Official Title:	**Is the Rehabilitation Robotic a Safe and Effective Choice for Stroke Patients?**

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Introduction

The number of incident strokes, prevalent stroke survivors, disability-adjusted life-years (DALYs) lost due to stroke, and stroke-related deaths is increasing in the word (1). Stroke is the most common cause of complex disability in Taiwan (2). After the acute phase of stroke, many patients are left with impairment of upper-limb movement (hemiparesis) because of the hand weakness and abnormal contractions. Motor recovery of the hand is the slowest and most difficult, leading to limited hand activities and occupational disability. Therefore, facilitating motor recovery of hand after stroke is crucial in stroke rehabilitation.

The mechanisms of recovery after stroke are multifactorial and the effect of rehabilitation programs is complex (3). Activity-dependent neural plasticity of the cortical maps adjacent to the lesion probably occurs, particularly during the acute period after stroke (4). In order to stimulate such plasticity, many new rehabilitation methods, including rehabilitation robots, have been developed according to the principles of motor learning (5). Robotic systems can provide repetitive, reproducible, interactive forms of physical therapy that can be quantified (6). The advantages of using robots in neuromotor rehabilitation includes favoring attention and reducing the effort of the patient during training (7), boosting motivation and adherence to treatment (8), as well as help in multi-sensory and sensorimotor integration (9). Some results are very promising, showing that robot-assisted therapy is safe and well tolerated and that it has a positive impact on muscle strength and function in the paretic arm (10-12). However, the quality of these evidence is still controversial and inconclusive. The effectiveness of robotic over conventional therapy is arguable and the best therapy strategy is still not clear. Furthermore, there is little understanding of the neurological mechanisms involved in functional recovery of the hand (13). In this study, the investigators hypothesize that the

robot based assistance would outperform conventional therapy during the subacute stage of stroke.

Study objective

1. To establish whether robot assisted therapy provides any additional motor recovery for the hand when administered during the subacute stage in a Chinese adult population diagnosed with stroke.
2. To evaluate the feasibility and efficacy of robot-assisted hand rehabilitation in improving arm function abilities in subacute hemiplegic patients.

Outcome evaluation

(A) Fugl-Meyer assessment (FMA) scale (14): The investigators used FMA scale to evaluate sensorimotor recovery of patients with particular attention to the hand and wrist section (maximum score=24) to assess the functional capacity of the affected hand.

(B) The Motricity Index (MI) scale (15): The investigators used MI scale to assess the motor recovery rate of the patients (100% = maximum MI).

(C) Functional Independence Measure scale (FIM) (16): The investigators used FIM to assess the degree of independence and need-of-assistance in basic activities of daily living at enrolment and at the end of the study. FIM is an 18-item ordinal scale rated from 1 (total dependence) to 7 (total independence) per item; 13 items of this scale, the sub-scale Motor- FIM, were used to evaluate motor disability.

(D) Visual analogue scale (VAS) (17): The investigators used VAS (0 extremely simple- 10 extremely difficult) to access the feasibility of the device in terms of the number of patients who completed the program; side effects (the physiotherapist was required to report any adverse events occurring during the study in regard to the use of the robotic hand); and the level of operator difficulty for the physiotherapist in managing the device.

Intervention

The experimental group will receive 30 minutes robotic training sessions, 3 times per week for a total of 30 sessions supervised by a research assistant. The robotic hand is a passive exoskeleton system, which was developed by the laboratory of the Department of Biomedical Engineering in Chung-Yuan Christian University. Participants will be placed in the robot and practice common hand tasks involving single finger range of motion exercise, grasping, and pinching objects. Immediately following this robot training, these subjects will receive schedule (1-hour sessions, 3 times/week, 30 total sessions) of conventional

