A Randomised Controlled Trial of Bilateral Movement-based Computer Games Training to Improve Motor Function of Upper Limb and Quality of Life in Sub-acute Stroke Patients

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Acknowledgement

- **Health and Medical Research Fund (HMRF # 02133096)**
- **Research Project Team**

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INTRODUCTION

In 2017, 25,861 inpatient discharges and deaths were related to cerebrovascular diseases (HK)

(HealthyHK, Department of Health, HKSAR, 2017)

~ 80% stroke patients reported significant impairments in the hemiplegic upper limbs

(Lawrence et al., 2001)

<15% post-stroke patients could restore normal function in daily activities

(Hendricks et al., 2002)

Sensorimotor impairment could significantly affect the motor function of upper limbs and quality of life

(Teasell et al., 2005; Nichols-Larsen et al., 2005; Buggea et al., 2001)

Motor recovery after stroke is related to the **neuroplasticity** of the brain

(Chen et al., 2010; Dancause & Nudo, 2011; Hosp & Luft, 2011; Takeuchi & Izumi, 2012)

Majority of rehabilitation protocol for stroke patients are based on **motor learning theory**

Functional gain would be greater if the training methods are **meaningful**, **repetitive** and **intensive**

(Kleim & Jones, 2008; Arya et al., 2011)

Virtual Reality-based Therapy

- **interactive simulations**
- computer-generated scenario that appears similar to the real world
- **motivate** patients to **engage** in rehabilitation
- **optimise motor learning process**
  - intellectual stimulation involved in playing
  - immediate feedback from game scores
  - physical benefits from the exercise
  - having game levels suitable for a range of abilities
  - connecting with the game
  - social interaction during group play

Laver et al. 2015; Rizzo et al. 2005; Brunner et al. 2014; King et al. 2010

Bilateral Movement Training

- more **effective** than unilateral training
- using the non-paretic limb to enhance functional recovery of the paretic limb
- facilitative coupling effects between the upper limbs
- **promotes neural plasticity**
- **facilitates control** of the paretic limb's movement

Summers et al. 2007; Whitall et al. 2000; Stewart et al. 2006; Van Delden etal. 2012; Cauraugh et al. 2005; Coupar et al. 2010

OBJECTIVES

To investigate whether **bilateral movement-based computer training (BMCT)** would be **superior** to the **conventional training**, in improving the **motor control** and **functional use** of paretic upper limb and quality of life in sub-acute stroke patients.

METHODS

ClinicalTrials.gov ID : NCT03618732

Geriatric Day Hospital at Shatin Hospital
New Territories East Cluster of Hospital Authority

The study protocol was approved by:

- ✓ **The Joint Chinese University of Hong Kong (CUHK)-New Territories East Cluster (NTEC) Clinical Research Ethics Committee (CREC)**

The study was conducted according to:

- ✓ The Declaration of Helsinki for human experiments and
- ✓ The good clinical practice standards of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

Stratified, Single-blinded, Randomized Controlled Trial

Geriatric Day Hospital, Shatin Hospital

Patients with sub-acute stroke were screened

Stratified by **sex/ age/ type of stroke** and randomly allocated to 1 of 2 groups

BMCT Group

Standard conventional physiotherapy training
+
30-minute Bilateral Movement-based Computer Training (BMCT)

VDCT Group

Standard conventional physiotherapy training
+
30-minute of Video-Directed Conventional Training (VDCT)

16 treatment sessions over 8-week period

Study Design – Clinical Trial

Stratified

Age
- 45 to 64 years-old
- 65 to 85 years-old

Gender
- Male
- Female

Type of stroke
- Infarct
- Haemorrhage

Randomized

- stratified blocked randomization
- random number table
- random selection from the blocks of 4

Single-blinded

- Blinded assessor

Inclusion criteria	Exclusion criteria
between 45 and 85 years of age	used a cardiac pacemaker
diagnosed with an ischaemic brain injury or an intracerebral haemorrhage by MRI or CT 1 week to 6 months previously	any additional medical, cardiovascular and orthopaedic condition that would hinder their proper assessment and treatment
suffered a single stroke	had receptive dysphasia
able to hold the game controller with the paretic hand	involved in a drug study or other clinical trial.
Abbreviated Mental Test score ≥ 7 /10	
able to follow instructions	
willing to give informed consent.	

