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Clinically Relevant Biomedical Factors for Design & Development of Practical Upper Limb Exoskeleton Rehabilitation Robots

실용적인 상지 외골격 재활 로봇
설계 및 개발을 위한
임상 적합성 기반 의공학적 인자

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서울대학교 대학원
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남 형 석

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Clinically Relevant Biomedical Factors for Design & Development of Practical Upper Limb Exoskeleton Rehabilitation Robots

By

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A thesis submitted to the Department of Medicine in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Biomedical Engineering at Seoul National University College of Medicine

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ABSTRACT

Clinically Relevant Biomedical Factors for Design & Development of Practical Upper Limb Exoskeleton Rehabilitation Robots

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Introduction: There has been rapid growth in both the development and clinical application of rehabilitation robots in the past decade. However, the goal of providing maximal task-specific repetition of the limb movements to facilitate neuroplasticity and functional recovery in neurorehabilitation, which is significantly superior to conventional rehabilitation therapies, has not yet been achieved. The aim of this study is to identify clinically relevant biomedical factors, distinguishable from simple biomechanical factors, for the design and development of practical but simple neurorehabilitation robots, focusing on exoskeleton-type robots.

Methods: A demand survey was performed on 48 potential users with stroke or neuromuscular diseases to identify the patients' practical needs, which may serve as a goal for rehabilitation therapy. As spasticity is a common problem when applying rehabilitation robots to patients with central nervous system disorders, biomechanical response to spasticity was evaluated in 20 chronic stroke patients with various grades of spasticity to characterize the spasticity induced resistance and to determine the minimal torque output required for motors in major robot joints. An inertial measurement unit (IMU) sensor based motion capture system was used to determine workspace and range of motion (ROM) for major upper extremity joints in ten healthy subjects, while performing the Action Research Arm Test (ARAT) and top ranked activities of daily living (ADLs) from the demand survey. The same evaluation method was applied to nine stroke patients with Brunnstrom stages ranging from 3 to 6 to identify the characteristics of patient movements and stroke recovery patterns. For user-intent driven control, an image-processing based robot control system was proposed and a prototype for a hand rehabilitation robot was developed. A usability study was performed with physicians, engineers, therapists, and stroke patients to evaluate the robot's clinical feasibility.

Results: In the demand survey, handling foods, dressing, and moving close items were highly necessary ADL functions for both exoskeleton and external robot arm types. Stroke patients demonstrated high demand for self-exercise with exoskeleton. The maximal resistance torques caused by low (modified Ashworth scale (MAS) 0, 1), intermediate (MAS 1+), and high (MAS 2 and 3) grade spasticity were 3.68 ± 2.42, 5.94 ± 2.55, and 8.25 ± 3.35 Nm for the elbow flexor ($p < 0.001$, between each grade) and 4.23 ± 1.75, 5.68 ± 1.96, and 5.44 ± 2.02 Nm for the wrist flexor ($p < 0.001$, for low versus intermediate, low versus high grade spasticity). In healthy subjects, the size of the workspace during the ARAT tasks was 0.53 m (x-axis, left-right) × 0.92 m (y-axis, front-back) × 0.89 m (z-axis, up-down) for the dominant hand. For ADL tasks, the workspace size was 0.71 m × 0.70 m × 0.86 m for the dominant hand which was significantly larger than the non-dominant hand ($p \leq 0.011$). The ROM for major joints of the upper extremity during the ARAT tasks were 109.15 ± 18.82° (elbow flexion / extension), 105.23 ± 15.38° (forearm supination / pronation), 91.99 ± 20.98° (shoulder internal / external rotation), and 82.90 ± 22.52° (wrist dorsiflexion / volarflexion), whereas the corresponding ROM for the dominant side during the ADL tasks were 120.61 ± 23.64°, 128.09 ± 22.04°, 111.56 ± 31.88°, and 113.70 ± 18.26°, respectively. Of the parameters that showed significant differences in values between healthy subjects and patients and also significant correlation with clinical measures, the average amplitude of the forearm supination / pronation angle during the ARAT domain 4 tasks demonstrated the greatest decline in severely impaired patients compared to normal subjects (29.83%) and also largest difference between severely and mildly impaired patients (48.46%). For the usability test for the image processing based user-intent driven hand rehabilitation robot, the participants found the device interesting (5.7 ± 1.2), motivating (5.8 ± 0.9), and as having less possibility of injury or safety issues (6.1 ± 1.1); however, the levels of difficulty (4.8 ± 1.9) and comfort (4.9 ± 1.3) were relatively low.

Conclusions: The results of this research will serve as a basis for the design and development of a practical and portable but clinically relevant neurorehabilitation exoskeleton robot.

Keywords: Neurorehabilitation Robot; Stroke; Upper Extremity; Biomedical Factor; Exoskeleton

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LIST OF ABBREVIATIONS

ADL Activity of daily living

ARAT Action Research Arm Test

BIG Bilateral impairment group

BMI Brain-machine interface

CNS Central nervous system

CoV Coefficient of Variance

CPP Catch point percentage

EEG Electroencephalogram

EMG Electromyography

F-M Fugl-Meyer

IMU Inertial measurement unit

MAS Modified Ashworth scale

MRI Magnetic resonance imaging

RMSE Root mean square error

ROM Range of motion

UIG Unilateral impairment group

1. INTRODUCTION

1.1 Research on Upper Limb Exoskeleton Robots

Because of the high incidence of stroke and the recent trend toward developing rehabilitation robots, many types of rehabilitation robots for stroke rehabilitation have been developed [1, 2]. Over the past few years, there have been considerable improvements in neurorehabilitation robotics. However, not many types of neurorehabilitation robots have entered the developmental stage for large-scale randomized controlled clinical trials, nor have they been widely commercialized. Part of the reason for this would be regulation issues pertaining to medical devices; however, it seems the main reason is that those pre-developed rehabilitation robots do not provide sufficient “task-specific high repetition” while appropriately maintaining motivation [3]. From a clinical perspective, it is undeniable that more task-specific repetition of the paralyzed extremity would lead to better recovery in patients with limb paralysis caused by central nervous system (CNS) injuries or disorders. In fact, most of the rehabilitation robots focus on providing high repetitions unless they are developed for assistance.

In general, electromechanical devices and robots for upper limb rehabilitation are classified into two categories: end-effector robots and exoskeletons [4]. Exoskeletons have a structure in which the robot joints correspond to human joints [5]. These types of robot are generally large and expensive, and they are usually fixed in space, which makes them only usable in occupational therapy rooms in hospitals. Armeo® series exoskeleton robots are the most widely used exoskeletons in clinics. End effector type robots are relatively simple in structure. These robots usually let the patients hold a handle with their hands and the handle generates power according to its trajectory and direction. The joint of the robot does not correspond with human anatomical structure; therefore, there are various types of end-effector robots [5]. InMotion™ is the most representative type of the end-effector type robot. End-effector robots are generally not in a wearable form; therefore, they are mostly fixed in one space and are mainly used in the clinics. While it is not clear whether either type of rehabilitation robot is better than another, numerous systematic reviews and meta-analyses showed conflicting results on the efficacy of robot-assisted arm rehabilitation [2, 4]. There is growing evidence that robot-assisted training improves both muscle strength and functional abilities, however, whether the amount of increase in outcome measures is clinically significant remains questionable, especially when considering cost-effectiveness.

Regardless of the robot type, the most important reason that the efficacy of robot-assisted training is currently not more prevalent or desired is that it simply does not provide sufficient amount of task-specific repetition. Many factors contribute to this limitation including patient’s medical status, functional status, socioeconomic factor, hospital accessibility, insurance policies, etc. Because all these factors are not easily controllable in many aspects, it is necessary to develop a rehabilitation robot that is affordable, clinically feasible, and portable, which will make the robot more accessible, and eventually maximize the task-specific repetition of the paralyzed limb.

1.2 Previous Robot Development and its Lessons

1.2.1 Clinical Application Experience with a Two-axis Mirror Robot

Several years ago, we developed a two-axis upper limb robot for robotic mirror therapy in stroke patients [6]. This device was operated based on multiple inertial measurement unit (IMU) sensors, which reflect the movement of the intact arm and actuates the robotic arm on the hemiplegic side, while the patient is looking at the mirror to provide an illusion that the paretic arm is really moving naturally. During the development and preliminary clinical trial of the robotic mirror therapy device, the robot could not actuate the elbow joint for patients with spasticity at grade 2 on the modified Ashworth Scale (MAS) even though a pilot test was successfully performed for healthy subjects and some selected patients. MAS grade 2 corresponds to a marked increase of spasticity; however, many stroke patients have spastic joints at greater than MAS grade 2. After the failure, the robot was equipped with motors with greater torques and the clinical study showed beneficial effects regarding proprioception, spatial hemineglect, and neuroplasticity supported by functional magnetic resonance imaging (MRI) findings [7].

1.2.2 Development Experience with Multi-axis Upper Extremity Exoskeleton

In the beginning stage of our rehabilitation robot research, we designed and developed a seven-axis upper extremity exoskeleton to expand the application of robotic mirror therapy to the whole upper extremity (Fig. 1). Validation for the exact reflection of the intact arm to the robotic arm through multiple IMU sensors was performed. However, this development could not go further because of medical device approval issues.

In addition to the medical device approval issues, the seven-axis robot was actually not clinically feasible for use in clinics or at home due to its large size. Therefore, we designed a second version of the exoskeleton with only four axes: shoulder internal / external rotation, elbow flexion / extension, forearm supination / pronation, and wrist dorsiflexion / volarflexion. Considering that most of the hemiplegic stroke patients show earlier recovery in their proximal limb compared to their distal limb, we eliminated the shoulder structure to reduce size and weight, and therefore provided more portability. A desktop height-adjustable elbow support with movable wheels was designed and manufactured to substitute and assist shoulder function. While this device also requires the clearance of medical device related regulations, the most appropriate user-intent driven control method remains unsolved and is under development (Fig. 2).

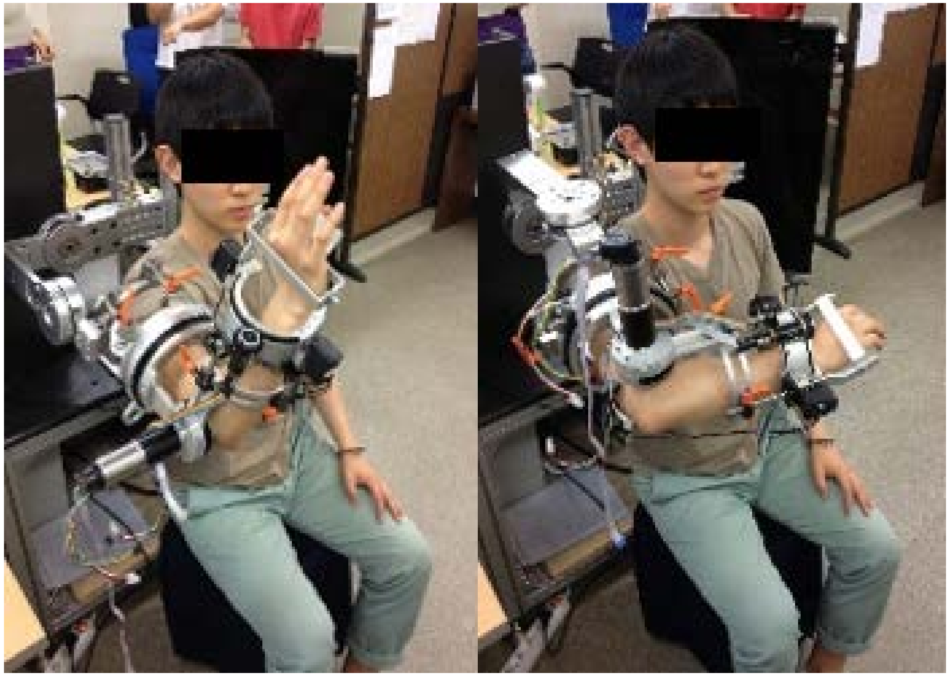

Fig. 1. A 6-axis semi-wearable upper limb exoskeleton prototype is shown.

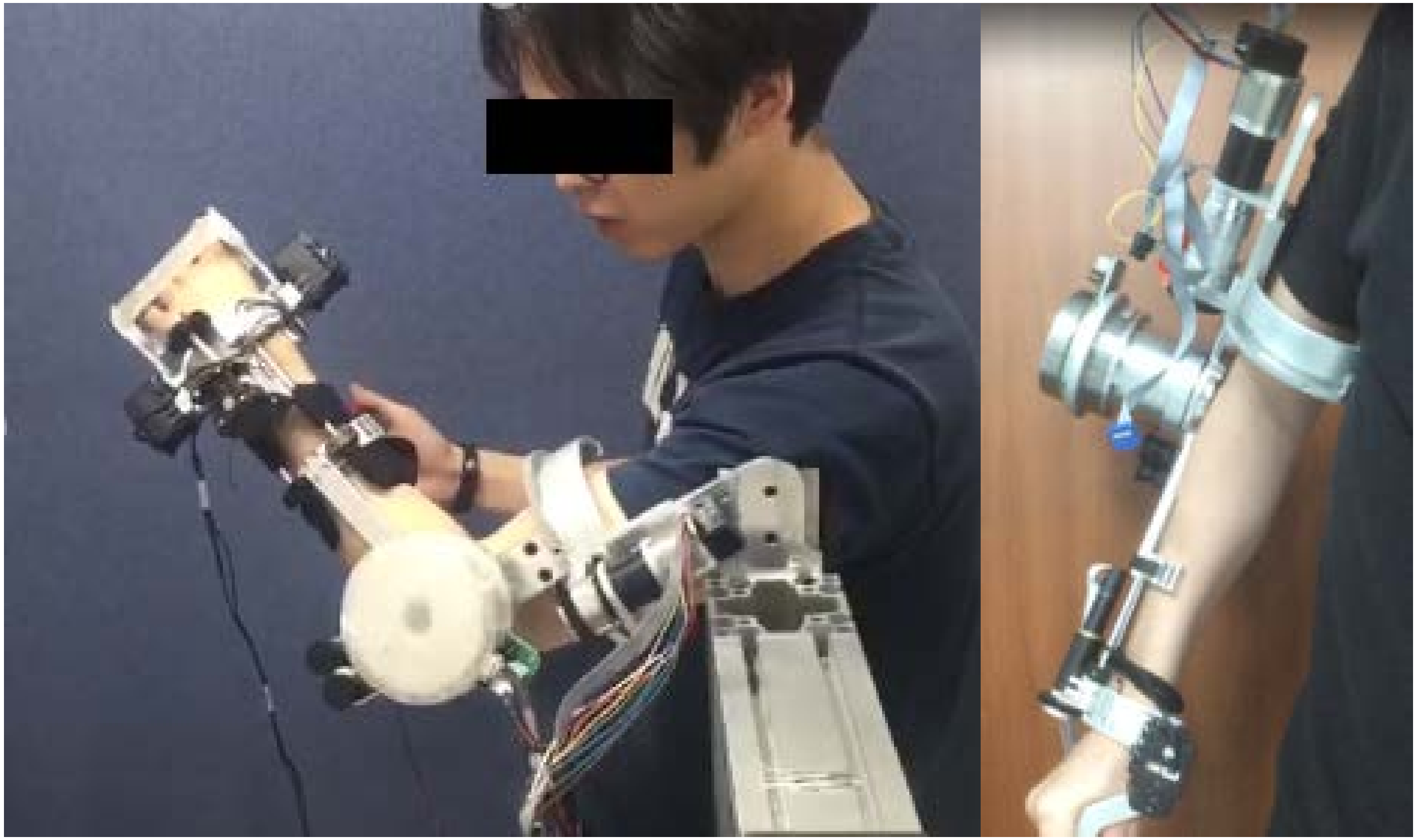

Fig. 2. A 4-axis upper limb wearable exoskeleton is shown. The weight of the robot is approximately 3.7kg.

1.2.3 Non-invasive Brain Machine Interface Control Methods

Most of the rehabilitation robots on the market are controlled via a monitor based user interface, usually in the form of a game or virtual task. To control the robotic arm by user-intent, commonly used methods are the electromyography (EMG) based method and torque sensor based method. The concept itself is relatively simple, but in reality, it is difficult to cancel out the noise and properly sense and actuate the robot, and it is not usable in patients with complete paralysis.

Electroencephalography (EEG) based brain-machine interface (BMI) control methods have been investigated over the years for robotic arm control. There are some studies that report successful control of robots by EEG in a switch controller-like manner; however, to the best of our knowledge, motor-imagery EEG based control does not seem to be feasible for practical use. In our research team's preliminary studies, we attempted to record EEG signals while actually performing the reaching task and also gain EEG signals from motor imagery [8]. After regression learning, new EEG signals were given to control the external robotic arm, but the decoded EEG did not show sufficient accuracy in terms of positional data. For the completion of the robotic arm task, an image-guided compensation algorithm regarding position and orientation was applied.

1.3 Potential Factors for Investigation

1.3.1 Robot Function (Purpose of the robot)

To focus on the accessibility and portability of the rehabilitation robot, it is important to specify the main purpose of the robot. In general, rehabilitation robots are classified into one of the two types depending on their purpose: robots for neurorehabilitation purposes, which aim to enhance functional recovery of the limb by facilitating neuroplasticity, and robots for assistive purposes, which focus on performing desired tasks, usually activities of daily living (ADL). Robots for neurorehabilitation tend to be either exoskeleton or end-effector type, and robots for assistance more likely have the form of an external robotic arm, such as a feeding robot or the JACO™ robotic arm. For neurorehabilitation, it is very essential to facilitate the repetitive feedback loop consisting of brain – motor execution – motor actuation – visual and sensory feedback to maximize neuroplasticity.

To the best of our knowledge, no specific robot has been commercially and widely utilized to assist in performing ADLs that require the upper extremities, although some are being used in limited circumstances [9]. Robots used only for treatment purposes are fixed at a certain location in a hospital, and they do not require portability in that setting. For the robots to be applicable in daily activities, they need to be portable, simple, controllable according to the user's intent, and be able to involve real target objects instead of providing monitor screen or virtual reality. Most of the robots use force sensors, torque sensors, or surface electromyography to recognize user's intent [10]. However, it is difficult for the people with severe limb impairment to generate sufficient input signals for such sensors. Recently, active research on BMI is being conducted to extract user intent directly from the brain signals. However, it is very challenging to perform precise control of the robot with electroencephalography signals, which is the most commonly used non-invasive brain signal, because the signal-to-noise ratio is very low. Furthermore, BMI technology involving invasive brain signals such as intracortical signals or electrocorticography, is yet far from practical utilization [8, 11, 12]. Therefore, it is important to clarify the purpose of the robot in the development and design stage, to simplify and adapt the robot structure, including whether it needs to be in the form of an external robotic arm or exoskeleton, so that it may be practically applied to ADL with simple control modalities. In order to clarify the purpose, the practical demands of the potential users with functional impairment need to be evaluated to avoid a situation where a perfect robot for both control and function is developed but nobody seeks to use it.

1.3.2 Robot Structure (Resistance and range of motion)

Robots for neurorehabilitation are mainly used by patients with CNS lesion or disorders. The most common disease that requires neurorehabilitation robots is stroke. In designing neurorehabilitation robots, understanding of the disease characteristics is particularly important.

In minimizing the mass and complexity of the exoskeleton, spasticity may act as a major challenge in neurorehabilitation robot design because the resistance induced by spasticity may require higher torque output to actuate the joint than in a healthy person. Therefore, the robot may require a motor with a higher output torque to be able to perform the desired movements.

Spasticity is characterized by a velocity-dependent increase of resistance caused by the exaggeration of the stretch reflex when the joint is passively stretched [13]. Spasticity occurs in upper motor neuron disorders including CNS lesions, and its incidence ranges from 30 to 60% in stroke and 65 to 78% in spinal cord injury [14-16]. Spasticity significantly affects sensorimotor function [17]. Especially in the chronic stage, spastic joints commonly present non-reflex hypertonic features, which mainly arise from soft tissue changes such as the shortening of the muscle and fibrotic changes [13]. When non-reflex hypertonic features progress and predominate, they may cause contracture or rigidity, which is represented as grade 4 in the MAS [18]. Non-reflex hypertonicity and rigidity are different from spasticity in that they are not affected by passive velocity and direction [19]. In stroke, rigidity usually appears as a sequelae of severe spasticity in the chronic stage. The target users for neurorehabilitation robots among the stroke patients, especially for those developed as assistive devices, would be patients in a chronic state, and a high percentage of them demonstrate considerable spasticity. Therefore, spasticity would be an important factor in designing neurorehabilitation robots to be widely and practically used.

