

Game-based Robotic Training for Upper Limb Function after Stroke

by

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Thesis submitted in fulfilment of the requirements for the degree of

Master by Research, Physiotherapy

under the supervision of

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Supervisor Declaration

This is to certify that the thesis entitled “**Game-based Robotic Training for Upper Limb Function after Stroke**” submitted by **Esminio Lacaden Rivera II** in fulfilment of the requirements for the degree of Master by Research (Physiotherapy) is in form ready for examination.

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Student Declaration

I, Esminio Lacaden Rivera II, declare that this thesis is submitted in fulfilment of the requirements for the award of Master by Research (Physiotherapy), in the Graduate School of Health at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

Name: Esminio Lacaden Rivera II

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Thesis Abstract

Game-based robotic training (GBRT) can assist clinicians to provide high-dosage and high-repetition training to individuals with motor dysfunction after stroke. It has been used in clinical settings to improve upper limb (UL) function despite insufficient evidence to support its benefits. Therefore, the aim of this thesis was to explore the effectiveness of GBRT and the perceptions of people with stroke and their family members (or carers) after 10 sessions of GBRT to provide insights on the possible barriers and facilitators of this novel rehabilitation tool. Two studies were conducted: 1) a systematic review that compared the effectiveness of GBRT to conventional therapy (CT) in improving UL function; and 2) a mixed-method study that gathered qualitative and quantitative data on the perspectives, experiences, and satisfaction of end-users after GBRT.

The systematic review compared the effects of GBRT to CT and the effects of GBRT in combination with CT to CT alone on UL function, independence (primary outcomes), quality of life and impairments such as hypertonia, muscle strength and range of motion (secondary outcomes). We performed a meta-analysis to pool the results of the trials and subgroup analysis to investigate if the type of robot and chronicity of stroke could influence the primary outcomes.

The second study in this thesis explored the experiences, perceptions, and satisfaction of participants with stroke and their family members or carers after 10 sessions of an individualized GBRT program targeted to treat impairments to the hand, wrist, elbow, and shoulder. We also present pre-post preliminary data on the potential changes in UL function and quality of life after GBRT. Participants experiences and opinions about GBRT were collected using semi-structured interviews and their satisfaction with the devices employed during the training was measured using a Likert-scale survey developed by the research team. The training constituted 10 one-hour sessions delivered over a three-week period. Observations and perceptions of family members or carers were collected using an online survey via Redcap to provide insights on satisfaction with the intervention, potential observed changes in UL utilization during day-to-day activities and mental outlook of the participants with stroke.

Twelve participants with stroke with an average time since stroke of 66.9 months and eight carers had completed the study. The findings in this thesis showed that GBRT was not superior to CT in improving function, independence or reducing impairments to the UL after a stroke. When applied in combination with CT, GBRT was significantly better than CT alone in improving UL function, however the magnitude of the effect was small and potentially not clinically meaningful. Furthermore, the majority of the studies included in the systematic review had moderate to high risk of bias, which compromises the generalization of the findings.

Besides the lack of evidence to support the benefits of GBRT over CT, in the second study of this thesis, participants with stroke and their family members/carers expressed high levels of satisfaction with the treatment and acknowledged that GBRT provided high volume training in an enjoyable and motivating environment. They also reported perceived benefits in motor function and felt more confident to use the affected UL during activities of daily living after the training, which was confirmed by their family members/carers. The changes in function and reduction of impairments reported by the participants were contrasted by the pre-post outcome measures collected in the study, that showed no significant changes after training.

In conclusion, GBRT has shown to be a well-accepted intervention among participants with stroke that could increase their motivation and engagement towards highly repetitive training, especially during the chronic phase, where adherence to treatment tends to decrease. However, its effects were not superior to CT. Clinicians should consider employing GBRT as an adjunct to CT to facilitate the promotion of high-volume training and to optimize rehabilitation outcomes. Future research with higher methodological rigor is required to provide certainty on the potential benefits of GBRT to improve UL function, independence and reduce impairments after a stroke.

Chapter 1

Introduction

1.1 Background

1.1.1 Overview on Stroke

The World Health Organization defined stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin”.¹ It can be classified according to its pathophysiology, vascular territory, and chronicity.

According to pathophysiology, there are many causes of stroke that could be mainly classified as ischemic or hemorrhagic. The word ischemic originates from two Greek words, “iskho”, which means “restrain” and “haima” which means “blood”, hence, in an ischemic stroke the blood supply to the brain is blocked or restrained by an embolus, commonly originated in the heart or by a thrombus formed within an artery of the brain.² The occlusion of the blood vessels to the brain can cause hypoxia and, if not restored, can lead to irreversible tissue damage.³ A haemorrhagic stroke is an event wherein the blood vessels in the brain rupture. Aneurysms and arteriovenous malformations are the two main causes of the weakening of the lining of the blood vessels. When they burst there is bleeding in the brain parenchyma (brain tissue), which is known as Intracerebral Haemorrhage, or in the subarachnoid space, which is known as Subarachnoid Haemorrhage.⁴

According to O’Sullivan et al (2009), stroke can be classified according to the vascular territory compromised, such as: Middle Cerebral Artery (MCA), Anterior Cerebral Artery (ACA), Internal Carotid Artery (ICA), and Posterior Cerebral Artery (PCA).⁵ The most common artery affected is the MCA, often leading to hemiplegia contralateral to the lesion, aphasia, and greater impairments to the UL than to the lower limb. A stroke to the ACA often results in hemiplegia with impairments that are more prominent in the lower limb than in the UL. When the ICA is occluded, the clinical signs present as a combination of the MCA and ACA syndromes. Finally, strokes to the PCA usually presents with hemiplegia, agnosia and hemianopsia.

Recovery after stroke is considered time-dependent. In research and clinical settings, the first 2 weeks after a stroke are defined as the acute stage, the period between 3 weeks and 6 months is considered the subacute stage and the period greater than 6 months is considered as chronic.⁶ The

acute phase of a stroke is when the most significant improvements occur due to physiological changes that result in spontaneous recovery.⁷ Recovery relatively plateaus after the third month after onset (subacute phase), with less significant spontaneous recovery occurring afterwards. After 6 months (chronic phase), spontaneous recovery usually reaches its limit and further recovery will usually depend on interventions and training received.⁸

1.1.2 Epidemiology and risk factors of stroke

A stroke is a serious health problem that causes personal and economic burden. Stroke is considered the second leading cause of disability and the third leading cause of death worldwide. In Australia, stroke is one of the main causes of disability and death.^{9, 10} According to Deloitte Access Economics (2020), a new stroke occurred at every 19 minutes in 2020 in Australia, which means that 27,428 Australians experienced a new stroke, making a total of 445,087 Australians living with a stroke in 2020.¹¹ In the same report, it was stated that in 2050, this number is projected to increase to 819,900 Australians living with a stroke. In 2020 alone, the economic cost of stroke was \$6.2 billion.

The risk factors for stroke are classified as modifiable and non-modifiable. The modifiable risk factors include hypertension, heart disease, Diabetes Mellitus, hyperlipidemia, obesity, smoking, excessive alcohol consumption, and use of oral contraceptive pills. The non-modifiable risk factors are age, sex, race and hereditariness.¹² Eighty percent of stroke is usually preventable by lifestyle modifications, including engaging in sufficient levels of physical activity, smoking cessation and a healthy diet.¹³ Lifestyle modifications can reduce blood pressure, total cholesterol, body mass index and blood glucose levels. Hypertension is the most prevalent risk factor for stroke.¹⁴ It causes damage to the structure of the blood vessels and increases the risks for formation of blood clots that could potentially block the blood vessels to the brain causing a stroke.¹⁵ Controlling blood pressure can decrease the risk of stroke occurrence.¹⁶ According to the American Heart Association, for each 10 mmHg lower systolic blood pressure, there is a decrease in the risk of stroke by a third in persons aged from 60 to 79 years.¹⁷

1.1.3 Reduction of Upper Limb Function after Stroke

The domains most affected following a stroke are physical function, social roles, and executive function (such as problem solving).⁸ A recent study showed that 80% of stroke survivors reported a reduction in UL function after the stroke, with almost 60% having permanent impairments to their UL.¹⁸ This is problematic due to the role of the UL in functionality, mobility and independence in day-to-day activities.¹⁹

UL dysfunction is caused primarily by weakness or paralysis, particularly at the initial stages post-stroke.²⁰ However, sensory loss and cognitive or perceptual deficits such as unilateral neglect also impact UL function.²⁰ In the later stages, weakness and paralysis are accompanied by secondary impairments such as spasticity, pain, and abnormal muscle synergies that often result in adaptive behaviors adopted by the individuals to move their UL. The repeated use of these adaptive behaviors may reduce UL function further.²¹ The primary and secondary impairments affecting the UL after a stroke can lead to the “Learned non-use phenomenon”, where people tend not to use the affected UL.²⁰ The learned non-use phenomenon is where the individual “can but does not use the affected UL”, which often causes further muscle weakness, disuse atrophy, muscle contractures and joint deformities.^{22, 23} It is one of the reasons why recovery is poorer in the upper limb when compared to the lower limb.^{24 25} Functional recovery in the UL requires control of a higher number of degrees of freedom in isolation and in combination when compared to the lower limbs (e.g., fingers and thumb movements to pick up small objects, while maintaining stability in the wrist, elbow and shoulder joints).²⁶ After a stroke, most people regain the ability to walk, but the majority will experience functional limitations to the UL.²⁷

Niet et al (2007), in a cross-sectional study, compared the activities of the affected UL to the non-affected UL in individuals with a chronic stroke.²⁸ In their 24 hour- monitoring period at the participants’ home or at the rehabilitation center, they found that the affected UL usage was significantly lower than the non-affected by almost three times, regardless of the severity of impairments. Another consequence of the impairments after stroke is the occurrence of an abnormal motor behaviour called “learned bad-use,” wherein a compensatory movement is used habitually to

complete tasks, which can cause inaccuracy of motor output.²⁰ Raghavan et al emphasized that if this compensatory movement is not corrected, it can lead to inaccuracy of movement and later to further decline in performance.²⁰

Reduction of the functionality of the UL negatively affects overall physical function, reducing autonomy in activities of daily living (ADLs).²⁹ This was described in a longitudinal study that included 82 participants with stroke from four rehabilitation centers, where it was found that UL function, especially hand function, was directly correlated to independence in ADLs.³⁰ In another study, Yamamoto et al (2020) showed that reduced UL function affected autonomy in ADLs in 58 people with stroke. Using a retrospective cross-sectional design, they observed a strong relationship between impairments detected in the motor section of the Fugl-Meyer Assessment (FMA) and independence measured by the Functional Independence Measure (FIM). When analyzing the UL section of the FMA, they found that UL function was related to independence, particularly in tasks like grooming, bathing, dressing and stair-climbing.¹⁹ This relationship of UL function and independence in ADLs is supported by the International Classification of Functioning, Disability and Health (ICF) Framework that suggests that limitation to activity would result in limitations to being involved in an one's role in the society.³¹

Finally, the loss of UL function can also yield a lower perceived quality of life (QoL).^{32, 33} A qualitative study interviewed stroke survivors during the subacute phase and showed that they felt that their way of life has been altered due to the reduction of UL function.³⁴ Moreover, it negatively impacted their hobbies and activities, such as “creative activities”, relationships and roles in the family and society, resulting in loss of self-identity, disrupted self, and feeling of being devalued and useless. Morris et al (2012) also found that even in people with chronic stroke, reduced UL function negatively affected QoL.³² In their cross-sectional study of 85 people with chronic stroke, they found that UL dysfunction was negatively correlated to QoL, with poorer QoL observed in people with more severe UL dysfunction.

1.1.4 Upper Limb Function Recovery after Stroke

Motor recovery in stroke varies from person-to-person. It is dependent on the interaction of multiple factors, such as clinical factors (extent of injury, type of stroke, co-morbidities, and rehabilitation therapy), sociodemographic factors (age, gender, race, socioeconomic status), and genetic factors.³⁵ The model proposed by Buma et al (2013) has tried to explain how cortical and plastic changes contribute to recovery following stroke.³⁶ In this model, neuroplasticity and cortical reorganization are a result of internal and external stimuli, leading to skill reacquisition through repair, and compensation mechanisms in the brain.

Neuroplasticity relies on two mechanisms: namely learning-dependent and non-learning dependent. The non-learning dependent mechanism explain spontaneous neurological recovery, which happens during the early stages after a stroke due to various intrinsic mechanisms, such as salvation of the ischemic penumbra, physiological and neuroanatomical reorganization, alleviation of diaschisis and reperfusion.^{37, 38} The learning-dependent mechanism suggests that plasticity occurs through an input-like activities in rehabilitative therapies. This means that the damaged part of the brain and its surroundings may adapt by increasing or changing neural connections as a result of learning.³⁹

Kleim and Jones (2008) supported the idea that rehabilitation is essential to improve neuroplasticity and functional outcomes after a neurological injury.⁴⁰ They presented a list of key principles that are essential to the reorganization of the brain after injury: 1) people with stroke should actively use their affected limbs; 2) neuroplastic and behavioural changes are specific to the training being performed; 3) high repetition and high intensity are important ; 4) early intervention matters as delays in treatment increase the chances for the development of abnormal movement patterns; 5) feedback is essential to elicit neuroplasticity; 6) neuroplasticity occurs easily at a younger age; 7) learned skills could be transferred to another skill; and 8) compensatory strategies to perform skills could impair learning. One overarching theme among these factors is that stroke survivors must be actively involved in training the affected UL. Rehabilitation should provide opportunities for training that is repetitive, intensive, and salient.

Repetition has a vital role in promoting neuroplasticity and improving functional outcomes.⁴¹ Much research has been performed on the minimum number of repetitions that can induce neuroplasticity, but until now there has been no consensus. A proof-of-concept study supported the idea that high-dosage task-specific training is feasible and could result in positive changes in outcomes, using a within-subjects, repeated measures design.⁴² In this study, it was observed that when more than 300 repetitions per session (delivered in 1-hour sessions, 3 sessions per week over 6 weeks) were performed there was a significant and clinically worthwhile change in UL function measured by the Action Research Arm Test (ARAT), and this change was maintained after one-month post-intervention. An overview of the literature emphasized that repetitions of less than 100 per session will not lead to changes in the brain.⁴³ Although the evidence is still unclear about the exact number of repetitions necessary to induce neuroplasticity in humans, the common message is that highly repetitive training is essential for motor recovery, as it can stimulate neuroplasticity that is responsible for reacquiring skills after stroke.⁴⁴

Feedback also has a significant role in stroke rehabilitation, particularly external feedback.⁴⁵ There are two types of external feedback 1) Knowledge of Results and 2) Knowledge of Performance. Knowledge of Results or explicit feedback informs the individual about the “correctness, exactness, success or failure” of the task outcome. For example, an unpleasant tone is activated when a patient failed to reach a target. Meanwhile, knowledge of performance/implicit feedback is a cue given to the patient about his/her movement execution.⁴⁶ For example, the therapist pushes down the trunk due to excessive lateral trunk flexion when practicing overhead reaching activities. Feedback is necessary as it will not just provide cues for a successful performance of the task, but it will also provide cues to determine if the movement needed for the task is correctly executed or not.⁴⁴

1.1.5 Interventions to improve Upper Limb Function

Interventions to improve UL function are focused on the reacquisition of skills that have been lost due to the injury and are based on the principles of neuroplasticity. From 1997 to 2017 there has been an increase in the number of published Clinical Practice Guidelines (CPG) for stroke

rehabilitation, with more than 300 CPGs being identified in 2017.⁴⁷ The Clinical Practice Guidelines (CPGs) were developed to pool and assess the effectiveness and safety of various existing interventions and are informed by systematic reviews, randomized controlled trials (RCT) and expert opinions with the goal of improving patient care.⁴⁸

According to the various CPGs, such as those from the American Heart Association/American Stroke Association, Canadian Stroke Best Practice Recommendation and Clinical Practice Guidelines for Stroke Management by the Stroke Foundation Australia, Constraint-induced Movement Therapy (CIMT) is highly recommended as the “gold standard” intervention for recovery of UL function.⁴⁹⁻⁵² CIMT is a high-intensive, high-dosage intervention, where the unaffected UL is constrained to force the use of the affected UL during task-specific actions. According to Kwakkel et al (2015), there are three components to a CIMT protocol: 1) intensive, the graded practice of the affected UL for 6 hours a day for 2 weeks; 2) unaffected UL is contained in a mitt to promote the use of the affected UL during 90% of total awake hours; and 3) utilization of adherence-enhancing behavioural methods to transfer learned skills in a clinical setting to a real-world setting.⁵³

There is sufficient evidence to support the use of CIMT after stroke, particularly among people in the sub-acute and chronic phase of stroke, from various systematic reviews and RCTs that showed significant improvements in UL function. However, CIMT has limitations.⁵⁴⁻⁵⁶ A systematic review presented various barriers of CIMT.⁵⁷ Firstly, CIMT requires high volumes of training, which can limit its feasibility due to the time and costs involved. Moreover, adherence tends to be a barrier as people with stroke often do not tolerate the intensity nor are motivated to use the constraint gloves in their daily lives. Due to this reason, the modified version was introduced to reduce the intensity from the original 6 or more hours of therapy.⁵⁸ Lastly, CIMT has strict selection criteria. To be eligible, individuals need to present with at least 10 degrees of active wrist extension and thumb abduction/ extension, have at least 10 degrees of extension in at least 2 additional digits, and be able to repeat these movements 3 times per minute. This excludes many people with stroke with severe UL impairments. The National Stroke Guideline strongly recommends a modified approach to CIMT

that involves 2 hours of active training and 6 hours of restraint of the unaffected arm daily for 2 weeks.⁵² However, even the application of the modified version is problematic. An exploratory RCT with 23 participants with stroke revealed that the 6-hour restraining of the unaffected UL was unachievable. The mean wearing time was only 2.7 hours a day.⁵⁹ Moreover, the modified version of CIMT still requires participants to have partial active extension of the wrist and fingers, which could still exclude a significant number of people with severe UL dysfunction after stroke.⁵³

Another recommendation for UL recovery from various CPGs is task-specific training.⁵⁰⁻⁵² The principle behind task-specific training is that an improvement of action is achieved by practicing that action. Task-specific training has 3 key elements: 1) high-repetition; 2) challenges the patients' abilities; and 3) activities need to be functional and goal-oriented.⁵⁰ Task-specific training has been shown to improve UL function.⁶⁰ However, a pragmatic observational study has reported that people with stroke only truly received task-specific training for less than half of the training sessions and achieved an average repetition of only 32, which is suboptimal to elicit neuroplastic changes to the brain.^{61, 62} This could mean that currently stroke rehabilitation using CTs would not suffice to induce neuroplasticity.

1.1.6 Robotics Therapy in Stroke Rehabilitation

Industry 4.0 or the fourth industrial revolution pertains to the era where new technologies, such as robots, were recognized to have an extensive capability in manufacturing service and communications.⁶³ Since then, these technologies had helped workers from various fields to increase productivity and efficiency.⁶⁴ In 1985, the first surgical robot, called PUMA, was used to perform a brain biopsy.⁶⁵ Since then, robotics utilization in health has increased in all areas, including rehabilitation, forming a new field called Rehabilitation Robotics due to an increasing demand for more efficient and precise rehabilitation strategies.⁶⁶ Robotics can be used in stroke rehabilitation to help clinicians provide intensity and repetitive training to stimulate the brain and improve functional outcomes.

Most studies in rehabilitation robotics use the mechanical design to classify the therapeutic robotic devices in - End-effector (EE) and Exoskeleton (EXO).⁶⁷ EXO is a device that mirrors the

structure of the limb to be trained (Figure 1.1). Joints in the limb, where movement occurs have a corresponding segment in the EXO device. Given its mechanical design, EXOs allows for independent, concurrent, and precise practice of movements during training. EEs usually has a simpler design when compared to EXOs. The only attachment of the device to the user is the most distal aspect of the limb under training (Figure 1.2). Given the differences in the mechanical design, researchers had tried to investigate if the type of robot could affect patient outcomes. Lee et al (2020) directly compared EXO and EE in a randomised clinical trial (RCT) among participants with moderate-to-severe UL impairments from a stroke.⁶⁸ They observed that EE was better for improving UL function and participation, however, caution is warranted when interpreting their results, since they reported that the number of repetitions received per session by the EE group was greater than in the EXO group.



Figure 1. 2 Example of an exoskeleton-based device (ArmeoSpring™)



Figure 1. 1 Example of an end-effector-based device (MIT- MANUSTM™)

Robotic training is a task-specific training that can be highly repetitive, challenging, functional and goal-oriented.⁶⁹⁻⁷¹ The Technology-supported Task-Oriented Arm Training (T-TOAT) method was developed to guide clinicians and researchers to implement task-specific principles when using technology devices such as robotics.⁷² In an RCT that applied T-TOAT principles, a robotic device was used during the part-practice training of functional components.⁷³ For example, the practice of drinking from a cup was broken down into small parts: reach out for the

cup, grasp the cup, lift cup, bring cup to mouth, empty cup in mouth, and place cup back on the table. Finally, after employing robotics to train every component of the task, the whole-task of drinking from a cup was practiced. During the practice of each component, challenge and repetitions were provided. T-TOAT was then compared to a control group that received a similar protocol, but without the robotic component. The results showed no significant differences between the two groups in UL function, but there was a significant difference in quality of life measured using the SF-36, particularly in physical health subsection, indicating a better mental outlook of participants that joined the robotic-assisted training. Moreover, the within group difference suggested that those participants who received T-TOAT improved UL function.

Another advantage of robotic training is that it allows high volume of training with a high number of repetitions achieved in a short period of time.⁴³ An observational study showed that robotic training for the UL could provide an average up to 851 movements over an average of 42 minutes.⁷⁴ An RCT that investigated the effectiveness of robot-assisted training demonstrated that robotic training achieved on average a total number of repetitions per session of 1344, while intensive CT achieved on average 650 repetitions per session.⁷⁵ In this study, the authors showed that the group with higher repetitions (i.e., the group that underwent robotic training) yielded a significant difference (mean difference 5.95, 95% CI 0.49 to 11.40) when compared to the intensive CT group that received a lower repetition (mean difference -3.19 95% CI -8.08 to 1.69). The change in score (5.95) indicates that this change could be clinically worthwhile, with an MCID of 5.9.⁷⁶ Despite the significant and clinically worthwhile change in ADLs, in the current study, there were no significant differences in UL function between the robotic group and the intensive CT group. This could have occurred due to some methodological issues in the study such as the small sample size, and heterogeneity of the participants. However, despite these methodological limitations, sub-group analysis revealed that there was a significant difference in the UL function between the robotic group (mean difference: 2.29 95% CI 0.85 to 3.72) and the intensive conventional group (mean difference: 0.43 95% CI -1.00 to 1.86) in participants with severe UL impairment. This finding is important because patients with severe arm impairments are typically difficult to treat, due to limited treatment options. The front-line treatment for patients with arm weakness (CIMT), cannot be used

by patients with significant weakness in the fingers and wrist and another option would be welcomed.⁵⁷.

A systematic review revealed that robotic training was superior to UL CT for the outcomes of UL function and ADLs.⁷⁷ In a multicentre RCT that compared robotic training and Enhanced Upper Extremity Therapy to improve UL function and independence after stroke, it was noted that the change in the robotic group was greater than the minimal clinically important difference of the UL Fugl-Meyer Assessment (6.98 points, 95% CI 5.55 to 8.42).⁷⁸ This could indicate that the effect of robotic training on UL function is clinically worthwhile.

1.1.7 Game-based Robotic Therapy in Stroke Rehabilitation

It is known that adherence to training is key to rehabilitation success after stroke.⁷⁹ However, an observational study revealed that adherence to training was low in patients with chronic stroke.⁸⁰ The study found that the adherence of 98 patients with stroke peaked at 6-weeks post-stroke with an index of 59.9% indicating a medium-level adherence. This adherence index decreased to less than 50% after the 16th week post-stroke, indicating a low-level adherence. A cross-sectional study reported that one of the reasons for participants not adhering to rehabilitation exercises was that “exercise is boring”. Strategies are then needed to make the training fun and motivating.

Gamification is one of the strategies identified to make a training engaging, fun and motivating. It has the potential to optimize the effects of robotic training. One common strategy is adding a gaming component to robotic training, named game-based robotic therapy (GBRT).⁸¹ The gamification of robotic training integrates games to robotics to provide external feedback to the patient.⁸² Moreover, gamification can be motivating and fun, thus leading to potentially more repetitions and greater adherence to training.

In GBRT, the feedback is in the form of games that provide visual and auditory stimuli that could lead to an increased activation of the sensorimotor cortex of the brain, contributing to motor recovery.⁴⁴ Virtual reality (VR) has been widely used in stroke rehabilitation to gamify therapy interventions. VR is defined as the “use of interactive simulations created with computer hardware

and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events.⁸³ Given this feature, clinicians started to use VR to provide high-repetitive and high-intensive training that is motivating and engaging. A systematic review that investigated the effectiveness of VR has shown that patients with chronic stroke had an improvement in their UL function with a moderate effect size (0.4) after VR training.⁸⁴ Bao et al (2013) showed that using Kinect-based VR training (total of 15 1-hour sessions) increased the sensorimotor cortex activation in participants with stroke and resulted in statistically significant and clinically important improvements to UL function.⁸⁵ According to a systematic review, there were two reasons why gaming can improve training with a robotic device.⁸⁶ Firstly, games can further increase the enthusiasm of patients to use a robotic device since they can personalize their rehabilitation based on their interests and preferences. Secondly, games can make robotic training fun, enjoyable and interesting, which motivates users to continue training and perform more repetitions.

There are several RCTs that investigated the effectiveness of GBRT for UL function, independence and quality of life, but to date, none have investigated the effectiveness of GBRT compared to CT in a systematic review using a meta-analysis. Furthermore, to our knowledge, there are no studies that investigated and integrated the perspective of users and family members/carers towards the utilization of GBRT for UL training after stroke. There is a growing interest from clinicians and people with stroke in undertaking GBRT and many clinics already offer this type of treatment to their clients, even without a strong evidence-based support.⁸⁷ Hence, research exploring the effectiveness and users' perceptions is important to provide evidence-based recommendations on the use of GBRT and an indication of the barriers and facilitators of this novel intervention.

1.2 Overall thesis aims

Despite limited evidence, GBRT is being implemented in current practice; therefore, the overall aim of this thesis was to investigate the potential effectiveness of GBRT and explore the perceptions and experiences of users towards GBRT using Tyromotion ® devices.

1.2.1 Aims specific to studies

To achieve our overall thesis aim, two studies were performed, and their aims are described below.

Study 1: Comparing the effectiveness of Game-based Robotic Training and Conventional Therapy for Upper Limb Dysfunction in People with Stroke: A Systematic Review

Primary aim: To investigate the effectiveness of GBRT when compared to CT for UL function and independence.

Secondary aim: To investigate the effectiveness of GBRT when compared to CT for quality of life and UL impairments including muscle strength, hypertonia, and range of motion (ROM).

Study 2: Game-based Robotics Training for Upper Limb function after Stroke: A mixed-methods study.

Primary aim: To explore the perceptions, opinions, and satisfaction of participants with stroke following 10 sessions of GBRT using Tyromotion ® devices.

Secondary aim: To explore the perception and opinions of carers/family members about the experiences and changes in UL function of participants with stroke after GBRT using Tyromotion ® devices.

Tertiary aim: To perform preliminary assessments of changes in UL function and Quality of Life in participants with stroke after undergoing GBRT using Tyromotion ® devices.

Chapter 2

Comparing Effectiveness of Game-based Robotic Training and Conventional Therapy for Upper Limb Dysfunction in People with Stroke: A Systematic Review

Abstract

Introduction: Following a brain injury such as stroke, exercise training is effective, although in high intensities and dosages. Providing high-intensity and high-dosage training can be difficult. Robotics have been proposed as a solution for people with stroke to perform high-dosage training with minimal supervision. To optimise the effect of robotic training and increase the adherence, gamification was introduced. Hence, this systematic review investigates the effectiveness of game-based robotic training (GBRT) compared to conventional therapy (CT) to improve upper limb (UL) function and independence.

Methods: A systematic review and meta-analysis of (randomized) clinical trials, that compared the effectiveness of GBRT and CT to improve UL dysfunction after stroke was performed. We conducted searches from inception to March 2019 on PubMed, Embase, Medline, Cochrane Library, Pedro, Web of Science, CINAHL, and Scopus. Two independent reviewers performed screening, study selection, data extraction and assessed risk of bias (using Cochrane Risk of Bias tool version 2). A meta-analysis was conducted using the random effects model and the certainty of the evidence was assessed using the GRADE approach.

Results: We included 49 studies in the review and 45 in the meta-analysis. We found no differences between GBRT alone and CT for functional performance (SMD=0.02, 95% CI -0.18, 0.23) with moderate quality of evidence and independence (SMD= 0.18, 95%CI -0.05 to 0.40) with high quality of evidence. There was also no difference between GBRT+CT versus CT alone for independence (SMD 0.22, 95%CI -0.04 to 0.47) with low quality of evidence. For UL function, a significant difference in favour of GBRT+CT was found (SMD 0.23 95% CI 0.11 to 0.34) with moderate quality of evidence.

Conclusion: GBRT was not superior to CT in improving UL function or independence. When combined to CT, GBRT was not superior to CT for independence but was as significantly better for improving UL function. However, the effect size was small with relatively narrow 95% CI, which may not be clinically worthwhile.

2.1 Introduction

Stroke is one of the most disabling and most costly diseases worldwide.^{88 89} In Australia, approximately 445,087 people are living with a stroke with an estimated health system expenditure of \$6.2 billion in 2020. By 2050, it is projected that there will be 819,900 Australians living with stroke.¹¹ Reduction of upper limb (UL) function is a commonly reported problem in stroke survivors, and most (~60%) will live with reduced UL function 6-month post stroke.⁹⁰ UL impairment leads to an overall reduction of physical function, independence, and quality of life (QoL).^{18, 29}

Rehabilitation is the process of promoting, maintaining, and sustaining motor recovery.⁹¹ Neuroplasticity is responsible for sensorimotor recovery and is the target of many rehabilitation interventions after stroke.⁹² There are several treatment strategies that can induce neuroplasticity, but the performance of high dosage training (high-repetition and high-frequency) is essential.⁹³ To date, the most effective intervention tailored to promote the recovery of UL function is constraint-induced movement therapy (CIMT), which has been highly recommended due to strong evidence in improving UL function.⁹⁴ However, CIMT requires a large number of hours to prepare and deliver, especially in the initial phases of implementation, and the selection criteria is rather restrictive, as it excludes stroke survivors with severe impairments.^{53, 95}

In contrast, a therapy robot can offer high dosage exercise, accurate monitoring of patient's progress, adaptable levels for stroke severity, and potentially allow for reduction of therapist supervision during the training session.⁹⁶ Rehabilitation robotic devices can be classified as End-effectors (EEs) and exoskeletons (EXOs), according to their difference in mechanical design. In EE devices, the patient is connected to the robot at one distal end, while in EXO devices, patients are connected to the robot at multiple joints.⁶⁸ Robotic therapy, without considering the game component, has shown promising results in assisting stroke survivors to improve their UL function.⁹⁷ Often patients are satisfied with the treatment when undergoing training using a robotic device.⁹⁸

Game-based technologies in rehabilitation integrate games with rehabilitative exercises/training to provide challenge and external feedback to the patient.⁸² There are several game

devices that have been used in stroke rehabilitation, such as video games (Wii games and XaviX games) that have shown to improve UL function, range of motion and independence.⁹⁹ Game-based interfaces may motivate and encourage a patient to adhere to high-dosage training.

The Australian Stroke Management Guideline has a weak recommendation on the use of technology-based interventions, such as robotic and game-based therapy to treat the UL after a stroke due to the lack of strong evidence to support it.⁵² Despite this, there is a growing interest by clinicians and people with stroke in accessing technology-based interventions for rehabilitation, which has resulted in an increase in its utilization in both clinical practice and research in recent years.¹⁰⁰ Another advancement in rehabilitation is to combine the two interventions, termed Game-based Robotic Training (GBRT). GBRT has features of both robot therapy and game-based therapy, which could increase the potential of motor recovery through neural plasticity and neuromuscular adaptations. Many new rehabilitation technologies are combining both robotics and gaming and are being tested in randomized controlled trials (RCT).¹⁰¹⁻¹⁰⁴

To our knowledge, no systematic review has investigated the effectiveness of GBRT for treating UL dysfunction after stroke, and it is unknown whether GBRT works best as a stand-alone therapy or when used in combination with CT. Therefore, in this systematic review, we aim to explore the effectiveness of GBRT, as stand-alone training or in addition with CT, compared to CT for the UL function and independence of people after a stroke. Secondly, we aim to evaluate the effectiveness of GBRT, as stand-alone training or in addition with CT, compared to CT on strength, range of motion (ROM), spasticity/hypertonia and quality of life (QoL).

2.2 Methods

This is a systematic review with meta-analysis. The protocol has been registered in PROSPERO (CRD42019125744) and the review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline.¹⁰⁵

2.2.1 Identification of Studies

The searches were conducted on PubMed, Embase, Medline, Cochrane Library, PEDro, Web of Science, CINAHL, and Scopus databases from inception to March 2019, without language or date restrictions. Studies published in languages other than English were interpreted by individuals able to read the language, and with experience in reading academic literature. Search terms included keywords and MESH terms for stroke, neurological rehabilitation, stroke rehabilitation, robotics, exoskeleton, end-effector, neurological assessment, physical examination, recovery of function, physical functional performance, activities of daily living, and quality of life. The search terms were developed with the advice from a librarian (see Appendix A for the full search strategy.) To ensure that recently published trials were included, an updated search was conducted from March 2019 to August 2021. Articles found from the search were imported into EndNote, where duplicates were removed, and later imported into the review management software Covidence for screening.

2.2.2 Eligibility criteria

Studies were eligible when:

1) *Design*: randomized controlled study and controlled clinical trial

2) *Participants*: adult participants (older than 18 years) with a reduction in UL function (as defined in the included trials) after stroke were included. Trials comprising a mixed population (e.g., stroke and another neurological condition) were included if at least 75% of the sample was composed by participants with a stroke. The number of participants, age, gender, type of stroke, affected UL, and time since stroke were recorded to assess the similarity of the included trials.

3) *Interventions*: To be included, trials must have utilized GBRT that is a training that used any robotic device that fits the definition of “*therapy robot can be defined as a reprogrammable and multifunctional manipulator designed to perform different rehabilitation tasks through various programmed motions*”.¹⁰⁶ Moreover, to be included, the intervention must have a gaming component. The definition used to assess if the robotic intervention also had gamification was

“Visual and/or auditory feedback was considered as a game if they were interactive, goal-oriented and had a form of a scoring system (e.g., points system)”.

