

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

ARRoW-CP: Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery - Protocol for a Randomized Controlled Trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-061580
Article Type:	Protocol
Date Submitted by the Author:	03-Feb-2022
Complete List of Authors:	Guinet, Anne-Laure; Universite Paris-Saclay, IBISC Laboratory; Fondation Ellen Poidatz, Pôle Recherche&Innovation Payan-Terral, Sandrine; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Bams, Michel; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Otmame, Samir; Universite Paris-Saclay, IBISC Laboratory Bouyer, Guillaume; Universite Paris-Saclay, IBISC Laboratory Khouri, Nejjib; Hôpital universitaire Necker-Enfants malades; Fondation Ellen Poidatz, Pôle Recherche&Innovation Desailly, Eric; Fondation Ellen Poidatz, Pôle Recherche & Innovation
Keywords:	Paediatric orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric neurology < NEUROLOGY, Developmental neurology & neurodisability < PAEDIATRICS, REHABILITATION MEDICINE, Clinical trials < THERAPEUTICS

SCHOLARONE™
Manuscripts

TITLE PAGE**a. Author and Co-author's name**

Mrs. Anne-Laure Guinet

Pr. Samir Otmane

Mr. Guillaume Bouyer

Dr. Michel Bams

Dr. Neijib Khouri

Mrs. Sandrine Payan-Terral

Mr. Eric Desailly

b. The name, postal address, e-mail, telephone, and fax numbers of the corresponding author.

Mrs. Anne-Laure Guinet, physiotherapist, and PhD student (computer science & rehabilitation science) at Ellen Poidatz Foundation and IBISC lab-IRA2 team.

anne-laure.guinet@fondationpoidatz.com

1, rue Ellen Poidatz 77310 Saint Fargeau Ponthierry – France 01060658282

c. The full names, institutions, city, and country of all co-authors.**Pr. Samir Otmane**

University professor at Paris-Saclay University, Evry University, IBISC lab
1, rue de Pelvoux 91000 Evry - France

Mr. Guillaume Bouyer

Assistant professor at Paris-Saclay University, Evry University, IBISC lab
1, rue de Pelvoux 91000 Evry - France

Dr. Michel Bams

Physical Medicine and Rehabilitation Doctor at the Ellen Poidatz rehab center
1, rue Ellen Poidatz 77310 Saint Fargeau Ponthierry – France

Dr. Neijib Khouri

Surgeon at Hôpital Universitaire Necker in Paris and consultant at the Ellen Poidatz rehab center
149, rue de Sèvres 75015 Paris – France

Mrs. Sandrine Payan-Terral

Executive manager of the rehabilitation team at the Ellen Poidatz rehab center
1, rue Ellen Poidatz 77310 Saint Fargeau Ponthierry – France

Mr. Eric Desailly

PhD in biomechanics and Director of Research and Innovation at the Ellen Poidatz Foundation
1, rue Ellen Poidatz 77310 Saint Fargeau Ponthierry – France

d. Up to five keywords or phrases suitable for use in an index (it is recommended to use MeSH terms).

Keywords: cerebral palsy, surgery, active video game, augmented reality, gait performance.

1
2
3 **e. Word count - excluding title page, references, figures and tables.**
4

5 Article type: Protocol for a Randomized control trial

6 Words (excluding abstract): 3197

7 Abstract – words: 298

8 Figure: 1

9 Table: 1

10 Supplementary Material: 3

11 References: 61
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ARRoW-CP: Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery - Protocol for a Randomized Controlled Trial

A-L. Guinet, M. Bams, S. Payan-Terral, S. Otmane, G. Bouyer, N. Khouri, E. Desailly

Abstract

Introduction. The natural history in people with cerebral palsy (CP) is a gradual decline in ambulatory function as children grow and age. Single-event multilevel surgery (SEMLS) aims to realign the musculoskeletal system to reverse this tendency. Recent studies show that rehabilitation after surgery should include intensive exercises and functional gait training to improve walking capacities. Fun and motivation are also critical keys to successful therapy in pediatric rehabilitation. Various interventions have shown positive effects, high-interest levels, and engagement with active video games (AVG). The combination of AVG and gait training seems to be an exciting approach for the postoperative rehabilitation of children with CP. In this study, we will investigate if an overground gait training program with an AVG can improve the gait performance of children with CP.

Methods and analysis. The ARRoW-CP study is a randomized clinical controlled trial. A total of 14 children and adolescents between the age of 12–18 years with CP will be included. The minimum time between surgery and inclusion will be seven weeks, and participants will have a Functional Mobility Scale 50 meters rating superior or equal to 2. Both groups will follow a gait training program of four weeks to improve their gait performance. The intervention group will participate in the overground gait training protocol with the ARRoW-CP game. The control group will consist of gait training on a treadmill with a maximal duration of 30 minutes. Measurements will occur before the gait training, directly after, and six months later. The primary objective is anaerobic performance. Secondary objectives are aerobic performance and enjoyment.

Ethics and dissemination. Ethical approval has been obtained from the French Ethical Committee Sud-Est and the French Commission of Informatics Freedom. The study has been registered in ClinicalTrials.gov (NCT04837105). Publications in peer-reviewed journals and conferences will disseminate the findings.

