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Immersive virtual reality enhanced reinforcement induced physical therapy (EVEREST)

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Immersive virtual reality enhanced reinforcement induced physical therapy (EVEREST)☆

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ABSTRACT

Background: Motor impairment of the upper limb (UL) post-stroke is prevalent, adversely affecting patients' quality of life. Previous research has shown that constraint-induced movement therapy (CIMT) is effective in UL rehabilitation. However, CIMT's rigorous regimen may hinder patient adherence, potentially affecting treatment efficacy. Immersive virtual reality (IVR) is an innovative approach for stroke rehabilitation. It utilizes VR technology to create dynamic environments and modify avatars efficiently, offering a less exhausting alternative to CIMT. We propose an IVR-based therapeutic approach that integrates positive reinforcement components to enhance motor coordination, offering an alternative to CIMT. This study aimed to evaluate the effect of incorporating positive reinforcement components into IVR-enhanced physical therapy (PT) on motor coordination.

Method: Eighteen stroke patients were randomly allocated to two groups: the intervention group ($n = 10$) received 30 ± 10 min/day of IVR therapy with PT, while the control group ($n = 8$) received PT alone. PT sessions, lasting 40 ± 10 min/day, were conducted on the ward in accordance with national guidelines. The mean number of sessions across all participants was 6.6, with a standard deviation of 2.98. Session frequency was tailored to individual hospital stays, adjusted due to pandemic-related early discharge protocols. For participants with stroke who received IVR (intervention group), the task involved reaching for 35 targets randomly distributed across seven different locations in the VR environment. The number of movement repetitions varied, depending on their ability to repeat the task and the length of stay in the stroke unit. The movement of the virtual image of the UL was reinforced by visual feedback to the participants, that is, the participants perceived their motor coordination as if their image of the UL was moving to a greater speed than the real UL monitored real-time while the participants were trying to reach a target. The primary outcome measure was investigated by the Fugl-Meyer assessment (FMA) scale for the affected UL, with secondary measures including a kinematic dataset (e.g., time to target) and a questionnaire assessing participant perception and achievement during therapy.

Results: The IVR group exhibited significant improvements in FMA scores ($P = 0.02$) between the first and fifth session, signifying a substantial recovery of UL motor function, with the fifth session showing higher scores. The time to target in the last session reduced compared with that in the first session, suggesting motor learning and recovery ($P = 0.03$). The patients were highly engaged and motivated during the sessions because they felt like they were in charge of controlling the virtual image of their upper body.

Conclusions: The results suggest that positive reinforcement within the IVR could encourage motor recovery of the affected hand and may facilitate the application of motor learning and neuroplasticity principles during neurological rehabilitation.

Abbreviations: ADL, Activities of daily living; BA, Border angle; BI, Barthel index; CIMT, Constraint-induced movement therapy; CT, Conventional therapy; FMA, Fugl-Meyer; IVR, Immersive virtual reality; PT, Physical therapy; RIMT, Reinforcement-induced movement therapy; UL, Upper limb; VR, Virtual reality.

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1. Introduction

A stroke occurs when blood flow to the brain is disrupted or insufficient, resulting in brain injury and subsequent impairments in both physical and cognitive functions [1–3]. Notably, approximately 70 % of stroke survivors experience motor impairments, particularly in the upper limbs (UL), which can significantly hinder self-care and participation in social activities [4–8]. Despite a marked reduction in stroke-related mortality in England, with a 50 % decrease in deaths during the first decade of the 21st century, it remains the fourth leading cause of death, and many survivors continue to live with substantial disabilities [9,10].

Adamovich et al. [11] note that stroke patients with UL impairment face substantial challenges, with functional recovery often being variable, and some individuals may experience permanent UL paresis. The treatment of UL hemiparesis is time-critical and involves a range of therapeutic modalities [12,13]. These studies underscore the importance of implementing effective rehabilitation strategies to optimize functional recovery.

Prolonged inactivity of the impaired hand can lead to learned non-use, which results from repeated unsuccessful attempts to use the affected limb and reliance on compensatory strategies [14–16]. Therefore, effective rehabilitation is essential for patients with UL impairments. Repetitive task training, particularly for improving UL function [17,18], promotes neuroplasticity by reshaping brain networks and enhancing motor control [19–21]. This repetition is crucial for improving motor learning, restoring functionality, and enabling daily activities [19,22,23].

Constraint-induced movement therapy (CIMT) is recognized as one of the most effective treatments for stroke patients. It involves constraining the unaffected limb to encourage use of the affected limb [18,24,25]. However, researchers have raised concerns about the intensive nature of CIMT, which often requires a demanding therapeutic schedule and can lead to patient fatigue [25–28].

Consequently, recent advancements in virtual reality (VR) offer promising alternatives to CIMT in stroke rehabilitation [29,30]. VR provides dynamic environments with adjustable targets, potentially alleviating the fatigue associated with CIMT [31]. In virtual rehabilitation, patients receive visual feedback from simulated environments via immersive or non-immersive systems [32,33]. Immersive systems, such as headsets, fully engage users in three-dimensional environments, relying solely on sensory input from the system to create a sense of presence [34,35]. Non-immersive systems project virtual environments onto screens, enabling interaction with two-dimensional images through devices like keyboards or controllers, thus allowing engagement with both the real and virtual worlds [36,37].

VR holds significant potential to advance motor learning and neurorehabilitation by dynamically adjusting stimuli to real-time movements and offering adaptive feedback [28,38]. Through key rehabilitative principles such as goal-oriented tasks, repetition, and dosage [11], VR fosters neuroplasticity and enhances recovery outcomes. While direct evidence of neuroplastic changes during VR training remains limited, neuroimaging research is driving the refinement of VR technologies to meet optimal treatment standards [39]. As VR becomes increasingly embedded in daily life, its integration into rehabilitation is expected to expand [40,41]. Consequently, ongoing evaluation of its efficacy is essential to inform future designs and applications.

VR environments may enhance patient motivation for engaging in repetitive, motor-intensive tasks vital for rehabilitation [42,43]. Studies have shown that basic VR games with adaptive difficulty improve mobility, motor performance, and psychological well-being compared to conventional therapy [42,43]. Neurological patients often experience low motivation for therapy, influenced by factors such as therapy goals, therapist engagement, and logistical, financial, and environmental barriers [44,45]. Post-stroke depression further contributes to reduced motivation [46]. To address these challenges, innovative approaches have been explored. For example, combining VR with modified CIMT encourages stroke patients to use the affected hand without restricting the unaffected side, allowing both hands to move freely [43]. Additionally, a study using the "Recovery Rapids" kayaking game in a virtual environment demonstrated increased rehabilitation engagement in patients with chronic hemiparesis [47].

Building on these innovations, recent studies have highlighted the potential of immersive VR (IVR) systems for post-stroke UL rehabilitation. For instance, Chen et al. demonstrated that an IVR-based exercise system significantly improved motor function, as measured by active range of motion (ROM) in shoulder flexion and abduction, within a two-week period in randomized controlled trials. This is a notable advancement in the field of IVR interventions [48]. Similarly, a review examining the effectiveness of VR in UL rehabilitation found that VR-supported exercise therapy resulted in significant improvements in motor function, ROM muscle strength, and independence in daily activities [49]. Other studies have also reported improvements in motor performance and biomechanical function when using VR technologies, as opposed to standard entertainment-based VR games [50,51]. Furthermore, Turolla et al. (2013) conducted the largest study on VR physical therapy, involving 205 patients, and provided compelling evidence of improvements in Fugl-Meyer (FM) scores following the intervention [52]. While these studies significantly contribute to the understanding of VR's role in enhancing motor function in stroke patients, it is important to note that, to our knowledge, our study is the first to introduce virtual enhancements—such as increasing hand speed while targeting a moving object—within an IVR environment.

