.e., direction or form). For targeted movements, 1 going is presented (middle and lower graph) for each direction. For large amplitude and targeted movements, solid and dashed black lines correspond to homolateral and contralateral directions of the moving arm. The grey line corresponds to the straight direction. For the geometrical movements, black and grey points were the start point of the square and the circle, respectively. The square was 25 cm long on each side and the circle had a radius of 12.5 cm.

Kinematic analyses

For each task, the X and Y coordinates of the distal effector were acquired as a function of time. These variables were analyzed for each task by a specific customized program that was created in LabWindows/CVI (8.5) environment.

For the large-amplitude movements, we analyzed the amplitude, the Standard Deviation (SD) of the mean amplitude (SD_{ampl}), straightness, velocity, the SD of the mean velocity ($SD_{velocity}$), peak velocity and smoothness indices. For the targeted movements, we analyzed the target inaccuracy and the straightness indices. Each of these indices was analyzed during 5 consecutive cycles and averaged. These indices are described below.

The amplitude (in cm) corresponds to the shortest distance between the starting point and the farthest point reached (Figure 3). The SD_{ampl} (in cm) was used as an index of the amplitude variation during the 5 cycles of movement (the lower the index, the more constant the amplitude). The straightness corresponds to the amplitude divided by the path length covered by the subject. Ratios closer to 1 indicate more rectilinear paths, whereas ratios closer to 0 indicate longer paths to realize the movement (Figure 3). The velocity (in cm/s) corresponds to the ratio between the path length and the elapsed time. The $SD_{velocity}$ (in cm/s) was used as an index of the velocity variation during the 5 cycles of movement (the lower the index, the more constant the velocity). The peak velocity (in cm/s) corresponds to the maximum velocity. The smoothness corresponds to the ratio between the velocity and the peak velocity (ratios closer to 0 indicate less smooth movements)[75]. The target inaccuracy (in cm) corresponds to the distance between the target position the subject had to reach and the end position achieved by the subject (Figure 3). For this measure, higher scores indicate more inaccurate movements.

For the geometrical movements, the goal was to quantify the ability of the subjects to draw a square or a circle. The X and Y coordinates acquired during 5 consecutive cycles were normalized to 100% as a function of time, and these values were called Performances (Figure 4). These X and Y Performances were compared with X and Y reference shapes (called References) using a correlation test (Figure 4). These References correspond to the normalized X and Y coordinates of a perfect square (25 cm long on each side) and a perfect circle (12.5-cm radius). Correlation coefficients closer to 1 indicate that the subject was capable of drawing the requested shape.

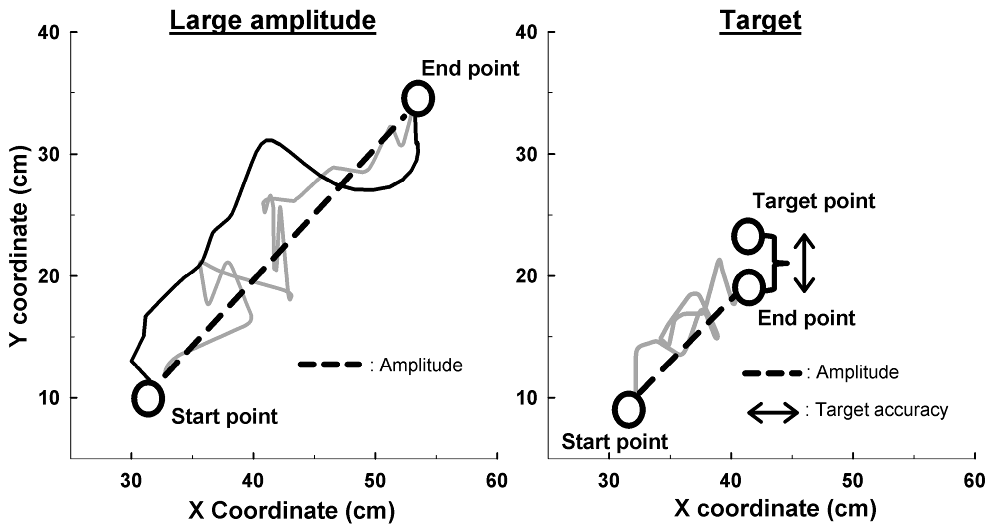

Figure 3: Illustration of the calculation of kinematic indices in large amplitude and targeted movements. The grey solid line corresponds to the going movement (left and right graphs), and the black solid line corresponds to the coming movement (left graph). For the two tasks, the amplitude corresponds to the distance between the start point and the end point. For the movement of large amplitude, the straightness corresponds to the ratio between the double of the amplitude (because of the going and coming) and then, the path length covered by the subject (grey and black solid lines).For the targeted movement, the straightness corresponds to the ratio between the amplitude and the path length covered by the subject (grey solid line). The target inaccuracy corresponds to the distance between the end point and target point.

Statistical analyses

For the first two tasks (i.e., large amplitude and targeted movements), a two-way analysis of variance (ANOVA) [groups (healthy vs. stroke) and directions (homolateral, contralateral and straight)] was performed for each kinematic index using SigmaStat 3.5 software (WPCubed GmbH, Germany). A Bonferroni adjusted post hoc (Holm Sidak) test was used to analyze differences between groups.

For the third task (i.e., geometrical movements), we performed a Pearson correlation test between Performances and References for each shape (square and circle) and coordinate (X and Y). We also performed a two-way ANOVA [groups (healthy vs. stroke) and shapes (square and circle)] for each coordinate (X and Y) using SigmaStat 3.5 software (WPCubed GmbH, Germany). A Bonferroni adjusted post hoc (Holm Sidak) test was used to analyze differences between groups. Homoscedasticity (normal distribution and equality of variance) was verified for all comparisons, and the accepted significance level was 0.05.

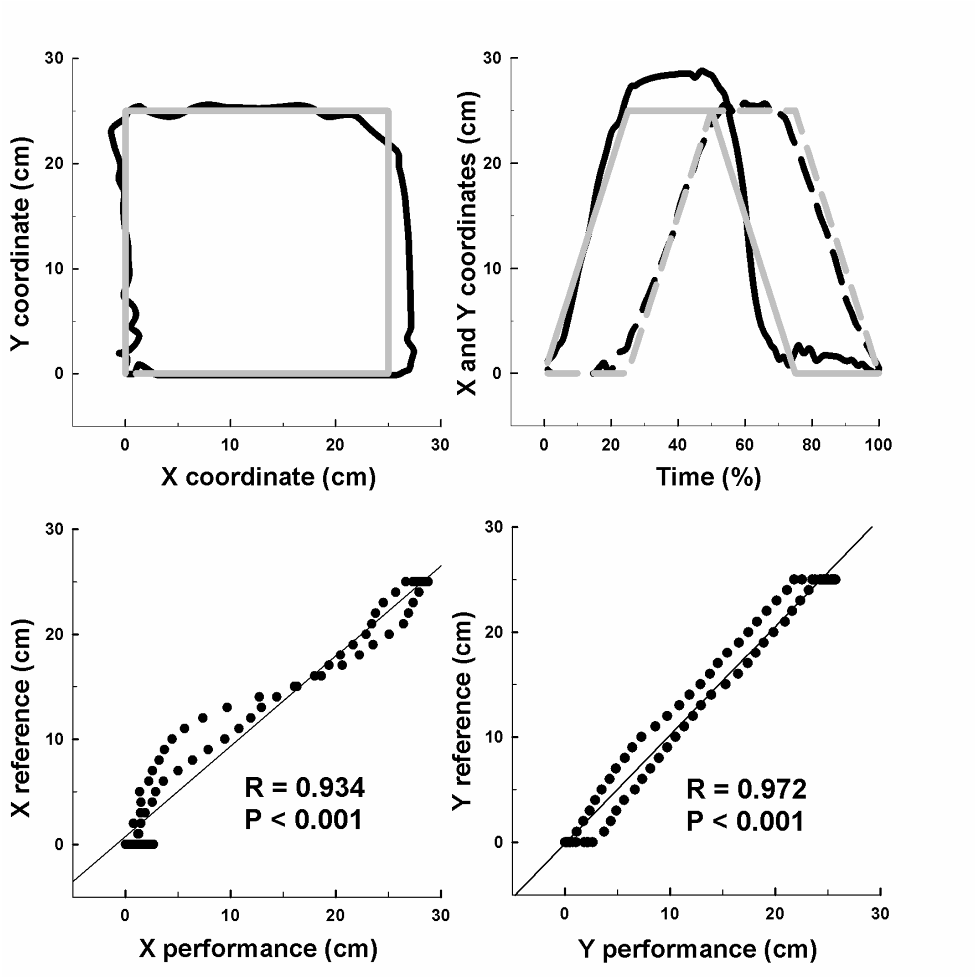

Figure 4: Illustration of the kinematic analysis of geometrical movements. The upper graphs illustrate the normalized square performed by one subject (black line) and the square of the reference (grey line). The left-upper graph illustrates the presentation of these squares on the visual interface. The right-upper graph illustrates evolutions of X (continuous line) and Y (discontinuous line) coordinates as a function of time (%). The lower graphs illustrate the Pearson correlation test between Performances (i.e., subject's square) and References (i.e., square of reference) for X (left-lower graph) and Y (right-lower graph) coordinates. R corresponds to the coefficient correlation, and p illustrates the significant relationship between Performance and Reference

4. Results

One patient, who had the lowest Stroke Impairment Assessment Set (SIAS) score (i.e., 49/76), was excluded from the analysis because he was unable to perform all of the tasks. Typical traces of the three tasks performed by one healthy subject and one patient are illustrated in Figure 2. The mean (SD) values for each group (control vs. stroke) and for each separate movement (i.e., directions or shapes) are presented in Table 2. Figure 5 shows the results for each group for all merged movements.

Interaction between groups and movements

For each kinematic index in the three tasks, the two-way ANOVA did not reveal any interaction ($p>0.05$) between the groups and the movements (i.e., directions or shapes).

Comparison between groups

For the large-amplitude movements, the amplitude was not significantly different between groups ($p>0.05$); however, stroke patients had more difficulty reaching constant amplitude at each cycle of movement ($p<0.001$). Indeed, the SD_{ampl} value was approximately 2 times greater in the stroke group. Furthermore, the path length was less rectilinear in the stroke group ($p<0.001$) (i.e., the straightness ratio was 13% lower in the stroke group). The velocity was not significantly different between groups ($p>0.05$), and the $SD_{velocity}$ showed that the stroke patients were able to maintain a constant velocity similar to the healthy subjects ($p>0.05$). Interestingly, movements of stroke patients were less smooth than those of healthy subjects ($p<0.001$). Indeed, the smoothness ratio was 12% lower in the stroke group.

For the targeted movements, the target inaccuracy was not significantly different between groups ($p>0.05$). The path length, however, was less rectilinear in the stroke group ($p<0.001$). Indeed, the straightness ratio was 27% lower in the stroke group.

For the geometrical movements, stroke patients had significantly more trouble drawing the requested shape than the healthy subjects ($p<0.01$). Indeed, the X and Y correlation indices were 24% and 19% lower, respectively, in the stroke group.

Table 2. For the three tasks, results of the kinematic indices in control and stroke groups.

Large amplitude	**Homolateral**		**Contralateral**		**Straight**	
	Control (n=10)	Stroke (n=9)	Control (n=10)	Stroke (n=9)	Control (n=10)	Stroke (n=9)
Amplitude (cm)	35.6 (6.2)	35.1 (6.2)	32.6 (4.9)	34.0 (8.3)	33.0 (6.8)	30.8 (8.9)
SD_{ampl} (cm)	2.6 (1.4)	4.0 (2.1)	2.5 (0.84)	3.9 (1.03)	1.7 (0.8)	3.6 (2.1)
Straightness	0.97 (0.02)	0.86 (0.09)	0.97 (0.02)	0.84 (0.13)	0.98 (0.02)	0.89 (0.12)
Velocity (cm/s)	26.4 (14.1)	22.3 (12.3)	22.6 (10.6)	20.0 (11.5)	20.0 (8.8)	16.4 (6.6)
$SD_{velocity}$ (cm/s)	14.6 (9.6)	16.0 (7.3)	12.6 (6.3)	14.9 (7.6)	14.6 (6.8)	14.5 (4.9)
Peak velocity (cm/s)	49.2 (25.8)	56.4 (18.5)	42.6 (19.2)	51.5 (19.6)	42.6 (17.6)	45.0 (13.2)
Smoothness	0.53 (0.06)	0.39 (0.13)	0.53 (0.04)	0.38 (0.11)	0.47 (0.04)	0.36 (0.08)
Target	**Homolateral**		**Contralateral**		**Straight**	
	Control (n=10)	Stroke (n=9)	Control (n=10)	Stroke (n=9)	Control (n=10)	Stroke (n=9)
Target inaccuracy (cm)	1.4 (1.1)	2.4 (1.5)	2.7 (0.8)	2.4 (1.4)	0.6 (0.3)	1.4 (1.9)
Straightness	0.92 (0.12)	0.61 (0.11)	0.92 (0.07)	0.57 (0.14)	0.95 (0.07)	0.77 (0.20)
Geometrical forms	**Square**		**Circle**			
	Control (n=10)	Stroke (n=9)	Control (n=10)	Stroke (n=9)		
X correlation	0.94 (0.05)	0.72 (0.39)	0.95 (0.07)	0.69 (0.31)		
Y correlation	0.95 (0.05)	0.77 (0.31)	0.96 (0.03)	0.75 (0.18)		

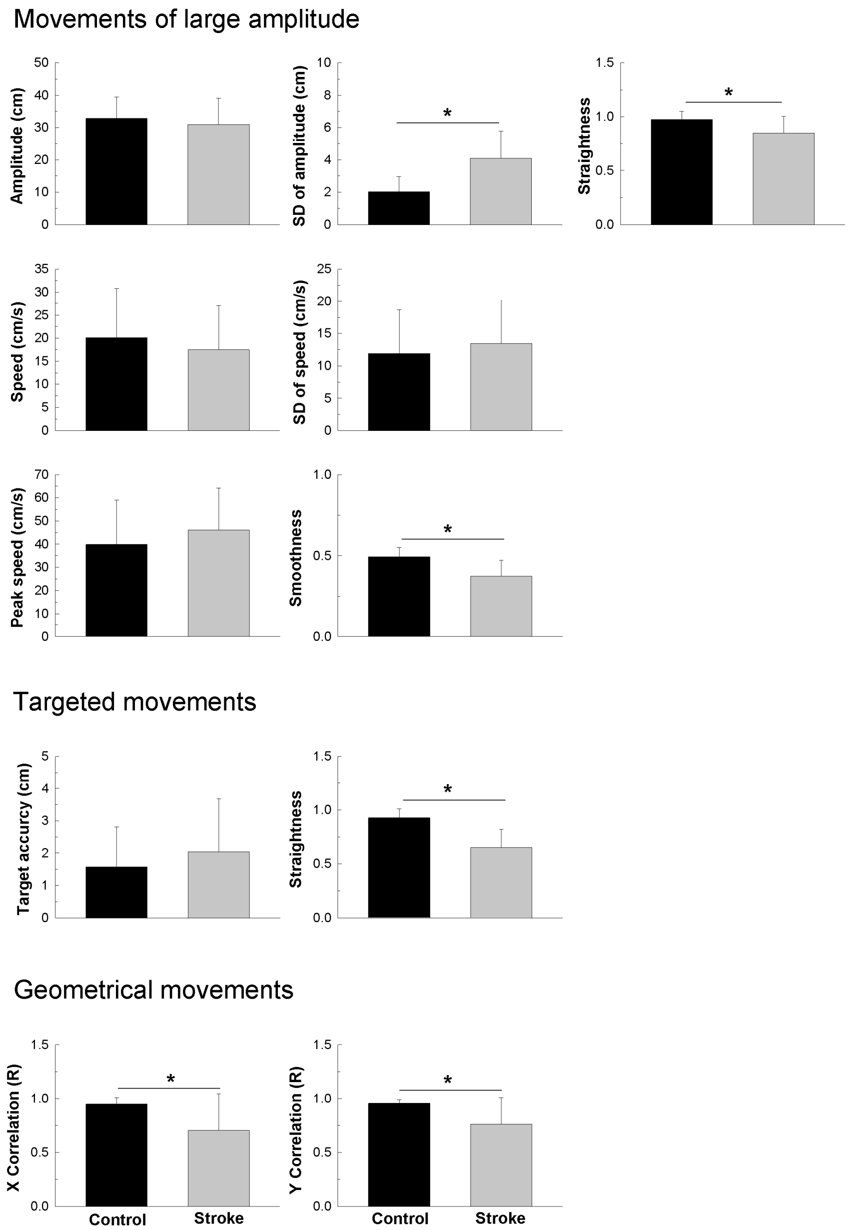

Figure 5: The results of the Bonferroni adjusted post hoc (Holm Sidak) tests comparing control and stroke groups in studied indices. * indicates that there was a significant difference ($p < 0.01$) between the two groups.

5. Discussion

This study presented a lot of kinematic indices, which were obtained with a distal effector robotic device in stroke patients and healthy matched subjects. By choosing the most relevant indices, we attempted to establish an objective, standardized protocol to assess upper limb impairments in stroke patients.

Elaboration of the standardized protocol

For the large-amplitude movements, our results showed that the amplitude, velocity, $SD_{velocity}$ and peak velocity could be rejected because they were similar in patients and healthy subjects. The amplitude rejection was surprising because Khan et al.[19] and Reikensmeyer et al.[20] observed that this index was improved after rehabilitation. Thus, we hypothesized that this index was altered before treatment. The rejection could have two explanations. First, the stroke patients in the present study had moderate to minor impairments, which is shown by high SIAS values in Table 1 (this was not the case in the previous studies). Secondly, movements were carried out at spontaneous velocities in the present study and at maximum velocity in the Khan et al.[19] and Reikensmeyer et al.[20] studies. This last protocol (i.e., maximum velocity) could limit the reaching amplitude by increasing spasticity[148].

For the large-amplitude movements, our results showed that SD_{ampl}, straightness and smoothness should be retained because they were different in patients and healthy subjects. Interestingly, SD_{ampl} is an original index that has never been used before, whereas the straightness index was calculated with the same method as Khan et al.[19], but has never been used with a distal effector robotic system. Although the smoothness can be calculated in various manners[34,60,75,144], our method was in agreement with Finley et al.[60] and Rohrer et al.[75] who described smoothness as a relevant index in assessing stroke patients.

For the targeted movements, our results showed that the index of target inaccuracy could be rejected and that the straightness should be retained (for the reasons detailed above). This result was not in agreement with Daly et al.[34], who used target inaccuracy in patient assessments. The difference could be due to the fact that the stroke patients in the Daly et al. study had severe impairments[34]. The present results suggested that stroke patients with moderate to minor impairments could reach targets similarly to healthy subjects, but they took longer to point out the target.

For these two first tasks, contrary to Finley et al.[60], but similar to Daly et al.[34], only one direction (i.e., homolateral) of movement was retained. This choice could be for three reasons. First, the present results did not reveal any interaction between groups and directions, which means that all directions have the same relevance. Secondly, preserving only one direction could limit the exhaustion bias and assessment time. Lastly, we suggest retaining the homolateral rather than the contralateral direction because the homolateral direction combines flexion and abduction of the shoulder and extension of the elbow, which allows movements away from primitive motor synergies[149].