The control intervention should be any form of CT which includes stand-alone active therapy regimen or active exercise (e.g. constraint-induced movement therapy, motor relearning program, neurodevelopmental techniques, mirror therapy, task-specific training, muscle strengthening, arm ergometry) or active therapy combined with passive training such as stretching.

4) *Outcome measures.* Our primary outcomes were UL function and independence; impairments including spasticity/hypertonia, ROM and muscle strength), and quality of life (QoL) were secondary outcomes. UL function was appraised using outcome measures that sought to evaluate the ability of the affected UL to perform activities that involve various functional movements like reaching, prehension, and various tasks like opening a jar, turning a door using a key and picking up small objects.¹⁰⁷ Independence was appraised using tools that evaluated the level of assistance required to carry out activities of daily living.

Secondary outcomes included QoL and impairments, such as UL muscle strength, ROM, and spasticity/hypertonia. QoL was assessed using generic or stroke-specific tools that measured perception of well-being in various aspects of life such as physical, emotional, mood, energy, and social roles. Muscle strength was assessed using tools that measured the ability of the muscles of the UL to cause active joint movement while gravity or any external force was present. ROM was evaluated using tools that measured active or passive available movement on a joint of the UL. Finally, spasticity/hypertonia was assessed using tools that measured the response of UL muscles in response to passive movement slowly or at speed.

Applying the selection criteria, a pair of review authors (ELR, CQO, PS, AM, ML) independently screened titles and abstracts of the retrieved records, and later screened the full texts of the articles included during the title and abstract screening stage. Disagreements were resolved through discussion with a third reviewer (CQO, ML) that did not participate in the screening stage.

2.2.3 Data extraction

Extraction of the data was performed using standardised forms and independently by a pair of reviewers (ELR, PS, ML and AM), using Covidence. Data extracted consisted of: the characteristics of the trials (authors, year, design and sample size); population (age, sex, type of stroke, time since stroke in months, UL affected); intervention received by the experimental and the comparator groups (description of each intervention, dosage, frequency and progression); description of the robotic device and games utilized; clinical outcomes and the magnitude of treatment effects in each of the trials using mean and standard deviation or median and interquartile ranges of post-intervention scores.

2.2.4 Assessment of Risk of Bias

The Cochrane Risk of Bias (RoB) tool version 2 was utilized to assess the quality and risk of bias of the included studies, which was done independently by two reviewers (ELR, AM, PS, ML, AV, CQO).¹⁰⁸ Discrepancies were discussed and disagreements were resolved by a third reviewer. The tool consists of five domains: bias arising from the randomization process, bias due to deviations from the intended intervention, bias due to missing outcome data, bias in the measurement of the outcome and bias in the selection of the reported result. Each domain has several questions, which is answerable by *yes*, *probably yes*, *probably no*, *no* and *no information*. After assessing all the domains, the tool proposes an overall risk of bias based on the judgement of each domain.

2.2.5 Analysis

A descriptive summary of the extracted data from each included trial, including information about the GBRT, was reported. In case of unclear or missing data, the corresponding author of the trial was contacted via email. If unresponsive for longer than 2 weeks, the trial was not included in the meta-analysis.

Data from trials were combined into two analyses: GBRT vs CT, and GBRT+CT vs CT. In the case of multiple outcome measures for a single outcome, the tools that were reported as the primary outcome of the trial were extracted for the analysis. If not reported, the outcome tools

validated for stroke or the tools recommend by the Academy of Neurologic Physical Therapy were extracted for the analysis. In the case of multi-arm interventions (i.e., two interventions in experimental group or control group), in either the experimental or control group, the intervention that was considered the most commonly used in practice (clinical and research) was used for analysis.¹⁰⁹

The software RevMan 5.3 was used to perform the statistical analysis, using a random effects model.¹¹⁰ The post-intervention scores for each outcome were reported as the mean difference (MD) in the case of comparable outcome measurement instruments. If this was not the case, standardised mean differences (SMD) were calculated, all with their 95% confidence intervals (95% CI). Sub-group analyses were planned for 1) time since stroke (less than 6 months, more than 6 months) and 2) type of robot (end-effector and exoskeleton). Cohen's d was used to interpret the magnitude and direction of the SMD: <0.2 was considered trivial, 0.2 to 0.5 was small effect, and 0.5 to 0.8 was moderate effect and >0.8 was large effect.¹¹¹ Moreover, the authors arbitrarily considered a SMD of >0.3 as clinically worthwhile or as the smallest worthwhile effect (SWE). In the case where data were not available in a study, results were presented descriptively.

The overall certainty of the evidence was assessed using the Grading of Recommendations Assessment Development and Evaluation (GRADE).¹¹² The certainty of the evidence started as "high" since all trials included were RCTs. The certainty of the evidence was downgraded by one level when one of the following domains were not met: 1) limitations of the study design (>25% of the participants came from studies with a high risk of bias), 2) inconsistency (statistical heterogeneity $I^2 > 40\%$) or inconsistent findings among studies (<75% of the participants presented findings in the same direction), 3) indirectness (when population, intervention and outcome measure were inapplicable), 4) imprecision of results (total number of participants across studies were <300 for each outcome) and 5) publication bias using tests for asymmetry of funnel plots (asymmetric pattern on the forest plot).¹¹³

2.3 Results

2.3.1 Search results

The electronic search strategy identified 2,938 publications. After duplicates were removed, 650 publications remained. After title and abstract screening, the full text of 128 publications were screened. Finally, 49 trials were included in the systematic review and 45 were included in the meta-analysis. Four trials did not present the data required for inclusion in a meta-analysis. Figure 2.1 demonstrates the flow of studies and the reasons for exclusion of studies.

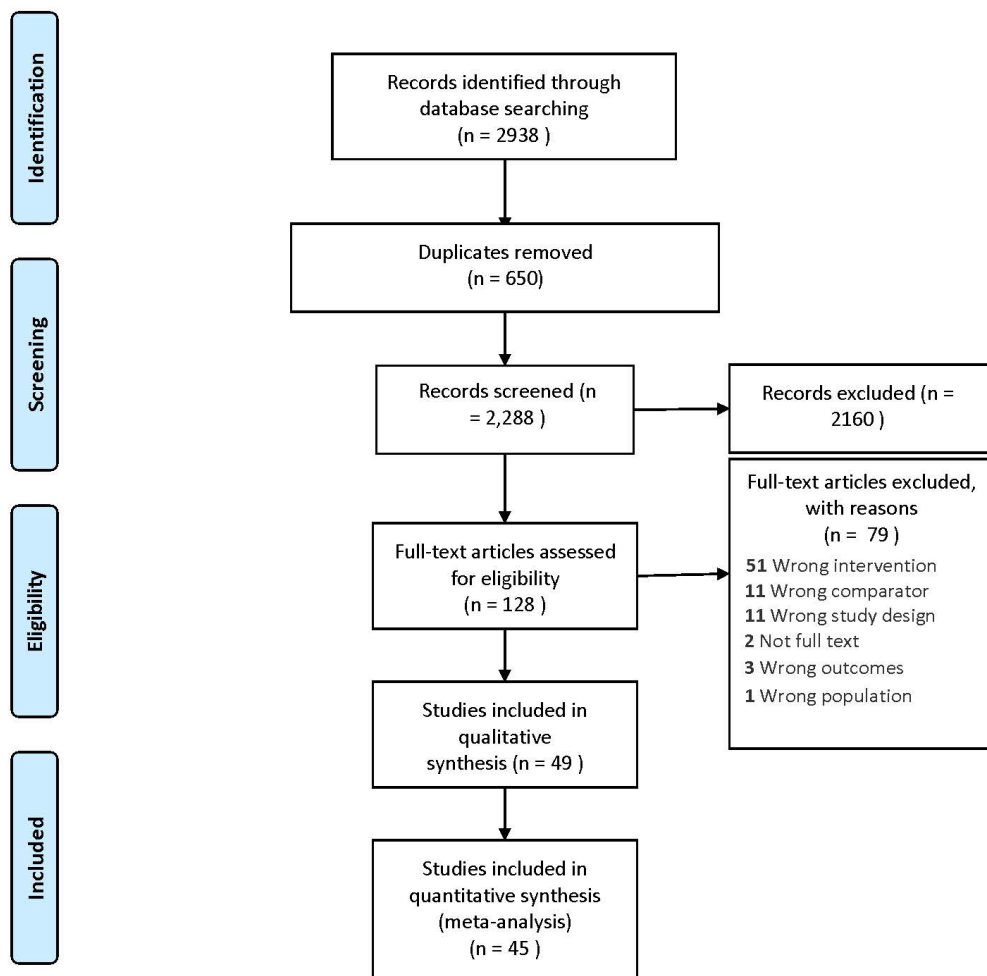


Figure 2. 1 PRISMA Flow diagram

2.3.2 Characteristics of studies

Participants: The 45 studies included a total of 2,521 participants. In 39 trials, 51% (n=1128) of participants had a stroke for at least six months and 49% (n=1069) had a stroke for less than 6 months. Six trials did not report time since stroke. Out of the 27 trials (n=1,865) that reported type of stroke, 26% (n=479) of the participants had a haemorrhagic stroke and 74% (n=1,386) had an ischemic stroke. Three trials did not report the sex of the participants, but overall, 60% (n=1,437) were males and 40% (n=946) were females (Table 2.1).

Interventions: Eighteen trials compared GBRT to CT and 27 trials compared GBRT as an additional treatment to CT, and CT alone. Among the 41 trials that reported the type of robot, 41% (n=17) utilized exoskeletons, while 59% (n=24) utilized end-effector devices. Two trials did not describe the devices used enough to be classified as either EXO or EE. Across trials, robotic training used the principles of progressive resistance training. Training usually started in a passive mode (complete assistance from the device provided) and progressed to a resisted mode (force provided against the desired movement by the device). Only 24 trials described the games used to train the UL such as tracking games, games that mimicked ADLs, and hobbies, such as golfing. Participants received GBRT training between two to ten sessions per week, from one to eight weeks, from 30 minutes to 3 hours per session, with a total training volume that ranged from 6 hours to 120 hours. The training dosage between control and intervention groups in 87% (n=39) of the included trials was equivalent (i.e., frequency of training and duration of training per session), in 11% (n=5) was different, with higher dosages being provided to the intervention group, and in 2% (n=1) could not be determined due to lack of information. CT included: passive stretching, range of motion exercises, mobilization, training of activities of daily living, electrical stimulation, hot packs, Proprioceptive Neuromuscular Facilitation (PNF, Kabat), and Neurodevelopmental Techniques (Bobath) (Table 1).

Primary Outcomes. Thirty-eight trials measured UL function using the Fugl-Meyer Assessment (FMA), Manual Function Test (MFT), Wolf Motor Function Test (WMFT), and Jebsen Hand Function Test (JHFT). The FMA was used in the meta-analysis. Twenty-three trials measured

independence employing the Functional Independence Measure (FIM) and Barthel Index (BI) or the Modified BI.

Secondary Outcomes Seventeen trials reported at least one measure of muscle strength such as the standard Medical Research Council (MRC) Manual Muscle Test (MMT), JAMAR dynamometer, and Motricity Index (MI); 18 trials measured hypertonia using the Modified Ashworth Scale (MAS), 9 trials measured ROM using goniometry and other means like using a 9-camera optoelectronic system. (QoL was assessed in 7 trials using the Stroke Impact Scale (SIS) or the 36-Item Short Form Survey (SF-36).

Table 2. 1 Characteristics of included trials

<i>Author, year (Design)</i>	<i>Participants</i>	<i>Intervention (GBRT)</i>	<i>Control intervention</i>	<i>Outcome domain and Outcome measure</i>
Aprile 2020 ¹¹⁴ (RCT)	Exp N=111; Age: 69.5±10.9; Gender (m/f): 68:43 Type of stroke (H/I): 30:81; Time since stroke: 1.58±1.35	GBRT Frequency: 5 days/week for 6 weeks Dosage 45 min/day Robot: EE Game: virtual environment by carrying out various target-oriented tasks	Control: Task-oriented exercises, sensorimotor reorganization, and spasticity inhibition Frequency: 5 days/week for 6 weeks Dosage 45 min/day	Strength MRC Hypertonia: MAS Functional performance: FMA Independence: MBI Quality of Life: SF-36
	Con N=113; Age: 68.5±11.5; Gender (m/f): 64:49 Type of stroke (H/I): 29:84; Time since stroke: 1.49±1.33			
Bartolo 2014 ¹¹⁵ (RCT)	Exp N=12; Age: 63.5±11.6; Gender (m/f): 8:4 Type of stroke (H/I): NR; Time since stroke: NR	GBRT+CT Frequency: 6 days/weeks for 2 weeks Dosage: 60 minutes/day CT and 30 minutes GBR Robot: EXO Game: Volitional tasks (e.g., cleaning a window) and goal-directed tasks (e.g., catching falling water in a mug)	Control: Bobath + Kabat's Frequency: 6 days/ weeks for 2 weeks Dosage: 90 minutes / day	Functional performance: FMA Independence: FIM
	Con N=16; Age: 51.2±7.0 9; Gender (m/f): 10:6 Type of stroke (H/I): NR; Time since stroke: NR			
Bondarenko 2016 ¹¹⁶ (RCT)	Exp N=36; Age: 52±4; Gender (m/f): 18:18 Type of stroke (H/I): NR; Time since stroke: NR	GBRT Frequency: 5 days/weeks for 3 weeks Dosage: 40 minute/session Robot: NR Game: Tennis	Control: Description NR in full details Frequency: 5 days/weeks for 3 weeks Dosage: NR	Hypertonia: MAS Range of Motion: ROM Functional performance: FMA
	Con N=16; Age: 58±5; Gender (m/f): 10:6 Type of stroke (H/I): NR; Time since stroke: NR			
Budhota 2021 ¹¹⁷ (RCT)	Exp N=21; Age: 56.3±10.4; Gender (m/f): 11:11	GBRT+CT	Control: OT mobilization and Neurodevelopmental technique	Strength: Grip Strength

	Type of stroke (H/I): 10:12; Time since stroke: NR	Frequency: 5 days/ weeks for 3 weeks	Frequency: 5 days/ weeks for 3 weeks	Functional performance: FMA
	Con N=21; Age: 54.6±10.9; Gender (m/f): 14:8 Type of stroke (H/I): 12:10; Time since stroke: NR	Dosage: 60-minute GBRT, 30-minute OT Robot: EE Game: Point-to-point reaching task	Dosage: 90 minutes	
Bustamate-Valles 2016 ¹¹⁸ (RCT)	Exp N=10; Age: 44.1±12.6; Gender (m/f): 3:7 Type of stroke (H/I): NR; Time since stroke: NR	GBRT Frequency: 3- 4x/ weeks for 6-8 weeks Dosage: 120 minute/session Robot: EE Game: Custom-made games and commercial videogames with a Logitech wheel	Control: Manual mobilizations, heat, ultrasound, therapeutic TENS, and repetitive tasks for occupational therapy Dosage: 120 minutes/session Frequency: 3- 4 sessions/ week in 6-8 weeks	Functional performance: FMA
	Con N=10; Age: 64.1±8.4; Gender (m/f): 4:6 Type of stroke (H/I): NR; Time since stroke: NR			
Byl 2013 ¹¹⁹ (RCT)	Exp N=5; Age: 54.2± 20.5; Gender (m/f): 4:1 Type of stroke (H/I): NR; Time since stroke: 122.4± 56.04	GBRT Frequency: 2x/week for 6 weeks Dosage: 90 minutes/session Robot: EXO Game: Flower, joints, paint, reach, pong, pinball, circle, and handball	Control: Task-specific training Frequency: 2x/ weeks for 6 weeks Dosage: 90 minutes/session	Range of motion: Active ROM Strength: Standard MMT Hypertonia: MAS Functional performance: FMA Quality of Life: SIS (Self-care subscale)
	Con N=5; Age: 59.3±6.8; Gender (m/f): 4:1 Type of stroke (H/I): 29:84; Time since stroke: 176.8±52.8			
Calabro 2019 ¹²⁰ (RCT)	Exp N=25; Age: 65±3; Gender (m/f): 11:14 Type of stroke (H/I): NR; Time since stroke: 10±2	GBRT+CT Frequency: 5x/week for 8 weeks Dosage: (45-minute OT, 30-minute gait, 30-minute speech, 45-minute biomechanical training, 30-minute rest, 45 minutes GBRT) Robot: EE Game: NR	Control: ADL training + biomechanical training Dosage: 45-minute OT, 30-minute gait, 30-minute speech, 45-minute biomechanical training, 30-minute, 45-minute CT Frequency: 5x/week for 8 weeks	Functional performance: FMA
	Con N=25; Age: 64±3; Gender (m/f): 14:11 Type of stroke (H/I): NR; Time since stroke: 10±2			
	Exp	GBRT		

Carpinella 2020 ¹²¹ (RCT)	N=19; Age: 67.0 (58.0–70.0)*; Gender (m/f): 10:9 Type of stroke (H/I): 6:13; Time since stroke: NR	Frequency: 5x/week for 4 weeks Dosage: 45 minutes/session Robot: EE Game: NR	Control: UL mobilization and task-oriented exercise Frequency: 5x/week for 4 weeks Dosage: 45 minutes/session	ROM: ROM Hypertonia: MAS Functional performance: FMA Independence: FIM
	Con N=19; Age: 59.0 (46.0–69.0)*; Gender (m/f): 10:9 Type of stroke (H/I): 7:12; Time since stroke: NR			
Chen 2021a ¹²² (RCT)	Exp N=10; Age: 47.1±11.11; Gender (m/f): 10:0 Type of stroke (H/I): 6:4; Time since stroke: 2.5±1.76	GBRT Frequency: 5x/week for 4 weeks Dosage: 45 minutes/session Robot: Exo Game: Shooting targets, whack-a-mole, drinking water, wiping face, cleaning windows, and frying egg	Control: Passive stretching, movement, and functional training Frequency: 5x/week for 4 weeks Dosage: 45 minutes/session	Functional performance: FMA Independence: MBI
	Con N=10; Age: 54.9±14.5; Gender (m/f): 7:3 Type of stroke (H/I): 5:5; Time since stroke: 1.65±1.26			
Chen 2021b ¹²³ RCT	Exp N=10; Age: 46.2±7.02; Gender (m/f): 8:2 Type of stroke (H/I): 3:7; Time since stroke: 3.20±2.77	GBRT+CT Frequency: 5x/week for 4 weeks Dosage: 45 minutes/session Robot: Exo Game: shooting targets, Whack-a-Mole, and cleaning windows	Control: general cognitive and occupational rehabilitation with passive movement training and task-specific activities Frequency: 5x/week in 4 weeks Dosage: 45 minutes/session	Functional performance: FMA Independence: MBI
	Con N=10; Age: 48.6±9.95; Gender (m/f): 7:3 Type of stroke (H/I): 1:9; Time since stroke: 2.84±2.04			
Chinembiri 2021 ¹⁰³ (RCT)	Exp N=20; Age: 57.3±9.23; Gender (m/f): NR Type of stroke (H/I): 9:11; Time since stroke: NR	GBRT+CT Frequency: 5x/week for 6 weeks Dosage: 70 minutes per session Robot: EE Game: Harvested fruits and vegetables	Control: Conventional neglect training, ADL training. Frequency: 5x/ weeks for 3 weeks Dosage: 60 minutes per session	Functional performance: FMA Independence: MBI
	Con N=20; Age: 57.7±7.4; Gender (m/f): NR			

	Type of stroke (H/I): 9:11; Time since stroke: NR			
Choi 2016 ¹²⁴ (RCT)	Exp N=20; Age: 60.8±12.5; Gender (m/f): 12:8 Type of stroke (H/I): 7:13; Time since stroke: 1.23 ±0.52	GBRT+CT Frequency: 5x/ week for 3 weeks Dosage: 30 minutes robotic training and 30 minutes conventional therapy Robot: EE Game: Isometric Exercises (hit apples and ROM exercises: (dolphin circus game and a skateboard game)	Control: Conventional neglect training, ADL training. Frequency: 5x/ weeks for 3 weeks Dosage: 60 mins per session	Quality of Life: Korean MBI
	Con N=18; Age: 63.2±12.5; Gender (m/f): 8:10 Type of stroke (H/I): 6:12; Time since stroke: 1.25±0.56			
Daunoraviciene 2018 ¹²⁵ (RCT)	Exp N=17; Age: 65.88±4.87; Gender (m/f): 11:6 Type of stroke (H/I): 4:13; Time since stroke: 1.99±0.81	GBRT Frequency: 5x/ weeks for 6 weeks Dosage: 30 minutes/day Robot: EXO Game: various 3D virtual environment	Control: Exercising, physical activities, active table games etc. Frequency 5x/week Dosage: 35-60 minutes/day for 6 weeks	Hypertonia: MAS Functional performance: FMA Independence: Modified FIM
	Con N=17; Age: 65.47±4.05; Gender (m/f): 11:6 Type of stroke (H/I): 2:15; Time since stroke: 2.22± 1.42			
Dehem 2019 ¹²⁶ (RCT)	Exp N=23; Age: 67.3±11.1; Gender (m/f): 11:12 Type of stroke (H/I): 7:16; Time since stroke: 28.1 ±4.4	GBRT+CT Frequency: 4x/week for 6 weeks Dosage: 45 minutes (25% GBR, 75%CT) Robot: EE Game: reference trajectory (e.g., golf path) while passing through checkpoints (e.g., golf balls)	Control: Motor rehabilitation, matched with their personal needs and the centre's means Frequency: 4x/week for 6 weeks Dosage: 45 minutes/session	Functional performance: FMA Quality of Life: SIS
	Con N=22; Age: 68.6±19.1; Gender (m/f): 10:1 Type of stroke (H/I): 3:19; Time since stroke: 27.5±6.5			
Esquenazi 2021 ¹⁰⁴ (RCT)	Exp N=21; Age: 62.7±15.9; Gender (m/f): 12:9 Type of stroke (H/I): 3:18; Time since stroke: 0.6±0.53	GBRT Frequency: 4x/week Dosage: 1 hour per session Robot: Exo	Control: Therapist-Assisted tabletop Intervention Frequency: 4x/week Dosage: 1 hour/session	ROM: Passive ROM Hypertonia: MAS Functional performance:

	Con N=19; Age: 58.05±11.6; Gender (m/f): 12:7 Type of stroke (H/I): 7:12; Time since stroke: 0.47±0.25	Game: Virtual reality training environment *Total session: NR	*Total sessions: NR	FMA Independence: FIM
Fischer 2007 ¹²⁷ (RCT)	Exp N=5; Age: 57.4±9.48; Gender (m/f): 4:1 Type of stroke (H/I): NR; Time since stroke: 51±34.60	GBRT Frequency: 3x/ weeks for 6 weeks Dosage: 1 hour Robot: NR Game: NR	Control: Grasp-and-release of the virtual and actual objects Frequency: 3/ week for 6 weeks. Dosage: 1 hour	Functional performance: FMA
	Con N=5; Age: 71.6±13.90; Gender (m/f): 3:2 Type of stroke (H/I): NR; Time since stroke: 134.4± 182.66			
Franceschini 2020 ¹²⁸ (RCT)	Exp N=25; Age: 74.0 (68.3- 80.3)*; Gender (m/f): 12:13 Type of stroke (H/I): 2:23; Time since stroke: 31.0 (29.0- 33.0)*	GBRT+CT Frequency: 5 days/ week for 6 weeks Dosage: 45 minutes GBRT+ unknown CT dosage Robot: EE Game: NR	Control: CT (# of reps matched GBR), assisted stretching, shoulder and arm exercises, and functional reaching tasks. Frequency: 5 days/ week for 6 weeks Dosage: matched GBRT	Hypertonia: MAS ROM: pROM Functional performance: FMA
	Con N=23; Age: 77.0 (60.3-72. 0)*; Gender (m/f): 14:9 Type of stroke (H/I): 4:19; Time since stroke: 31.0 (28.0; 33.0)*			
Gandolfi 2019 ¹²⁹ (RCT)	Exp N=16; Age: 59.31± 14.40; Gender (m/f): 12:4 Type of stroke (H/I): NR; Time since stroke: 71.99 ±37.2	GBRT+CT Frequency: 2/week for 5 weeks Dosage: 45 minutes (10 minutes passive mobilization and stretching, 35 min GBRT Robot: EE Game: Collect the coins, drive the car, wash the dishes, and burst the balloons	Control: Passive mobilization and stretching followed by UL exercises Frequency: 2/week for 5 weeks Dosage: 45 minutes	Strength: MRC Hypertonia: MAS Functional performance: FMA
	Con N=16; Age: 59.13±14.97; Gender (m/f): 10:6 Type of stroke (H/I): NR; Time since stroke: 61.19±26.4			

Gueye 2021 ¹⁰² (RCT)	Exp N=15; Age: 66.6 ± 12.3; Gender (m/f): 14:11 Type of stroke (H/I): 5:20; Time since stroke: 0.49± 0.21	GBRT+CT Frequency: 4x/week for 3 weeks Dosage: at least 180 minutes Robot: EXO Game: NR	Control: Conventional PT and OT training regimen Frequency: 4x/week for 3 weeks Dosage: at least 180 minutes	Functional performance: FMA Independence: FIM
	Con N=25; Age: 68.1 ± 11.97; Gender (m/f): 15:10 Type of stroke (H/I): 1:24; Time since stroke: 0.54±0.24			
Hung 2019 ¹³⁰ (RCT)	Exp N=10; Age: 57.5 (54.15-62.16; Gender (m/f): 6:4 Type of stroke (H/I): 3:7; Time since stroke: 26 (15.75-34.5)	GBRT+CT Frequency: 5x/week for 4 weeks Dosage: 90-100 minute/session (70- 75 RT, 20 functional-based activities) Robot: EE Game: NR	Control: Muscle tone normalization, fine motor training, gross motor training, muscle strengthening, and functional activity practice Frequency: 5x/week for 4 weeks Dosage: 90-100 minutes/session	Strength: MRC Hypertonia: MAS Functional performance: FMA
	Con N=10; Age: 55.54 (49.41-61.56); Gender (m/f): 4:6 Type of stroke (H/I): 4:6; Time since stroke: 25(15-32.5)			
Jiang 2021 ¹⁰¹ (RCT)	Exp N=23; Age: 62.43±11.3; Gender (m/f): 14:9 Type of stroke (H/I): 7:16; Time since stroke: 0.66±0.18	GBRT+CT Frequency: 10x/week for 2 weeks Dosage: 30 minutes/session Robot: Exo Game: NR	Control: NDT, functional tasks and muscle strengthening Frequency: 10x/week for 2 weeks Dosage: 30 minutes/session	Strength: MI Hypertonia: MAS Functional performance: FMA Independence: FIM
	Con N=22; Age: 66±11.5; Gender (m/f): 15:7 Type of stroke (H/I): 4:18; Time since stroke: 0.64±0.23			
Keeling 2021 ¹³¹ (RCT)	Exp N=9; Age: 54.3±15.6; Gender (m/f): 8:1 Type of stroke (H/I): 2:7; Time since stroke: 1.41±0.84	GBRT+CT Frequency: 5x/week for 2 weeks Dosage: 60 minutes/session Robot: EE Game: NR	Control NDT, functional tasks and muscle strengthening Frequency: 10 sessions/week for 2	Functional performance: FMA Independence: FIM
	Con			

	N=10; Age: 42.8±25.5; Gender (m/f): 9:1 Type of stroke (H/I): 1:9; Time since stroke: 1.2±0.51		weeks Dosage: 30 minute/session	
Klamroth-Marganska 2014 ¹³² (RCT)	Exp N=38; Age: 55±13; Gender (m/f): 15:7 Type of stroke (H/I): 9:13; Time since stroke: 1.34± 0.75	GBRT+CT Frequency: 3x/week for 8 weeks Dosage: 45 minutes Robot: EXO Games: Ball games, a labyrinth game and different kitchen activities	Control: Mobilization, games and/or ADL training Frequency: 3x/ week for 8 weeks Dosage: 45 min	Strength: Grip strength using Jamar Hypertonia: MAS Functional performance: FMA Quality of Life: SIS
	Con N=35; Age: 58±14; Gender (m/f): 14:8 Type of stroke (H/I): 10:12; Time since stroke: 1.38± 0.67			
Lee 2016 ⁹⁸ (RCT)	Exp N=22; Age: 50.27±11.1; Gender (m/f): 15:7 Type of stroke (H/I): 9:13; Time since stroke: 1.34± 0.75	GBRT+CT Frequency: 5x/ week for 2 weeks Dosage: 30 minutes/session, 2 sessions/day Robot: EE Game: Basic continuous passive motion exercise mode, basic controlled assisted movement exercise mode, grinding millstone and jumping rope	Control: Stretching and strengthening exercises and passive and/or active assistive ROM exercises. Frequency: 10 sessions/week for 2 weeks Dosage: 30 minutes/session	Strength: Standard MMT Hypertonia: MAS Functional performance: MFT Independence: Korean MBI
	Con N=22; Age: 52.32±8.66; Gender (m/f): 14:8 Type of stroke (H/I): 10:12; Time since stroke: 1.38± 0.67			
Lee 2021 ¹³³ (Cross-over RCT)	Exp N=14; Age: 59.56±8.29; Gender (m/f): 9:5 Type of stroke (H/I): 5:9; Time since stroke: 29±31.5	GBRT Frequency: 2x/ week for 6 weeks Dosage: 60 minutes/session Robot: Exo Game: flying a spaceship, filling a shopping cart, and playing a Breakout clone	Control: Stretching and strengthening exercises and passive and/or active assistive ROM exercises. Frequency: 2x/ week for 6 weeks Dosage: 60 minutes/session	Strength: Grip strength Functional performance: FMA Independence: MBI
	Con N=10; Age: 53.5±12.3; Gender (m/f): 7:3 Type of stroke (H/I): 6:4; Time since stroke: 29.04±33.55			
Lencioni 2021 ¹³⁴ (RCT)	Exp N=10; Age: 68 (54.5-74.5); Gender (m/f): 6:9	GBRT	Control: Usual care (mobilisation and task-oriented exercises)	

	Type of stroke (H/I): 4:11; Time since stroke: NR	Frequency: 5 sessions per week (total 20 sessions)	Frequency: 5 sessions per week (total 20 sessions)	ROM: ROM Functional performance: FMA
	Con N=20; Age: 59 (46.9-68.4); Gender (m/f): 9:8 Type of stroke (H/I): 6:11; Time since stroke: NR	Dosage: 45 minutes/session Robot: EE Game: NR	Dosage: 45 minutes/session	
Liao 2012 ¹³⁵ (RCT)	Exp N=10; Age: 55.51±11.17; Gender (m/f): 4:6 Type of stroke (H/I): NR; Time since stroke: 23.90±13.4	GBRT+CT Frequency: 5 days/ week for 4 weeks Dosage: 90 to 105 minutes/day GBRT and 15 CT Robot: EE Game: NR	Control: NDT, strengthening, ADLs and functional task exercises Frequency: 5 days/weeks for 4 weeks Dosage: 90 to 105 min/day	Functional performance: FMA Independence: FIM
	Con N=10; Age: 54.6±8.2; Gender (m/f): 3:7 Type of stroke (H/I): NR; Time since stroke: 22.20±17.47			
Liu 2016 ¹³⁶ (RCT)	Exp N=16; Age: 56±12; Gender (m/f): 10:6 Type of stroke (H/I): NR; Time since stroke: NR	GBRT+CT Frequency: 3x/ week for 4 weeks Dosage: 30 minutes/session Robot: NR Game: NR	Control: Self-exercise rehabilitation plan Frequency: 3x/ week for 4 weeks Dosage: 30 minutes/session	Hypertonia: MAS Functional performance: FMA
	Con N=15; Age: 52±14; Gender (m/f): 8:7 Type of stroke (H/I): NR; Time since stroke: NR			
Orihuela-Espina 2016 ¹³⁷ (RCT)	Exp N=9; Age: 56.22±13.72; Gender (m/f): 5:4 Type of stroke (H/I): 0:9; Time since stroke: 2.44±0.88	GBRT Frequency: 5X/week for 8 weeks Dosage: 40 to 60 minutes/session Robot: EE Game: NR	Control: Strengthening, stretching, and palmar grasp exercise Frequency: 5x/week for 8 weeks Dosage: 40 to 60 minutes/session	Strength: MI Functional performance: FMA
	Con N=8; Age: 55.0±25.78; Gender (m/f): 6:2 Type of stroke (H/I): 0:8; Time since stroke: 2.18±1.25			
	Exp	GBRT		

Padua 2020 ¹³⁸ (RCT)	N=36; Age: 66±10; Gender (m/f): NR Type of stroke (H/I): 4:32; Time since stroke: 2.13±1.5	Frequency: 5x/week for 6 weeks Dosage: 45 minutes/session Robot: EE Game: NR	Control: Exercises for hand, arm and shoulder oriented to sensor-motor reprogramming, inhibition of the hypertonus, functional improvement and task-oriented exercise Frequency: 5x/week for 6 weeks Dosage: 45 minutes/session	Strength: MI Functional performance: ARAT Independence: BI
	Con N=39; Age: 65±12; Gender (m/f): NR Type of stroke (H/I): 8:31; Time since stroke: 1.90±1.41			
Patel 2019 ¹³⁹ (RCT)	Exp N=7; Age: 62±10.8; Gender (m/f): 5:2 Type of stroke (H/I): NR; Time since stroke: 0.39±0.10	GBRT+CT Frequency: 8 sessions total Dosage: 1-hour GBR + 3-hour CT Robot: Exo Game: Monkey Business, Space Pong, and Piano Trainer.	Control: strengthening, ROM, mobility, activities of daily living, and transfer training Frequency: 5 days a week Dosage: 3 hour/session	Strength: Pinch force Functional performance: FMA
	Con N=6; Age: 57.14±11.3; Gender (m/f): 4:2 Type of stroke (H/I): NR; Time since stroke: 0.43±0.31			
Perini 2021 ¹⁴⁰ (RCT)	Exp N=9; Age: 58.7±20.6; Gender (m/f): 5:4 Type of stroke (H/I): NR; Time since stroke: 35.3±44.5	GBRT+CT Frequency: 2 sessions/day (3 days per week for - 3.2 to 4 weeks Dosage: 45 minutes stimulation with task-oriented and 45 minutes GBRT Robot: Exo Game: NR	Control: Task-oriented exercise Frequency: 5 sessions per week for 4-5 weeks Dosage: 45 minutes/session	Functional performance: FMA
	Con N=9; Age: 61.4±9; Gender (m/f): 4:5 Type of stroke (H/I): NR; Time since stroke: 42±44.7			
Prange 2013 ¹⁴¹ (RCT)	Exp N=35; Age: 60.3±9.7; Gender (m/f): NR Type of stroke (H/I): 7:28; Time since stroke: 87.6±40.8	GBRT Frequency 3x/ weeks for 6 weeks Dosage: 30 minutes/session Robot: EXO Game: Computer-based gaming	Control: Reaching for targets (bow, pegs in holes, placing disks, etc.) Frequency 3x/ weeks for 6 weeks Dosage: 30 minutes/session	Functional performance: FMA
	Con N=33; Age: 58 ±11.4; Gender (m/f): NR			

