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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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 et al. 2012; Cauraugh et al. 2005; Coupar et al. 2010
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

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**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

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**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

<table>
<thead>
<tr>
<th>Activity</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper arm and hand function training</td>
<td>30 minutes</td>
</tr>
<tr>
<td>- Passive stretching and weight bearing exercise</td>
<td>5 minutes</td>
</tr>
<tr>
<td>- Assisted or active mobilizing exercise</td>
<td>5 minutes</td>
</tr>
<tr>
<td>- Progressive resisted exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>- Task-orientated exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>Lower limb training</td>
<td>30 minutes</td>
</tr>
<tr>
<td>- Passive stretching and warm up exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>- Assisted, active mobilizing exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>- Progressive resisted exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>Balance, functional and endurance training</td>
<td>30 minutes</td>
</tr>
<tr>
<td>- Static or dynamic standing balance exercise</td>
<td>10 minutes</td>
</tr>
<tr>
<td>- Functional mobility training</td>
<td>10 minutes</td>
</tr>
<tr>
<td>- Gait and endurance training</td>
<td>10 minutes</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Hitting single stationary targets</th>
<th>Hitting multiple moving targets</th>
<th>Interacting with various stationary and moving targets or clicking on balloons to pop them</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required movement in all directions and increasing reaction speed</td>
<td>Interacting with multiple moving targets which required directional control, strategy and timing</td>
<td>Required strength, endurance and timing</td>
</tr>
</tbody>
</table>
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**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMA-UE</td>
<td>Fugl-Meyer Assessment - Upper Extremity</td>
</tr>
<tr>
<td>ARAT</td>
<td>Action Research Arm Test</td>
</tr>
<tr>
<td>GS</td>
<td>Grip strength</td>
</tr>
</tbody>
</table>

**Health-related Quality of Life**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36</td>
<td>Hong Kong Short-form Health Survey (version 2)</td>
</tr>
<tr>
<td>PCS</td>
<td>Physical Component Summary</td>
</tr>
<tr>
<td>MCS</td>
<td>Mental Component Summary</td>
</tr>
</tbody>
</table>

**At baseline before treatment (A₀)**
- FMA-UE
- ARAT
- GS

**After 8 intervention sessions (A₁)**
- FMA-UE
- ARAT
- GS

**After 16 intervention sessions (A₂)**
- FMA-UE
- ARAT
- GS

**4 weeks after the end of the whole intervention period (Aₐ)**
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 \( \leq 0.05 \)
• 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

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

Values are mean ± standard deviation, n (%), or n.
<table>
<thead>
<tr>
<th>Measures</th>
<th>Time point</th>
<th>BMCT group Mean changes (95% CI)</th>
<th>VDCT group Mean changes (95% CI)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMA-UE</td>
<td>A₂</td>
<td>14.84 (12.42, 17.26)</td>
<td>6.54 (5.05, 8.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ARAT</td>
<td>A₂</td>
<td>13.64 (9.65, 17.63)</td>
<td>6.61 (3.88, 9.33)</td>
<td>0.006</td>
</tr>
<tr>
<td>GS (affected)</td>
<td>A₂</td>
<td>4.89 (3.21, 6.57)</td>
<td>1.72 (0.78, 2.67)</td>
<td>0.002</td>
</tr>
<tr>
<td>GS (non-affected)</td>
<td>A₂</td>
<td>1.38 (0.27, 2.49)</td>
<td>1.04 (-0.00, 2.08)</td>
<td>0.639</td>
</tr>
<tr>
<td>SF-36 (PCS)</td>
<td>A₂</td>
<td>3.85 (1.82, 5.88)</td>
<td>3.23 (1.48, 4.97)</td>
<td>0.701</td>
</tr>
<tr>
<td>SF-36 (MCS)</td>
<td>A₂</td>
<td>4.75 (1.78, 7.72)</td>
<td>2.85 (0.01, 5.68)</td>
<td>0.455</td>
</tr>
</tbody>
</table>

A₂: 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 A₀ to A₁, A₂, 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
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
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.
We sincerely thanks

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- Ms. Carol LI, SH/GDH PT in-charge
- All the colleagues and subjects from SH/GDH who participated in this study