It is also crucial to recognize that the effectiveness of VR in rehabilitation is influenced by a variety of factors, including the specific experimental protocols employed, the individual motor function needs of patients, and the technological characteristics of the VR system used. These variables play a pivotal role in determining the success of clinical applications, highlighting the need for personalized VR interventions that allow patients to select the most appropriate therapy protocol for their condition. Therefore, while the current literature provides substantial evidence for the efficacy of VR in stroke rehabilitation, further research is needed to explore the full range of VR-based interventions and their tailored applications for individual patients.

Relevant to our investigation, [53] proposed a new treatment that combines CIMT and reinforcement-induced movement therapy (RIMT). They demonstrated the efficacy of RIMT by speeding up the hindered hand in VR using the goal-oriented reaching task. After the RIMT intervention, FMA scores of stroke patients improved; however, their study did not report the subjective feeling of being completely engaged in VR. Although they pioneered positive reinforcement utilizing computer-simulated limbs in the display, the RIMT concept should be developed to use immersive VR (IVR).

Visual feedback in IVR simply displays the simulated UL. Only the simulated hand should be seen during the task. If people watch their real hand move in front of them while viewing the simulated hand on the display, the discrepancy in visual feedback of motor coordination will induce a sense of loss of ownership of the simulated UL or, in certain situations, the subjective awareness of the loss of bodily control.

Our study by [54] that used IVR on healthy subjects with a weight attached to their dominant hand to simulate the impairment of a stroke patient is also relevant to our investigation. Their system was portable (head-mounted VR), and the objective was to reach a target in VR without forcing the subjects to use their dominant hand, with an option to use either hand. The movement of the virtual avatar of the UL was reinforced by visual feedback to the participants, that is, the participants perceived their motor coordination as if their UL was moving to a greater degree than what was occurring in everyday life. These findings suggest that positive reinforcement within IVR can influence hand usage decision-making. Thus, herein, we modified the protocol developed by [54] for stroke survivors to accommodate the specific requirements of the patients, including extended task completion time and breaks to prevent fatigue, as detailed in the method section.

In this study, we aimed to evaluate effectiveness of an adaptive and alternative approach to VR-based stroke rehabilitation in improving UL motor function among stroke patients. Our hypothesis was that incorporating positive reinforcement in IVR would result in greater improvements in UL motor function compared to traditional stroke rehabilitation methods. Through a randomized controlled trial, we examined the effects of this approach using the FMA to measure improvements in UL functionality.

2. Methods

2.1. Participants

Eighteen subjects (69.4 ± 13.5 years, eight women) with acute post-stroke hemiparesis (16 ischemic strokes) were recruited in the study at the stroke unit of the Royal Berkshire Hospital (RBH) in Reading, United Kingdom (Table 1). Treatment was initiated within a mean of 7.3 days (± 4.04 days) following hospital admission. The sample size was limited by the number of patients that could be enrolled over the project's duration. For NHS REC procedures and restrictions: https://www.myresearchproject.org.uk. The experiment was approved by the ethics committee Health Research Authority and Health and Care Research Wales (IRAS project ID: 264096) and performed according to relevant guidelines and regulations.

The participants were screened for study eligibility by the clinical team according to the inclusion and exclusion criteria. The inclusion criteria were (i) age ≥ 18 years; (ii) recent stroke (ischemic/hemorrhagic) within the last 4 weeks; (iii) Montreal Cognitive Assessment score ≥ 23; (iv) ability to sit independently in a chair; (v) upper limb weakness; and (vi) ability to speak and read English. The exclusion criteria were (i) visual field defect; (ii) visual or sensory neglect; (iii) strokes affecting both upper limbs; (iv) poor static and dynamic balance in sitting; (v) shoulder subluxation or dislocation; (vi) upper limb weakness due to conditions other than stroke; (vii) presence of emotional and/or cognitive deficits (such as global aphasia, apraxia, dementia, and depression) that could interfere with the understanding and execution of the task; and (viii) history of photosensitive epilepsy.

Participants provided written informed consent after being informed about the aims and procedure of the experiment. They were allocated to either receive IVR and conventional PT (intervention group, 10 patients) or receive conventional PT alone (control group, 8 patients) (Table 1). Both groups received conventional PT on the ward, administered in accordance with national guidelines. The patient allocation, conducted through a randomization process, occurred at a 1:1 ratio using pre-prepared sealed opaque envelopes. These envelopes, numbered by the Trust the Research & Development department before recruitment began, contained information identifying the assigned group for each patient. To ensure equitable and unbiased distribution, an online random number generator utilizing atmospheric noise assigned numbers to each envelope [55]. The research team sequentially opened the sealed envelopes (numbered 1–30) to determine group allocation for each participant. Additionally, the assigned number served as the participant identification number throughout the study. This rigorous randomization process aimed to enhance the validity and reliability of the research findings. Participants could withdraw consent at any time during the study, yet the collected data were retained and used without additional procedures on or in relation to the participant.

2.2. Experimental setup

We utilized the same method as used for healthy subjects [54]. An integrated IVR system consists of a VR headset (Oculus Rift) and a small motion capture sensor (Leap Motion) attached to the headset (Fig. 1) Both products are CE marked. This system can monitor the actual UL movements of the participants and create a virtual image of the

Table 1
Demographic characteristics and stroke subtypes.

Patient ID	Group	Sex	Age	Stroke type	Lesion site	MoCA	NIHSS	Affected side	Dominant hand	Initial FM
ET001	Intervention	F	38	Ischemic	Right LACI	28	10	Left	Right	62
ET002	Control	M	76	Ischemic	Right posterior cerebral circulation	24	10	Left	Right	62
ET004	Intervention	F	73	Ischemic	Right LACI	26	7	Left	Right	59
ET005	Control	M	42	Ischemic	Right total anterior cerebral circulation	23	17	Left	Left	0
ET006	Control	M	81	Ischemic	Right partial anterior cerebral circulation	28	7	Left	Right	58
ET007	Intervention	M	62	Ischemic	Right posterior cerebral circulation	27	4	Left	Right	46
ET008	Intervention	M	88	Ischemic	Right total anterior cerebral circulation	27	9	Left	Right	32
ET009	Intervention	F	82	Ischemic	Right partial anterior cerebral circulation	24	3	Left	Right	64
ET010	Control	M	66	Ischemic	Left posterior cerebral circulation infarction	24	2	Right	Right	66
ET011	Control	F	88	Ischemic	Right total anterior cerebral circulation stroke	23	17	Left	Right	51
ET012	Control	M	77	Ischemic	Right pontine infarct	24	9	Left	Right	31
ET013	Intervention	M	76	Ischemic	Left partial anterior cerebral circulation	23	10	Right	Left	47
ET014	Intervention	F	65	Ischemic	Right total anterior cerebral circulation stroke	25	5	Left	Right	0
ET015	Control	F	70	Ischemic	Right partial anterior cerebral circulation infarct	26	6	Left	Right	66
ET016	Control	F	72	Ischemic	Right lacunar infarct	26	9	Left	Left	0
ET017	Intervention	F	59	Haemorrhage	Left LACI	24	12	Right	Right	15
ET018	Intervention	M	67	Ischemic with haemorrhagic transformation	Right MCA infarct	24	7	Left	Right	9
ET019	Intervention	F	67	Ischemic	Right LACI	24	6	Left	Right	55

F = Female; M = Male; LACI = Lacunar Cerebral Infarction; MCA = Middle Cerebral Artery; MoCA = Montreal Cognitive Assessment; NIHSS = National Institutes of Health Stroke Scale and FM = Fugl Meyer.