For the geometrical movements, our results showed that the X and Y correlation indices should be retained. Although geometrical movements have been analyzed in various manners[76,77,144,150], the present study was the first study to use a simple index to evaluate the capacity to draw a perfect circle or a perfect square in a free, unconstrained mode.

We propose that the two geometrical shapes should be retained. Although the two-way ANOVA did not reveal any interaction between groups and shapes, we hypothesized that both shapes could assess various aspects of coordination. The square involves sharp changes in direction, which require quick changes in the control of agonist and antagonist muscles, whereas the circle involves high regularity in movements, which requires a continued adaptation in the control of agonist and antagonist muscles. Further studies must be carried out to determine if treatments could improve these specific movements.

The standardized protocol should include specific indices (SD_{ampl}, straightness, smoothness, X and Y correlations) obtained from four movements (i.e., homolateral large amplitude and targeted movements and square and circle movements).

A correlation study between our kinematic and clinical scores did not reveal any significant relationship ($p>0.05$). However, the sample of patients is small and the “Stroke Impairment Assessment Set“ scale is not a specific motor impairment scale that could enable us to perform these correlation studies. Then, as already performed by Bosecker et al.[78] with MIT-Manus, further correlation studies between our protocol and other clinical scales (e.g. Fugl-Meyer) should be carried out in larger samples of patients, to determine if the protocol reflects the amount of upper arm motor impairment. Moreover, further studies will assess the complete validity of this protocol, and the variability of results in dominant and non-dominant hand. Finally, the effect of specific treatments will be assessed with this protocol.

Advantages of this study

The REAplan robotic device could easily be used for all stroke patients in routine assessments. Indeed, patients could easily be placed in an ergonomic and standardized sitting position, and the protocol appears to be able to detect abnormalities in stroke patients compared with age-matched healthy subjects. In addition, therapists and researchers could easily and quickly use the specific customized program.

Although the REAplan is more limited in degrees of freedom than other systems[15,27,29,151–153], it permits a quantitative assessment of stroke patients that could easily be used in further randomized controlled trials (RCTs) or in daily clinical assessments.

The present study was the first study to compare kinematic indices (in a free, unconstrained mode) of tasks performed with an effector distal robot by stroke patients and age-matched healthy subjects.

Limitations

There were several limitations in the present study. First, our results have to be interpreted carefully since they could be affected by the small sample and the moderate to light impairments of patients. Then, future studies are necessary to confirm our results. However, most differences shown by our indices were highly significant ($p<0.001$; statistical power = 1). Secondly, kinematic indices could have a floor effect. Indeed, one patient was excluded from the study analysis because he was too weak to perform all of the tasks. In agreement with Sivan et al.[12], we believe that kinematic indices could be a complement to the Fugl-Meyer test, which has a ceiling effect[154]. However, further studies are necessary to adapt this protocol with an assistance model in order to apply kinematics to more severely impaired patients. Lastly, further studies are necessary to evaluate the reliability and responsiveness of our protocol. Indeed, Wagner et al.[54] have proved the intra-examiner reliability and the responsiveness of some kinematic indices that have been evaluated in simple forward reaching tasks with an optical tracking system. No study, however, has examined the reliability and responsiveness of the kinematic indices for the measurement of upper limb functions with robotic device[12].

6. Conclusions

This preliminary study proposes a new standardized, objective and protocol to assess upper limb impairments in stroke patients, which will enable us to realize a larger study that will analyze intra- and inter examiner reliability and responsiveness of this protocol. In future RCTs, researchers will be able to use our tool to objectify upper limb impairments before and after stroke patients' treatments as RAT.

Acknowledgements

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Chapter 4

Using the robotic device REAplan as a valid, reliable, and sensitive tool to quantify upper limb impairments in stroke patients

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1. Abstract

Objective –To validate a protocol assessing upper limb kinematics with a planar robot among stroke patients. Design – Prospective cohort study. Subjects – Age-matched healthy subjects (n=25) and stroke patients (n=25). Methods – Various kinematic indices (n=44) were obtained from four tasks performed by subjects with REAplan, a planar end-effector robotic device. The metrological properties of this protocol were studied. Results – In stroke patients, 43 kinematic indices showed moderate to excellent reliability (Intraclass Correlation Coefficients [ICC] range [0.40-0.95]; and Minimal Detectable Changes range [9.9%-131%]). In healthy subjects, 25 kinematic indices showed moderate to excellent reliability (ICC range [0.40-0.91]) and 3 indices showed a laterality effect ($p<0.05$). Many of these indices (27 of 44) were altered in stroke patients in comparison to healthy subjects ($p<0.05$). The Box & Block test (manual dexterity) and Upper Limb Sub-score of Fugl-Meyer Assessment (motor control) showed moderate to good correlations with, respectively, 13 and 4 indices ($r>0.40$). Finally, a Principal Component Analysis allowed the elaboration of a short version of the protocol, reducing the number of indices to five (i.e., Amplitude, $CV_{straightness}$, Speed Metric, $CV_{jerk\ metric}$ and $CV_{speed\ metric}$). Conclusion – This study provides a standardized, valid, reliable and sensitive protocol to quantify upper limb impairments in stroke patients by using a planar robot.

Keywords: Robotics, outcome assessment, biomechanics, stroke, upper extremity, Reproducibility of Results, Reference Standards.

2. Introduction

Fifteen million people worldwide experience cerebral vascular accidents each year and one-third of them display permanent neurological impairments[9]. Recent recommendations have described the necessity of intensive and prolonged rehabilitation[139] and regular assessments[39] in stroke patients. Robotic devices have the potential to achieve these recommendations because they are able to both intensively rehabilitate[92] and assess[12,39] the damaged upper or lower limb.

Several systematic reviews[12,39] have recommended the use of kinematic measures to assess active movements of the upper limb in stroke patients. These measures can be computed by robotic devices while stroke patients carry out standardized movements with their affected upper limb. Following various treatments, some clinical trials have shown kinematic improvements, using tasks such as reaching to one target[34,55], multiple targets[60,81], moving as far as possible toward specific directions[19,20] or performing hand to mouth movements[55]. Among all the kinematic indices computed by these authors, the amplitude[19,20], velocity[19,20,55,60,81], smoothness[34,55,60,81], straightness[19,60] and inaccuracy[34] of movements showed improvements after treatment in stroke patients.

The metrological properties of kinematic indices can be analyzed by several methods, such as construct validity, minimal detectable change (MDC) and reliability. Construct validity examines correlations between different assessment tools[12]. Indeed, several kinematic indices seem to be correlated with upper limb motor control (for review[39]). However, previous studies have not established any correlation between kinematic indices and gross manual dexterity. This relationship could be suggested because the motor control of the proximal upper limb, as assessed with kinematics, is important to initiate and control the movement to reach the object, when exercising manual dexterity. For example, in the Box and Block test (BB), the subject has to reach the cube before grasping it[121]. The MDC determines if a variable modification corresponds to a true functional change or to a measurement error[155], while reliability assesses the ability of a tool to provide the same results on repeated measures[40]. Finley et al.[156] have demonstrated excellent reliability for repeated kinematic assessments with a planar robotic device (MIT-Manus) in healthy adults. Wagner et al.[54] have shown moderate to excellent reliability of various kinematic indices in stroke patients and have computed their MDCs. These indices were obtained from simple forward-reaching tasks using an optical tracking system. No study has examined the reliability and MDC of a protocol assessing kinematics in stroke patients with a robotic device.

Previously, we[117] proposed a preliminary protocol including kinematic indices obtained in various tasks, underlining the lack of a gold standard to quantify upper limb movements in stroke patients. REAplan, a planar end-effector robotic device allowing the mobilization of the upper limb in a horizontal plane[38], was used to compute these indices. Objectives of the study are as follow: verifying the intra-rater reliability of kinematic indices in stroke patients and healthy subjects; calculating the MDC in stroke patients; assessing the laterality effect in healthy subjects; identifying which kinematic indices are altered in stroke patients; and studying the construct validity of the protocol.

The secondary objective of this study was to provide a short version of this protocol, allowing researchers and clinicians to easily assess stroke patients' upper limb kinematics in clinical and research settings, as recommended by Balasubramanian et al.[39].

3. Materials and Methods

Subjects

Fifty subjects participated in our study: 25 healthy subjects (the control group) and 25 stroke patients (the stroke group). These patient's characteristics are described in Table 1. Patient's inclusion criteria were a history of ischemic or hemorrhagic stroke (with no restriction of localization), the ability to understand verbal instructions and the capacity to actively move the planar end-effector robot without assistance; beyond this capacity, sensitive deficits, muscle strength and spasticity of the affected upper limb were not considered. Patient's exclusion criterion was the presence of secondary cognitive disorders (i.e., hemineglect, apraxia or comprehension aphasia) that could alter the task comprehension. In both groups, the exclusion criteria were any other significant orthopedic (e.g. upper limb fracture, muscle tears, or shoulder and elbow pain) or neurological disease that could alter active mobility of the upper limbs. For the control group, the subjects were selected in function of the included patients to match both groups for age and Body Mass Index (Table 1). Stroke patients were recruited in the rehabilitation department of our Faculty hospital. The study was approved by Ethics Board of our Faculty of Medicine. Each subject freely participated in the study and signed an informed consent.

Clinical assessments

In stroke patients, neurological impairments of the affected upper limb were assessed by the Upper Limb Sub-score of the Fugl-Meyer Assessment (USFMA)[49,157] and the BB[121]. The first scale assesses motor control and muscle tone, and the second test assesses the gross manual dexterity of the patient's upper limb. The results of these assessments are presented in Table 1.

Table 1: Characteristics of healthy subjects and stroke patients

Characteristics	Stroke (n=25)	Healthy (n=25)
Gender, male/female, n	18/7	15/10
Age, years, mean (SD)	64.8 (15.9)	63.1 (16.0)
BMI, kg/m^2, mean (SD)	25.6 (2.8)	23.7 (4.3)
Dominant arm, right/left, n	24/1	23/2
Affected arm, right/left, n	5/20	N/A
Post-stroke time, months, mean (SD)	31.5 (55.0)	N/A
USFMA (0-66), median [IQR]	51 [37-62]	N/A
BB, mean (SD)	19.7 (14.6)	N/A

BMI: body mass index; USFMA: Upper Limb Sub-score of the Fugl-Meyer Assessment; BB: Box and Block test; N/A: not applicable; IQR: interquartile range.

For the age and BMI, there is no significant difference between groups (p-value=0.70 and 0.07, respectively).

Kinematic assessments

Apparatus

The robot used in the present study was the research prototype of a rehabilitation robot named REAplan, which is illustrated in Figure 1[38]. REAplan is a planar end-effector robot capable of mobilizing the patient's upper limb in a horizontal plane via a handle that the patient can grasp or to which it may be attached via a brace or an orthosis if the hand is too weak.

Like most rehabilitation robots, REAplan is equipped with force and position sensors. The former are intended to measure the interaction force between the patient and the robot to determine a reference force through a force controller. The position sensors measure the kinematics of the patient’s hand to determine the reference force on positional basis and on the basis of the specific exercise to be performed with the robot. For this study, the only reference force used was a slightly viscous friction force to avoid the strange sensation of moving the hand on a frictionless surface. For the purposes of the study, the kinematic information provided by the position sensors was recorded during the exercise, allowing us to produce our analyses off-line (acquisition frequency: 100 Hz). This planar robot is also equipped with a screen positioned in front of the patient that was intended to give him or her visual feedback on the exercise.

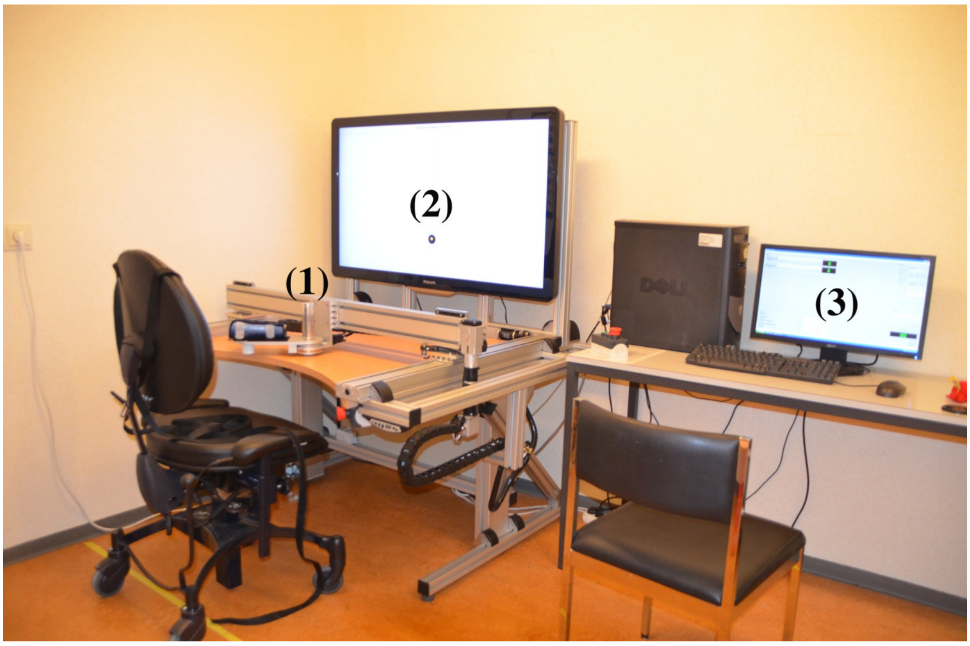

Figure 1: View of REAplan. 1: planar end-effector robot; 2: visual interface for the subject; 3: physiotherapist's interface

Position of subjects

All subjects were installed in an ergonomic and standardized sitting position. The start position was placed at 13 cm in front of the subject. The angle between each subject's hip and trunk was maintained at 120° to limit lumbar constraints. The subjects' feet were on a footrest to stabilize them, and their trunk was secured to minimize compensatory movements.

Tasks

All subjects were requested to perform four different tasks with REAplan at spontaneous velocities. The tasks, illustrated in Figure 2, were presented to subjects via the visual interface (Figure 1). Movements were performed by the affected arm in stroke patients (n=25) and the dominant arm in healthy subjects (n=25). A subgroup of these healthy subjects (n=15) performed also the tasks with the non-dominant arm to study the effect of laterality on the protocol.

For the Free Amplitude task, the subject had to reach straight out in front of them as far as they could and brought the arm back to the starting position. For the Target task, the subject made movements in the most precise and direct manner toward a specific target placed at a distance of 14 cm in front of the subject[34]. After performing this task, the planar robot brought the subject's arm back to the starting position. For the Square and Circle tasks, the subject had to draw two geometrical shapes: a square of 6 cm side and a circle of 4 cm radius. These shapes were performed clockwise with the right upper limb, and counter-clockwise with the left one. To summarize this protocol, the subjects performed rhythmic (i.e. Free Amplitude and Circle tasks) and discrete (i.e., Target and Square tasks) movements.

The experiment started with a ten-minute training phase to limit learning bias. For the data-acquisition phase, the order of tasks was randomly assigned. Each task was performed ten consecutive times. The rest period between each task was one minute.

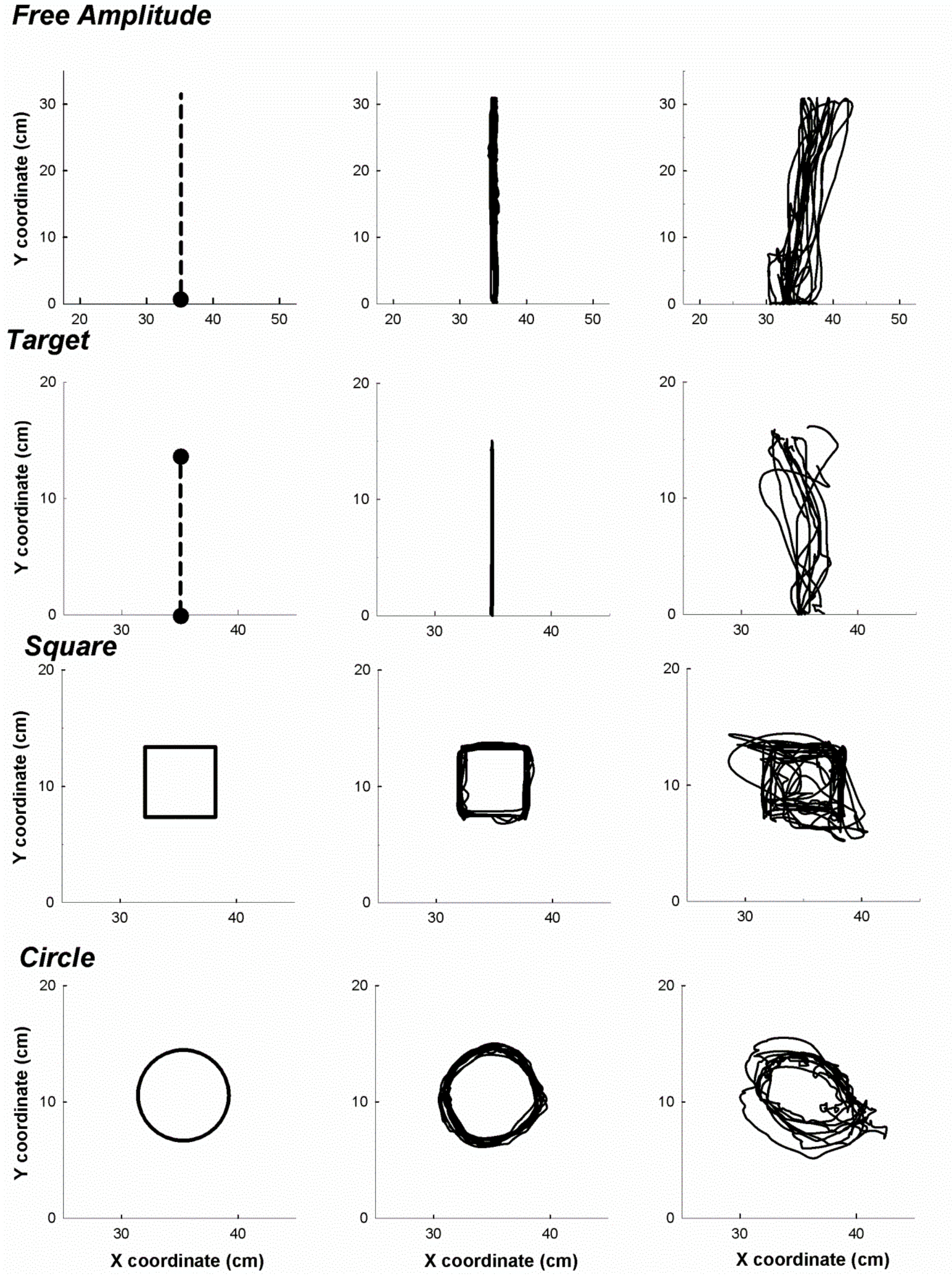

Figure 2: Illustration of the requested tasks presented on the visual interface (left graphs), the tasks performed by a healthy subject (middle graphs) and a stroke patient (right graphs).