Strengths and limitations of this study:

This study is the first randomized control trial to evaluate the impact of an active video game on gait performance in children with cerebral palsy after surgery

The active video game ARRoW-CP game is dedicated to children with cerebral palsy using a PROGame design framework, including a multidisciplinary team.

The addition of gait training to conventional care may improve the aerobic and anaerobic gait performance in children with CP after surgery.

The enjoyment could decrease over time because of the relative limitation of game elements and game mechanics deployed in the ARRoW-CP game.

For peer review only

Introduction

Cerebral palsy is commonly defined as a "group of permanent disorders of the development of movement and posture, causing activity limitation"¹ The overall prevalence of CP remains constant (2.11 per 1000 births)² with an estimated prevalence of 17 million people worldwide.³ Individuals with CP present various clinical symptoms, including a non-exhaustive list of neurological, orthopedic, movement, cognitive, vision/hearing, aerodigestive disorders.

Musculoskeletal disorders are secondary impairments contributing to restricted mobility in childhood and adulthood.⁴⁻⁶ Since 1985, therapeutic interventions to correct orthopedic disorders include single-event multilevel surgery (SEMLS). This surgery proposes to realign the musculoskeletal system during one operative period, practicing tendon transfer, muscle lengthening, derotation, deflexion osteotomy, and joint stabilization. In a recent systematic review presenting the state of the evidence on effective interventions for children with CP, SEMLS has been classified as effective ('probably do it W+') for improving both Gross Motor, walking speed, and walking capacity but also contracture and alignment deformities.⁷ To date, systematic reviews on the effect of SEMLS reported improvement in passive range of motion, kinematics and kinematics gait parameters, overall gait index, and energy efficiency.^{8,9} Results disputed the long-term effect on temporospatial gait parameters, gross motor function, and the activity and participation domain.¹⁰

A recent review has proposed a model of 5-step that could guide clinicians during postoperative rehabilitation.¹¹ The authors suggested that the fourth phase, which included more intensive exercises, functional gait training, and resistive muscle strengthening, should be optimized to improve the gross motor function and walking speed after surgery. Functional gait training has been defined as actively practicing walking to improve walking ability.¹² Intervention could be overground gait training (OGT) or treadmill gait training (TT), with or without body support.

Previously, Grecco et al. demonstrated the efficacy of the treadmill gait training program, including functional mobility and gross motor function in children with CP after SEMLS.¹³ Recently, a systematic review showed that gait training was a safe and effective intervention to improve walking capacity in children with CP outside postoperative context.¹² In particular, the minimal clinically important difference (MCID) for an increase in walking speed (0.1 m/s) was achieved after intervention in 12 studies/14 (studies level between II and III). The authors discussed two points: OGT could have a more significant effect on locomotor abilities than TT because OGT is more representative of natural walking,¹⁴ and feedback could enhance patient outcomes.¹⁵ These points were important to consider after SEMLS because the bone and muscle gestures modified the overall gait pattern of children. Novak et al. highlighted the importance of context-focused therapy and goal-directed training for children with CP.^{7,16} Functional gait training should consider those recommendations and involve motor learning strategies: task-specific, variable practice, high intensity, augmented feedback during therapy sessions, and motivation of the patient.¹⁷⁻¹⁹

New technologies have been introduced in rehabilitation practice in recent years, both for upper and lower limbs therapy. These systems include extensive technology ranging from fully immersive virtual reality (VR) to augmented reality (AR). The head-mounted displays (HMD) (e.g., Oculus Quest; HTC VIVE, Microsoft HoloLens), Cave Automatic Virtual Environment (video displaying on the walls and floor)²⁰ and game console (e.g., Nintendo Switch, PlayStation) are some of these systems.

To 'actively practice the task of walking,' systems combining treadmill training and exergame delivered through a screen in a semi-immersive environment have been tested with good results.²¹⁻²³ However, motor learning principles are not always fully integrated into VR/AR systems because of the lack of knowledge about which feedback modality and which intensity level should be provided in the rehabilitation context.²⁴

To our knowledge, even if OGT was recommended for functional gait training, no AR system with active video games exists to provide high-intensity, with progressive difficulty, and variable modalities, including feedback. To this end, we have developed the active video game ARRoW-CP combining OGT based on the previous results¹² and literature²⁵ and motor learning theory.^{17–19,26} In this active video game, continuous feedback and terminal feedback, both with different audio and visual modalities, are combined. The ARRoW-CP game, architecture, framework development, and feedback characteristics are available in **Supplementary File 1**.

The current study, denoted as the ARRoW-CP study, will investigate whether a gait training protocol through an active video game in AR can increase the physical fitness levels of children with CP following surgery. We hypothesize that the active video game ARRoW-CP is as effective as treadmill training and more enjoyable for children.

Methods and analysis

Study Design

This study is a randomized control trial with OGT using the active video game ARRoW-CP in AR (OGT-AR) and Treadmill Training control groups (TT). All children and adolescents participate in a four-week gait training intervention to improve their walking function in one of these two groups. During this period, children continue their usual physical therapy program (5 weekly 45-minute sessions). This postoperative protocol has been standardized following a 5-step framework.¹¹ These usual rehabilitation sessions include muscle stretching exercises, muscle strengthening exercises (active resistance exercises), functional exercises (sit-to-stand, transfer, balance, walk, stairs).