	Type of stroke (H/I): 8:25; Time since stroke: 81.6±37.2			
Prange 2015 ¹⁴² (RCT)	Exp N=35; Age: 58±11.4; Gender (m/f): 24:19 Type of stroke (H/I): 8:25; Time since stroke: 1.68± 0.78	GBRT Frequency:3 sessions per week for 6 weeks Dosage: 30 minutes per session Robot: EXO Game: 1D, 2D (and 3D movements games)	Control: standardized set of arm exercises Frequency:3 sessions per week for 6 weeks Dosage: 30 minutes per session	Functional performance: FMA
	Con N=33; Age: 60.3± 9.7; Gender (m/f): 17:19 Type of stroke (H/I): 7:28; Time since stroke: 1.56±0.71			
Remy-Neris 2021 ¹⁴³ (RCT)	Exp N=107; Age: 58.08±14.05; Gender (m/f): 67:40 Type of stroke (H/I): 64:42; Time since stroke: 1.83±0.71	GBRT+CT Frequency:5 sessions per week for 4 weeks Dosage: 1.5 hours per session Robot: EXO Game: NR	Control: CT+ Self-rehabilitation (stretching and active exercise) Frequency:5 sessions per week for 4 weeks Dosage: 1.5 hours per session	Hypertonia: MAS Functional performance: FMA Independence: FIM Quality of Life: SIS
	Con N=108; Age: 58.53±13.27; Gender (m/f): 73:35 Type of stroke (H/I): 33:75; Time since stroke: 1.77±0.75			
Rodgers 2019 ¹⁴⁴ (RCT)	Exp N=257; Age: 59.9±13.5; Gender (m/f): 156:101 Type of stroke (H/I): 60:197; Time since stroke: 7.66 (3.35-18.04)*	GBRT+CT Frequency: 3x/week for 12 weeks Dosage: 45 minutes Robot: EE Game: NR	Control: Repetitive functional tasks Frequency: 3x/week for 12 weeks Dosage: 45 minutes	Functional performance: ARAT Independence: BI (ADL index) Quality of Life: SIS
	Con N=259; Age: 59.4±14.3; Gender (m/f): 159:100 Type of stroke (H/I): 57:202; Time since stroke: 8.48 (3.78-17.95)*			
	Exp	GBRT		

Saleh 2017 ¹⁴⁵ (RCT)	N=10; Age: NR; Gender (m/f): NR Type of stroke (H/I): NR; Time since stroke: 70±49	Frequency: 4 days/ weeks for 2 weeks Dosage: 180 minutes/session Robot: EE Game: moving virtual targets and objects in 3D space	Control: "reach and grasp" exercises and functional tasks Frequency: 4 days/week for 2 weeks Dosage: 180 minutes/session	Functional performance: JTHF
	Con N=10; Age: NR; Gender (m/f): NR Type of stroke (H/I): NR; Time since stroke: 90±53			
Takahashi 2016 ¹⁴⁶ (RCT)	Exp N=30; Age: 65.2±10.9; Gender (m/f): 21:9 Type of stroke (H/I): NR; Time since stroke: 1.57±0.23	GBRT+CT Frequency: Daily for 6 weeks Dosage: 40 minutes CT and 40 minutes GBRT Robot: EE Game: NR	Control: Stretching, ROM, reaching, grasping/releasing, and pinching, as well as ADL training. Frequency: Daily for 6 weeks Dosage: 80 minutes CT	Strength: MI Hypertonia: MAS Range of motion: ROM Functional performance: FMA Independence: FIM
	Con N=26; Age: 64.6±11.5; Gender (m/f): 18:8 Type of stroke (H/I): NR; Time since stroke: 1.54±0.27			
Taveggia 2016 ¹⁴⁷ (RCT)	Exp N=27; Age: 73±10; Gender (m/f): 9:18 Type of stroke (H/I): NR; Time since stroke: NR	GBRT+CT Frequency: 5 sessions for 6 weeks Dosage: 30 minutes GBRT and 30 minutes CT Robot: EXO Game: Visual feedback with 3D virtual environment	Control: Bobath approach Frequency: 5 sessions for 6 weeks Dosage: 60 minutes CT	Hypertonia: MAS Strength: MI Independence: FIM
	Con N=27; Age: 68±13; Gender (m/f): 14:13 Type of stroke (H/I): NR; Time since stroke: NR			
Terranova 2021 ¹⁴⁸ (RCT)	Exp N=25; Age: 60.72±12.38; Gender (m/f): 15:10 Type of stroke (H/I): NR; Time since stroke: 18.96±9.68	GBRT+CT Frequency: 3 sessions for 12 weeks Dosage: 60 minutes GBRT/session + CT Robot: EE Game: NR	Control: CIMT+ CT Frequency: 5 sessions/week (10 weeks CT, 2 weeks CT) Dosage: 6 hours/sessions for CIMT+ CT	Hypertonia: MAS Functional performance: FMA Independence: FIM Quality of Life: SIS
	Con N=26; Age: 59.35±14.48; Gender (m/f): 11:15 Type of stroke (H/I): NR; Time since stroke: 14.32±7.53			

Thielbar 2014 ¹⁴⁹ (RCT)	Exp N=7; Age: 54±7; Gender (m/f): 4:3 Type of stroke (H/I): NR; Time since stroke: 46.6±32.5	GBRT+CT Frequency: 3 sessions for 6 weeks Dosage: 1 hour/session Robot: EXO Game: Key combination mode, song mode	Control: High intensity, task-oriented on fine motor control, dexterity, in-hand manipulation, and finger individuation. Frequency: 3 sessions for 6 weeks Dosage: 1 hour/session	Strength: Grip strength Functional performance: FMA
	Con N=7; Age: 59±6; Gender (m/f): 5:2 Type of stroke (H/I): NR; Time since stroke: 47.9±47.4			
Tomic 2017 ¹⁵⁰ (RCT)	Exp N=13; Age: 56.5±7.4; Gender (m/f): 12:1 Type of stroke (H/I): 1:12; Time since stroke: 1.16±0.31	GBRT+CT Frequency: 5 days/ weeks for 3 weeks Dosage: 30 minutes CT and 30 minutes GBRT Robot: EXO Game: Interactive gaming with a focus on reaching.	Control: CT like ROM, stretching and facilitation of active movement ADLs training Frequency: 5 days/ weeks for 3 weeks Dosage: 60 minutes per session	Functional performance: FMA Independence: BI
	Con N=13; Age: 58.3± 5.2; Gender (m/f): 9:4 Type of stroke (H/I): 2:11; Time since stroke: 1.23± 0.25			
Wolf 2015 ¹⁵¹ (RCT)	Exp N=51; Age: 48; Gender (m/f): 25:26 Type of stroke (H/I): NR; Time since stroke: 3.8±1.75	GBRT+CT Frequency: 5x/ week for 8-12 weeks Dosage: 3 hour/ session Robot: EE Games: NR	Control: ROM, weight-bearing activities; AAROM with cane, shoulder /elbow/forearm, wrist/hand exercises; and task-based activities Frequency: 5x/week for 8-12 weeks Dosage: 3 hour/session	Functional performance: FMA
	Con N=48; Age: 54.7±12.2; Gender (m/f): 31:17 Type of stroke (H/I): NR; Time since stroke: 4.18±1.52			
Wu 2021 ¹⁵² (RCT)	Exp N=14; Age: 55.13±12.72; Gender (m/f): 10:4 Type of stroke (H/I): NR; Time since stroke: 18±8.65	GBRT Frequency: 5/week for 4 weeks Dosage: 90-105 minutes/session Robot: EXO Games: Picking up and placing apples	Control: Therapy-based Bilateral Arm Training Frequency: 5x/ week for 4 weeks Dosage: 90-105 minutes/session	Functional performance: FMA Quality of Life: SIS
	Con N=14; Age: 57.04±8.78; Gender (m/f): 12:2			

	Type of stroke (H/I): NR; Time since stroke: 17.29±13.29			
Yoo 2013 ¹⁵³ (RCT)	Exp N=11; Age: 50.9±10.9; Gender (m/f): 7:4 Type of stroke (H/I): 3:8; Time since stroke: 45.8±41.8	GBRT+CT Frequency: 3 days/week for 6 weeks Dosage: 60 minutes CT and 30 minutes GBRT Robot: EE Game: 3D reaches forward reach task reach task	Control: Specific details about the therapy was not reported Frequency: 3 days/week for 6 weeks Dosage: 60 minutes CT	Strength: Grip strength Functional performance: WMFT Independence: MBI
	Con N=11; Age: 49.7±8.9; Gender (m/f): 6:5 Type of stroke (H/I): 4:7; Time since stroke: 41.5±33.1			

N=sample size, age (mean± SD) in years, gender (Male: Female), Type of stroke (Haemorrhagic: Ischemic), Affected UL (Left: Right), Time since stroke in months (mean± SD) Mean, GBRT- game-based robotic training., CT- conventional therapy, OT- occupational therapy, ADL-activities of daily living, ROM- range of motion, MMT- manual muscle testing, SIS- Stroke Impact Scale, MAS- Modified Ashworth Scale, FIM- Functional Independence Measure, MBI- Modified Barthel Index, BI- Barthel Index, pROM- passive range of motion, MRC- Medical Research Council, MI- Motricity Index, ARAT- Action Research Arm Test, JTHF- Jebsen-Taylor Hand Function, WMFT- Wolf Motor Function Test, Exp-experimental, Con- control, NR-not reported, EE- end-effector, Exo- Exoskeleton, *Median (IQR)

2.3.3 Risk of Bias

Most of the trials included had “some concerns” across all outcomes of interest. The overall risk of bias for the outcome functional performance of the UL was high risk in 15 trials (41%), some concerns in 20 trials (54%) and low risk in 2 trials (5%). For the outcome independence, the overall risk of bias was high risk in 10 trials (50%) and some concerns in 10 trials (50%) and no trial was graded as low risk of bias (see Figure 2.2 and 2.5 for the complete ROB for the primary outcomes).

2.3.4 Game-based Robotics Training versus Conventional Therapy

2.3.4.1 Game-based Robotics Training versus Conventional Therapy: UL Function

Seventeen trials (n=525) compared GBRT to CT for UL function (Figure 2.2). Pooled results yielded an SMD of 0.02 with the 95% CI (-0.18 to 0.23) spanning the line of no difference, indicating that there was no difference between GBRT and CT for UL function, with a high percentage of participants (35%) deriving from high-risk trials and with small heterogeneity ($I^2=31\%$). The GRADE assessment showed that the certainty of the evidence for UL function was moderate (downgraded for design) (see Appendix B for full GRADE assessment).

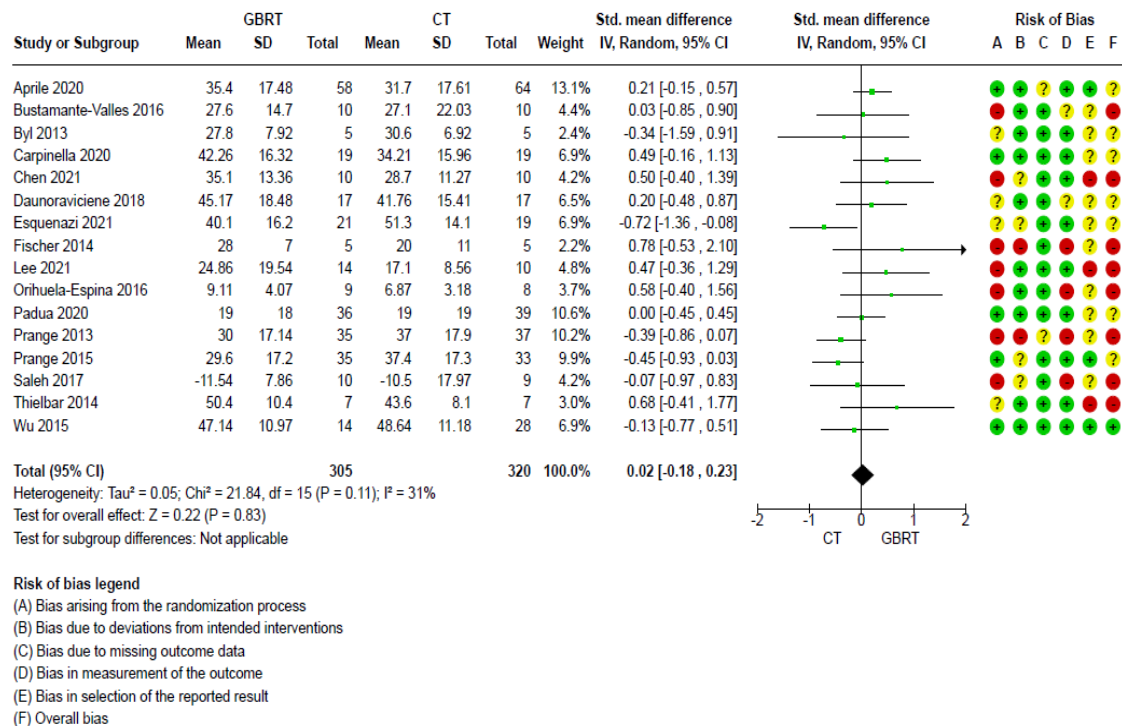


Figure 2. 2 SMD (95% CI) of effect of GBRT on functional performance of the upper limb compared with conventional therapies by pooling data from 17 trials (n=525)

2.3.4.2 Game-based Robotics Training versus Conventional Therapy: Independence

Seven trials (n=353) compared GBRT to CT for independence (Figure 2.3). Pooled results yielded a trivial effect size of SMD: 0.18 with the 95% CI (-0.05 to 0.40) spanning the line of no difference, indicating that there was no difference between GBRT and CT for independence. The GRADE assessment showed that the certainty of the evidence for no difference for independence was high with low heterogeneity and a low percentage of participants coming from high-risk trials (Appendix B for full GRADE assessment).

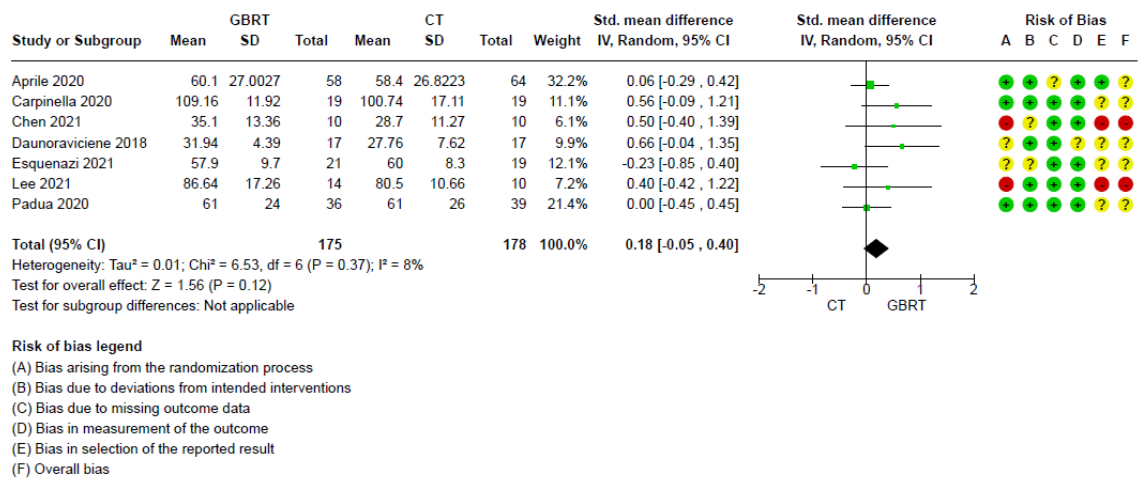


Figure 2. 3 SMD (95% CI) of effect of GBRT on independence compared with CT by pooling data from 6 trials (n=353)

2.3.5 Addition of Game-based Robotics to Conventional Therapy

2.3.5.1 Addition of Game-based Robotics Training to Conventional Therapy versus Conventional Therapy Alone: UL Function

Twenty-two trials (n=1,234) compared CT in addition to GBRT to CT alone for UL function (Figure 2.4). The pooled results yielded a small effect size of SMD: 0.23 with the 95% CI (0.11 to 0.34) not spanning the line of no difference, indicating that there was a difference between the groups for UL function in favour of GBRT +CT. Moreover, the CI was below the nominated SWE, indicating that the effect estimate was not clinically worthwhile. The GRADE assessment showed that the certainty of the evidence for the difference in UL function was moderate (downgraded for design) (Appendix B for full GRADE assessment).

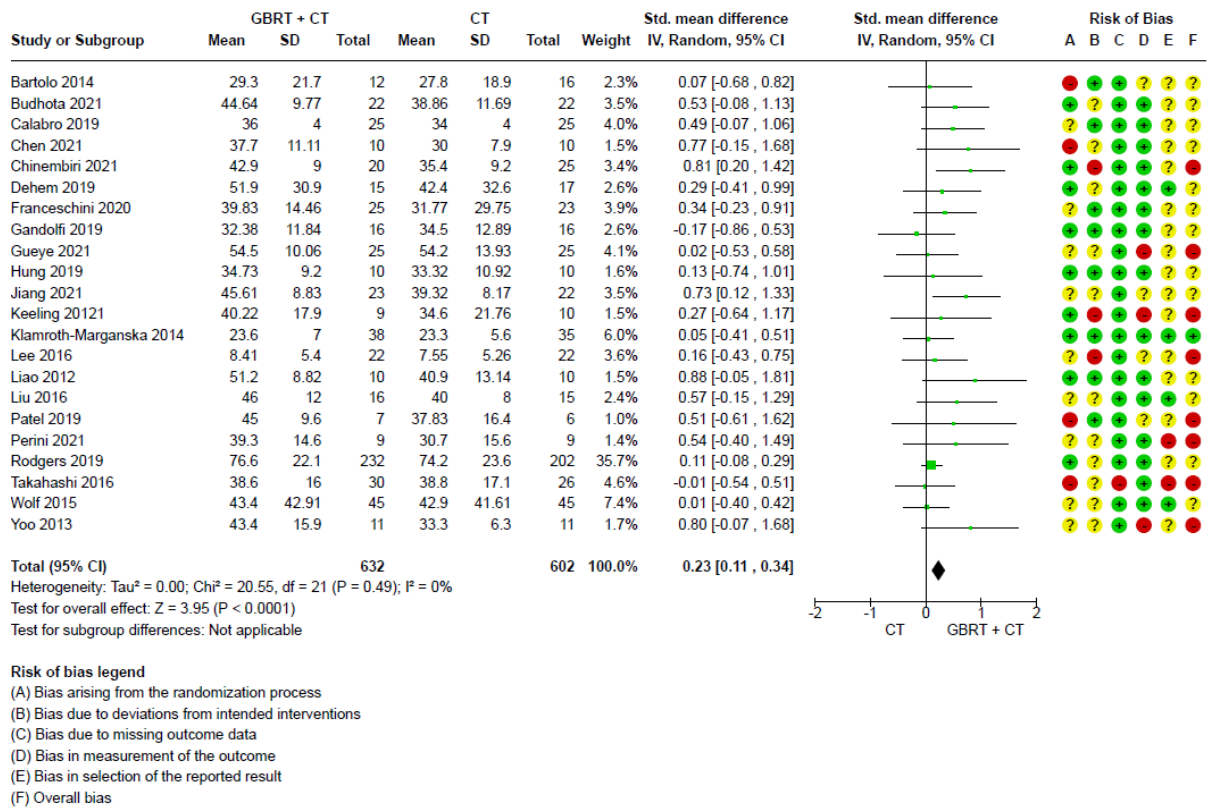


Figure 2. 4 SMD (95% CI) of the effect of GBRT with CT on functional performance of the upper limb compared with CT by pooling data from 22 trials (n=1,234)

2.3.5.2 Addition of Game-based Robotics Training to Conventional Therapy versus Conventional Therapy Alone: Independence

Thirteen trials (n=881) compared CT in addition to GBRT to CT alone for independence (Figure 2.5). The pooled results yielded a small effect size of SMD: 0.22 with the 95% CI (-0.04 to 0.47) spanning the line of no difference, indicating that there was no difference between the groups for independence. The GRADE assessment showed that the certainty of the evidence for no difference was low (downgraded for design and inconsistency) (Appendix B for full GRADE assessment).

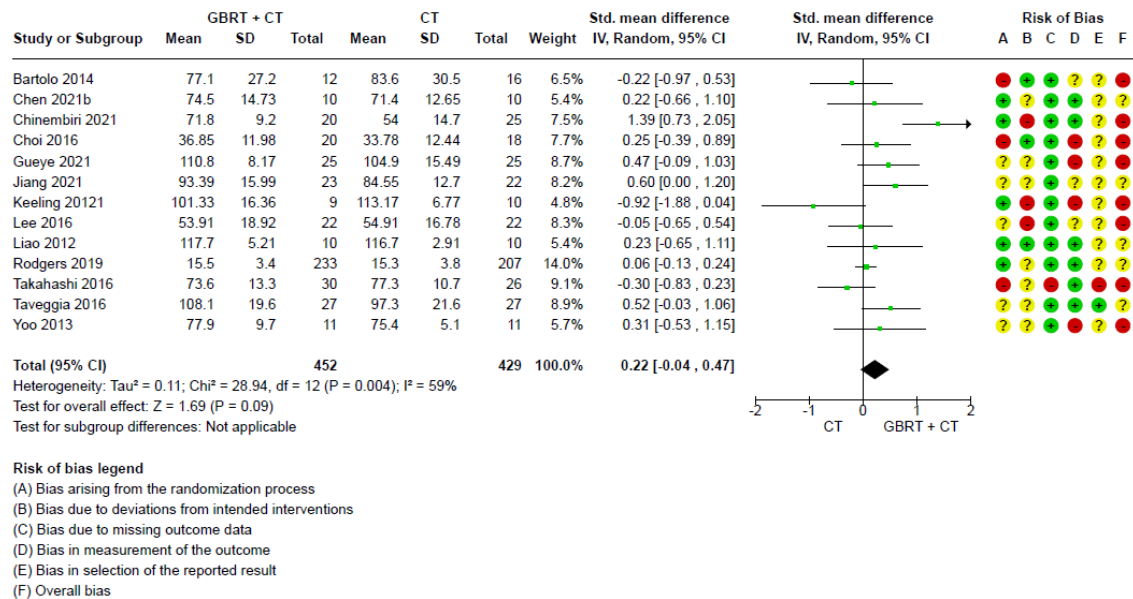


Figure 2. 5 SMD (95% CI) of effect of GBRT with CT on independence compared with CT by pooling data from 13 studies (n=702)

2.3.6 Subgroup analysis

2.3.6.1 Type of robot

We defined two subgroups of robots: EE and EXO. When comparing GBRT and CT, the 95% CI for all subgroups spanned the line of no difference indicating no differences between EE and EXO in UL function (EE: SMD= 0.18, 95% CI -0.03 to 0.39, EXO: SMD= -0.18, 95% CI, -0.53 to 0.16) and in independence (EE: SMD= 0.21, 95% CI -0.03 to 0.46, EXO: SMD= 0.06, 95% CI, -0.63 to 0.75).

When comparing CT in addition to GBRT to CT alone, for the subgroup EE, we found a small treatment effect size of SMD 0.22 with the 95% CI (CI 0.10 to 0.35) not spanning the line of no difference in favour of EE for UL function. However, the CI was lower than the nominated SWE indicating that the estimated effect was possibly not clinically worthwhile. The GRADE assessment showed that the certainty of the evidence for the difference in UL function in favour of EE was low (downgraded due to design and imprecision).

For the subgroup EXO, the 95% CI spanned the line of no difference for UL function (EXO: SMD 0.26, 95%CI -0.01 to 0.54) and for independence (EE: SMD=0.18, 95% CI -0.15 to 0.51, EXO: SMD= 0.34, 95% CI -0.00 to 0.68) (see Appendix C for forest plots). The effect estimate

was not considered clinically worthwhile. The GRADE assessment varied from very low to high certainty of no differences between EE and EXO (see full GRADE assessment and reasons for downgrade in Appendix B)

2.3.6.2 Time since stroke

We defined two subgroups concerning the time since stroke: less than 6 months and 6 months or more. When comparing the GBRT and CT, the 95% CI for all subgroups spanned the line of no difference for UL function (< 6 months: SMD= -0.02, 95%CI -0.33 to 0.30, 6 months or more: SMD=-0.12, 95%CI -0.41 to 0.17).

When comparing CT in addition to GBRT to CT alone for the subgroup 6 months or more, we found a small treatment effect size of SMD 0.31 with the 95% CI (CI 0.09 to 0.53) not spanning the line of no difference for the subgroup 6 months or more for UL function. However, the lower border of the CI was lower than the nominated SWE indicating that the estimated effect was possibly not certain to be clinically worthwhile. The GRADE assessment showed that the certainty of the evidence for the difference in UL function in favour of the subgroup 6 months or more was high.

For the subgroup less than 6 months, the 95% CI spanned the line of no difference for UL function (<6 months: SMD=0.19, 95%CI -0.02 to 0.39) and independence (< 6 months: SMD= -0.02, 95%CI -0.33 to 0.30, 6 months or more: SMD=-0.12, 95%CI -0.41 to 0.17) (see Appendix C for forest plots). The GRADE assessment varied from very low to high certainty for no differences between groups (see full GRADE assessment and reasons for downgrade in Appendix B).

2.3.7 Secondary Outcomes

2.3.7.1 Quality of Life

When comparing GBRT and CT, we found a small treatment effect of SMD= 0.2 with the 95% CI (-0.88 to 0.48) spanning the line of no difference, indicating that there was no difference between groups in QoL. The GRADE assessment revealed that the certainty of evidence for no difference in QOL was low due to small sample size (n=144) and high heterogeneity ($I^2=63\%$).

The comparison between addition of GBRT to CT and CT alone, revealed a trivial treatment effect of SMD= 0.16 with the 95% CI (-0.34 to 0.02) spanning the line of no difference, indicating no difference between the groups in QoL. The GRADE assessment revealed that the certainty of evidence for no difference was high. (See appendix C for detailed forest plot and appendix B for the full GRADE assessment).

2.3.7.2 Range of Motion

When comparing GBRT and CT, we found a trivial treatment effect of SMD= 0.1 with the 95% CI (-0.41 to 0.61) spanning the line of no difference, indicating that there was no difference between groups in ROM. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was moderate due to small sample size (n=60).

The comparison between addition of GBRT to CT and CT alone, revealed a small treatment effect of SMD= 0.25 with the 95% CI (0.34 to 0.84) spanning the line of no difference, indicating no difference between the groups in ROM. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was very low due to small sample size (n=117), 59% of participants came from high-risk trials and high heterogeneity ($I^2=59\%$). (See appendix C for detailed forest plot and appendix B for the full GRADE assessment).

2.3.7.3 Muscle Strength

When comparing GBRT and CT, we found a small treatment effect of SMD= 0.2 with the 95% CI (-0.02 to 0.43) spanning the line of no difference, indicating that there was no difference between groups in muscle strength. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was low due to small sample size (n=300) and 31% of participants came from high-risk trials.

The comparison between addition of GBRT to CT and CT alone, revealed a trivial treatment effect of SMD= -0.09 with the 95% CI (-0.15 to 0.33) spanning the line of no difference, indicating no difference between the groups in muscle strength. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was moderate due to high heterogeneity ($I^2=29\%$). (See appendix C for detailed forest plot and appendix B for the full GRADE assessment).

2.3.7.4 Hypertonia

When comparing GBRT and CT, we found a trivial treatment effect of SMD= -0.13 with the 95% CI (-0.38 to 0.12) spanning the line of no difference, indicating no difference between groups in hypertonia. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was low due to small sample size (n=254).

The comparison addition of GBRT to CT and CT alone revealed a small treatment effect of SMD= -0.23 with the 95% CI (-0.54 to 0.31) spanning the line of no difference indicating no difference between the groups in hypertonia. The GRADE assessment revealed that the certainty of evidence for no difference for this outcome was moderate due to high heterogeneity ($I^2=58\%$). (See appendix C for detailed forest plot and appendix B for the full GRADE assessment).

2.4 Discussion

2.4.1 Main findings

This systematic review provided evidence on the effectiveness of UL training using robotic devices with a game component as stand-alone training or as an adjunct to CT. The results showed that when GBRT is combined with CT, it yielded a significant difference in UL function, although the treatment effect was small and may not be clinically worthwhile. Moreover, we found that when using GBRT for UL training after stroke, the type of robot and the chronicity of the condition might matter for improvements in UL function, with EE, and longer time since injury presenting better outcomes. Finally, the certainty of the evidence for each outcome of interest varied from low to high. The main reasons for the downgrade were: 1) several trials were appraised as high risk of bias 2) high heterogeneity and 3) the small sample size of the included trials.

2.4.2. Comparing with existing evidence

It is established that robotic therapy can lead to high-volume task-oriented training, which is vital for motor recovery as it can increase the potential for neuroplasticity.¹⁵⁴⁻¹⁵⁶ Previous studies indicated that a training regimen using robots can provide high-repetition and high-intensive training that ranges from 240 to 1344 repetitions of movement in a 30- to 45-minute session.^{74, 75, 121} To

further optimize the effect of robotic training by increasing adherence, motivation and user engagement, gamification was introduced.¹⁵⁶

The Optimizing Performance Through Intrinsic Motivation and Attention for Learning (OPTIMAL) theory hypothesized that external feedback, like the visual and auditory feedback provided in games, could increase the focus on the task to be done, which could, in turn, facilitate motor learning and increase motor performance.¹⁵⁷ However, our results indicated that robotic training with a game component, as a stand-alone training, did not improve UL function, independence, quality of life or UL impairments (muscle strength, ROM and hypertonia) more than conventional therapy did. This finding is in corroboration with a systematic review conducted by Chien et al (2020), where no significant differences were seen in UL function between robotic training (without gamification) and CT, even when the dose received by both groups was matched.¹⁵⁸ Similarly in the present systematic review, the CT group matched the given dose for the GBRT group in the majority of studies. The GRADE assessment for this finding suggested that the certainty of the evidence for the no effect in UL function was moderate due to the high percentage of the population coming from high-risk trials. This could indicate that additional high-quality trials could still change this finding. This systematic review found that GBRT, as an adjunct to CT, seemed to be a better mode of implementation of robotics in therapeutic settings after stroke. We found a significant small treatment effect, indicating that combinations of these interventions could lead to slight greater benefits in UL function. Similarly, previous studies had shown that the combination of CT and robotic training can lead to better outcomes in people with stroke.⁸ Hsieh et al (2016), in their single-blinded RCT, found that a combination of robotic training and CIMT resulted in a greater improvements in UL function than robotic training alone.¹⁵⁹ Moreover, there was a clinically worthwhile and significant difference favouring the combined treatment to enhance independence in activities of daily living. This was confirmed by a systematic review conducted by Norouzi-Gheidari et al (2012), in which non-significant differences between robotic and CT were observed, even when the dosage delivered to both groups was matched.¹⁶⁰ However, when robotic and CT were combined, it resulted in a significant change. A plausible reason for this is that receiving both treatments could lead to more comprehensive training; GBRT offers a practice of

tasks through simulation, whereas CT offers an actual practice of tasks. This finding is supported by Brokaw et al (2014) wherein they suggested that both types of therapies are “distinct but complementary”, hence having both could provide a more holistic training that could optimise gains.¹⁶¹ Moreover, the gaming component of the combined training could have resulted in a greater training intensity due to the engaging, fun and competitive nature of playing games.^{139, 162} However, although significant, there was uncertainty about the treatment effect and whether it is clinically worthwhile because the treatment effect’s 95% CI spanned the nominated smallest worthwhile effect. Our subgroup analysis showed two factors to consider to further optimize a rehabilitation program with robots, aside from combining it with CT: type of robot and time since stroke.

For the subgroup type of robots, the EE group had a small significant treatment effect size for the outcome UL function favouring the combination of GBRT with CT. We could not provide evidence to support the superiority of EXO over CT, as a stand-alone training or as an adjunct. This finding could be related to the differences in the mechanical design between the two types of robots, which dictates the number of degrees of freedom required to control the device. EXOs are rigid devices that control multiple joints simultaneously, though the user’s movement is limited to what the robot allows.⁶⁸ EEs are less restrictive, since the robot is attached only to the most distal part of the limb, allowing for more voluntary control from the participant. Another difference is the greater number of degrees of freedom controlled by the robot in an EXO (at least 7 degrees of freedom) in comparison to EE (at least 2 degrees of freedom). Having less degrees of freedom in EEs, might require the user less time to adapt to how to perform the movements and more time to focus on the training.⁶⁸ However, the assumption that EE is superior to EXO could be inaccurate since the evidence had low certainty due to the majority of the participants deriving from trials with a high risk of bias and small sample sizes. This could indicate that the resulting effect size might be different to the true effect, which could lead to an imprecise assumption between the two robotic devices.

Moreover, for the subgroup analysis time since stroke, a more favourable outcome for UL function was observed for the 6 months or more group, favouring the combination of GBRT and CT.

The findings of this review are consistent with the findings of Wu et al (2021), where people with stroke had better UL function compared to acute stroke after robotic training.¹⁵² They argued that since spontaneous neurological recovery is possible in acute stroke patients, gains may be observed regardless of the type of training. This finding must be taken with precaution as the width of the confidence interval could be regarded as “very wide”, which indicates that more data is needed to make more conclusive and precise recommendation.

2.4.3. Strength & limitations

To our knowledge, this review and meta-analysis are the first to explore the effectiveness of a robotic regimen with a game component in UL function, independence, QoL and a range of common impairments after stroke. The GRADE assessment has shown that the certainty of the evidence for the primary outcomes of the functional performance of the UL and independence, is high and moderate, respectively. Meanwhile, the GRADE assessment for the secondary outcomes varied from very low to high. Participants coming from high-risk trials were the most common cause of the downgrade in the GRADE assessment. One of the limitations of this review is that trials with different duration of intervention have been pooled for meta-analysis. Hence leading to increased clinical heterogeneity that could have resulted in inaccuracy of the findings.¹⁶³

Some of the findings in this systematic review were uncertain or imprecise mostly due to the quality of the included studies and the sample size. Further studies are needed in this topic and should consider a rigorous methodology including randomisation and blinding. We also found that most studies included lacked transparency by not having a registered protocol or not indicating deviations from protocol. Moreover, future studies should further investigate the role of GBRT in increasing motivation, engagement, attention and, in turn, adherence to training. This could be done by comparing GBRT over a robotic training, without a game component. Moreover, the result of this study had revealed the importance of being transparent into training dosage to make a more accurate comparison between GBRT and CT.

2.5 Conclusion

Our findings suggested that GBRT and CT were equally effective in improving UL function, independence, QoL, muscle strength, hypertonia, and ROM. Moreover, when combining GBRT with CT, using an EE-based robotic device, we found a small, but possibly not clinically relevant effect in UL function. This could indicate that GBRT associated with CT could provide a more holistic training to people with stroke and an opportunity to practice high-repetitive and high-dosage training under various environment (actual/real and virtual).