For a neurorehabilitation robot to perform a desired movement in the presence of up to a certain degree of spasticity, the robot should have a motor with sufficient output torque to overcome the resistance created by the spastic muscles [20], or it should have a specific dynamic control algorithm to avoid high resistance during robot-actuated movement; and to prevent overloading from mechanical or anatomical compensation in adjacent joints [18]. Large fixed robots for treatment only in rehabilitation facilities have high torque output motors; however, actuation with excessive torque output may cause injury to spastic or rigid joints. Furthermore, in order to develop a robot in a portable and wearable form for use in daily living, the appropriate range of torque output requirements for the motors should be determined. Some guidelines and measurements have been established for spastic joints; however, to the best of our knowledge, definite evidence based on the measurements of patients with spasticity is rare [20-22], and Alibiglou et al. [23] reported in 2008 from a study on the spastic ankle joints of 20 stroke patients that quantitative measures and clinical assessments lack significant correlation.

Since it is important to minimize the size and complexity of the neurorehabilitation robot, the number of axes and the workspace of the robotic hand or the end-effector should be minimized, but at the same time the robot needs to be able to perform essential tasks in daily activities and functions. In the viewpoint of specific task performance, human movement using the arm and actuation of the robot may seem similar; however, when considering the mechanism of the performance, they are actually significantly different. Moreover, it is possible to say that the biological and engineering mechanisms are very opposite [24]. There have been numerous attempts to analyze the 3D movements of the upper extremity during ADL using image based motion analysis, IMU sensor based motion analysis, magnetic sensor systems, etc. Positional and angular data during ADL such as drinking water, fastening a button, touching the perineum, eating food, and combing hair were evaluated [25-27]. Chen and Lum [28] performed a study with a spring operated exoskeleton to assess the change in joint movements when assisted by the robot. It is important to have a database on the position and joint angles while performing essential daily activities; however, the movement patterns between healthy subjects and stroke patients differ significantly, and the exoskeleton cannot be actuated exactly in the same manner as the human limb. To optimize the design of the robot and to focus on the recovery of specific functions, the dimensions of the essential workspace, range of motion (ROM) of major joints of the upper extremity in the normal motion of healthy subjects, and the characteristics of joint movements in stroke patients, all need to be evaluated.

1.3.3 Robot Control Method

To maximize neuroplasticity in using rehabilitation robots, the robot should move according to the user’s intent, or at least the patient should be able to anticipate the robot’s movement. Because EMG and torque sensor based controls are not applicable to patients with flaccid paralysis or with only minimal volitional movements, in this thesis we attempted to apply an image processing based approach that can reflect user-intent. Visual compensation using camera images in the BMI control of the robotic arm has recently been introduced [29]. Bang et al. [30] suggested an upper limb rehabilitation robot system for precision control by image processing.

1.4 Objectives

The aim of the present study was to identify clinically relevant biomedical factors, distinguishable with simple biomechanical factors, for the design and development of practical but simple rehabilitation robots, focusing on exoskeleton type robots. First, a survey was performed to assess potential users' practical demands on robot function. Biomechanical response to spasticity was evaluated with stroke patients with various grades of spasticity to determine the minimal torque output of the robot motor. The workspace and ROM for major joints in healthy subjects were evaluated while performing the Action Research Arm Test (ARAT) and ADLs with high demand. The characteristics of joint movement in stroke patients were identified. Finally, based on determined biomedical factors, an image processing based user-intent driven hand rehabilitation robot was developed, and a pilot usability test was performed.

2. METHODS

2.1 Demand Investigation for Upper Limb Exoskeleton and Brain-Machine Interface on potential users (patients)

A. Survey Development and ADL Items

For differentiation of utilizing external robotic arm and upper limb exoskeleton for assistance, it was defined and explained to the survey participants that the external robotic arm will assist as a helper external to the body performing the desired movement or providing and placing the object that is needed for them to complete the task. Exoskeleton was described that it would be in a completely wearable form to assist the movements of the paralyzed part of the body, including the fingers in the form of a glove. For control of the robot, the subjects were told to assume a perfect BMI control system and a robot that could perform all of the tasks completely. The subjects were informed about the three categories of BMI technology from non-invasive to invasive to have a concept of BMI, however, for the survey they were instructed to assume the best BMI system without significant risks. Regarding each different task, it was assumed that the robot was specifically designed for the designated ADL task, therefore, a robot for assisting eating and another robot for assisting brushing teeth may have different forms of hardware and control mechanisms regardless of total degree of freedom of the robot. It was also assumed that a robot hand or a glove type exoskeleton with precise control is mounted on the robot. They were instructed not to take the possibility of realization into consideration, but rather focus on the importance and necessity of the ADL items themselves.

Fourteen ADLs were selected for rating in regards to both the external robotic arm and upper limb exoskeleton, and 4 additional items were selected for exoskeletons. The survey items were extracted from the commonly used ADL assessment tools, such as the modified Barthel Index (MBI) [31] or Functional Independence Measure (FIM) [32], as well as some results from our preliminary research. After the extraction, a professional committee meeting consisting of 4 physiatrists, 2 rehabilitation robot engineers, and 2 neuroscience engineers reviewed the survey items and selected relevant survey items. The 14 selected ADL items were: 1) washing face, 2) brushing teeth (including squeezing toothpaste), 3) hairdressing, 4) dressing (putting shirts on and off), 5) eating, 6) handling foods (i.e. peeling a banana, opening a bottle cap, etc.), 7) cleaning (cleaning one's desk), 8) moving close items, 9) smartphone (using a smartphone or smart tablet), 10) computer (using a computer), 11) phone calls (dialing and receiving a phone call), 12) writing, 13) switch control, and 14) purse (putting in and taking out bills and cards from a purse / wallet). The 4 additional items for exoskeletons were: 1) transfer (assisting bed to chair, chair to standing, etc.), 2) toilet use, 3) self-exercise (of the upper extremity), and 4) wheelchair control (both manual and electric). These items were not included for the external robotic arm category they were considered not appropriate to be assisted by an external robot, and the assistance method was clearly explained to the survey participants. The survey form and detailed instructions are provided in the supplemental materials (Supplement 1).

B. Participants

The survey was conducted on volunteers with severe functional impairments of either unilateral or bilateral upper extremities caused by various neuromuscular diseases, who are considered to be potential users of the external robotic arm or upper limb exoskeleton controlled by a BMI system upon its development. A total of 48 patients from the outpatient clinic of the Department of Rehabilitation in a tertiary hospital volunteered to answer the survey. All participants provided written, informed consent before enrollment.

C. Procedure

For each ADL selected, all participants were asked to rate their current level of dependence on another person using a 5-point Likert scale (1: totally dependent, 2: mostly dependent; 3: half dependent; 4: mostly independent, 5: totally independent). Then, the participant rated the objective importance of the function from the viewpoint of a developer based on their experience with severe functional impairment. External robotic device and exoskeletons were rated separately, also using a 5-point Likert scale (1: unimportant; 2: of little importance; 3: moderately important; 4: important; 5: very important). The same items were presented to determine the subjective necessity of the function from the viewpoint of a consumer based on their current daily activities. They were asked if they would need to use it if a perfect robot with the mentioned function was provided (1: not necessary, 2: of little necessity, 3: moderately necessary, 4: necessary, 5: highly necessary). A short free interview was done after the survey to assess detailed information on their answers.

D. Statistical Analysis

Descriptive statistical analyses were performed for the rating scores of each survey items. Independent *t* tests for comparison of necessity between unilateral impaired group and bilateral impaired group regarding each ADL items and type of robot were performed. Paired *t*-tests were performed to compare the necessity of each item between the two subgroups and also between the two types of robotic devices. A *p* value less than 0.05 was considered statistically significant.

2.2 Biomedical Factor Investigation

2.2.1 Biomechanical Response of Exoskeleton in Spastic Elbows and Wrists

A. Robot Design and Settings

The robot used in this study was the 2-axis (elbow extension / flexion, wrist dorsiflexion / volarflexion) planar upper limb exoskeleton robot system initially designed and developed by our research team for a robotic mirror therapy system for functional recovery of a hemiplegic arm [6]. This robot is equipped with two brushless DC motors (EC45flat and EC90flat, Maxon Motor AG, Sachseln, Switzerland) with sufficient torque outputs to overcome spasticity of the participants and the robot is fixed to a metal frame desk. Torque sensors (TFF-500, CTAplus Co., Ltd., Daegu, South Korea; FT01-20NM, Forsentek Co., Ltd., Shenzhen, China) are mounted on each joint to measure reaction torques between the human arm and the robot actuators during the robotic therapy. For the real time monitoring platform, LabVIEW® (National Instruments (NI) Corp., Austin, TX, USA) was used to control and monitor the robotic movements in real time. The schematic structure of the system and a photo of a participant during the trial are shown in Fig. 3.

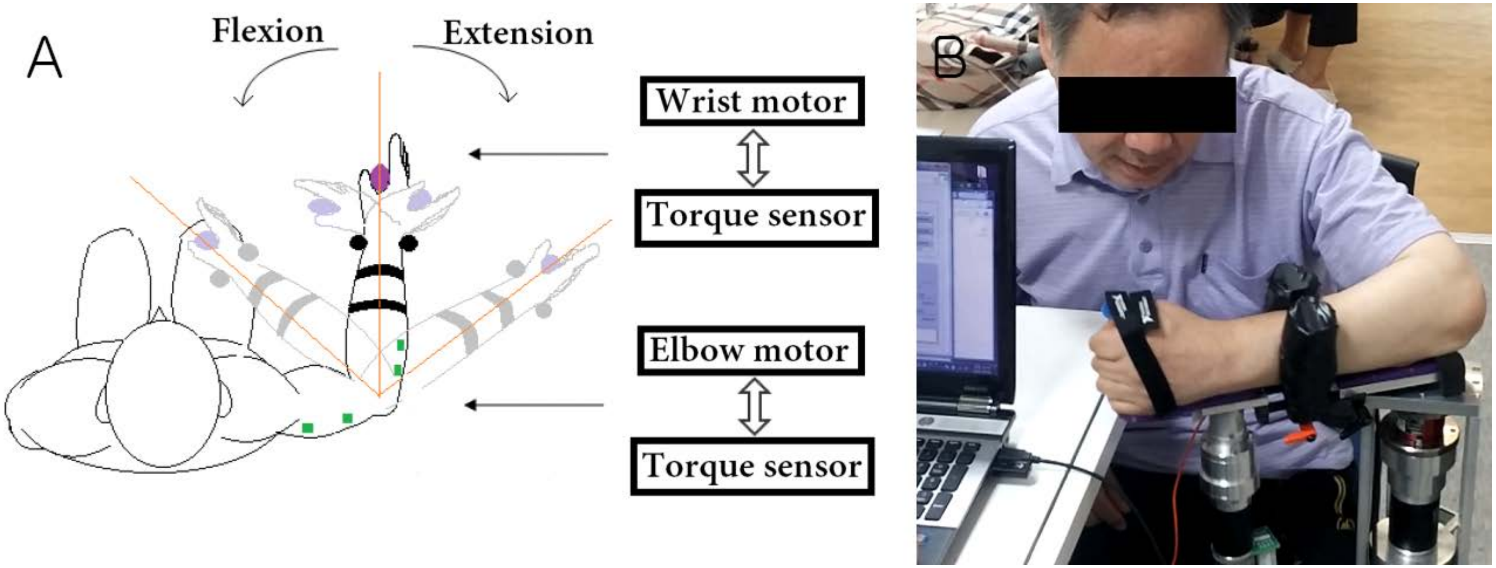

Fig. 3. (A) Schematic structure of the system is shown. (B) A subject is equipped with a two-axis rehabilitation robot for measurement of the resistance torque.

A. Participants

For evaluation, chronic stroke patients with a spastic upper limb were recruited. Subjects matching all of the following inclusion criteria were included in the study: 1) spasticity of the hemiplegic upper limb with a MAS grade between 1 and 3 in the elbow and / or the wrist flexor; 2) a history of stroke with more than 1 year since onset; and 3) alert mental status sufficient for following instructions during the study. The clinical experiment was performed between July and September in 2015. A total of 20 chronic stroke patients and one healthy subject for comparison volunteered for the study with written informed consent from the department of rehabilitation medicine in two hospitals: Seoul National University Hospital (SNUH) and Seoul National University Boramae Medical Center (SNUBMC).

B. Clinical Test Settings and Procedure

For each subject, two skilled rehabilitation specialists independently assessed the spasticity of the elbow flexor, elbow extensor, and wrist flexor using the MAS scale. Considering the variability of spasticity, the higher grade was used for classification. After the subjects were equipped with the exoskeleton robot, the maximum flexion and extension angle range for each joint was configured for each subject in order to prevent injuries. The maximum flexion and extension angle were determined by a clinical decision based on physical examinations performed by rehabilitation specialists, and are the extent to which the joint angle cannot be further extended or flexed due to severe spasticity, contracture, or pain. All subjects were given three consecutive passive isokinetic movements back and forth by the robot within its ROM.

Three different angular velocities at the elbow joint (20, 40, and 60 ° /s) and six different velocities at the wrist joint (20, 40, 60, 80, 100, and 120 ° /s) were applied. The resistance torque at each joint and the corresponding angular position were continuously recorded throughout the process. The test-retest reliability coefficients of the torque sensor for the elbow and wrist were 0.977 and 0.931, respectively.

C. Extracted Parameters

In each trial for flexor spasticity, the maximal resistance torque during the extension, the resistance torque value at the maximal flexion state (0%ROM), 1/3 point (1/3ROM) and 2/3 point (2/3ROM) of the ROM, and full extension (100%ROM) were calculated based on the measured torque data. For each trial of extensor spasticity, the same parameters were extracted in the opposite direction, from full extension to full flexion. The changing pattern of the stiffness for each trial was computed and represented in graphs as $d\tau / dt$, because all movements in a single trial were isokinetic, making $d\Theta / dt$ a constant (Equation 1).

$$\text{Stiffness } (Nm/rad) = \frac{d\tau}{d\Theta} = \frac{d\tau}{dt} \times \left(\frac{d\Theta}{dt}\right)^{-1}$$

$$\propto k \ \frac{d\tau}{dt} \ (Nm/sec) \qquad (1)$$

In Equation 1, τ is the torque measured by the sensor, θ is the angular position, and $d\tau / dt$ and $d\theta / dt$ are time derivatives of τ and θ. The k stands for a constant coefficient. A sudden increase in the resistance torque during movement, where the time derivative of the torque ($d\tau$ / dt) increase to a peak, was assumed as equivalent to a "catch" phenomenon [33]. The angle at which the catch phenomenon occurs was defined as the catch angle, and the catch angle (*deg*) was converted to catch point percentage (CPP, %ROM) according to Equation 2, where the difference between catch angle and initial angle is divided by total ROM. The CPP shows a low value when the catch phenomenon occurs early during the passive ROM, and is 100% if there is no catch.

$$\text{Catch point percentage (\%ROM)}$$
$$= \frac{|\ \text{catch angle } (deg) - \text{ initial angle } (deg)|}{\text{total ROM } (deg)} \times 100 \tag{2}$$

Throughout the study, the resistance torques caused by flexor spasticity during actuation in the extension direction are given in positive values whereas the resistance torques caused by extensor spasticity in the flexion direction are given in negative values. A representative graph of the outcome parameters is shown in Fig. 4.

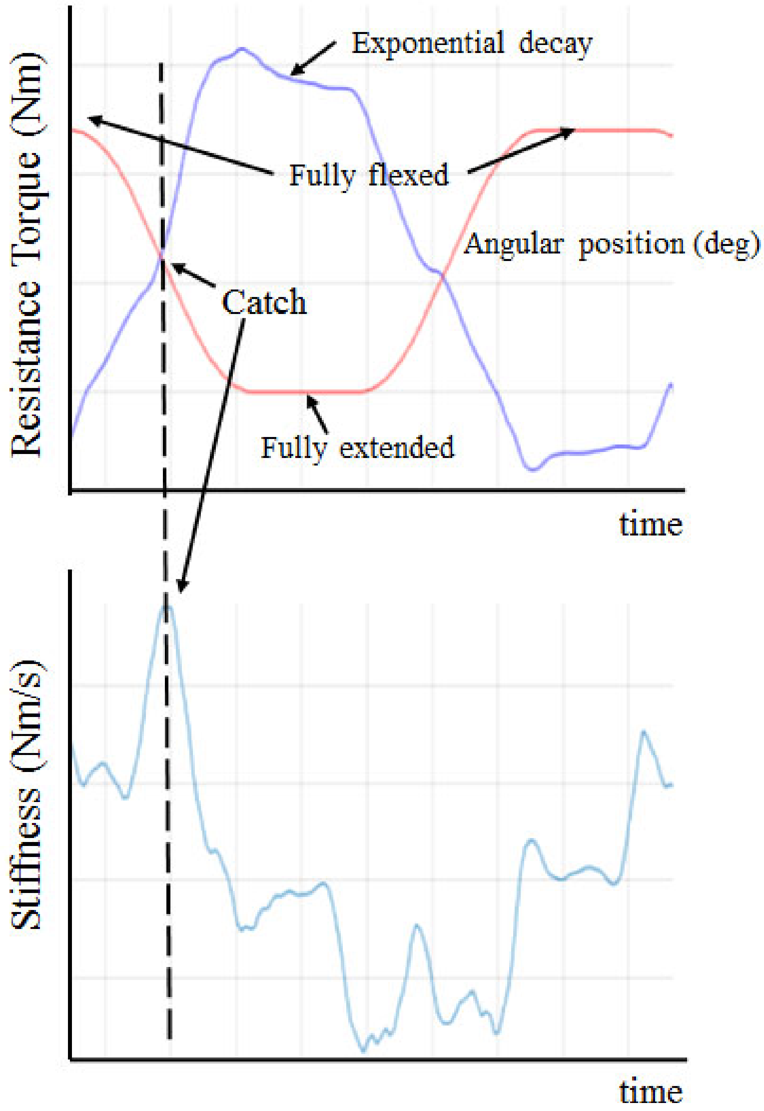

Fig. 4. A representative graph of the outcome parameters is shown. Blue lines indicate resistance torque values and red lines show corresponding angular positions. The catch phenomenon and the exponential decay of torque at the end of range of motion are indicated.

D. Statistical Analysis

The degree of spasticity was categorized into three grades based on the MAS; low (MAS grade 0, 1), intermediate (MAS grade 1+), and high grade (MAS grade 2, 3) spasticity. Statistical analyses were performed for spasticity of the elbow flexor, elbow extensor, and wrist flexor. The maximal resistance torque values for the three spasticity grades over all trials were compared using the analysis of variance (ANOVA) method followed by post-hoc analyses. Resistance torque values at 0%, 1/3, 2/3, and 100% ROM were compared using the repeated measures ANOVA (RM-ANOVA) method with ROM position as within-subjects factor and spasticity grades as between-subject factor, followed by post hoc analyses. During the post-hoc analyses, ANOVA tests were performed for comparison of resistance torques between the three groups, and independent *t* tests were used for comparison between two groups. Maximal resistance torque values and catch angles at each actuated angular velocities were also compared between the three spasticity grades using the ANOVA test. Catch angles between intermediate and high spasticity grades were compared using the independent *t* test.

2.2.2 Upper Limb Motion Characterization in Major Movements & Tasks

A. Upper extremity motion capture system and its validation

For upper extremity motion capture, Perception Neuron® (Noitom Ltd., Beijing, China), a wearable multi-IMU based modular motion capture system was used. In this study, we utilized 25 IMU sensors for upper body assessment; 3 sensors for body axis, 4 sensors for each arm, and 7 sensors for each hand including fingers (Fig. 5). A user interface software, Axis Neuron (Noitom Ltd., Beijing, China), was used for motion recording and also data extraction. Data sampling rate was set to 60 Hz.

To validate the system's accuracy and consistency, root mean square error (RMSE) analyses for elbow flexion / extension and wrist dorsiflexion / volarflexion axis were performed with electro-goniometer as a reference. In real motion with the system worn to the body, it is not possible to isolate single joint movement in a single plane with all other joint fixed. Therefore, coefficient of variation (CoV) analyses for forearm supination / pronation and elbow flexion / extension for the angles from gyrosensor, and *z*-axis (up-down direction) and *y*-axis (front-back direction) distances from accelerometers in forearm and hand sensors were performed with the data collected during the tasks.