Kinematic analyses

For each task, the elapsed time of the end-effector position was recorded by the planar robot. These variables were analyzed for each task by a specific customized program in a LabWindows/CVI (8.5) environment. Each index mentioned below was computed for each of the ten cycles of movement and then averaged.

For the Free Amplitude task, we computed the amplitude, velocity, straightness, peak velocity and two smoothness indices (the speed and jerk metrics[75]). For the Target task, the amplitude index was replaced by the target inaccuracy index. For the Square and Circle tasks, we computed the velocity, peak velocity, speed metric, jerk metric and shape inaccuracy indices. The Coefficient of Variation (CV), calculated from the subjects' ten cycles of movement, was computed for each index. Some of these indices are described below.

Straightness corresponds to the amplitude divided by the path length covered by the subject[19] (ratios closer to 1 indicate more rectilinear paths, whereas ratios closer to 0 indicate longer paths to realize the movement). The speed metric[75] corresponds to the ratio of the mean velocity and the peak velocity (ratios closer to 0 indicate less smooth movements). The jerk metric[75] corresponds to the ratio of the absolute mean jerk (corresponding to the variations of acceleration) and the peak velocity (ratios closer to 0 indicate smoother movements). Target inaccuracy[34] corresponds to the distance between the target position that the subject had to reach and the end position achieved by the subject (higher scores indicate more inaccurate movements). Shape inaccuracy quantifies the subject's ability to draw a square or a circle posted on the visual interface. This index corresponds to:

$$\frac{\sum_{i=1}^{n}\sqrt{(Rx_i - Px_i)^2 + (Ry_i - Py_i)^2}}{n}$$

where n corresponds to the number of positions acquired during the exercise and related to the analyzed shape, Pxi and Pyi correspond to the X and Y coordinates of its positional data point and Rxi and Ryi correspond to the X and Y coordinates of the orthogonal projection of its point on the reference shape (cf. illustration in the Figure 3). Thus, the shape inaccuracy index corresponds to the average of the distances between the measured performance points and their corresponding reference points (higher scores indicate more inaccurate movements).

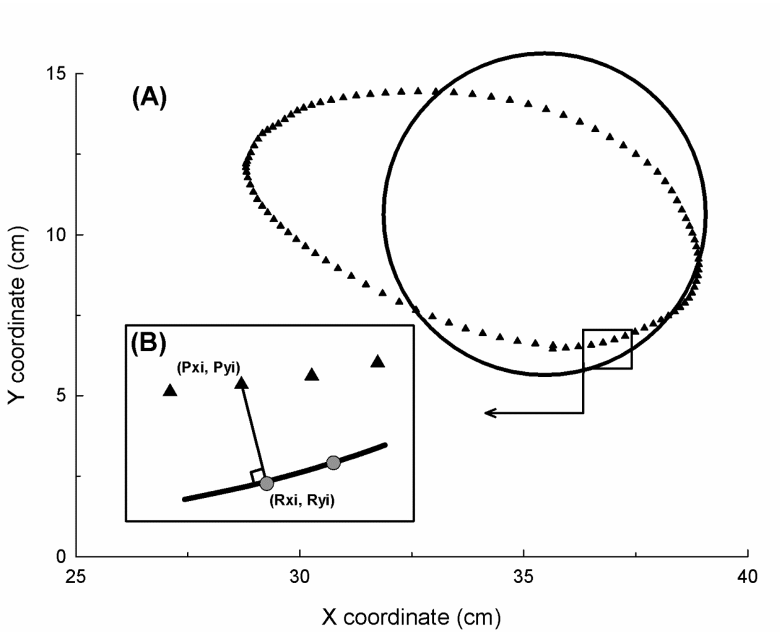

Figure 3. Illustrations of (A) the circle of reference (black circle) and a circle performed by a stroke patient (black triangle symbols) and of (B) the calculation of the shape inaccuracy index. Each reference point (grey circle symbol, [Rxi, Ryi]) corresponds to the minimal orthogonal projection of the performance point (Pxi, Pyi) on the shape of reference. The distances between all the related reference and performance points were measured and averaged to obtain the shape inaccuracy result.

Statistical analysis

For each section, the normal distribution and equality of variance were verified for all comparisons, and the significance level was 0.05. Statistical tests were performed using SigmaStat 3.5 software (WPCubed GmbH, Munich, Germany), except for reliability (SPSS 16.0 software [SPSS Inc., Chicago, USA]) and Principal Component Analysis (PCA) (StatView 5.0 software [Sas institute, North Carolina, USA]).

Learning effects

The learning effect was assessed through ten consecutive cycles of movement in 15 stroke patients. Each cycle of movement was analyzed separately, and the data were then submitted to a one-way repeated measures analysis of variance (ANOVA).

Intra-rater reliability in stroke patients and healthy subjects

Intra-rater reliability represents the ability to provide the same results on repeated measures in the same subjects using the planar robotic device[40]. Some stroke patients (n=15) and healthy subjects (n=15) performed all tasks twice, one to seven days apart.

For each group, we assessed intra-rater reliability with the Intraclass Correlation Coefficient (ICC). The ICC is related to the variability of results across repeated measures within the subjects (i.e. between-subjects variability) and to the measurement error (i.e., within-subject variability)[158]. ICC consistency parameters were calculated in a two-way mixed model. Reliability was rated as excellent, moderate and poor with ICC scores >0.75, 0.40-0.75 and <0.40, respectively[40].

Minimal Detectable Change in stroke patients

The MDC corresponds to the minimal change that exceeds the measurement error in the score. A small MDC corresponds to a better ability to detect a real change in patients[155]. The MDC parameter (MDC_{95}) was calculated from the data obtained during the intra-rater reliability section for stroke patients and at a 95% confidence interval, as follows[54]:

$$\mathrm{MDC_{95}} = \mathrm{SEM} \times 1.96 \times \sqrt{2},$$

where 1.96 is the 2-sided z table value for the 95% confidence interval and is used to account for the variance between 2 measurements. The lower the MDC_{95}, the lower the probability of observing a change related to a measurement error. The Standard Error of Measurement (SEM) is related to the measurement error across repeated measures and was calculated as[54]:

$$\mathrm{SEM} = \mathrm{SD_x} \times \sqrt{(1 - \mathrm{R_x})},$$

where SD_x is the standard deviation for all observations from test sessions 1 and 2, and R_x corresponds to the calculated ICC.

The MDC_{95} unit is the same as that of the original measurement. To facilitate comparisons between kinematic indices, the MDC% was calculated as[54]:

$$\mathrm{MDC\%} = \frac{\mathrm{MDC}}{\mathrm{mean}} \times 100,$$

where the mean is the average of all the observations in stroke patients between the two sessions. The lower the MDC%, the lower the probability will be of observing a change related to a measurement error.

Laterality effect in healthy subjects

Fifteen healthy subjects performed the tasks described above with the dominant and non-dominant hands. The dominant one corresponded to the main hand used in activity of daily living such as writing. For each kinematic index, a paired t-test was performed to assess which kinematic indices were influenced by laterality.

Comparisons between stroke and healthy subjects

Age-matched stroke patients (n=25) and healthy subjects (n=25) performed the tasks described above with their impaired and dominant upper limb, respectively. For each kinematic index, a one-way ANOVA was performed to determine the kinematic indices that were altered in stroke patients.

Construct validity

Correlations between each kinematic index and clinical assessments were analyzed by (i) a Pearson correlation test for the BB and (ii) a Spearman correlation test for the USFMA in 25 patients. A correlation was good, moderate or poor if the correlation coefficient (r) was >0.60, 0.30-0.60 and <0.30, respectively[40].

Principal Component Analysis

PCA determines several orthogonal axes (Varimax), called principal components, composed of a set of correlated kinematic indices. The number of principal components was the smallest one representing at least 75% of the variance. Correlations between the 44 indices assessed in 25 stroke patients were established in two steps.

First, for each individual task, the kinematic indices were included in a PCA to provide the index most correlated to each principal component. Second, from all the indices selected in the first step, a PCA was performed to provide, for all merged tasks, those that were the most correlated to each principal component. These last selected indices were put together to provide a short version of the protocol.

4. Results

Among the 25 patients, two patients cannot perform the geometrical tasks because of limited motor control (i.e., USFMA = 7 and 8/66). All results are presented in Tables 2, 3 and 4 and are illustrated in Figure 2.

No learning effect was found for the different tasks (data not shown). Indeed, for each index, the results of the ten consecutive cycles of movement were similar (p-value>0.05). A laterality effect was shown in only three indices of the Free Amplitude task. Indeed, the amplitude and the straightness indices were respectively 1.6 cm and 0.02 lower for the non-dominant upper limb in healthy subjects, and that the jerk metric index was $4.8/s^2$ higher for this limb (p-value<0.04).

In stroke patients, all indices of the Free Amplitude and Target tasks had a moderate to excellent reliability (ICC range [0.50 - 0.95], Table 2), except the $CV_{peak\ velocity}$ index of the Target task, which presented poor reliability (ICC=0.04). All indices of the two geometrical shapes had a moderate to excellent reliability (ICC range [0.40 - 0.93]). In healthy subjects and for all merged tasks, 25/44 kinematic indices had moderate to excellent reliability (ICC range [0.40 - 0.91]).

The MDC% was calculated for each index (Table 2). The indices the most likely to detect a change in patients were:

- the amplitude, velocity, straightness, peak velocity, jerk metric and speed metric indices of the Free Amplitude task (MDC% range [9.9% - 33.7%]);
- the straightness and speed metric indices of the Target task (MDC% were 14.6% and 22.4%, respectively);
- the velocity, peak velocity, jerk metric and speed metric indices of the Square task (MDC% range [20.4% - 32.8%]);

- the peak velocity and speed metric indices of the Circle task (MDC% were 37.7% and 29.5%, respectively).

For the four merged tasks, 27 of 44 indices were significantly altered in stroke patients (p-value<0.05) (Table 3). This result was partly related to the fact that the ten cycles of movements were less identical in stroke patients than in healthy subjects. Indeed, the significantly altered CV indices were higher (difference range [2.4% - 12.8%]) in the stroke group. Second, the stroke patients' movements were less smooth for all tasks. Indeed, the jerk metric (excepting for the Square task) was higher (difference range [$5.7/s^2$ – $14.5/s^2$]) and the speed metric was lower (difference range [0.06 - 0.10]) in the stroke group. Third, movements of unidirectional tasks were less rectilinear in patients: ratios were 0.09 (Target task) and 0.10 (Free Amplitude task) lower in the stroke group. Finally, movements were less accurate by 1.6 cm for the Target task and by 0.4 (Circle task) and 0.6 (Square task) cm for the geometrical tasks in the stroke group. The movements of the Target and Square tasks had a higher peak velocity of 5.5 cm/s and 5.9 cm/s in the stroke group, respectively.

The construct validity studied the correlation between each kinematic index and clinical scales. The indices that showed moderate to good correlations with the manual dexterity assessed with BB were (Table 3):

- $CV_{velocity}$ and straightness indices of the Free Amplitude task (r = -0.41 and 0.42, respectively);
- the velocity, $CV_{velocity}$, straightness, target inaccuracy, peak velocity, $CV_{peak\ velocity}$ and $CV_{speed\ metric}$ indices of the Target task (r range [-0.60 - 0.41;]);
- the shape inaccuracy index of the Square task (r = -0.41);
- the $CV_{velocity}$, $CV_{peak\ velocity}$ and the $CV_{jerk\ metric}$ indices of the Circle task (r range [-0.46 to -0.61]).

The indices that showed moderate to good correlation with motor control assessed with the USFMA were (Table 3) the $CV_{velocity}$ and peak velocity indices of the Target task (r = -0.51 and -0.47, respectively); the $CV_{velocity}$ and the $CV_{jerk\ metric}$ indices of the Circle task (r = -0.49 and -0.61, respectively).

A PCA was carried out to determine a short version of the protocol (Table 4). The first step of the PCA enabled us to select four representative kinematic indices of the Free Amplitude task and three indices for each of the other tasks. It enabled us to determine the five most representative indices, obtained from all tasks, allowing 79% of the variance. There were the amplitude and the $CV_{straightness}$ of the Free Amplitude task, the peak velocity of the Target task, the $CV_{jerk\ metric}$ of the Square task and the $CV_{speed\ metric}$ of the Circle task.

Table 2: Results of intra-rater reliability and MDC in 15 stroke patients for each task and index.

	Stroke patients (n=15) Mean (SD) Session 1	Session 2	ICC	MDC_{95}	MDC%
Free amplitude					
Amplitude (cm)	29.8 (2.9)	29.5 (3.4)	**0.84**	3.4	11.6
$CV_{amplitude}$ *(%)*	3.6 (2.5)	3.6 (2.3)	**0.82**	2.8	77.4
Velocity (cm/s)	10.9 (5.5)	9.7 (5.7)	**0.95**	3.4	33.2
$CV_{velocity}$ *(%)*	17.4 (6.0)	16.2 (7.1)	**0.80**	8.0	47.8
Straightness	0.90 (0.11)	0.88 (0.09)	**0.90**	0.09	9.9
$CV_{straightness}$ *(%)*	5.7 (6.2)	6.5 (5.3)	**0.78**	7.4	121.6
Peak velocity (cm/s)	30.8 (11.3)	28.7 (11.3)	**0.95**	6.8	22.7
$CV_{peak\ velocity}$ *(%)*	22.0 (16.0)	25.5 (25.0)	**0.88**	19.8	83.5
Jerk metric $(1/s^2)$	30.3 (7.0)	32.4 (10.7)	**0.88**	8.6	27.4
$CV_{jerk\ metric}$ *(%)*	20.5 (7.7)	19.2 (5.8)	**0.57**	12.2	61.7
Speed metric	0.35 (0.09)	0.33 (0.09)	**0.77**	0.12	33.7
$CV_{speed\ metric}$ *(%)*	18.2 (6.3)	19.0 (8.6)	**0.72**	10.9	58.3
Target					
Target inaccuracy (cm)	1.7 (0.8)	1.5 (0.9)	**0.80**	1.0	63.0
$CV_{target\ inaccuracy}$ *(%)*	37.6 (12.8)	37.3 (12.2)	**0.50**	24.0	64.2
Velocity (cm/s)	6.9 (4.0)	6.5 (4.2)	**0.88**	3.8	57.6
$CV_{velocity}$ *(%)*	25.2 (11.8)	23.2 (8.4)	**0.53**	19.3	79.5
Straightness	0.89 (0.09)	0.91 (0.08)	**0.69**	0.13	14.6
$CV_{straightness}$ *(%)*	7.9 (6.3)	7.1 (5.8)	**0.82**	7.0	93.5
Peak velocity (cm/s)	16.9 (8.0)	15.4 (8.4)	**0.87**	8.1	50.3
$CV_{peak\ velocity}$ *(%)*	26.0 (8.1)	26.6 (9.9)	0.04	24.2	91.9
Jerk metric $(1/s^2)$	55.9 (17.3)	59.2 (30.0)	**0.85**	25.9	44.9
$CV_{jerk\ metric}$ *(%)*	22.0 (6.9)	24.2 (12.2)	**0.73**	14.1	60.9
Speed metric	0.41 (0.08)	0.42 (0.06)	**0.77**	0.09	22.4
$CV_{speed\ metric}$ *(%)*	19.8 (5.8)	15.1 (4.3)	**0.61**	9.6	54.7
Square					
Velocity (cm/s)	9.5 (3.7)	8.7 (4.5)	**0.93**	3.0	32.8
$CV_{velocity}$ *(%)*	21.3 (9.7)	17.7 (7.5)	**0.59**	15.5	79.4
Peak velocity (cm/s)	30.7 (7.3)	29.5 (9.5)	**0.93**	6.1	20.4
$CV_{peak\ velocity}$ *(%)*	19.5 (5.4)	19.5 (6.8)	**0.44**	12.6	64.6
Jerk metric $(1/s^2)$	33.2 (6.4)	32.5 (8.8)	**0.74**	10.7	32.5
$CV_{jerk\ metric}$ *(%)*	20.1 (7.0)	21.6 (4.7)	**0.60**	10.3	49.6
Speed metric	0.31 (0.08)	0.30 (0.06)	**0.80**	0.09	29.0
$CV_{speed\ metric}$ *(%)*	18.6 (7.5)	20.2 (7.4)	**0.51**	14.2	73.2
Shape inaccuracy (cm)	1.7 (0.5)	1.5 (0.3)	**0.45**	0.8	52.0
$CV_{shape\ inaccuracy}$ *(%)*	17.8 (9.5)	15.6 (6.9)	**0.46**	16.5	99.2
Circle					
Velocity (cm/s)	14.8 (7.6)	14.2 (8.3)	**0.89**	7.2	49.6
$CV_{velocity}$ *(%)*	19.5 (10.4)	16.3 (8.2)	**0.87**	9.4	52.3
Peak velocity (cm/s)	35.4 (13.6)	33.7 (12.9)	**0.87**	13.0	37.7
$CV_{peak\ velocity}$ *(%)*	17.4 (8.4)	17.3 (7.4)	**0.81**	9.4	54.0
Jerk metric $(1/s^2)$	35.2 (10.0)	34.1 (13.4)	**0.80**	14.4	41.7
$CV_{jerk\ metric}$ *(%)*	19.9 (7.7)	21.4 (8.0)	**0.49**	15.4	74.6
Speed metric	0.41 (0.08)	0.41 (0.10)	**0.76**	0.12	29.5
$CV_{speed\ metric}$ *(%)*	15.2 (5.2)	15.7 (9.8)	**0.57**	13.9	90.0
Shape inaccuracy (cm)	1.0 (0.3)	0.9 (0.5)	**0.77**	0.5	57.8
$CV_{shape\ inaccuracy}$ *(%)*	29.1 (8.8)	27.7 (12.9)	**0.40**	23.4	82.4

The indices that showed a moderate to excellent reliability are in bold (ICC≥0.4).

Table 3: Results of the one-way ANOVA test comparing 25 stroke patients and 25 healthy subjects, the Pearson correlation test (BB) and the Spearman correlation test (USFMA) in 25 stroke patients for each task and index.