Chapter 3

Game-based Robotics Training for Upper Limb function after Stroke: A mixed-methods study

Abstract

Introduction: Game-based robotic training (GBRT) could provide high-intensity, high-repetition training and increase adherence to rehabilitation and motivation of people with stroke. Given this, we explored the experiences and perspectives of participants with stroke after GBRT for the UL. We also explored the opinions and observations from their family member/carers. Lastly, we performed a preliminary assessment of changes in the Upper Limb function and Quality of Life after GBRT.

Methods: This study utilized mixed methods with a pre-post study design, semi-structured interviews and satisfaction surveys. The intervention consisted of 10 1 hour-sessions of GBRT to the upper limb using Tyromotion® devices, three times per week for 3 weeks. Potential changes in upper limb function and quality of life was measured using various standardized outcome measures. Family members or carers of the participants with stroke answered a survey on their perceptions of the training. Qualitative data were analysed using inductive thematic analysis, while quantitative data were analysed using descriptive statistics, and paired T-test or Hodges-Lehmann statistics.

Results: Twelve participants with stroke and 8 carers completed the studies. Five themes emerged from the semi-structured interviews reflecting positive perceptions and experiences from the training. The Satisfaction Surveys demonstrated that participants with stroke were highly satisfied with the training. There were no statistically significant changes pre and post GBRT for all the measures of upper limb function and quality of life. The perceived changes in upper limb function after GBRT and the high levels of satisfaction reported by the participants with stroke were mostly confirmed by their family member or carer.

Conclusion: Overall, this study has shown that people with stroke found GBRT enjoyable and motivating. The majority of participants perceived improvements to their upper limb function after training, which corroborated with the perceptions of their family members or carers. However, those changes were not supported by the performance-based outcome measures.

3.1 Introduction

Reduced upper limb (UL) function is one of the major problems faced by approximately 60% of the stroke survivors, which limits their physical function, independence, and quality of life.^{18, 29} Currently, the Stroke Guidelines recommend several interventions tailored to improve UL function, such as constrain-induced movement therapy (CIMT) and task-specific training.^{50, 52} Despite being considered the gold standard for UL rehabilitation after stroke, CIMT has several limitations. For example, the eligibility criteria for CIMT is very restrictive, meaning that a considerable proportion of stroke survivors with severe impairments are ineligible.⁵⁷ Moreover, the delivery and preparation of CIMT is time consuming and some individuals do not tolerate the restriction for the long periods of time required.⁵⁷ One of the most commonly utilised interventions for treating the UL after stroke is task-specific training, which is based on the repetitive training of a functional task and its components and has shown to be effective in stroke populations.⁵⁰ However, the intensity provided, and the amount of functional practice employed by therapists aiming to deliver task-specific training has been questionable.⁶²

Separately, there is evidence of low post-stroke exercise adherence rates especially after discharge from the rehabilitation hospital. This means that stroke survivors might not receive the recommended or sufficient dosage of training, which could compromise their recovery outcomes.^{80, 164} Even when stroke survivors do engage in exercise programs, 50% are still unable to incorporate their affected UL into normal daily activities even 6 months post-stroke.^{90, 165}

Interventions with the help of rehabilitation robots (robotics) have been developed to reduce some of the barriers identified above and to assist clinicians in providing high-dose training and potentially reduce the intensity of the labour required.⁴³ Previous research shows that robotic-assisted therapy can deliver a higher dosage of training, at a lower daily monetary cost, in the same amount of time of conventional therapies (CTs).¹⁶⁶ Additionally, several systematic reviews have highlighted the potential of robot-assisted rehabilitation in improving UL impairments and function after stroke without any adverse events.^{160, 167, 168} To further optimise the effects of robotic-assisted training, gamification of robotic training (GBRT) has been introduced. The gaming aspect can provide a fun and motivating training experience, which could improve outcomes by increasing

adherence.⁸⁶ Furthermore, motivating training options may enhance motor recovery as it encourages patients with stroke to perform an intensive and highly repetitive exercise, which is essential to yield neuroplastic changes to the brain after injury.^{86, 169, 170}

Currently, there are few studies that have explored the perspectives and experiences of end-users (people with stroke) after completing GBRT that found that a robotic training with game component is generally a well-accepted intervention, regarded as enjoyable and beneficial.^{171, 172} However, in these studies, the perspectives of family members or carers of the participants were not explored. Family members/carers opinions and point of views are relevant because these people are often significantly involved in the care of the person with stroke. They can be a useful source of information about a person's response to a training or health service and if their rehabilitation needs are being met.¹⁷³ Considering the end-user' and family member/carers perspectives, it is important to inform robotic rehabilitation programs that are patient-centred and, in turn, provide better care for patients.

Furthermore, there are few studies that investigated the experiences of patients with stroke towards GBRT for the entire UL using a set of robotic equipment targeted at different joints.^{114, 138} Therefore, this study aimed to engage with people with stroke, and their family member/carers to investigate their perspectives when using a suite of GBRT devices (Tyromotion®), that together provide training to the entire UL (i.e., finger, wrist, elbow, shoulder). Tyromotion® provides a set of devices that target the entire upper limb through an interactive therapy using a vast list of games. Moreover, this brand was chosen as a representative of GBRT since it is becoming widely utilized in Australia. According to the official distributor of Tyromotion® (CantleyMedical), there were approximately 30 rehabilitation centres/hospitals Australia that have at least one Tyromotion® device in 2020.

The primary aim of this study was to examine the experiences and perceptions of people with stroke following ten sessions of GBRT using Tyromotion ® devices. Our secondary aims were a) to examine the perception and opinion of carers or family members about the participants' (with stroke) experiences and responses to GBRT using Tyromotion ® devices.; and c) to perform a

preliminary analysis of possible changes in UL function following ten sessions of a multi-joint GBRT using Tyromotion ® devices.

3.2 Methods

3.2.1 Design

This mixed-methods study consists primarily of qualitative data that addressed the perceptions and experiences of participants with stroke. Furthermore, two 5-point Likert-Scales were developed and employed to assess participant's satisfaction and family/carers perceptions and observations. A pre-post design was utilized to provide preliminary data on potential changes in UL function and QoL after GBRT, using standardised outcome measures.

The protocol of this study was reviewed and approved by the University of Technology Sydney Human Research Ethics Committee under the number ETH18-3022. All participants provided written consent prior to joining the study.

3.2.2 Participants with Stroke

3.2.2.1 Recruitment and Selection Criteria

Participants with stroke were recruited from a community-based rehabilitation facility that provides exercise programs for people with neurological conditions (NeuroMoves gyms and Advanced Rehabilitation Centre) and on relevant social media and websites. We placed public notices on social media forums and stroke New South Wales (NSW) websites, such as EnableMe and the Stroke Recovery Association NSW to invite participants. Contact details of potential participants were obtained after initial contact had been made with the research team. Recruitment commenced on May 3, 2019 and finished in January 2020.

Adults (18 years or over) with a unilateral haemorrhagic or ischemic stroke for at least 6 months, with adequate communication ability and intact cognitive function (Mini-Mental Status Exam score ≥ 24 points) were eligible.¹⁷⁴ Participants were excluded if they scored 6 (maximal score) in the items Arm Function, Hand movements and Advanced Hand Activities of the Motor Assessment Scale¹⁷⁵ (to avoid ceiling effect), had severe muscle contracture in the shoulder, elbow, wrist or fingers that did not allow the use of robotic device, had severe spasticity (>2 on the Tardieu

scale)¹⁷⁶ on elbow, finger and wrist or had a visual impairment that did not allow them to see and interpret images on a computer screen. Once participants were enrolled in the study, they were asked to maintain their regular training routine (e.g. physiotherapy or occupational therapy). We aimed to recruit 12 participants with stroke as recommended by Julious et al (2005) for a feasibility study.

3.2.2.2 Baseline Assessments

Participants completed questionnaires about demographics (including type of and time since stroke, age, previous and current rehabilitation received and co-morbidities). Prior to training, participants underwent initial assessments (approximately 2 hours) of their UL function and quality of life (Appendix F). All assessments were performed by a physiotherapist (CQO) with experience in performing the assessments used and that was not involved in the delivery of the intervention. The baseline assessments took approximately 1.5 hours. See below for the description of the tools:

The Upper Limb Fugl-Meyer Assessment (FMA) is an assessor-based tool that measures UL recovery after stroke.¹⁷⁷ FMA is recommended to be a core measure to be included in a stroke trial by the Stroke Recovery and Rehabilitation Roundtable consensus.¹⁷⁸ It consists of 5 domains (motor function, sensory function, joint range of motion and joint pain) and each item is rated using a 3-point scale (0- cannot perform, 1 performs partially and 2- performs fully). In this study, we utilised the motor function domains. Scores range from 0 to 66, with higher scores indicating better UL function. Intra-rater reliability was rated as excellent for all domains (FMA total score: $r=0.98-0.99$, UL motor domain: $r=0.995-0.996$, sensation: $r=0.95-0.96$, and joint range/pain: $r=0.86$ to 0.996). The inter-rater reliability was also excellent for UL motor function ($r=0.98-0.995$). Excellent construct validity when compared to Barthel Index ($r=0.75$) was reported.^{179, 180}

The Action Research Arm Test (ARAT) is an observational tool to measure UL performance.¹⁸¹ ARAT is also recommended by as a core measure to be included in a stroke trial by the Stroke Recovery and Rehabilitation Roundtable consensus.¹⁷⁸ The test consists of 19 items grouped in four subtests (grasp, grip, pinch, and UL gross movement) rated using a 4-point scale (0- no movement to 3-movement performed normally). The inter-rater and retest reliability was rated as

high (ICC >0.98) for participants with stroke and the criterion validity was excellent ($r=0.94$) when compared with the UL Fugl-Meyer Assessment Scale.

The Motor Activity Log (MAL) is a patient-reported questionnaire that assesses the amount of use^{182, 182} and quality of movement (QOM) of the affected UL after a stroke in 30 activities of daily living (e.g. button shirt, use fork).^{182, 183} Participants are asked to rate the AOU and QOM of their affected UL using scores ranging from 0 to 5 (0- did not use the paretic UL to 5- used my affected UL as before/ usage of affected UL was good). Internal consistency was high (AOU: $\alpha=0.88$ and QOM $\alpha=0.91$) and it has reasonable construct validity when compared to accelerometry ($r=0.7$).¹⁸⁴

The Stroke Specific Quality of Life (SSQoL) is a patient-reported questionnaire that contains 12 domains (mobility, energy, UL function, work/productivity, mood, self-care, social roles, family roles, vision, language, thinking, and personality) to assess health-related quality of life (QoL) specific in people with stroke.¹⁸⁵ It is a 5-point Likert-scale with 3 different response sets: a) 1: total help to 5: no help needed; b) 1: could not do it at all to 5: no trouble at all; and c) 1: strongly agree to 5: strongly disagree. Test-retest ($r=0.92$) was rated as excellent and internal consistency ($\alpha=0.75$ to 0.89) was rated as adequate to excellent.¹⁸⁶ Criterion validity was rated as fair ($\rho=0.25$ to 0.31) and construct validity was established ($r=0.3$ to 0.5) in comparison to the Beck Depression Inventory, the Barthel Index, the 36-Item Short Form Health Survey and the National Institutes of Health Institutes of Health Stroke Scale.¹⁸⁷

3.2.2.3 Post-intervention Assessment

The post-intervention assessment took on average one hour to be completed. Immediately after the last training session, participants repeated the baseline assessments and completed a Satisfaction Survey and the Participant Perception of Treatment Scale (Appendix F):

The Satisfaction Survey was developed by the research team to assess satisfaction, experience, and perception of the participants with the devices and games employed for GBRT. The survey consisted of a 5-point Likert scale to capture the participants' degree of agreement/disagreement on the overall satisfaction, experience, and perceptions towards safety,

comfort, willingness, and enjoyment when using the devices. The areas explored in the satisfaction survey were adapted from the Acceptability of Robotic Therapy questionnaire developed by Mazzoleni et al (2014).¹⁷¹

The Participant Perception of Treatment Effectiveness is a tool to quantify perceived change after receiving an intervention. It is scored from +7 to -7, where +7 means the perceived change is “a great deal better”, 0 means “almost the same”, and -7 means “a very great deal worse”.¹⁸⁸

3.2.2.4 Follow-up Assessment

One week after the termination of training, the quality of life and physical assessments collected at baseline were re-performed to test for maintenance of any possible changes. The semi-structured interview was also held at this time. The follow-up assessment lasted approximately 1.5 hours.

3.2.2.5 Semi-structured Interviews

During the follow-up assessment session, participants with stroke were invited to attend a one-on-one, audio-recorded semi-structured interview (see Appendix H), which was held in a private room at the University of Technology Sydney, Moore Park Campus. A member of the research team (CQO), who did not participate in the delivery of the GBRT and who had previous experience in interviews, conducted all interviews. Participants with stroke were interviewed individually unless they requested the presence of their carer/family member. The interview aimed to explore participants’ opinions, beliefs and experiences with the training protocol, devices, and games.

3.2.2.6 Training protocol

All participants with stroke received an individualised GBRT program based on their impairments and functional abilities using the Tyromotion ® rehabilitation suite. Box 3.1 describes the principles used to ensure an individualised protocol for each participant. Figure 3.1 describes the decision framework used to set up the robotic training based on the participant’s abilities. Figure 3.2 provides examples of the games utilized during training.

Box 3. 1 Specific training regimen using Tyromotion

Training Regimen using Tyromotion	
1.	Dosage of training, including intensity, level of difficulty, presence, and level of assistance from the robotic device and duration of exercise per machine was based on the impairments and activity limitations identified during the baseline assessments (see Figure 3.2).
2.	Participants could choose any game of their preference. If he/she wished to change the game, they were allowed to do so but the level of difficulty always started at the previous completed level on that particular game of choice (see Figure 3).
3.	Pablo (forearm trainer) was not used if there was no movement in both the forearm and wrist since Pablo is a sensory-based device and not robotic device and therefore, does not provide assistance to the patient.
4.	2D games were used for joints where more than 2 planes of movement are possible (Shoulder and wrist joint) and 1D games for the joints where 1 plane of movement is possible (Elbow, hands and fingers joints).
5.	Control mode is the way the patient controls the game. In Amadeo, movement control was used to allow movement of the fingers. In Diego, frontal plane control was used as this mode allows the patient to do activities that mimics overhead reaching and other functional tasks of the shoulder. Finally, in Pablo, motion control was used as this mode senses movement of the wrist and forearm.

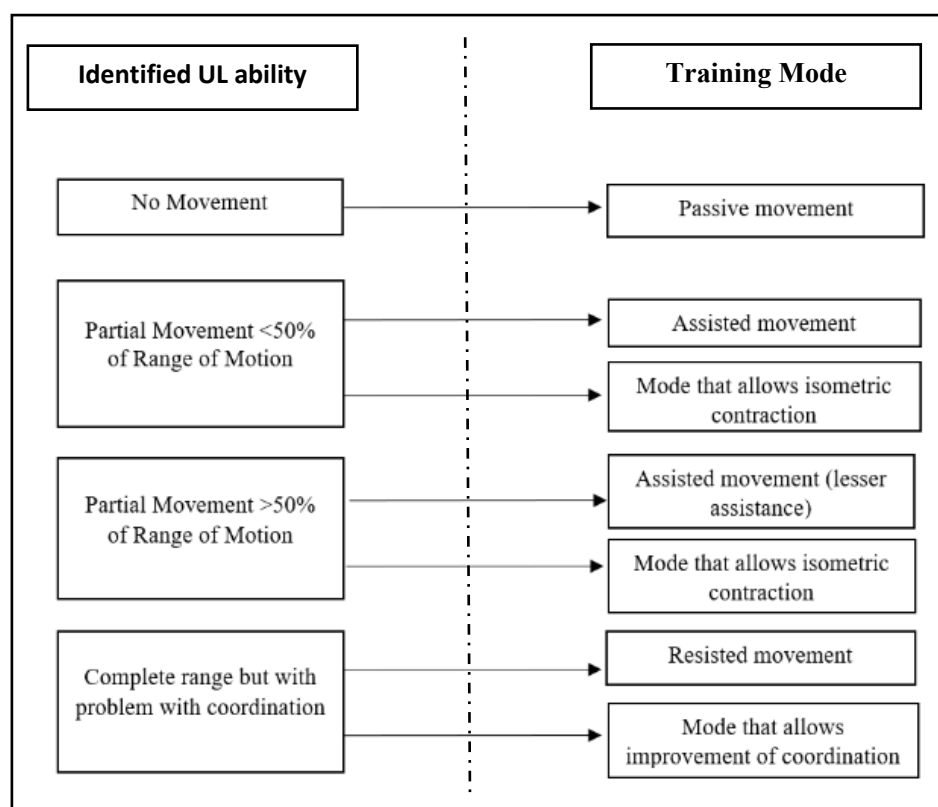


Figure 3. 1 Protocol based on identified limitation on baseline assessment

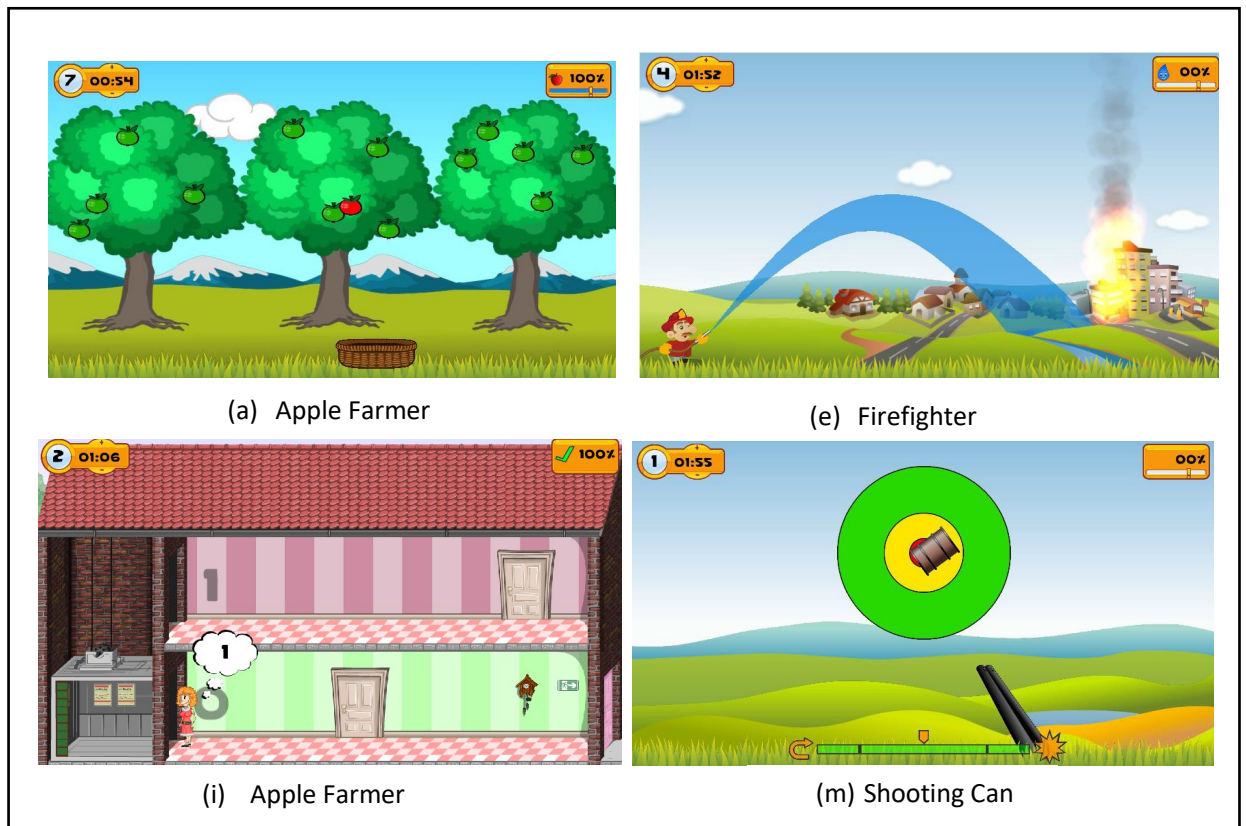


Figure 3. 2 Example of games used in the training

The training program consisted of 10 sessions, delivered over a 3-week period based on the findings of Veerbeek et al (2017)¹⁶⁸ Each training session took 60 minutes and was delivered by a Physiotherapist trained by a Tyromotion® representative. It is worth noting that the 60 minutes was the total training time per session. Set-up time, breaks and rests were not counted as part of the training sessions. In case of rest/breaks and changes to set up required during training, the training time was paused and resumed once the break/rest or set up was finalised. The rehabilitation protocol consisted of three Tyromotion® gaming devices that targeted the shoulder-elbow (Diego®), forearm-wrist (Pablo®), and fingers and thumb (Amadeo®). Table 3.1 describes the training devices employed in the study.

Table 3. 1 Devices used in the training and their description

Device	Description	
Amadeo TM	Fingers and thumb training. A distal end-effector robot that allows training of different grasping movements. It utilizes sensors to send feedback to the participant on their performance in a given task and provides assistance or resistance, as needed.	
Pablo stick TM and Multiball TM	Elbow and wrist training. A 2-dimensional handheld multiball therapy or stick device. It is sensory-based and used to train gross grasp, wrist and the forearm movements in 1 or 2 dimensions.	
Diego TM	Shoulder training. An intelligent gravity compensation device. Provides unilateral and bilateral assistance by supporting the weight of the UL. Allows bilateral or unilateral movements of the arm at the shoulder joint. As seen in the image, the elbow and the wrist are connected to a four retractable rope, which is controlled by four separate motors equipped with sensors.	

**Images from Tyromotion Manual and official website*

The initial session was used to determine the level of difficulty for each of the gaming programs. As participants became better at playing the games, the difficulty (level) was increased over

the 10 sessions. At the start of each session, training difficulty was set at one gaming level below the level achieved in the preceding session. Set-up time, breaks and rests were not counted as part of the training sessions. In case of rest/breaks, the training time was paused and resumed once the break/rest was finished.

3.2.3 Family members/carers

3.2.3.1 Recruitment and Selection Criteria

Family members or employed carers who lived with the participant with a stroke or provided assistance in mobility and/or self-care activities for at least 4 hours per day and that were fluent in English were invited to take part in the study. They were invited to join the study via a letter of invitation provided to the participant with a stroke to pass onto their chosen family member/carer during the study. In the case of multiple family members/carers, only one carer/family member answered the survey if he/she fitted the selection criteria of the study. Their contact details were obtained after they consented to join the study.

3.2.3.2 Family members/carers Perception and Observation Questionnaire

The family members/carers completed an online questionnaire via RedCap or paper-based survey, according to their preference. The link to the online survey or printed copy of the questionnaire was made available when their clients/family member with stroke completed the training sessions. The questionnaire was developed by the researchers and consisted of Likert-scale questions on the amount of assistance provided during self-care and mobility tasks and their perceptions about the participants with stroke in relation to the robotic training, including perceived changes and opinions on the protocol and devices. The estimated time for completion was 30 minutes. (Appendix I)

3.2.4 Data Analysis

Qualitative data from the semi-structured interviews were analyzed using inductive thematic analysis as described by Braun and Clarke (2015).¹⁸⁹ The process started with familiarization with the data by reading the transcripts and listening to the interviews repeatedly (more than twice). After that, two researchers (ELR, MC) performed the open coding independently. The first step in the coding process was the identification of the unit of analysis, which is a word, phrase, sentence, or

paragraph that basically portrays one idea. This was followed by assigning a code to each unit, which was a word or a phrase that represented the meaning of the unit of analysis. Consensus amongst the coding researchers was reached through discussion. If there were disagreements, a third more experienced researcher, was consulted (CQO, EP).

After coding, categorization was performed. All codes with a common meaning were merged to a common code by three authors (ELR, CQO, EP). A visual map on Idea Flip software was created to illustrate the relationship between codes, which helped to identify themes and subthemes (see Appendix J). Multiple discussions were held until the authors were confident that the themes and subthemes accurately and comprehensively reflected the data from the semi-structured interviews.

Descriptive statistics were used to summarize the data from the demographic questionnaires. Data from the Participant's (with stroke) Satisfaction Survey, Participant Perception of Treatment Effectiveness scale and Family members/Carers Perception and Observation Questionnaire were analyzed using frequencies.

Pre and post assessment data was initially analysed using Shapiro-Wilk Test to determine normality of data since sample size was small¹⁹⁰. If data were normally distributed, then paired T-tests were used to analyse the change in score in line with 95% Confidence Interval (CI). If data were not normally distributed, median differences with 95% CI using Hodges Lehman Estimator was performed¹⁹¹. Moreover, individual scores were also presented in a graph to illustrate change score and compared to the minimal clinical important difference (MCID), if available in the literature. The following MCIDs were used: UL function (FMA (motor) MCID = 5.25, ARAT MCID = 5.7, MAL QOM = 1.0, MAL AOM = Not published MCID)^{192, 193} and QoL (SSQoL MCID = Not published MCID). For outcome measures with no published MCID, 15% of their total score was considered as the MCID¹⁹⁴. Hence, for SSQoL the MCID was set to 36.75 (total score=245) and MAL AOM was set to 0.75 (total score=5).

3.3 Results

3.3.1 Participants with Stroke

We recruited 12 participants with stroke, and they all completed the intervention and assessments. Their characteristics are described in Table 3.2. The mean age of participants was 56.6 (SD= 11.4) years; the mean duration post-injury was 66.9 (SD= 37.0) months; the mean Mini Mental Status Exam (MMSE) score was 29.9 (SD=0.3); and the mean Motor Assessment Scale (MAS) was 2.7 (SD= 2.3). Many of the participants were male (58%) and had an ischemic stroke (67%). Moreover, all the participants had a single stroke, two reported that they had hypertension, three reported that they were diagnosed with a cardiac problem (irregular heart rhythm, pacemaker and ischemic heart disease). Finally, mostly (n=10) were actively enrolled in a rehabilitation program apart from the study.

Table 3. 2 Characteristics of Participants with Stroke at baseline

	Age	Gender	Type of stroke	Time since Stroke (months)	MMSE (0 to 30)	Motor Activity Scale			FMA UL Function (baseline) (0 to 66)
						Upper Arm (0 to 6)	Hand Movement (0 to 6)	Advanced Hand Movement (0 to 6)	
P1	52	F	I	46	30	6	6	5	58
P2	64	F	I	37.88	29	1	0	0	5
P3	53	M	H	42.95	30	6	6	3	53
P4	54	M	I	58.2	30	6	0	0	19
P5	70	M	H	96	30	0	0	0	4
P6	59	F	H	32.43	30	6	6	4	59
P7	46	F	I	91.49	30	1	0	0	9
P8	68	M	I	43.66	30	0	0	0	5
P9	69	M	I	129.92	30	4	5	5	35
P10	31	F	H	136.85	30	6	4	4	36
P11	63	M	I	43.92	30	2	1	0	11
P12	50	M	I	43.46	30	4	5	2	32
Mean (SD)	56.58 (11.35)	7:5 (M:F)	4:8 (H:I)	66.90 (36.99)	29.92 (0.29)	3.5 (2.5)	2.75 (2.77)	1.92 (2.15)	27.17 (21.26)

M- Male, F- female, H-haemorrhagic, I- ischemic, MMSE- Mini-mental Status Scale, FMA- Fugl-Meyer Assessment

3.3.1.1 Experiences and Perceptions after GBRT

Thematic analysis of the semi-structured interviews resulted in five main themes with 15 subthemes describing the experiences and perceptions of the participants with stroke about GBRT (Figure 3.3). Overall, the participants with stroke thought that the intervention was beneficial and enjoyable.

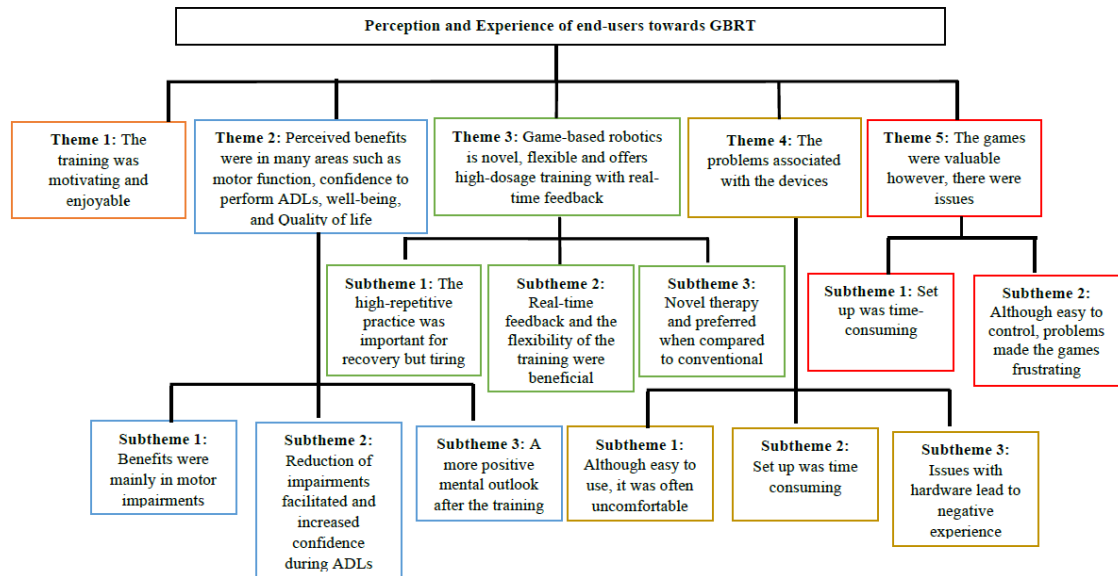


Figure 3. 3 Schematic diagram of themes and subthemes illustrating participants with stroke perspectives and experiences using GBRT (*see quotations below illustrating each theme*). Note that each colour corresponds to a theme and its subthemes.

Theme 1: The training was motivating, enjoyable and helpful.

The first theme described the overall perception and experience of the participants towards the training. Overall, participants' perception and experiences were positive. There was a perceived benefit in joining the training, while having a good experience. They described the intervention as "enjoyable", "motivating" and "pleasant". This was reinforced by the fact that all of participants were willing to join GBRT, if given the chance.

All participants with stroke agreed that they benefited from the GBRT. One participant even suggested that this type of training regimen should be available to all and one participant was surprised to have experienced benefits from joining the study.

“To be honest with you, the fact that I was going to benefit from the experience was a surprise for me. I did not anticipate that there would be a benefit. I thought that I was just making a contribution rather than receiving a benefit.” - P7

However, three participants experienced no benefits after training.

Theme 2: Benefits were in many areas: motor function, confidence to perform ADLs, well-being, and Quality of life

Most participants perceived improvements in impairments, activity limitations and mental outlook after training. Perceived improvements in muscle control, strength, endurance, and joint range of motion were reported. All participants with stroke had reported “ease of movement” on at least one joint, which could be either during active range of motion or when another person was moving their UL to provide assistance. The majority (n=9) had reported that the reason for the “ease of movement” was due to reduced stiffness or spasticity in the joints.

“The benefit from lifting my hand and the range of motion I think is improved a lot. I can lift my arm higher, I can do this, I can swing my hand. I could not do that before... Now the stiffness has changed. Now it is good, it is more relaxed, it is not rigid.” – P4

Conversely, one participant reported no improvements in strength and four participants reported no changes in range of motion despite receiving GBRT.

Most participants (n=10) reported that there were reductions in motor impairments that seemed to have translated into better performance in various ADLs. Furthermore, for some (n=4) the reduction of impairments increased their confidence in performing activities with the affected UL as illustrated by the quote below.

“I think supination was a little bit better. It might’ve gained a couple more degrees than it was before. Before when I was washing my face, it was a little bit harder when I didn’t have that extra degree. Now it’s a lot easier. And to

sort of, when I am brushing my teeth to pick up water and put it into my mouth, I am a lot more precise”-P1

“It’s more responsive the fingers...It helps me when I am doing the dishes because I can hold the dishes more confidently”- P9

Other areas of improvement in ADLs were bed mobility (e.g., use of the arm when getting in and out of bed), hygiene (e.g., washing hair), dressing, helping in household chores (e.g., wiping counters) and driving (e.g., grabbing the steering wheel). Furthermore, five participants reported a better mental outlook after GBRT because they felt a “sense of accomplishment”, increased “hope” and that they felt “good” after the training.

“Yes, it felt good because it had movements. Anytime my left arm had movement is positive. It’s beneficial and positive.”—P10

“Yeah because if there’s a movement there you can see, there is hope. Some people because it doesn’t move, it mean “I lost my hand movement” but if you find out that there is still movement hopefully he/she they will do more exercises”—P3

Theme 3. Game-based robotics is novel, flexible and provides high-dosage training with real-time feedback

The third theme illustrated the characteristics and the features of GBRT that participants acknowledged as important. Participants valued the versatility of the training and found that the training was specific to their needs after the stroke. Highly repetitive training was one of the key perceived components of GBRT. Participants described the training as having “good number of repetitions” and “an elegant way to bombard the repetition”. Four participants reported tiredness after training, which they perceived as important for recovery. Fatigue was commonly experienced early in the training period but decreased as the training progressed.

“There were good number of repetitions. In the beginning, I have to ask for a break in between. But as it went by, I remember with the fingers especially after

three minutes I had to have a break, but in the last session I remember so vividly I did the whole 10 minutes.” – P11

Another feature of the training that was perceived as positive by the participants was the real-time feedback. Six participants said feedback was “motivating”, helped them to be engaged with the task and acted as a guide during the training.

“It helped my brain to think from moving from one side to another, sending the message, and also activating my hands to move. So, it gives me vision to see something in front of me so I can make my judgement. So, the judgement sending the message here in my head- so you have to pick up something in that game. So you are struggling to move but it helps to make you think that you are supposed to catch it.”- P4

Another feature of the GBRT perceived as positive by the majority of participants (n=7) was the flexibility in providing assistance or resistance according to their needs. One participant described this feature as “incredible” because it helped them to move their affected UL.

“I liked it because it is designed in a way to move your weaker hands... you can see that it is helping the weak side to move. When I went home, I felt like I have done a lot of training”-P4

Theme 4: The problems associated with the devices

Six participants reported experiencing issues with at least one device used in the training. Although generally perceived as easy to use, participants reported that the severity of their motor impairment affected their comfort in using the devices. For 3 participants, the presence of stiffness in the hand and fingers impacted the proper fitting of the hand to the devices. Moreover, three participants reported that setting up the devices was “time consuming”, “frustrating”, and “distracting” and affected their overall experience negatively.