Description of the two gait training interventions

The therapists participate in the training sessions before the start of the study. During these sessions, a member of the project team presents them the process and objectives of this study and the gait training protocol proposed for the two groups. They have trained with the Microsoft HoloLens and the ARRoW-CP game via a tutorial application.

ARRoW-CP: Overground Gait Training in AR

The intervention group receives the OGT-AR protocol through the active video game ARRoW-CP using the Microsoft HoloLens headset (**Figure 1**). ARRoW-CP sessions are monitored by physiotherapists, assistant-physiotherapist, or research assistants.

The intervention consists of 4 weeks of OGT-AR (3 sessions per week), including a series of walking sprints. This protocol is adapted from Zwinkels et al.²⁵. Every training session consists of a prescribed intensity, volume, and time (**Table I**).

Before the first session of each week, the target velocity is calculated during a Muscle Power Sprint Test (MPST).⁴⁴ This test is made through the ARRoW-CP game and is presented as a “calibration” to the participant. During this test, the player does not receive feedback. The highest velocity of 6 sprints defines the target speed (see *Intervention – Outcomes* section below for more details about MPST). This test is repeated every week to adapt the game's difficulty to the child's progress.

Treadmill Gait Training

The control group protocol consists of 4 weeks of GT on a treadmill (3 sessions per week), with a maximal duration of 30 minutes. This protocol is adapted from Grecco et al.¹³

Before the first session, the target velocity is estimated during a treadmill speed test: participants walk on a treadmill with increasing speed (initially 0.5 km/h and increased 0.5 km/h each minute). Each minute, the therapist asks about the shortness of breath, and the subjective responses are classified using the 1-10 Borg Rating of Perceived Exertion Scale. The test stopped if the score was higher than 5. The target velocity is 80% of the maximum speed achieved during the test.

1
2
3 The first 5 minutes are a warm-up time; the speed gradually increases until reaching the target velocity.
4 The child walks for a maximum of 20 minutes at their target velocity. Then, the treadmill speed gradually
5 diminishes over the final 5 minutes. Training could be interrupted at any time at the child's request or
6 the therapist's judgment. Treadmill sessions are monitored by a physiotherapist, assistant
7 physiotherapist, or a research staff member.
8

9 **Randomization Procedure**

10 After baseline measures, eligible participants are randomized to the intervention or control group based
11 on a computerized randomization program. Block randomizations are calculated in block sizes of fours
12 and six. The randomization procedure is only available to an independent researcher who will not be
13 involved in the delivery of the interventions or the performance of the measurements.
14
15

16 **Participants**

17 All participants will be recruited from the Ellen Poidatz Rehabilitation Center. The children will be
18 operated in several hospitals in Paris: Necker Enfants Malades University Hospital, Trousseau
19 University Hospital, or Robert Debré University Hospital. The French Ethical Committee Sud-Est
20 granted ethics approval. Additionally, all parents, and participants from 12 years of age, will provide
21 informed consent prior to study initiation. All participants should have a cooling-off period prior to the
22 inclusion (minimum 15 days between information and consent). The National Commission of
23 Informatics (CNIL) guarantees confidentiality and data access. A Data Protection Officer has been
24 designated for all research studies conducted in this rehabilitation center. According to the General Data
25 Protection Regulation (EU) 2016/679 (GDPR), he guarantees the respect of data protection and the
26 subject's rights. The study has been registered in ClinicalTrials.gov (Identifier: NCT04837105).
27
28

29 Inclusion criteria are children with CP admitted for inpatient rehabilitation following SEMLS, 12–18
30 years of age, functioning preoperatively at GMFCS I–III. The study's minimum time between surgery
31 and inclusion is seven weeks (step 4 of the postoperative rehabilitation process). They should have a
32 Functional Mobility Scale 50 meters rating superior or equal to 2 (ability to walk on 50m using a walker
33 or frame without help from another person).
34

35 All children should cooperate, understand and follow simple instructions in French to practice the game.
36 Only voluntary patients whose parents consent for their child's participation in the study are included.
37 Criteria for non-inclusion include a diagnosis of photosensitive epilepsy in the medical record and the
38 patient's case history mentioning seizures that occurred while playing a video game, visual cognitive or
39 auditory impairment that would interfere with playing the game. The patient should have normal or
40 corrected vision and hearing.
41
42

43 **Patient and Public Involvement**

44 Patient involvement. No public involved.
45

46 **Outcomes**

47 Outcome measures will take place at baseline (T0), immediately after four weeks of GT (T1), and six
48 months later (T2).
49

50 See **Supplementary File 2** for outcomes details and criterion validity.
51

52 *The 6 minutes walk test (6MWT)*

53 The six-minute walk test is increasingly used in pediatrics clinics to monitor patients' abilities, or for
54 clinical research as a criterion for evaluating the effectiveness of a rehabilitation protocol^{27–29} The
55 6MWT assesses distance walked over six minutes as a submaximal test of aerobic capacity/endurance.
56 The reference guide detailing the recommendations and instructions was updated in 2013.^{30,31}
57
58
59
60

Muscle power sprint test (MPST)

The MPST evaluates the anaerobic performance of youth with CP over 6x15 meters at their maximal speed.³² Velocity (m/s), acceleration (m/s²), force (kg/s²) and power (watts) are calculated.

Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of six sprints, and mean power (MP) averages over six sprints.

Shuttle Run Test (SRT)

The 10-meters shuttle run test is an adapted version of the 20-meter shuttle run test³³ to accommodate children with cerebral palsy (CP) classified Level I or Level II on the Gross Motor Function Classification System (GMFCS).³⁴ In this study, the SRT-II will be used because of the postoperative context. The SRT-II starts at 2 km/h. Speed is increased by 0.25 km/h at every level (minute). The test is over when the child cannot go to the next cone in time.

Questionnaire

The 16-items of the Physical Activity Enjoyment Scale (PACES) will be used to assess enjoyment for both the control and test groups.³⁵ The PACES is a valid and reliable measure of physical activity enjoyment.^{36,37} It has been used in many studies assessing the effectiveness of VR therapy.^{38,39} This questionnaire will be presented to the participant at the end of the last session.

Sample size and statistical analysis

According to a study by Grecco et al., an average augmentation of 83% (range 80-85%) in 6MWT was calculated following 12-weeks of treadmill training in a postoperative context.¹³ The distance traveled during the 6MWT increases from before: 166.4 ± 39.1 m to after: 304.7 ± 75.8 m. The effect size was calculated: $d = 2.29$. We hypothesize that participants following the ARRoW CP protocol will show the same effect on the 6MWT.

With an $\alpha = 0.05$ and $\beta = 0.20$ (power = 0.80), a sample size of 6 subjects per group will be required.

When taking a failure rate of 10 % into account, 14 subjects should be included.

The required sample size was calculated with G.Power 3.1.9.7. The parameter was t-tests – Means; preliminary analysis was the difference between two independent means (two groups).

The effect of the GT protocol will be analyzed using a multivariate repeated-measures ANOVA. The differences between and within T0, T1, and T2 for the intervention and control groups will be calculated. A posthoc test will be executed to investigate group differences further. Quantitative descriptive statistics will be used to present patient characteristics and global results. All statistical analyses will be performed using R with a statistical significance level of $p = 0.05$.

DISCUSSION

This approach has evolved from two directions: interest to improve walking capacity after SEMLS for children with CP and from concern that the usual postoperative rehabilitation approach has not produced sustainable improvements in participation and activity in daily life for these children.⁸

Active video game development framework

This work followed the active video game development framework PROGame, proposed by Amenguai Alcover et al.³⁸ A participative process including both professional healthcare and patients has been conducted.

The first step was the *project initiation*. The team identified the need for an active video game, the stakeholders, and user categories (users and experts). They also clarified the game functionality and constraints. They selected the therapy to transfer into the active video game. The operational objectives were to be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to

1
2
3 be fun. These identifications were based upon prior experience and literature review.^{12,39–41} The team
4 used communication tools like an oral presentation of preliminary results, open debates, surveys, and
5 meeting reports. The aim was to support incremental development between team members (with their
6 specialty) and share knowledge. At this stage, the project proposed a general description. The second
7 step was the *interaction mechanism*, all technical solutions were explored, and an algorithm for gait
8 parameters detection was developed and tested.^{40,41} During the third step, the *interactive elements*, the
9 team investigated actual commercial or active video games to get inspired. Team exploration and
10 discussion are aimed at games like Pokémon Go or Zelda, in which the gamer must explore the world
11 and accomplish missions. These games appear very popular with the younger generation. The
12 development team was composed of therapists (3 physiotherapists), researchers (2 in computer science,
13 1 in rehabilitation science, 1 in movement science), and a software engineer. These steps occurred
14 between January 2020 and June 2021. All details are available in **Supplementary File 3**.

15
16
17 The aim was to think together about the best solution for improving postoperative results, especially
18 walking capacity. New technologies were young people's preferred solution. These solutions seem to be
19 an up-and-coming tool for rehabilitation purposes, allowing to manipulate the environment, offer
20 interaction, optimize feedback, and many other potentialities.^{42,43}

21 22 23 **Feedback the critical point for motor learning**

24 The feedback retraining paradigm is based on the conversion, supplementation, and augmentation of
25 sensory information that are usually accessible only by an internal focus of attention to accessible
26 information.^{44–46} In this paradigm, augmented feedback is defined as augmented sensory information
27 provided by an external resource (therapist or display) to the patient.^{26,47} The information provided to
28 the user could be relative to the movement's pattern or result on the environment or the outcome of a
29 movement for the goal.^{48–51} Sensory channels used to deliver information are visual, auditory, or haptic,
30 linked to the proprioception properties of humans.⁵² The timing of feedback delivery is critical.
31 Concurrent feedback is delivered while the skill is being performed. Terminal feedback is delivered after
32 the skill is performed with or without delay.^{53,54} In most studies, even if feedback effectively improves
33 motor activities, the characteristics applied during interventions were generally inconsistent with motor
34 control feedback theory. Authors suggest that timing, frequency, and autonomy should be adjusted to
35 optimize the long-term effect.^{53–55} A strategy that provides feedback to the user on demand promotes
36 learning. Then, by reducing the frequency and timing of the feedback, the user can develop a sense of
37 self-regulation.⁵⁶