Sample size
- a pilot study predicted an effect size of 0.64
- the alpha level was set at 0.05 and the design was based on a power of 80%
- assuming the possible drop-out rate of 10%, **the sample size required was estimated to be 88 subjects**

90 minutes standard Conventional Physiotherapy Training	
Upper arm and hand function training (30 minutes)	• Passive stretching and weight bearing exercise (5 minutes) • Assisted or active mobilizing exercise (5 minutes) • progressive resisted exercise (10 minutes) • Task-orientated exercise (10 minutes)
Lower limb training (30 minutes)	• Passive stretching and warm up exercise (10 minutes) • Assisted, active mobilizing exercise (10 minutes) • Progressive resisted exercise (10 minutes)
Balance, functional and endurance training (30 minutes)	• Static or dynamic standing balance exercise (10 minutes) • Functional mobility training (10 minutes) • Gait and endurance training (10 minutes)

BMCT Group

Subjects were required:

- to hold the game controller in their paretic hand, which incorporated in a standard handlebar, the other end of which was held by the non-paretic hand
- to **play the computer games** on a notebook computer (which was connected to a large separated television screen) by using the game controller
- to move the paretic arm in a **bilateral**, nearly **symmetrical** and **self-assistive** pattern with the non-paretic arm

BMCT Group

- **16 treatment sessions over 8-week period, 30 min training per session**
- **3 different games for 10 minutes each**

Hitting single stationary targets	Hitting multiple moving targets	Interacting with various stationary and moving targets or clicking on balloons to pop them
Required movement in all directions and increasing reaction speed	Interacting with multiple moving targets which required directional control, strategy and timing	Required strength, endurance and timing

VDCT Group

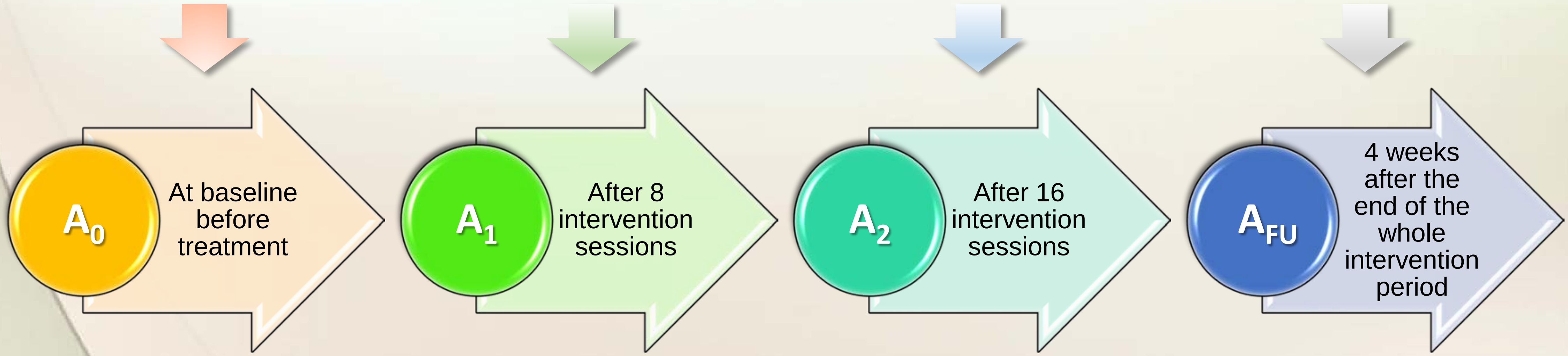
- **16 treatment sessions over 8-week period**
- **continued to exercise for 30 minutes in response to a video**

The video was used to:

- instruct the patients how to continue to do the exercises
- prescribed the exercise movements of the upper limb that the subject had performed during the physiotherapy **conventional training**
- to **equalize** the **treatment dosage**