(A) (B)

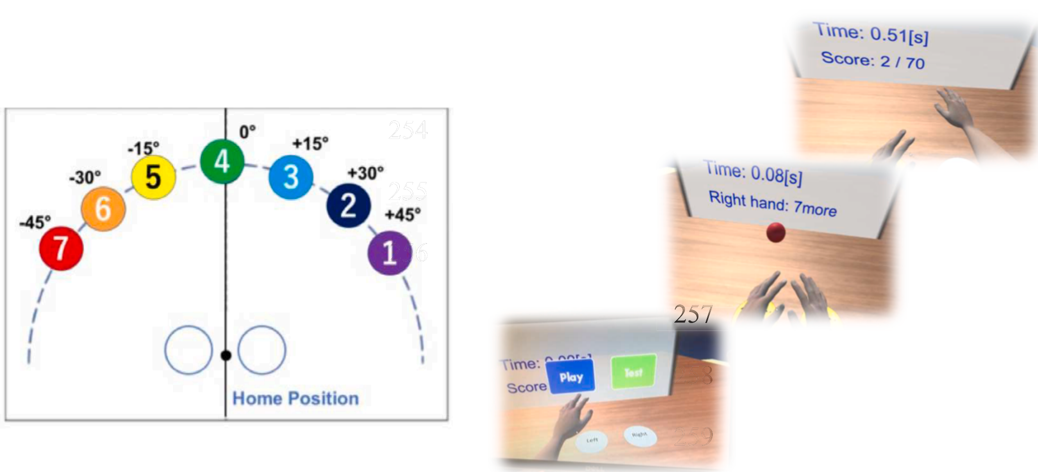
Fig. 1. Sample setup of the immersive virtual reality (IVR) system integrated with motion capture. (A) A person wearing an IVR headset with an attached Leap Motion sensor, placing both hands on a table. (B) Sample setup at the Royal Berkshire Hospital.

corresponding UL in the IVR environment. In our implementation of the visual enhancement intervention, we incorporated a function into the IVR system to amplify the visual representation of the virtual hand in terms of kinematics. This amplification involved displaying the virtual hand at a distance α times greater than the actual hand's position vector from the home position (visual amplification, $\alpha = 1.4$), effectively speeding up the motion of the hand and UL. Despite this enhancement, we ensured the natural appearance of the virtual UL posture through adjustments made using an inverse kinematics program. Stroke survivors go through task-oriented training of the UL in the IVR environment.

2.3. Task

Participants were asked to sit comfortably on a chair and place their UL on a table in front of them (Fig. 1A). Seven targets were arranged in a semi-circular orientation within the IVR environment (Fig. 2A). As a goal-oriented task, participants were asked to reach for the target immediately by choosing their healthy or impaired UL (Fig. 2B). To implement reinforcement-induced PT, the velocity of the virtual hand of the impaired UL was amplified in the virtual environment in the direction of the target. The target was turned blue and was set to be immediately disappeared, when reached by the virtual hand.

As opposed to 2-second duration allocated for healthy individuals [54], we extended the time to 4 s upon the ball's appearance, considering the greater time needed by stroke patients. If the patients could not reach a target within 4 s, the target was set to be disappeared, and the trial was invalidated. In the VR environment, participants receive feedback on both time to reach the target and the number of reached targets. Following a successful reach to a target within the 4-second window, participants could observe the time taken to reach the specific movement. This approach was uniformly applied to all subjects, as per the restrictions outlined in the NHS ethical application.



(A) (B)

Fig. 2. (A) Virtual target locations that appeared randomly. (B) The participants placed their hands at the home positions, and the target appeared randomly along with the semicircle. The participants were asked to reach for the target immediately by choosing their virtual impaired or unaffected hands.

2.4. Procedure

The experiment included three stages: familiarization, intervention, and washout (Fig. 3). At each stage, visual amplification is consistently applied to the affected side (right or left), in contrast to the healthy experiment where the visual amplification depended on the experimental phase, specifically for the right side. The visual amplification, defined as increasing the velocity of the virtual hand corresponding to the impaired UL by 1.4 times compared to the actual hand motion, will be described.

The aim of the familiarization stage was to acquaint the participants with the task. In this stage, five targets (excluding the far right and far left targets) appeared randomly in a semi-circular array in the virtual environment (see Fig. 2 A), each target appeared four times. For example, participants completed 20 reaching trials, equally divided between using the right hand (the five targets appearing twice) and the left hand in 10 trials each (the five targets appearing twice). This stage was applied only once at the beginning of each session.

Subsequently, the primary stage in this experiment was the intervention stage/free choice stage, wherein the participants were free to choose the right or left hand (unaffected or affected limb) to reach the target that randomly appeared in seven different positions. To accommodate the motor performance of patients in this study, we reduced the number of times they reached for the ball from 70 to 35 (5 times per target). This adjustment was implemented due to our consideration about potential participant fatigue. Post-stroke fatigue, prevalent throughout the acute and chronic phases following a stroke, significantly impacts rehabilitation outcomes [56]. This consideration is essential in treatment planning, given the heightened likelihood of fatigue in stroke survivors due to brain damage and limb weakening compared to healthy individuals. To avoid fatigue, participants were given 2-minute rest periods between each task.

In this stage, participants repeated the reaching task, which included 35 targets repeated 5 times for each target, at their own pace. The number of task repetitions varied for each person in each session. Each task, comprising 35 targets, lasted 3–5 min. The term "session" refers to the time when patients receive IVR training, occurring once per day. The number of sessions is determined by the duration of the patient's hospital stay until discharge or completion of 15 sessions—whichever comes sooner.

The final stage was the washout session to wash out the effect of the amplified visual feedback, similar to the intervention stage (35 target per task) but gradual reduction in the velocity of amplification in the IVR environment to 1.2 times faster with respect to that of the actual hand motion. This stage was intended to commence from the 10th session and extend until the 15th session. However, because of early discharge of patients, we could complete this 'washing out' stage with only two patients. The entire session lasted for 20–40 min, depending on the patient's condition.