38 39 40 **The serious aspect of the ARRoW-CP game**

41 ARRoW-CP active video game combines many of the motor learning theories: context-focused therapy
42 and goal-directed training, task-specific, variable practice, high intensity, augmented feedback during
43 therapy sessions, and motivation of the patient.⁵⁷ To find the best feedback modalities for our active
44 video game, we have conducted preliminary studies exploring the impact of feedback modalities on
45 walking speed, both in healthy adults and in children with CP. A study on healthy adults showed that
46 specific feedback helped increase walking speed, provided that the game instruction was explicit.
47 Typically, feedback combining a focus of attention with knowledge of results, a spatial representation
48 with world-locked holograms, and a method of presentation with rich holographic content (like
49 animation, color changes) increased walking speed in healthy subjects.⁵⁸ This step allowed us to modify
50 and adapt feedback modalities. A second study has occurred with children with CP. Results showed that
51 *scenarios* combining world-locked holograms that disappeared over time helped children with CP reach
52 their target speed. On the other hand, a body-locked hologram that advances in front of the user at the
53 target speed was better able to control the walking speed of the patient.⁵⁹

54
55
56 ARRoW-CP is an adaptation of the validated protocol from Zwinkels et al. The original protocol consists
57 of 8 weeks, twice a week.²⁵ Every training session consisted of a 30s walking sprints following the
58 prescribed intensity, volume, and time: Week 1 to week 2: 8 sprints, work/rest ratio 1:4; Week 3 to week
59 4: 10 sprints, work/rest ratio 1:4; Week 5 to week 8: 12 sprints, work/rest ratio 1:3. Because of the
60 postoperative context, the intensity should be reduced. At the beginning of the fourth step of the

1
2
3 rehabilitation process, even if gait training is recommended, children did not precisely recover to their
4 pre-operative level; some children needed crutches or k-walkers. Moreover, a further aspect not to be
5 underestimated: fatigue and pain.⁶⁰ The choice of intensity, volume, and time in the ARRoW CP
6 protocol is based on practical experience from expert clinicians and literature^{12,13,61}
7

8 CONCLUSION

9
10 This article presents in detail the gait training protocol tested through an RCT. Both the control group
11 and experimental group have evidence-based physical therapy training. This article also presents the
12 game development framework of the ARRoW-CP active video game. This game is based on the most
13 recent motor learning approach. This is the first study assessing the efficacy of postoperative gait
14 rehabilitation using an active video game. If our hypothesis is validated, the ARRoW-CP game will
15 intensify gait training. This innovative strategy will have a significant clinical impact by improving
16 walking capacity for children after SEMLS. Publishing the study protocol of the RCT offers the
17 opportunity to collaborate with other teams and to give more details about the study. Results will be
18 available in 2022.
19

20
21
22
23 **Acknowledgements:** Authors would like to thank all participants and people involved in this work. This
24 study is a part of the ARRoW CP project supported by the Ellen Poidatz Foundation and Association
25 Nationale Recherche et Technologie (ANRT), in collaboration with the University of Paris-Saclay,
26 University of Evry, IBISC, Team IRA2.
27

28 **Authors' contributions:** ALG, GB, and ED, conceived the study, participated in its design, and
29 participated to the manuscript. SPT, MB, NK participated in the coordination of the study. All authors
30 read and approved the final manuscript.
31

32 **Funding statement:** The *Association Nationale Recherche et Technologie* (ANRT/ grant number
33 convention CIFRE 2018/0973).
34

35 **Competing interests:** Not applicable.
36

37 **Data sharing statement:** Not applicable.
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Image capture from ARRoW-CP active video game. On the left, this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. A child wearing the Microsoft HoloLens AR headset is in the middle to see holograms. On the right, game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard)

	WEEK 1	WEEK 2	WEEK 3	WEEK4
Frequency (session/week)	3	3	3	3
Sprint Duration (s)	30	30	30	30
Rest Time (min:s)	2:00	2:00	1:30	1:30
Sprint Repetition	4	6	8	10
Total time (min)	10	15	18	22

Table I. Details of the gait training protocol deployed in the active video game ARRoW-CP

1. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol Suppl.* 2007;109(suppl 109):8-14. doi:10.1111/j.1469-8749.2007.tb12610.x
2. Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology.* 2013;55(6):509-519. doi:10.1111/dmcn.12080
3. Graham HK, Rosenbaum P, Paneth N, et al. Cerebral palsy. *Nat Rev Dis Primers.* 2016;2(1):15082. doi:10.1038/nrdp.2015.82
4. Park E-Y. Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. *Health and Quality of Life Outcomes.* 2018;16(1). doi:10.1186/s12955-018-0891-1
5. Himuro N, Mishima R, Seshimo T, et al. Change in mobility function and its causes in adults with cerebral palsy by Gross Motor Function Classification System level: A cross-sectional questionnaire study. *NeuroRehabilitation.* 2018;42(4):383-390. doi:10.3233/NRE-172340
6. Benner JL, Hilberink SR, Veenis T, Stam HJ, van der Slot WM, Roebroek ME. Long-Term Deterioration of Perceived Health and Functioning in Adults With Cerebral Palsy. *Arch Phys Med Rehabil.* 2017;98(11):2196-2205.e1. doi:10.1016/j.apmr.2017.03.013
7. Novak I, Morgan C, Fahey M, et al. State of the Evidence Traffic Lights 2019: Systematic Review of Interventions for Preventing and Treating Children with Cerebral Palsy. *Curr Neurol Neurosci Rep.* 2020;20(2):3. doi:10.1007/s11910-020-1022-z
8. McGinley JL, Dobson F, Ganeshalingam R, Shore BJ, Rutz E, Graham HK. Single-event multilevel surgery for children with cerebral palsy: a systematic review. *Dev Med Child Neurol.* 2012;54(2):117-128. doi:10.1111/j.1469-8749.2011.04143.x
9. Lamberts RP, Burger M, du Toit J, Langerak NG. A Systematic Review of the Effects of Single-Event Multilevel Surgery on Gait Parameters in Children with Spastic Cerebral Palsy. Martinuzzi A, ed. *PLOS ONE.* 2016;11(10):e0164686. doi:10.1371/journal.pone.0164686
10. Amirmudin NA, Lavelle G, Theologis T, Thompson N, Ryan JM. Multilevel Surgery for Children With Cerebral Palsy: A Meta-analysis. *Pediatrics.* 2019;143(4):e20183390. doi:10.1542/peds.2018-3390
11. Guinet A-L, Khouri N, Desailly E. Rehabilitation after single-event multilevel surgery for children and young adults with cerebral palsy: A systematic review. *American Journal of Physical Medicine & Rehabilitation.* Published online August 13, 2021. doi:10.1097/PHM.0000000000001864
12. Booth ATC, Buizer AI, Meyns P, Oude Lansink ILB, Steenbrink F, van der Krogt MM. The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology.* 2018;60(9):866-883. doi:10.1111/dmcn.13708
13. Grecco LAC, de Freitas TB, Satie J, Bagne E, Oliveira CS, de Souza DR. Treadmill training following orthopedic surgery in lower limbs of children with cerebral palsy. *Pediatr Phys Ther.* 2013;25(2):187-192; discussion 193. doi:10.1097/PEP.0b013e3182888495
14. Emara HA, El-Gohary TM, Al-Johany AH. Effect of body-weight suspension training versus treadmill training on gross motor abilities of children with spastic diplegic cerebral palsy. *European Journal of Physical and Rehabilitation Medicine.* 2016;52(3):8.

15. Gharib NM, El-Maksoud GMA, Rezk-Allah SS. Efficacy of gait trainer as an adjunct to traditional physical therapy on walking performance in hemiparetic cerebral palsied children: a randomized controlled trial. *Clin Rehabil*. 2011;25(10):924-934. doi:10.1177/0269215511400768
16. Novak I, McIntyre S, Morgan C, et al. A systematic review of interventions for children with cerebral palsy: state of the evidence. *Developmental Medicine & Child Neurology*. 2013;55(10):885-910. doi:10.1111/dmcn.12246
17. Cano-de-la-Cuerda R, Molero-Sánchez A, Carratalá-Tejada M, et al. Theories and control models and motor learning: Clinical applications in neurorehabilitation. *Neurologia (English Edition)*. 2015;30(1):32-41. doi:10.1016/j.nrleng.2011.12.012
18. Sullivan KJ, Kantak SS, Burtner PA. Motor learning in children: feedback effects on skill acquisition. *Phys Ther*. 2008;88(6):720-732. doi:10.2522/ptj.20070196
19. Orand A, Ushiba J, Tomita Y, Honda S. The comparison of motor learning performance with and without feedback. *Somatosensory & Motor Research*. 2012;29(3):103-110. doi:10.3109/08990220.2012.687419
20. Cruz-Neira C, Sandin DJ, DeFanti TA, Kenyon RV, Hart JC. The CAVE: audio visual experience automatic virtual environment. *Commun ACM*. 1992;35(6):64-72. doi:10.1145/129888.129892
21. Cho C, Hwang W, Hwang S, Chung Y. Treadmill Training with Virtual Reality Improves Gait, Balance, and Muscle Strength in Children with Cerebral Palsy. *The Tohoku Journal of Experimental Medicine*. 2016;238(3):213-218. doi:10.1620/tjem.238.213
22. Biffi E, Beretta E, Cesareo A, et al. An Immersive Virtual Reality Platform to Enhance Walking Ability of Children with Acquired Brain Injuries. *Methods Inf Med*. 2017;56(2):119-126. doi:10.3414/ME16-02-0020
23. Gagliardi C, Turconi AC, Biffi E, et al. Immersive Virtual Reality to Improve Walking Abilities in Cerebral Palsy: A Pilot Study. *Annals of Biomedical Engineering*. Published online April 27, 2018. doi:10.1007/s10439-018-2039-1
24. Demers M, Fung K, Subramanian SK, Lemay M, Robert MT. Integration of Motor Learning Principles Into Virtual Reality Interventions for Individuals With Cerebral Palsy: Systematic Review. *JMIR Serious Games*. 2021;9(2). doi:10.2196/23822
25. Zwinkels M, Verschuren O, de Groot JF, et al. Effects of High-Intensity Interval Training on Fitness and Health in Youth With Physical Disabilities: *Pediatric Physical Therapy*. 2019;31(1):84-93. doi:10.1097/PEP.0000000000000560
26. Dursun E, Dursun N, Alican D. Effects of biofeedback treatment on gait in children with cerebral palsy. *Disability and Rehabilitation*. 2004;26(2):116-120. doi:10.1080/09638280310001629679
27. Apolo-Arenas MD, Jerônimo AF de A, Caña-Pino A, Fernandes O, Alegrete J, Parraca JA. Standardized Outcomes Measures in Physical Therapy Practice for Treatment and Rehabilitation of Cerebral PALSY: A Systematic Review. *JPM*. 2021;11(7):604. doi:10.3390/jpm11070604
28. Gillett JG, Lichtwark GA, Boyd RN, Carty CP, Barber LA. The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy. *Gait & Posture*. 2019;70:323-329. doi:10.1016/j.gaitpost.2019.03.023