	Stroke (n=25) Mean (SD)	Healthy (n=25) Mean (SD)	Correlation coefficient (r) BB	USFMA
Free amplitude				
Amplitude (cm)	26.2 (7.3)	29.2 (3.0)	0.30	0.22
$CV_{amplitude}$ (%)	4.5 (3.1)***	2.1 (1.6)	-0.35	-0.34
Velocity (cm/s)	10.2 (6.4)	10.5 (3.9)	-0.30	-0.16
$CV_{velocity}$ (%)	18.3 (8.2)**	12.1 (5.7)	**-0.41**	-0.32
Straightness	0.89 (0.1)***	0.98 (0.02)	**0.42**	0.28
$CV_{straightness}$ (%)	5.5 (5.3)***	1.6 (1.4)	-0.27	-0.31
Peak velocity (cm/s)	27.6 (12.7)	23.6 (6.8)	-0.34	-0.20
$CV_{peak\ velocity}$ (%)	22.9 (17.7)	15.7 (10.3)	0.06	0.08
Jerk metric ($1/s^2$)	33.0 (9.0)***	26.0 (3.9)	-0.38	-0.31
$CV_{jerk\ metric}$ (%)	21.1 (6.9)	17.5 (6.9)	-0.24	-0.21
Speed metric	0.36 (0.09)***	0.44 (0.06)	0.04	0.02
$CV_{speed\ metric}$ (%)	18.2 (6.1)***	11.4 (5.2)	-0.27	-0.23
Target				
Target inaccuracy (cm)	2.6 (2.8)**	1.0 (0.4)	**-0.51**	-0.20
$CV_{target\ inaccuracy}$ (%)	39.4 (16.5)	47.3 (15.6)	-0.07	0.06
Velocity (cm/s)	6.5 (3.8)	5.1 (1.7)	**-0.44**	-0.38
$CV_{velocity}$ (%)	30.2 (15.3)	27.0 (18.4)	**-0.57**	**-0.51**
Straightness	0.88 (0.11)**	0.98 (0.3)	**0.41**	0.33
$CV_{straightness}$ (%)	9.8 (12.2)**	1.7 (1.4)	-0.37	-0.32
Peak velocity (cm/s)	15.9 (7.7)**	10.4 (2.5)	**-0.52**	**-0.47**
$CV_{peak\ velocity}$ (%)	29.8 (10.3)	30.0 (16.5)	**-0.60**	-0.37
Jerk metric ($1/s^2$)	52.9 (17.3)**	38.4 (12.8)	-0.24	-0.30
$CV_{jerk\ metric}$ (%)	26.8 (12.5)	35.5 (16.3)	-0.03	-0.06
Speed metric	0.41 (0.07)***	0.49 (0.07)	0.13	0.21
$CV_{speed\ metric}$ (%)	22.7 (10.0)**	15.5 (5.6)	**-0.53**	-0.31
Square				
Velocity (cm/s)	8.7 (3.9)	8.5 (2.6)	-0.06	-0.01
$CV_{velocity}$ (%)	21.1 (9.1)***	8.3 (2.3)	-0.36	-0.13
Peak velocity (cm/s)	29.2 (8.1)**	23.3 (5.3)	-0.31	-0.14
$CV_{peak\ velocity}$ (%)	19.6 (6.2)	14.1 (14.0)	-0.11	-0.01
Jerk metric ($1/s^2$)	31.4 (7.0)	31.9 (7.5)	0.03	-0.13
$CV_{jerk\ metric}$ (%)	20.5 (7.9)	17.4 (5.3)	0.23	0.12
Speed metric	0.30 (0.08)***	0.36 (0.05)	0.25	0.12
$CV_{speed\ metric}$ (%)	18.6 (6.7)***	12.3 (4.8)	-0.28	-0.12
Shape inaccuracy (cm)	1.8 (1.0)**	1.2 (0.1)	**-0.41**	-0.14
$CV_{shape\ inaccuracy}$ (%)	18.5 (10.3)**	11.7 (5.9)	-0.30	-0.13
Circle				
Velocity (cm/s)	13.7 (7.5)	13.8 (5.4)	0.05	-0.28
$CV_{velocity}$ (%)	19.7 (9.7)***	9.9 (4.4)	**-0.61**	**-0.49**
Peak velocity (cm/s)	34.1 (13.8)	27.6 (8.3)	-0.04	-0.31
$CV_{peak\ velocity}$ (%)	16.5 (7.3)***	10.0 (3.5)	**-0.46**	-0.31
Jerk metric ($1/s^2$)	34.3 (10.4)*	28.6 (7.9)	-0.23	-0.41
$CV_{jerk\ metric}$ (%)	19.1 (7.6	16.7 (5.6)	**-0.60**	**-0.61**
Speed metric	0.39 (0.10)***	0.49 (0.06)	0.32	-0.11
$CV_{speed\ metric}$ (%)	14.8 (5.5)***	9.3 (3.7)	-0.32	-0.32
Shape inaccuracy (cm)	1.0 (0.6)**	0.6 (0.3)	-0.13	-0.15
$CV_{shape\ inaccuracy}$ (%)	29.1 (13.8)**	19.7 (6.7)	-0.19	-0.06

* correspond to the indices significantly altered in stroke patients (*p<0.05; **p<0.01; ***p<0.001).

The indices with a significant correlation (p<0.05) are in bold.

Table 4: Results of the second step of the PCA in 25 stroke patients for the 13 kinematic indices selected in the first step of the PCA.

	PC 1 (r)	PC 2 (r)	PC 3 (r)	PC 4 (r)	PC 5 (r)
Free amplitude					
Amplitude (cm)	0.06	0.18	0.34	**0.79**	0.07
$CV_{straightness}$ (%)	0.00	**-0.86**	0.01	-0.23	0.05
Peak velocity (cm/s)	**0.81**	0.33	0.02	0.32	-0.11
$CV_{speed\ metric}$ (%)	-0.20	-0.56	0.46	-0.14	-0.08
Target					
Peak velocity (cm/s)	**0.93**	0.07	0.13	0.06	-0.18
$CV_{jerk\ metric}$ (%)	**-0.60**	-0.09	-0.15	0.38	0.21
Speed metric	**0.83**	-0.15	-0.17	-0.05	0.17
Square					
Velocity (cm/s)	0.36	**0.61**	-0.08	0.44	-0.36
$CV_{jerk\ metric}$ (%)	-0.08	0.00	0.09	0.14	**0.92**
$CV_{shape\ inaccuracy}$ (%)	0.24	**0.64**	0.36	-0.36	0.36
Circle					
$CV_{velocity}$ (%)	-0.06	-0.21	0.37	**-0.71**	-0.13
Jerk metric (1/s²)	**0.86**	0.28	-0.04	0.08	0.05
$CV_{speed\ metric}$ (%)	0.06	-0.02	**0.86**	0.04	0.12
Variance proportions (%)	33	17	12	9	8

PC= Principal Component

For each principal component, the correlated indices are in bold and the selected, and the most correlated index is underlined.

5. Discussion

Main objective: metrological properties of a standardized protocol

To pursue the development of a preliminary protocol[117], designed to quantitatively assess the upper limb kinematics in stroke patients by using the REAplan robotic device. This objective was reached by analyzing a number of metrological properties for the protocol.

Our results showed that some indices seem particularly useful in discriminating between patients and healthy subjects. The straightness (unidirectional tasks) and the smoothness (all tasks) of movements were altered in patients, confirming results of several authors[19,60,75,117,144]. The Coefficient of Variation was also abnormal in patients, and seems useful in assessing the ability to maintain a similar pattern of movement in repetitive tasks. Even if some patients (n=19) performed movements with their affected but non-dominant upper limb, it did not influence the comparison between groups. Indeed, our results showed that almost all the kinematic indices (41/44) were not influenced by laterality.

In stroke patients, the demonstration of a high reliability of kinematic indices obtained from various tasks is in agreement with Wagner et al.[54]. Indeed, these authors have also shown moderate to excellent reliability of kinematic indices obtained from a simple forward-reaching task measured with an optical tracking system. Only one index, the Coefficient of Variation of peak velocity index (Free Amplitude task), should be excluded from the present protocol because of its poor reliability. However, many indices (19/44) showed poor reliability in healthy subjects. De Vet et al.[158] thought that ICC analyses in healthy subjects could be negatively influenced by the small variability between healthy subjects. A paired t-test was carried out and revealed no significant difference between the two sessions for each kinematic index (p-value>0.05). This analysis suggests that all the indices may be reliable in healthy subjects.
The MDC was used to determine the minimal change that exceeds the measurement error in each index score[54,155]. A real improvement of upper limb kinematic indices in stroke patients could only be suggested when this improvement exceeds the MDC values given in our results (Table 2).

The construct validity of our protocol was determined by showing some correlations between kinematic indices and clinical scales. A recent review has reported correlations with the Upper Limb Sub-score of the Fugl-Meyer Assessment but has not reported any correlation with the Box and Block test[39]. The present study confirms that some kinematic indices could have correlations with the motor control of the upper limb, as assessed by the Upper Limb Sub-score of the Fugl-Meyer Assessment[39]. However, our study demonstrates that an even larger number of kinematic indices have correlations with gross manual dexterity assessed by the Box and Block test. The proximal motor control of the upper limb, involved in USFMA and BB, could explain these correlations. However, the better correlation observed with the BB test could be related to the parametric statistics used, which was not the case for the USFMA. Correlations could have been better if the proximal and distal items of the USFMA had been split up. However, the whole score of USFMA was chosen because no study has validated a subscale of the Fugl-Meyer scale for the proximal upper limb only[12].

The poor correlation of some indices (e.g., smoothness in all tasks) could be because our protocol is able to reflect some specific movement characteristics that are otherwise difficult to quantify and that are not traditionally assessed by clinical scales. The kinematics, Box and Block test and Upper Limb Sub-score of the Fugl-Meyer Assessment assess the body functions and structures domain of the International Classification of Functioning Disability and Health (ICF)[12]. Further studies should determine the correlations between kinematics and the other ICF domains such as activity (e.g., Abilhand[147]) and social participation (e.g. SATIS-Stroke[159]).

The kinematic results were compared between the dominant and non-dominant hand in healthy subjects. Surprisingly, the majority of the variables were not affected by hand dominance. A difference between the dominant and non-dominant sides was found in only 3 of 44 indices. This difference was slight and lower than the MDC assessed in stroke patients (see Table 2). This symmetry could be related to the major contribution of the shoulder and elbow when using REAplan. Greater involvement of the wrist and the hand could lead to a larger laterality effect. Indeed, Ozcan et al.[160] suggested that the digital dexterity (as assessed by the

VALPAR Component Work Sample-4) was better for the dominant hand than for the non-dominant one.

Second objective: a standardized short protocol

The second objective of this study was to provide a short version of this protocol. Our study investigated a large variety of tasks and indices that involved elements of unidirectional (i.e. Free Amplitude and Target tasks) or multidirectional/graphical (i.e. Circle and Square tasks) movements. Moreover, these tasks could be rhythmic (i.e. Free Amplitude and Circle tasks) or discrete (i.e., Target and Square tasks), which involves different neuronal mechanisms[138,161,162].

The short version of the protocol requires all tasks and five indices. However, for the Target task, the peak velocity index should be replaced by the speed metric one for the two following reasons. First, these two indices are highly correlated to the first principal component (Table 4). Second, the speed metric index shows higher alteration in stroke patients and higher change after a treatment than the peak velocity one[60,75,117]. The final short protocol and its metrological properties are presented in the Table 5. This short version could facilitate the use and acceptance of robotic assessment in routine clinical practice, as recommended by Balasubramanian et al.[39]. Indeed, clinicians could use this short protocol to easily monitor the patients' improvements during their rehabilitation. This protocol could also help the clinicians to define and adapt the patients' rehabilitation program. Further studies should be conducted to determine the sensitivity to change of this short version by assessing upper limb improvements in stroke patients during recovery.

Table 5: metrological properties of the short kinematic protocol

	ICC	MDC%
Free amplitude		
Amplitude (cm)	**0.84**	11.6
*$CV_{straightness}$ (%)**	**0.78**	121.6
Target		
*Speed metric**	**0.77**	22.4
Square		
$CV_{jerk\ metric}$ (%)	**0.60**	49.6
Circle		
*$CV_{speed\ metric}$ (%)**	**0.57**	90.0

The indices that showed a moderate to excellent reliability are in bold (ICC>0.4). * correspond to the indices significantly altered in stroke patients (p<0.001).

No index is significantly altered in the non-dominant upper limb (p>0.05). No index is correlated with BB and USFMA.

Limitations and Perspectives

There were several limitations to the present study.

First, the REAplan conception allows end-effector movements in 2 spatial dimensions only (2D), what could limit its benefits in kinematic assessment and in rehabilitation. Although these planar distal movements, the shoulder and elbow movements involve 3D displacements. Further studies could apply this protocol to an exoskeleton robotic device[38,124] or an optical tracking system[58], which assess upper limb movements in 3D.

Second, three tasks (i.e., circle, square and target tasks) were made in a short workspace, so that it could limit their relevance. This choice is justified by the following reasons. Previous studies showed that reaching targets placed at a distance of 14 cm in front of the subject are enough to objectify altered movements in stroke patients[75]. The shapes were smaller than in a previous study[117] where the most severely affected patients have had difficulties to draw the shapes because of their large size.

6. Conclusions

This study provides a standardized, valid, reliable, sensitive and concise kinematic protocol to objectively and quantitatively assess upper limb impairments in stroke patients by using a planar robotic device such as REAplan. A short protocol was provided reducing the number of indices to five (i.e., Amplitude, $CV_{straightness}$, speed metric, $CV_{jerk\ metric}$ and $CV_{speed\ metric}$). Future studies should extend the use of this assessment tool to other populations of patients, such as those with cerebral palsy, orthopedic trauma, Parkinson's disease, and others. This protocol is independent to the REAplan and could be implemented to other devices. A robot is not only a rehabilitation tool but also an assessment tool. It offers more specific and accurate kinematic indices than we could obtain with pencil movements performed on a sheet of paper. This device allows easy and quick evaluation of upper limb kinematics that could be useful in daily clinical practice and in clinical research.

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Part 2
A robotic device to rehabilitate upper limb movements

Upper limb robot-assisted therapy in cerebral palsy: A single-blind randomized controlled trial

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1. Abstract

Background – Several pilot studies have evoked the interest of Robot-Assisted Therapy (RAT) in children with Cerebral Palsy. Objective – To assess the effectiveness of RAT in children with cerebral palsy (CP) through a single-blind randomized controlled trial.

Patients and Methods – Sixteen children with CP were randomized into 2 groups. Eight children performed 5 conventional therapy sessions per week over 8 weeks (Control group). Eight children completed 3 conventional therapy sessions and 2 robot-assisted sessions per week over 8 weeks (Robotic group). For both groups, each therapy session lasted 45 minutes. Throughout each RAT session, the patient attempted to reach several targets consecutively with the REAplan. The REAplan is a distal effector robot that allows for displacements of the upper limb in the horizontal plane. A blinded assessment was performed before and after the intervention with respect to the ICF framework: body structure and function (upper limb kinematics, Box and Block test, QUEST, strength and spasticity), activities (Abilhand-Kids, PEDI) and participation (MHAVIE).

Results – During each RAT session, patients performed 744 movements on average with the REAplan. Among the variables assessed, the smoothness of movement ($p<0.01$) and manual dexterity assessed by the Box and Block test ($p=0.04$) improved significantly more in the Robotic group than in the Control group.

Conclusions – This single-blind randomized controlled trial provides the first evidence that RAT is effective in children with CP. Future studies should investigate the long-term effects of this therapy.

Key words: Rehabilitation; Robotics; Cerebral Palsy; Kinematics; Motor learning ; Pediatrics; International Classification of Functioning, Disability and Health.

2. Introduction

Cerebral Palsy (CP) is a neuro-developmental disease related to non-progressive cerebral abnormalities that occur before birth or early in life, and it affects 2 to 3 children out of every 1000[163]. The CP children have hemi-, quadri- or di-plegia, which could be associated with abnormal sensibility, motor control, strength and tonus (i.e., spasticity) of the upper limb[6,7]. These impairments may restrict a CP child's functional capacity and participation in activities of daily living (ADL)[4,90].

Recent recommendations state that intensive rehabilitation is necessary for improving motor function in children with CP[4,90]. These recommendations, based on motor learning theories, suggest that repetitive and assist-as-needed movements that are associated with sensory feedback and an attractive environment are likely to promote reorganization of the neuronal networks (i.e., neuroplasticity) and motor development after brain injuries[4,164,165].

Robot-Assisted Therapy (RAT) of the upper limb has the potential to satisfy these recommendations in CP children[22,35,99,166]. RAT is conducted using robotic devices that enable the patients to perform specific upper limb movements[14]. The main interest in using robots is to allow the patients to achieve a large amount of movement in a limited time. For instance, children with CP were able to perform 640 movements during 60-minute RAT sessions[35]. Additionally, the attractive human/machine interface has the capacity to motivate the child to perform his or her therapy[14]. This visual interface can be adapted to be kid-friendly through playful games such as car races[22,35,99] or to perform exercises that mimic ADL, such as reaching for a cup[22]. Moreover, robotic devices allow the patient to receive visual, auditory or sensory feedbacks[35,99]. Finally, the haptic interaction of the robot gives performance-based assistance to the patients[38,105]. This assistance can enhance the neuronal plasticity by enabling the patients to initiate and accomplish movements as actively as possible[105].

RAT efficacy has been studied in stroke patients[92]. A recent meta-analysis concluded that RAT could improve upper limb structure and function and the ADL of these patients. Some pilot studies have described the feasibility and interest in using this therapy in CP children[22,35,99,100,167]. However, there are no currently published randomized controlled trials, and a recent review has noted that such studies are needed to confirm the usefulness of RAT in CP children[4].

Pilot studies have investigated RAT efficacy in place of, but not combined with, conventional therapy (CT)[22,35,99,100,167]. In everyday life, the combination of RAT, involving substantial movement, and CT could enable the therapist to re-allocate his or her time and energy to transferring the benefits of these repetitive movements (for instance, motor control improvement in stroke patients[92]) to ADL and patient social integration.

According to these considerations, the purpose of this study was to assess the effectiveness of RAT combined with CT compared to conventional therapy alone in children with CP. This comparison was performed in a single-blind, randomized controlled trial. The assessment protocol was in accordance with the 3 International Classification of Functioning (ICF) domains.

3. Materials and Methods

The Ethics Board of our Faculty of Medicine approved this study. All parents freely accepted the participation of their children in the study and provided written informed consent.

Patients Selection

Sixteen patients were recruited from a school for children with physical disabilities (Institut Royal de l'Accueil du Handicap Moteur, Brussels, Belgium). This sample size was dependent on the recruitment possibilities in the school. MG and AR enrolled the children. The patients' characteristics are described in Table 1. The inclusion criteria were a history of CP; a maximum age of 18 years; the ability to understand simple instructions; and moderate to severe impairments of the upper limbs, corresponding to a Manual Ability Classification System (MACS) score greater than 1. The exclusion criteria were epileptic patients and upper limb therapeutic intervention within the previous 6 months, such as a Botulinum toxin injection or neuro-orthopedic surgery. The patients were equally randomized into 2 groups (1:1): a Robotic group and a Control group. A stratified randomization assigned participants to their groups after the first evaluation using a computer-generated random number. The same persons (MG and AR) generated each allocation sequence. The stratification classified the subjects according to their upper limb manual capacity, as assessed by the MACS score (moderate disability, MACS range [2-3]; and severe disability, MACS range [4-5]). The trial was registered at ClinicalTrials.gov, number NCT01700153.

REAplan

The robot used in this study was a robot research prototype named REAplan, which is illustrated in Figure 1a[38]. REAplan is an end-effector robot than can move the patient's upper limb in a horizontal plane via a handle that the patient can grasp or to which he or she may be attached by an orthosis if his or her hand is too weak.