“I found also with the hand one (when) I was trying to squeeze; I was turning every muscle on. So, it was kind of like hurting in the straps and things, so it was

a little bit sore, whereas the shoulder one (it) was easier cos you just had to move your arm and your forearm and your shoulder. It was a bit easier to use”—P6

“It always cuts into my hand because my hand is bigger. So when the wrist sits there, you need something to cushion it up properly. So my wrist whenever I go here, it always cuts into my hand because my hand is bigger and the grid is too rigid so it need to do that so it get cushion your hand”—P4

“Often, it took a little time adjusting the contractions that was right for me as an individual. So that you know, I just felt that if some of those settings could be plotted the next time I attended or for what it would be it will just be repeated or less precision required from the operator”—P7

Theme 5. The games were valuable, however, there were issues

Most participants (n=11) appreciated the gaming component of training. They describe it as “directive” and found that the tasks were important for recovery “helpful”, “enjoyable”, “interesting”, and “fun”. Participants felt that the games were helpful to boost their performance and kept them engaged in the training. The accuracy and sensitivity of the software to movement was considered positive, and one participant described it as “quite wonderful”. Moreover, game-based therapy was considered as a good way to “trick the mind” to do more repetitions as illustrated by the quote below:

” I think the computer-based training is a distraction to the monotonous task of rehabilitation so having someone being occupied while they doing rehabilitation is fantastic. I think I did more repetitions because I did not realize I was doing the repetition; I was playing games. So, I was kinda tricking my brain.”-P12

Three participants found that the games design and animation seemed to be simple and often “too basic”, “child-like” and “would require updating”. Two participants experience glitches (e.g.,

program sometimes did not show the correct response for a movement) during the training, which affected their overall experience negatively.

“Some mistake on the on the program because they should have the writing blocking. There’s no icon, there’s people getting there who cannot leave and they got big timing on a couple of tape and then it then block the view and we can’t see and it confuse us.”- P5

Participants suggested several ways to improve the GBRT, which included changes in the games, and hardware. Some of the recommendations were: to add a program to count repetitions of movements during the games; to add more variety and have more interactive games; to add a program that could provide real-time position of limbs during training; to change the music to more age-appropriate; to modify hand support so that it could accommodate users with bigger hands; to add a cushion for support to the wrist area and Pablo TM stick; to develop a physical blocker between fingers; to strengthen the magnets used in Amadeo TM to prevent frequent detaching; and to utilize the Nintendo Wii games TM together with GBRT.

3.3.1.2 Satisfaction with GBRT

The results from the satisfaction surveys are presented in Figures 3.4 and 3.5. Ten participants felt that the intervention addressed their rehabilitation needs, majority of participants (n=7) reported experiencing increased UL strength, half (n=6) were neutral when asked about improvements in ADLs, and in addition, half of participants (n=6) reported increased confidence to performing ADLs.

Participants with stroke generally reported a positive experience undergoing GBRT. Majority of the participants (n=10) reported feeling good after the training and enjoyed the robotic and gaming components of the training. Nine participants experienced tiredness after the training. Finally, most of the participants (n=11) agreed that the training was interesting and would like to undergo the same training again (n=11), if given the chance.

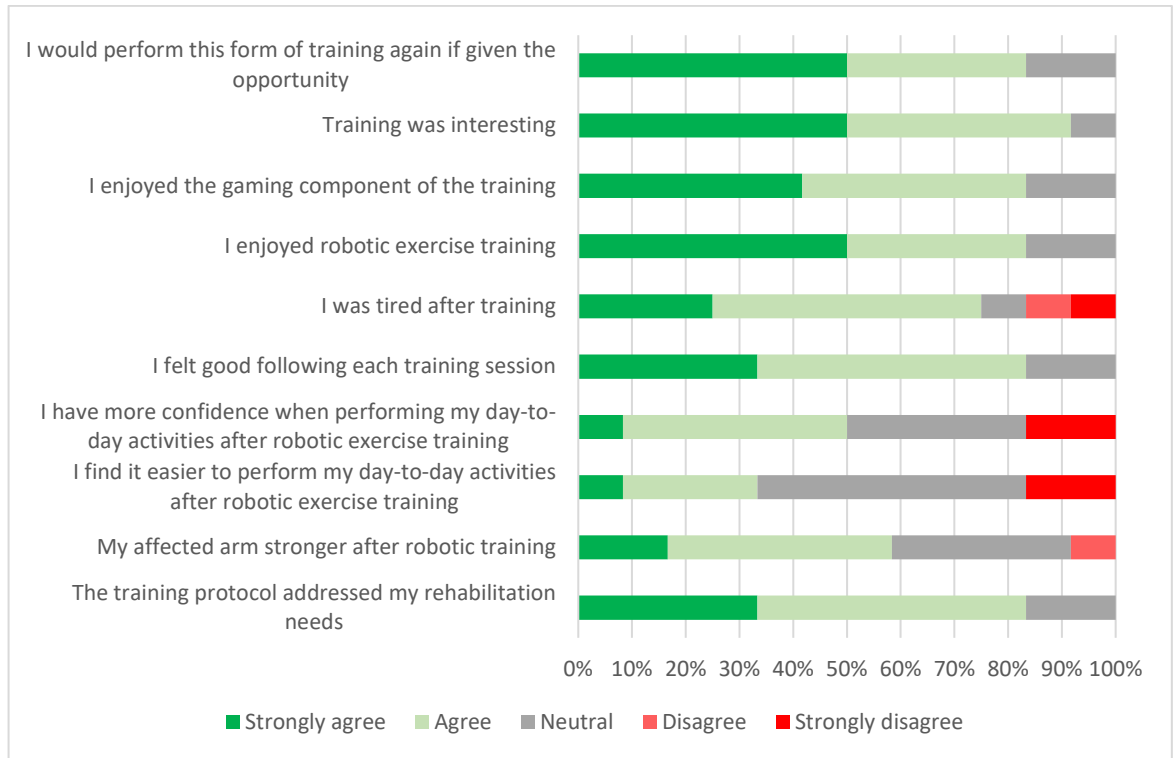


Figure 3. 4 Overall perceived benefits and overall experience of participants with stroke

The surveys also revealed that most participants (n=9) were satisfied with the device used for hand training and found the training motivating and safe. Three participants found the device uncomfortable. All participants were satisfied with the device used to train the forearm and wrist and found it comfortable and safe, with majority of participants (n=7) reported feeling motivated when using it. Most participants (n=11) were satisfied with the shoulder and elbow training device and found it safe, while ten felt motivated while using it and ten found it comfortable.

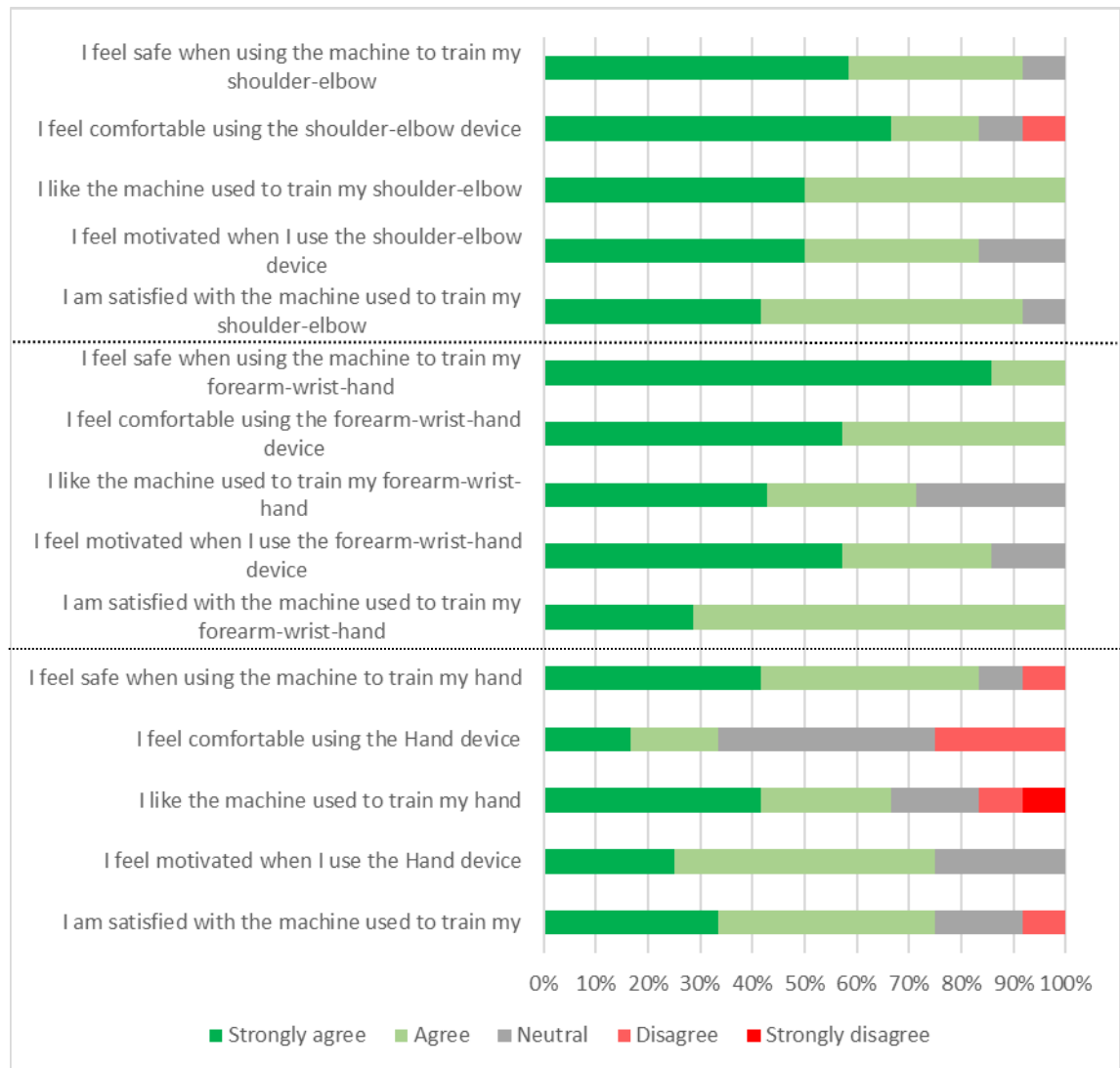


Figure 3. 5 Satisfaction of participants with stroke specific to device used.
 Note: The top portion illustrates the perception and experiences of participants with stroke towards the shoulder-elbow training device, the middle portion illustrates the participants' responses for the forearm-wrist-hand training device, and the bottom portion illustrates the responses for the hand training device.

3.3.1.3 Adherence, retention, adverse effects and preliminary data of changes in UL function and QoL

Twelve participants were enrolled in the study. Six participants completed the planned training sessions (i.e., 10 training sessions in 3 to 4 weeks) and six participants completed ten training sessions but with changes in their training schedule due to unforeseen appointments (e.g., medical or unexpected personal appointments). No drop-outs were reported.

No serious adverse events were reported at any stage of enrolment in the study. However, two participants experienced pain during sessions, and a few had reported muscle soreness after sessions, especially at the early stages of training. The pain and soreness went away after resting or removal of the source of pain (e.g. wrist hitting the metal side of the hand support).

There was no significant nor clinically worthwhile changes after GBRT as described in Table 3.3 The 95% CI spanned the MCID for UL function and QoL. Figure 3.6 shows individual scores for each participant (see Appendix E for individual scores for each outcome measure).

Table 3. 3 Mean change/Median change in functional performance of the UL and QoL

Outcome Measure (scoring)	Mean (SD)/Median (IQR)**			Mean/Median Difference (95% CI)**		
	Pre (T0)	Post (T1)	Follow Up (T2)	Post-Pre	Follow up-Post	Follow up-Pre
UL FMA (motor subsection) (0 to 66)	27.25 (21.29)	29.25 (21.91)	29.58 (23.56)	2.00 (-0.13 to 4.13)	0.33 (-2.07 to 2.75)	2.33 (-0.20 to 4.87)
ARAT (0 to 57)**	8.5 (1-50.50)	16.00 (16.00-54.5)	19.00 (0.25 – 54.50)	0.00 (0.0 to 6.5)	0.0 (0.0 to 3.0)	1.5 (0.00 to 6.5)
MAL AMT (0 to 5)**	0.89 (0.00-2.5)	1.04 (0.00-2.47)	0.98 (0.00-2.23)	0.0 (-0.16 to 0.3)	-0.12 (-0.27 to 0.02)	0.04 (-0.16 to 0.18)
MAL QOL (0 to 5)**	0.68 (0.00-2.19)	1.13 (0.00-2.43)	0.98 (0.00-2.24)	0.13 (-0.15 to 0.52)	0.0 (-0.19 to 0.15)	0.13 (-0.05 to 0.47)
SSQoL (49 to 245)	167.25 (34.27)	172.83 (34.26)	184.42 (35.27)	5.58 (-7.02 to 18.19)	11.58 (-5.30 to 28.46)	17.17 (3.53 to 30.80)

Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT), Motor Activity Log Amount (MAL AMT), Motor Activity Log Quality (MAL QOL), Stroke-specific Quality of Life (SSQoL)

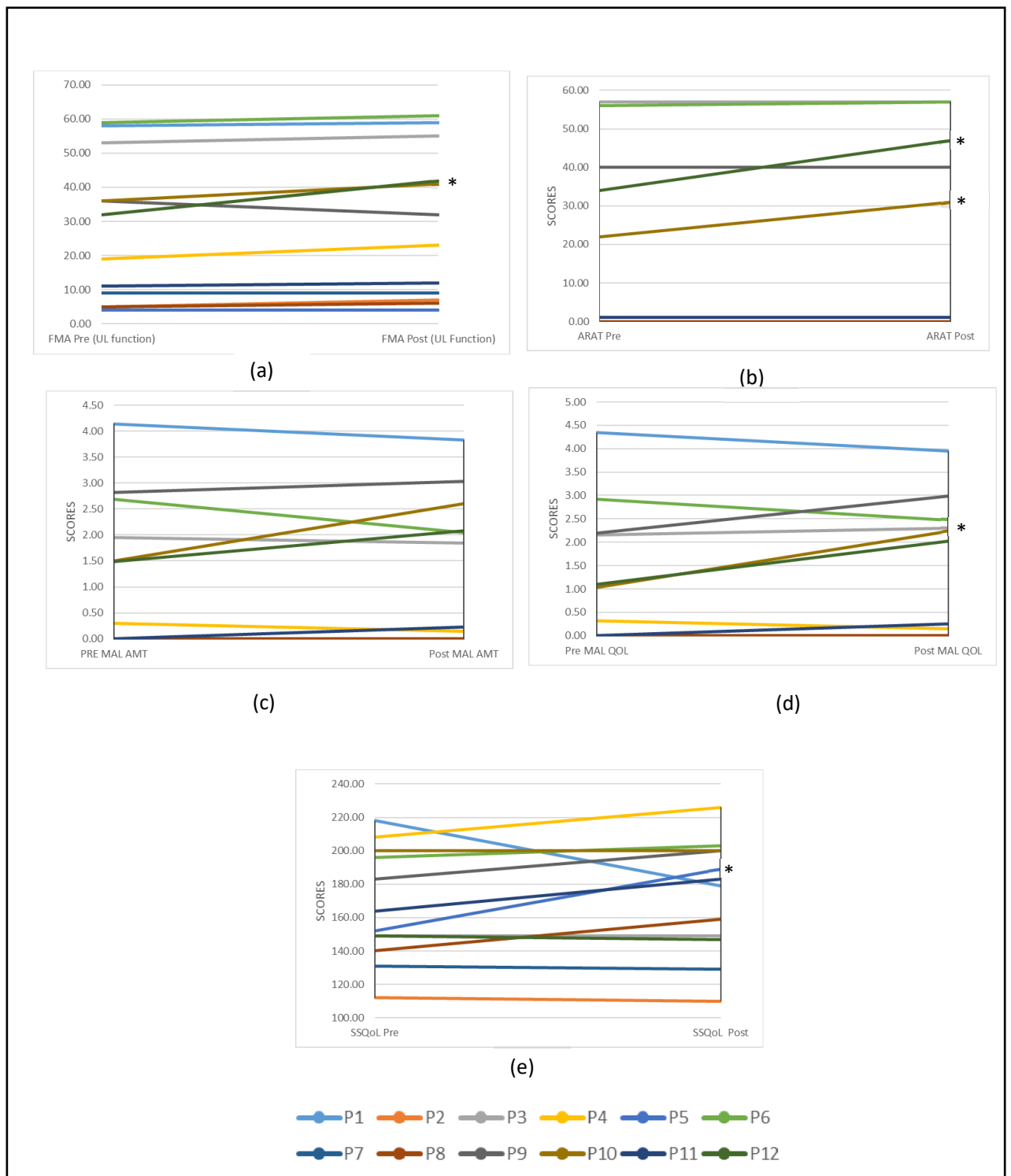


Figure 3. 6 Individual pre-assessment and post assessment scores for UL function and QoL: (a) FMA, (b) ARAT) (c) MAL AMT (d) MAL QOM (e) SSQoL * indicates it surpassed a published minimal clinical

3.3.1.4 Participant Perception of Treatment Effectiveness

Eleven participants (92%) reported that their condition improved after GBRT, while one participant (8%) reported experiencing no changes in their condition. The mean score for the

Participant Perception of Treatment Effectiveness scale was +3.25, indicating that participants felt that their condition was “*somewhat better*” after GBRT (Table 3.4).

Table 3. 4 Individual scores on Perception of Treatment Effectiveness

Scale		Participants
Almost the Same	0	P5
A little better	+ 1	P3, P7, P8
Somewhat better	+ 2	P9, P10, P11, P12
Moderately better	+ 3	P2
A good deal better	+ 4	None
A great deal better	+ 5	P1, P4, P6,
A very great deal better	+ 6	None

3.3.2 Perceptions of Family Members/Carers

The family members/carers from the 12 participants with stroke that joined the study were invited to complete the questionnaire, however only 8 returned it (Table 3.5). The mean age of family members/carers was 49.67 (SD=18.24) years. The majority were males (62.5%) and had 50% had a bachelor’s degree.

Table 3. 5 Demographic Profile of Clinicians and Family Member/Carer

	<i>Family Member/Carer</i>
Sample Size	8
Age, years (SD)	49.67 (18.24)
Gender	Male:5, Female: 3
Highest Educational Attainment	High School: 3, Bachelor’s Degree: 4, prefer not to say: 1

3.3.2.1 Family members/carers Observation Questionnaire

Family members/carers observed that the people with stroke who joined the study had a better UL function after GBRT (n=5). Three disagreed that their family member/clients with stroke performed day-to-day tasks easier and more confidently. Moreover, family members/carers observed that the participant with stroke enjoyed both the gaming (n=8) and the robotics (n=7) components of the training and were interested (n=8) and motivated (n=8) during the training period (Figure 3.7).

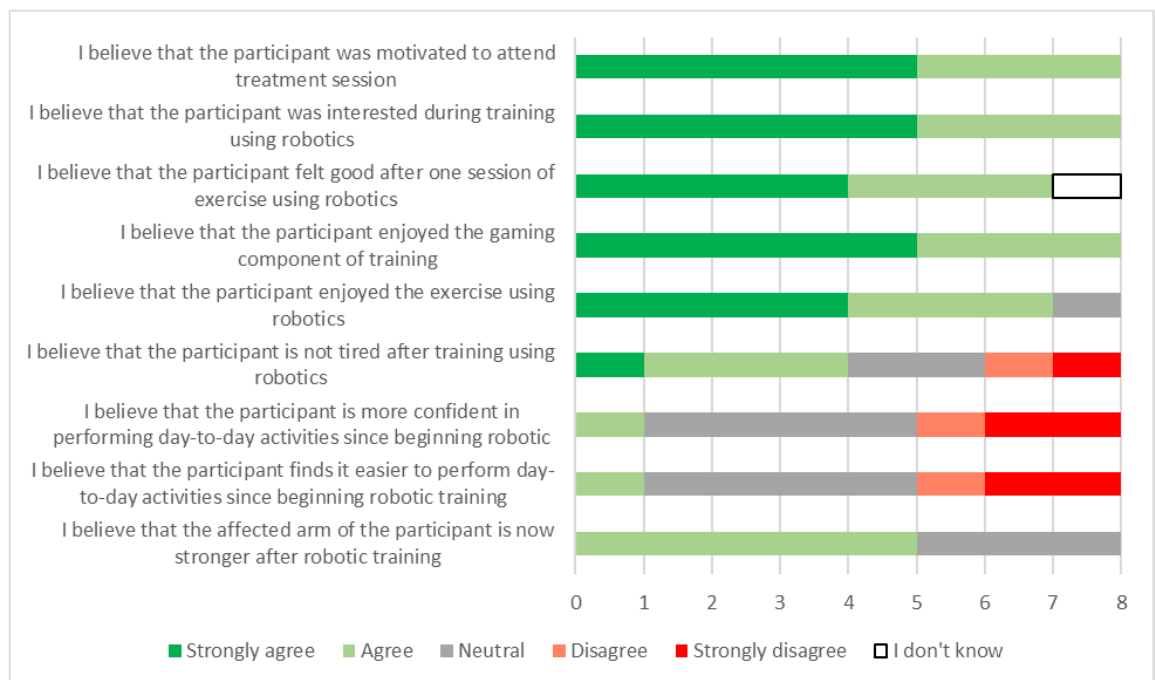


Figure 3. 7 Family member/carers observation on their family member/client with stroke after GBRT

The positive aspect of GBRT from the perspective of the family and carers were: “enjoyable training” (n=8), “more positive attitude towards condition” (n=6), “use of UL more in ADLs”, “more confidence in using UL in ADLs” and “more independent on ADLs” (n=1). Meanwhile, the negative aspects from the perspective of family member/carers were: “no improvement in using the UL” (n=3), “no improvement in confidence in using the affected UL” (n=2), “not an interesting training” (n=2), “no changes in attitude towards condition” (n=2), and “no changes in the level of assistance required” (n=2).

3.4 Discussion

The current study evaluated the overall perceptions and experiences of people with stroke after GBRT. It also explored the opinions of their family members or carers. There were four key findings in this study: 1) Participants with stroke had an overall positive experience undergoing GBRT; 2) The issues with the devices (e.g., hand support too small, frequent attachment/detachment to the device, glitches) caused discomfort and wastage of treatment time; 3) There was a discordance in the changes and benefits detected by the patient-reported outcome measures and the performance-based measures; 4) The feedback and the games could help facilitate high-repetitive training.

Our participants found GBRT an enjoyable and motivating training modality and majority perceived benefits to their affected UL, which was frequently confirmed by their family member/carer as illustrated in Figures 3.8 and 3.9. This finding is confirmed by Mazzaoleni et al that investigated the acceptability of end-effector GBRT in 34 participants with chronic stroke and found a perceived enjoyment between moderate to strong.¹⁷¹ In our study, the vast majority of participants 10/12 reported enjoyment from taking part in GBRT and all participants acknowledged having had a positive experience, which was confirmed by their family members/carers as illustrated in Figure 3.8.

All participants with stroke in the present study reported willingness to undergo further training, if available, which was evident by the 100% attendance to sessions from all participants. Adherence is the key to reacquiring lost motor skills after a stroke.⁸⁰ In our study, there is an indication that GBRT could facilitate greater adherence, which could be related to the gamification component that can provide a fun way to train as revealed by our qualitative data. This could be explained by a phenomenon called *hedonic motivation*, which refers to the phenomenon of undergoing or continuing to undergo a treatment because the participant perceives the treatment as fun, interesting and enjoyable. A qualitative systematic review argued that hedonic motivation is more noticeable in training with games because, by nature, they are interactive and pleasurable.⁸⁶ Adding games into robotic training, which is known to provide high-volume and high-repetitive training, could be a way to attract users to adhere to rehabilitation programs.^{86, 195}

All stroke participants in this study reported a willingness to undergo highly repetitive training despite feeling tired after each session, since they recognized that a high volume of therapy is important for improvements. High- repetitive training is vital for neuroplasticity that could elicit sensorimotor recovery. Kleim and Jones (2008) on their work presenting the ten principles of neuroplasticity, highlighted that active participation, high number of repetitions and high intensity are key elements to induce neural reorganization following injuries to the brain such as stroke.⁴⁰ Those elements can be facilitated by GBRT. In our study, we counted the number of repetitions performed by the participants during training. Participants performed at least 150 repetitions in 20 minutes, which was significantly greater than the previously reported average of approximately 38 repetitions performed by patients with stroke per session in an out-patient clinic.¹⁹⁶

In our study, two features of GBRT allowed participants to achieve high-repetition training: 1) ability to help and 2) ability to provide motivating and real-time feedback. The ability to help was important especially for those with severe impairments. It is worth emphasizing that providing assistance, using the robotic device, does not diminish active participation¹⁹⁷. Hospital charts of 16 participants with sub-acute stroke who underwent training with robotic devices revealed that the assist-as-needed component of the training promoted active participation. In addition, the ability to provide feedback plays an important role in motor recovery¹⁹⁸. In our study, participants with stroke and family members/carers valued the feedback, in the form of games and considered it motivating. Participants reported that the games “tricked their mind”, since it can change their focus from doing movements to the games on the screen hence, facilitating more repetitions.

The Australian Stroke Guideline recommended (weak) robotics to be utilised after stroke regardless of the level of UL impairment.⁵² A recent systematic review that investigated the effectiveness of robotics for UL showed that patients with moderate-to-severe UL dysfunction could benefit more from this type of intervention.¹⁵² This is inconsistent with our findings. Even though most (75%) of our participants with stroke had moderate-to-severe UL dysfunction (UL motor FMA ranging from 4 to 58), our findings revealed non-significant nor clinically worthwhile changes in UL function and QoL. However, this is in discordance with the findings from the Participant Perception

of Treatment Scale, where 11 out of 12 participants with stroke believed that their condition was better after GBRT. The areas where they reported benefits were in motor function, and performance in ADLs (Figure 3.9), which is contrary to the findings of Mazzaoleni et al., where the perceived benefits aligned with the measured changes in UL impairments after robotic training.¹⁷¹ The participants perceived the training as beneficial and a significant change in UL function of approximately 2 points in the UL Motor Status Scale was detected. However, their study protocol was longer than ours and consisted of a total of 18 training sessions. Similarly, to the present study, Saleh et al (2017) employed 10 training sessions of robotic training in 10 individuals with chronic stroke. However, they found a significant within-group change in the UL function.¹⁴⁵ The only evident difference between our study and that of Saleh et al was that their training sessions were 2 hours longer than ours. From this comparison, we can infer that the dosage, including the duration of GBRT sessions and the overall duration of training seem to play a role in promoting significant changes in UL in participants with stroke.

An alternative reason that could explain the discordance between patient-reported and performance-based measurements could be an overestimation of the changes by the participants, which could be related to the 1) novelty effect; 2) lower expectation of rehabilitation outcomes; and 3) Hawthorne effect. Firstly, the novelty effect is defined as “the perceived usability of something on the account of newness”.¹⁹⁹ In our study, all participants with stroke were new to GBRT, which could have resulted in a bias towards overestimation of reported changes in the UL due to *excitement* with the opportunity to access the novel treatment. Secondly, the level of expectation could have affected the participants’ perception of change. It is a misconception among people with a stroke that recovery is impossible after 6 months post-injury, which could account for a lowered expectation for recovery after that time.²⁰⁰ This could have resulted in an overestimation of the perceived improvement, which means that even a subtle change could have been perceived as important and significant.²⁰¹ Thirdly, the Hawthorne effect is a phenomenon where participants tend to report the effects of a treatment differently due to being aware of the nature and purpose of the study.²⁰² Our participants were informed about the nature and purpose of the study prior to enrolment, which could have led them to providing more positive perspectives and opinions about the training they received.

Family members/carers can be a good source of information about their family members'/clients' (with disability) responses to training. They can also provide reliable information on whether the needs of their family members/clients with disability were met or not.¹⁷³ Moreover, often family member/carers can identify changes that the patient with stroke might not detect.²⁰³ In our study, family members/carers confirmed that the rehabilitation needs of their family members/clients with stroke, in terms of the UL function, were met with GBRT (Figure 3.9). Five out of eight reported that they observed that their family member/client had a stronger affected UL after GBRT. However, the changes might have been too small to be detected by the outcome measures used in this study. They also confirmed the findings on UL function during ADLs measured by the MAL, which revealed no improvements in the usage or quality of movements in the affected UL.

Data from the interviews and the Participant with stroke Satisfaction survey revealed issues with the hardware and the software/game component of the GBRT devices utilised. Hardware issues were those related to the mechanical design of the devices, which included: hand support being too small for users with large hands, frequent attachment/detachment to the robot, fingers hitting each other during squeezing and hard surface (absence of cushion) of the device used to train grasp. Those issues led participants to experience some discomfort and frustration during the training, negatively affecting their overall experience. Our findings are supported by Laparidou et al in their systematic review of the experiences of participants with stroke after UL robotics, where participants also suggested that hardware issues caused discomfort and wasting of treatment time to readjust the machine.⁸⁶ Moreover, soft-tissue-related injuries (e.g., abrasion) were identified as hazard when using robotic devices in rehabilitation.²⁰⁴ Therefore, strategies to lessen skin damage and discomfort, such as cushioning and frequent skin checks are recommended when employing robotic training, especially to individuals with reduced sensation or cognition.

The identified software-related issues were glitches (i.e., erratic movement of an object on the screen), and appropriateness and variety of games and sound. Participants reported frustration during the training when glitches appeared, feeling bored due to lack of variety and appropriateness

of games and feeling disturbed because of the inappropriateness of the sounds. Software-related issues were identified as one of the major barriers in a training using robotic devices as it can lead to feelings of frustration.⁸⁶ Since games are used to increase engagement, it can be assumed that if those issues are not addressed, it can cause otherwise. A strength of this study was the integration of perceptions and experiences from people with stroke and the ones directly involved in their care. This strategy provided us with the opportunity to compare perspectives from these groups, thus giving us more holistic findings. Another strength of this study was its mixed-method design that allowed us to compare participants' perceptions with the quantitative data obtained by the performance-based outcome measures.

However, this study has its limitations. The sample size for the family members/carers was less than the planned sample size, which could affect the generalizability of the results. Power calculation was also not performed for the quantitative data. However, the primary data in this study is the qualitative data and the sample size was based on the recommendations from Fugard and Potts, who suggested a sample size of 12 participants as appropriate in qualitative studies.²⁰⁵ Moreover, in this study, both the assessor and the therapist delivering the intervention were part of the research team, which could have affected judgement during assessments and training. To lessen the impact of this, the assessor was not present during the training sessions and the therapist that delivered the intervention was not present during the interviews and when the Satisfaction Surveys were collected. Also, only the perceptions and experiences of people with chronic stroke were explored in this study, so the findings might not reflect on those with acute and sub-acute stroke. Finally, the outcome measures used in this study were validated to be utilized for stroke population and some were recommended by the Stroke Recovery and Rehabilitation Roundtable.¹⁷⁸ However, some tools, particularly the ARAT are not highly sensitive to individuals with low motor function.²⁰⁶ This could be the reason why no measurable change was observed using this tool as 70% of our sample consisted of participants with moderate-to-severe UL dysfunction (70%).

In this study, we found no significant changes in UL function and QoL, but concluding that GBRT is ineffective could be inaccurate, considering that the training protocol was short and power

calculation was not performed for the quantitative measures. Future studies should consider investigating the optimal dosage of training by either increasing the number of training sessions (more than 10 training sessions) or the duration of sessions (more than 60 minutes). Moreover, a power calculation must be considered in studies aiming to assess effectiveness of GBRT to ensure that significant and clinically worthwhile treatment effects could be detected, if any.

Our findings provided insights into the positive and negative aspects of GBRT. Device-related issues (software and hardware issues) could have a negative impact on the overall patient experience. Our study revealed that these issues could lead to frustration, distractions and inefficient use of time and affect the participants' performance during training, impacting their potential for gains. For clinicians, it is important to consider participants' comfort and the time taken to set up. Some participants reported discomfort on the wrist and fingers, which could have affected their performance and outcomes. Discomfort can be reduced by enhancing the position of the wrist and fingers with cushioned blocks between fingers. Moreover, the use of games, including the presence of sound, should be discussed prior to the start of the training as some users have their own preferences and some might be very sensitive to loud or unexpected noises. Therefore, it is of the utmost importance for clinicians to develop strategies to overcome those issues if they occur during a session. Furthermore, these are important points for device developers to address when upgrading the system or developing new systems.

Also, the dosage of training must be carefully planned as exercise-induced fatigue is common due to the highly repetitive nature of GBRT. Since no statistical or clinical important differences were found in this study, it is recommended to consider adjusting the dosage of the therapy regimen. Lastly, clinicians should consider developing strategies to implement GBRT in a way that they could treat multiple patients/clients at one time (semi-supervised practice) to reduce their workload and costs involved with training.

For industries developing robotic devices, the current study shows that the overall experience of the participants with stroke was positive, but there were issues, particularly with the devices and software used. Based on the participants' experiences, GBRT devices should ensure comfortable

positioning of the joints during training, add program to count repetition of targeted movements during games, add a greater variety of interactive games, and consider audio feedback music that is age-appropriate.

In conclusion, the findings of this study demonstrated that GBRT was considered an enjoyable, motivating, and beneficial training regimen according to the participants with stroke, which was confirmed by their family members/carers. Besides participants reports of improved UL function and reduction in impairments, there was no significant nor clinically worthwhile differences detected after training, which could be a result of an overestimation of patient-reported outcome measures. A more positive mental outlook was revealed to be a result of the training because it provided participants with the feeling of self-accomplishment and hope. Therefore, clinicians might consider GBRT to increase volume and adherence to training in people with chronic stroke. Finally, despite the overall positive perception and experience of GBRT, the findings have revealed issues particularly with the devices used, which interfered with the participants' overall experience and could affect adherence and performance, if not addressed.

Chapter 4

Discussion

4.1 Summary of Key findings

Besides the lack of strong evidence to support the implementation of GBRT into clinical practice, there is a growing interest from clinicians and people with stroke to access robotic training, and many private clinics and rehabilitation hospitals in Australia have already purchased GBRT devices.⁸⁷ Our findings from the systematic review and the mixed-methods study have indicated that GBRT could be used in clinical practice as a tool to increase the volume of therapy, motivation, and engagement of participants with chronic stroke, while providing a highly repetitive and intensive training. It is an intervention that was highly appreciated by participants with stroke and their family members/carers. In this thesis, it was also found that GBRT was equally effective to CT, and as an adjunct to CT, resulted in a significant treatment effect, but that was possibly not clinically worthwhile and, therefore, its effectiveness is still questionable. Lastly, we provided insights on the issues with the robotic devices that affected comfort and overall experience of end-users during GBRT. These limitations need to be considered before the implementation of GBRT in clinical settings. This chapter summarises and integrates the critical findings of this thesis, besides presenting the potential facilitators and barriers for this intervention.