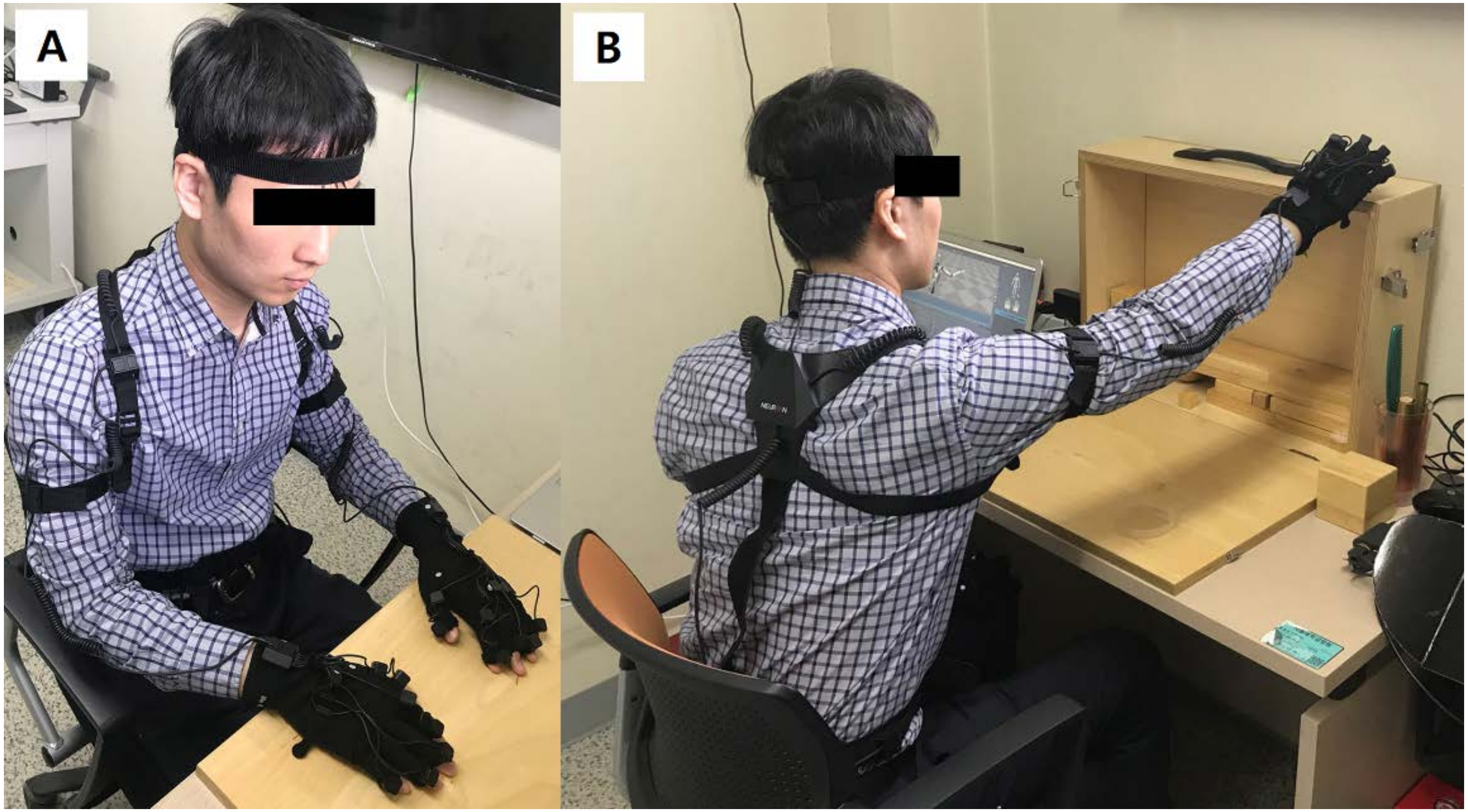

Fig. 5. (A) A volunteer subject is wearing the IMU-based upper extremity motion capture system. (B) The subject is performing a task in Action Research Arm Test.

B. Participants

Ten healthy volunteers (6 males, 4 females) and nine patients with hemiplegic stroke were recruited for this study and participated after providing written informed consent. Their mean age was 29.3 ± 4.7 years old (age range: 23 - 35). Enrolled stroke patients' mean age was 57.4 ± 17.2 years old (age range: 22 - 73). Four patients had left hemiplegia and five patients had right hemiplegia. There were 2 (B-stage 3), 2 (B-stage 4), 3 (B-stage 5), and 2 (B-stage 6) for each Brunnstrom stage (Supplement 2). Their mean ARAT score was 34.8 ± 21.6 points, where 57 points is the maximum score.

C. Tasks and procedure

All subjects wore the IMU sensor based motion capture system on both upper extremities. After sensor calibration, they performed all 19 test items of the ARAT with both right and left hands alternatively (Supplement 3). They also performed 6 pre-specified ADL tasks: 1) opening a water bottle and drinking, 2) peeling off a banana, 3) putting on and off of the buttons on a shirt, 4) hair combing, 5) squeezing toothpaste and toothbrushing, and 6) opening the door knob. These pre-specified ADL tasks were selected from the survey results from the previous section regarding stroke patients' practical needs due to their hemiplegia. During the ADL tasks, the subjects were instructed to perform the task most naturally, not specifying which hand to hold or manipulate the object. For all stroke patients, ARAT score and Brunnstrom stage were evaluated.

D. Extracted parameters

Using the Axis Neuron software, acceleration and position data of the wrist and hand sensors from the accelerometer and Euler angles for sensors of all major joints with reference to their proximal segment sensors during the ARAT and ADL tasks were extracted. For each ARAT domain and ADL tasks, the size of workspace in three orthogonal coordinates and angular position and ROM for each upper extremity joint were calculated.

For healthy subjects, grasping / pinching and reaching movement during tasks in ARAT domain 1 and 3 were additionally analyzed regarding initial grasping / pinching position and ROM during reaching movement.

For all subjects, the average amplitude and maximum amplitude of the movement segments, and logsum and logsum per time (logsum / time) were extracted and analyzed. Logsum was defined as the integration of all displacements or changes for corresponding measurements.

E. Statistical analysis

For validation purposes, intra-subject covariance and inter-subject covariance were calculated for repetitive grasping / pinching and reaching tasks. Paired *t* tests were performed to compare workspace dimensions and ROM between dominant and non-dominant arms. Paired *t* tests were also performed for comparison of major joint angles in grasping / pinching position and reaching position, initial position between grasping and pinching, and reaching position from grasping and pinching. For all calculated parameters, independent *t* tests were performed between healthy subjects and stroke patients. For all parameters that showed significant difference between healthy subjects and stroke patients, correlation analyses were performed with the ARAT score as the dependent variable. A *p* value less than 0.05 was considered statistically significant.

2.3 Feasibility Study for User-intent Driven Robot Control Methods

2.3.1 Image-processing Based Control and its Feasibility

2.3.1.1 Development of an Image-processing Based Hand Rehabilitation Robot

A. Design of a simple two-axis hand rehabilitation robot

In this development, we selected forearm supination / pronation as the essential joint motion in recovery from stroke. For the execution of the task, a hand grasp / release motion was included in the design. Based on the fact that most stroke patients experience proximal limb recovery in the early stage, we assumed that most of the potential users for this device would have a certain extent of shoulder power and movement. The forearm support structure was manufactured in the form of a skateboard with four small wheels mounted at the bottom, so that the user could roll the whole device freely in any direction with their residual and / or recovered shoulder movement. Contrary to our initial design, in this pilot study the height adjustment function was excluded for simplicity. This design structure was intended to make the device feasible to use at the hospital bedside or at home. The initial design is shown in Fig. 6.

In the current design, the exoskeleton body part for the hand was placed at the volar side of the hand, while most of the hand robots' exoskeleton body are placed at the dorsum side. This was to prevent hand injury that may be caused by the excessive grasp motion of the robot.

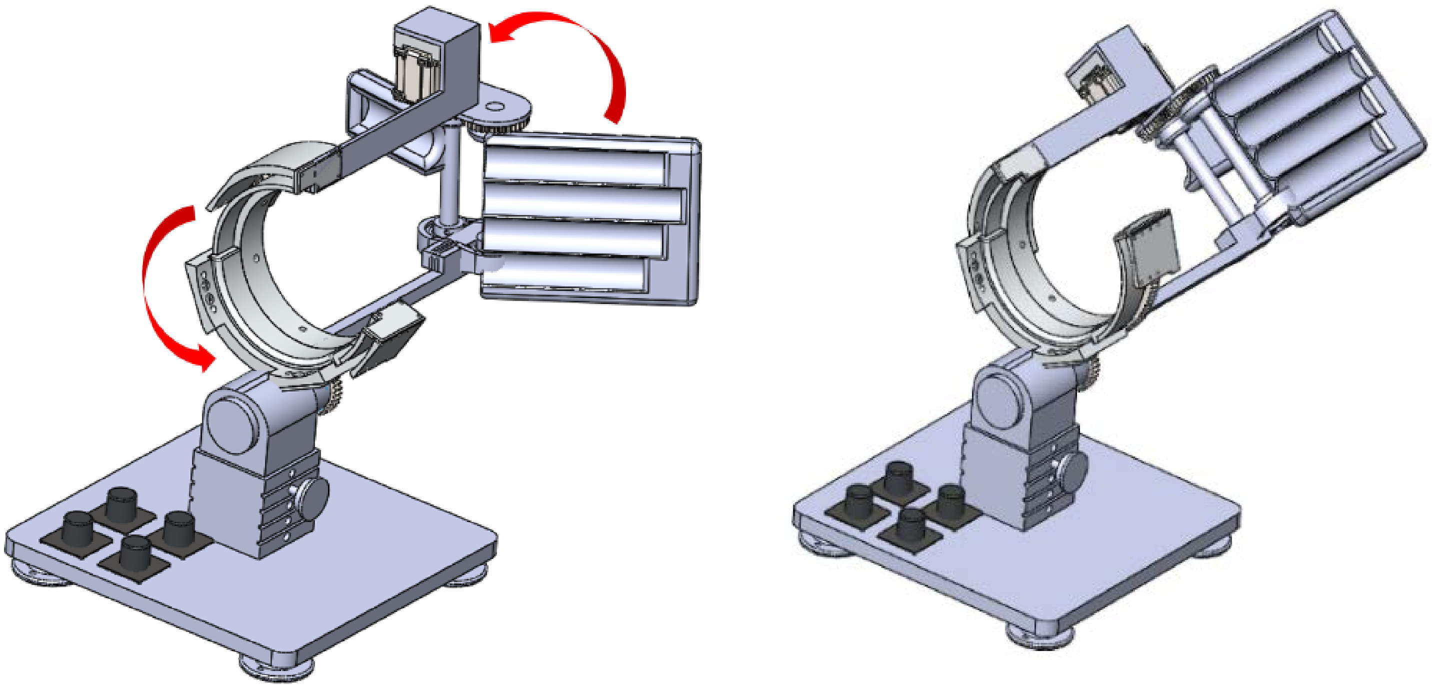

Fig. 6. Initial design for image-processing based user-intent driven 2-axis hand rehabilitation robot is shown.

B. Image-processing algorithm for recognizing user-intent

In this hand rehabilitation robot, the camera is mounted on the exoskeleton. This is different from other types of image guided robot control devices in which most of the cameras are placed external to the robot in a fixed coordinate system. This concept comes from a snake-eye view, in contrast to human-eye view. In this robot, the “image-guided” concept refers to targeting the object and deriving the appropriate orientation for grabbing the object.

When the patient attempts to grab a target object, the “measurement” button is pressed. Then the camera detects the long axis of the object, and the software calculates the difference between the grasp axis and the long axis of the object. Then it automatically rotates to provide appropriate orientation to grab the object. Once the robot is oriented in the right position, the user confirms the position and the robot hand grabs the object. Fig. 7 shows the basic concept and process of the robot.

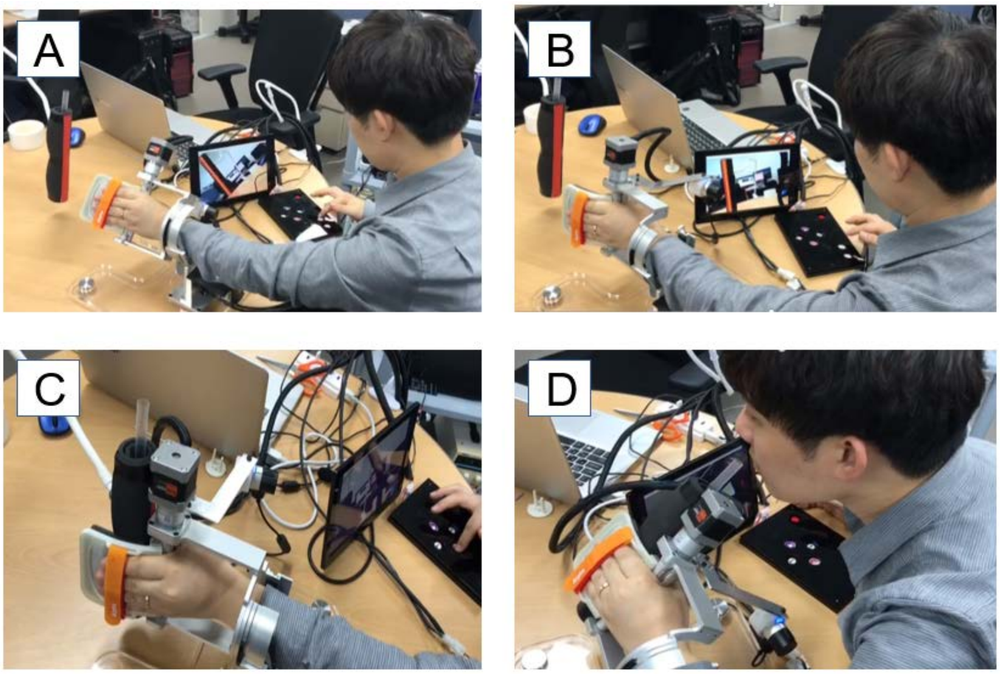

Fig. 7. Main concept of the image-processing based user-intent driven hand rehabilitation robot is shown. (A) The user aims the robot hand at the target (assumed as a water bottle with a straw) and confirms the target object shown in the display. (B) The robot recognizes the target object and the long axis, and automatically rotates the forearm supination / pronation axis to the appropriate orientation of the robot hand. (C) The user moves the robot to the object with the proximal muscle power (mainly shoulder). (D) The user rotates the axis with the controller so that he can drink water.

2.3.1.2 Preliminary Usability Test

A. Participants

For the usability test, 20 volunteers were recruited. The participants consisted of six physicians, five engineers, five rehabilitation therapists, two chronic stroke patients, and two caregivers of stroke patients. Patients and caregivers were both categorized as "patients". All participants were instructed to evaluate the device in their perspectives of professional experience.

B. Procedure

All participants mounted their left arm and hand on the robot. They were instructed to use the hand rehabilitation robot freely with the software, which the mounted camera recognizes the long axis of the target object and automatically rotates to the appropriate orientation. The users also operate the robot using the switch control pad with their right hand. After 10 minutes of use, they were asked to fill out the survey form. The survey consisted of 10 items in a seven-point scale, including sub-items, asking for the respondent's overall satisfaction, interest, motivation, expected improvement in recovery, difficulty, discomfort, safety, comparison to other therapeutic robots, willingness to use, and expected efficacy after commercialization. Additional opinions on the robot were also obtained.

C. Statistical Analysis

Descriptive statistical analyses were performed.

2.4 Statistical Analysis and Study Approval

All statistical analyses in this study were performed using SPSS v21.0 (SPSS Inc., Chicago, IL, USA). All parts of this study involving ethical issues or procedural justification were approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 1505-017-668, 1504-104-666, 1610-043-797) and Seoul National University Boramae Medical Center (IRB No. 20150514/16-2015-56/061).

3. RESULTS

3.1 Practical Robot Functions in Demand

A. Demographic data

A total of 48 subjects (42 men, 6 women) participated in the survey. The mean age was 42.6 ± 22.2 years and the mean duration since onset was 99.7 ± 54.7 months. All subjects in unilateral impairment group (UIG, n = 24) had chronic stroke and no functional use of the hemiplegic arm whereas there were no significant impairments of the contralateral arm. Bilateral impairment group (BIG, n = 24) consisted of patients with cervical spinal cord injury (n = 5), Duchenne muscular dystrophy (n = 18), and amyotrophic lateral sclerosis (n = 1). Half of the subjects (n = 12) reported partial functional use of at least one upper extremity, and the other half (n = 12) reported no functional use of both upper extremities. Detailed demographic data of the subgroups are shown in Table 1.

Table 1. Demographic Data of Demand Survey Participants

	Unilateral impairment group	Bilateral impairment group	Total
No. of subjects	24	24	48
Chronic stroke	24		
Cervical spinal cord injury		5	
Duchenne muscular dystrophy		18	
Amyotrophic lateral sclerosis		1	
Men : Women (n)	20:4	22:2	42:6
Average age (years)	61.2 ± 5.3	24.8 ± 17.0	42.6 ± 22.2
Average duration since onset (months)	109.5 ± 51.8	90.1 ± 56.7	99.7 ± 54.6

B. Unilateral impairment group (UIG)

In subjects with unilateral upper extremity impairment, handling foods (2.6 ± 1.3, level of dependence), computer (2.9 ± 1.5), cleaning (3.4 ± 1.5), self-exercise (3.4 ± 1.7) showed high dependency.

Regarding external robotic arm, handling foods (75.0%, important or very important), using computer (75.0%), hairdressing (70.8%), and using smartphones (66.7%) were considered objectively important functions as well as subjectively necessary. However, moving close items (75.0%, necessary or highly necessary) and dressing (62.5%) were the most highly necessary functions whereas their importance was relatively rated in lower priority. Assistance in brushing teeth (37.5%, not necessary or of little necessity), switch control (37.5%), phone calls (33.3%), and eating (33.3%) showed low necessity with external robotic arms.

Importance and necessity showed generally higher ratings regarding upper limb exoskeleton. Handling foods (87.5%, important or very important), self-exercise (87.5%), transfer (87.5%), and smartphone (83.3%) were considered objectively important functions. Regarding necessity, handling foods (75.0%, necessary or highly necessary), self-exercise (66.7%), moving close items (75.0%), dressing (66.7%), washing face (66.7%), hairdressing (66.7%), and smartphone (66.7%) were rated high. Brushing teeth (66.7%) and eating (62.5%) were relatively rated high in necessity compared to low rank in importance. Switch control (37.5%, not necessary or of little necessity), phone calls (37.5%), and wheelchair control (33.3%) were functions that were considered not necessary for an exoskeleton. Detailed data for UIG are shown in Table 2, Fig. 8, and Fig. 9.