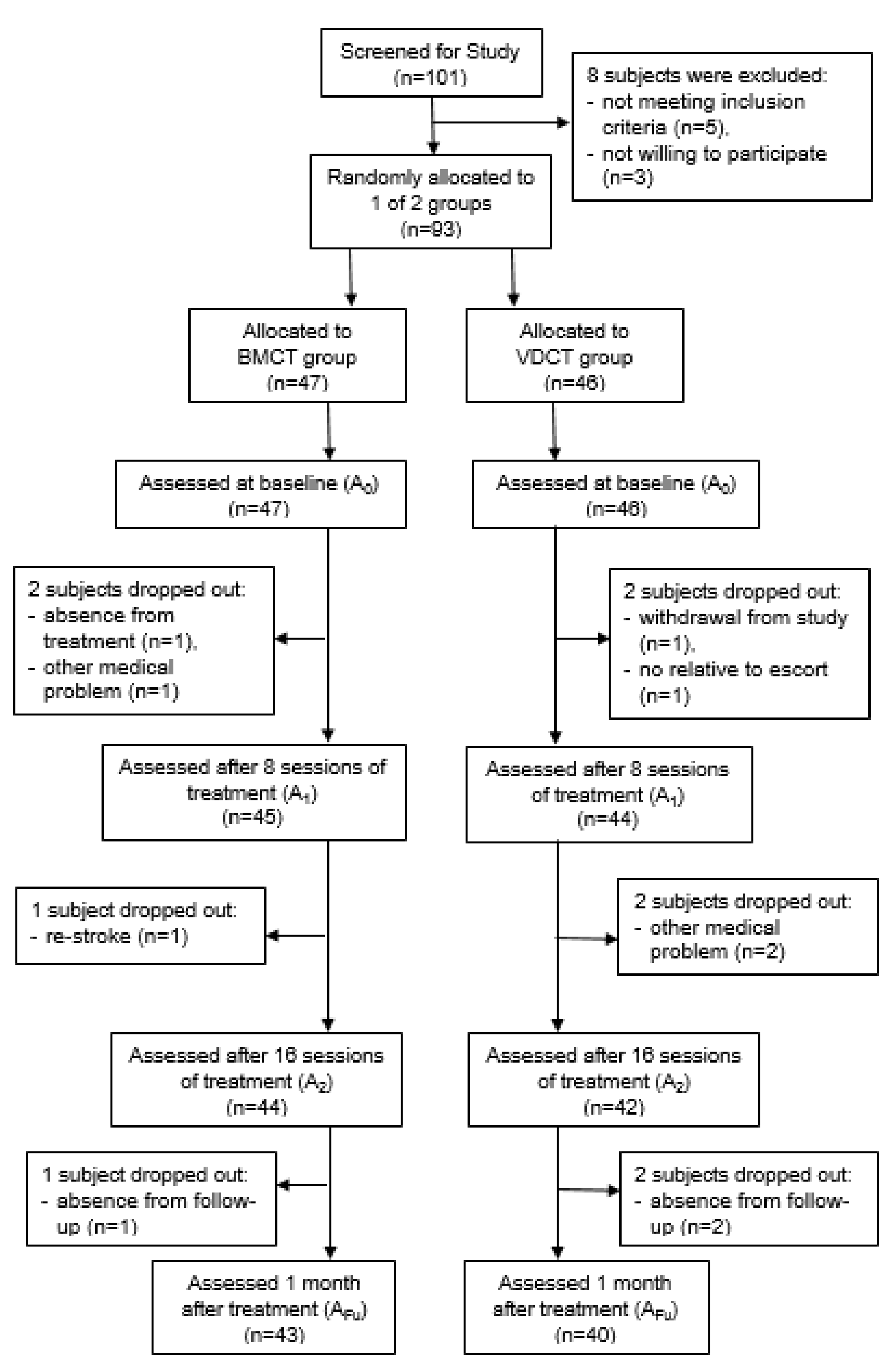
Study Outcomes

Motor Control and Function of Paretic Upper Limb		Health-related Quality of Life	
FMA-UE	Fugl-Meyer Assessment - Upper Extremity	**SF-36**	Hong Kong Short-form Health Survey (version 2)
ARAT	Action Research Arm Test	**(PCS)**	Physical Component Summary
GS	Grip strength	**(MCS)**	Mental Component Summary