2.5. Primary outcome measure (Clinical outcome)

The Fugl Meyer for UL was used to evaluate the functional motor condition as the primary outcome in this study. The evaluation was conducted by a physiotherapist who actively participated in the program. It is important to note that the physiotherapist was not blinded to the participants' intervention assignment. The FMA is crucial for determining motor recovery and disease severity [57]. It has five domains: motor function, sensory function, balance, joint range of motion, and joint pain [58,59]. The motor function domain is the most widely used and plays a primary role in monitoring motor recovery after stroke. The items in the FMA motor function domain are based on patient motion, coordination, and reflex action in the shoulder, elbow, forearm, wrist, and hand. Each domain contains multiple items, each scored on a 3-point ordinal scale (0 = cannot perform, 1 = performs partially, 2 = performs fully). The total score varies from 0 to 66. The measurements of FMA were utilized to assess the efficacy of IVR feedback in restoring motor coordination affecting the patient's QoL. Our initial plan was to collect FMA from participants at the beginning, middle, and end of their participation in the study. However, because of the COVID-19 pandemic, the length of hospitalization varied, and patients could be discharged to free the space without notifying our research team. Hence, depending on the length of the total stay, we evaluated the motor performance of the patients in the first, fifth, and tenth sessions. The control group underwent only evaluations during corresponding sessions, ensuring consistent assessment across both groups with the same timescales as the intervention group. Note that the ethical approval granted by the NHS in the UK only allowed a certain period for our clinical study with maximum 30 patients to initially make a contact, not allowing us to extend our study to recruit more patients.

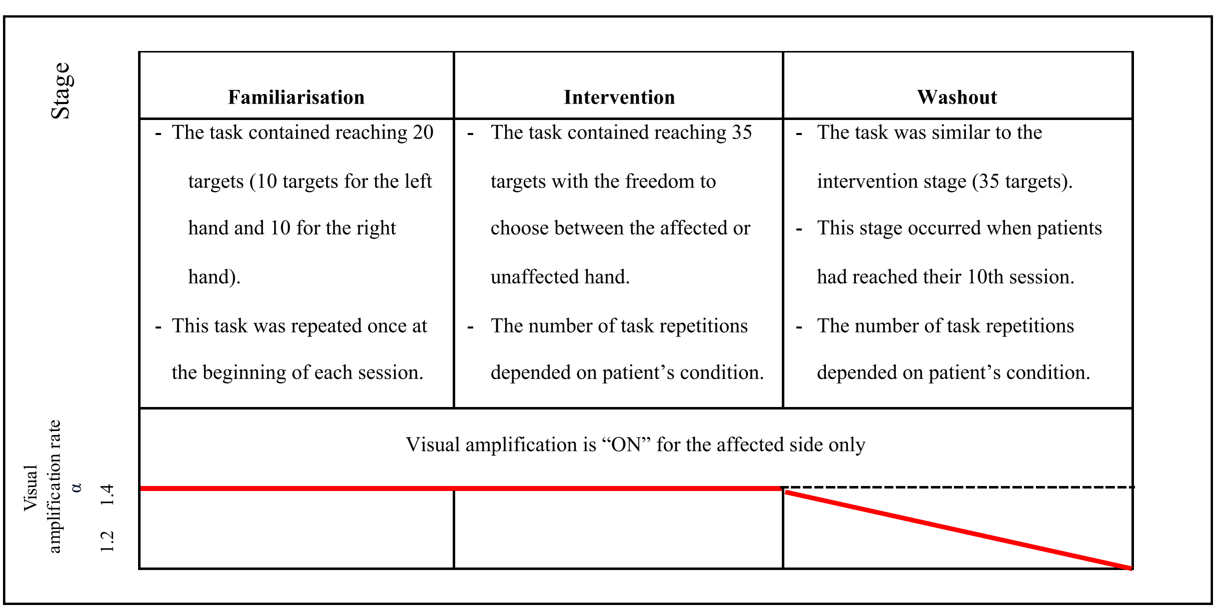


Fig. 3. Flow of experiment. The experiment consisted of three experimental stages (Familiarisation, intervention, and washout). The visual amplification is always ON.

2.6. Secondary outcome measures

2.6.1. Questionnaire

We used a questionnaire administered at the end of the last session to evaluate patient experience, provide information regarding the sense of agency (subjective awareness of initiating and controlling one's own activities) [60], and obtain comments about the training sessions in the IVR environment. The questionnaire contained four short items that required participants to respond with a simple "yes," "no," or "somewhat.".

The following questions were asked:

- Did you feel that you were controlling the virtual hand?
- Did you feel a sense of achievement during the virtual reality therapy?
- Did you feel dizzy when looking around in the virtual reality?
- Did you feel any fatigue in any of your muscles during the therapy?
- If you have any comments or feedback on your experience, please include them below.

2.6.2. Barthel index (Clinical outcome)

The Barthel index (BI; modified 10-item version) is used to measure the amount of independence and mobility of patients in their activities of daily living (ADL), such as feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, chair transfer, ambulation, and stair climbing [61]. The evaluation was conducted by a physiotherapist who was not involved in the training. This tool indicates the need for assistance in care and is widely used as a measure of functional disability [62]. Depending on the item, functional categories may be rated 0–1, 0–2, or 0–3 points. The range of possible total scores is 0–20. Two measurements were taken at both the baseline and discharge stages.

2.6.3. Virtual reality kinematic dataset outcome

2.6.3.1. Border angle (BA). To evaluate the effects of visual enhancement along with the decision-making process to use the right or left hand, we measured participants' usage of their unaffected hand in the VR environment during training sessions. This involved calculating the border angle (BA) from the first two tasks, with each task consisting of 35 targets, totaling 70 targets for each patient across the sessions. To this end, the probability of affected hand usage was plotted as a function of the target angles, and then a psychometric function was fitted to the plots as a function of the target angles; (see Fig. 2B in [54]). The angle at which the psychometric function corresponds to a 50 % probability was defined as the BA.

2.6.3.2. Time to target. To determine the time to target for each subject, the time to reach the target of the affected hand for each target was recorded, encompassing the duration from the ball's onset to the time participant reached the target. Each trial commenced with participants placing their hands at the starting point (home position), triggering the appearance of the ball upon accurate hand placement on the home position. Following this, participants reached the target, returned their hands to the starting position, and repeated the process for successive targets in different locations (35 balls). We considered that it is important to compare the time to target during the therapy across the sessions to evaluate the improvements; we hypothesized that smaller values of the time to target indicated effective motor learning resulting in motor recovery.

2.6.3.3. Observation of patient's strategy. The physiotherapist who participated in the training sessions reported all vital observations, which were necessary to comprehend the patient's treatment strategies.

2.7. Analysis and statistics

To establish the efficacy of IVR feedback in the recovery of motor coordination, we initially analyzed the statistical difference in FMA scores between the first and fifth sessions for each patient in both groups (Wilcoxon signed rank test). Additionally, to compare the FMA improvements between groups, we conducted an independent statistical test (Mann-Whitney *U* test). For further analysis, we performed paired comparisons test (Wilcoxon signed-rank test or the paired Student's *t*-test) to evaluate Barthel index, Border angle and time to target. Prior to these analyses, we conducted the Shapiro-Wilk test to assess the normality of the distribution. The level of significance was set at $p < 0.05$. In addition, repeated measures analysis of variance (ANOVA) mixed model was employed to determine the influence of two factors, namely the target locations and the sessions, on the time to target.

The answers derived from the questionnaire were not compared statistically between the groups. However, subjective experience is crucial for determining whether a larger community would be interested in and benefit from the IVR physical treatment.