Table 2. Dependency, Importance, and Necessity for Assistive Robots in Unilateral Impairment Group (n=24)

ADL item*	Dependency[a]	External Robotic Arm				Upper Limb Exoskeleton			
		Importance[b]	Necessary[c]	Highly necessary[d]	Not necessary[e]	Importance[b]	Necessary[c]	Highly necessary[d]	Not necessary[e]
Handling foods	2.6 ± 1.3	75.0 (1)	70.8 (2)	33.3 (4)	20.8 (11)	87.5 (1)	75.0 (1)	45.8 (3)	16.7 (13)
Computer	2.9 ± 1.5	75.0 (1)	54.2 (6)	33.3 (4)	25.0 (7)	70.8 (12)	50.0 (15)	25.0 (14)	25.0 (6)
Cleaning	3.4 ± 1.5	45.8 (11)	41.7 (11)	16.7 (10)	20.8 (11)	70.8 (12)	58.3 (12)	29.2 (12)	29.2 (4)
Self-exercise	3.4 ± 1.7					87.5 (1)	66.7 (3)	50 (2)	8.3 (18)
Moving close items	3.5 ± 1.4	62.5 (6)	75.0 (1)	37.5 (2)	25.0 (7)	79.2 (7)	75.0 (1)	33.3 (11)	20.8 (11)
Dressing	3.5 ± 1.3	54.2 (9)	62.5 (3)	41.6 (1)	16.7 (14)	79.2 (7)	66.7 (3)	54.2 (1)	12.5 (16)
Washing Face	3.8 ± 1.6	45.8 (11)	45.8 (9)	25 (7)	29.2 (5)	83.3 (4)	66.7 (3)	41.7 (7)	12.5 (16)
Transfer	3.8 ± 1.2					87.5 (1)	58.3 (12)	25 (14)	25.0 (6)
Hairdressing	3.8 ± 1.4	70.8 (3)	58.3 (4)	37.5 (2)	20.8 (11)	79.2 (7)	66.7 (3)	45.8 (3)	16.7 (13)
Brushing teeth	3.8 ± 1.1	58.3 (7)	33.3 (14)	25 (7)	37.5 (1)	70.8 (12)	66.7 (3)	41.7 (7)	16.7 (13)
Phone calls	3.8 ± 1.6	58.3 (7)	37.5 (13)	16.7 (10)	33.3 (3)	79.2 (7)	37.5 (18)	16.7 (17)	37.5 (1)
Writing	3.8 ± 1.2	66.7 (4)	54.2 (6)	16.7 (10)	29.2 (5)	75.0 (11)	62.5 (9)	45.8 (3)	25.0 (6)
Wheelchair control	3.9 ± 1.3					66.7 (16)	50.0 (15)	29.2 (12)	33.3 (3)
Purse	4.0 ± 1.4	54.2 (9)	50.0 (8)	25.0 (7)	25.0 (7)	66.7 (16)	54.2 (14)	25.0 (14)	25.0 (6)
Smartphone	4.0 ± 1.3	66.7 (4)	58.3 (4)	29.2 (6)	25.0 (7)	83.3 (4)	66.7 (3)	37.5 (10)	20.8 (11)
Switch control	4.1 ± 1.4	37.5 (14)	41.7 (11)	16.7 (10)	37.5 (1)	58.3 (18)	45.8 (17)	16.7 (17)	37.5 (1)
Eating	4.1 ± 1.2	45.8 (11)	45.8 (9)	16.7 (10)	33.3 (3)	70.8 (12)	62.5 (9)	41.7 (7)	29.2 (4)
Toilet use	4.3 ± 1.2					83.3 (4)	62.5 (9)	45.8 (3)	25.0 (6)

* ADL items are listed in the order of highest dependence to lowest dependency

[a] dependency in 5-Likert scale: 1(totally dependent) to 5(independent), mean ± standard deviation

[b] percentage of respondents who replied corresponding ADL as important (4) or very important (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group

[c] percentage of respondents who replied corresponding ADL as necessary (4) or highly necessary (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group

[d] percentage of respondents who replied corresponding ADL as highly necessary (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group

[e] percentage of respondents who replied corresponding ADL as not necessary (1) or of little necessity (2) in a 5-Likert scale, numbers in ( ) indicate ranking in the group

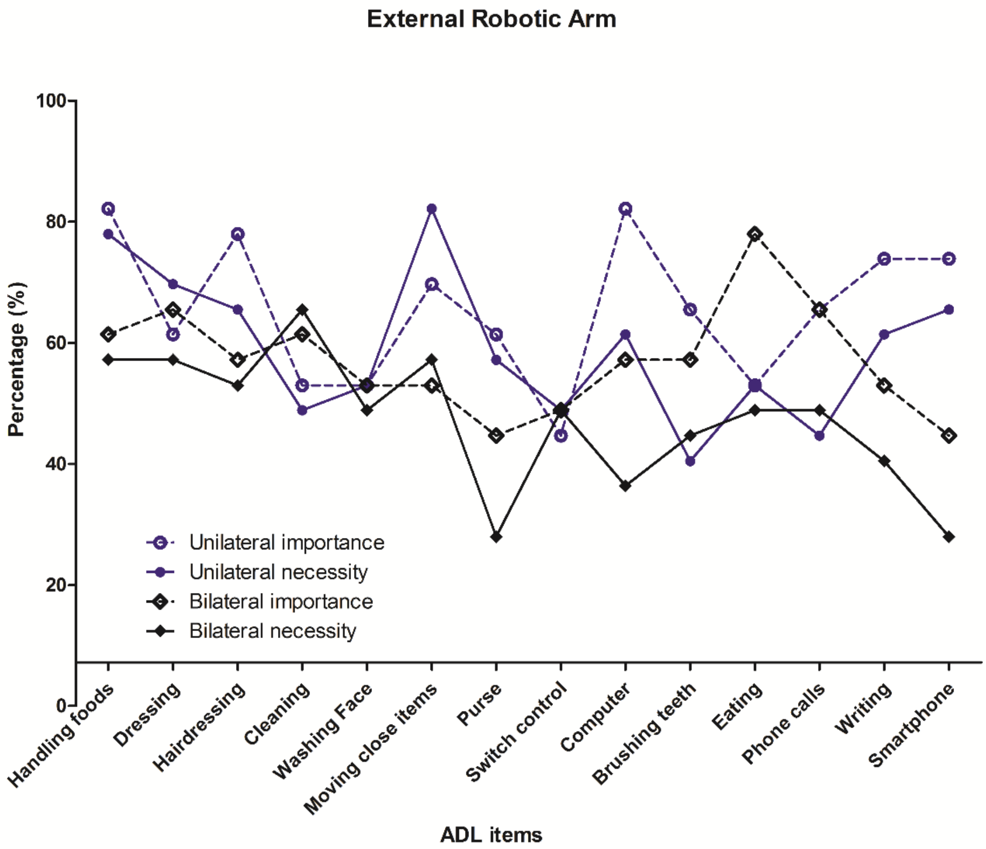

Fig. 8. The percentage of respondents who replied 'important' or 'very important' for importance (dotted line) and 'necessary' and 'highly necessary' for necessity (solid line) of an external robotic arm to each activities of daily living (ADL) function in each impairment group (unilateral impairment group: circle, bilateral impairment group: rhombus). The ADLs in the *x*-axis are in the order of high to low dependency for all survey participants.

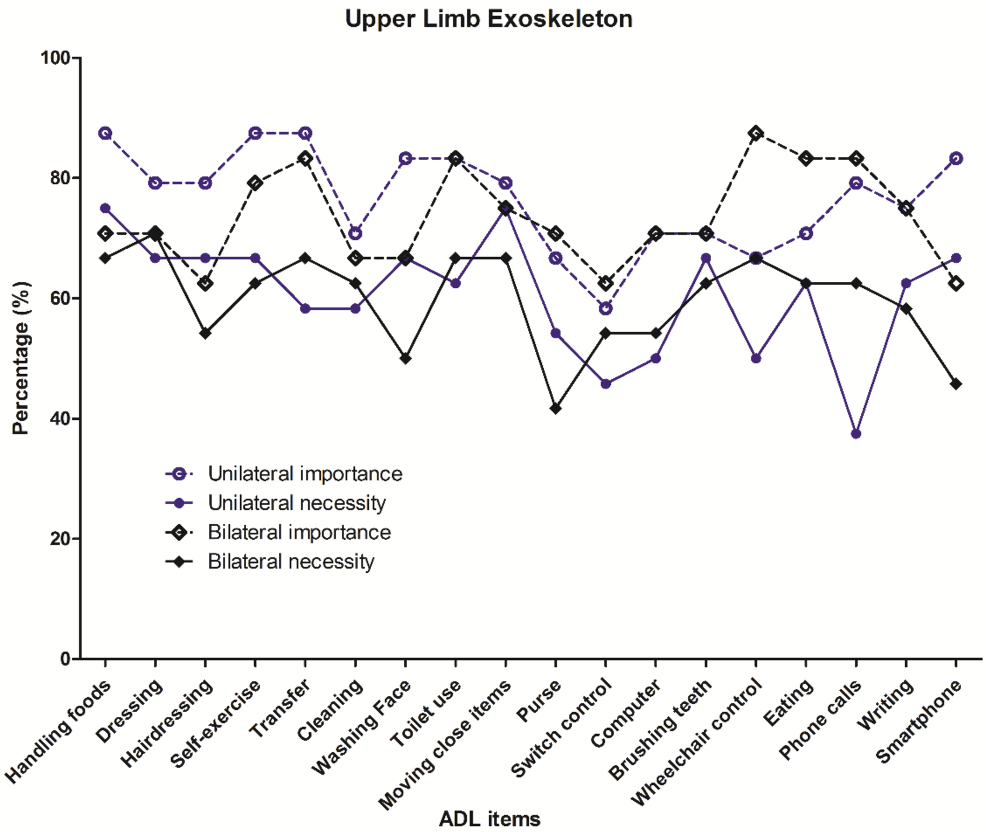

Fig. 9. The percentage of respondents who replied 'important' or 'very important' for importance (dotted line) and 'necessary' and 'highly necessary' for necessity (solid line) of an upper limb exoskeleton to each activities of daily living (ADL) function in each impairment group (unilateral impairment group: circle, bilateral impairment group: rhombus). The ADLs in the *x*-axis are in the order of high to low dependency for all survey participants.

C. Bilateral impairment group (BIG)

In subjects with bilateral upper extremity impairment, toilet use (1.6 ± 1.2), hairdressing (1.7 ± 1.2), dressing (1.7 ± 1.3), transfer (1.8 ± 1.4) and handling foods (2.0 ± 1.4) showed high dependency.

For an external robotic arm, assistance in eating (70.8%, percentage of being rated important or very important), dressing (58.3%), phone calls (58.3%), handling foods (54.2%), and cleaning (54.2%) were considered important functions as well as necessary functions. Eating (33.3%, percentage of being rated very necessary) and hairdressing (33.3%) showed highest percentage of being rated highly necessary functions for an external robotic arm. In contrast, smartphone (58.3%, not necessary or of little necessity), purse (54.2%), writing (50.0%), and computer (50.0%) showed low necessity with external robotic arms.

Importance and necessity regarding upper limb exoskeleton also showed generally higher ratings in the BIG. Wheelchair control (87.5%, 66.7%, important or very important, necessary or highly necessary, respectively), transfer (83.3%, 66.7%), toilet use (83.3%, 66.7%), eating (83.3%, 62.5%), phone calls (83.3%, 62.5%), moving close items (75.0%, 66.7%), dressing (70.8%, 70.8%), handling foods (70.8%, 66.7%), and self-exercise (79.2%, 62.5%) showed both high importance and necessity. High proportion of subjects replied writing (54.2%) as highly necessary function for upper limb exoskeleton. Smartphone (41.7%, not necessary or of little necessity), washing face (37.5%), purse (33.3%), and computer (33.3%) were considered less necessary functions for an exoskeleton. Detailed data for BIG are shown in Table 3, Fig. 8, and Fig. 9.

Table 3. Dependency, Importance, and Necessity for Assistive Robots in Bilateral Impairment Group (n=24)

ADL item[*]	Dependency[a]	External Robotic Arm				Upper Limb Exoskeleton			
		Importance[b]	Necessary[c]	Highly necessary[d]	Not necessary[e]	Importance[b]	Necessary[c]	Highly necessary[d]	Not necessary[e]
Toilet use	1.6 ± 1.2					83.3 (2)	66.7 (2)	45.8 (4)	16.7 (12)
Hairdressing	1.7 ± 1.2	50.0 (6)	45.8 (5)	33.3 (1)	16.7 (14)	62.5 (16)	54.2 (13)	33.3 (12)	16.7 (12)
Dressing	1.7 ± 1.3	58.3 (2)	50.0 (2)	29.2 (3)	29.2 (11)	70.8 (9)	70.8 (1)	45.8 (4)	12.5 (14)
Transfer	1.8 ± 1.4					83.3 (2)	66.7 (2)	58.3 (1)	25.0 (8)
Handling foods	2.0 ± 1.4	54.2 (4)	50.0 (2)	25.0 (5)	29.2 (11)	70.8 (9)	66.7 (2)	37.5 (10)	25.0 (8)
Washing Face	2.0 ± 1.6	45.8 (9)	41.7 (6)	12.5 (13)	33.3 (8)	66.7 (14)	50.0 (16)	25.0 (18)	37.5 (2)
Self-exercise	2.1 ± 1.6					79.2 (6)	62.5 (7)	41.7 (7)	8.3 (18)
Purse	2.2 ± 1.5	37.5 (13)	20.8 (13)	16.7 (10)	54.2 (2)	70.8 (9)	41.7 (18)	33.3 (12)	33.3 (3)
Cleaning	2.3 ± 1.2	54.2 (4)	58.3 (1)	29.2 (3)	33.3 (8)	66.7 (14)	62.5 (7)	29.2 (16)	12.5 (14)
Switch control	2.3 ± 1.7	41.7 (12)	41.7 (6)	25.0 (5)	41.7 (6)	62.5 (16)	54.2 (13)	29.2 (16)	20.8 (10)
Moving close items	2.4 ± 1.3	45.8 (9)	50.0 (2)	12.5 (13)	20.8 (13)	75.0 (7)	66.7 (2)	33.3 (12)	12.5 (14)
Brushing teeth	2.6 ± 1.8	50.0 (6)	37.5 (10)	16.7 (10)	33.3 (8)	70.8 (9)	62.5 (7)	33.3 (12)	29.2 (5)
Eating	2.8 ± 1.8	70.8 (1)	41.7 (6)	33.3 (1)	45.8 (5)	83.3 (2)	62.5 (7)	41.7 (7)	29.2 (5)
Wheelchair control	3.0 ± 1.4					87.5 (1)	66.7 (2)	58.3 (1)	12.5 (14)
Phone calls	3.1 ± 1.7	58.3 (2)	41.7 (6)	25.0 (5)	41.7 (6)	83.3 (2)	62.5 (7)	45.8 (4)	20.8 (10)
Writing	3.1 ± 1.7	45.8 (9)	33.3 (11)	16.7 (10)	50.0 (3)	75.0 (7)	58.3 (12)	54.2 (3)	29.2 (5)
Smartphone	3.4 ± 1.7	37.5 (13)	20.8 (13)	20.8 (8)	58.3 (1)	62.5 (16)	45.8 (17)	37.5 (10)	41.7 (1)
Computer	3.5 ± 1.7	50.0 (6)	29.2 (12)	20.8 (8)	50.0 (3)	70.8 (9)	54.2 (13)	41.7 (7)	33.3 (3)

* ADL items are listed in the order of highest dependence to lowest dependency
[a] dependency in 5-Likert scale: 1(totally dependent) to 5(independent), mean ± standard deviation
[b] percentage of respondents who replied corresponding ADL as important (4) or very important (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group
[c] percentage of respondents who replied corresponding ADL as necessary (4) or highly necessary (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group
[d] percentage of respondents who replied corresponding ADL as highly necessary (5) in a 5-Likert scale, numbers in ( ) indicate ranking in the group
[e] percentage of respondents who replied corresponding ADL as not necessary (1) or of little necessity (2) in a 5-Likert scale, numbers in ( ) indicate ranking in the group

D. Unilateral impaired group vs bilateral impaired group

For external robotic arm, only necessity for smartphone showed significant difference between unilateral group (3.4 ± 1.5) and bilateral group (2.4 ± 1.6, p = 0.008). For upper limb exoskeleton, only necessity for wheelchair control showed significant difference (3.1 ± 1.7 vs 4.1 ± 1.3, unilateral vs bilateral, p = 0.041). Detailed data for all necessity ratings are shown in Fig. 10.

E. External robotic arm vs upper limb exoskeleton

In most of the cases, upper limb exoskeletons demonstrated higher ratings in necessity compared to external robotic arm. In UIG, upper limb exoskeleton showed significantly higher necessity in washing face (3.9 ± 1.2 vs 3.2 ± 1.5, p = 0.004), brushing teeth (3.8 ± 1.4 vs 3.0 ± 1.5, p = 0.005), and eating (3.5 ± 1.7 vs 3.0 ± 1.5, p = 0.005). In BIG, significantly higher necessity for upper limb exoskeleton was shown in dressing (4.0 ± 1.1 vs 3.4 ± 1.4, p = 0.010), moving close items (3.8 ± 1.1 vs 3.4 ± 1.1, p = 0.046), purse (3.2 ± 1.6 vs 2.5 ± 1.4, p = 0.038), switch control (3.5 ± 1.3 vs 3.1 ± 1.5, p = 0.038), computer (3.4 ± 1.7 vs 2.7 ± 1.5, p = 0.005), eating (3.5 ± 1.7 vs 3.0 ± 1.7, p = 0.020), phone calls (3.7 ± 1.6 vs 3.0 ± 1.6, p = 0.026), writing (3.7 ± 1.6 vs 2.8 ± 1.5, p = 0.003), and smartphone (3.1 ± 1.8 vs 2.4 ± 1.6, p = 0.008). Detailed data for all necessity ratings are shown in Fig. 10.

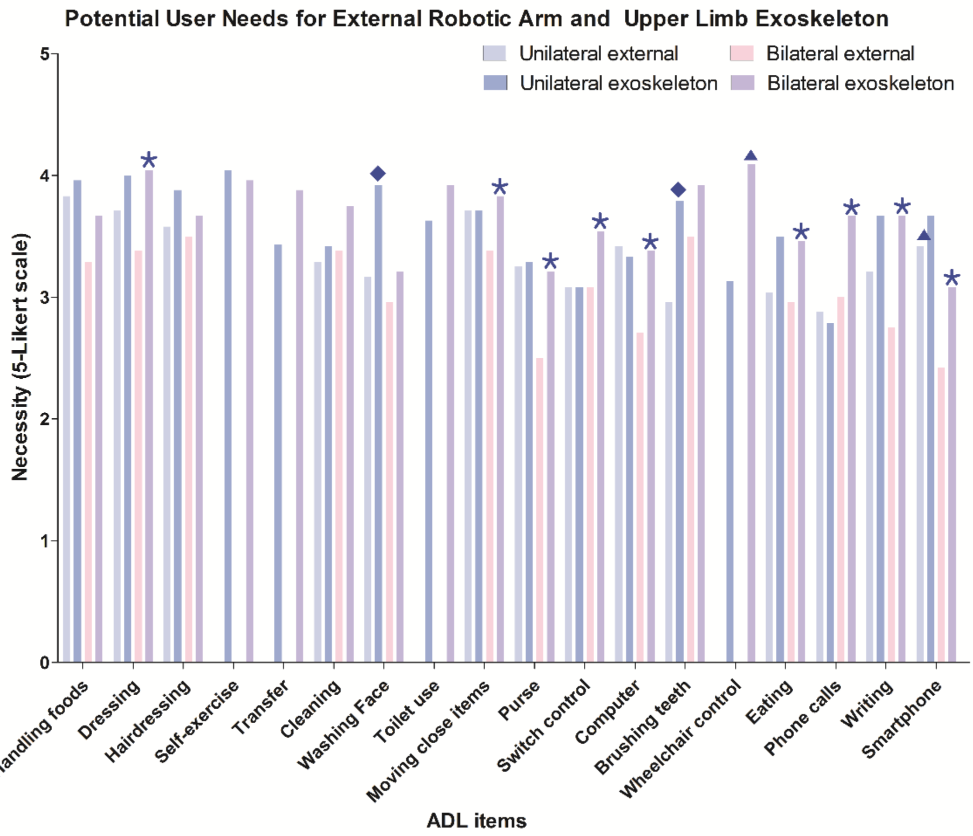

Fig. 10. Potential user needs (necessity in 5-Likert scale) are shown for each activities of daily living (ADL) item regarding external robotic arm and upper limb exoskeleton in both unilateral (UIG) and bilateral impairment group (BIG). The ADLs in the *x*-axis are in the order of high to low dependency for all survey participants. ADLs with significantly higher necessity for exoskeleton than external robotic arm in UIG (asterisks, *) and BIG (rhomboids, ◆) are indicated ($p < 0.05$). Triangles (▲) indicate significant difference between UIG and BIG ($p < 0.05$).

3.2 Minimum Requirements for Motor Power in Major Joints to Overcome Spasticity

A. Demographic Data

Demographic data of the subjects are shown in Table 4. Mean age was 60.6 ± 5.4 years and the mean duration since stroke onset was 9.7 ± 3.7 years. Age, height, body weight, duration since onset, and possible ROM range did not significantly differ between the spasticity grades, except for wrist flexor spasticity, for which the ROM range was approximately 16 degrees smaller at the high grade compared to the low grade of spasticity.