29. Geiger R, Strasak A, Treml B, et al. Six-Minute Walk Test in Children and Adolescents. *The Journal of Pediatrics*. 2007;150(4):395-399.e2. doi:10.1016/j.jpeds.2006.12.052
30. American Thoracic Society. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med*. 2002;166:111-117.
31. Hoder J. The 6 minute walk test : Instrument details. Shirley Ryan AbilityLab. Published June 24, 2021. <https://www.sralab.org/rehabilitation-measures/6-minute-walk-test>
32. Verschuren O, Bongers BC, Obeid J, Ruyten T, Takken T. Validity of the Muscle Power Sprint Test in Ambulatory Youth With Cerebral Palsy: *Pediatric Physical Therapy*. 2013;25(1):25-28. doi:10.1097/PEP.0b013e3182791459
33. Léger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. *Journal of Sports Sciences*. 1988;6(2):93-101. doi:10.1080/02640418808729800
34. Verschuren O, Takken T, Ketelaar M, Gorter JW, Helder PJ. Reliability and validity of data for 2 newly developed shuttle run tests in children with cerebral palsy. *Physical therapy*. 2006;86(8):1107-1117.
35. Kendzierski D, DeCarlo KJ. Physical Activity Enjoyment Scale: Two Validation Studies. *Journal of Sport and Exercise Psychology*. 1991;13(1):50-64. doi:10.1123/jsep.13.1.50
36. Motl RW, Dishman RK, Saunders R, Dowda M, Felton G, Pate RR. Measuring enjoyment of physical activity in adolescent girls. *Am J Prev Med*. 2001;21(2):110-117. doi:10.1016/s0749-3797(01)00326-9
37. Román PÁL, Pinillos FG, Martínez AVN, Rus TI. Validity and reliability of Physical Activity Enjoyment Scale questionnaire (PACES) in children with asthma. *Journal of Asthma*. 2014;51(6):633-638. doi:10.3109/02770903.2014.898773
38. Deutsch JE, Hoehlein B, Priolo M, Pacifico J. Custom game paced video games played by persons post-stroke have comparable aerobic intensity but higher accuracy, greater enjoyment and less effort than off-the-shelf game. In: ; 2019.
39. Fehlings D, Switzer L, Findlay B, Knights S. Interactive Computer Play as “Motor Therapy” for Individuals With Cerebral Palsy. *Seminars in Pediatric Neurology*. 2013;20(2):127-138. doi:10.1016/j.spen.2013.06.003
40. Guinet AL, Bouyer G, Otmane S, Desailly E. Reliability of the head tracking measured by Microsoft HoloLens during different walking conditions. *Comput Methods Biomech Biomed Engin*. Published online October 2019:159-161. doi:10.1080/10255842.2020.1714228
41. Guinet A-L, Bouyer G, Otmane S, Desailly E. Validity of HoloLens Augmented Reality Head Mounted Display for Measuring Gait Parameters in Healthy Adults and Children With Cerebral Palsy. *Sensors (Basel, Switzerland)*. 2021;21:2697. doi:10.3390/s21082697
42. Lamontagne A, Keshner EA, Bugnariu N, Fung J. Virtual Reality Reveals Mechanisms of Balance and Locomotor Impairments. In: *Virtual Reality for Physical and Motor Rehabilitation*. Virtual Reality Technologies for Health and Clinical Applications. Springer, New York, NY; 2014:169-202. doi:10.1007/978-1-4939-0968-1_9
43. Keshner EA, Lamontagne A. The Untapped Potential of Virtual Reality in Rehabilitation of Balance and Gait in Neurological Disorders. *Front Virtual Real*. 2021;2:641650. doi:10.3389/frvir.2021.641650