In this study with stroke patients, we noted that they adopted certain or individual intriguing methods while undergoing therapy. The observations were made from the perspective of a physiotherapist. These findings were considered important in the study because they revealed how the patients coped or utilized other motor movements to complete the task. Hence, the patients were separated into distinct groups based on the similarity of their strategies.

3. Results

Two patients in the intervention group withdrew from the trial owing to difficulty to complete the task (ET014), a perception of therapy being ineffective, or a desire to concentrate more on the lower limb (ET009). Our study demonstrated feasibility in participant recruitment, enrolling 18 S patients successfully at Unit in the RBH, UK within the specified timeframe Table 1. Using IVR, an innovative approach for improving UL function in the stroke unit, sessions were conducted with minor reported discomforts, including a heavy headset and forearm spasms, but no serious adverse effects. This underscores the feasibility of real-world research and the team's commitment to advancing stroke rehabilitation. However, adherence to the intervention protocol faced hurdles, including early patient discharge and logistical constraints in session delivery, mostly due to the restriction over the COVID-19.

Two significant observations emerged from the study. Firstly, each patient underwent a varying number of sessions, as outlined in Fig. 4, and Tables 2 and 3. This number was correlated with the duration of hospitalization *(as shown in the supplementary files table A)*. The mean number of sessions across all participants was 6.6, with a standard deviation of 2.98, with some patients receiving five sessions and others having more or fewer; there was no standard quantity for sessions. More specifically, the intervention group had a mean of 6.2 sessions (SD = 3.25) (Table 2), whereas the control group had a mean of 7.4 sessions (SD = 2.15) (Fig. 4). Secondly, each patient was able to repeat the number of tasks per session according to their condition and endurance level. Some patients repeated the task twice (one task = 35 targets), while others repeated it more times per session. Consequently, patients were categorized into three main groups (Table 3).

3.1. For the primary outcome (FMA)

The FMA score measured predominantly in the first and fifth sessions (seven and eight patients in the intervention and control groups, respectively) *as shown in the supplementary files Table B.* One patient's (ET017) data was eliminated from the intervention group because he underwent only four sessions, and we could not repeat the evaluation due to his discharge from the stroke unit. Additionally, two patients (ET013 and ET019) who stayed longer in the hospital were evaluated

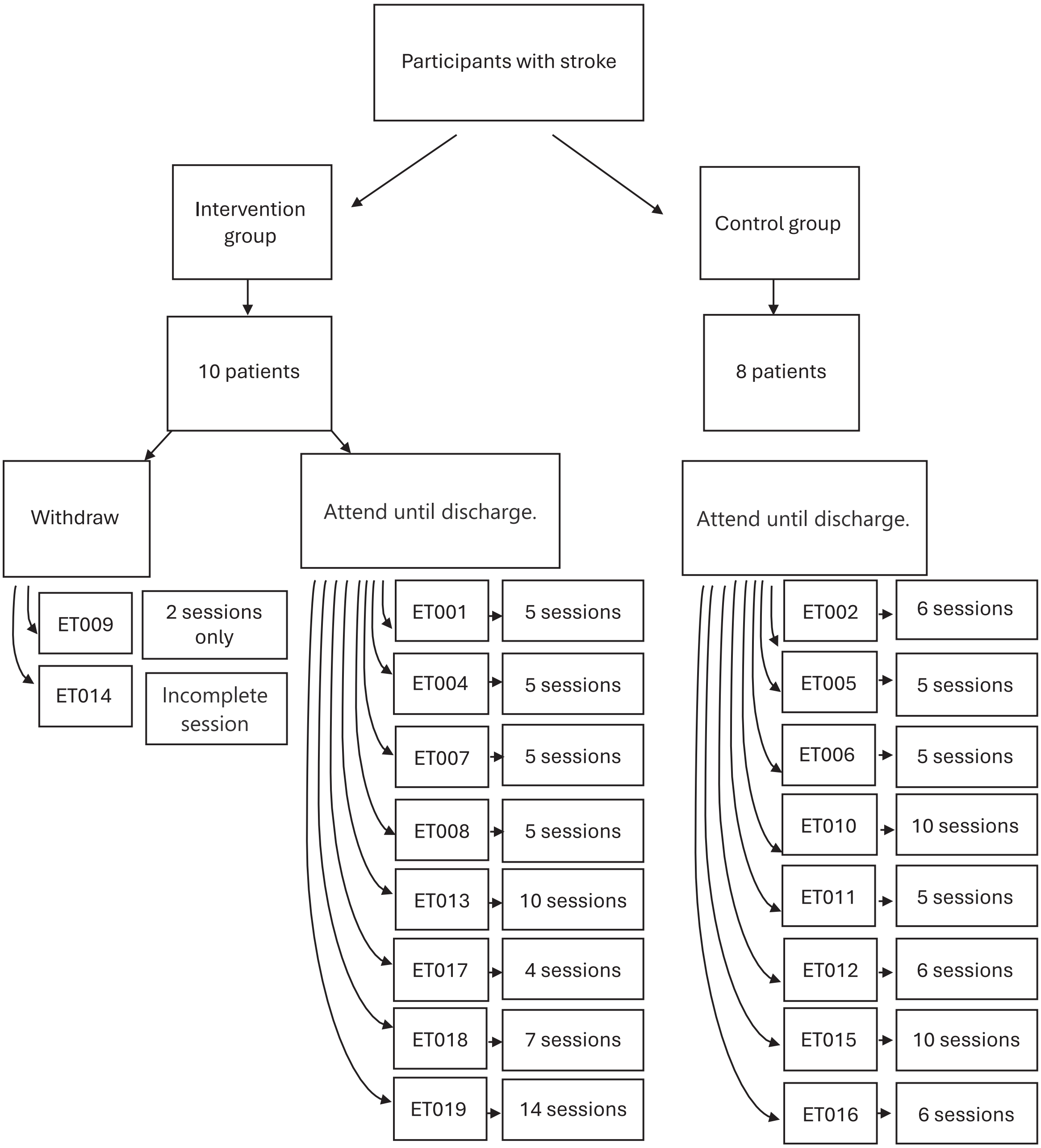


Fig. 4. Flow chart illustrating the participant flow throughout the study.

Table 2
Number of sessions for each patient.

Two sessions	Four sessions	Five sessions	Seven sessions	10–14 sessions
ET009 (withdraw)	ET017 (DC)	1. ET001 2. ET004 3. ET007 4. ET008	ET018	1. ET013 2. ET019

DC = discharge.

three times. Nevertheless, data from only the first and fifth sessions were analyzed. As opposed to the intervention group, two patients in the control group (ET010 and ET015) had a full score at the beginning of the study. However, we repeated the assessment in the fifth session to ensure that there was no deterioration in their motor function, as neurological deterioration is common in some stroke patients [63] and we observed that their scores remained unchanged.

From our findings, it was observed that all seven patients in the intervention group demonstrated improvement in the FMA score after receiving IVR-enhanced visual feedback, constituting 100 % of the group. In contrast, only 25 % of the control group, consisting of two out of eight patients, demonstrated improvement in the FMA score. Moreover, 75 % of all patients exhibited no change in the FMA score between the first and fifth sessions.