4.1.1 Potential Facilitators for Implementation of GBRT.

The Technology Acceptance Model is a model that is used to understand what factors cause individuals to use technology.²⁰⁷ In this model, it is proposed that there are two factors that can lead to acceptability and actual use of new technologies, namely perceived ease of use and perceived usefulness. The overall findings of this thesis suggested that GBRT is an acceptable treatment regimen and that the factors that could possibly lead to its utilization in clinical settings are: 1) Participants with stroke were confident that the training was beneficial. Moreover, both participants with stroke, and their family members/carers were optimistic about the training 2) generally, GBRT was considered easy to use. 3) GBRT has the potential to increase adherence to high-dosage training.

4.1.1.1 GBRT is easy to use and perceived to be beneficial

This study showed that participants with stroke believed that they benefited from the training and reported improvements in their UL, particularly *ease of movement* or the ability to move

the affected UL actively or passively. Overall, the majority of the participants (n=11 out of 12) perceived that their condition improved after the training, which was consistent with previous research.^{86, 171, 208} Furthermore, participants with stroke and their family members/carers were optimistic about GBRT. Most participants with stroke (n=10 out of 12) agreed that their rehabilitation needs were met after undergoing the training. Most family members/carers (n=5 out of 8) agreed that their family member/client with stroke had a stronger UL after the training. This overall sense of optimism can be related to some of the features of GBRT, such as high-dosage training, real-time feedback, and ease to use.

Most participants with stroke appreciated that GBRT provided highly repetitive training. This was evidenced by the fact that the participants performed at least 150 repetitions in 20 minutes, which was like previous studies that employed robotic training and achieved from 240 to 1344 repetitions in a 30 to 45-minute session.^{74, 75, 121} Highly repetitive activity is vital for motor recovery and skill reacquisition, as it can stimulate reorganization of the brain through restitution and compensation.⁴⁰ An intervention that can provides highly repetitive training could affect participants' attitude towards that intervention,²⁰⁹ once our participants with stroke seemed to highly regard the importance of repetitive training to achieve their goals.

One of the limitations of CIMT, which is considered the gold standard UL intervention after stroke, is that individuals with severe impairments are often excluded from training, especially those in the chronic phase after a stroke.⁵⁷ The data from the semi-structured interviews showed that even participants with severe UL impairments experienced a high-dosage training (at least 200 repetitions in 20 minutes), because of the ability of the device to detect even small movements and to assist in completing a movement. These findings are supported by Grosmaire et al., who found that the assistance to the UL provided by robotic devices led to active highly repetitive training (at least 640 movements per hour) in people with severe UL impairments.¹⁹⁷

Another feature of GBRT that could increase optimism and motivation towards training is the real-time feedback. The findings reported in Chapter 3 demonstrated that games increased the focus and engagement of participants with stroke towards the task being performed. This could

explain why participants valued the gaming component of the training. Additionally, the semi-structured interviews showed that the participants with stroke considered the feedback encouraging and an important guide during the training. Hence, we can conclude that the use of games to provide feedback may have an important role in stroke rehabilitation, because it could increase the chance for motor recovery by guiding users on the tasks being performed and facilitating high-volume practice. This is supported by the *Optimizing Performance Through Intrinsic Motivation and Attention for Learning (OPTIMAL) Theory* that suggests that having an external focus, such as games, can increase the focus on the task's goal, which could lead to motor learning due to an increased motor performance.¹⁷⁰

Finally, the ease of use of the devices employed during GBRT may have affected the participants' (with stroke) optimism towards the intervention. In a study by Ghazali et al. (2019),²¹⁰ ease of use affected users' attitudes towards technology and its perceived usefulness. The semi-structured interviews suggested that most participants (n=7) with stroke found that GBRT was easy to use and that the training was simple.

4.1.1.2 Role of Games in Adherence and Motivation

Adherence to the training is vital for the success of any intervention in stroke rehabilitation²¹¹. In Chapter 3, participants with stroke attended all planned sessions, and there were no dropouts during the study. They also reported high levels of satisfaction. All participants with stroke said that they would continue the training if they were given a chance, as revealed in the Satisfaction Survey and in the semi-structured interviews. Previous research showed that games can facilitate adherence to training due to a sense of enjoyment and pleasure.^{86, 212, 213}

4.1.2 Potential barriers in using the intervention

Despite the findings presented above, the studies in this thesis indicated that the clinical application of GBRT could be problematic. In this subsection, the possible factors that could hinder adoption of GBRT in clinical settings are presented: 1) uncertainty if GBRT could lead to a treatment effect that is clinically worthwhile 2) Issues with the devices, both hardware and software.

4.1.2.1 Uncertainty in the effectiveness and clinically worthwhile effects

The systematic review and meta-analysis presented in Chapter 2 demonstrated no differences in effectiveness between GBRT and CT to treat UL dysfunction after a stroke. The meta-analysis showed no superiority in the differences in UL function (SMD 0.02 95% CI -0.18 to 0.23), independence (0.18 95% CI -0.05 to 0.40), quality of life (QoL) (SMD=-0.2, 95%CI -0.88 to 0.48), strength (SMD=0.20, 95% CI -0.02 to 0.43), range of motion (ROM) (SMD: 0.10, 95% CI -0.41 to 0.61) and hypertonia (SMD=0.20, 95% CI -0.02 to 0.43). These findings contrast with a previous systematic review that investigated the effectiveness of robotic training to improve UL function and found that the robotic-assisted training was superior to CT in improving UL function after stroke.¹⁵²

Combining GBRT and CT was superior to CT alone for UL function. When comparing GBRT, in addition to CT, to CT alone, the meta-analysis showed no differences for independence (SMD= 0.22 95% CI -0.04 to 0.47), QoL (SMD=-0.16, 95%CI -0.34 to 0.02), strength (SMD: -0.09, 95% CI -0.15 to 0.33), hypertonia (SMD: -0.23, 95% CI -0.54 to 0.31) and ROM (SMD: 0.25, 95% CI -0.34 to 0.84). UL function had a statistically significant effect favouring GBRT with CT (SMD 0.23 95% CI 0.11 to 0.34), however the narrow 95%CI indicates that effect was trivial to small. This finding corroborate with other systematic reviews that indicated that robotic training in general, as an adjunct to CT, can be superior to CT alone.^{161, 214} Zhang et al (2016) showed a moderate effect size (SMD=0.56 95% CI 0.19 to 0.93) favouring the combination of therapies, however with the lower bound of the CI being trivial, it is still uncertain if the resulting treatment effect was clinically worthwhile.

The reason for the small significant effect when GBRT is used as an adjunct to CT could be attributed to the fact that both treatments in the same training regimen could offer a more holistic rehabilitation; while GBRT offers intensive training in a simulated world, CT provides the practice of tasks in the real world.¹⁶¹ The opportunity of experiencing both interventions could yield a positive rehabilitation outcome. This assumption has been confirmed by a single-blinded RCT by Hsieh et al., wherein they investigated the impact of sequencing robotic-assisted training and CIMT in people with chronic stroke on UL function.¹⁵⁹ Participants underwent robotic training in the first

two weeks, followed by two weeks of CIMT. Participants improved the quality of movement and participation in ADLs after receiving the sequenced intervention. Despite our finding suggesting that GBRT+CT was slightly more beneficial than CT alone, there is still uncertainty whether the treatment effect was clinically worthwhile because the 95% CI spanned the nominated minimal clinical important difference.

Moreover, in this thesis, we performed a preliminary investigation of the changes in UL function, impairments, and QoL after GBRT. Similarly, to the findings in the systematic review, the study presented in Chapter 3, showed no significant differences in the outcomes of interest. However, individual data showed that some participants with stroke had an increase in scores after training; with a few exceeding the minimal clinically significant difference (MCID) of the tools employed. Hence, the lack of significance of the participants' combined results could be attributed to the small sample size and the fact that the study was not powered for its quantitative aspects.

Another factor that may have influenced the lack of significant results was the length of sessions and duration of intervention. An RCT that employed a similar training protocol with the same number of sessions, but with an extra 2 hours of session duration, found a significant change in UL function in the group that received GBRT.¹⁴⁵ This may indicate that our training sessions were too short to elicit changes in UL function.

4.1.2.2 Issues with the devices

The results reported in this thesis indicated that GBRT was a well-accepted intervention amongst participants with stroke and their families/carers. However, participants in our study reported experiencing issues with the devices used to deliver GBRT that negatively affected their overall experience. In Chapter 3, a list of issues reported by the participants' (with stroke) has been provided. The main issues with the hardware components were related to comfort and positioning and resulted in increased time required to readjust or to reset the devices (e.g., frequent detachment of the magnet that connects the fingers to the device), and discomfort (e.g., for a large hand, the wrist was hitting the metal component of the hand support). These findings are confirmed by similar studies that found that device position and attachment/ detachment was often difficult to both

clinicians and patients/clients and time consuming.⁸⁶ Moreover, soft tissue-related injuries (e.g., abrasion) was an identified hazard using devices in rehabilitation.²⁰⁴

Meanwhile, issues with the software also occurred and led to overall negative experiences such as feelings of frustration during the training. This was similar to a systematic review that explored the perception of users towards robotic training that reported that software-related issues, such as unresponsive software, were considered major barriers because it led to patients/clients feeling frustrated during training.⁸⁶

4.2 Limitations

This thesis consisted of two studies. Each study had its limitations in methodology that could affect the accuracy or the generalizability of the findings presented in this thesis:

Definition of games: In the systematic review, we included trials that used robotic training that utilized games as external feedback. In many trials, it was not clearly reported if games were used or not. Hence, the research team decided to introduce a definition for “games” during the screening phase to include trials in the review. We defined games as “*An audio and visual feedback that is interactive, goal-oriented and consist of a scoring system (e.g., points system)*”. This definition is not the standard definition of games and could be restrictive or permissible to trials with no intention to use games to be included or those with intention to be excluded.

Small sample size (Participants with stroke): In the mixed-method study, the aim was to explore the perceptions and experiences towards GBRT of people with stroke and the people directly involved in their care. The qualitative component did not require sample size computation. We targeted eight to 12 participants as the literature suggested that by this sample size, data saturation can be achieved.²¹⁵ However, the quantitative component requires power calculation for a more accurate result, particularly for the tools that measured change in UL function and QoL. This could be done by presenting the minimum number of participants needed to detect possible significant changes, if any²¹⁶. Since the quantitative analysis was not the primary aim of the study, the only way for us to reduce the impact of a small effect size is to carefully interpret the results.

Short training protocol: The total number of training sessions were 10 and each session duration was 1-hour long, which is less than previous studies that demonstrated effectiveness of robotics and could have contributed to the lack of changes in UL function and QoL.²¹⁷⁻²¹⁹ In previous pilot studies that aimed at investigating the effects of robotic training, the total number of training sessions was 10 in 3 weeks but with a longer session duration (more than 1 hour).^{98, 145} However, the primary aim of the present study was to investigate participants' perceptions and therefore, the authors considered 10 sessions sufficient exposure for the participants to form opinions about the training.

Inability to blind people directly involved in the study: The thesis utilized a pre-post research design of participants with stroke, with no control group. Hence, randomization and blinding were not possible or applicable. With no randomization and blinding, biases like ascertainment bias, information bias, and reporting bias can arise.¹⁰⁸ Ideally, research members should not be involved directly in the implementation of the training protocol and assessments. However, due to lack of funding to employ assessors and therapists, two research members were the ones who implemented the training protocol (ELR) and performed assessments (CQO). To reduce those potential bias, ELR was not present during the assessments, particularly during interviews and Satisfaction Surveys, and CQO was not present during training.

No validation and reliability testing of survey questionnaires: Two assessment tools employed in this thesis were developed by the research team: the Participants with stroke Satisfaction survey and the Family members/carers Perception and Observation. These tools did not undergo any pilot testing nor had their validity and reliability assessed. This issue could make our findings questionable, since the questionnaires did not undergo the necessary validation process. To reduce the impact of this, the research team made sure to discuss and reviewed the questionnaires several times to assure that the essential constructs were included. Furthermore, the Participants with stroke Satisfaction Survey was developed based on a previous study by Mazzolei et al (2014).¹⁷¹

Generalizability of the findings (acceptability of GBRT): Participants with stroke underwent training using three Tyromotion devices that were purchased by the University of Technology

Sydney. The findings on acceptability of GBRT in this thesis are limited to the use of Tyromotion devices and may not be generalised to other UL robotic devices, especially EXOs. EEs and EXOs have different mechanical designs that might affect the execution of movement differently. EEs control less degrees of freedom, allowing individuals to perform movements freer, whereas EXOs are more rigid and bulkier and control several joints of the UL.^{67, 68} This difference in mechanical design could lead to different treatment outcomes.

Inconsistencies in the self-reported questionnaires: There were various self-reported questionnaire employed in this study that demonstrated inconsistent responses across time points. For example: one participant had a decreased perception of his QoL by 39 points in the SSQoL between the baseline and the post-intervention time points, but rated that his condition has improved “a great deal better” in the Participant Perception of Treatment Effectiveness Scale. Those reductions could be related to the inherent bias from self-reported questionnaires (e.g. social desirability bias and recall bias).²²⁰ Furthermore, reduction in quality of life scores might have happened due to personal problems not related to their participation in the study, once the SSQoL includes many life domains not related to UL function.^{185, 220}

The severity of UL impairments was not considered: The severity of UL impairments was not an inclusion criteria in this thesis, however previous , research suggests that robotics could be more effective in participants with moderate-to-severe arm impairments.¹⁵² Contrary, in our sample, there were no changes in UL function, even though participants had a baseline UL FMA (motor subsection) from 4 to 58, with 70% presenting moderate (from 32 to 36) to severe impairments (from 5 to 19).

Potential mismatch in the training intensity between the intervention and control groups: Previous studies indicated that training intensity has a vital role in promoting recovery after a brain injury such as stroke.¹⁵⁶ But despite its importance, the included trials in the systematic review lacked transparency in reporting the intensity of training provided to participants. Hence, it is unsure if the intervention and control groups received training at similar and comparable intensities. If one group received higher intensity training, this could have led to a result favouring that group.

4.3 Clinical Implications

The findings in this thesis suggested that in many essential rehabilitation outcomes, GBRT alone, or as an adjunct to CT was equally effective to CT, except for UL function. GBRT+CT showed a small significant effect, but with uncertainty on being clinically worthwhile, when compared to CT alone. There was also no significant nor clinically worthwhile changes when we tested the effects of GBRT in UL function and QoL of our participants with stroke after 10 training sessions. Clinicians should interpret our results with caution as the lack of statistically significant changes in the studies presented in this thesis could be related to the fact that most of the trials included in the systematic review had issues with quality and moderate to high risk of bias. Furthermore, our mixed-methods study was not powered to identify statically significant changes in the outcomes of interested. This could have compromised the accuracy and reliability of our findings.²²¹

The duration of the GBRT protocol employed in this study was relatively short (3 times per week for 3 weeks, 1 hour per session) and could have been suboptimal to promote recovery of the UL in people with chronic stroke. Despite the lack of changes after GBRT, the participants and their family members/carers perceived benefits in many areas, especially motor function, ease of movement and increased confidence to perform ADLs. Participants enjoyed, were motivated during the training and acknowledged that GBRT allowed for high repetition of movements, which they considered essential for recovery after stroke.

Based on our findings, clinicians that are willing to introduce GBRT to their clinical practice, should consider this intervention to increase motivation, engagement, and adherence to therapy, which could in turn, result in better rehabilitation outcomes. In regard to selecting the type of device, our systematic review showed a slight better effect of end-effectors in comparison to exoskeletons to improve UL function. Some participants with stroke exceeded the MCID for some of the outcome measures (FMA- 1 participant, ARAT- 2 participants, MAL QOL- 1 participant, SSQoL- 1 participant) in our mixed-methods study, despite of our short training duration. Hence, clinicians should consider utilizing GBRT over a longer duration of treatment and for longer

sessions. Moreover, GBRT should be used in a group setting to facilitate semi-supervised practice, reduce workload and optimize revenue. Evidence has suggested that training using robotics could be performed with less supervision from clinicians without a negative impact on the effectiveness of training.¹¹⁴

Furthermore, clinicians should select games that are realistic and adjust the auditory feedback according to participants' preferences to provide an overall positive experience during training. During GBRT, clinicians should also be aware of patient's comfort and attend for joint alignment and any signs of redness on skin, as often adjustments are required. Lastly, companies developing robotic devices for rehabilitation should address issues related to the participants' comfort, alignment, the appropriateness and variety of games and audio feedback to increase the overall experience of the end-users.

4.4 Recommendation for Future Studies

The collective findings of this thesis provided preliminary evidence on the potential factors that could facilitate the utilization of GBRT in clinical practice, however a few gaps in the literature remain. The findings of the systematic review described in Chapter 2 are based on many RCTs with a high-risk of bias, which highlights the need for higher quality RCTs to assess the effectiveness of GBRT to improve UL function after a stroke. The main sources of risk of bias found in our systematic review that future studies should avoid are the absence or lack of details about randomisation and absence of pre-registered protocol.

Future studies should also focus on identifying differences in responses to GBRT according to the duration of stroke. Our subgroup analysis showed that people with more than 6 months after stroke tended to have better outcomes in UL function. However, our results should be taken with caution due to a wide confidence interval for effectiveness leading to an imprecise finding. Moreover, since the result of the systematic review revealed that GBRT is better when combined with CT. Additional studies, particularly crossover RCTs must be performed to investigate the best sequencing of GBRT and CT to improve UL function after stroke.

Moreover, it is essential to investigate the impact of the severity of the UL impairments on the effectiveness of GBRT, which was not taken into consideration in this thesis. Previous literature has shown that the severity of impairments can affect the suitability and applicability of an intervention.^{53, 222} Therefore, future studies should focus on determining the effectiveness of GBRT on the various severities of UL motor function and investigate the acceptability of GBRT in relation to motor function. This could provide further insights on modifications and improvements that are tailored to the individuals' deficits, ensuring patient-centred approach.

In the systematic review, the studies included did consider the number of repetitions achieved during training when comparing GBRT and CT. In most cases, authors just mentioned that the experimental and control groups were dose-matched in terms of training duration and nature (e.g., task-specific, high-intensive, or highly repetitive). Future studies should consider comparing GBRT and any CT with matching intensity and be more transparent when reporting dosage. This would eliminate the potential impact of an imbalanced intensity, which could increase the accuracy and precision of the findings regarding which interventions are more effective in improving essential outcomes after stroke. The lack of significant changes in UL function and quality of life after GBRT reported in Chapter 3, could be related to the insufficient dosage of training to elicit changes. Therefore, future studies investigating the effects of GBRT after stroke should investigate the optimal dosage of training, especially in individuals with a chronic stroke. Furthermore, the disagreement between patient-reported and performed-based outcome measures should be taken in consideration. Moreover, future studies should consider providing greater training dosage than what was utilized in this thesis. Lastly, a powered sample size calculation should be performed when evaluating the effects of GBRT on UL function.

In this thesis, three devices were used to provide upper limb training for participants with reduced arm/hand function after a stroke. Each device trained specific joints/movement of the UL at a time, which could facilitate the training as it decreases the degrees of freedom of the task. Future studies should investigate different devices that allow multi-joint training at the same time, once majority of the ADLs involving the UL require multi-joint coordinated movements.

Besides, many rehabilitation settings and clinics in Australia having implemented GBRT to their practice, the findings in Chapter 3 revealed a need to further investigate the implementation of this intervention, using frameworks such as the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework²²³ or the Theoretical Domain Framework²²⁴ to explore the actual implementation of GBRT. Exploring the actual utilization, which includes cost analysis for clinics and participants, physical space taken and training requirements for therapists, would capture the worthiness of purchasing the robotic device and the feasibility of integrating it into the clinical setting.

4.5 Conclusion

The collective findings of this thesis showed the potential factors that could affect the utilization of GBRT in clinical settings. Firstly, there is potential to improve UL function, especially when added to CT, using an end-effector-based robotic device during the chronic phase of a stroke. However, there is uncertainty whether the resulting treatment effect was clinically worthwhile. Secondly, participants with stroke and their family members/carers found GBRT enjoyable, motivating, targeted to their rehabilitation needs and experienced benefits in many areas. In contrast, when measured using performed-based outcome measures, there were no detected changes in UL function or QoL. Thirdly, GBRT could be employed in clinical settings to increase adherence to training as it provides highly repetitive practice with engaging and motivating real-time feedback. However, the issues with the device and the games could hinder the overall experience and comfort during the training and should be addressed.

Therefore, our findings revealed that GBRT as a sole intervention or an adjunct to CT, may not be superior to CT in promoting clinically worthwhile changes in UL function and impairments after stroke, however, due to great participant enjoyment and high levels of satisfaction with the training, it might be considered as an intervention to increase engagement, adherence, and the volume of training, which is crucial to promote better rehabilitation outcomes.

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Appendices

Appendix A Search Strategies in each Databases

Appendix B GRADE Assessment in all outcomes

Appendix C Annotated Forest plots of all outcomes

Appendix D UTS HREC Confirmation of Approval

Appendix E Individual change scores (Post score-baseline score) of Participants with Stroke in all outcome measures

Appendix F Participant Information Sheet and Consent Forms (Participant with Stroke, and Family Member/Care)

Appendix G Screening, Initial, Post-assessment and Follow up assessment tools

Appendix H Semi-Structure Interview Guide Questions

Appendix I Family members/carers Perception and Observation Questionnaire (Online version)

Appendix J Mapping of themes using IdeaFlip Software

Appendix K Integration of quantitative data into qualitative

Appendix A Search Strategy

PubMed

1. Neurological Rehabilitation [MeSH]
2. Stroke rehabilitation [MeSH] or rehabilitation
3. Robotics [MeSH] or robotic device
4. Exoskeleton Device [MeSH] or robotic-assisted
5. Stroke [MeSH] or cerebrovascular accident
6. Neurologic examination [MeSH]
7. Physical examination [MeSH]
8. Motor impairment
9. Recovery of function [MeSH]
10. Physical Functional Performance [MeSH]
11. Activities of Daily Living [MeSH] or independence
12. Quality of life [MeSH]

Embase

1. 'Neurorehabilitation'/exp
2. 'stroke rehabilitation'/exp
3. 'robotics'/exp
4. 'rehabilitation robot'/exp
5. 'robotic exoskeleton'/exp
6. 'cerebrovascular accident'/exp
7. 'neurologic examination'/exp
8. 'physical examination'/exp
9. 'motor dysfunction assessment'/exp
10. 'convalescence'/exp
11. 'physical performance'/exp
12. 'daily life activity'/exp
13. 'quality of life'/exp

Medline

1. Neurological Rehabilitation.mp. or Neurological Rehabilitation/
2. Stroke rehabilitation.mp. or Stroke Rehabilitation/
3. robotics.mp. or Robotics/
robotic device.mp.
4. Exoskeleton Device.mp. or Exoskeleton Device/
5. robot*-assisted.mp.
stroke.mp. or Stroke/
6. neurologic examination.mp. or Neurologic Examination/
7. Physical examination.mp. or Physical Examination/
8. motor impairment.mp.
9. recovery of function.mp. or "Recovery of Function"/
10. Physical Functional Performance.mp. or Physical Functional Performance/
11. Activities of Daily Living.mp. or "Activities of Daily Living"/
12. independence.mp.
13. Quality of life.mp. or "Quality of Life"/

Cochrane

1. MeSH descriptor: [Neurological Rehabilitation] explode all trees
2. MeSH descriptor: [Stroke Rehabilitation] explode all trees
3. MeSH descriptor: [Rehabilitation] explode all trees
4. MeSH descriptor: [Robotics] explode all trees
5. MeSH descriptor: [Exoskeleton Device] explode all trees
6. robotic device/robotic-assisted/end-effector device
7. MeSH descriptor: [Stroke] explode all trees/ cerebrovascular accident

8. MeSH descriptor: [Neurologic Examination] explode all trees
9. MeSH descriptor: [Physical Examination] explode all trees
10. Motor impairment" OR "motor dysfunction"
11. MeSH descriptor: [Recovery of Function] explode all trees
12. "Physical Functional Performance"
13. MeSH descriptor: [Activities of Daily Living] explode all trees
14. Independence
15. MeSH descriptor: [Quality of Life] explode all trees

PEDro

1. Robot
2. Stroke

Web of Science

1. ALL="Neurological Rehabilitation"
2. ALL="Stroke Rehabilitation"
3. ALL=rehabilitation
4. ALL=robotics
5. ALL="robotic device"
6. ALL= (("exoskeleton device" OR robotic-assisted) OR "end-effector device")
7. ALL=(stroke OR "Cerebrovascular Accident")
8. ALL= "Neurologic Examination"
9. ALL= "Physical Examination"
10. ALL= ("motor impairment" OR "Motor dysfunction")
11. ALL= "Recovery of function"
12. ALL= Physical Functional Performance
13. ALL= "Activities of Daily Living"
14. ALL= "Quality of Life"

CINAHL

1. Neurological Rehabilitation”
2. “Stroke rehabilitation” or rehabilitation
3. Robotics or “robotic device”
4. “Exoskeleton Device” or robotic-assisted
5. Stroke or “cerebrovascular accident “
6. “Neurologic examination”
7. “Physical examination”
8. “Motor impairment”
9. “Recovery of function”
10. “Physical Functional Performance”
11. “Activities of Daily Living” or independence
12. “Quality of life”

Scopus

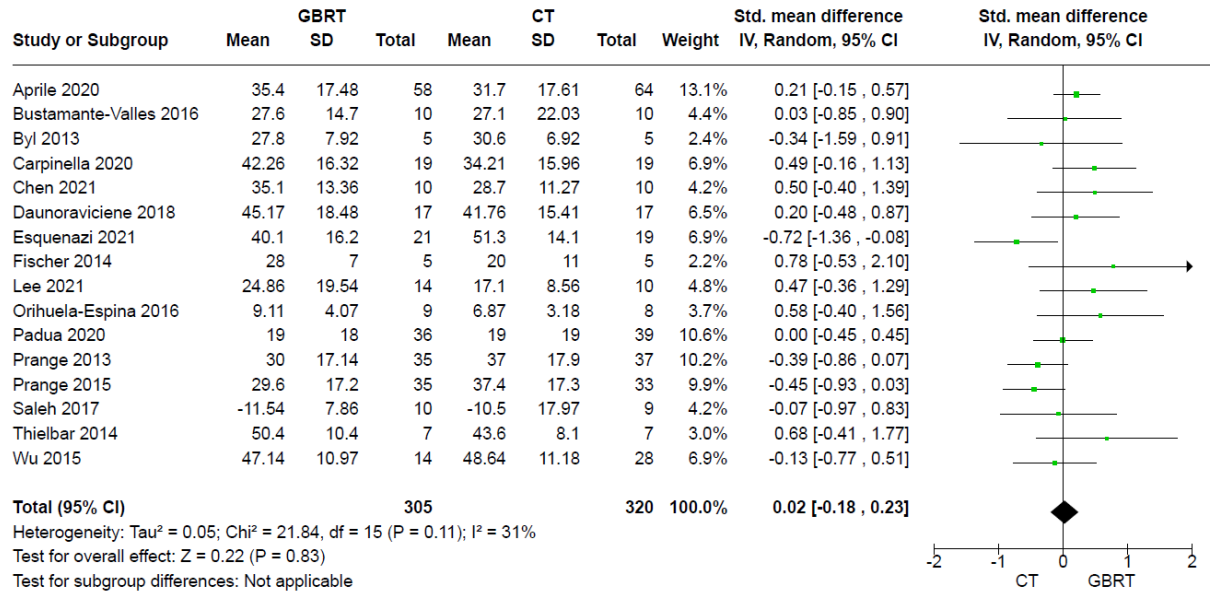
((ALL (stroke OR "Cerebrovascular Accident")) AND ((ALL ("Stroke rehabilitation" OR rehabilitation)) OR (ALL ("Neurological Rehabilitation"))) AND ((ALL (robotics OR "robotic device")) OR (ALL ("Exoskeleton Device" OR robotic-assisted OR "end-effector device"))) AND ((ALL ("Neurologic examination")) OR (ALL ("Motor impairment" OR "motor dysfunction")) OR (ALL ("Recovery of function")) OR (ALL ("Physical Functional Performance")) OR (ALL ("Activities of Daily Living" OR independence)) OR (ALL ("Quality of life")) OR (ALL ("Physical Examination")))))

Appendix B Summary of GRADE assessment for primary and secondary outcomes

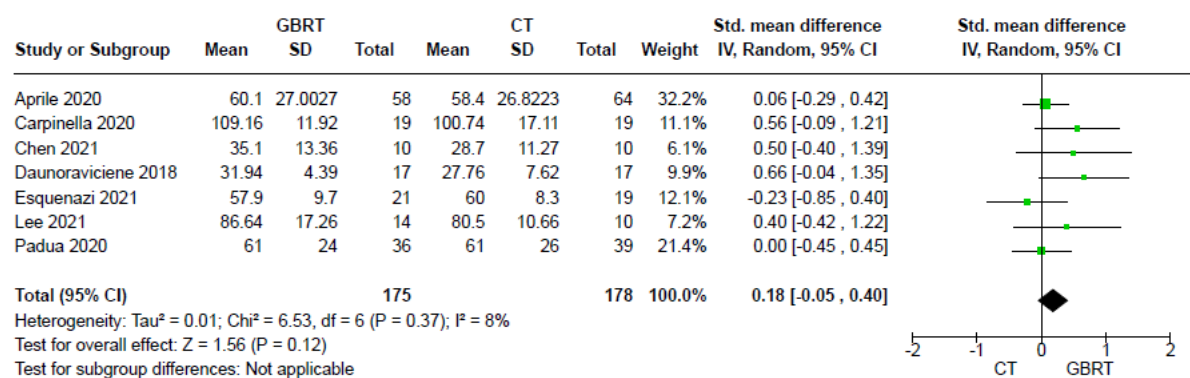
Outcome	Reason to downgrade	Grade
GBRT vs CT		
Primary Outcome		
Functional Performance	35% of participants came from high-risk trials	Moderate
Subgroup		
End-effector	None	High
Exoskeleton	42% heterogeneity, 36% of participants came from high-risk trials, and 258 participants	Very low
<6 months	51% heterogeneity	Moderate
6 months or more	72% of participants came from high-risk trials and only 187 participants	Low
Independence	None	High quality
Subgroup		
End-effector	Only 293 participants	Moderate
Exoskeleton	41% heterogeneity, 50% of participants came from high-risk trials, only 40 participants	Very low
<6 months	Subgroup analysis not applicable	
6 months or more		
Secondary Outcome		
Strength	31% of participants came from high-risk trials, only 300 participants	Low
Hypertonia	Only 254 participants	Moderate
ROM	Only 60 participants	Moderate
QoL	Only 144 participants, 63% heterogeneity	Low
GBRT+ CT vs CT		
Functional Performance	57% of participants came from high-risk trials	Moderate
Subgroup		
End-effector	None	High
Exoskeleton	Only 229 participants and 44% of these participants came from high-risk trials	Low
<6 months	60% of participants came from high-risk trials	Moderate
6 months or more	None	High
Independence	34% of participants came from high-risk trials, 59% heterogeneity	Low
Subgroup		
End-effector	30% participants came from high-risk trials, 67% heterogeneity	Low
Exoskeleton	35% participants came from high-risk trials and only 143 participants	Low

• <6 months	60% participants came from high-risk trials	Moderate
• 6 months or more		High
<i>Secondary Outcome</i>		
Strength	29% heterogeneity	Moderate
Hypertonia	58% heterogeneity	Moderate
ROM	59% of participants came from high-risk trials, 54% heterogeneity, only 117 participants	Very low
QoL		High

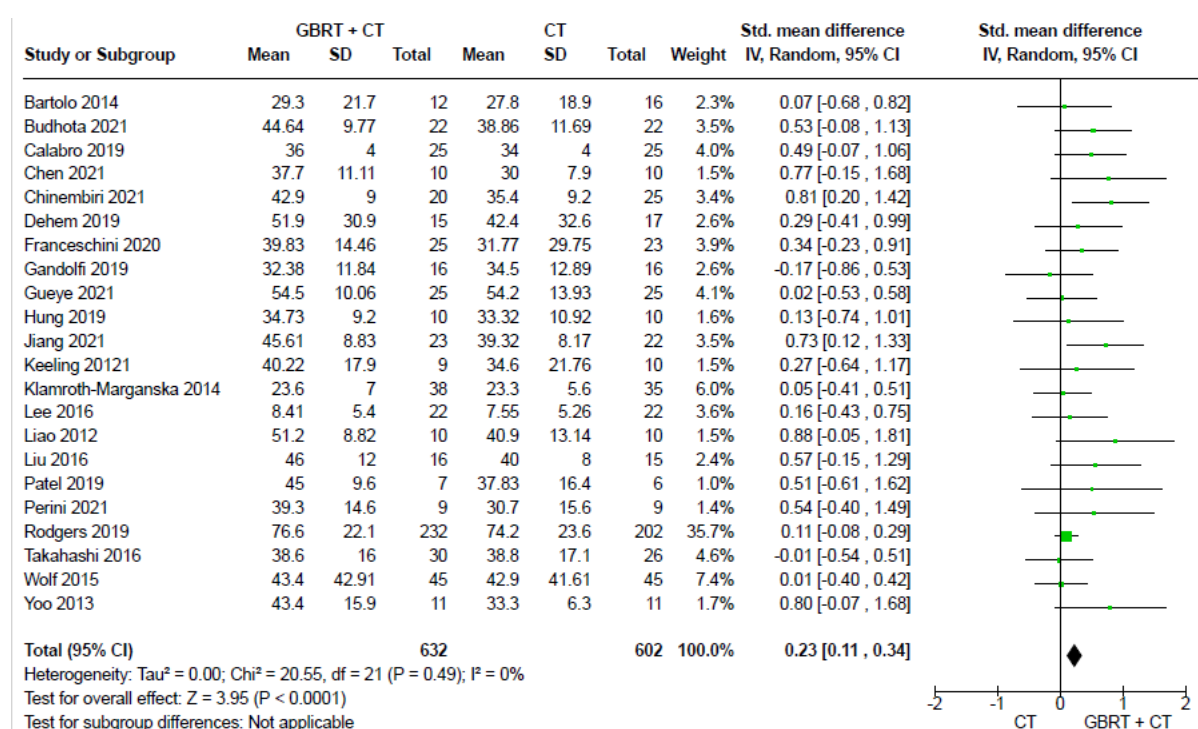
Appendix C Annotated Forest Plots for all the Outcomes