Table 4. Demographic Data of Enrolled Stroke Patients for Spasticity Resistance Evaluation

	Elbow Flexor Spasticity				Wrist Flexor Spasticity				Total
	Low	Intermediate	High	*p**	Low	Intermediate	High	*p**	
Subjects (n)	7	6	7		8	6	6		20
Gender (M/F)	5/2	5/1	7/0		5/3	6/0			17/3
Age (years old)	60.6±5.5	57.5±7.4	62.1±4.2	0.315	61.5±5.9	59.2±4.8	60.8±6.0	0.592	60.6±5.4
Height (cm)	161.8±9.0	171.8±4.0	166.5±4.3	0.092	162.1±9.3	167.7±3.9	168.3±5.9	0.345	165.7±7.3
Body weight (kg)	66.3±9.4	73.3±12.4	71.6±9.3	0.593	66.0±9.1	73.8±9.7	70.8±10.8	0.408	69.8±9.9
Etiology (Inf / Hem / Etc)	0/6/1	3/3/0	4/3/0		0/7/1	3/3/0	4/2/0		7/12/1
Laterality (left / right)	5/2	2/4	3/4		5/3	3/3	2/4		10/10
Years Since Onset	9.8±4.3	8.8±3.6	10.1±3.4	0.560	9.9±4.3	9.2±2.9	10.0±4.0	0.867	9.7±3.7
Range of Motion (°)	110.0±23.3	112.5±9.6	106.9±18.3	0.887	132.5±17.9	126.8±15.1	116.5±24.4	<0.001	Elbow: 109.3±18.5 Wrist: 126.1±20.3

Low: MAS grade 0, 1 ; Intermediate: MAS grade 1+ ; High: MAS grade 2, 3 ; Inf: infarction ; Hem: hemorrhage ; Etc: others, e.g. brain tumor

* Kruskal-Wallis test between spasticity grades, $p < 0.05$ considered significant

B. Torque Resistance Response for Elbow Flexors

The maximal resistance torques caused by the elbow flexor with low, intermediate, and high grade spasticity averaged over all angular velocities were 3.68 ± 2.42, 5.94 ± 2.55, and 8.25 ± 3.35 Nm, respectively, with statistically significant differences between the grades ($p < 0.001$ by ANOVA and all post-hoc analyses). The maximum resistance torque for the elbow flexor was 1.77 Nm in a healthy subject. The maximum resistance torque value during extension of the elbow joint among all subjects and trials was 21.28 Nm, which occurred in the subject with MAS grade 2 in the elbow flexor. The RM-ANOVA test for torque values at 1/3, 2/3, and 100 % ROM demonstrated that the resistance torque value showed significant differences between spasticity grades showing a tendency of increase with increasing spasticity ($p < 0.001$ for interaction of ROM and spasticity grade by RM-ANOVA). The ANOVA tests for resistance torques at 1/3 ROM, 2/3 ROM, and 100 % ROM also demonstrated significant differences between spasticity grades showing increasing resistance torque with increasing spasticity ($p = 0.001$ for 1/3 ROM, $p < 0.001$ for 2/3 ROM and 100 % ROM). The results for elbow flexors are shown in Table 5 and Fig. 11.

C. Torque Resistance Response for Elbow Extensors

For the elbow extensor, the maximal resistance torques averaged over all angular velocities were -4.95 ± 3.30, -9.65 ± 4.35, and -8.35 ± 3.66 Nm for low, intermediate, and high grade spasticity, respectively ($p < 0.001$ by ANOVA, p < 0.001 for low vs intermediate, low vs high grade spasticity), compared to -2.82 Nm in a healthy subject.

The maximum resistance torque during flexion of the elbow joint among all subjects and trials was -18.84 Nm, which occurred in a subject with MAS grade 1+ in both the elbow flexor and extensor. The RM-ANOVA test for resistance torques at 1/3, 2/3, and 100% ROM showed significant interaction of ROM and spasticity grades ($p < 0.001$). The ANOVA test regarding resistance torques for 1/3, 2/3, and 100% ROM and maximal resistance torque showed significant differences between the spasticity grades ($p < 0.01$); however, post hoc analysis demonstrated that the resistance torque at 100% ROM and the maximal value were not significantly different between intermediate and high spasticity. The results for elbow extensors are shown in Table 5 and Fig. 11.

D. Torque Resistance Response for Wrist Flexors

The maximal resistance torques caused by the wrist flexor averaged over all angular velocities were 4.23 ± 1.75, 5.68 ± 1.96, and 5.44 ± 2.02 Nm for low, intermediate, and high grade spasticity, respectively ($p < 0.001$ by ANOVA, $p < 0.001$ for low vs intermediate, low vs high grade spasticity), compared to 0.56 Nm in a healthy subject. The maximum resistance torque during extension of the wrist joint among all subjects and trials was 11.34 Nm, which occurred in a subject with MAS grade 2 in the wrist flexor. The maximum resistance torque in the flexion direction was -7.5 Nm among all subjects, who did not show specific wrist extensor spasticity. The RM-ANOVA test for resistance torques at 1/3, 2/3, and 100% ROM showed significant interaction of ROM and spasticity grades ($p < 0.001$). The ANOVA test for torque values at 1/3, 2/3, and 100% ROM also showed significant differences between spasticity grades

($p < 0.001$), while resistance torque at 100% ROM between intermediate and high spasticity grades was not significantly different ($p = 0.869$). Because intermediate and high spasticity did not show meaningful difference, the independent *t* test was performed as a part of post-hoc analysis between low grade and intermediate plus high grades. The resistance torques at 2/3, 100% ROM and the maximal value were significantly different ($p < 0.001$). The results for wrist flexors are shown in Table 5 and Fig. 11.

Table 5. Resistance Torque Values to Spastic Elbow and Wrist Joints

Spastic Muscle (No. of trials for low, intermediate, high grade spasticity)	Angular Position	Reference (healthy subject)	Low Grade Spasticity (MAS 0,1)	Intermediate Grade Spasticity (MAS 1+)	High Grade Spasticity (MAS 2,3)	*p* value (ANOVA)	Posthoc Analysis Low vs Intermediate	Low vs High	Intermediate vs High
Elbow Flexor (75/36/78)	0%ROM	-2.17	-3.61±2.52	-4.06±2.62	-4.36±2.05	0.150	>0.05	>0.05	>0.05
	1/3ROM	0.99	0.06±0.84	0.83±1.57	0.93±1.81	0.001	0.025	0.001	0.939
	2/3ROM	0.79	1.66±1.80	4.05±2.99	4.64±2.77	<0.001	<0.001	<0.001	0.463
	100%ROM	0.37	3.44±2.45	5.57±2.05	7.85±3.34	<0.001	0.001	<0.001	<0.001
	Maximal Torque	1.77	3.68±2.42	5.94±2.55	8.25±3.35	<0.001	<0.001	<0.001	<0.001
Elbow Extensor (138/17/34)	0%ROM	0.70	4.04±2.13	2.66±1.31	4.37±1.34	0.011	0.018	0.653	0.010
	1/3ROM	0.79	0.39±0.83	-0.27±0.74	0.56±0.82	0.003	0.006	0.501	0.002
	2/3ROM	1.16	-1.64±2.03	-4.72±3.29	-2.40±1.76	<0.001	<0.001	0.157	0.001
	100%ROM	-2.68	-4.86±3.15	-9.31±4.49	-7.79±3.42	<0.001	<0.001	<0.001	0.281
	Maximal Torque	-2.82	-4.95±3.30	-9.65±4.35	-8.35±3.66	<0.001	<0.001	<0.001	0.418
Wrist Flexor (96/71/68)	0%ROM	-0.19	-1.30±1.19	-1.58±1.28	-2.03±1.77	0.006	0.412	0.004	0.154
	1/3ROM	-0.08	0.05±0.66	0.56±0.80	-0.22±0.92	<0.001	<0.001	0.079	<0.001
	2/3ROM	-0.07	1.17±0.87	2.07±1.26	1.54±1.34	<0.001	<0.001	0.096	0.021
	100%ROM	0.44	4.14±1.75	5.52±1.93	5.36±2.03	<0.001	<0.001	<0.001	0.869
	Maximal Torque	0.56	4.23±1.75	5.68±1.96	5.44±2.02	<0.001	<0.001	<0.001	0.730

MAS: modified Ashworth Scale; ANOVA: analysis of variance; ROM: range of motion

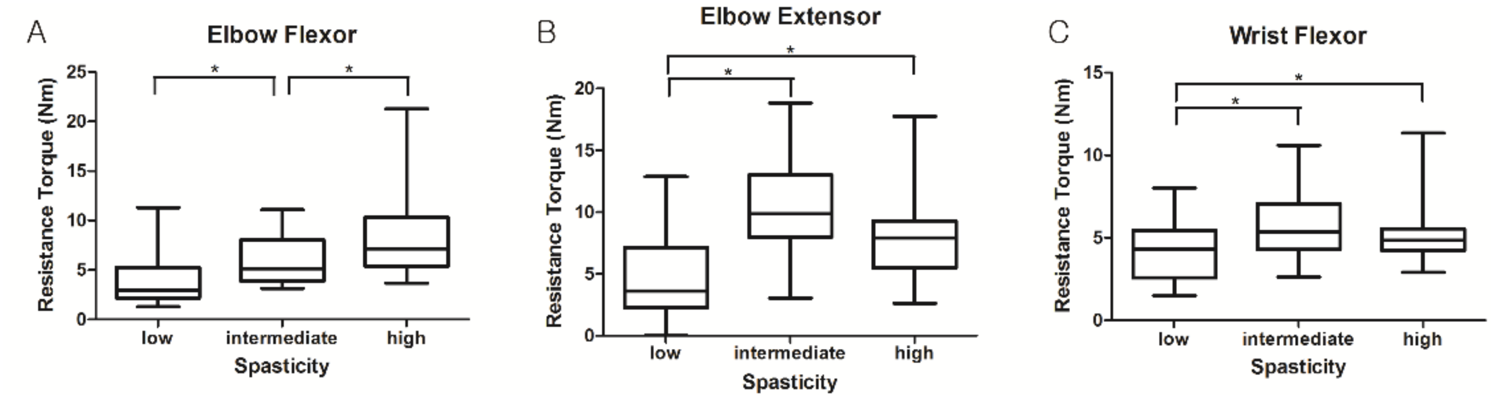

Fig. 11. Box-and-whisker plots are shown for maximal resistance torque of (A) elbow flexor, (B) elbow extensor, and (C) wrist flexor. Analysis of variance test showed significant differences between spasticity grades. Asterisks indicate significant differences between the grades by posthoc analysis ($p < 0.05$).

E. Effect of Robot Speed

In each spasticity grade for elbow flexors, the maximal resistance torques were compared by the angular velocity of the isokinetic robotic movement. There were no significant differences according to the angular velocities (p = 0.231, 0.478, 0.766), but a trend was shown for the resistance torque to increase with velocity. In contrast, the CPP demonstrated a significant tendency to decrease with increasing angular velocity in subjects with low and intermediate spasticity, which means that the catch occurred more quickly when the robotic movement speed was faster (p = 0.009 and 0.004). Data are shown in Fig. 12.

For wrist flexor spasticity, the robot speed did not significantly affect the maximal resistance torque, nor did it show any specific tendency relative to angular velocity (p = 0.917, 0.697, and 0.989 for low, intermediate, and high spasticity, by ANOVA, data not shown).

F. Catch Point Percentage

The catch angle for each trial was converted into CPP (%ROM) and the average CPP was calculated by the degree of spasticity. The estimated CPP for intermediate and high elbow flexor spasticity was 57.56 ± 30.91 %ROM and 49.11 ± 21.32 %, respectively ($p < 0.001$). The mean torque at the moment of the catch did not show significant differences between the spasticity grades (data not shown). With regard to the wrist flexor spasticity, the CPP for intermediate and high spasticity were 73.2 ± 22.4 and 76.3 ± 23.5 %ROM, respectively ($p > 0.05$).

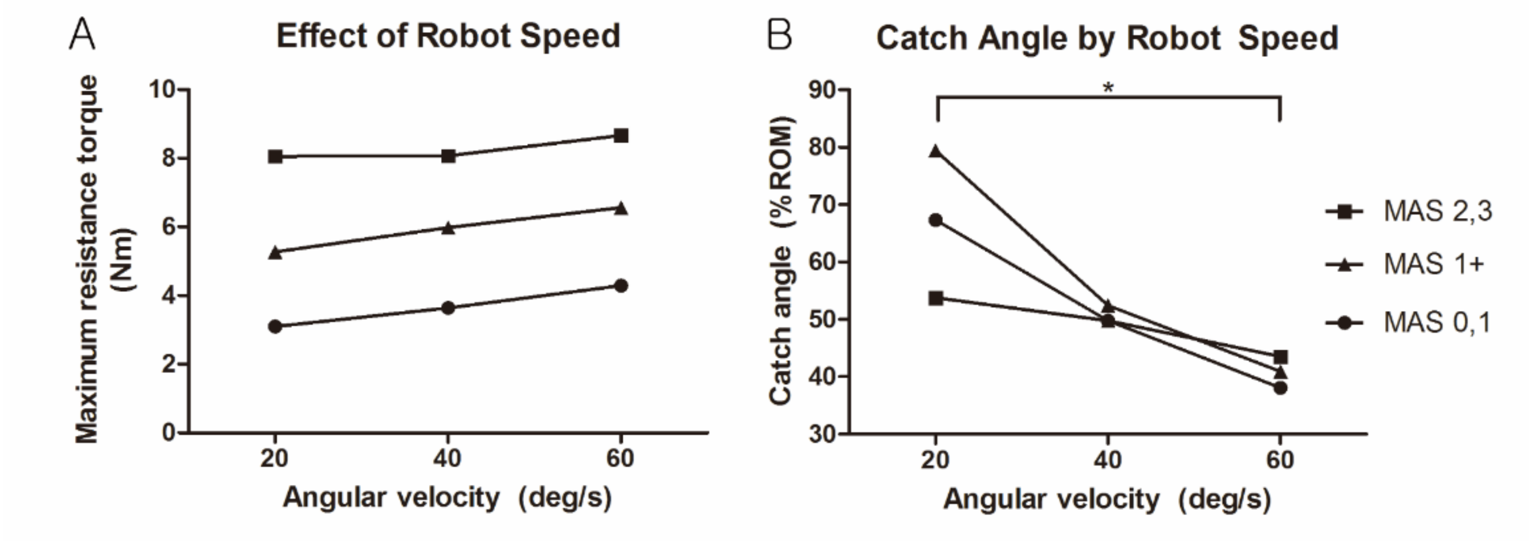

Fig. 12. (A) Maximum resistance torque and (B) catch angle according to the angular velocity of the robot in each grade of elbow flexor spasticity are shown. Catch angle for low (MAS 0, 1) and intermediate (MAS 1+) spasticity showed significant decrease with increasing velocity.

3.3 Range of Motion and Movement Characteristics in Major Movements & Tasks

3.3.1 Healthy Subjects

A. Validation of the upper extremity motion capture system

Validation was performed for 6 reaching tasks within the ARAT tasks for 10 healthy subjects. The range of RMSE for elbow flexion / extension angle ranged from 2.11° to 4.75° (average: 3.61 ± 1.32°), and 0.42° to 1.22° (average: 0.85 ± 0.40°) for wrist dorsiflexion / volarflexion angle. During the reaching task, the mean change of forearm supination / pronation was 36.65 ± 6.98°, with intra-subject CoV of 17.29% and inter-subject CoV of 19.05%. The change of elbow flexion / extension was 69.96 ± 16.89°, and intra-subject and inter-subject CoV were 11.67% and 24.14%, respectively. Distance data extracted from the sensors during the reaching tasks were evaluated and also compared with real movement distance. Regarding the accelerometer on the forearm sensor, average of the calculated movement distance were 34.14 ± 4.15 cm in z-axis and 33.54 ± 4.79 cm in y-axis, where measured distance in each direction was 34.0 cm and 33.5 cm, respectively. Data calculated from hand sensors were 36.78 ± 3.09cm and 32.35 ± 4.64 cm, respectively. Intra-subject CoV ranged from 5.5 to 9.5% while inter-subject CoV ranged from 8.4 to 14.3%. Full results are shown in Table 6.

Table 6. Coefficient of Variation during Major Movements for IMU-based Upper Extremity Motion Capture System

Sensor type	Movement / direction	Mean±SD of change during task (across subjects)	Intra-subject CoV average	Inter-subject CoV	Estimated real distance
Gyrosensor	Forearm supination/ pronation	36.65 ± 6.98°	17.29%	19.05%	-
	Elbow flexion/ extension	69.96 ± 16.89°	11.67%	24.14%	-
Accelerometer (forearm sensor)	*z*-axis distance* (up/down)	34.14 ± 4.15 cm	6.18%	12.17%	34.0 cm
	y-axis distance* (front/back)	33.54 ± 4.79 cm	7.16%	14.28%	33.5 cm
Accelerometer (hand sensor)	*z*-axis distance* (up/down)	36.78 ± 3.09 cm	5.56%	8.41%	34.0 cm
	y-axis distance* (front/back)	32.35 ± 4.64 cm	9.49%	14.33%	33.5 cm

* Estimated distance between initial object position and target position is approximately 39cm for *y*-axis and 40cm for *z*-axis. Note that this is distance regarding center of object, while calculated distance from accelerometers refers to position of the sensor (forearm and hand dorsum).

B. Workspace and ROM in basic upper extremity movements

All 10 subjects were right-handed. For orthogonal coordination, axes were defined as following: left-right direction as x-axis, front-right direction as y-axis, and up-down direction as z-axis. For the ARAT tasks, size of the workspace for the right hand with reference to the sensor on the dorsum of the hand was 0.53 ± 0.11 m for x-axis, 0.92 ± 0.08 m for y-axis, and 0.89 ± 0.10 m for z-axis. For the left side, average workspace size was 0.62 × 0.80 × 0.86 m (in x, y, z-axis order). For pre-specified ADL tasks, the workspace for the dominant hand was 0.71 ± 0.22 m, 0.70 ± 0.17 m, and 0.86 ± 0.11 m (in x, y, z-axis order). Workspace of the non-dominant hand was significantly smaller, with average size of 0.52 × 0.53 × 0.65 m (p = 0.001, 0.011, and 0.001 for x, y, and z-axis, respectively). Detailed data are shown in Table 7.

For ROM in major upper extremity joints, the angular range was similar between right and left sides. Elbow flexion / extension and forearm supination / pronation showed highest value for ROM in both ARAT and ADL for the dominant arm. The ROM values were 109.15 ± 18.82° and 105.23 ± 15.38° (elbow flexion / extension and forearm supination / pronation, respectively) for ARAT tasks and 120.61 ± 23.64° and 128.09 ± 22.04° for ADL tasks. The ROM of the dominant side were significantly greater than the non-dominant side for all joint directions except wrist dorsiflexion / volarflexion, which showed similar values (113.70 ± 18.26° vs 110.08 ± 12.16°, right vs left, p = 0.526). Detailed data are shown in Table 7.

Table 7. Range of Motion Angle between Right and Left Upper Extremities During ARAT and ADL Tasks

	Axis	Right	Left	*p*[a]
ARAT	*x*-axis (left-right, hand sensor)	0.53 ± 0.11m	0.62 ± 0.07m	0.082
	y-axis (front-back, hand sensor)	0.92 ± 0.08m	0.80 ± 0.11m	0.049*
	z-axis (hand sensor)	0.89 ± 0.10m	0.86 ± 0.08m	0.224
	Shoulder abduction/adduction	50.16 ± 11.14°	55.34 ± 13.48°	0.249
	Shoulder flexion/extension	79.52 ± 19.34°	75.71 ± 21.56°	0.478
	Elbow flexion/extension	109.15 ± 18.82°	106.89 ± 12.83°	0.705
	Forearm supination/pronation	105.23 ± 15.38°	108.64 ± 12.64°	0.426
	Shoulder internal/external rotation	91.99 ± 20.98°	84.44 ± 44.75°	0.584
	Wrist dorsiflexion/volarflexion	82.90 ± 22.52°	81.26 ± 11.16°	0.833
ADL tasks	*x*-axis (left-right, hand sensor)	0.71 ± 0.22m	0.52 ± 0.13m	0.001*
	y-axis (front-back, hand sensor)	0.70 ± 0.17m	0.53 ± 0.15m	0.011*
	z-axis (hand sensor)	0.86 ± 0.11m	0.65 ± 0.13m	0.001*
	Shoulder abduction/adduction	58.84 ± 14.53°	35.43 ± 10.09°	<0.001*
	Shoulder flexion/extension	68.41 ± 17.56°	40.49 ± 18.54°	0.002*
	Elbow flexion/extension	120.61 ± 23.64°	102.53 ± 19.51°	0.044*
	Forearm supination/pronation	128.09 ± 22.04°	108.00 ± 16.23°	0.027*
	Shoulder internal/external rotation	111.56 ± 31.88°	77.04 ± 21.28°	0.030*
	Wrist dorsiflexion/volarflexion	113.70 ± 18.26°	110.08 ± 12.16°	0.526

[a] *p* value for paired *t* test between right and left side

* *p* value less than 0.05 considered statistically significant

C. Characteristics of grasping / pinching and reaching

Upper extremity posture during grasping / pinching and reaching was analyzed as a subset analysis of the motion data extracted from grasping / pinching and reaching tasks in ARAT domains 1 and 3. Comparing grasping and pinching posture, shoulder was more significantly abducted during pinching (19.39 ± 7.84°) compared to grasping (15.33 ± 6.91°, p = 0.040) and more extended during pinching (29.12 ± 12.33°) than grasping (22.99 ± 10.63°, p = 0.038). Elbow flexion / extension, forearm supination / pronation and shoulder internal / external rotation did not significantly differ between the two postures. During reaching after grasping, elbow was extended for 87.87 ± 25.18° from initial flexed posture and pronated for 36.65 ± 6.98° from initial posture. The degree of elbow extension and forearm pronation while reaching after pinching were similar (p = 0.849 and 0.294, respectively). Detailed results are shown in Table 8.