The data obtained from FMA in both groups were not normally distributed, we performed the Wilcoxon signed-rank test for the paired sample comparison of the data. As shown in the box plot in Fig. 5, the FMA scores differed significantly between the first and fifth sessions for the intervention group ($P = 0.02$) but not for the control group ($P = 0.16$), indicating that IVR enhanced the motor function of the affected upper limb. Additionally, we conducted the Mann-Whitney U test to compare the FMA improvement between both groups, revealing a significant difference ($P = 0.0477$).

Table 3
The number of task repetition per session.

Task repetition in each session	Patient ID	Number of sessions	Task repetitions in each session
Increase of task repetitions per session	ET001	5	3, 3, 4, 5, 6
	ET004	5	2, 4, 4, 4, 6
	ET009	2	4, 8
	ET017	4	2, 3, 4, 7
Reduction in the number of task repetitions per session after a steady increase	ET007	5	2, 3, 4, 5, 3
	ET008	5	5, 7, 7, 8, 6
	ET013	10	3, 6, 7, 8, 8, 10, 7, 8, 8, 9
Fluctuation in the repetition of a task	ET018	7	4, 3, 4, 6, 5, 5, 4
	ET019	14	5, 6, 6, 6, 6, 6, 6, 10, 5, 8, 8, 8, 8, 6

The first row under each patient's ID indicates the number of sessions, whereas the second row indicates the number of times they could repeat the task in each session.

Furthermore, our results revealed significant differences between the intervention and control groups in terms of median improvement, effect sizes, and Z-statistics. The intervention group demonstrated a substantial median improvement of 7 points (IQR: 6), with a Cohen's d effect size of 1.29 and a Z-statistic of 3.44. Conversely, the control group exhibited minimal improvement, with a median change of 0 points (IQR: 8), a Cohen's d effect size of 0.54, and a Z-statistic of 1.53. These findings underscore the efficacy of the intervention in enhancing motor function compared to the control condition.

3.2. Secondary outcome

3.2.1. Questionnaire

Only seven patients responded to the questionnaire *(Table C in the supplementary files*). In the questionnaire, participants provided feedback regarding their experiences during the virtual reality therapy sessions. Five respondents affirmed a strong sense of control over the avatar, while two indicated a moderate level of control. All participants reported feeling a sense of achievement during the therapy. In terms of experiencing dizziness while navigating the virtual environment, the majority (five participants) reported no such sensations, while two acknowledged mild sensations. Additionally, all participants denied feeling fatigued during the sessions. Finally, they provided comments regarding the therapy, such as "

> "I found the therapy to be enjoyable and fun, especially as it encouraged me to use my affected hand more, making the experience both engaging and motivating," and "It improved my hand coordination and control, and I felt as though my affected hand was moving normally, as if I had control over it." However, one of them stated that the "The headset was quite heavy, but it did not prevent me from fully engaging in the therapy sessions."

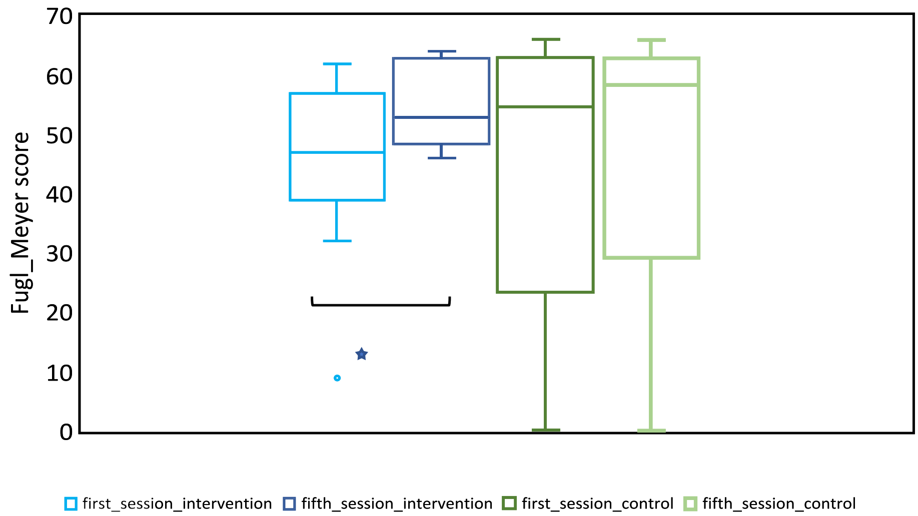


Fig. 5. Box plot of Fugl-Meyer Assessment (FMA) scores for the intervention group (n = 7) and control group (n = 8). In the intervention group, a significant improvement in FMA scores was observed between the first and fifth sessions ($p < 0.05$), as determined using the Wilcoxon signed-rank test. This indicates motor recovery improvement in the intervention group over time. In contrast, no significant changes were found in the control group. The FMA score evaluates motor function, with higher scores reflecting motor recovery.

3.2.2. *Barthel index (BI)*

In terms of BI, not all individuals were evaluated twice; only nine participants (four in the intervention group and five in control group) had their data recorded twice (*Table* D *in the supplementary files*). As we had a small data size and some of them were not normally distributed, we considered that our data were not normally distributed. Therefore, the Wilcoxon signed-rank test was used. We found that BI scores did not differ significantly between the first and last sessions in the intervention group (p = 0.07), whereas they differed significantly in the control group (p = 0.04). The effect sizes for the intervention group (first and last session) and the control group (first and last session) are 1.027 and 1.613, respectively, as calculated using Cohen's d.

3.2.3. *Virtual reality kinematic dataset outcome*

3.2.3.1. Border Angle (BA). Three of nine patients were excluded from further analysis as the BA could not be calculated because they chose a biased strategy, such as using their affected hand for all the targets (ET001, ET009, and ET017). Owing to the normal distribution of the BA data across all sessions, we used the paired Student's *t*-test to assess the differences in BA between sessions and the results indicated that there was no statistically significant difference first and last session, as indicated by a p-value (P = 0.38).

3.2.3.2. Time to target. One participant was excluded from further analysis (ET008), for the reason that his response time was affected because of spatial neglect, for example, lack of attention towards the targets near the affected side and he needed to be reminded to refocus his attention. Furthermore, he employed a distinct approach when attempting to reach the target.

We found that patients with left-side impairment consistently reached targets closest to the affected side, while those with right-side impairment consistently reached targets on the opposite side. A repeated measures ANOVA showed no significant difference in target locations (p = 0.67) but a significant difference between sessions ($p < 0.01$). Therefore, we combined the average value of the response time of targets 5, 6, and 7 for the left sided patients and targets 1, 2 and 3 for the right sided patients. We then proceeded to compare the results obtained from the first and last sessions.

We performed the Wilcoxon signed rank test on eight patients in order to reveal the improvement of motor recovery between the first and last session in terms of the time to target of the affected hand. Based on the box plot depicted in (Fig. 6), there is a statistically significant difference found between the first session and the last session (P = 0.03), and a moderate effect size (Cohen's d = 0.506), suggesting the motor recovery of the affected limb in terms of kinematics. In contrast, we found that there was no motor learning on the unaffected upper limb (P = 0.20).