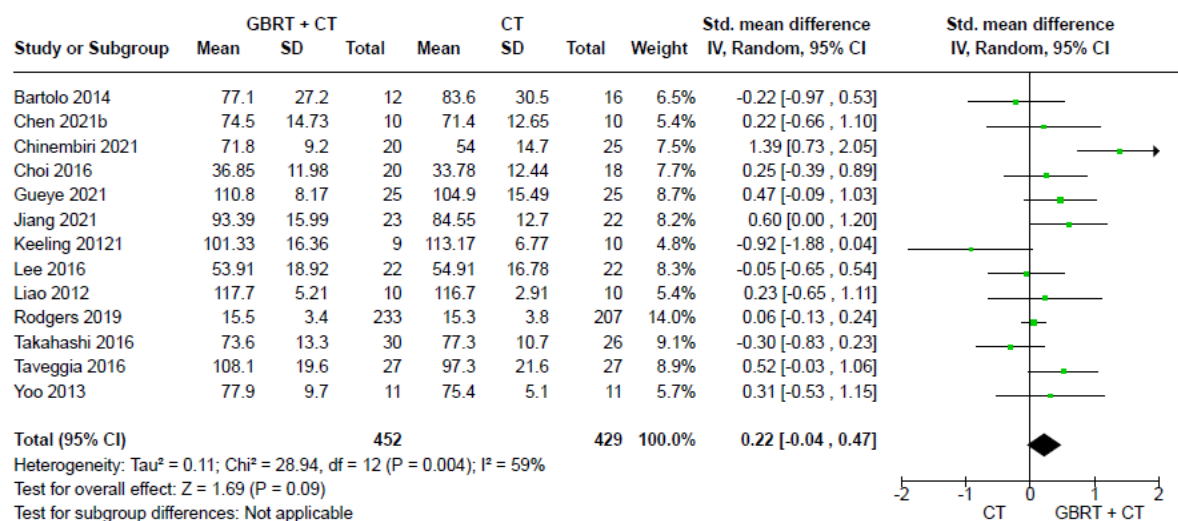
GBRT versus CT, outcome: Functional Performance



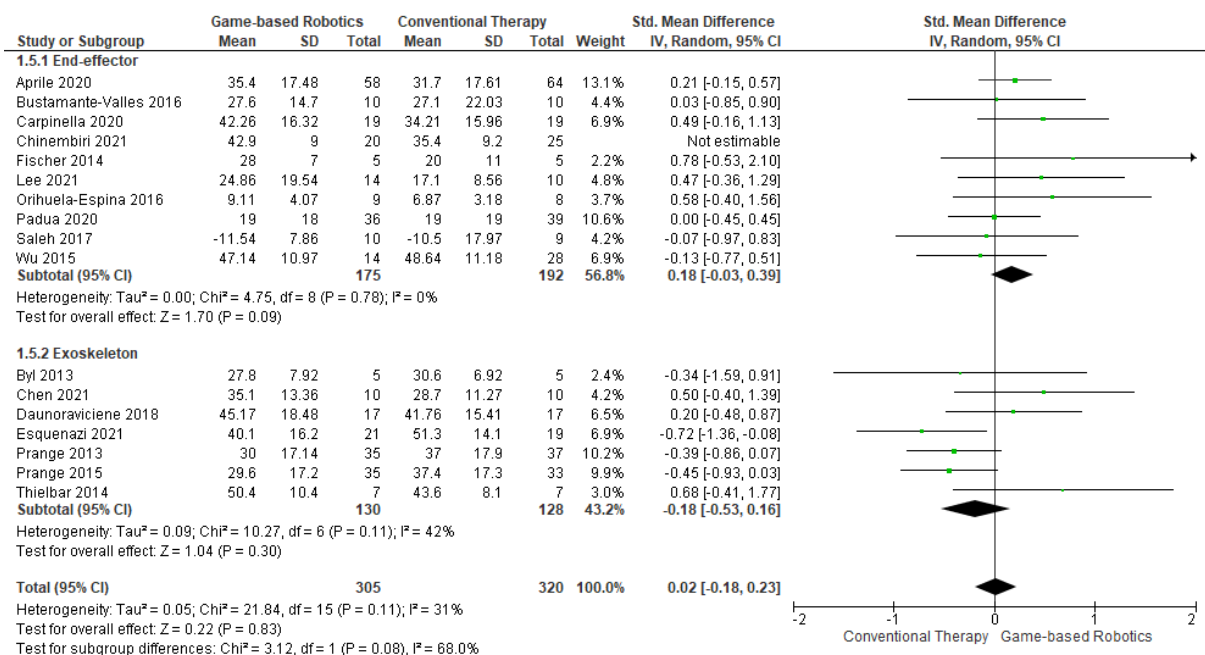
GBRT versus CT, outcome: Independence



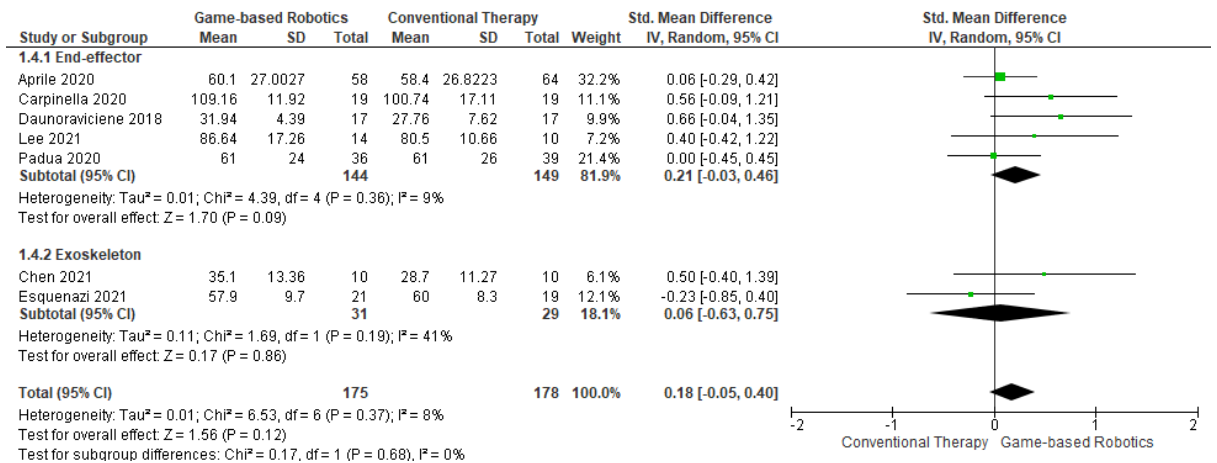
GBRT with CT versus CT, outcome: Functional Performance



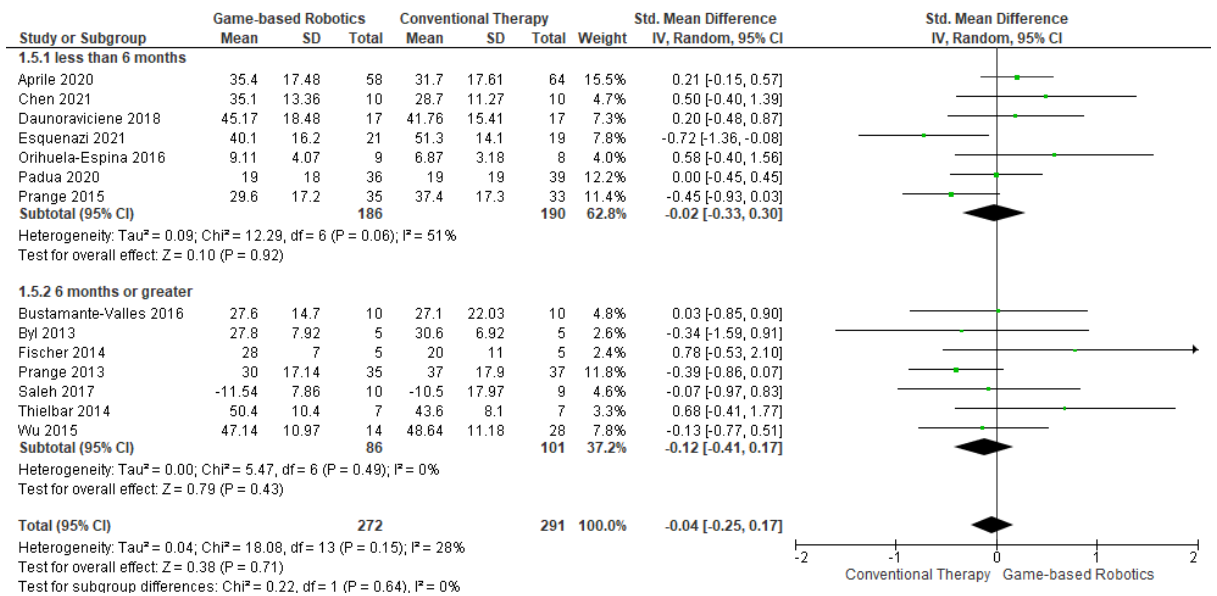
GBRT with CT versus CT, outcome: Independence



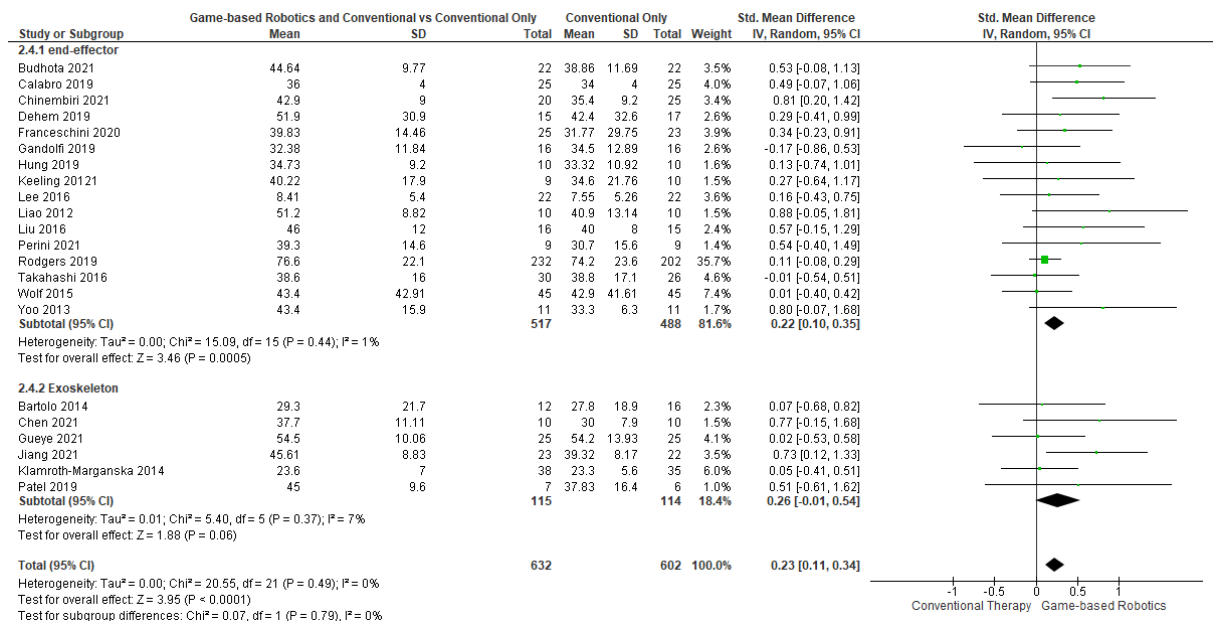
GBRT versus CT, subgroup analysis: Type of robot, outcome: Functional Performance



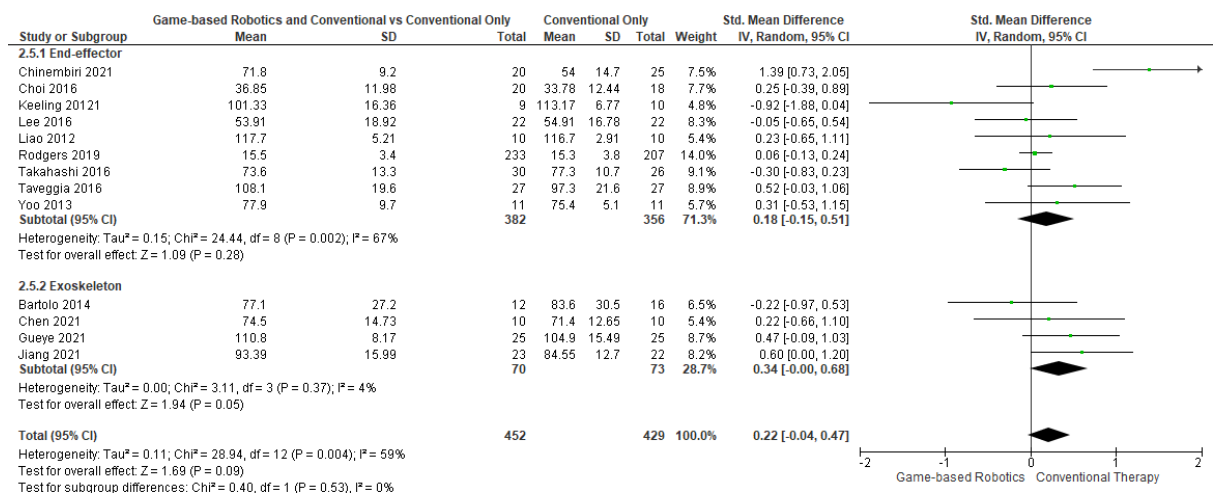
GBRT versus CT, subgroup analysis: Type of robot, outcome: Independence



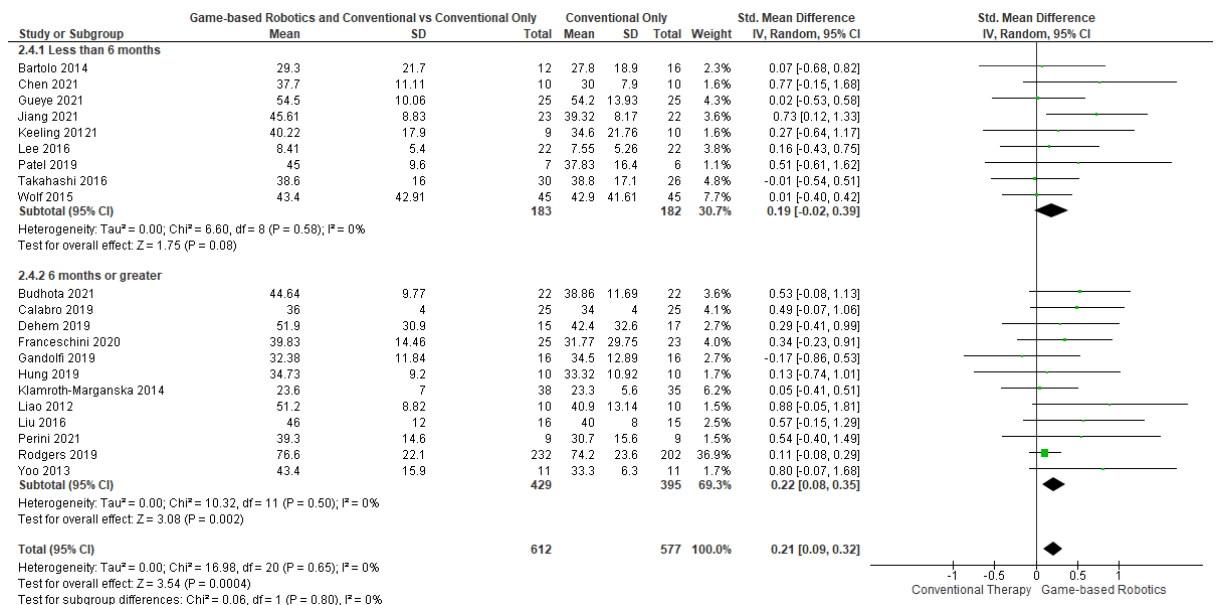
GBRT versus CT, subgroup analysis: Time since Stroke, outcome: Functional Performance



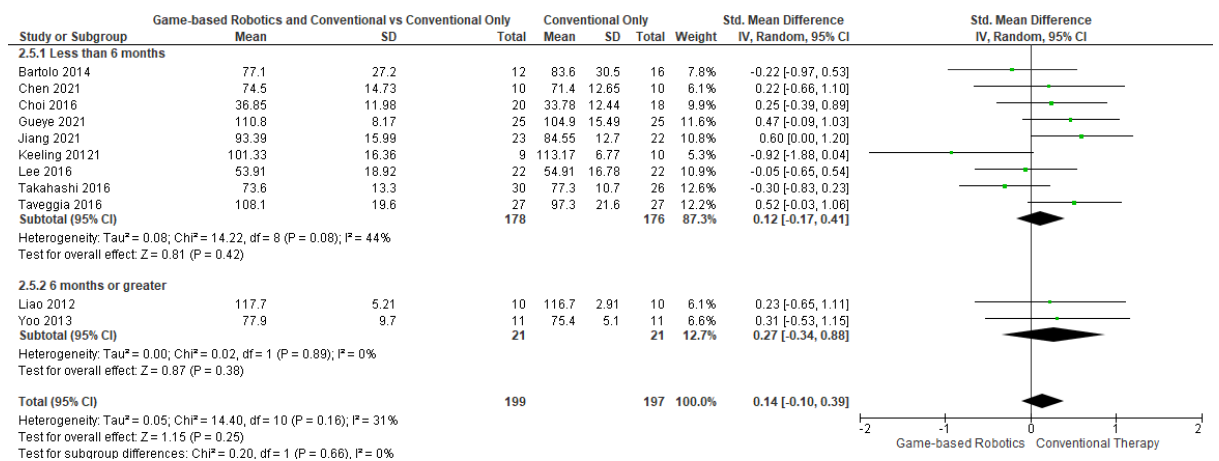
GBRT with versus CT, subgroup analysis: Type of Robot, outcome: Functional Performance



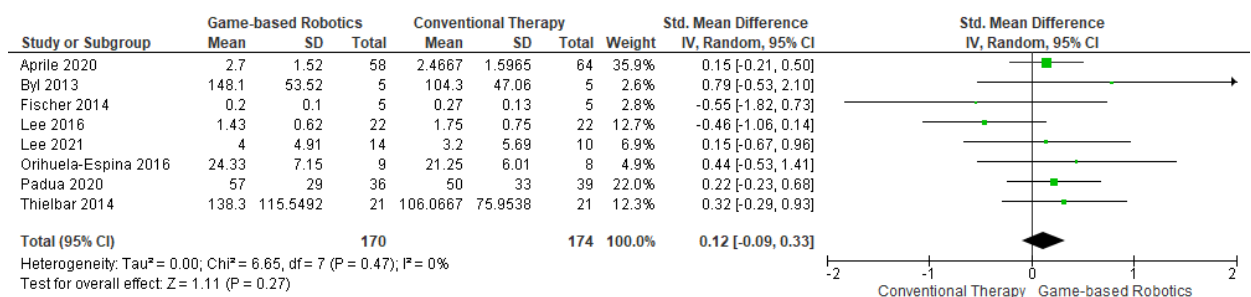
GBRT with CT versus CT, subgroup analysis: Type of Robot, outcome: Independence



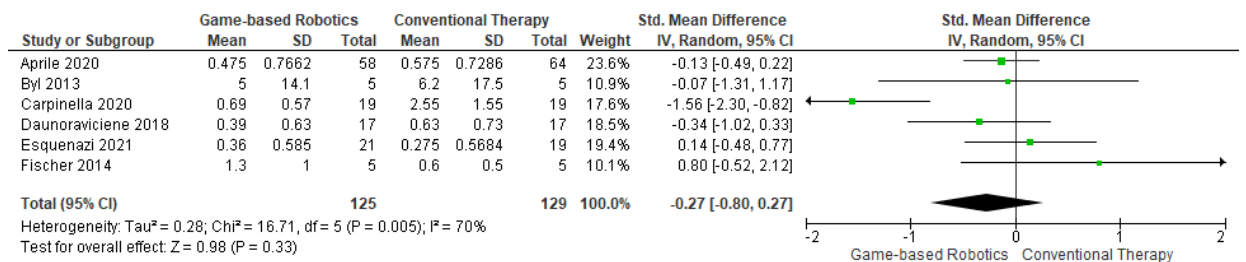
GBRT with CT versus CT, subgroup analysis: Time since Stroke, outcome: Functional Performance



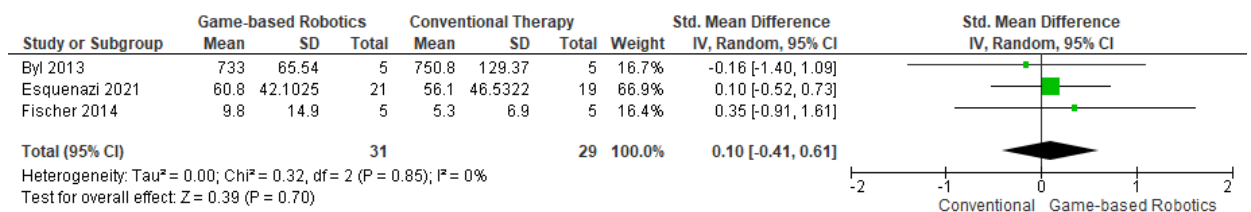
GBRT with CT versus CT, subgroup analysis: Time since Stroke, outcome: Independence



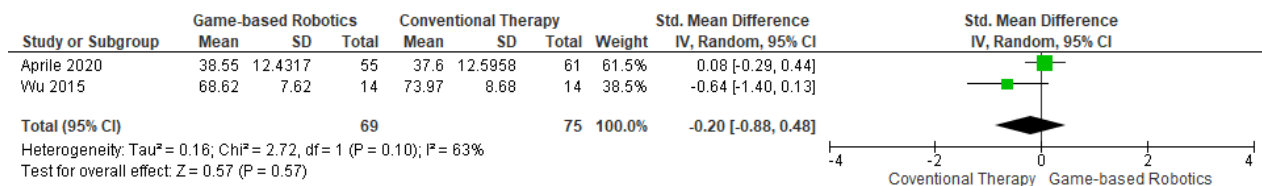
GBRT versus CT, outcome: Strength



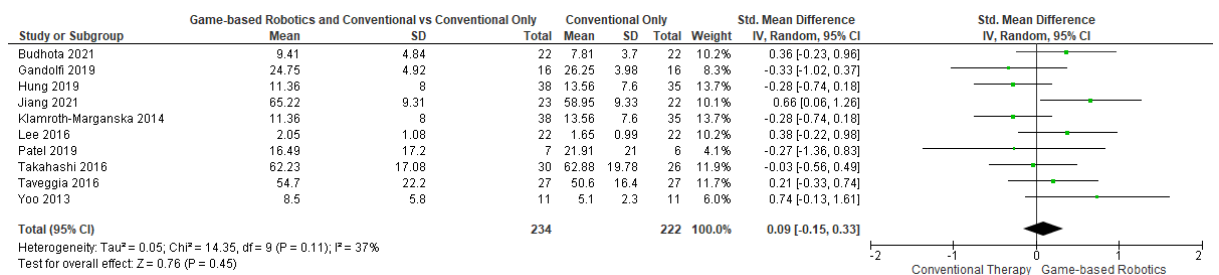
GBRT versus CT, outcome: Hypertonia



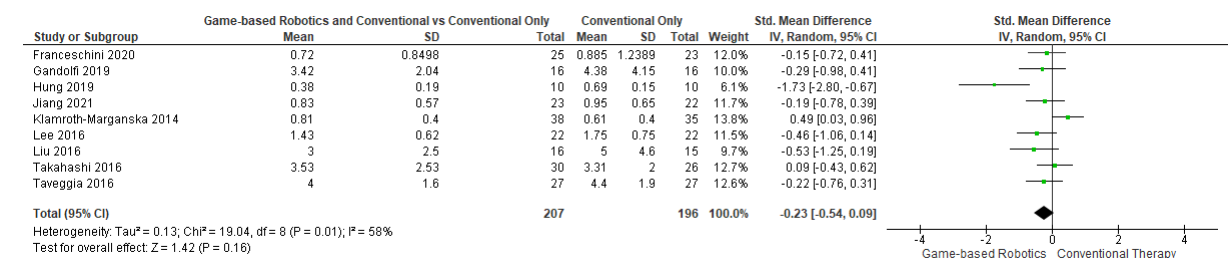
GBRT versus CT, outcome: ROM



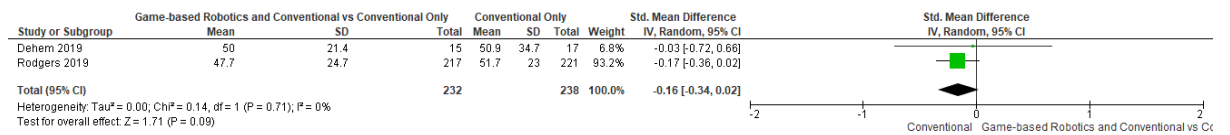
GBRT versus CT, outcome: QoL



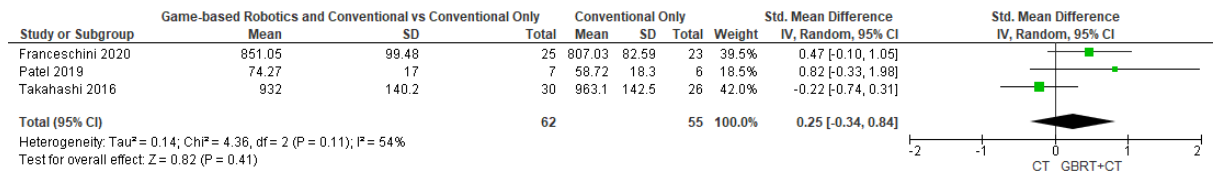
GBRT+ CT versus CT, outcome: Strength



GBRT+ CT versus CT, outcome: Hypertonia



GBRT+ CT versus CT, outcome: QoL



GBRT+ CT versus CT, outcome: ROM

Appendix D Individual change scores (Post score-baseline score) of Participants with Stroke in all outcome measures

Participants	UL FMA (Motor)	ARAT	MAL AMT	MAL QOL	SSQoL
P1	1.00	0.00	-0.31	-0.40	-39.00
P2	2.00	0.00	0.00	0.00	-2.00
P3	2.00	0.00	-0.10	0.15	0.00
P4	4.00	0.00	-0.15	-0.17	18.00
P5	.00	0.00	0.00	0.00	37.00
P6	2.00	1.00	-0.63	-0.45	7.00
P7	.00	0.00	0.00	0.00	-2.00
P8	1.00	0.00	0.00	0.00	19.00
P9	-4.00	0.00	0.22	0.78	17.00
P10	5.00	9.00	1.10	1.21	0.00
P11	1.00	0.00	0.23	0.25	19.00
P12	10.00	13.00	0.60	0.91	-2.00

Appendix E UTS HREC Confirmation of Approval



UNIVERSITY
OF TECHNOLOGY
SYDNEY

Human Research Ethics Committee
Ethics Secretariat
C/O Research and Innovation Office
15 Broadway, Ultimo NSW 2007
T: +61 2 9514 9681
Research.Ethics@uts.edu.au

PO Box 123
Broadway
NSW 2007 Australia
www.uts.edu.au

UTS CRICOS PROVIDER CODE 00099F

3 May 2019

Dr Camila Quel De Oliveira
Graduate School of Health
UNIVERSITY OF TECHNOLOGY SYDNEY

Dear Camila,

Re: UTS HREC ETH18-3022 – Dr Camila Quel De Oliveira, Dr Arianne Verhagen, Dr Peter Stubbs, Dr Alana McCambridge (for Mr Esminio II Rivera, PhD student) – “Robotic-Assisted Game-Based Rehabilitation for upper limb function in people with chronic stroke: A Feasibility Study”

Thank you for your response to the Committee's comments for your project titled, "Robotic-Assisted Game-Based Rehabilitation for upper limb function in people with chronic stroke: A Feasibility Study". The Committee agreed that this application now meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and has been approved on that basis. You are therefore authorised to commence activities as outlined in your application, subject to any conditions detailed in this document.

You are reminded that this letter constitutes ethics approval only. This research project must also be undertaken in accordance with all UTS policies and guidelines including the Research Management Policy (<http://www.gsu.uts.edu.au/policies/research-management-policy.html>).

Your approval number is UTS HREC REF NO. ETH18-3022.

Approval will be for a period of five (5) years from the date of this correspondence subject to the submission of annual progress reports.

The following standard conditions apply to your approval:

- Your approval number must be included in all participant material and advertisements. Any advertisements on Staff Connect without an approval number will be removed.
- The Principal Investigator will immediately report anything that might warrant review of ethical approval of the project to the Ethics Secretariat (Research.Ethics@uts.edu.au).
- The Principal Investigator will notify the UTS HREC of any event that requires a modification to the protocol or other project documents, and submit any required amendments prior to implementation. Instructions can be found at <https://staff.uts.edu.au/topic/Pages/Researching/Research%20Ethics%20and%20Integrity/Human%20research%20ethics/Post-approval/post-approval.aspx#tab2>.
- The Principal Investigator will promptly report adverse events to the Ethics Secretariat (Research.Ethics@uts.edu.au). An adverse event is any event (anticipated or otherwise) that has a negative impact on participants, researchers or the reputation of the University. Adverse events can also include privacy breaches, loss of data and damage to property.
- The Principal Investigator will report to the UTS HREC annually and notify the HREC when the project is completed at all sites. The Principal Investigator will notify the UTS HREC of

any plan to extend the duration of the project past the approval period listed above through the progress report.

- The Principal Investigator will obtain any additional approvals or authorisations as required (e.g. from other ethics committees, collaborating institutions, supporting organisations).
- The Principal Investigator will notify the UTS HREC of his or her inability to continue as Principal Investigator including the name of and contact information for a replacement.

I also refer you to the AVCC guidelines relating to the storage of data, which require that data be kept for a minimum of 5 years after publication of research. However, in NSW, longer retention requirements are required for research on human subjects with potential long-term effects, research with long-term environmental effects, or research considered of national or international significance, importance, or controversy. If the data from this research project falls into one of these categories, contact University Records for advice on long-term retention.

If you have any queries about your ethics approval, or require any amendments to your research in the future, please do not hesitate to contact Research.Ethics@uts.edu.au.

Yours sincerely

Production Note:

Signature removed
prior to publication.

Professor Meera Agar

Chairperson

UTS Human Research Ethics Clinical Trials Subcommittee

Appendix F Participant Information Sheet and Consent Forms (Participant with Stroke)



PARTICIPANT INFORMATION SHEET Participant with Stroke

TITLE OF THE STUDY

Robotic-Assisted Game-Based Rehabilitation for upper limb function in people with chronic stroke: A Feasibility Study

WHO IS DOING THE RESEARCH?

Esminio L. Rivera II is a Master by Research in Physiotherapy student at UTS. This study will be supervised by the Physiotherapy academic staff of the University of Technology Sydney, Graduate School of Health: Dr. Arianne Verhagen, Dr. Camila Quel De Oliveira, Dr. Peter Stubbs and Dr. Alana McCambridge

WHAT IS THIS RESEARCH ABOUT?

Nowadays, technology plays a very important role in healthcare like the use of robotics to treat diseases, provide assistance to people with disabilities, and many more. One of the trending application of robotics is to help people after a stroke to perform exercises to improve the movements and use of their arms. Robotics is gaining an important role in rehabilitation in these days, because unlike any other treatment, it 1) assist both the therapist and patient to achieve their goal better and faster 2) it is fun and motivating as patients can play games while using the robots 3) it can monitor progress or improvement of arm and hand movements and 4) it can provide many repetitions of movement which is a very important aspect of re-learning of arm/hand skills.

However, this is an area that needs more research. There are few studies that explored the opinions and views of people who had stroke, their therapists and their carer/family member about the robot-assisted game-based rehabilitation. Hence, this study aims to better understand if robot-assisted game-based rehabilitation is an accepted treatment for people after stroke. By doing this, we can understand the strengths and weaknesses of robotic rehabilitation. Moreover, this will provide a sneak peek of the possible effects of such intervention in the arm affected by stroke.

WHY I HAVE BEEN ASKED?

You have been invited to participate in this study because you are a person who had stroke for at least 6 months that affected your ability to move your arm.

IF I SAY YES, WHAT WILL IT INVOLVE

If you decide to participate you will be involved in the screening, baseline assessment, training, post-intervention assessment and focus group discussion phases of the study. All phases will take place at Level 2, UTS Moorepark Campus, Graduate School of Health, Physiotherapy Department Moore Park Rd and Driver Avenue Moore Park, NSW 2021

Pre-assessment Phase

At the start, you will be asked to provide your personal details to the researcher, such as name/age/contact detail/details about your stroke/other health problems/cigarettes and alcohol consumption/occupation/Physiotherapy/Occupational Therapy sessions. You will be asked also to answer questions to check the status of your cognitive function such as memory, attention span, concentration, language and communication skills, ability to plan and ability to understand instruction.

Your arm movements will be assessed by a physiotherapist by asking you to perform activities that will evaluate the muscle strength, motion and coordination of your shoulder, elbow, forearm, wrist and hand. Also, you will answer a questionnaire about how much and how well you can use your arm and hand during your day-to-day activities. All assessments in this phase will take approximately 2 hour

Training/Intervention Phase

You will be undertaking an exercise program for your whole arm using robotic devices. You will receive training for 10 session in 3 weeks. Each session is 1h long (10h in total) which will be supervised by a therapists who is trained to use the robots that will be used in this study. Every devices uses games (which is flashed in a monitor) which is controlled by these three robotic devices below:

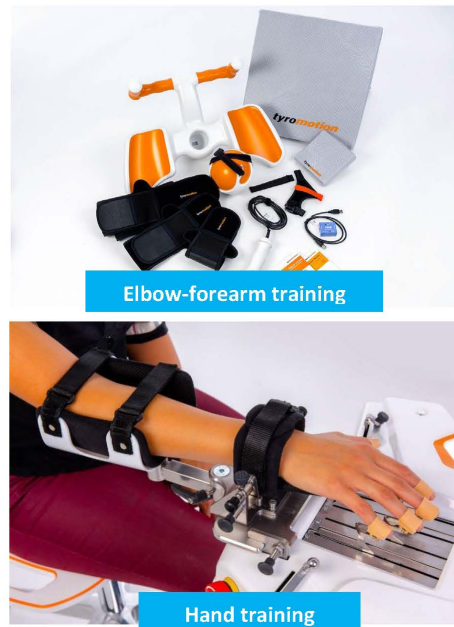


Image source: Tromotion User Manual

Post-intervention and Follow-up assessment

Immediately after the last session (post-intervention assessment) and one week after the last session (Follow-up assessment), the function of your arm will be reassessed by a physiotherapist using the same process on the baseline assessment. Also, you will be answering a questionnaire about the usefulness and your experience of the devices. Both post-intervention and follow-up assessment will take approximately 1 hour each.

Focus group

Lastly, you will be invited to join a focus group discussion with the other participants of the study. The focus group is a group discussion about your experience and feelings (likes/dislikes) on taking part in the training. You will be free to share your views and opinions about the devices and training. This discussion will be audio-recorded and your identity will be kept confidential in any recordings of this present study. The focus group discussion will take approximately two hours.

As soon as we have enough numbers of participants (6-8 participants), we will contact you via phone to invite you to attend the focus group session at UTS Moore Park Campus.

ARE THERE ANY COSTS TO JOIN TO THE STUDY?

Joining in this study is free of charge. You maybe compensated for your travel costs through taxi and/or petrol vouchers and if you decide to join the focus group discussion, you will receive Au\$30 gift voucher as a monetary compensation.