REAplan is fitted with force and position sensors (acquisition frequency: 100 Hz), allowing for control of the lateral ($\bar{F}_{lat}$) and longitudinal ($\bar{F}_{long}$) interaction forces between the patient and the robot. Below, the description of these two interaction forces ($\bar{F}_{lat}$ and $\bar{F}_{long}$) and how these forces are automatically adapted in function of the patient's performance.

The patient has to perform the movement along a reference trajectory. This reference trajectory corresponds to the ideal path that the patient must follow to perform the exercise. $\overline{F}_{lat}$ corresponds to a lateral interaction force, perpendicular to the reference trajectory, that helps the patient stay on the path. The higher this interaction force, the more the robot is helping the patient stay on the reference trajectory. $\overline{F}_{long}$ corresponds to a longitudinal interaction force, parallel to the reference trajectory, that helps the patient move along the trajectory at a reference velocity. The higher this force, the more the robot helps the patient move along the reference trajectory at this reference velocity. For this study, the reference velocity was standardized at 5 cm/s. After reaching the end of a given trajectory (i.e., the target), $\overline{F}_{long}$ and $\overline{F}_{lat}$ are automatically adapted in function of the patient's performance. If the patient reaches the target with a velocity that is below the reference velocity, $\overline{F}_{long}$ increases to help the patient with respect to the reference velocity, and vice versa. If the patient does not maintain the reference path when he moves toward the target, $\overline{F}_{lat}$ increases to help the patient follow the path, and vice versa.

The size of the workspace was adapted to the child's morphology, within a square that was 0.8 m long on each side. Indeed, this workspace was as large as possible to stimulate the children, with regards to their arm lengths, to perform the largest movements with the robot. A screen and a speaker were installed in the robot to give visual and auditory feedback for performance.

Interventions

Both groups (Robotic and Control) received 5 sessions of therapy per week over the course of 8 weeks (40 sessions in all). Each session lasted 45 minutes. For the Control group, all of the sessions were CT. The Robotic group received 2 RAT sessions and 3 CT sessions per week.

The children underwent their CT sessions with their regular physiotherapists and occupational therapists. The physiotherapists practiced neurodevelopmental therapy, and occupational therapists specifically focused on the ADL. The therapists maintained their standard protocols and adapted the rehabilitation to match each child's needs.

All RAT sessions were supervised by the same physiotherapist (MG), who is experienced with the use of robot. RAT sessions consisted of many duplicate exercises. Each exercise consisted of 160 consecutive movements toward a specific target, as suggested by Fasoli et al.[35], with the REAplan robotic device (for illustration, see Figure 1b). A force field helped the children to reach the targets (see the REAplan section). The reaching of each target consecutively resulted in audio feedback, the deletion of the target and the appearance of a new target on the screen. This new target was randomly placed on the visual screen at a distance of 10 cm from the last one. These targets were enlarged for children with visual impairments. For half of the exercises, the target was motionless as long as the patient did not reach it. For the other half, the target was dynamic, moving a distance of 1 cm vertically or horizontally every 0.5 seconds.
The amount of movement, adapted to each patient, was as high as possible to stimulate improvements but was also adapted to the child's tiredness. Each child could have an optional rest between exercises and during each exercise (of approximately 1 minute). Finally, the RAT sessions were in the form of video games. An avatar (the cursor that the child had to move) and a cartoon animal (the target that the child had to reach) were integrated into a appropriate landscape (Figure 1b). The cartoon animal and its corresponding landscape were changed each week. Finally, at the end of each exercise, a personalized feedback was posted on the visual interface to congratulate the child and give him his time score for achieving the 160 targets.

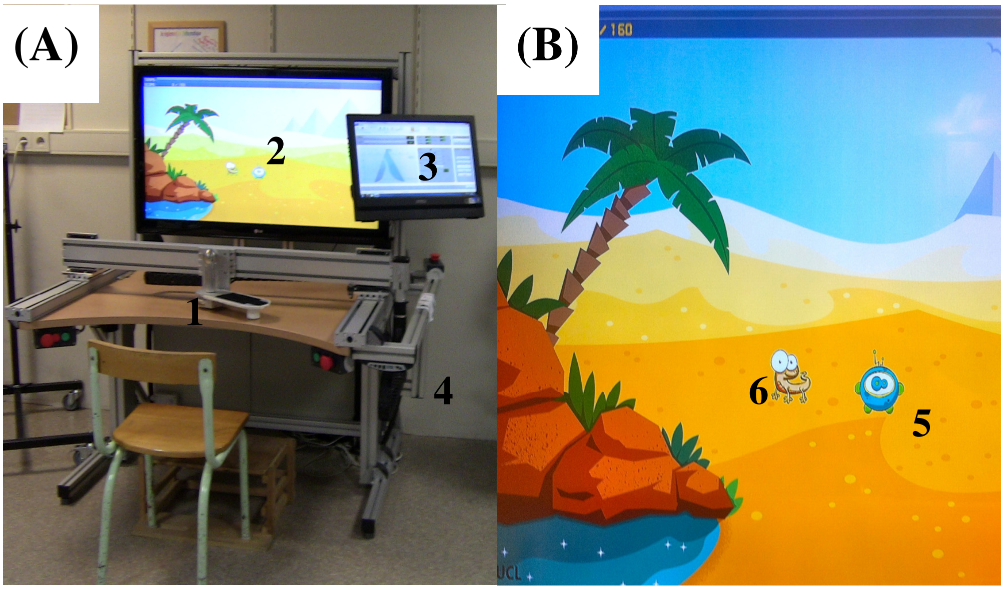

Figure 1: (A) View of REAplan. 1: planar end-effector robot; 2: visual interface for the patient; 3: physiotherapist's interface; 4: adaptive button for the table height. (B) Zoomed-in view of the visual interface during a session of robotic-assisted therapy. 5: Cursor to move; 6: Target to reach.

ICF assessment

All of the children were assessed before and after the intervention through a protocol that took into account the 3 domains of the ICF.

The primary outcome was upper limb kinematics. The first part of this PhD thesis[116,117] provided a standardized protocol to quantitatively assess active movements of the upper limb in stroke patients, including several kinematic indices. The short version of this protocol (5 indices) was used for this study. This protocol consisted of performing 4 different tasks (Free Amplitude, Target, Square and Circle), as described below.

For the Free Amplitude task, the subject had to reach straight out in front of them as far as they could and brought the arm back to the starting position. For the Target task, the subject made movements in the most precise and direct manner

toward a specific target placed at a distance of 10 cm in front of the subject. After performing this task, the robot brought the subject's arm back to the starting position. For the Square and Circle tasks, the subject had to draw two geometrical shapes: a square of 6 cm side and a circle of 4 cm radius. These shapes were performed clockwise with the right upper limb, and counter-clockwise with the left one. These tasks were performed with REAplan, without any assistance (i.e., no interaction forces) and at spontaneous velocities.
For the Free Amplitude task, the computed indices were the amplitude and the coefficient of variation (CV) of the straightness. For the Target task, the speed metric index was calculated. For the Square and Circle tasks, the $CV_{\text{jerk metric}}$ and $CV_{\text{speed metric}}$ indices, respectively, were computed. Each index of this short protocol was computed for each of the 10 cycles of movement and was then averaged.
The kinematic assessment started after a 10-minute training phase to limit learning bias. For the acquisition phase, the order of tasks was randomly assigned. Each task was performed 10 consecutive times, during which the end-effector position was recorded (acquisition frequency: 100 Hz). The rest period between tasks was 1 minute. This kinematic assessment was performed 3 times within the 2 weeks preceding the intervention to evaluate a possible learning effect of the protocol and then once after the intervention. The same blinded physiotherapist (DD) performed each kinematic assessment.

For the secondary outcomes of the body structure and function domain of the ICF, the assessment included the Box and Block test (BB)[132]; the 4 subscales (dissociated movements, grasps, weight bearing and protective extension) of the Quality of Upper Extremity Skills Test (QUEST)[48,168]; the Modified Ashworth Scale (6 muscular groups were tested: shoulder adductors, elbow flexors and extensors, pronators, wrist and finger flexors)[169]; and the strength of 2 muscular groups (elbow flexors and extensors), assessed with a hand-held dynamometer (Microfet2TM, Orsay, France)[170]. For the calculation of muscle torque, the result obtained with the dynamometer was multiplied by the distance measured between the lateral epicondyle and radial styloide[171]. All of these assessment tools were reliable and valid for the studied population[13] and were used by the same blinded occupational therapist (DH).

The secondary outcomes of the activity and participation domains of the ICF correspond to 3 questionnaires. For the activity domain, the French versions of the Abilhand-Kids[172] and Pediatric Evaluation of Disability Inventory (PEDI)[50] questionnaires were filled out by each child's therapist. For the participation domain, the French version of Life Habits was completed by each child's parent[173].

Statistics

Statistical tests were performed using SigmaStat 3.5 software (WPCubed GmbH, Munich, Germany). For tests with parametric measures, the normal distribution and equality of variance were verified for all comparisons. For each test, the significance level was 0.05.

For each parametric and non-parametric measure, a 1-way analysis of variance (ANOVA) or a Mann-Whitney test was performed to verify the parity of the baseline results between groups. To verify the learning effect of the primary outcome, a 1-way repeated ANOVA was performed for each kinematic index on the 3 measures computed before the intervention.

For each parametric variable, a 2-way repeated ANOVA was performed to analyze the interaction between the time (before vs. after interventions) and groups (Control vs. Robotic groups). For each significant interaction, a Bonferroni-adjusted post hoc (Holm Sidak) test was used to analyze the differences in the change between groups. For each non-parametric variable, a Mann-Whitney test and a Wilcoxon test were performed to analyze the treatment effects between groups and within each group, respectively.

4. Results

The recruitment and baseline assessments were performed in September 2012, and the interventions were started in October 2012. The final interventions were completed in December 2012. The final assessments were performed between one and seven days following the final rehabilitation session. The flowchart of this study is illustrated in Figure 2.

All 16 patients completed the study. During each RAT session, the patients performed 744 (224) (mean [SD]) movements on average with the REAplan. For the Robotic group, the children performed 15 (0) sessions of RAT and 23 (0.9) sessions of CT. For the Control group, the children received 38.4 (1.7) sessions of CT. No adverse events were reported. All results are presented in Tables 1, 2 and 3 and are illustrated in Figure 3.

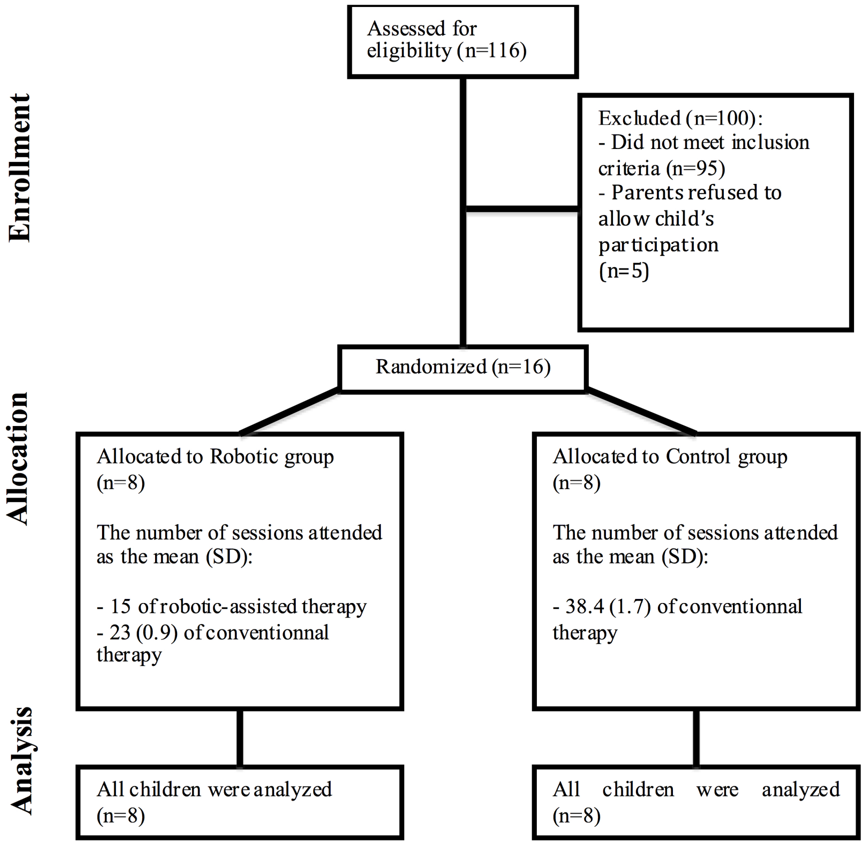

Figure 2: Flow diagram of the participants through each stage of the study (i.e., Enrollment, Allocation and Analysis) (adapted from CONSORT [Moher et al., 2010]).

Similarity between groups at baseline and learning effect

Before the interventions, the results of the kinematic indices were similar between groups, except for the $CV_{straightness}$ of the Free Amplitude task (p=0.03) (Table 1). There was no learning effect for the primary outcome (Table 1). Indeed, for all merged tasks, the kinematic indices were similar within the 3 measures computed before the intervention (p>0.09). For this reason, the average of these 3 kinematic measures was considered to be the baseline results.

Effect of therapy

For the body structure and function domain, an interaction between the time and groups revealed that the smoothness in discrete and unidirectional upper limb movements only improved in children who received RAT ($p<0.01$) (Table 2). Indeed, for the Target task, the speed metric index increased from 0.42 (0.05) to 0.49 (0.03) in the Robotic group, but this index score did not change in the Control group (0.46 [0.05] to 0.46 [0.06]). For the 3 other tasks (Free Amplitude, Square and Circle), the kinematics indices did not change after intervention ($p>0.05$).

An interaction between time and groups showed that the manual dexterity of the upper limb improved significantly more in children who received RAT than children who only received CT ($p=0.04$) (Table 2). Indeed, the BB score improved from 13.0 (7.3) to 16.6 (9.9) blocks/min in the Robotic group, while this score increased only slightly from 13.4 (9.6) to 13.8 (9.7) in the Control group.

The capacity to perform analytical movements of the upper limb similarly improved in both groups ($p<0.05$) (Table 3). Indeed, the scores of the dissociated movements subscale of the QUEST significantly increased for the Robotic (median increased from 37.0 to 63.3/100) and Control (median increased from 44.4 to 68.8) groups ($p<0.04$). However, these improvements were not different between the groups ($p=0.87$) (Table 3).

There was no significant effect of treatment for the other scales and for the 3 questionnaires assessing the activity and participation domains ($p>0.06$) (Tables 2 and 3).

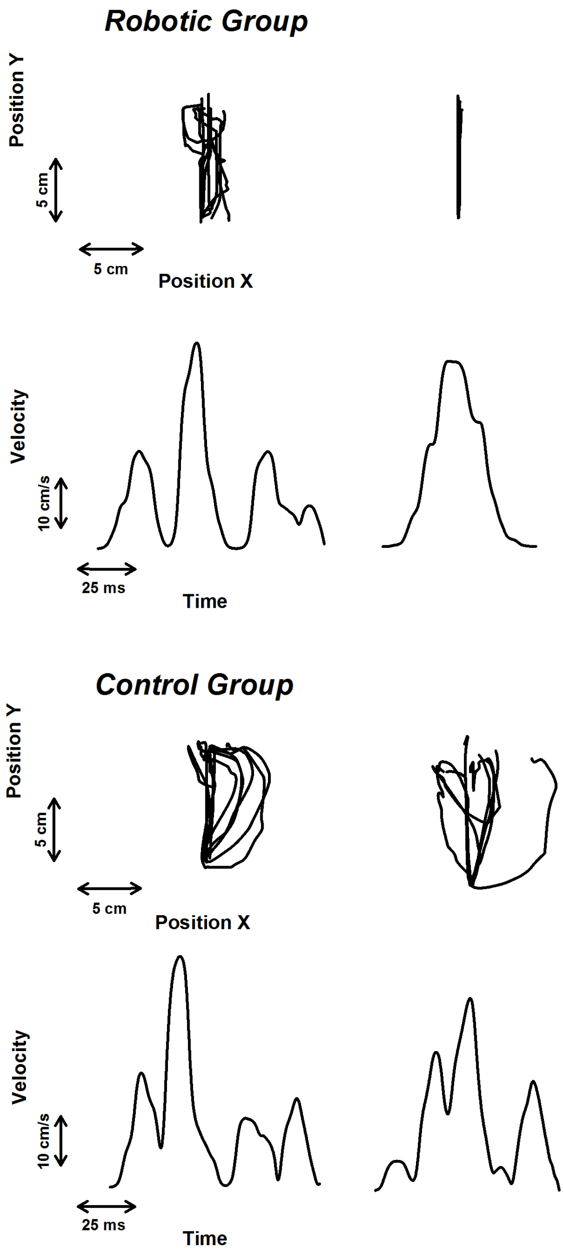

Figure 3: For the Target task in each group (Robotic and Control), illustration of the typical traces computed for 1 child before (*left graphs*) and after (*right graphs*) treatment. The upper graphs show the displacement plots of 10 consecutive trials. The lower graphs show the velocity curve of 1 in-progress trial.

Table 1: Characteristics of the subjects included in the Robotic and Control groups and results of the baseline measurement comparison between the groups and the learning effects of the upper limb kinematics in all children.

	Robotic Group Mean (SD) (n=8)	Control Group Mean (SD) (n=8)	P-value	Test 1 Mean (SD) (n=16)	Test 2 Mean (SD) (n=16)	Test 3 Mean (SD) (n=16)	P-value
Characteristics							
Age, years, mean (SD)	10.8 (4.6)	11.0 (3.5)					
MACS (1-5), median [Q1-Q3]	3 [2-3.3]	2.5 [2-4]					
Quadri/Di/Hemi-plegic, n	4/4/0	3/4/1					
Dominance, R/L, n	3/5	4/4					
Kinematic indices							
Amplitude (cm)	14.9 (7.2)	20.1 (5.0)	0.12	17.5 (7.0)	17.8 (6.6)	17.1 (7.0)	0.62
$CV_{straightness}$ *(%)*	6.9 (3.0)	3.7 (2.3)	0.03*	5.6 (3.7)	4.9 (3.5)	5.4 (5.0)	0.83
Speed metric	0.42 (0.05)	0.46 (0.05)	0.10	0.45 (0.05)	0.43 (0.07)	0.45 (0.06)	0.25
$CV_{jerk\ metric}$ *(%)*	18.8 (2.8)	20.1 (2.7)	0.36	19.5 (5.1)	20.1 (7.1)	16.4 (5.0)	0.09
$CV_{speed\ metric}$ *(%)*	17.9 (4.1)	20.9 (7.9)	0.39	18.7 (4.5)	19.1 (4.8)	20.5 (5.4)	0.66
BB (blocks.min^{-1})	13.0 (7.3)	13.4 (9.6)	0.93				
QUEST (/100)†							
Dissociated mvts	37 [21.1-43.8]	44.4 [25-54.7]	0.54				
Grasp	51.9 [18.5-72.5]	51.9[25.9-75.0]	0.80				
Weight bearing	45.5 [23.0-77.6]	74.0[29.1-97.5]	0.66				
Protective extension	0.0 [0.0-50.0]	41.7 [8.3-87.5]	0.45				
Muscle torques (N.m)							
Elbow flexion	9.9 (5.3)	11.7 (5.2)	0.52				
Elbow extension	9.3 (4.0)	11.5 (5.8)	0.40				
MAS (/4)†							
Shoulder adduction	1.0 [0.0-1.3]	0.0 [0.0-0.0]	0.28				
Elbow flexion	2.0 [0.8-2.0]	0.5 [0.0-2.0]	0.57				
Elbow extension	0.0 [0.0-0.3]	2.0 [0.0-2.0]	0.13				
Elbow pronation	1.5 [0.0-2.0]	0.5 [0.0-2.0]	0.78				
Wrist flexion	1.0 [0.8-2.0]	0.0 [0.0-2.0]	0.20				
Finger flexion	0.0 [0.0-1.3]	0.0 [0.0-0.5]	0.51				
Abilhand-Kids (Logits)	-1 (3.6)	-1.2 (3.4)	0.92				
PEDI (/63)†	21 [20-39.5]	27 [18.5-46]	0.90				
Life-Health (/248)†	106.5 [67.5-136.8]	148 [137-153.5]	0.15				

Q1=First quartile; Q3=Third quartile; R=Right; L=Left; MACS=Manual Ability Classification System; BB=Box and Block test; MAS=Modified Ashword Scal

† indicates results with Median [1st quartile-3rd quartile]; * corresponds to a significant baseline difference.