3.2.4. *Patients' strategies via the therapist's observation*

We subgrouped the patients based on the similarity of their strategies and highlighted the following three significant characteristics from the therapist's observation:

3.2.4.1. Patients categorized based on the frequency hand usage (Affected or unaffected hand). Based on the recorded data, we identified two categories of patients;

3.2.4.1.1. The frequency of using the affected side. This category comprised two types of patients who predominantly used their affected hand to reach the majority of targets, potentially indicating self-motivation and competitiveness. The first type achieving ≥ 80 % of

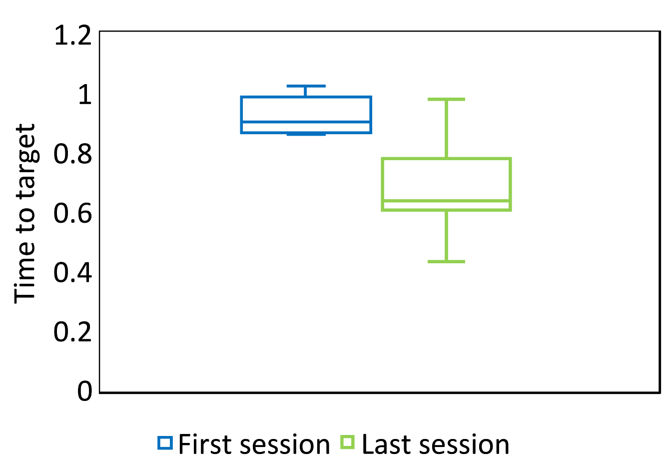


Fig. 6. Distribution of the time to target [s] of the affected side in the first and last sessions. The Wilcoxon signed-rank test revealed a statistically significant improvement ($p < 0.05$), indicating faster response times in the last session compared to the first.

the affected hand usage (28 targets out of 35), The second type patients used 71 % to 77 % (25 to 27 targets out of 35). Notably, this method was not used for every session; for example, patient ET001 used both methods.

3.2.4.1.2. The frequency of using the unaffected side. This category included patients who did not use the affected hand to reach targets because they wanted to train the opposite side; they used the affected 25 % (0 to 8 times out of 35).

3.2.4.2. Patients categorized based on strategy for reaching targets. Each patient employed a unique strategy for achieving the targets. For instance, some patients utilized trunk movement to assist in reaching the target, while others switched to their unaffected hand if they were unable to reach the target, returned to their starting position, and repeated the task. Additionally, certain patients exhibited circumduction movements rather than moving in a direct line. Moreover, some patients tapped the table upon successfully reaching the target.

3.2.4.3. Patient categorised based on factors affecting performance. Some patients exhibited characteristics that could affect their performance. For instance, neglecting the affected side resulted in overlooking targets close to that side, while leaning towards the affected side led to neglecting targets on the opposite side. Others had hand deformities, although this did not impact the efficacy of the system. Additionally, negative mood and lack of sleep were observed to have detrimental effects on session performance.

4. Discussion

The primary goal of this pilot study was to investigate the effectiveness of IVR technology in the UL rehabilitation of stroke patients, as opposed to traditional CIMT that combines positive reinforcement in PT. Our study by [54] confirmed that positive reinforcement in IVR influences hand usage decisions in healthy participants. In this study, we modified the IVR system in order to meet the specific requirements of the patients by reducing the target number and extending the time limit to reach the targets. The efficacy of the IVR-enhanced PT was validated using the FMA to test the improvement of the UL motion with respect to the control group.

Based on our findings, it is evident that the intervention group, which received IVR combined with PT, exhibited improvement in the FMA score in all patients compared to the control group which received only PT. This observation is promising, indicating a positive trajectory that may offer insights into the efficacy of the IVR intervention. The positive outcomes observed in the intervention group suggest the effectiveness of IVR in enhancing motor function. However, the question persists: Can this improvement be attributed solely to the system, the physiotherapy sessions, or their combined synergistic impact, serving as compelling evidence of efficacy?

VR is frequently compared to conventional therapy (CT) administered by physio- and occupational therapists in studies on stroke rehabilitation. The updated Cochrane review by Laver et al. [6] concluded that the efficacy of VR-based therapy was not superior to that of CT in enhancing upper limb function. Specifically, they reported that VR "may be beneficial in improving UL and activities of daily living (ADL) when used as an adjunct to CT (to increase overall therapy time)". It is essential to note that their study primarily focused on commercial video gaming consoles, a prevalent choice in VR-based rehabilitation due to their ease of use, enjoyment, and cost-effectiveness [64,65]. Nevertheless, present-day researchers are increasingly avoiding these approaches as these systems are primarily designed for healthy individuals, thereby presenting significant challenges for patients [64]. Consequently, our study implemented an IVR system that is tailored to the specific requirements, benefits, and conditions of the patients.

The inherent simplicity of this approach may contribute to the observed enhancement in their FMA scores, aligning seamlessly with the overarching objectives of stroke rehabilitation, especially in terms of early initiation to mitigate the disease's impact. Notably, in the 2022 *meta*-analysis, Everard and colleagues observed a particularly notable efficacy of VR interventions among patients with mild to moderate motor impairments.

This highlights the importance of assessing impairment severity in VR interventions. VR's reliance on a minimum level of UL motor function, particularly evident in individuals with severe impairment, suggests it may not be ideal for rehabilitating patients with a low UE-FMA score [66].

Given that the participants in our study were in acute conditions, with initially high FMA scores, the observed improvement between the first and last sessions aligns with the findings of [66]. Notably, even patients with initially low FMA scores demonstrated improvement, although the degree of improvement was minimal. This suggests that for individuals with low FMA scores, VR might not be the optimal option. However, VR remains of interest for these patients, as it has demonstrated potential in offering effective mirror therapy and cognitive rehabilitation [65,67].

The combination of therapies in our study, emphasizing both task-oriented exercises and repetitive movements, holds the potential to facilitate patient recovery through intensive treatment. While traditional CIMT emphasizes intensive training with forced use of the affected side, our study diverged from this approach. Instead of imposing constraints on the patients, we employed positive reinforcement in VR, thus promoting engagement without inducing fatigue or exhaustion. In IVR training, it involved task-oriented exercises, particularly actions like reaching for ball—a movement integral to ADL that frequently necessitates the use of the arm [68,69]. Additionally, the task contained repetitive movements [70].

Previously, the direct effects of VR therapy on neuroplasticity were still being explored, with limited evidence available [6]. However, recent studies have indicated that VR interventions aligned with neurorehabilitation principles may be particularly effective in targeting neuroplasticity [66].

Definitive conclusions regarding the effectiveness of IVR should be approached with caution, given the observed differences in FMA scores between the groups. Especially in the control group, the presence of participants with both zero and maximum FMA scores introduces variability that may impact the overall result. It is noteworthy to consider that, as indicated by their baseline FMA scores, participants in the control group may have had a narrower scope for improvement compared to those in the intervention group. Moreover, it is essential to underscore that there was no deliberate control exerted in patient selection; the pivotal element lies in the random allocation of patients. This random assignment contributes robustness to the study design, serving as a mechanism to manage potential biases. It is recommended that future studies establish an initial standardised degree of motor function in order to facilitate a more equitable and precise comparison among groups.