Statistical Analysis

- demographics and baseline characteristics
- changes in the mean scores from baseline (A_0) to the primary endpoint (A_2)
- **Analysis of covariance (ANCOVA)** adjusted with the baseline measurements
  - to investigate the **significance of any observed differences between the groups** in the scores changes.
  - the significance level was set at a ***p*-value ≤ 0.05**
- all of the analyses were kept blinded to the allocation
- all of those randomized were included in the intention-to-treat population
- carried out with the help of Statistical Analysis System, SAS software (version 9.4) by the Centre for Clinical Research and Biostatistics (CCRB), CUHK



RESULTS

Demographics and baseline characteristics

Group	BMCT (n=47)	VDCT (n=46)
Male	27 (57.4)	28 (60.9)
Female	20 (42.6)	18 (39.1)
Age	65.1 ± 10.2	66.0 ± 9.0
Infarct	38 (80.9)	38 (82.6)
Haemorrhage	9 (19.1)	8 (17.4)
Post-stroke days	57.6 ± 24.7	63.4 ± 39.6

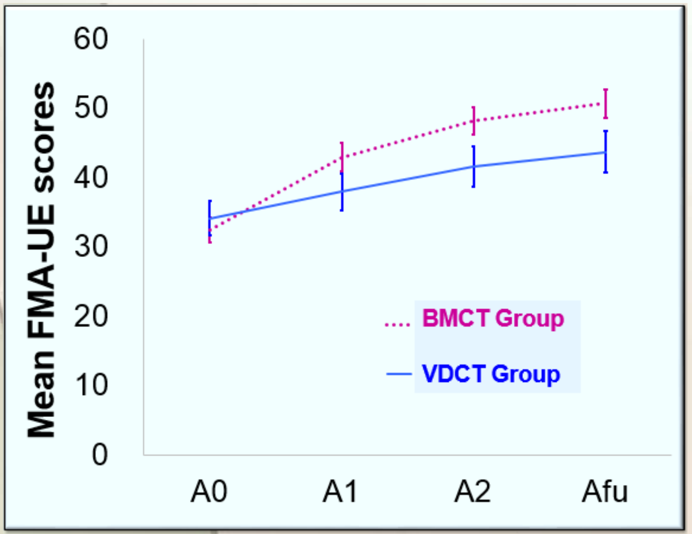
Values are mean ± standard deviation, n (%), or n.

Measures	Time point	BMCT group	VDCT group	
		Mean changes (95% CI)	Mean changes (95% CI)	*p-values*
FMA-UE	A_2	14.84 (12.42, 17.26)	6.54 (5.05, 8.02)	<0.001
ARAT	A_2	13.64 (9.65, 17.63)	6.61 (3.88, 9.33)	0.006
GS (affected)	A_2	4.89 (3.21, 6.57)	1.72 (0.78, 2.67)	0.002
GS (non-affected)	A_2	1.38 (0.27, 2.49)	1.04 (-0.00, 2.08)	0.639
SF-36 (PCS)	A_2	3.85 (1.82, 5.88)	3.23 (1.48, 4.97)	0.701
SF-36 (MCS)	A_2	4.75 (1.78, 7.72)	2.85 (0.01, 5.68)	0.455