Table 2: Two-way ANOVA results for parametric variables comparing the treatment effects between the Robotic and Control

	T1-T0 Mean difference (SD)		Group effect P-value	Time effect P-value	Interaction Group x Time effect P-value	Effect size Cohen's *d*
	Robotic group (n=8)	Control group (n=8)				
Kinematic indices						
Free amplitude						
Amplitude (cm)	1.7 (1.6)	0.6 (3.1)	0.15	0.37	0.08	0.48
$CV_{straightness}$ (%)	0.8 (6.4)	1.1 (2.5)	0.05	0.92	0.45	-0.06
Target						
Speed metric	0.07(0.05)	0.00 (0.05)	0.75	<0.01*	0.01*	1.52
Square						
$CV_{jerk\ metric}$ (%)	-0.8 (6.5)	0.4 (8.2)	0.49	0.50	0.50	-0.17
Circle						
$CV_{speed\ metric}$ (%)	2.5 (6.8)	0.0 (7.1)	0.26	0.75	0.92	0.36
BB (blocks.min^{-1})	3.6 (3.6)	0.4 (2.1)	0.79	0.04*	0.02*	1.14
Muscle torques (N.m)						
Elbow flexion	1.5 (4.9)	2.9 (3.3)	0.59	0.53	0.07	-0.34
Elbow extension	0.6 (2.5)	2.1 (3.1)	0.45	0.31	0.09	-0.54
Abilhand-Kids (Logits)	-0.2 (0.8)	-1.1 (1.3)	0.71	0.15	0.06	0.93

* indicates significant results (p<0.05).

Effect size was rated as large, medium and small with Cohen'd scores >0.8, 0.5-0.8 and <0.5, respectively.

Table 3: Results of the Mann-Whitney and Wilcoxon tests for non-parametric variables comparing the treatment effects between the Robotic and Control groups and within each group

	Mann-Whitney test		Wilcoxon test			
	Robotic group (n=8)	Control group (n=8)	Robotic group (n=8)		Control group (n=8)	
	T1-T0	T1-T0	T0	T1	T0	T1
QUEST (/100)						
Dissociated movements	23.5 [5.7;41.0]	28.1 [21.9;36.4]	37.0 [21.1;43.8]	63.3 [41.3;74.3]*	44.4 [25;54.7]	68.8 [44.9;83.3]*
Grasp	9.3 [-9.5;23.1]	12.7 [1.9;23.2]	51.9 [18.5;72.5]	59.3 [41.7;85.2]	51.9 [25.9;75.0]	55.6 [39.8;75.8]
Weight bearing	10.3 [3.0;24.5]	0.0 [-9.0;0.0]	45.5 [23.0;77.6]	65.0 [30.0;88.0]	74.0 [29.1;97.5]	71.0 [16.0;94.5]
Protective extension	0.0 [0.0;19.5]	0.0 [0.0;2.1]	0.0 [0.0;50.0]	27.8 [12.5;100]	41.7 [8.3;87.5]	52.8 [9.0;92.4]
MAS (/4)						
Shoulder adduction	0.0 [-0.3;0.0]	0.0 [0.0;0.0]	1.0 [0.0;1.3]	0.0 [0.0;1.3]	0.0 [0.0;0.0]	0.0 [0.0;0.0]
Elbow flexion	0.0 [-0.3;0.0]	0.0 [0.0;0.0]	2.0 [0.8;2.0]	1.5 [0.0;2.0]	0.5 [0.0;2.0]	1.0 [0.0;2.0]
Elbow extension	0.0 [0;0.3]	0.0 [0.0;0.5]	0.0 [0.0;0.3]	0.0 [0.0;2.0]	2.0 [0.0;2.0]	2.0[1.8;2.0]
Elbow pronation	0.0 [-1.0;0.0]	0.0 [-0.3;0.0]	1.5 [0.0;2.0]	1.0 [0.0;2.0]	0.5 [0.0;2.0]	0.0 [0.0;0.5]
Wrist flexion	0.0[-1.0;0.0]	0.0 [0.0;0.0]	1.0 [0.8;2.0]	0.5 [0.0;1.3]	0.0 [0.0;2.0]	0.0 [0.0;2.0]
Finger flexion	0.0 [0.0;0.0]	0.0 [0.0;0.0]	0.0 [0.0;1.3]	0.5 [0.0;1.0]	0.0 [0.0;0.5]	0.0 [0.0;0.0]
PEDI (/63)	0.0 [-1.5;2]	2.0 [-2.5;3.5]	21.0 [20.0; 39.5]	24.0 [20.3;32.3]	27.0 [18.5;46.0]	42.5 [18.0;48.5]
Life-H (/248)	8.5[-6.3;30.0]	12.0[-9.0;21.0]	106.5 [67.5;136.8]	113.5[101.3;135.5]	148.0[137.0;153.5]	154.0[139.0;163.0]

The values are presented as Medians [First Quartiles; Third Quartiles]. T0 and T1 correspond to the results before and after the intervention, respectively. T1-T0 corresponds to the difference between the results obtained after (T1) and before (T0) the intervention.

Abbreviation: MAS=Modified Ashword Scale.

* indicates a significant difference ($p<0.05$).

5. Discussion

The aim of this study was to compare the effect of conventional therapy (CT) to the combination of RAT and CT in children with CP in a single-blind randomized controlled protocol. This comparison took into account the 3 domains of the ICF[11].

Body structure and function domain

Some upper limb kinematic indices, assessed by the robot REAplan, and manual dexterity, assessed by the Box and Block test, had significantly more improvement after RAT and CT than after CT alone. Both results suggest a motor learning effect[164]. Indeed, the RAT of this study consisted of repetitive discrete movements (reaching targets), and the observed improvements were specifically related to discrete movements (Target Task of the kinematic assessment and BB).

The assessment protocol of this study followed current recommendations. Indeed, kinematics was chosen as a primary outcome to quantitatively and objectively assess upper limb movements[39], avoiding the disadvantages (e.g., non-parametrical statistics) of qualitative, subjective and ordinal scales[12,39]. After that, this protocol was established to be easily reproduced in clinical routines. Because a robotic device, such as the REAplan, has the potential to rehabilitate and assess patients[116], we suggest that combining both abilities in one tool is more advantageous in clinical routines than adding other kinematic assessment tools, such as an expensive optoelectronic system.

However, one can argue that the kinematic improvement observed in the Robotic group could be related to the child's learning of the specific robot tasks. Even so, the 3 kinematic assessments performed before the intervention did not show any leaning effect. More importantly, the Robotic group transferred the improvement to a more functional task (BB) that was not directly related to robot therapy. Indeed, improvement in the BB test showed a high effect size (Cohen's d = 1.1), which suggests that RAT can significantly influence gross manual ability in children. However, although minimal detectable change in CP is unknown, the change measured (3.6 blocks/min) is below the known minimum for stroke patients (6 block/min)[174] and cannot therefore be assumed to represent a meaningful improvement. These results are consistent with an observational study that has shown kinematic improvements after RAT in children with CP[61]. Finally, randomized controlled trials assessing RAT efficacy in stroke patients have also shown improvements in kinematics and manual dexterity, as assessed by a robot[34,175] and the BB[23], respectively.

The dissociated movements of the QUEST showed improvements in both groups, but no difference between groups. Previous observational studies identified significant improvements on this same subscale after RAT[35,61]. The present results illustrate the necessity of a control group in clinical trials to avoid misinterpretation of the results[110]. The improvement observed in both groups could be explained by the fact that this study started after the summer holidays (lasting 2 months), during which most children did not have rehabilitation. This observation suggests that CT, with or without RAT, could preserve the children's capacity to dissociate upper limb movements.

Activity and participation domains

The improvements of impairments after only 8 weeks of RAT seem promising. However, these improvements did not translate into improved ADL. This result is disappointing because the patients yearn to improve their capacity for ADL as well as their social integration. These results can be explained by the following hypotheses. First, the various exercises were designed to stimulate the patients to repeat discrete reaching movements. However, ADL involves discrete reaching movements (e.g., pushing on a light switch) along with rhythmic reaching movements (e.g., washing the upper body) and grasping movements (e.g., open a bag chips) (for these examples, see Abilhand-Kids[172]). Further studies should expand the exercises to enable the patients to repeat a wide variety of movements (e.g., rhythmic, discrete, with or without hand implication), as suggested by Krebs et al.[61]. Moreover, these exercises could be in the form of ADL[22] or serious games[176]. Second, the activity and participation assessments were presented in the form of questionnaires completed by parents and therapists[50,172,173]. Because the parents and therapists were not blinded, their judgment could have been altered. To increase the responsiveness of this activity assessment, future studies should also use tools to assess the child's performance in ADL, such as the Melbourne Assessment of Unilateral Upper Limb Function[177] or the Assisting Hand Assessment[178].

Limitations and perspectives

This study lays the groundwork for future research on the use of RAT in CP.

Even though the sample size was sufficient to show significant results, it was too small to generalize the results to the clinical setting and to determine the subgroups of children who will be more responsive to RAT. Finally, the sample size did not allow the stratification to take other factors, such as the patients' ages, into account. This bias was limited because the mean age of each group was similar (Table 1). Then, further multicenter trials should be planned to (1) confirm these results with a larger sample and variety of settings[110], (2) add other stratification factors, such as the patients' age, since learning capacities and video games playing experience are not the same among young children and adolescents and (3) establish the correlations between the improvements and the children's characteristics (e.g., impairment severity, age, etc.).

In this study, the proportion of robotic sessions (2/5) was limited by the feasibility of performing the study at school, and the number of RAT sessions (n=15) was chosen in agreement with previous studies[35,99]. However, we still do not know whether more intensive use of the robot or the use of RAT over a longer period of time would yield better results. Additionally, we do not know whether similar results could be obtained with reduced use of the robot. This issue could be addressed through a study conducted over a longer period of time with a regular evaluation of the evolution of the patients' function instead of only at the beginning and after therapy.

This study assessed the effect of RAT directly after therapy but not a few months later for logistical reasons. There was no long-term follow-up, therefore the results do not provide any indication that benefits are maintained or of the necessity to repeat RAT regularly or to use it continuously. This limitation could be addressed by evaluating the evolution of improvements over time, as Krebs et al.[61] have shown for kinematics.

Finally, Sakzewski et al.[90] are interested in combining Botulinum toxin with other upper limb therapies. Future studies should evaluate the effectiveness of the combination of RAT with Botulinum toxin injection in the upper limb. This combination showed promising results in a pilot study and could maximize the improvements to upper limb impairments and activities after RAT[179].

6. Conclusions

In conclusion, this study is the first single-blind randomized controlled trial to assess the efficacy of RAT in children with CP. This therapy improved upper limb kinematics and manual dexterity but did not improve functional activities and social participation. Further studies should confirm these preliminary results on larger populations and assess if RAT could lead to more functional improvements in the long term. The REAplan robotic device provides an intensive and assist-as-needed therapy associated with motivational and performance feedbacks. Robotic devices offer children fun and intensive rehabilitation that a human therapist cannot provide. These robots can be easily integrated as a relevant complement to therapy in the clinical setting.

Acknowledgements

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General discussion and perspectives

General discussion and perspectives

1. Synthesis of the PhD thesis

This PhD thesis investigated the clinical interest of robotic devices to assess and rehabilitate upper limb movements in cerebral palsy (CP) children and stroke adults. For each part of the thesis, a synthesis is provided below.

A robot to assess upper limb movements

The present PhD thesis used the REAplan robot to develop a standardized, norm-referenced, reproducible, valid, responsive and concise protocol to objectively and quantitatively assess upper limb kinematics in CP children and stroke adults. This objective was fulfilled because a standardized protocol was developed that assessed upper limb kinematics in CP children[120] and healthy children[129,180] as well as in stroke adults[116,117] and healthy adults[180] using the REAplan robot. This protocol showed reproducible results in both populations[116,120], which were quantified with minimal detectable change (MDC) values[116]. These MDC values could be used to (i) calculate the sample size of future randomized controlled trials (RCTs)[110] and (ii) identify meaningful improvement after an intervention[155]. Furthermore, age effects and reference standards of this protocol were established in 370 healthy subjects aged 3-93 years old[180], which was recommended by Balasubramanian[39]. Then a short version of this protocol was provided to facilitate the assessment of upper limb kinematics in routine clinical practice[116]. This protocol could thus be used to monitor patients' progress over time and to detect changes in upper limb kinematics after a specific intervention[12,40]. For instance, we showed that upper limb kinematics improved significantly more in children who received robot-assisted therapy (RAT) than in those who only received conventional therapy (CT)[120]. However, further studies should confirm the responsiveness of this protocol by assessing kinematic changes after other interventions such as constraint-induced movement therapy (CIMT)[79] or Hand-Arm Bimanual Intensive Therapy (HABIT)[106].

The construct validity of this protocol was also established in CP children and stroke patients[116,129], showing that upper limb kinematics quantified specific movement characteristics (i.e., the quality of upper limb movements) that were not assessed by usual clinical scales. However, other analyses should be added in the first part of this thesis (first chapter)[129]. In this chapter, the correlations between upper limb kinematics and psychomotor abilities of the upper limb, assessed by Bruininks-Oseretsky test of motor proficiency (BOTMP), were computed in healthy children aged 3 to 12 years. These correlation results could be biased because both scales (kinematics and BOTMP) are influenced by age[129]. Therefore, for each child, the raw results of the kinematic indices and BOTMP subtests were converted into Z-scores. Correlations between the Z-scores of each kinematic index and each BOTMP subtest were performed with a Spearman correlation test, using SigmaStat 3.5 software (WPCubed GmbH, Munich, Germany). The results are presented in Table 1. Interestingly, all the kinematic indices showed no or poor correlation with both BOTMP subtests. These results confirmed that the correlations between kinematics and psychomotor abilities of the upper limb observed in the first chapter of the thesis corresponded to an age effect[129]. These poor correlations between upper limb kinematics and motor abilities were consistent with the fourth chapter of the first thesis part[116]. Indeed, it could be suggested that our protocol is able to reflect some specific movement characteristics (smoothness, straightness, reproducibility) that are otherwise difficult to assess by clinical scales (e.g. Fugl-Meyer test, BOTMP).

Table 1: Results of the Spearman's correlation test for Z-scores of each kinematic index and each BOTMP subtest

	Coefficient correlation (r)	
	Visual-Motor Control	*Velocity and Dexterity*
Free amplitude		
Amplitude (cm)	0.00	0.10
$CV_{amplitude}$ (%)	**-0.22**	-0.04
Straightness	-0.01	0.06
$CV_{straightness}$ (%)	0.14	-0.07
Velocity (cm/s)	-0.05	0.05
$CV_{velocity}$ (%)	0.14	-0.03
Smoothness	0.12	**0.22**
$CV_{smoothness}$ (%)	0.00	-0.13
Target		
Target Inaccuracy (cm)	-0.01	-0.01
$CV_{target\ inaccuracy}$ (%)	-0.03	**-0.25**
Straightness	0.07	0.17
$CV_{straightness}$ (%)	0.03	-0.13
Velocity (cm/s)	-0.02	0.06
$CV_{velocity}$ (%)	0.07	-0.09
Smoothness	-0.07	0.13
$CV_{smoothness}$ (%)	**-0.26**	-0.06
Square		
Shape inaccuracy (cm)	-0.01	0.17
$CV_{shape\_inaccuracy}$ (%)	0.09	0.06
Velocity (cm/s)	0.07	0.01
$CV_{velocity}$ (%)	0.17	0.05
Smoothness	-0.08	0.01
$CV_{smoothness}$ (%)	0.12	0.02
Circle		
Shape inaccuracy (cm)	**-0.23**	0.06
$CV_{shape\_inaccuracy}$ (%)	0.02	0.06
Velocity (cm/s)	-0.07	0.05
$CV_{velocity}$ (%)	0.06	-0.02
Smoothness	-0.12	0.02
$CV_{smoothness}$ (%)	0.03	-0.05

Indices with a significant correlation ($p < 0.05$) are shown in bold

Finally, the content of this kinematic protocol has evolved through the PhD thesis. This progress was essential to adapt the computation of tasks and kinematic indices in function of our clinical and statistical results. For instance, the calculation of shape inaccuracy index was modified in the last chapters in comparison to the third one (first thesis part). This change was essential to analyze the subject's ability to draw a shape without any normalization of the patient's performance. To summarize the results of this PhD thesis, the annexes 1 and 2 provide the details of the final kinematic protocol.

A robot to rehabilitate upper limb movements

The first part of this PhD thesis developed a standardized RAT protocol in CP children according to the neuro-rehabilitation recommendations and investigated the efficacy of RAT in such children through a single-blind RCT, considering the three domains of the International Classification of Functioning, Disability, and Health (ICF). This objective was fulfilled; a RAT protocol that followed the current recommendations in CP neurorehabilitation[4] was created using the REAplan robot[120]. Notably, these recommendations encourage the execution of repetitive and motivating movements[4,101], which should be assisted as needed and associated with feedbacks[16,102]. By using our protocol, CP children performed many movements (744 [224], mean [SD]) in a limited period of time (45 minutes). This finding is (i) consistent with previous studies[17,35] and (ii) unfeasible for human therapists in routine clinical practice[103]. These repetitive movements were assisted as needed due to the interaction forces between the patient and the robot, as in previous studies[16,38,105,120]. In addition to this assistance, inference rules were created to modulate the intensity of these interaction forces. These inference rules allowed for assistance and challenge of the patients' movements in real time as a function of their impairments (e.g., spasticity) and performances (e.g., were the movements kinematically correct?). These methods and inference rules are currently being filed as a patent. Additionally, the exercises of this RAT protocol corresponded to a kid-friendly video game that motivated children to perform many movements. Such motivating programs have already been implemented in several previous protocols[22,99,104,181–183], whereas several other studies have developed rudimentary target tasks[18,34,35,97]. We believe that serious games (*rehabilitating game*s, ed.) are essential in promoting motivation and recovery in patients (cf. perspectives below)[101]. Finally, patients received visual, sensory and auditory feedbacks similar to that provided by other devices[18,34,35,97,99], as recommended by Molier et al.[102].