Table 8. Major Joint Angle Position and Change During Grasping / Pinching and Reaching

Axis	Grasping Initial Position	ROM during Reaching	*p*	Pinching Initial Position	ROM during Reaching	*p*	Grasp -Pinch p^a	Reaching difference p^b
Shoulder abduction/ adduction	15.33±6.91° (abduction)	22.48±19.81° (toward abduction)	0.006*	19.39±7.84° (abduction)	23.67±13.35° (toward abduction)	<0.001*	0.040*	0.015*
Shoulder flexion/extension	22.99±10.63° (extension)	47.80±17.70° (toward flexion)	<0.001*	29.12±12.33° (extension)	41.83±13.69° (toward flexion)	<0.001*	0.038*	0.948
Elbow flexion/extension	87.87±25.18° (near fully flexed)	69.96±16.89° (toward extension)	<0.001*	84.82±20.25° (near fully flexed)	67.91±14.16° (toward extension)	<0.001*	0.543	0.849
Forearm supination/pronation[c]	34.37±11.07° (supinated)	36.65±6.98° (toward pronation)	<0.001*	30.98±13.71° (supinated)	36.02±12.44° (toward pronation)	<0.001*	0.181	0.294
Shoulder IR/ER	0.68±23.56° (inward direction)	16.55±23.02° (toward external rotation)	0.049*	2.01±13.74° (inward direction)	18.10±13.02° (toward external rotation)	0.002*	0.794	0.860
Wrist deviation	8.94±12.12° (to thumb side)	-1.76±10.21° (to finger side)	0.599	1.05±8.19° (to thumb side)	4.81±8.85° (to thumb side)	0.120	0.004*	0.522
Wrist rotation	4.59±7.35° (toward palm down)	7.12±4.59° (toward palm up)	0.001*	0.80±5.25° (toward palm down)	4.75±4.05° (toward palm up)	0.005*	0.023*	0.385
Wrist dorsiflexion / volarflexion	18.79±16.35° (dorsiflexed)	6.79± 6.00° (toward volarflexion)	0.006*	11.30±13.90° (dorsiflexed)	7.28±11.22° (toward volarflexion)	0.070	0.166	0.123

[a] Comparison between grasping and pinching posture by paired *t* test

[b] Comparison between ROM change during reaching after grasping and pinching by paired *t* test

[c] Full pronation: 0°, full supination: 180°

* *p* value less than 0.05 considered statistically significant

3.3.2 Stroke Patients

Of the parameters that showed significant differences in values between healthy subjects and patients and also significant correlation with clinical measures, the average amplitude of forearm supination / pronation angle during the ARAT domain 4 tasks demonstrated the greatest decline in the value of severely impaired patients compared to healthy subjects (29.83%) and also the largest difference between severely and mildly impaired patients (48.46%). During ADL tasks, logsum per time for supination / pronation showed a profound difference between severity levels (38.33%). The average amplitude of acceleration in the *x*-axis (left-right) and *z*-axis (up-down) of the hand and wrist sensors during the ARAT tasks demonstrated a range of 45 to 60% value compared to healthy subjects, with a 21.6 to 37.8 % difference along the severity spectrum. Detailed results are shown in Table 9 and Fig. 13.

Table 9. Average Amplitude Angles and Acceleration for Significantly Declined Parameters in Stroke Patients by Brunnstrom Stage

Task	Position / Direction	Brunnstrom stage				Normal	Difference between severely and mildly impaired[a]	Residual value in severely impaired[b]
		3	4	5	6			
Angle (gyrosensor data, degree)								
ARAT full	Wrist dorsiflexion/volarflexion	7.23	8.62	11.61	14.31	13.57	52.17%	53.28%
ARAT domain 4	Forearm supination/pronation	11.40	16.14	23.06	29.92	38.22	48.46%	29.83%
ARAT domain 1	Forearm supination/pronation	8.67	10.56	14.08	16.78	18.03	44.98%	48.09%
ARAT domain 1	Elbow flexion/extension	9.12	14.49	22.29	22.23	32.91	39.84%	27.71%
ARAT domain 3	Elbow flexion/extension	9.12	15.32	19.23	21.96	32.28	39.78%	28.25%
ARAT domain 3	Shoulder internal/external rotation	7.78	10.70	14.60	13.45	15.60	36.35%	49.87%
ARAT domain 2	Wrist dorsiflexion/volarflexion	7.71	7.73	9.88	12.38	13.68	34.14%	56.36%
ARAT full	Forearm supination/pronation	9.94	12.71	14.89	16.15	19.30	32.18%	51.50%
ARAT full	Elbow flexion/extension	10.49	14.67	19.33	19.39	28.21	31.55%	37.19%
Acceleration (accelerometer data, m/s^2)								
ARAT full	Hand *x*-axis	0.22	0.24	0.31	0.35	0.37	35.14%	59.46%
ARAT full	Hand *z*-axis	0.25	0.32	0.35	0.39	0.47	29.79%	53.19%
ARAT full	Hand *y*-axis	0.21	0.30	0.33	0.32	0.40	27.50%	52.50%
ARAT full	Wrist *x*-axis	0.18	0.20	0.28	0.25	0.29	24.14%	62.07%
ARAT full	Wrist *y*-axis	0.17	0.22	0.27	0.25	0.37	21.62%	45.95%

[a] Percentage value of (B-stage 6 – B-stage 3) / Normal
[b] Percentage value of B-stage 3 / Normal

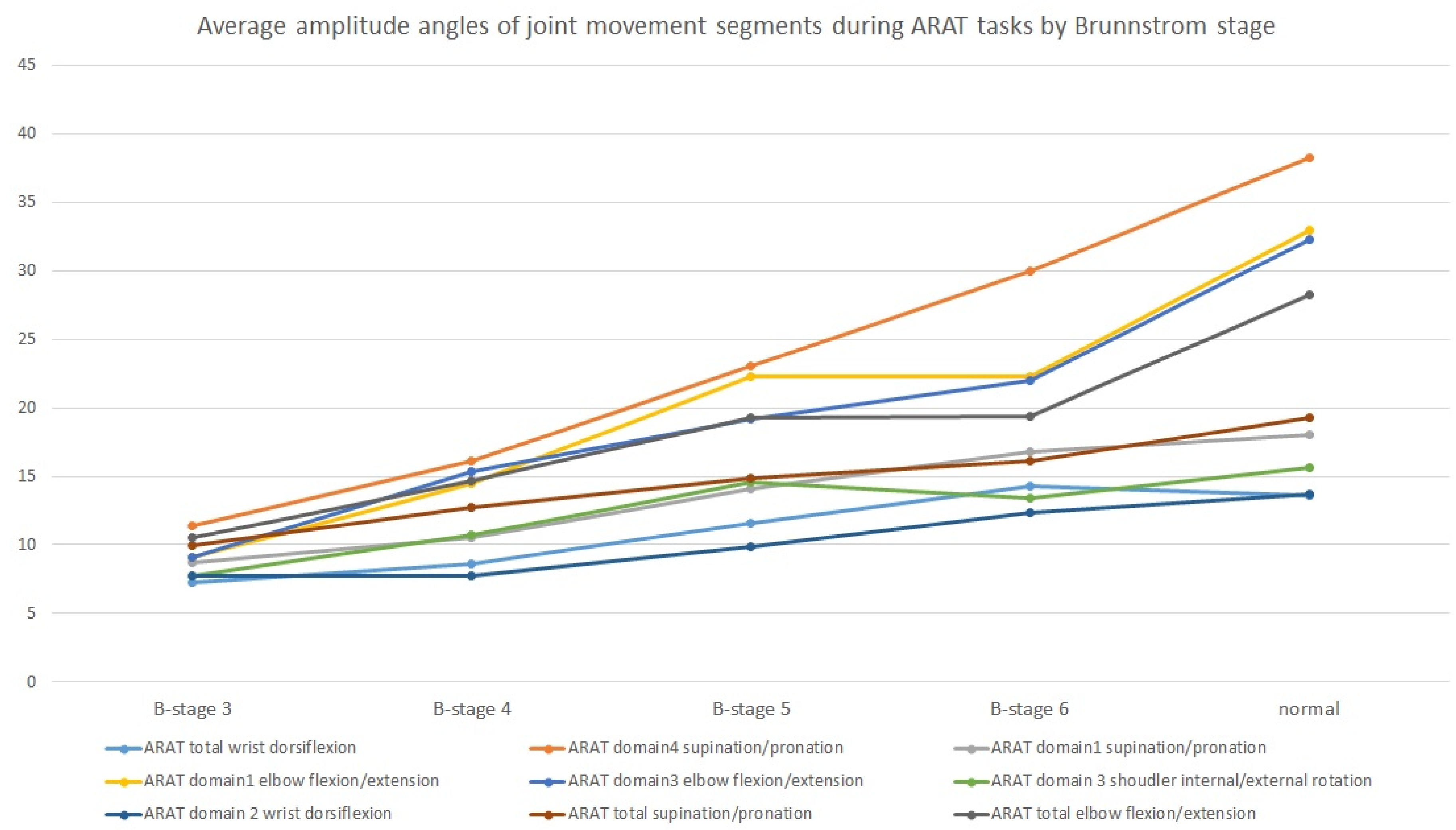

Fig. 13. Average amplitude angles of joint movement segments during ARAT tasks by Brunnstrom stage are shown.

3.4 Preliminary Usability Test for Image-processing Based Hand Rehabilitation Robot

For overall satisfaction regarding the robot's ability to help stroke rehabilitation, physiatrists replied with the highest score (6.0 ± 0.9), followed by robot engineers (5.4 ± 0.5), therapists (4.6 ± 0.5), and patients (4.0 ± 1.2). Participants found the device interesting (5.7 ± 1.2), motivating (5.8 ± 0.9), and also having less possibility of injury or safety issues (6.1 ± 1.1). However, the level of difficulty (4.8 ± 1.9), expectance of improvement (5.1 ± 1.0), and comfort (4.9 ± 1.3) were relatively low. Detailed response results are shown in Fig. 14.

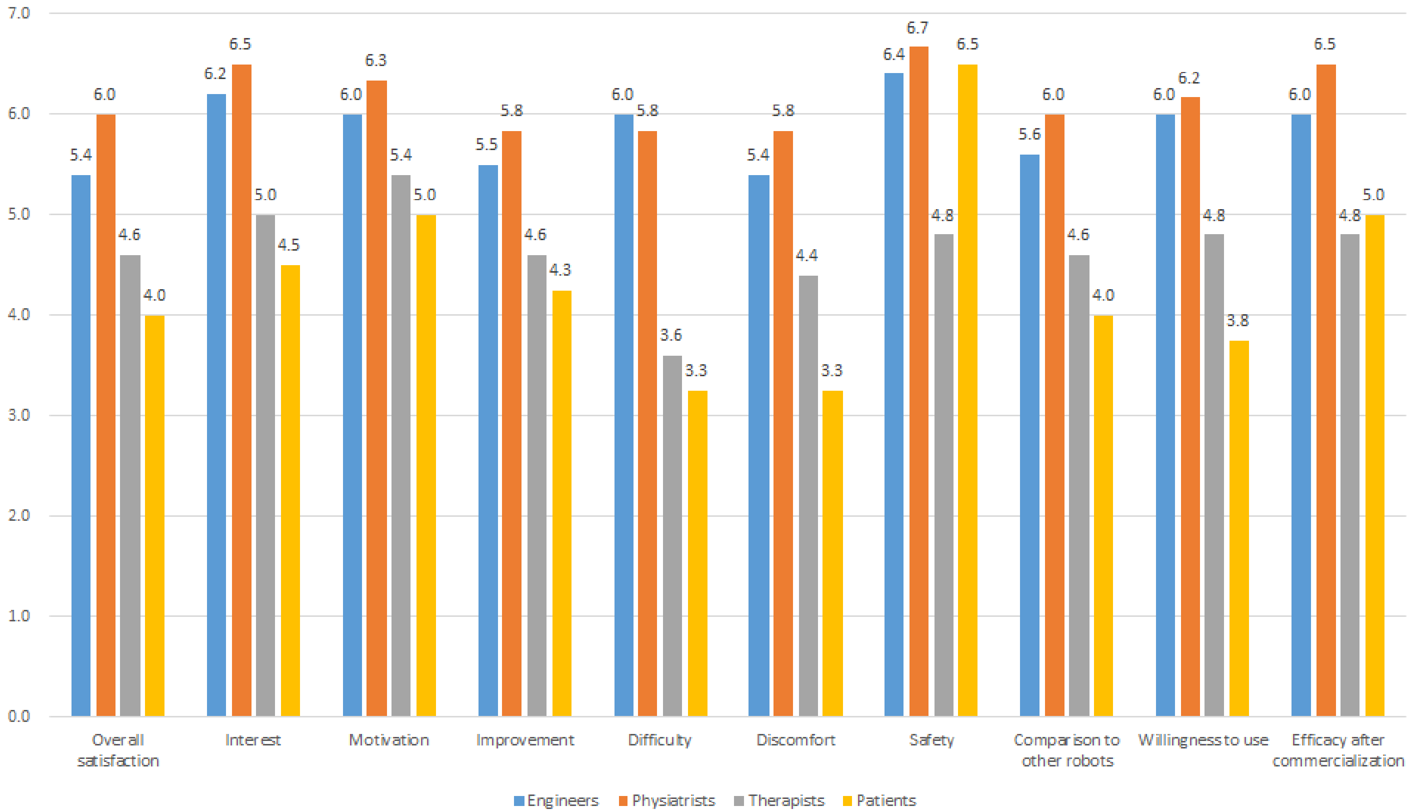

Fig. 14. Usability test results for an image-processing based hand rehabilitation robot are shown for 4 categories of respondents. The scores are in a 7-point scale with 7 points representing most satisfactory or safe and 0 points for least satisfactory or unsafe.

4. DISCUSSION

4.1. Demand survey for potential users of robots

Highly rated ADLs should be taken into consideration when designing a BMI controlled robot for rehabilitation or ADL assistance, especially if the robot is going to be simple and portable with selected functions. There have been several previous studies on the functional priorities of patients with specific diseases [34-36]. However, to our knowledge, this is the first study to assess the needs of potential users by the type of robot and laterality of the impairment.

Chronic stroke patients with hemiplegia generally rated bimanual ADLs as the most necessary functions for both types of robot. Nearly 80% of stroke patients who have hemiplegia become able to perform most one-handed ADLs and several two-handed ADLs according to the degree of hemiparesis. All 24 stroke patients in this study also had hemiplegia and were able to use the unaffected arm properly. Therefore, ADLs that require both upper extremities were rated as the most necessary functions that a robot should provide. Handling foods, dressing, and hairdressing are functions that require both hands for its performance. However, the most important and necessary function for an exoskeleton in stroke patients was self-exercise of upper extremity, getting a higher score than bimanual functions. The mean duration since stroke onset was about 110 months in our study population. Many of these chronic stroke patients had moderate to severe spasticity in major upper extremity joints. The rate of spasticity after stroke is reported to be approximately 30 to 60 percent [37]. During a short interview after the survey, participants stated that they would like to have an upper extremity robot that could help them exercise at home, in addition to the therapies that they receive in rehabilitation centers. It seems that personal robots with exercise functions would help patients continue their exercises at home to enhance functional recovery and decrease spasticity, which would increase their ADL performance level. It has also been reported in many studies that a decrease in spasticity leads to better ADL performance and a lower burden for care [14, 38]. In addition, several studies showed greater functional improvement when robotic rehabilitation therapy was provided for up to 5 hours a day for 12 weeks compared to that of a lesser treatment dose, which indicates that continuing exercise with robots throughout the day would result in better outcomes [39-41].

In BIG, eating and hairdressing as well as cleaning, handling foods, dressing, and moving close items were ADLs that received relatively high scores for the necessity of external robotic arms. For exoskeletons, dressing, toilet use, transfer, wheelchair control, moving close items, and handling foods showed high demand. A previous study on amyotrophic lateral sclerosis (ALS) patients also showed that "using the bathroom" was among the highest priorities for a BMI in addition to communication and controlling motorized wheelchairs [35]. Self-exercise of the upper extremity also received the high scores in both importance and necessity. Self-exercise function of the robot in this survey was defined as the ability of the exoskeleton, with or without any kind of user-robot interaction, to provide passive ROM or active ROM exercises, in the manner that the user may select and control the moving joint and the extent of ROM. This result is in agreement with previous studies, which found that patients with spinal cord injury replied that restoration of walking and arm and hand functions along with bladder and bowel control were all high priorities, and that they would like to use a BMI to control functional electrical stimulation in order to enhance functional recovery [34, 42]. Patients in this study wanted to control the exoskeleton with a BMI to perform their upper extremity exercises.

Fig. 1 and 2 shows the importance and necessity of each type of robot in both impairment subgroups. The ADLs in the *x*-axis are given in the order of level of dependency, from highly dependent to near independent. It is easily noticed that the importance and necessity is not in proportion with dependency. The results in these figures show ADLs that were considered important, but not actually necessary for everyday lives. In regards to both robot types, UIG did not need to do phone calls or use computers with the robot. This may be because they have an intact arm, and are older in age compared to patients in other disease categories. For exoskeletons, stroke patients did not require wheelchair control or transfer assistance, as they could manage it with their intact arm or using a cane.

In general, the ratings for importance and necessity for the exoskeleton were higher than those for the external robotic arm as shown in Fig. 3. UIG showed significantly higher necessity for exoskeleton compared to external robotic arm in washing face, brushing teeth, and eating. In BIG, dressing, moving close items, purse, switch control, computer, eating, phone calls, writing, and smartphone showed higher necessity for exoskeletons. While bimanual ADLs such as hairdressing, handling foods and dressing showed high scores for both types of robot, patients with unilateral impairment demonstrated higher demands for using exoskeletons for grooming related activities, whereas subjects with bilateral impairments tended to give higher scores to activities necessary for social functioning and interactions.

4.2. Biomechanical Response of Exoskeleton to Spasticity

The main results of the spasticity study were resistance torque values for robotic elbow and wrist joints during actuation for patients with spastic arms. The mean torque values for various levels of spasticity in the elbow flexor ranged from 3.68 to 8.25 Nm, with statistically significant differences between the grades. Considering that the maximal resistance torque in a healthy subject was 1.77 Nm and the calculated torque required for maintaining isokinetic rotation of the forearm and the hand (not the robot) from the elbow joint against gravity based on the human database (Size Korea, http://sizekorea.kats.go.kr) is approximately 0.97 Nm and 1.14 Nm, respectively, the amount of resistance produced by spasticity during the isokinetic actuation is considerable [43]. Park et al. [44] showed that the resistance torque measured during physical examination was approximately 3 Nm in MAS grade 1+ and between 4 and 6 Nm in MAS grades 2 and 3 for individual subjects. In their study, passive movement conducted by an examiner was paused during the moment of the catch, and was continued after the resistance was decreased. In the present study, the robotic joint maintained isokinetic movement without giving the spastic joint sufficient time for the resistance to be decreased, resulting in higher resistance values than those of the previous study. This resistance pattern is consistent with other studies, in that the resistance torque kept increasing beyond the point of maximal stiffness with continuation of the movement, as observed in various situations such as passive movement by an examiner [33], both slow and fast isokinetic movements [45, 46], and even in active and non-isokinetic cases [47]. In addition, the mean torques measured at the 2/3 ROM point during extension of the elbow joint were 4.05 and 4.64 Nm, respectively, for intermediate and high spasticity, which is similar to the results of a previous study [44]. Considering that the maximal value measured during the study was 21.28 Nm, it appears that maximum output torque range buffer for the spastic elbow flexor component need not to exceed 21.28 Nm. However, it does need to be modified according to the target population or desired function of the robot. The required torque for each joint to actuate the robot would include the torque needed to rotate the robot frame distal to the joint (τ_{robot}), human arm mass distal to the joint (τ_{arm}), and torque to overcome spasticity ($\tau_{spasticity}$), which can be calculated approximately as shown in Equation 3:

$$\tau_{total} = \tau_{\text{robot frame}} + \tau_{arm} + \tau_{spasticity}$$

$$= r_{COM_{robot\ frame}} \times F_{robot} + r_{COM_{arm}} \times F_{arm} + \tau_{spasticity} \qquad (3)$$

where COM represents center of mass (COM), *r* is distance from the joint axis to the COM, and F is force. Parameters $r_{COMrobot\ frame}$ and r_{COMarm} represents the distance from the joint axis to the center of mass of the robot frame and human arm, respectively, and F_{robot} and F_{arm} refers to the force needed to move the robot frame and human arm to perform intended movement, respectively.