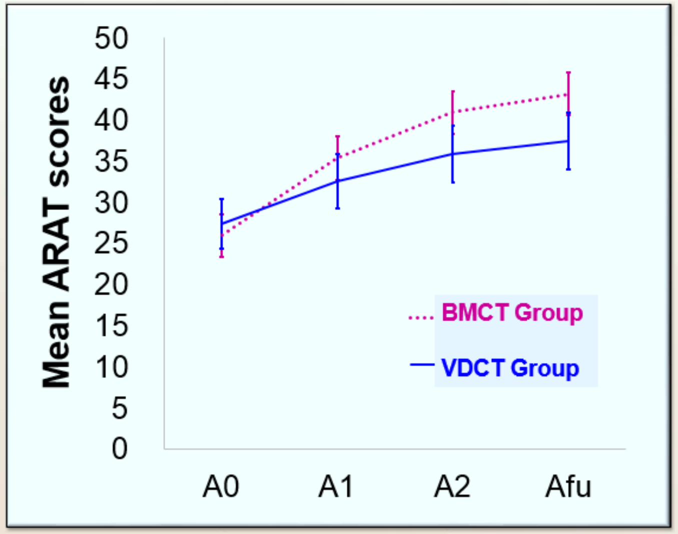
A_2 : After 16 intervention sessions

p-values: The *p*-values of intervention effect are obtained by ANCOVA analysis adjusted with baseline

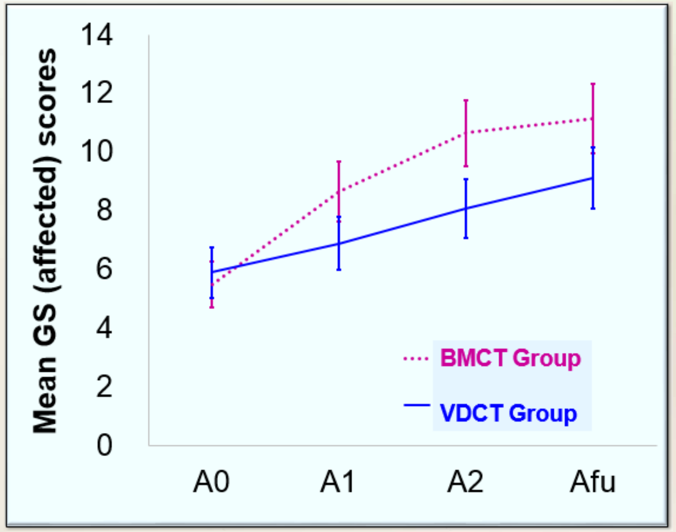
Mean changes in **FMA-UE scores, ARAT scores and GS (affected hand) scores** were statistically ***significantly greater in the BMCT group than the VDCT group*** from baselines A_0 to A_1, A_2, and A_{FU}



FMA-UE scores
All p-values < 0.001



ARAT scores
All p-values < 0.05



GS (affected hand) scores
All p-values < 0.05

DISCUSSION

Subjects receiving BMCT demonstrated significant improvement in their movements, strength and coordination, and in the functional use of their paretic upper limb

- practicing highly repetitive bilateral movements in an non-immersive simulated environment
- Self-assisted, interactive, enriched and task-orientated
- all movements were shown in real time at real speed as immediate feedback
- optimize the motor learning process
- promote cortical reorganization and possibly contribute to functional recovery

Health-related quality of life

- measured by patient-reported SF-36 in this study
- no significant differences in the mean changes of scores between the BMCT and VDCT groups
- might be due to SF-36 is a generic outcome measure for assessing quality of life in stroke patients
- the objective of this study was focused on the aspect of impairment and functional limitation of upper limb.
- the improvement may not be truly reflected in the changes of SF-36 scores

Clinical Implications

- The bilateral movement in this study was generated through virtual reality
- The positive results provide scientific evidence for the efficacy of this new treatment modality for rehabilitating upper limb function after a stroke
- Implementation of this technology at home or in day care centres
  - is **inexpensive** and **easy to operate**
  - could **motivate patients to exercise**
  - to **maintain or even improve physical health** after being discharged from rehabilitation

CONCLUSION

- Application of **BMCT** is **superior** to VDCT in **improving motor control and function** of paretic upper limb in sub-acute stroke patients.
- **BMCT** could be a **useful complement** to conventional therapy in stroke rehabilitation.

Thank You

We sincerely thanks

- Professor Herman LAU, BBH/SCH/SH HCE
- Dr. Elsie HUI, SH M&G COS(M&G)
- Ms. Carol LI, SH/GDH PT in-charge
- All the colleagues and subjects from SH/GDH who participated in this study