Additionally, the RCT performed in this PhD thesis showed that the combination of CT and RAT more significantly improved upper limb kinematics and manual dexterity in CP children compared with CT alone. The limitations and perspectives of this study are discussed in the second part of this thesis[120], including the lack of improvement in performing activities of daily living (ADL) and the necessity of combining RAT with other interventions (e.g., botulinum toxin injections[179]). This first study could be the foundation for further studies of using RAT in CP.

2. Perspectives

Robotic assessment

This PhD thesis standardized a protocol to assess upper limb kinematics in CP children and stroke adults. Further studies could use this norm-referenced protocol to (i) assess alterations of upper limb movements in other neurological diseases such as multiple sclerosis[134,135] or Parkinson's disease[136,137] and (ii) monitor the evolution of upper limb kinematics in patients during interventions such as RAT[34,60,61,120], CIMT[79] and Botulinum toxin injection[72,73,80]. Moreover, kinematics assesses the body functions and structures domain of the ICF. Further studies should assess the relationship between this protocol and other scales that assess the activity (e.g., *Abilhand-Kids*[172] in CP children and *Abilhand*[147] in stroke adults) and participation domains (e.g., *Stroke Impact Scale*[51] in adults and *Assessment of Life Habits*[173] in CP children). Next, upper limb kinematics was computed with a planar end-effector robotic device, while kinematics could also be assessed using optoelectric[54–58] or electrogoniometer[59] systems (for review, see tables 3 and 4 of the general introduction). Further studies could compare results of upper limb kinematics computed with a planar end-effector robotic (e.g. REAplan) to results of three-dimensional assessment devices (e.g. optoelectric system). Such a comparison could finalize the validation of our kinematic protocol. Finally, this protocol assessed the quality of upper limb movements without any assistance provided by the robot. Further studies could use the robotic advantages (e.g., assistance, reactivity) to quantitatively and objectively assess specific neurological impairments[6,7,10] such as force[25] and muscles overactivity[20,184].

To illustrate this perspective, the muscles overactivity of the upper limb was recently quantified in twelve stroke patients using the REAplan robot[185]. Each patient had moderate to severe elbow flexor spasticity, corresponding to a Modified Ashworth Scale score greater than 0. For this experiment, the REAplan robot passively moved the patients' upper limbs at various velocities (10, 20, 30, 40 and 50 cm/s) in a back-and-forth trajectory (Figure 1). For each velocity condition, ten back-and-forth upper limb movements were performed. During these movements, the end-effector recorded the force needed (in Newtons) to passively mobilize the upper limb (Figure 1). Each patient performed this protocol with both the impaired and non-impaired upper limbs. Moreover, the patients performed this protocol with their impaired upper limbs before, just after and a day after receiving an anesthetic block (Lidocaine 1%) injection. This injection was performed on the axilla near the musculo-cutaneous nerve. The results of this study, illustrated in Figure 1 and presented in Table 2, showed that the force needed to mobilize the patients' upper limb was significantly greater in the impaired arm than in the non-impaired arm ($p<0.001$). Moreover, greater mobilization velocity was associated with greater force required to mobilize the patients' impaired arms ($p<0.001$). Finally, in the 40 cm/s condition, this force was significantly lower just after the anesthetic block injection than before and the day after this injection was given ($p<0.05$). This study showed that robotic devices could objectify muscles overactivity of the upper limb.

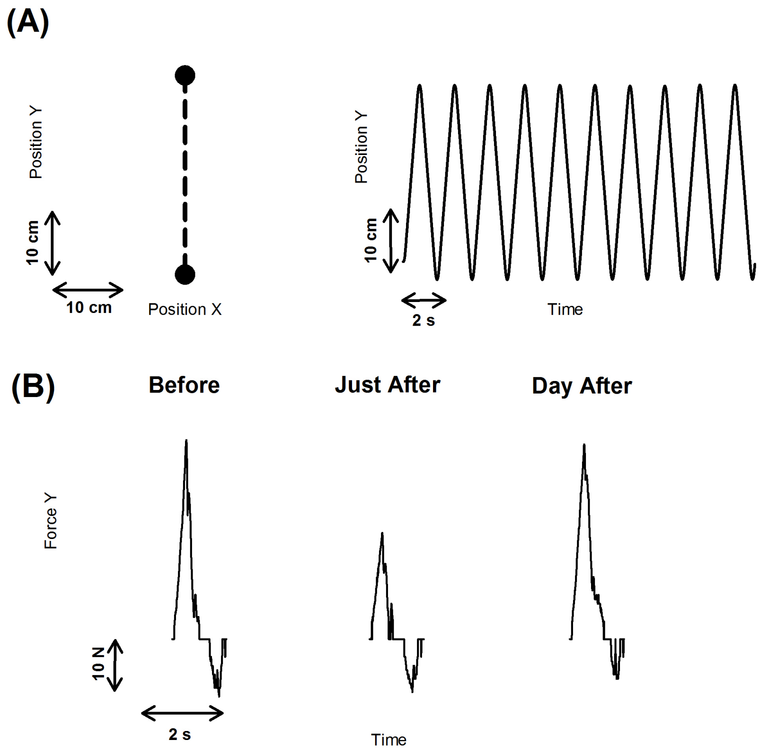

Figure 1: Typical traces of passive mobilization of a stroke patient's impaired upper limb. This mobilization was performed at 40 cm/s. (A) Illustrations of the requested task presented on the visual interface (left column) and the evolution of the end-effector positions as a function of time during ten back and forth movements (right column). (B) Illustrations of the force necessary to passively mobilize the upper limb during one back and forth movement before (left column), just after (middle column) and the day after (right column) anesthetic block injection. The positive and negative force values respectively correspond to the necessary force to pull (extension movements) and brake (flexion movements) the upper limb during the movement.

Table 2: The results of 1-way repeated analysis of variance (ANOVA) comparing the muscles overactivity between the non-impaired and impaired arms for each velocity condition and before the anesthetic block injection (T0). Moreover, the results of 2-way ANOVA analyzing the injection effect as a function of velocity.

	Stroke patients n=12									
	10 cm/s mean (SD)		20 cm/s mean (SD)		30 cm/s mean (SD)		40 cm/s mean (SD)		50 cm/s mean (SD)	
	N-I	I	N-I	I	N-I	I	N-I	I	N-I	I
Overactivity of the elbow flexors, in N										
T0	8.2 (3.5)	32.4 (17.5)	9.7 (3.2)	40.6 (18.3)	10.5 (4.3)	49.8 (17.0)	10.3 (4.0)	60.4 (24.5)	10.8 (5.6)	64.4 (23.4)
Mean of the difference										
T0 – T1		3.8 (11.6)		5.7 (9.2)		5.4 (11.8)		15.2 (16.8)*		16.4 (14.4)*
T2 – T1		2.3 (6.7)		7.9 (8.9)		4.0 (10.0)		12.4 (14.2)*		8.0 (10.0)*
T0 – T2		1.5 (7.4)		-2.1 (7.0)		1.4 (13.0)		2.9 (13.8)		8.4 (12.0)*

Abbreviations: N-I = non-impaired arm; I = impaired arm; SD = standard deviation; T0 = before the injection of anesthetic block; T1 = just after the injection; T2 = day after the injection. For each velocity condition, the muscles overactivity of the impaired arm was significantly higher than that in the non-impaired arm ($p<0.001$).

* indicates significant results for the injection effect ($p<0.05$).

Robotic rehabilitation

This PhD thesis developed a standardized RAT protocol in CP children according to neuro-rehabilitation recommendations. The exercises included in this protocol enabled children to repeat discrete reaching movements (i.e., reaching targets). We are now developing other exercises to adapt this protocol to adult populations and to expand the variety of movements, as it has been suggested by previous studies[61,120]. The exercises that should be developed, which are illustrated in Figure 2, correspond to simple discrete (e.g., reaching targets without following a specific path), complex discrete (e.g., reaching targets while following a specific path) and cyclic tasks (e.g., repeating closed loops). Moreover, these exercises are not performance based. Further developments should include a game that would adapt its scenario as a function of a patient's performance in real time. This last perspective is being investigated by the research project ROB*i*GAME (main investigator: Pr. Thierry Lejeune). Indeed, ROB*i*GAME aims to combine a clever game with an interactive robot. This combination would adapt the game scenario and robotic assistance as functions of the motivational, cognitive and motor performances of the patient in real time.

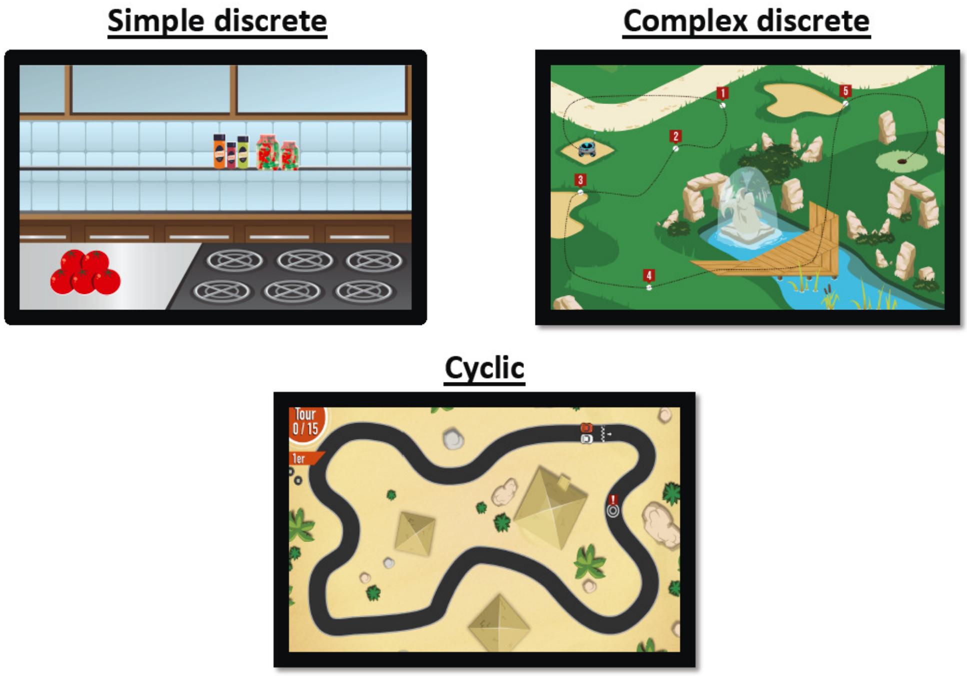

Figure 2: Illustrations of three exercises computed by the REAplan robot. The simple target task corresponds to reaching targets without following a specific path (here, a tomato). The complex target task corresponds to reaching targets while following a specific path (here, golf balls). Cyclic tasks correspond to repeating closed loops (here, playing a car racing game).

Further studies could also investigate the benefits of upper limb RAT in stroke patients. The evidence-based recommendations of upper limb interventions and RAT in stroke patients are summarized in the general introduction of this thesis (cf. supra). Most RCTs investigating the efficacy of RAT have been performed in chronic stroke patients[17,25,34,93,94,96] (>6 months after stroke), whereas patient recovery has been primarily observed in the acute (<1 months after stroke) and sub-acute (<3 months after stroke) stroke stages[10,186]. The lack of studies in the acute stage of stroke rehabilitation could be related to the difficulty in distinguishing between real treatment effects and spontaneous recovery[186]. Moreover, most trials have assessed patients' upper limb impairments but not their abilities to perform ADL and their social integration[12,18,34,92,95,97,98] unless these assessments were recommended by the World Health Organization[41]. To enhance the evidence supporting RAT in stroke patients, a multi-center single-blind RCT began in May 2014 to investigate the efficacy of RAT in acute stroke patients while considering the three ICF domains. For this study, sixty acute stroke patients are being recruited from the Cliniques universitaires Saint-Luc (Brussels), the Centre Neurologique William Lennox (Ottignies) and the Valida Hospital (Brussels). The patients are randomized into two groups (control and robotic groups), and the therapeutic intervention lasts nine weeks. For the control group, all rehabilitation sessions (fifteen sessions/week) correspond to CT. For the robotic group, RAT replaces four of these fifteen CT sessions such that thirty-six sessions of RAT are performed during the nine weeks. For each center, a therapist blinded to the patient allocation assesses the patients before the intervention, just after the end of the nine-week program, and at six months post stroke using a protocol that considers the three ICF domains. This study is registered at ClinicalTrials.gov (NCT02079779).

Three-dimensional (3D) robotic devices

This PhD thesis highlighted the interests of a robot that allows end-effector movements in two spatial dimensions (2D). Further studies could also assess the interests of 3D exoskeleton robots. Indeed, we believe that 2D end-effector robots are clinically different from 3D exoskeletons to rehabilitate upper limb movements. On one hand, the adaptations of current 3D exoskeleton robots (e.g., ARMin[27]) to patient morphology appear to be more time and energy consuming than those of 2D end-effector robots (e.g., MIT-manus[34]), which could limit their application in clinical routines. On the other hand, 3D exoskeleton robotic devices have the advantages to increase movements' accuracy by independently moving and controlling the different joints of the mobilized limb. These devices also enable patients to perform realistic movements for ADL such as reaching for a cup at a certain height[15].

Today, both devices seem to have their own advantages. However, it could be suggested that further-developed 3D exoskeleton robots should be adapted to patients by clinicians as easily as planar robots. For example, Galinski et al.[187] developed a free-alignment mechatronic structure, for which alignment between the robot and patient joints is unnecessary. This structure could facilitate exoskeleton adaptation to patient morphology and enhance its acceptance in routine clinical practice. The development of such structures could lead to further studies comparing the interests of 2D versus 3D robotic rehabilitation, which has not yet been studied.

Bimanual robotic rehabilitation

This thesis focused on the unimanual REAplan robot; thus, bimanual robotic devices were not considered. The following part discusses how bimanual robotic devices, which are illustrated in Figure 3, could rehabilitate upper limb movements in CP children and stroke adults.

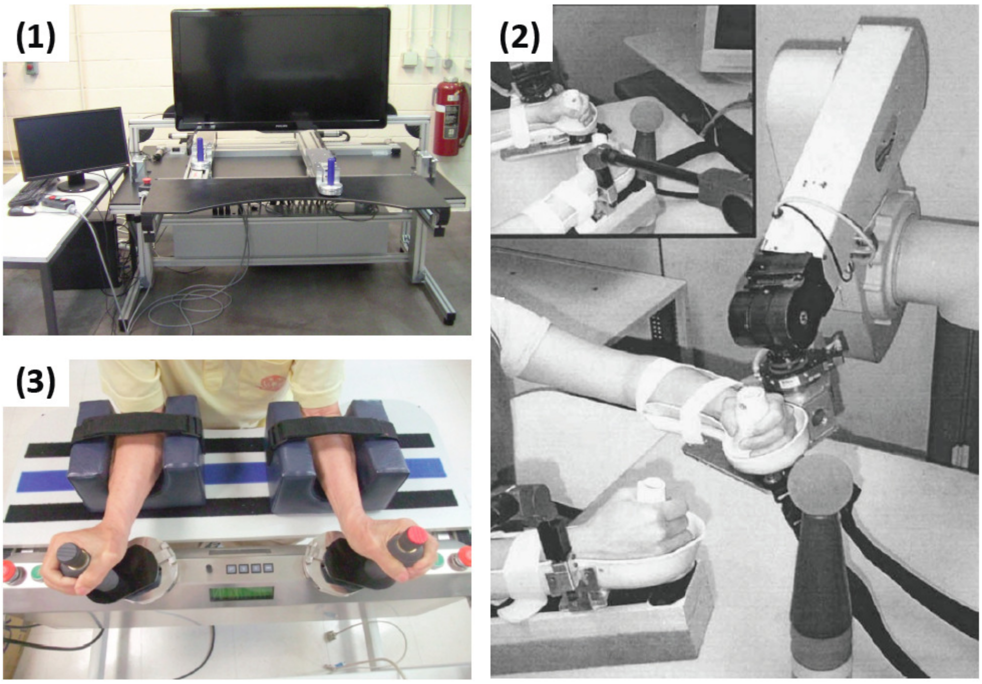

Figure 3: Illustrations of bimanual robotic devices: (1) REA^{2}Plan (inventor: Dr. Julien Sapin), (2) MIME[188] and (3) Bi-Manu-Track[189]. These three devices correspond to end-effector robotic devices that enable patients to perform proximal (REA^{2}Plan and MIME) or distal (Bi-Manu-Track) bimanual movements.

Bimanual rehabilitation, either involving robots (e.g., Bi-Manu-Track[189] [Figure 3]) or not (e.g., HABIT[106]), appears to improve upper limb impairments and abilities to perform ADL in CP children[87,106,190] and stroke adults[188,191–195]. Interestingly, recent RCTs[196,197] and systematic reviews[198,199] have shown similar efficacies of uni- and bimanual rehabilitation. These findings are consistent with current evidence-based recommendations in both populations[88,89]. The combination of uni- and bimanual exercises with[200,201] or without[202] a robot could optimize CP and stroke rehabilitation. Indeed, uni- and bimanual movements are involved in many ADL tasks[203]. Training these two types of movement could improve both of them[199,203,204]. Moreover, the neurophysiological effects appeared different for both concepts[203,205,206], possibly due to the involvement of additional neuroplastic mechanisms[205,207,208]. Additionally, one review suggested that the effectiveness of uni- versus bi-manual rehabilitation depended on the patients' severity (e.g., bimanual training was recommended in stroke patients with severe impairments) and the time post stroke (e.g., unimanual training was recommended in chronic stroke patients)[198]. These findings support that both concepts could be additional tools used throughout patients' rehabilitation. According to the above considerations, further studies should assess the interests of combining uni- and bimanual rehabilitation with[200,201] or without[202] a robot. This perspective is consistent with current recommendations promoting combination treatments to optimize upper limb rehabilitation[90,199].

Finally, most of the current bimanual robots (Figure 3) allow more rudimentary movements than current unimanual robots. For instance, The Bi-Manu-Track[189] robot allows only either pro/supination or flexion/extension movements of the wrist. It could be suggested that further-developed bimanual robots should involve movements of both upper limbs. For instance, the prototype REA^{2}Plan is an end-effector planar robot that can mobilize both upper limbs (shoulders and elbows) of the patients in a horizontal plane (Figure 3). As indicated above, uni- and bimanual movements are distinct philosophies in neuro-rehabilitation[203,205]. Thus, the further-protocols implemented in these bimanual robots should take into account the existing bimanual concepts[106,190,203].