In most chronic stroke patients, spasticity for the elbow joint usually appears in the elbow flexor muscles; however, in some patients, spasticity exists on the opposite side, or even on both sides [17]. Seven patients in this study also showed elbow extensor spasticity. The number of subjects and trials for elbow extensor spasticity was relatively small, but results suggested that resistance torques for low spasticity and intermediate to high spasticity have significant differences. Maximal resistance torques were in a similar range to results for elbow flexor spasticity. The data reported by Starsky et al. [46] showed a similar range during the flexion of an elbow joint with a spastic elbow extensor, but detailed data were not provided. It seems that similar specifications may be applied for the flexion direction of the elbow joint.

For the wrist flexors, the maximal resistance torque values showed statistically significant differences between low and intermediate to high grades of spasticity, and the differences of the values between the spasticity levels were relatively small compared to those for the elbow. However, the resistance created by the wrist flexor spasticity was nearly 10 times that of the healthy subject. Despite the fact that spasticity of the wrist flexors has been a critical problem in many stroke patients, it seems that mechanical assessment of the wrist flexors has been rare because the resistance torque value is relatively small owing to the fact that it is a distal and smaller joint. Malhotra et al. [48] evaluated the stiffness of wrist flexors by levels of spasticity, which showed no significant differences between spasticity levels; however, the maximal resistance torque values were not presented. Many neurorehabilitation robots in wearable form with shoulder joints do not have a wrist joint [49, 50], while large robots for use in treatment already possess motors in their wrist joints that can simply overcome these amounts of resistance [51, 52]. However, in the design of neurorehabilitation robots for portable use in daily living, wrist flexor spasticity must be considered.

As spasticity is commonly defined as “velocity dependent” [13], analysis regarding angular velocity of the robot joint was performed. In each MAS grades of elbow flexor spasticity, the maximum resistance torque showed a tendency to increase with increasing velocity; however, statistical analysis did not support this tendency. Seth et al. [53] reported that the robot’s velocity had a significant effect on robot resistance for the elbow joint; however, their study was performed on healthy subjects and patients with MAS grade 0, which may not be applicable to higher spasticity grades. However, the number of subjects and trials in the present study may have been insufficient to ensure sufficient statistical power. The CPP presented by %ROM demonstrated a significant decreasing tendency with higher velocity, which means that the catch occurred more quickly at higher velocities. This is consistent with clinical experiences and a study by Wu et al. [54] performed on patients with cerebral palsy using a manual spasticity evaluator. They found that the catch angle occurred later with increasing velocity because the examiner manually extended the elbow more quickly and with greater strength despite the increased resistance and early activated spastic muscle EMG signal, resulting in a greater catch angle. As mentioned earlier, it is known that spasticity consists of two major components: reflexive and tissue components [13]. The reflexive component is strongly associated with the catch phenomenon, whereas the tissue component is related to stiffness throughout the passive movement of the joint. The velocity-dependent feature of spasticity stems from the reflexive component, and therefore, the catch angle may be affected by the angular velocity; however, the maximal resistance appears at the end of the ROM range and this would not be affected by the velocity, but rather the level of spasticity. For practical utilization of a portable and wearable neurorehabilitation robot, it is important that the robot weight is made as light as possible. Potential users with impaired limbs require robots of even lighter weight than those healthy people may wear. However, robots must have sufficient power and capabilities as well as an appropriate control algorithm to help the user perform the desired movement and activities. Robots should be able to deal with spasticity in an appropriate and safe manner with a certain amount of output torque. In addition to setting an adequate torque range for spasticity induced resistance, other methods may be applied to create a light-weight exoskeleton. One possible method is to apply a pause during movement when the resistance exceeds the threshold of the motor. At the end of the ROM where the robot is actuated against spasticity, the activity of the spastic muscle remains for a certain amount of time with an exponential decay of the resistance torque (Fig. 2). Using this phenomenon, which is equivalent to the decrease of resistance during the catch while the examiner is still applying force to the joint, the robot can still be applied to a spastic limb, even with a low-torque output motor without resulting in excessive loading. A precise sensing and control system would be necessary for this type of system.

4.3. Kinematic Characteristics of Upper Extremity in Healthy Subjects and Stroke Patients

The purpose of this study was to provide clinically relevant information regarding workspace and major joint angle range while performing essential ADLs or important movements. By identifying these factors, it is possible to limit the extent of exoskeleton movements and therefore modify the design of the robot so that it can move within the designated workspace with relatively more simple structure. In this study we evaluated the ROM and workspace during performing the ARAT tasks, one of the common functional evaluation tool in the clinics, because it is well known to significantly correlate with the patients' functional status or recovery state [55-57]. ARAT consists of 4 domains: domain 1 and domain 3 tasks consists of grasping and pinching various size of objects such as wooden blocks or marbles and then moving them to top of the wooden box by reaching movement. Domain 2 mainly involves moving items on a table focusing on grip function, and domain 4 items are gross movement tasks that require lifting the arm to the head or face [58].

Validation of the IMU-based motion analysis system used in this study showed that the accuracy and reliability of the sensors themselves are very high regarding angles. However, in the form of upper body and extremity wearable multi-sensor system, it is impossible to move a single joint alone, but all joints systemically move in 3-dimension including body trunk and contralateral upper extremity. Intra-subject and inter-subject covariance was calculated for forearm supination / pronation and elbow flexion / extension to evaluate the system reliability regarding gyrosensor derived angular values and the range was acceptable considering that the reaching tasks were not identical in terms of posture and the target point of reaching was not exactly determined. For the position data derived from the accelerometers, we compared calculated data in y and z direction with the estimated real moving distance measured by a ruler. The calculated distance data was similar to that of the measured data, and variability was also acceptable. Also, the calculated workspace and ROM during ARAT were similar between the two extremities with no significant difference (Table 2). This may also support the reliability of the system derived parameter values. While it is difficult to say that it provides a completely accurate measure, but it seems reasonable to consider this system as providing consistent and meaningful data.

The workspace of right and left hand was mostly similar, since the ARAT repeat the same tasks with both hands alternatively. The slight difference between both sides would be probably due to the difference in posture and orientation by limb dominance. During the ADL tasks, the workspace of the dominant hand, which was right hand in all subjects, was significantly larger than the non-dominant side by up to nearly 20cm for all directions. In the view of stroke rehabilitation, most of the patients demonstrate hemiplegia up to over 80% [59], which means that the intact limb should be able to perform all normal functions. Patients with hemiplegia would use their intact hand as their dominant hand, therefore, in some occasions the exoskeleton may only need to cover smaller workspace than the dominant side.

The ROM of major upper extremity joints during essential daily activities are presented in Table 2. Forearm supination / pronation and elbow flexion / extension showed the highest values for the dominant side. The ROM for forearm supination / pronation was 128.09° and 108.00° in average for right and left sides during all ADL tasks. In a study performed with reflective marker based motion capture system, the whole ROM calculated by overlapping all 95% confidential interval range during various ADL tasks was 92° [26]. Another study done with electromagnetic sensor system reported at the maximal supination angle from full pronation was 110° during glass drinking and 75° while combing hair [25]. A study by van Andel et al. [60] evaluated 4 selected ADL tasks with optic marker based system and their reported ROM for forearm supination / pronation was approximately 130°. Regarding elbow flexion / extension ROM, other studies also showed similar results. Aizawa et al. [25] reported approximately 120° to 130° of ROM during various tasks, and Gates et al. [26] showed that peak flexion angle of the elbow joint was 121° in average during drinking from a cup, which was the highest value among the evaluated tasks. Another study reported an ROM of around 140° from full extension [60]. Wrist dorsiflexion / volarflexion ROM was also similar with other studies which ranged from 90° to 130°, where in our study it was 113.70° and 110.08° for right and left side, respectively. It would be important to ensure sufficient ROM for elbow flexion / extension, forearm supination / pronation, and wrist dorsiflexion / volarflexion movements during rehabilitation, because these joint movements are essential for performing ADL tasks while recovery for distal joints are relatively slow and not sufficient for a large portion of stroke patients [61-63].

The reason for evaluating major joint angular change during reaching after grasping

/ pinching was that these actions are most basic and at the same time most important movements for performing any kind of tasks [64, 65], and most of the activities are performed within the spatial range of these actions. Pinching was performed at a slightly but significantly more abducted and flexed posture of the shoulder joint, and also showed significant difference in fine tuning movements of the wrist joint. During the reaching movement, the elbow joint was extended for nearly 70° from almost full flexed position, and the forearm was rotated toward pronation direction for more than 36° from its initial supinated posture. In the current motion capture system, forearm supination / pronation and wrist rotation are given separately, and it is reasonable to assume that the sum of both forearm and wrist rotation would correspond to gross supination / pronation angle. Therefore, it seems that the extent of forearm rotation angle during reaching movement would reach near 45° in average.

In contrast to simple pure reaching movement, reaching movement associated with performing a task may differ significantly regarding arm postures, grasping position, and orientation [66, 67]. Human motor system has high redundancy in terms of multi-degree-of-freedom control system, and while task-relevant factors are specifically controlled, task-irrelevant variables are given relatively high variability [66]. In this study, shoulder abduction / adduction and flexion / extension angles showed significantly different posture between grasping and pinching, which reflects different position of the elbow joint while performing the task. Wrist deviation and rotation angles also showed significant difference reflecting difference in fine motor posture and movements. Given the difference in posture, the main components of the reaching movement: elbow flexion / extension and forearm supination / pronation did not significantly differ between the two types of tasks. This result may be applied to the swivel angle model suggested by Li et al. [66], where the shoulder joint angles can be simplified to a swivel angle regarding the orientation and posture, and the other distal joint angles account for essential reaching movements. In regular stroke rehabilitation, proximal muscle power recovery occurs in the early stage and more sufficiently compared to distal muscles [61-63], so it would be reasonable to motivate the patient to practice taking an appropriate posture for providing the right orientation of the exoskeleton (or upper extremity) using the proximal muscles voluntarily with the help of gravity support system, while the individual robot joint actuation focus on essential distal joint movements such as elbow flexion / extension, forearm supination / pronation and wrist movements.

For the workspace during ADL tasks and logsum / time (rate of displacement) during many tasks, healthy subjects and stroke patients showed significant differences in average, meaning that the workspace of hemiplegic patients is smaller, and the movement speed is also slower. However, logsum (accumulated displacement) itself had a rather larger value in stroke patients, suggesting that there may have been more jerky movements in patients. In the current experiment, the stroke subjects were instructed to complete all tasks with assistance if necessary, because it was hypothesized that even with assistance there would be some extent of postural difference regarding the angular range of the joints between healthy subjects and stroke patients, and also between mildly and severely impaired patients.

Most of the parameters that showed significant difference between healthy subjects and stroke patients and also significant correlation with clinical measures were average amplitude of motion segments throughout the tasks. This implies that the smoothness and voluntary movement magnitude get improved throughout the recovery process of stroke, and it may serve as a useful clinical outcome measure if simply accessible. If a wearable wrist sensor with an accelerometer and gyrosensor can access some of these parameters such as forearm supination / pronation average amplitude, it may provide clinically relevant data without the difficulty of wearing a suit system or taking patients to a motion lab. There have been many investigations regarding possible parameters from wearable sensors [68], but to our knowledge, the average amplitude during movements has not been sufficiently investigated in the clinical view.

4.4 Usability Test for an Image-processing Based Hand Rehabilitation Robot

The usability test results showed high scores for interest, motivation, and safety issues, but relatively low scores for difficulty, comfort, and expectance of improvement. Because this system did not use a computer display as the main interface but instead real objects, and that this may be used at home or at the bedside, the respondents replied that these features were interesting and that the robot may help patients be motivated for the therapy. The response from the patient group showed lower scores in most of the categories except safety. The patients responded that the device was not appropriate for their stroke recovery stage; however, they also commented that the device would be very useful for the patients that are not able to move the distal upper limb. The main issues from the free comments were that the gripping was not highly secure, and that the task was limited due to the low degree of freedom. At initial design, a height adjustment system was proposed so that the robot may grasp objects at various heights; however, for the current prototype it was not applied due to the structural complexity. In the next version, the height adjustment system using a gravity compensation method is planned to be applied. Another feature of the current prototype was that the hand part was placed at the palm side of the hand, in contrast to other commercial hand exoskeletons where it is place at the dorsum of the hand. The reason for this design was to prevent injury since it is difficult to control gripping pressure. However, in this prototype, it was a problem in that it was not easy for the user to determine if the object was sufficiently grasped so that it would not fall down. The structure and position of the motors seemed to interfere with the user's workspace, which should be modified in the next step prototype. The use of pressure sensors should be considered in the next step as well. In addition, a clinical proof-of-concept study should be performed, which was not available during this study due to IRB approval and FDA clearance issues. It is necessary that the investigational device exemption (IDE) for medical robots with non-significant risk to be practically applied in Korea, to facilitate the development and the proof-of-concept clinical studies for medical robots, so that the clinically relevant robots may enter the market and be used in clinics as soon as possible, whereas clinically irrelevant robots may stop development at an earlier stage.

4.5 Optimization of Neurorehabilitation Robot Design Regarding Clinical Settings

The purpose of this thesis was to evaluate and identify clinically relevant biomedical factors, to eventually develop a practical rehabilitation exoskeleton robot. It was not possible to evaluate clinical effects of the hand rehabilitation robot due to IRB and FDA approval issues, therefore, it is necessary to discuss the estimated expected therapeutic effects of the suggested robot based on previous clinical studies, and also suggest a direction for overall design and development of the rehabilitation robots with the viewpoint of optimization.

It is reported that minimal clinically important difference (MCID) for the Fugl-Meyer (F-M) upper extremity motor score is estimated to range from 4.25 to 7.25 points [69], whereas another study suggests 9 to 10 points [70]. In a multi-center randomized controlled clinical trial using the ARMin exoskeleton, it was reported that the robotic therapy group showed a 3.4 point improvement at the end of 8-week therapy compared to the initial score, and it was approximately 0.78 points larger than the conventional therapy group [52]. In the ARMin study, the stroke patients were mostly in the chronic stage, and they had received the robotic therapy for 45 minutes per session, three times a week, over 8 weeks. The weekly treatment dose was 2.25 hours, and the total treatment dose was 18 hours of robotic therapy. From the individual study data of the Cochrane review published in 2015, the total robotic treatment dose and improvement in F-M upper extremity motor score showed linear correlation as in Equation 4, with $r^2 = 0.57$, as shown in Fig. 15 [2, 39, 40, 52, 71-73].

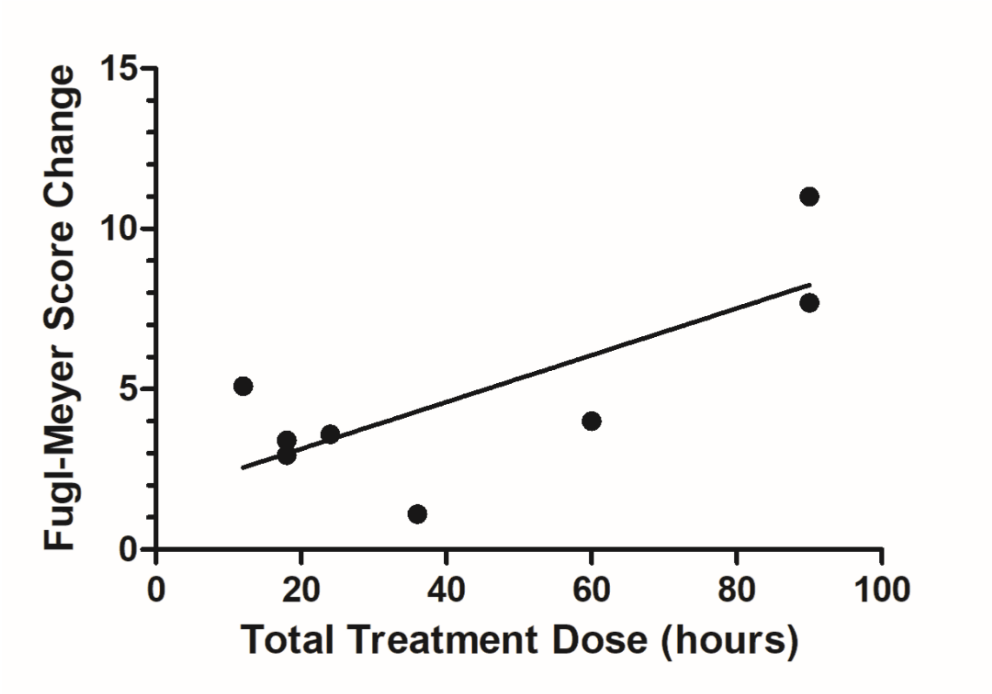

Fig. 15. Improvement in Fugl-Meyer upper extremity score after robot-assisted treatment showed linear correlation with total treatment dose.

$$\text{Fugl-Meyer Score Change (improvement)}$$

$$= \text{Total robot-assisted treatment dose (hours)} \times 0.073 + 1.680 \qquad (4)$$

In an intensive rehabilitation unit or clinic, one rehabilitation robot device can provide approximately 16 thirty-minute sessions assuming that it is run for 8 hours daily. However, for one patient, the robotic therapy should be provided at least 2 hours per day to achieve the sufficient repetition level, which an occupational therapist cannot provide to a single patient. A clinical study in Mexico showed that robot-assisted gait training for 24 two-hour sessions resulted in significant improvement in lower extremity F-M motor score compared to the control group consisting of 30-minute sessions [74]. In this case, one robot can be used by only four patients per day. Two hours per day would give 10 hours of weekly dose, and assuming linearity of correlation for the total treatment dose and the F-M motor score improvement to calculate ideally maximal expectation for improvement, it would be approximately 12 points increase of F-M upper extremity motor score after 3 months (12 weeks) of robotic therapy.

However, most of the rehabilitation robots used in earlier clinical studies did not include assistance for hand or finger movements, and therefore did not show significant improvements in F-M scoring of the hand and fingers, while they account for 14 points of the 66 points in the upper extremity (Supplement 4). Recently, there have been several clinical trials using robotic devices focusing on hand and finger recovery, with sufficient total treatment dose: 5 days a week for a duration of 3 to 8 weeks [75-78]. In these clinical studies, improvements in F-M score of distal limbs ranged from 3 to 6 points [75-78]. It is shown in various clinical studies that the improvement is generally specific to the joints targeted by the robotic therapy [79]. A recent study using InMotion^{TM} combined with task-specific training, for 90 to 100 minutes per day for 5 days a week over a 4-week period, showed an improvement of 7.7 points, where proximal F-M scores increased by 4.3 points and distal scores were improved by 3.4 points [80]. Therefore, it may be assumed that an optimized robotic therapy including hand and finger movements for a sufficient period of time would expect nearly 18-point increase in F-M upper extremity motor score, which is obviously a clinically significant improvement.

In contrast to optimization of the industrial robots, which are optimized for pre-determined specific tasks only, rehabilitation robots require flexibility of tasks. As evaluated in this study, it is necessary to determine workspace, ROM, and degree of freedom as eventual specifications of the robot, rather than specific limited tasks, although the workspace and ROM should be calculated from the desired tasks, among the top ranked survey ADLs.

To apply the concept of optimization in rehabilitation robots, it should be assessed with the viewpoint of maximizing task-specific repetition, especially to the range that conventional therapy may not achieve. In addition, it should be considered that each patient should be provided with maximal repetition as much as possible, but not just purchasing one rehabilitation robot in the clinic and utilizing it for the whole working day.