ARE THERE ANY RISKS?INCONVENIENCE?

There are no expected serious risk in joining the study. But like any other physiotherapy intervention there is a chance of muscle soreness, fatigue, , skin redness, joint strain and other exercise-related side effects which are a normal responses of the body to exercise and with correct supervision from the trained therapist all these side effect can be reduced or eliminated. Moreover, possible distress in answering some of questions in the survey or interview is likely. If, you feel very uncomfortable in answering any questions you have the choice not to answer.

If you felt emotional distress please tell it immediately to the researcher or to any person

DO I HAVE TO SAY YES?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part.

WHAT WILL HAPPEN IF I SAY NO?

If you decide not to participate, it will not affect your relationship with the researchers or the University of Technology Sydney. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason, by contacting Mr. Esminio L. Rivera II, the principal investigator of this study.

If in case you have withdrawn from the study, please take note that all information you provided from all the phases of the study will be erased from our database (for soft copy) and will be destroyed (hard copies like questionnaires)

CONFIDENTIALITY

By signing the consent form you consent to the research team collecting and using personal information about you for the research project. All this information will be treated confidentially. Only the investigator and the supervisors will have access to information you provided and during encoding unique subject code assigned for each participant will be used. Furthermore, during the voice recorded focus group your identity will be protected by making sure that your name or any details about you will not be cited. If in case, it will be cited that part of the recording will be deleted.

Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

WHAT IF I HAVE CONCERNS OR A COMPLAINT?

If you have concerns about the research that you think I or my supervisor can help you with, please feel free to contact one of the following:

Esminio L. Rivera II
Research Student
Phone: +61 [REDACTED]
Email: esminioii.rivera@student.uts.edu.au

Dr. Camila Quel De Oliveira
Principal Supervisor
Phone: +61 [REDACTED]
Email: Camila.QuelDeOliveira@uts.edu.au

You will be given a copy of this form to keep.

NOTE:

This study has been approved by the University of Technology Sydney Human Research Ethics Committee [UTS HREC]. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat on ph.: +61 2 9514 2478 or email: Research.Ethics@uts.edu.au], and quote the UTS HREC reference number. Any matter raised will be treated confidentially, investigated and you will be informed of the outcome.

CONSENT FORM

I _____ agree to participate in the research project entitled Robotic-Assisted Game-Based Rehabilitation for upper limb function in people with chronic stroke: A Feasibility Study being conducted by Mr. Esminio L. Rivera II, a Master of Physiotherapy student at Graduate School of Health at the University of Technology, Sydney. I understand that funding for this research has been provided by *the university*.

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research as described in the Participant Information Sheet.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time without affecting my relationship with the researchers or the University of Technology Sydney.

I understand that I will be given a signed copy of this document to keep.

I agree to be:

- ☐ Audio recorded
- ☐ Video recorded
- ☐ Photographed

I agree that the research data gathered from this project may be published in a form that:

- ☐ Identifies me
- ☐ Does not identify me in any way
- ☐ May be used for future research purposes

I am aware that I can contact [researcher's name] if I have any concerns about the research.

_____/_____/_____
Name and Signature [participant] Date

_____/_____/_____
Name and Signature [researcher or delegate] Date

_____/_____/_____
Name and Signature [witness*] Date

* Witness to the consent process

If the participant, or if their legally acceptable representative, is not able to read this document, this form must be witnessed by an independent person over the age of 18. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant (or representative) and that informed consent was freely given by the participant (or representative) (delete this section and the 'Signature of witness' section above if this form does not need to be signed by a witness to the consent process).

Appendix G Screening, initial, post-assessment and follow up assessment tools

ACTION

Patient Name: _____

RESEARCH

ARM TEST

Date: _____

Instructions

There are four subtests: Grasp, Grip, Pinch, Gross Movement. Items in each are ordered so that:

- if the subject passes the first, no more need to be administered and he scores top marks for that subtest;
- if the subject fails the first *and* fails the second, he scores zero, and again no more tests need to be performed in that subtest;
- otherwise he needs to complete all tasks within the subtest

Activity	Score
Grasp	
1. Block, wood, 10 cm cube (If score = 3, total = 18 and to Grip) Pick up a 10 cm block	_____
2. Block, wood, 2.5 cm cube (If score = 0, total = 0 and go to Grip) Pick up 2.5 cm block	_____
3. Block, wood, 5 cm cube	_____
4. Block, wood, 7.5 cm cube	_____
5. Ball (Cricket), 7.5 cm diameter	_____
6. Stone 10 x 2.5 x 1 cm	_____
Coefficient of reproducibility =	
0.98 Coefficient of scalability	
= 0.94	
Grip	
1. Pour water from glass to glass (If score = 3, total = 12, and go to Pinch)	_____
2. Tube 2.25 cm (If score = 0, total = 0 and go to Pinch)	_____
3. Tube 1 x 16 cm	_____
4. Washer (3.5 cm diameter) over bolt	_____
Coefficient of reproducibility =	
0.99 Coefficient of scalability =	
0.98	
Pinch	
1. Ball bearing, 6 mm, 3 rd finger and thumb (If score = 3, total = 18 and go to Grossmt)	_____
2. Marble, 1.5 cm, index finger and thumb (If score = 0, total = 0 and go to Grossmt)	_____
3. Ball bearing 2 nd finger and thumb	_____
4. Ball bearing 1 st finger and thumb	_____

5. Marble 3rd finger and thumb

6. Marble 2nd finger and thumb

Coefficient of reproducibility =

0.99 Coefficient of scalability

= 0.98

Grossmt (Gross Movement)

1. Place hand behind head (If score = 3, total = 9 and finish)

2. (If score = 0, total = 0 and finish)

3. Place hand on top of head

4. Hand to mouth

Coefficient of reproducibility =

0.98 Coefficient of scalability =

0.97

References

Carroll D. "A quantitative test of upper extremity function."
J Chronic Diseases. 1965;18:479-491.

Crow JL, Lincoln NNB, Nouri FM, De Weerd W. "The effectiveness of EMG biofeedback in the treatment of arm function after stroke."
International Disability Studies. 1989;11:155-160.

De Weerd WJG, Harrison MA. "Measuring recovery of arm-hand function in stroke patients: a comparison of the Brunnstrom-Fugl-Meyer test and the Action Research Arm test."
Physiotherapy Canada. 1985;37:65-70.

Lyle RC. "A performance test for assessment of upper limb function in physical rehabilitation treatment and research."
[Int J Rehabil Res. 1981;4:483-492.](#)

FUGL-MEYER ASSESSMENT UPPER EXTREMITY (FMA-UE) Assessment of sensorimotor function

UPPER EXTREMITY						
I. Reflex activity			none	can be elicited		
Flexors: biceps and finger flexors (at least one)			0	2		
Extensors: triceps			0	2		
Subtotal						
II. Volitional movement within synergies			none	partial	full	
Flexor synergy: Hand from contralateral knee to ipsilateral ear. From extensor synergy (shoulder adduction/ internal rotation, elbow extension, forearm pronation) to flexor synergy (shoulder abduction/ external rotation, elbow flexion, forearm supination). Extensor synergy: Hand from ipsilateral ear to the contralateral knee	Shoulder	retraction	0	1	2	
		elevation	0	1	2	
		abduction	0	1	2	
		(90°) external	0	1	2	
	Elbow	rotation flexion	0	1	2	
	Forearm	supination	0	1	2	
	Shoulder	adduction/internal	0	1	2	
		Elbow	rotation extension	0	1	2
		Forearm	pronation	0	1	2
	Subtotal					
III. Volitional movement mixing synergies, without compensation			none	partial	full	
Hand to lumbar spine hand on lap	cannot perform or hand in front of ant-sup iliac spine hand behind ant-sup iliac spine (without compensation) hand to lumbar spine (without compensation)		0	1	2	
Shoulder flexion 0°- 90° elbow at 0° pronation-supination 0°	immediate abduction or elbow flexion abduction or elbow flexion during movement flexion 90°, no shoulder abduction or elbow flexion		0	1	2	
Pronation-supination elbow at 90° shoulder at 0°	no pronation/supination, starting position impossible limited pronation/supination, maintains starting position full pronation/supination, maintains starting position		0	1	2	
Subtotal						
IV. Volitional movement with little or no synergy			none	partial	full	
Shoulder abduction 0 - 90° elbow at 0° forearm pronated	immediate supination or elbow flexion supination or elbow flexion during movement abduction 90°, maintains extension and pronation		0	1	2	
Shoulder flexion 90° - 180° elbow at 0°	immediate abduction or elbow flexion abduction or elbow flexion during movement		0	1	2	

pronation-supination 0°	flexion 180°, no shoulder abduction or elbow flexion			
Pronation/supination elbow at 0° shoulder at 30°- 90° flexion	no pronation/supination, starting position impossible limited pronation/supination, maintains start position full pronation/supination, maintains starting position	0	1	2
Subtotal IV				
V. Normal reflex activity assessed only if full score of 6 points is achieved in part IV; compare with the unaffected side		0 (IV), hyper	lively	normal
biceps, triceps, finger flexors	2 of 3 reflexes markedly hyperactive or 0 points in part IV 1 reflex markedly hyperactive or at least 2 reflexes lively maximum of 1 reflex lively, none hyperactive	0	1	2
Subtotal V (max 2)				
Total A (max 36)				

B. WRIST support may be provided at the elbow to take or hold the starting position, no support at wrist, check the passive range of motion prior testing		none	partial	full
Stability at 15° dorsiflexion elbow at 90°, forearm pronated shoulder at 0°	less than 15° active dorsiflexion dorsiflexion 15°, no resistance tolerated maintains dorsiflexion against resistance	0	1	2
Repeated dorsiflexion / volar flexion elbow at 90°, forearm pronated shoulder at 0°, slight finger flexion	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Stability at 15° dorsiflexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	less than 15° active dorsiflexion dorsiflexion 15°, no resistance tolerated maintains dorsiflexion against resistance	0	1	2
Repeated dorsiflexion / volar flexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Circumduction elbow at 90°, forearm pronated shoulder at 0°	cannot perform volitionally jerky movement or incomplete complete and smooth circumduction	0	1	2
Total B				

C. HAND support may be provided at the elbow to keep 90° flexion, no support at the wrist, compare with unaffected hand, the objects are interposed, active grasp		none	partial	full
Mass flexion from full active or passive extension		0	1	2

Mass extension from full active or passive flexion		0	1	2
GRASP				
a. Hook grasp flexion in PIP and DIP (digits II-V), extension in MCP II-V	cannot be performed can hold position but weak maintains position against resistance	0	1	2
b. Thumb adduction 1-st CMC, MCP, IP at 0°, scrap of paper between thumb and 2-nd MCP joint	cannot be performed can hold paper but not against tug can hold paper against a tug	0	1	2
c. Pincer grasp, opposition pulpa of the thumb against the pulpa of 2-nd finger, pencil, tug upward	cannot be performed can hold pencil but not against tug can hold pencil against a tug	0	1	2
d. Cylinder grasp cylinder shaped object (small can) tug upward, opposition of thumb and fingers	cannot be performed can hold cylinder but not against tug can hold cylinder against a tug	0	1	2
e. Spherical grasp fingers in abduction/flexion, thumb opposed, tennis ball, tug away	cannot be performed can hold ball but not against tug can hold ball against a tug	0	1	2
Total C				

D. COORDINATION/SPEED , sitting, after one trial with both arms, eyes closed, tip of the index finger from knee to nose, 5 times as fast as possible		marked	slight	none
Tremor	at least 1 completed movement	0	1	2
Dysmetria at least 1 completed movement	pronounced or unsystematic slight and systematic no dysmetria	0	1	2
		≥ 6s	2 - 5s	< 2s
Time start and end with the hand on the knee	at least 6 seconds slower than unaffected side 2-5 seconds slower than unaffected side less than 2 seconds difference	0	1	2
Total D				

TOTAL A-D (max 66)				
H. SENSATION , upper extremity eyes closed, compared with the unaffected side		anesthesia	hypoesthesia or dysesthesia	normal
Light touch	upper arm, forearm	0	1	2
	palmary surface of the hand	0	1	2
		less than 3/4 correct or absence	3/4 correct or considerable difference	correct 100%, little or no difference

Position	shoulder	0	1	2
small alterations in the position	elbow	0	1	2
	wrist	0	1	2
	thumb (IP-joint)	0	1	2
Total H				

J. PASSIVE JOINT MOTION , upper extremity, sitting position, compare with the unaffected side				J. JOINT PAIN during passive motion, upper extremity		
	only few degrees (less than 10° in shoulder)	decreased	normal	pronounced pain during movement or very marked pain at the end of the movement	some pain	no pain
Shoulder						
Flexion (0° - 180°)	0	1	2	0	1	2
Abduction (0°-90°)	0	1	2	0	1	2
External rotation	0	1	2	0	1	2
Internal rotation	0	1	2	0	1	2
Elbow						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Forearm						
Pronation	0	1	2	0	1	2
Supination	0	1	2	0	1	2
Wrist						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Fingers						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Total (max 24)				Total		
A. UPPER EXTREMITY				/36		
B. WRIST				/10		
C. HAND				/14		
D. COORDINATION / SPEED				/ 6		
TOTAL A-D (motor function)				/66		
H. SENSATION				/12		
J. PASSIVE JOINT MOTION				/24		
J. JOINT PAIN				/24		

MOTOR ACTIVITY LOG

		Amount	How Well	Comments
1	Turn light on			
2	Open drawer			
3	Pick up clothing			
4	Pick up phone			
5	Wipe counter			
6	Open car door			
7	Open refrigerator			
8	Turn door knob			
9	Operate TV remote			
10	Wash hands			
11	Dry hands			
12	Put socks on			
13	Take socks off			
14	Put shoes on			
15	Take shoes off			
16	Get out of a chair			
17	Pull the chair out			
18	Pull the chair in			
19	Pick up a glass			
20	Brush teeth			
21	Apply makeup, lotion, shaving cream			
22	Use key to open door			
23	Write on paper			
24	Use hand to stabilize while standing			
25	Carry object			
26	Use fork			
27	Use comb/brush			
28	Pick up cup with a handle			
29	Button shirt			
30	Eat finger foods			
Average				

Amount Scale		How well Scale
0	Did not use my weaker arm (not used).	The weaker arm was not used at all for that activity (never).
0.5		
1.0	Occasionally used my weaker arm, but only very rarely (very rarely).	The weaker arm was moved during that activity but was not helpful (very poor).
1.5		
2.0	Sometimes used my weaker arm but did the activity most of the time with my stronger arm (rarely).	The weaker arm was of some use during that activity but needed some help from the stronger arm or moved very slowly or with difficulty (poor).
2.5		
3.0	Used my weaker arm about half as much as before the stroke (half pre-stroke).	The weaker arm was used for the purpose indicated but movements were slow or were made with only some effort (fair).
3.5		
4.0	Used my weaker arm almost as much as before the stroke (3/4 pre-stroke).	The movements made by the weaker arm were almost normal, but were not quite as fast or accurate as normal (almost normal).
4.5		
5	Used my weaker arm as often as before the Stroke (same as pre-stroke).	The ability to use the weaker arm for that activity was as good as before the stroke (normal).

Reference: Taub, E., McCulloch, K., Uswatte, G., Morris, D.M., Bowman, M., Crago, J., King, D.K., Bishop, S., Allen, F. and Yakley, S., 2011. Motor activity log (mal) manual. *UAB Training for CI*

Stroke Specific Quality of Life Scale (SS-QOL)

Scoring: each item shall be scored with the following key

Total help - Couldn't do it at all - Strongly agree	1
A lot of help - A lot of trouble - Moderately agree	2
Some help - Some trouble - Neither agree nor disagree	3
A little help - A little trouble - Moderately disagree	4
No help needed - No trouble at all - Strongly disagree	5

Energy

1. I felt tired most of the time. _____
2. I had to stop and rest during the day. _____
3. I was too tired to do what I wanted to do. _____

Family Roles

1. I didn't join in activities just for fun with my family. _____
2. I felt I was a burden to my family. _____
3. My physical condition interfered with my personal life. _____

Language

1. Did you have trouble speaking? For example, get stuck, stutter, stammer, or slur your words? _____
2. Did you have trouble speaking clearly enough to use the telephone? _____
3. Did other people have trouble in understanding what you said? _____
4. Did you have trouble finding the word you wanted to say? _____
5. Did you have to repeat yourself so others could understand you? _____

Mobility

1. Did you have trouble walking? (If patient can't walk, go to question 4 and score questions 2-3 as 1.) _____
2. Did you lose your balance when bending over to or reaching for something? _____
3. Did you have trouble climbing stairs? _____
4. Did you have to stop and rest more than you would like when walking or using a wheelchair? _____
5. Did you have trouble with standing? _____
6. Did you have trouble getting out of a chair? _____

Mood

1. I was discouraged about my future.
2. I wasn't interested in other people or activities.
3. I felt withdrawn from other people.
4. I had little confidence in myself.
5. I was not interested in food.

Personality

1. I was irritable.
2. I was impatient with others.
3. My personality has changed.

Self Care

1. Did you need help preparing food?
2. Did you need help eating? For example, cutting food or preparing food?
3. Did you need help getting dressed? For example, putting on socks or shoes, buttoning buttons, or zipping?
4. Did you need help taking a bath or a shower?
5. Did you need help to use the toilet?

Social Roles

1. I didn't go out as often as I would like.
2. I did my hobbies and recreation for shorter periods of time than I would like.
3. I didn't see as many of my friends as I would like.
4. I had sex less often than I would like.
5. My physical condition interfered with my social life.

Thinking

1. It was hard for me to concentrate.
2. I had trouble remembering things.
3. I had to write things down to remember them.

Upper Extremity Function

1. Did you have trouble writing or typing? _____
2. Did you have trouble putting on socks? _____
3. Did you have trouble buttoning buttons? _____
4. Did you have trouble zipping a zipper? _____
5. Did you have trouble opening a jar? _____

Vision

1. Did you have trouble seeing the television well enough to enjoy a show?
2. Did you have trouble reaching things because of poor eyesight?
3. Did you have trouble seeing things off to one side?

Work/Productivity

1. Did you have trouble doing daily work around the house?
2. Did you have trouble finishing jobs that you started?
3. Did you have trouble doing the work you used to do?

TOTAL SCORE	_____
--------------------	-------

Reference

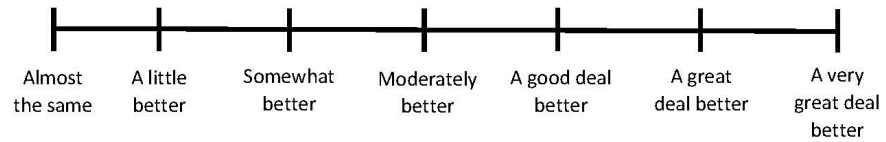
Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke-specific quality of life scale. [Stroke 1999 Jul;30\(7\):1362-9.](#)

Patient Name
Assessor:
Date:

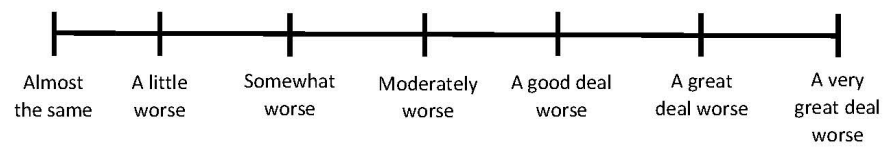
Participant Perception of Treatment Scale

Patient Name:
Question: Do you think your condition gets worse, better or the same?

If better...



If worse



MOTOR ASSESSMENT SCALE
MOVEMENT SCORING SHEET

Name : _____

	0	1	2	3	4	5	6
1. Supine to side lying							
2. Supine to sitting over side of bed							
3. Balanced sitting							
4. Sitting to standing							
5. Walking							
6. Upper arm function							
7. Hand movements							
8. Advanced hand activities							

Reference: Carr, J.H., Shepherd, R.B., Nordholm, L. and Lynne, D., 1985. Investigation of a new motor assessment scale for stroke patients. *Physical therapy*, 65(2), pp.175-180.

TARDIEU SCALE

This scale quantifies muscle spasticity by assessing the response of the muscle to stretch applied at specified velocities.

Grading is always performed at the same time of day, in a constant position of the body for a given limb. For each muscle group, reaction to stretch is rated at a specified stretch velocity with 2 parameters x and y.

Velocity to stretch (V)

- V1** As slow as possible
- V2** Speed of the limb segment falling
- V3** As fast as possible (> natural drop)

V1 is used to measure the passive range of Motion. (PROM). Only V2 and V3 are used to rate spasticity

Quality of muscle reaction (X)

- 0** No resistance throughout passive movement
- 1** Slight resistance throughout, with no clear catch at a precise angle
- 2** Clear catch at a precise angle, followed by release
- 3** Fatigable clonus (<10secs) occurring at a precise angle
- 4** Unfatigable clonus (>10secs) occurring at a precise angle
- 5.** Joint Immobile

Angle of muscle reaction (Y)

Measure relative to the position of minimal stretch of the muscle (corresponding at angle)

Spasticity Angle

- R1** Angle of catch seen at Velocity V2 or V3
- R2** Full range of motion achieved when muscle is at rest and tested at V1 velocity

Date	Joint/ Muscle	L/R	V	X	R1	R2	Active ROM	Power MRC	°

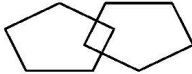
Ref: Boyd R, Graham K. Objective Measurement of clinical findings in the use of Botox type A for the management of children with Cerebral Palsy. European Journal of Neurology 6(Supp 4) S23-35 Tardieu G, Rondont O, Mensch J, Dalloz J, Monfraix C, Tabary J. Responses electromyographiques a l'etirement musculaire chez l'homme normal. Revue Neurologie + 97(1), 60-61 Gracies J, Marosszzeky J, Renton R, Sandaman J, Gandevia S, Burke D. Short term effects of dynamic splints on the upper limb in hemiplegic patients. Archives of Physical Medicine and Rehabilitation, 81 1547-1555.

Mini-Mental State Examination (MMSE)

Patient's Name:

Date:

Instructions: Ask the questions in the order listed. Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

(Adapted from Rovner & Folstein, 1987)

Source:

- Folstein MF, Folstein SE, McHugh PR: "Mini-mental state: A practical method for grading the cognitive state of patients for the clinician." *J Psychiatr Res* 1975;12:189-198.
- Source: www.medicine.uiowa.edu/igec/tools/cognitive/MMSE.pdf

Demographic Profile
Participant with Stroke

Please answer the questions below completely.

I. Personal Details:

Name:

Age:

Gender:

- ☐ Male
- ☐ Female
- ☐ LGBTQ+
- ☐ Prefer not to say
- ☐ Others (Please Specify)

Civil Status:

- ☐ Single
- ☐ De facto
- ☐ Married
- ☐ Divorced/Separated
- ☐ Widowed
- ☐ Others (Please specify)

Highest Educational Attainment:

- ☐ High school Graduate
- ☐ Certificate I,II,III,IV
- ☐ Diploma, Advance diploma and associate degree
- ☐ Bachelor degree
- ☐ Master degree (Research/Coursework)
- ☐ Doctoral Degree (extended, coursework and research)
- ☐ Others (Please specify):

Employment Status:

- ☐ Unemployed
- ☐ Employed (Casual, part time, full time)
- ☐ Self-employed
- ☐ Others (Please specify)

Profession:

Contact Number:

II. Stroke Profile (Please answer only those you can recall)

When were you diagnosed with stroke?

Was that the first time you had stroke?

What type of stroke are you diagnosed?

What artery is affected?

III. Comorbidities (Please answer if you have conditions belonging under each category)

Allergy:

Lung/Pulmonary (Allergies, asthma, COPD):

Cardiovascular/Heart (Hypertension, cholesterol, heart disease, Blood clot problem, diabetes:

Skin/Integumentary (Wound, allergies):

Muscles/Bone/Joints (Fracture, muscle problem, arthritis):

IV. Social History (Please answer the questions below)

Do you smoke?

Do you drink alcohol (If so, the amount and type)?

What do you do in your leisure time?

What's your current work?

Do you exercise? (Gym, sports, walking every morning)

V. Others:

Are you currently undergoing treatment from a therapist (Physiotherapist, Occupational Therapist, and Exercise Scientist/Physiologist) If yes, How long?

What are the usual exercises you are doing? (Please describe)

Did you experience using robotics in exercising your weak arm after stroke?

Who is your primary carer? (Family member, employed carer)

Patient Questionnaire

Name:

General Questions about robotics training

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	I don't know
My affected arm stronger after robotic training						
I was tired after training						
I find it easier to perform my day-to-day activities after robotic exercise training						
I have more confidence when performing my day-to-day activities after robotic exercise training						
I enjoyed robotic exercise training						
I enjoyed the gaming component of the training						
I felt good following each training session						
The training was interesting						
The training protocol addressed my rehabilitation needs						
I would perform this form of training again if given the opportunity						

Hand training

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	I don't know
I feel comfortable using the Hand device						
I feel motivated when I use the Hand device						
I like the machine used to train my hand						
I am satisfied with the machine used to train my hand						
I feel safe when using the machine to train my hand						

Elbow-Forearm training

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree

I feel comfortable using the Elbow-Forearm training					
I am motivated when I am using the Elbow-Forearm training					
I like the machine used to train my elbow-forearm					
I am satisfied with the machine used to train my elbow-forearm					
I feel safe when using the machine to train my elbow-forearm					

Shoulder-arm training

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
I feel comfortable using the Shoulder-arm device					
I am motivated when I am using the Shoulder-arm device					
I like the machine used to train my shoulder-arm					
I am satisfied with the machine used to train my shoulder-arm					
I feel safe when using the machine to train shoulder-arm					

Appendix H Semi-Structure Interview Guide Questions

1. Tell me about your experiences during the period that you attended the robotic training?
 - a. Probe: I want to know the good and the things that were not that good
2. Do you believe that you had benefited from participating in the robotic training? If yes, in what areas? If not, how could it be improved?
 - a. Probe: physical/functional/day-to-day activities/socially/well-being/psychological
3. What are your feelings about training devices?
 - a. Probe: I want to know the good and the things that were not that good
4. What is your opinion of using the robotic devices?
5. Would you or would not recommend to others and would you or would not use it again?
6. How long did it take you to get to the UTS Moorepark for training? How many hours of your day did you spend to attend the training?
7. Was there any cost involved?

Appendix I Family members/carers Perception and Observation Questionnaire (Online version)

Confidential

Page 2 of 11

Instruction: Please read carefully the INFORMATION SHEET AND CONSENT FORM below. If you agree, you can tick the "agree button" to proceed to the questionnaire. If you have doubts and want to ask for further details about the study, you can tick the "I don't agree button" for now and contact any person provided below.

Title of the Study

Robotic-assisted game-based rehabilitation for upper limb function in people with chronic stroke: A feasibility study

What is the research study about?

Nowadays, technology plays a very important role in healthcare like the use of robotics to treat diseases, provide assistance to people with disabilities, and many more. One of the trending application of robotics is to help people after a stroke to perform exercises to improve the movements and use of their arms. Robotics is gaining an important role in rehabilitation in these days, because unlike any other treatment, it 1) assist both the therapist and patient to achieve their goal better and faster 2) it is fun and motivating as patients can play games while using the robots 3) it can monitor progress or improvement of arm and hand movements and 4) it can provide many repetitions of movement which is a very important aspect of re-learning of arm/hand skills.

However, this is an area that needs more research. There are few studies that explored the opinions and views of people who had stroke, their therapists and their carer/family member about the robot-assisted game-based rehabilitation. Hence, this study aims to better understand if robot-assisted game-based rehabilitation is an accepted treatment for people after stroke. By doing this, we can understand the strengths and weaknesses of robotic rehabilitation. Moreover, this will provide a sneak peek of the possible effects of such intervention in the arm affected by stroke.

Who is conducting this research?

My name is Esminio Il L. Rivera and I am a research student at UTS. My supervisors are Dr. Camila Quel De Oliveira (Primary supervisor, email: Camila.QuelDeOliveira@uts.edu.au), Dr. Arianne Verhagen, Dr. Peter Stubbs and Dr. Alana McCambridge.

Inclusion/Exclusion Criteria

Before you decide to participate in this research study, we need to ensure that you are eligible to take part. You must be a family member who lives with a person that had a stroke or you are a carer who assists a person who had a stroke for at least 4 hours in his/her activities of daily living, such as transferring from bed to chair, eating, personal hygiene and going out and about.

Do I have to take part in this research study?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part. If you decide to participate, I will invite you to answer a questionnaire and you will be asked to:

1. Provide personal details like your name, age, gender, contact number and details about your role to the person who had a stroke during day-by-day activities and the time you spend with the person.
2. Answer an online survey. The survey has questions about any changes that you may have noticed in the ability to use their arm affected by the stroke. You can choose to answer the survey online or to accompany the patient at his/her last day of treatment session to answer the paper based survey. The questionnaire will be handed out to you and it will be retrieved on the same day. The survey should take approximately 30 min to answer

Are there any risks/inconvenience?

We don't expect serious harm in joining the study, however emotional distress is possible as questions may trigger unpleasant memories or sensitive topic maybe covered in the questionnaire. Moreover, joining the study may cause inconvenience and burden of commitment since you will be asked to commit some of your time to this study.

What will happen to information about me?

Access to the online questionnaire is via RedCap. By clicking the Agree button below, you give your consent to the research team collecting and using personal information about you for the research project. If you decide to answer the survey on paper, you will be asked to sign an informed consent form. All this information will be treated confidentially. Only the research student and the primary supervisor of the study will have an access to your data. Moreover, the data will be presented in such a way that your identification will not be disclosed. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

We would like to store your information for future use in research projects that are an extension of this research project. In all instances your information will be treated confidentially.

We plan to publish the results in scientific journals and conferences in the future. In any publication, information will be provided in such a way that you cannot be identified.

What will happen if I say no?

www.projectredcap.org



If you decide not to participate, it will not affect your relationship with the researchers or the University of Technology Sydney. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason, by contacting Mr. Esmínio L. Rivera II, the principal investigator of this study. If in case you have withdrawn from the study, please take note that all information you provided from all the phases of the study will be erased from our database (for soft copy) and will be destroyed (hard copies like questionnaires)

What if I have concerns or a complaint?

If you have concerns about the research that you think I or my supervisor can help you with, please feel free to contact us on the following:

Esmínio L. Rivera II

Research Student

Phone: +61. [REDACTED]

Email: esminioii.rivera@student.uts.edu.au

Dr. Camila Quel De Oliveira

Principal Supervisor

Email: Camila.QuelDeOliveira@uts.edu.au

If you would like to talk to someone who is not connected with the research, you may contact the Research Ethics Officer on 02 9514 9772 or Research.ethics@uts.edu.au and quote this number [UTS HREC Approval Number]

☐ I agree and give my consent

☐ I don't agree and I don't give my consent

Please provide your personal details below.

Name _____

Gender: _____

Age: _____

Contact Number _____

Email _____

- Highest Educational Attainment
- ☐ High school Graduate
 - ☐ Certificate I,II,III,IV
 - ☐ Advance diploma and associate degree
 - ☐ Bachelor degree
 - ☐ Master degree and Doctoral Degree (extended, coursework and research)
 - ☐ Others (Please specify):

Others (please specify) _____

ANSWER THE FOLLOWING QUESTIONS:

What is your relationship with the participant?

- ☐ Married/Partner
- ☐ Sibling
- ☐ Cousin/Aunt/Uncle/grandparents (please circle)
- ☐ Son/daughter/ grandchildren (please circle)
- ☐ Employed carer
- ☐ Others (Please specify):

Others (Please specify)

Are you spending time with the participant with stroke everyday?

- ☐ Yes
- ☐ No

On average, how much time do you spend with the participant per day?

- ☐ < 1 hour
- ☐ 1 hour to 4 hours
- ☐ 4 hours- 8 hours
- ☐ > 8 hours

How much assistance do you give to the participant with stroke in the following self-care activities?

	I am just there near him/her in case he/she needs my help	I am helping him/her a little but he/she does the task more	I am helping him/her and I think more effort is coming from me	I am completely assisting him/her in this activity	I am not assisting him/her on this activity	I don't know
Eating	☐	☐	☐	☐	☐	☐
Grooming	☐	☐	☐	☐	☐	☐
Bathing	☐	☐	☐	☐	☐	☐
Dressing	☐	☐	☐	☐	☐	☐
Toileting	☐	☐	☐	☐	☐	☐

How much assistance do you give the participant with stroke in activities that requires transfer and mobility?

	I am just there near him/her in case he/she needs my help	I am helping him/her a little but he/she does the task more	I am helping him/her and I think more effort is coming from me	I am completely assisting him/her in this activity	I am not helping him/her in this activity	I don't know
Bed, Chair, Wheelchair	☐	☐	☐	☐	☐	☐
Pushing wheelchair	☐	☐	☐	☐	☐	☐
Walking	☐	☐	☐	☐	☐	☐
Bed mobility (lying down to side lying to sitting)	☐	☐	☐	☐	☐	☐

Acceptability of Robotics

Instruction: Please read the following statement about the response of patient to the robotic training protocol by ticking the ONE box for your answer

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	I don't know
I believe that the affected arm of the participant is now stronger after robotic training	☐	☐	☐	☐	☐	☐
I believe that the participant is tired after training using robotics	☐	☐	☐	☐	☐	☐
I believe that the participant finds it easier to perform day-to-day activities since beginning robotic training	☐	☐	☐	☐	☐	☐
I believe that the participant is more confident in performing day-to-day activities since beginning robotic training	☐	☐	☐	☐	☐	☐
I believe that the participant enjoyed the exercise using robotics	☐	☐	☐	☐	☐	☐
I believe that the participant enjoyed the gaming component of training	☐	☐	☐	☐	☐	☐
I believe that the participant felt good after one session of exercise using robotics	☐	☐	☐	☐	☐	☐
I believe that the participant was interested during training using robotics	☐	☐	☐	☐	☐	☐
I believe that the participant was motivated to attend treatment sessions	☐	☐	☐	☐	☐	☐

Positive aspect/s of training using robotics

What is/are the positive aspect of training using the robotics? (you can tick more than 1):

- ☐ Participant uses his/her arm better in his/her daily activities
- ☐ Participant is more confident in using the affected arm
- ☐ Participant enjoys the treatment
- ☐ Participant's attitude towards his/her condition is more positive
- ☐ Participant is more independent with his/her daily activities
- ☐ Others (Please specify):

Others (Please specify) _____

Based on your answer above, what is the main reason
you would recommend the device/training to other
people with stroke? _____

What is/are the negative aspect of training using the robotics (you can tick more than 1):

- ☐ No improvements in how the participant uses his/her arm
- ☐ No improvements in the confidence of the participant using his/her arm
- ☐ Participant was not interested during the treatment
- ☐ Participant was not comfortable using the machine
- ☐ Participant's attitude towards his/her condition hasn't change
- ☐ Participant level required level of assistance has not changed
- ☐ Others (Please specify):

Others (Please specify) _____

IDEA FLIP