Robotics in routine clinical practice

The primary objective of this research was to investigate the clinical relevance of robotic devices to assess and rehabilitate upper limb movements in CP children and stroke adults. This objective was achieved via laboratory experiments and scientific publications[116,117,120,129,180]. Implementing robots in routine clinical practice appears to be important, as both clinicians and patients benefited from this experiment. This implementation could be made possible by transferring the scientific data from this thesis into clinical use, as recommended by Stein: *"Ultimately,* *rehabilitation robots must move out of the laboratory and into the clinic if they are to be used as a component of routine clinical care*[1]*"*. This transfer was achieved due to constant collaboration between clinicians, researchers, engineers and technicians throughout this research. This close collaboration enabled our team (i) to adapt the first research prototype of the REAplan robotic device (Figure 4a) into a device that patients can use in routine clinical practice (Figure 4b) and (ii) to develop ergonomic software (Figure 4c) that facilitates the use of robotic devices by clinicians during routine clinical practice.

This transfer could further enable clinicians to easily use robotics in routine clinical practice. However, some clinicians are reluctant to use rehabilitation technologies. Thus, patients and clinicians must be (i) informed of the complementary effects of robots and humans in rehabilitation[14], (ii) provided with evidence-based information[92] and (iii) enabled to experience the haptic interaction. Finally, training is essential to efficiently and safely assess and rehabilitate patients using a robotic device. A user manual is provided to facilitate this training.

Figure 4: Illustrations of the (A) previous and (B) actual versions of the REAplan robot. (C) Presentation of the main menu displayed on the therapist's interface, which enables the clinician to (right column) connect the patient and (left column) choose a therapeutic action ([1] assessment, [2] rehabilitation, [3] assessment evolution, and [4] rehabilitation evolution).

3. Conclusions

This thesis provides clinical evidence regarding the use of upper limb robotic devices in neuro-rehabilitation. This research developed a standardized assessment protocol using a robot and performed a single-blind RCT to assess the efficacy of RAT in CP children, considering the ICF model[41]. Future studies should extend the use of these protocols to other neurological impairments and pathologies (e.g., multiple sclerosis) and to other devices (e.g., 3D exoskeleton and bimanual robotic devices).

The thesis would not have been possible without close collaboration between engineers, technicians, clinicians and researchers. We would like to encourage further similar collaborations (i) to develop and validate new protocols using robotic devices and (ii) to transfer scientific data to clinical use. This PhD training allowed me to develop new skills in scientific, clinical and technical domains. My wish is to allow researchers and clinicians to benefit from this experience to stimulate new technological research projects in neuro-rehabilitation and to enable patients to benefit from these technologies.

"*Technology as destiny*"[1,2]. I definitely believe that technology and humans have complementary skills. By cleverly combining the two, the rehabilitation and assessment of CP children and stroke adults can be improved.

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Abbreviations

Abbreviations

2D	2 Spatial Dimensions
3D	3 Spatial Dimensions
ADL	Activities of Daily Living
ANOVA	Analysis of Variance
AVC	Accidents Vasculaires Cérébraux
BB	Box and Block test
BMI	Body Mass Index
BOTMP	Bruininks-Oseretsky Test of Motor Proficiency
CIMT	Constraint-Induced Movement Therapy
CP	Cerebral Palsy
CT	Conventional Therapy
CV	Coefficient of Variation
ICC	Intraclass Correlation Coefficient
ICF	International Classification of Functioning, Disability, and Health
IMoC	Infirmité Motrice d'origine Cérébrale
IQR	Interquartile Range
L	Left
MACS	Manual Ability Classification System
MAS	Modified Ashworth Scale
MDC	Minimal Detectable Change
N/A	Not Applicable
PCA	Principal Component Analysis
PEDI	Pediatric Evaluation of Disability Inventory
Q1	First Quartile
Q3	Third Quartile
QUEST	Quality of Upper Extremity Skills Test
R	Right
RAT	Robot-Assisted Therapy
RCT	Randomized Controlled Trial

SD	Standard Deviation
SEM	Standard Error of Measurement
SIAS	Stroke Impairment Assessment Set
USFMA	Upper Limb Sub-score of the Fugl-Meyer Assessment

Annexes

Annex 1

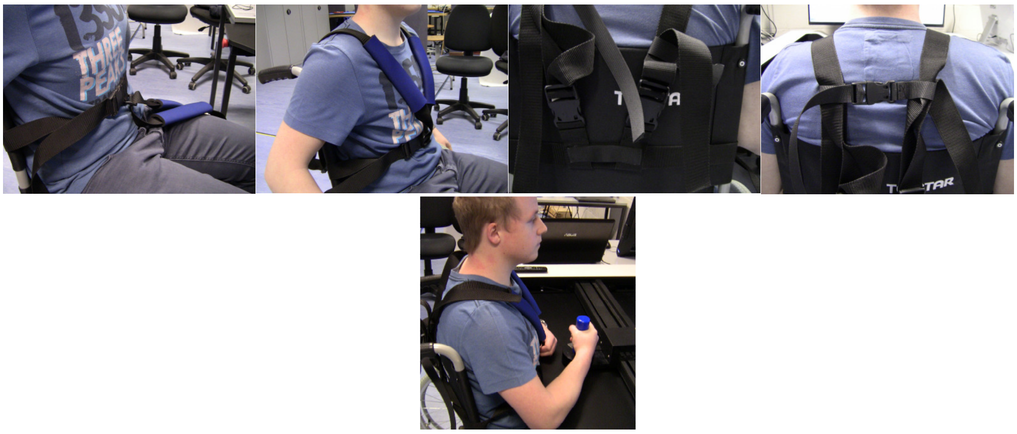
The first of part of this PhD thesis standardized a protocol to assess upper limb kinematics in Cerebral Palsy (CP) children and stroke adults, by using the REAplan robot. This annex aims helping clinicians and researchers to reproduce this protocol, by providing the details of patient installation, tasks instructions and interpretation of kinematic indices.

Patient installation

The standardization of patient's installation is essential to ensure patient's security and reliability of the procedure. This installation depends on patients' impairments/morphology and should be the same at each assessment session. Please respect these following instructions:

- Place the patient in a fixed and stable chair. To avoid any transfer, a wheelchair with reliable brakes is recommended.
- Place the patient in the middle and approximately 2 cm from the table edge (see illustrations below).

- The patient's feet should be stable. If necessary, place them on a footrest to stabilize them.
- A specific belt was developed to secure the patient's trunk, whatever the chair uses (classic chair or wheelchair). Secure the patient's trunk to minimize compensatory movements by respecting the following steps:



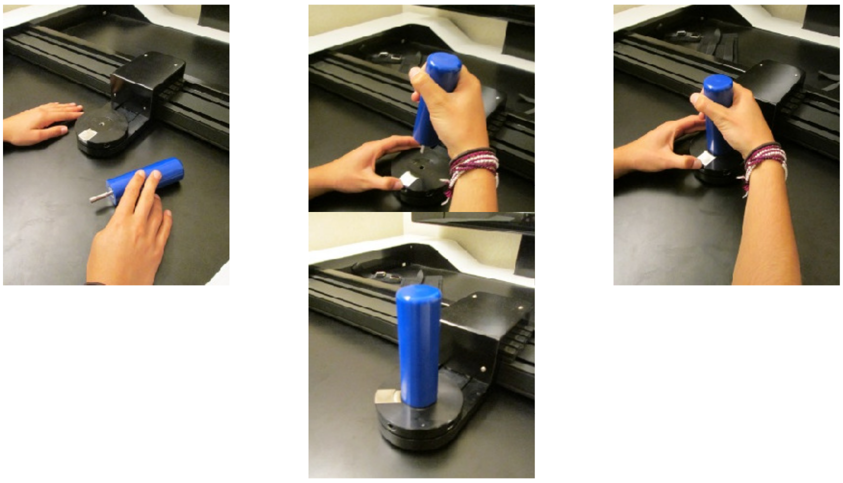
- Two handpieces were developed to adapt the assessment in function of patients' impairments. Choose the handpiece in function of the following instructions:

Cylindrical handpiece	Spherical handpiece

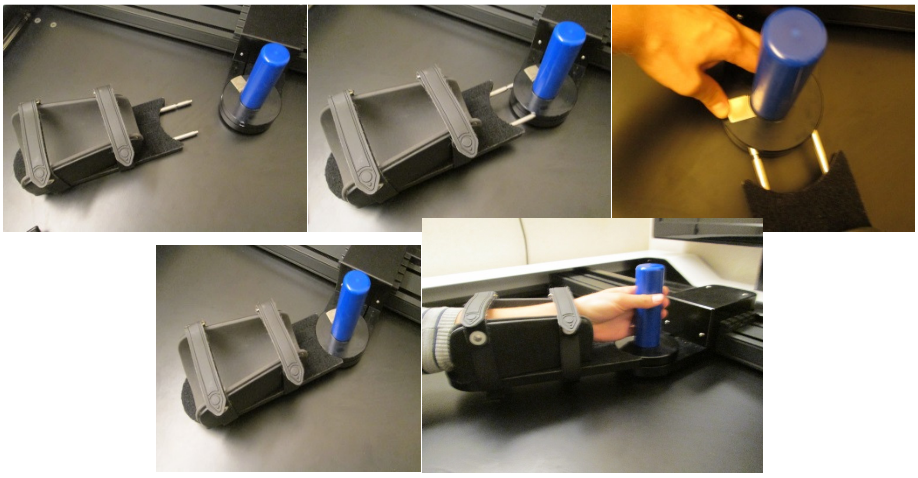
The cylindrical handpiece is recommended in patients without spasticity of the forearm pronating muscles.

The spherical handpiece is recommended in patients with spasticity of the forearm pronating muscles.

- Place the chosen handpiece by respecting the following steps:



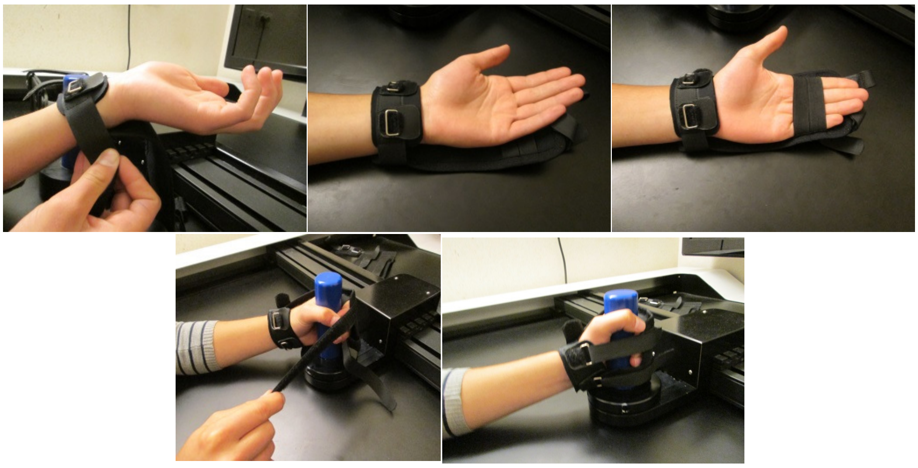
- A structure was developed to support the forearm in patients with shoulder weakness. Place the support by respecting the following steps:



Three shell sizes of this support are available. Choose the size according to the patient's morphology, as described below:

Medium shell	Large shell	Extra large shell
		
Recommended in small children	Recommended in small adults and tall children	Recommended in tall adults

- A glove was developed to support the hand in patients with hand weakness. Place the glove by respecting the following steps:



Three glove sizes are available. Choose the size according to the patient's morphology, as described below:

Medium glove

Recommended in small children

Large glove

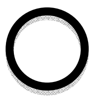
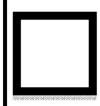
Recommended in small adults and tall children

Extra large glove

Recommended in tall adults

Tasks instructions

For each task, a training phase should precede the registration phase. For each task, ten consecutive movements are performed and no velocity instruction is provided to the patient. The specific instructions of each task are provided below.

Free amplitude	**Target**
"Reach straight out in front of you as far as possible and brought your arm back to the starting position."  Remarks: - No break between the ten back and forth movements; - Verbal Stimuli are allowed.	"Go to the target as direct and accurate as possible"  Remark: - For each trial, patient goes himself to the target but the robot performs the return movement.
Circle	**Square**
"Drive around the circle as best as you can, without stopping"  Remarks: - No break between the ten movements; - Verbal Stimuli are allowed. - The movements are performed clockwise with the right upper limb and counter-clockwise with the left one.	"Drive around the square as best as you can, without stopping"  Remarks: - No break between the ten movements; - Verbal Stimuli are allowed. - The movements are performed clockwise with the right upper limb and counter-clockwise with the left one.

Kinematic indices

Each task is linked to specific indices. These indices are listed in the following table. For each index and task, YES means that the index is computed while NO means that the index is not computed. The interpretation of each index is also provided.

Indices \ Tasks	Target	Free Amplitude	Circle	Square	**Interpretation**
Amplitude (cm)	NO	YES	NO	NO	Higher amplitude score indicates larger movements
CV Amplitude (%)	NO	YES	NO	NO	Higher CV amplitude score indicates more variability in the amplitude of movements
Inaccuracy (cm)	YES	NO	YES	YES	Higher inaccuracy score indicates more inaccurate movements
CV inaccuracy (%)	YES	NO	YES	YES	Higher CV inaccuracy score indicates more variability in the movements' accuracy
Straightness	YES	YES	NO	NO	Higher straightness score indicates more linear movements
CV Straightness (%)	YES	YES	NO	NO	Higher CV straightness score indicates more variability in the movements' linearity
Velocity (cm/s)	YES	YES	YES	YES	Higher velocity score indicates faster movements
CV Velocity (%)	YES	YES	YES	YES	Higher CV velocity score indicates more variability in the movements' velocity
Smoothness	YES	YES	YES	YES	Higher smoothness score indicates smoother movements
CV Smoothness (%)	YES	YES	YES	YES	Higher CV smoothness indicates more variability in the movements' smoothness

Abbreviation: CV = coefficient of variation

Annex 2

The first of part of the PhD thesis standardized a protocol to assess upper limb kinematics in Cerebral Palsy (CP) children and stroke adults, by using the REAplan robot. The four chapters did not provide all precisions about kinematic analyses. This annex aims helping researchers to reproduce analyses of these kinematic indices with REAplan or other devices.

For each task, the X and Y positions was recorded in function of time by the REAplan robot (frequency acquisition: 125 HZ). These acquisitions were analyzed by a specific customized program in a LabWindows/CVI (8.5) environment, as followed:

- X and Y position data were firstly filtered (Butterworth filter; cutoff frequency=12Hz; Order=2);
- The filtered X and Y position data were derived to obtain velocity data in function of time. Each velocity data was computed by the following ratio:

$$v_i = \frac{x_{(i+n)} - x_{(i-n)}}{2.n.\Delta t}$$

  Where v_i is a velocoty data for the frame i, $x_{(i+n)}$ is the n^{th} position supra, $x_{(i-n)}$ is the n^{th} position infra, n=5 and Δt is the elapsed time.

From these velocity and position data, the kinematic indices were computed as followed:

- Amplitude index (Free Amplitude task) corresponds to the farthest Y position obtained during the back and forth movement;
- Straightness index (Free Amplitude and Target tasks) corresponds to the optimal path divided by the path length covered by the subject; the optimal

path corresponds to the distance between the starting position and the final position of the movement.

- Target inaccuracy index (Target task) corresponds to the distance between the target position that the subject had to reach and the end position achieved by the subject;
- Shape inaccuracy index (Shape tasks) corresponds to:

$$\frac{\sum_{i=1}^{n} \sqrt{(Rx_i - Px_i)^2 + (Ry_i - Py_i)^2}}{n}$$

where n corresponds to the number of positions acquired during the exercise and related to the analyzed shape, Pxi and Pyi correspond to the X and Y coordinates of its positional data point and Rxi and Ryi correspond to the X and Y coordinates of the orthogonal projection of its point on the reference shape (cf. illustration in the Figure below). Thus, the shape inaccuracy index corresponds to the average of the distances between the measured performance points and their corresponding reference points (higher scores indicate more inaccurate movements).

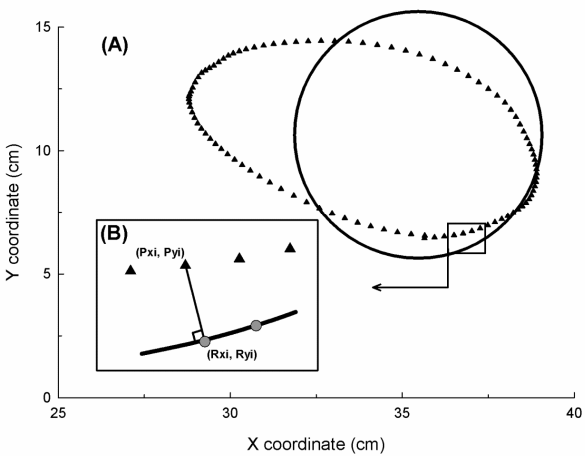


Figure. Illustrations of (A) the circle of reference (black circle) and a circle performed by a stroke patient (black triangle symbols) and of (B) the calculation of the shape inaccuracy index. Each reference point (grey circle symbol, [Rxi, Ryi]) corresponds to the minimal orthogonal projection of the performance point (Pxi, Pyi) on the shape of reference. The distances between all the related reference and performance points were measured and averaged to obtain the shape inaccuracy result.

- Velocity (all tasks) corresponds to the average of the velocity data computed during the movement.
- Smoothness index (all tasks) corresponds to the ratio of the mean velocity and the peak velocity. Mean velocity corresponds to the average of the velocity data computed during the movement. Peak velocity corresponds to the maximal velocity computed during the movement.
- Coefficient of Variation index (all tasks and all indices) is calculated from the subjects' 10 movements. For each index, the coefficient of variation corresponds to the ratio of the standard deviation and the average of the 10 kinematic results computed during the 10 movements.

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Cerebral palsy (CP) and stroke are major causes of permanent disabilities. These disabilities justify intensive interdisciplinary rehabilitation and regular assessments, which could be optimized using robotics. This PhD thesis investigated the clinical interest in robotic devices to assess and rehabilitate upper limb movements in CP children and stroke adults. This investigation was performed with the REAplan robot, which is an end-effector robotic device that moves the patient's upper limb in a horizontal plane using various assistance modes (i.e., active, active-passive, passive). The first part of this thesis investigated how a robotic device could quantitatively assess upper limb movements in both populations. A standardized protocol was developed to assess upper limb kinematics using the REAplan robot in CP children and stroke adults. The reproducibility, validity, responsiveness and reference standards of this protocol were established, and a short version of this protocol was provided to facilitate the assessment of upper limb kinematics in routine clinical practice. The second part of this thesis investigated how a robotic device could efficiently rehabilitate upper limb movements in CP children. A standardized protocol for robot-assisted therapy (RAT) was first developed according to the current recommendations in CP neuro-rehabilitation. This protocol was used in a single-blind randomized controlled trial that assessed the efficacy of RAT in CP children. This trial showed that the combination of conventional therapy (CT) and RAT could significantly improve upper limb kinematics and manual dexterity in CP children compared with CT alone. Thus, robotic devices could quantitatively assess and efficiently rehabilitate upper limb movements in CP children and stroke adults. These findings would not have been possible without close collaboration between engineers, technicians, clinicians and researchers. Further similar collaborations should be encouraged to facilitate technological integration in rehabilitation.