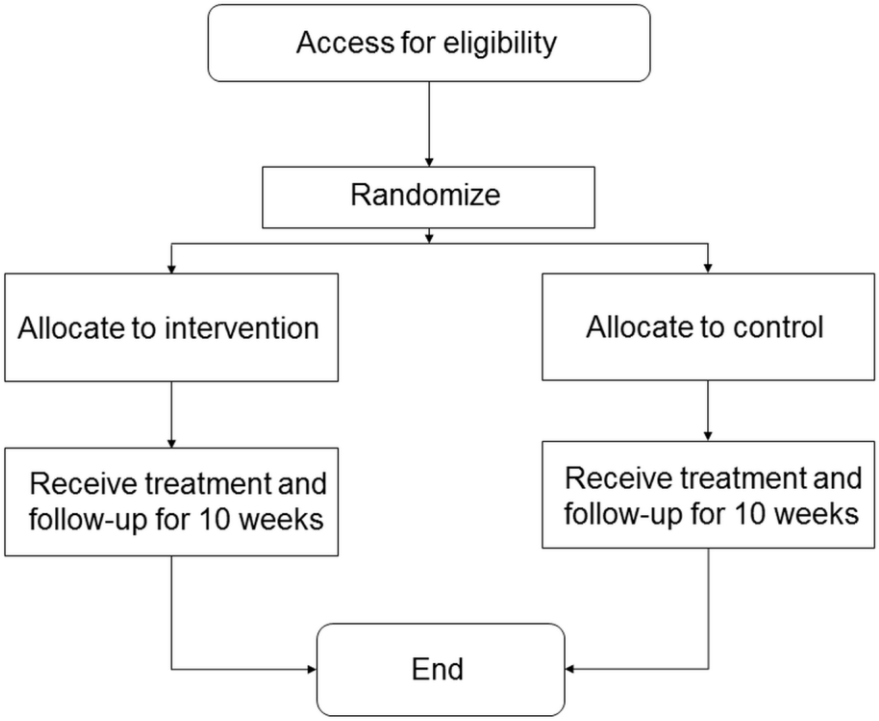
therapy from an occupational therapist. An occupational therapist will provide one-on-one individualized programs focused on arm and hand function. Treatment will include function-oriented specific tasks, such as reach, grasp, transport and release of various objects between different targets.

In conventional therapy group, participants will receive an one-hour of one-on-one treatment from an occupational therapist, focusing on arm and hand function. Treatment will include function-oriented specific tasks, such as reach, grasp, transport and release of various objects between different targets. The treatment schedule will parallel that given to the experimental group (1-hour sessions, 3 times/week, 30 total sessions). All patients would undergo basic rehabilitation following the guidelines (18) according to the Bobath concept (19).

Statistical analysis

Statistical analysis was performed with SPSS 22.0 (IBM, USA). The normality of variables was assessed using the Kolmogorov–Smirnov test. Confirmation of matching in initial conditions in co-factors among control and intervention groups was made using Wilcoxon Rank Sum (WRS) tests with continuity correction or Fisher's exact test (FET), depending on the nature of the variables (categorical, interval or ratio). For each group, improvements in dexterity performance were evaluated using Wilcoxon Sign Rank (WSR) test with continuity correction for paired samples. Comparative differences between control and intervention in these improvements were established using Wilcoxon Rank Sum tests with continuity correction. Cohen's d effect sizes and the 95% confidence interval for the contrast (continuous data) were further calculated. In all cases, statistical significance threshold was kept at $\alpha = 5\%$.

Steps of experiment



Study participants

(A) Inclusion criteria: Adult patients (>20 years old) with a diagnosis of hemorrhagic or ischemic stroke and who experience severe upper extremity hemiparesis.

(B) Exclusion criteria: severe pain and instability in the wrist of the affected arm, severe cognitive impairment, aphasia, hemispatial neglect, apraxia and joint contractures greater than 20 degrees in the affected hand.

(C) The number of estimated enrollment is thirty-six stroke patients (18 in intervention group and 18 in control control).

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