As mentioned previously, the purpose of developing a rehabilitation therapy robot is not just substituting occupational therapy or adding a 30-minute treatment session daily. Moreover, the algorithm and control method of the robot itself may not influence the brain recovery better than conventional therapy as long as the therapy consists of task-specific movements. Therefore, the optimal robot should be designed in a self-usable form with or without help from the caregiver, but without the therapist, as well as in a wearable and portable form. The weight issue should be discussed at this point. Based on our design experience considering appropriate output torque, size, and velocity, the weight of the motor and gear part together for each mechanical joint ranges from approximately 0.5 kg in distal joints to 1.0 kg in middle joints such as elbow flexion / extension, and to up to 2.0 kg for proximal joints such as shoulder flexion / extension and abduction / adduction. The hand rehabilitation robot developed in this study weighed 3.9 kg in total including the rolling bottom board (1.2 kg), and if the metal plates for support were removed, the exoskeleton weight itself was about 2.0 kg. For the patients or caregivers to freely move the robots from one place to another and install it on the table, it seems that 4 to 5 kg is the maximum tolerable weight. The KNRC self-feeding robot, which is a robot-arm type feeding assistant robot, weighed approximately 3.7 to 4.7 kg for their pre-market prototype [81]. These robots are not light enough to be lifted easily, but they are portable and movable within home settings.

Even after adequate development of a rehabilitation robot, there still exist a number of barriers for the robot to enter the market or the clinic: which may be classified into technological, behavioral, organizational, and economic barriers [82]. The device must be easily controllable for the patients and / or caregivers to let them adopt the use of the robot successfully [82], and strong clinical evidence for the efficacy of the neurorehabilitation robots should be established, since the evidence up to now is relatively weak [2]. In addition, the healthcare system should be adequately modified and also support the distribution and utilization of the robot for successful initial adoption, especially when the cost-effectiveness is not well established [82].

There was a study that calculated healthcare cost for comparison of a robot therapy group, an intensive therapy group, and a usual therapy group in the VA-ROBOTICS study using the MIT-Manus robot [72, 83]. The study showed that the intervention cost for a single session was lower for robot therapy ($140) compared to the intensive therapy ($218), and the total healthcare cost at 36 weeks showed approximately $2,000 in savings for the robotic therapy group compared to intensive therapy. However, the F-M score showed only 2.17 points difference, which may not have a clinically significant meaning.

Assuming full utilization of the robot in the hospital, 17 patients are able to use the Armeo® type robot during a week, and 4 patients can use the practical robot during a week, which is 2 hours daily per patient [74]. Assuming a rehabilitation clinic can afford to purchase one Armeo® Power ($190,000), which approximately 17 patients may use weekly, the practical robot price should be kept under $50,000 per robot to provide robotic therapy for a similar number of patients.

Summarizing this discussion section, the clinically relevant practical rehabilitation exoskeleton for treatment in a hospital should have at most 3 axes (or 2 axes + hand part) distal to the elbow, with proximal structures supported by gravity compensation, with total movable weight under 5 kg, and a final market price under $50,000, which is operable by the patient and / or the caregiver, to provide maximal task-specific repetition in the inpatient rehabilitation setting.

4.6 Limitations

This study has several limitations. For the demand survey, the number of subjects was not sufficient to generalize the needs of all upper extremity impaired persons. UIG was relatively homogeneous and representative of chronic stroke patients, however, BIG was mostly consisted of young muscular dystrophy patients and only 5 cervical spinal cord injured patients, potentially possessing limitations for generalization. However, most previous studies were performed with spinal cord injury or ALS patients. Therefore, this study may provide a reference for comparison between different disease entities. And most of the participants were not familiar with the concept of a BMI other than the explanation given to them just before the survey. There may have been some difficulties in imaging how it would be with the given technology and functions. If they had known more about BMIs and rehabilitation robots, the survey results would have been more accurate.

For the spasticity resistance study, the clinical assessment of spasticity with the MAS grading system was not clearly applicable for some subjects. As most of the volunteers were chronic stroke patients with an average of 9.7 years since stroke onset, the characteristics of their spasticity were very complex and did not typically fit to the definition of the MAS grade. For this study, two experienced physiatrists evaluated spasticity independently and there were disagreements between them concerning four subjects for the elbow and five subjects for the wrist. In those cases, the higher grade was taken for analysis. The trials were performed from a slow speed to a fast speed, in order to minimize the risk of musculoskeletal injury of the joint. However, preceding trials at the slower speeds could have decreased the spasticity temporarily, and the resistance torques for the faster speeds may have been underestimated. Ideally, randomization of the trial order in terms of angular velocity would have resulted in more accurate data. In addition, the numbers of subjects at each level of spasticity were not sufficient to generalize the results of the study

For the motion analysis, the number of subjects was relatively small to generalize the findings of motion analysis. However, the statistical analyses provided minimal requirements regarding validity and reliability. IMU-based sensors basically have its inevitable limitations, which include drift phenomenon in both position and angular values, and it would have affected the outcome measure values [84]. Also gimbal-lock phenomenon regarding especially shoulder joint angles may have occurred during data measurements [25]. In this point of view, the data may not be accurate in terms of absolute values, however, it seems that the general pattern of the data is reliable since the data are sufficiently consistent.

The hand rehabilitation robot prototype also had a number of limitations. The height adjustment system was not applied resulting in limited function of the robot. The contour of the hand part need to be more customized to the real contour of the user's hand to provide a better sense of grabbing objects. This may be solved by using 3-dimensional printers.

5. CONCLUSIONS AND FUTURE WORK

The results of this research will serve as a basis for the design and development of a practical and portable but clinically relevant neurorehabilitation exoskeleton robot. Clinical evidence should be supported for pilot developments to successfully enter the clinical market and become widely used among stroke patients.

The next step after this study would be developing a simple and portable neurorehabilitation robot by applying the biomedical factors described in this study. One suggestion could be estimating the elbow trajectory for operating in the essential workspace and making an elbow support with a constant elastic spring for gravity compensation and at the same time movable in 3-dimension within the intended trajectory area. The part distal to the elbow part may be designed by accommodating the described hand rehabilitation robot and minimizing the ROM according to this study for a smaller and lightweight design.

For optimal control of the robot, biomechanical analysis regarding joint torque during the essential movements may be necessary to provide support as needed and to avoid over-actuation of a joint. Millard et al. [85] presented an example of optimal control in lifting motion. Upper limb movement simulation using muscle-based modeling software may provide useful information [86].

Further research on user-intent driven actuation of the exoskeleton must be performed for better stimulation of neuroplasticity, using both brain signals and sensing of the volitional movements in the peripheral limb. A clinical proof-of-concept study should be performed prior to further developments to ensure the efficacy of the proposed concept.

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Supplemental Materials

Supplement 1. Survey for potential users' demand on assistive robots

**** This survey is to be performed by the examiner throughout the whole process to explain each questions and activities of daily living items, and ensure that the respondent is always aware of the rating scale.***

0. Please check your gender and age: M / F / Age: _____

1. Please check on your disease category that caused your impairment.

   1) Stroke

   2) Spinal cord injury

   3) Muscular dystrophy

   4) Motor neuron disease

   5) Peripheral nerve injury

   6) Any others: ______________________________

2. When was the onset of the impairment? Year ___________ Month ____ (____ years ago)

3. How well do you use your upper extremities?

   1) I can use both arms functionally (at least partially)

   2) I only use one arm functionally

   3) I can hardly use both arms functionally

4. Please check on your gait status.

   1) I can walk independently without any assistive tools.

   2) I can walk independently using some assistive tools.

   3) I need other person's assistance (regardless of assistive tool use)

   4) I hardly can walk despite any kind of help from others.

5. Is wheelchair your main method of moving?   Y / N

* As you have been informed during your consent, please assume that the following robots (external robotic arm and upper limb exoskeleton: shown in pictures) may be controlled perfectly according to your intent, to perform following activities of daily living tasks. Regarding each task, please reply of your **1) current dependence** on others, your ratings on **2) objective importance** of the function from the viewpoint of a developer based on your experience with severe functional impairment, and **3) subjective necessity** of the function from the viewpoint of a consumer based on your current daily activities. For the subjective necessity, please think if you would use the function if a perfect robot was provided for the specific function. **Please rate objective importance and subjective necessity for the external robotic arm and upper limb exoskeleton separately.**

*Ratings**

5-Likert scale	1	2	3	4	5
Dependence	Totally dependent	Mostly dependent	Half dependent	Mostly dependent	Totally dependent
Importance	Unimportant	Of little importance	Moderately important	Important	Very important
Necessity	Not necessary	Of little necessity	Moderately necessary	Necessary	Highly necessary

ADL items		External Robotic Arm					Upper Limb Exoskeleton				
Washing face	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Brushing teeth (including squeezing toothpaste)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Hairdressing	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Dressing (putting shirts on and off)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Eating	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Handling foods (i.e. peeling a banana, opening a bottle cap, etc.)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Cleaning (cleaning one’s desk)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Moving close items	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Smartphone (using a smartphone or a tablet)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Computer (using a computer: keyboard and mouse)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Phone calls (dialing and receiving a phone call)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Writing	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5

Switch control	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Purse (putting in and taking out bills and cards from a purse/wallet)	Dependency	1	2	3	4	5					
	Importance	1	2	3	4	5	1	2	3	4	5
	Necessity	1	2	3	4	5	1	2	3	4	5
Transfer (assisting bed to chair, chair to standing, etc.)	Dependency	1	2	3	4	5					
	Importance						1	2	3	4	5
	Necessity						1	2	3	4	5
Toilet use	Dependency	1	2	3	4	5					
	Importance						1	2	3	4	5
	Necessity						1	2	3	4	5
Self-exercise (of the upper extremity)	Dependency	1	2	3	4	5					
	Importance						1	2	3	4	5
	Necessity						1	2	3	4	5
Wheelchair control (both manual and electric)	Dependency	1	2	3	4	5					
	Importance						1	2	3	4	5
	Necessity						1	2	3	4	5

Supplement 2. Brunnstrom Stage [64]

1) Brunnstrom stage for arm

Stage	Arm
1	Flaccidity-no voluntary movement
2	Synergies developing-flexion usually develops before extension (may be a weak associated reaction or voluntary contraction with or without joint motion); spasticity developing
3	Synergies performed voluntarily Increased spasticity which may become marked
4	Some movements deviating from synergy a. Hand behind body b. Arm to forward-horizontal position c. Pronation-supination with elbow flexed to 90°; spasticity decreasing
5	Independence from the basic synergies a. Arm to side-horizontal position b. Arm forward and overhead c. Pronation-supination with elbow full extended; spasticity waning
6	Isolated joint movements freely performed with near normal coordination Spasticity minimal

2) Brunnstrom stage for hand

Stage	Hand
1	Flaccidity
2	Little or no active finger flexion
3	Mass grasp or hook grasp
	No voluntary finger extension or release
4	Lateral prehension with release by thumb movement
	Semivoluntary finger extension (small range of motion)
5	Palmar prehension
	Possible cylindrical and spherical grasp (awkward)
	Voluntary mass finger extension (variable range of motion)
6	All types of prehension (improved skill)
	Voluntary finger extension (full range of motion)
	Individual finger movements

Supplement 3. Action Research Arm Test Tasks [56]

Task	Score*		Time (sec)
	Left	**Right**	**Left/Right**
A. Grasp (grasp and reach out to top of the shelf)			
1. Block, 10 cm^3	0 1 2 3	0 1 2 3	
2. Block, 2.5 cm^3	0 1 2 3	0 1 2 3	
3. Block, 5 cm^3	0 1 2 3	0 1 2 3	
4. Block, 7.5 cm^3	0 1 2 3	0 1 2 3	
5. Cricket ball	0 1 2 3	0 1 2 3	
6. Sharpening stone	0 1 2 3	0 1 2 3	
Subtest score	/18	/18	
B. Grip			
7. Pour water from glass to glass	0 1 2 3	0 1 2 3	
8. Tube 2.25 cm	0 1 2 3	0 1 2 3	
9. Tube 1 cm	0 1 2 3	0 1 2 3	
10. Put washer over a bolt	0 1 2 3	0 1 2 3	
Subtest score	/12	/12	
C. Pinch (pinch and reach out to top of the shelf)			
11. Ball 6 mm 3rd finger and thumb	0 1 2 3	0 1 2 3	
12. Marble 1st finger and thumb	0 1 2 3	0 1 2 3	
13. Ball 6 mm 2nd finger and thumb	0 1 2 3	0 1 2 3	
14. Ball 6 mm 1st finger and thumb	0 1 2 3	0 1 2 3	
15. Marble 3rd finger and thumb	0 1 2 3	0 1 2 3	
16. Marble 2nd finger and thumb	0 1 2 3	0 1 2 3	
Subtest score	/18	/18	
D. Gross Movements			
17. Hand behind head	0 1 2 3	0 1 2 3	
18. Hand on top of head	0 1 2 3	0 1 2 3	
19. Hand to mouth	0 1 2 3	0 1 2 3	
Subtest score	/9	/9	
Total score	**/57**	**/57**	

* Scoring: 0 = unable to complete any part of the task within 60 sec; 1 = task partially performed within 60 sec; 2 = task completed but with great difficulty or abnormally long time; 3 = task completed normally within 5 sec

Supplement 4. Fugl-Meyer Assessment Scale for Upper Extremity Motor Function [59]

Upper Extremity				**Score (2/(1)/0)**
A.	Shoulder/Elbow/Forearm			
	I.	Reflex activity		
		Flexors	Biceps, Finger flexors	
		Extensors	Triceps	
	II.	a. Flexor synergy		
		Shouler	Retraction	
			Elevation	
			Abduction	
			Outward rotation	
		Elbow	Flexion	
		Forearm	Supination	
		b. Extensor synergy		
		Shoulder	Adduction/inward rotation	
		Elbow	Extension	
		Forearm	Pronation	
	III.	Hand to lumbar spine		
		Hand	Move to lumbar spine	
		Shoulder	Flexion 0˚- 90˚	
		Elbow 90˚	Pronation/supination	
	IV.	Shoulder	Abduction 0˚- 90˚	
			Flexion 90˚- 180˚	
		Elbow 0˚	Pronation/supination	
	V.	Normal reflex activity		
Total – Shoulder/Elbow/Forearm				/36
B.	Wrist			
		Elbow 90˚	Wrist stability	
		Elbow 90˚	Wrist flexion/extension	
		Elbow 0˚	Wrist stability	
		Elbow 0˚	Wrist flexion/extension	
		Circumduction		
Total - Wrist				/10
C.	Hand			
		Fingers mass flexion		
		Fingers mass extension		
		Grasp a		
		Grasp b		
		Grasp c		
		Grasp d		
		Grasp e		
Total – Hand				/14
D.	Coordination/Speed			
		Tremor		
		Dysmetria		
		Speed		
Total – Coordination/Speed				/6
Total Motor Score for the Upper Extremity				/66

Appendix

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Author: Hyung Seok Nam

Publication: Neural Systems and Rehabilitation Engineering, IEEE Transactions on

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국문초록

실용적인 상지 외골격 재활 로봇 설계 및 개발을 위한 임상 적합성 기반 의공학적 인자

서울대학교 의과대학 의학과
의공학교실 남형석

서론: 지난 수년간 재활 로봇은 빠른 속도로 발전되어 다양한 기능을 갖추고 실제 임상에 적용되고 있는 사례도 많다. 그러나 로봇의 본래 목적인 과제 지향적 반복적 움직임을 최대한 제공하여 기존의 치료 방식에 비해 유의하게 기능 회복과 뇌가소성을 촉진시킨 사례는 거의 없다고 알려져 있다. 본 연구의 목적은 단순한 인체공학적인 접근을 넘어, 실용적이면서도 간단한 외골격 뇌신경재활 로봇을 개발하기 위한 의공학적 인자를 정립하는 데에 있다.

방법: 우선 뇌졸중 및 신경근육질환으로 인한 상지 마비 환자 48 명을 대상으로 기술 수요 조사를 시행하였다. 로봇을 실제 사용하게 될 예비 사용자 대상의 설문 조사를 통해 로봇을 개발하는 실질적인 목적을

규명하고자 하였다. 중추신경계 손상 및 질환으로 인한 마비 환자는 특징적으로 경직 증상을 보이는 경우가 많다. 이에 경직 증상을 보이는 만성 뇌졸중 환자 20 명을 대상으로 하여, 경직이 있을 경우 외골격 로봇이 받게 되는 저항을 정량적으로 측정하였다. 이를 통해 외골격 로봇 주요 관절의 모터에 필요한 최소한의 토크 출력을 제시하고자 하였다. 건강한 자원자 10 명을 대상으로는 관성 측정 장치 기반 동작 분석 시스템을 이용하여 액션 리서치 암 테스트 및 상위 수요 일상 생활 동작 수행 시 손의 작업 공간 및 주요 관절의 가동 범위를 측정하였다. 같은 방법으로 브룬스트롬 3 단계에서 6 단계에 걸쳐 분포하는 뇌졸중 환자 9 명을 모집하여 편마비측 상지에서 보이는 동작 특성에 대해 분석하였다. 사용자 의도에 따른 로봇 제어를 위해 영상 처리 기반 제어 알고리즘을 제안하였고, 이를 이용한 시제품을 제작하여 의사, 공학자, 치료사 및 뇌졸중 환자를 대상으로 사용성 평가를 시행하였다.

결과: 예비 사용자 수요 조사 결과, 음식 다루기, 옷입기, 가까운 물건 옮기기 등이 외골격 및 외부 로봇팔 모두에 가장 필요한 동작으로 나타났다. 뇌졸중 환자의 경우 특히 로봇을 이용하여 자가 운동을 할 수 있기를 희망하였다. 팔꿈치 굴곡 및 손목 굴곡 경직으로 인한 로봇 저항은 경직이 낮은 그룹 (수정 애쉬워스 척도 0, 1)에서 각각 3.68 ± 2.42, 4.23 ± 1.75 Nm 이었고, 중간 경직 그룹 (1+)에서는 5.94 ± 2.55, 5.68 ± 1.96 Nm, 높은 경직 그룹 (2, 3)에서는 8.25 ± 3.35, 5.44 ± 2.02

Nm으로 나타났으며, 중간 경직 그룹과 높은 경직 그룹 간의 손목 굴곡 경직 차이를 제외하고는 모든 그룹간 경직 저항 토크가 유의한 차이를 보였다. 건강한 자원자에서 우세손의 작업 공간은 액션 리서치 암 테스트의 경우 0.53 m (좌우축) × 0.92 m (앞뒤축) × 0.89 m (상하축) 이었으며, 일상생활동작 수행 시에는 0.71 m × 0.70 m × 0.86 m 이었다. 일상생활동작 시에는 우세손의 작업 범위가 비우세손에 비해 유의하게 크게 나타났다. 액션 리서치 암 테스트 시 우세팔의 관절 가동 범위는 주관절 굴곡-신전 109.15 ± 18.82°, 전완 회내-회외 105.23 ± 15.38°, 견관절 내회전-외회전 91.99 ± 20.98°, 손목관절 굴곡-신전 82.90 ± 22.52° 였으며, 일상생활동작 시에는 각각 순서대로 120.61 ± 23.64°, 128.09 ± 22.04°, 111.56 ± 31.88°, 그리고 113.70 ± 18.26°로 나타났다. 건강인과 뇌졸중 환자 간에 유의한 차이를 보이면서 동시에 뇌졸중 회복 정도에 따른 유의한 상관 관계를 보인 동작 분석 관련 변수 중, 액션 리서치 암 테스트 4단계 검사 동작 시 전완 회내-회외의 평균 동작 크기가 중증 기능 장애 시 건강한 사람에 비해 가장 많이 저하되었으며 (29.83%), 경증 기능 장애와의 차이도 가장 크게 나타났다 (48.46%). 영상 처리를 통한 사용자 의도 파악 손재활 로봇 시제품 사용성 평가 결과 흥미성 (5.7 ± 1.2), 동기 유발 가능성 (5.8 ± 0.9) 및 안전성 (6.1 ± 1.1)에서는 좋은 평가를 받았으나 난이도 (4.8 ± 1.9), 편안함 (4.9 ± 1.3) 등에서는 상대적으로 낮은 점수를 받았다.

결론: 본 연구 결과를 바탕으로 임상적으로 유용하면서 동시에 간단하고 병상 또는 집에 휴대할 수 있는 외골격 뇌신경재활 로봇을 제작하는 데에 도움이 될 것으로 기대한다.

주요어: 뇌신경재활 로봇; 뇌졸중; 상지; 의공학적 인자; 외골격 로봇

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