As we shift our focus to the secondary outcome of patient independence in executing real-life tasks, the Barthel Index (BI) served as the instrumental metric for measuring their performance in crucial activities. However, the evaluation faced challenges, as not all BI data were consistently recorded, with some being only documented in the first or last session or not at all. This is because the length of hospitalization for stroke patients varied; some patients were discharged without notification, compromising the validity and reliability of the evaluation. As a result, the variation in the number of sessions is noteworthy; while some patients underwent five sessions, others underwent more or fewer. The accelerated discharge of patients due to the pandemic made it challenging to control this variation, which could potentially have influenced the study outcomes. Determining the optimal hospitalization duration for stroke patients is critical for effective rehabilitation planning. Studies suggest that stroke patients need time to show improvements in ADL. For example, one study [65] found a significant difference in FMA scores but none in BI scores (p = 0.193), indicating the impact of short rehabilitation durations on functional evaluation. Additionally, the location and extent of the brain lesion significantly influence patients' improvement and stroke outcomes [71]. Despite our hypothesis focusing on VR therapy benefits for the intervention group, both groups showed enhancements in BI scores from initial to final sessions (*Table D in the supplementary files*). However, statistically significant results were observed only in the control group, possibly due to limited data documentation.

Despite the challenges in conclusively asserting the efficacy of IVR in enhancing the motor function of the affected UL, our findings reveal several positive aspects.

Particularly notable is the fact that patients in the intervention group expressed enjoyment and engagement during the IVR sessions. The person using IVR equipment can "look around" the artificial world and interact with virtual features or objects. Through iterative visual-motor loops in the brain, the person might experience a feeling of controlling the virtual image of their body in such a way that the virtual world would be perceived as a real one. If individuals were to experience the ideal motor coordination of their ULs avatar, the successful matching of motor intention and resultant motor coordination in the IVR would enable brain networks to establish new neuronal pathways, facilitating spontaneous motion in their daily lives. Therefore, IVR-enhanced therapy may offer a powerful rehabilitation approach, allowing PT to be tailored to the specific needs of stroke survivors.

Furthermore, the accuracy and smoothness of the visual avatar in the virtual environment played a crucial role in the positive experience. Patients felt a sense of control over the virtual hand [72] and this was validated by the questionnaire responses. The study's results align with previous research [53,54] suggesting that the virtual therapy approach is effective in inducing a feeling of accomplishment [73] and control among patients.

These positive findings about the results can be categorized into four aspects. *Firstly,* the variability in the number of task repetitions within sessions should be considered. While there is indeed a range in the number of tasks performed from one session to another, it is noteworthy that some patients exhibited an increase in the repetition of tasks (Table 3). It suggests that IVR can enable patients to become more motivated, involved, and immersed in their rehabilitation, resulting in enhanced performance. However, other patients reported a gradual deterioration after a continual rise or fluctuation in session frequency. Potential explanations include insufficient sleep [74] and patient's mood [75] and endurance level [76], all of which could affect performance [77].

Secondly, it is essential to note that each patient employed a distinct strategy, particularly in evaluating which hand they utilized to reach the target. This differs from the approach observed in healthy participants as reported in the study by Sakabe et al. [54]. For example, several patients challenged themselves by using their impaired hand to reach at least 80 % of the targets in the semi-circular array. Other patients adopted the reverse strategy, employing the affected hand to reach no more than 25 % to reach the target. Considering that the task could be performed more than once per session, which depends on the patient's endurance level, the challenging technique was only used in some sessions. These particular motor performances may have been influenced by the patient's level of motivation throughout sessions [77]. The use of multisensorial stimulation and challenging levels encourages patients, which is an essential factor for sustaining treatment and enhancing rehabilitation outcomes [78]. Motor control training is hampered by low motivation and compliance, which can significantly impact its effectiveness.

Thirdly, it is imperative to highlight that the response time to reach the target using the affected hand demonstrated a notable reduction for all patients in the intervention group when comparing the initial and final sessions. This might demonstrate the treatment's efficacy by its potential to facilitate motor learning on the affected side. In study of [79] offers a valuable theoretical framework and insights into skill acquisition processes, essential for guiding future endeavours to enhance motor learning. Additionally, no difference was found on the unaffected side, likely because it is not impaired.

Promoting motor learning in UL rehabilitation may be possible by providing patients with more real time information about their results and performance during a single session [79]. As feedback can be simultaneously provided when using VR, it may also encourage more active participation from patients, which is associated with increased motivation to succeed [80,81]. It has long been hypothesized that motor recovery after stroke is a form of relearning [82,83]. This is due to the engaging and motivating nature of VR, which enables patients to improve their response time to target and complete tasks more efficiently through task-oriented and repetitive movement [84]. However, in patients aiming to improve the quality and precision of movement of the affected hand, focusing on a different aspect of performance may hinder their ability to reach the target quickly [85,86], similar to the response time to target data of certain patients in our study. *Lastly*, The IVR system in our study was safe and well-tolerated, with no serious adverse effects reported. Minor issues included one participant finding the headset slightly heavy (without impacting therapy engagement) and another experiencing a forearm spasm. These observations align with [48], which reported mild discomforts such as dizziness and eye strain, suggesting that our system may present fewer challenges, possibly due to design or protocol differences. While participants generally found the IVR system enjoyable and user-friendly, this could reflect a bias, as those with negative experiences might have withdrawn. Future research should critically evaluate both favourable and unfavourable feedback to refine IVR systems, ensuring broader patient acceptance and improved rehabilitation outcomes.

Like all other studies, this study had its limitations. Our greatest limitation seemed to be the intensity and frequency of the IVR therapy, which was beyond our control because it depended entirely on how long a patient required hospitalization.

Additionally, this study faced limitations related to a small sample size, which may impact the validity of the results. While this constraint was outside our control, we recommend that future research prioritize the recruitment of a larger sample size and seek collaborations with other institutions to enhance the generalizability of the findings.

Furthermore, the subjective measures should incorporate broader questions that focus on patient acceptance and motivation toward IVR therapy. This approach would provide a deeper understanding of their experiences and perspectives.

Another limitation was the discrepancies in baseline FMA scores between groups and the substantial amount of missing data in secondary outcomes. It is recommended that future studies include additional functional assessment measures, such as grip strength tests or the Action Research Arm Test to comprehensively evaluate various aspects of UL recovery and strengthen the clinical relevance of the results.

Our findings suggest a dose–effect relationship in VR therapy for upper limb rehabilitation. Further research is warranted to ascertain optimal intervention dosages and their impact on outcomes and activities of daily living. Future studies should also explore the effects of specific VR features, such as avatar motion trajectories or the use of physical items for grasping, on enhancing rehabilitation outcomes.

5. Conclusion

In conclusion, our study suggests that positive reinforcement in IVR may enhance motor function in stroke patients with UL impairment, as indicated by FMA scores. However, the exclusive contribution of the VR intervention versus a combination of PT and IVR remains uncertain. The intervention group significantly benefited from a task-oriented, intensive treatment combining PT and VR, with evident participant engagement, motivation, and potential motor learning indicated by faster reaction times.

6. Ethics approval and consent to participate

The experiment was approved by the ethics committee Health Research Authority and Health and Care Research Wales (IRAS project ID: 264096).

7. Consent for publication

All subjects consented to the publication of the results of this study.

8. Authors' contributions

YH, TK, and KN conceived and supervised the study. NS developed the IVR. SA modified the system to optimize patients need. SA performed the experiments, write the manuscript and statistical analysis. All authors contributed to the discussion of the results and revised the final manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.displa.2024.102962.

Data availability

The authors do not have permission to share data.

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