- 1
2
3 44. Levin MF. Feedback and virtual environments for motor learning and rehabilitation. *Schadae*.
4 Published online 2010:18.
5
6 45. Oliveira N, Ehrenberg N, Cheng J, Blochlinger S, Barrance P. Visual kinematic feedback
7 enhances the execution of a novel knee flexion gait pattern in children and adolescents. *Gait &*
8 *Posture*. 2019;74:94-101. doi:10.1016/j.gaitpost.2019.06.016
9
10 46. Alwhaibi RM, Alsakhawi RS, EIKholi SM. Augmented Biofeedback Training with Physical
11 Therapy Improves Visual-Motor Integration, Visual Perception, and Motor Coordination in
12 Children with Spastic Hemiplegic Cerebral Palsy: A Randomised Control Trial. *Physical &*
13 *Occupational Therapy In Pediatrics*. Published online July 31, 2019:1-18.
14 doi:10.1080/01942638.2019.1646375
15
16 47. Alahakone AU, Senanayake SMNA. A Real-Time System With Assistive Feedback for Postural
17 Control in Rehabilitation. *IEEE/ASME Transactions on Mechatronics*. 2010;2(15):226-233.
18 doi:10.1109/TMECH.2010.2041030
19
20 48. Sigrist R, Rauter G, Riener R, Wolf P. Augmented visual, auditory, haptic, and multimodal
21 feedback in motor learning: A review. *Psychon Bull Rev*. 2013;20(1):21-53. doi:10.3758/s13423-
22 012-0333-8
23
24 49. Chiviawosky S, Drews R. Effects of generic versus non-generic feedback on motor learning in
25 children. *PLoS ONE*. 2014;9(2):e88989. doi:10.1371/journal.pone.0088989
26
27 50. Gilmore PE, Spaulding SJ. Motor Learning and the Use of Videotape Feedback After Stroke.
28 *Topics in Stroke Rehabilitation*. 2007;14(5):28-36. doi:10.1310/tsr1405-28
29
30 51. Ronsse R, Puttemans V, Coxon JP, et al. Motor learning with augmented feedback: modality-
31 dependent behavioral and neural consequences. *Cereb Cortex*. 2011;21(6):1283-1294.
32 doi:10.1093/cercor/bhq209
33
34 52. Kassover M, Tauber C, Au J, Pugh J. Auditory biofeedback in spastic diplegia. *Journal of*
35 *Orthopaedic Research*. 1986;4(2):246-249. doi:10.1002/jor.1100040213
36
37 53. MacIntosh A, Lam E, Vigneron V, Vignais N, Biddiss E. Biofeedback interventions for
38 individuals with cerebral palsy: a systematic review. *Disability and Rehabilitation*. Published
39 online May 12, 2018:1-23. doi:10.1080/09638288.2018.1468933
40
41 54. Frikha M, Chaâri N, Elghoul Y, Mohamed-Ali HH, Zinkovsky AV. Effects of Combined Versus
42 Singular Verbal or Haptic Feedback on Acquisition, Retention, Difficulty, and Competence
43 Perceptions in Motor Learning. *Percept Mot Skills*. 2019;126(4):713-732.
44 doi:10.1177/0031512519842759
45
46 55. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A. Real-Time Avatar-Based Feedback to
47 Enhance the Symmetry of Spatiotemporal Parameters After Stroke: Instantaneous Effects of
48 Different Avatar Views. *IEEE Trans Neural Syst Rehabil Eng*. 2020;28(4):878-887.
49 doi:10.1109/TNSRE.2020.2979830
50
51 56. Wulf G, Shea C, Lewthwaite R. Motor skill learning and performance: a review of influential
52 factors. *Medical Education*. 2010;44(1):75-84. doi:10.1111/j.1365-2923.2009.03421.x
53
54 57. Demers M, Fung K, Subramanian S, Lemay M, Robert M. Do virtual interventions in individuals
55 with cerebral palsy make use of motor learning principles?: A systematic review (Preprint).
56 *JMIR Serious Games*. Published online August 25, 2020. doi:10.2196/23822
57
58
59
60

- 1
2
3 58. Guinet AL, Bouyer G, Otmane S, Khouri N, Desailly E. Exploring visual feedback modalities in
4 Augmented Reality to control the walking speed. Feasibility study. *Gait & Posture*.
5 2020;81:122-123. doi:10.1016/j.gaitpost.2020.07.095
6
7 59. Guinet AL, Biddiss E, Khan A, et al. Towards an AR game for walking rehabilitation:
8 Preliminary study of the impact of augmented feedback modalities on walking speed. *IEEE*
9 *International Symposium on Mixed and Augmented Reality (ISMAR-Adjunct)*. Published online
10 2020.
11
12 60. Høiness PR, Capjon H, Lofterød B. Pain and rehabilitation problems after single-event
13 multilevel surgery including bony foot surgery in cerebral palsy. A series of 7 children. *Acta*
14 *Orthop*. 2014;85(6):646-651. doi:10.3109/17453674.2014.960141
15
16 61. American College of Sports Medicine, Riebe D, Magal M. *ACSM's Guidelines for Exercise*
17 *Testing and Prescription*. 10th ed. Wolters Kluwer; 2016.
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Figure 1. Image capture from ARoW-CP active video game. On the left, this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. A child wearing the Microsoft HoloLens AR headset is in the middle to see holograms. On the right, game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard)

447x137mm (38 x 38 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ARROW-CP Serious game for gait rehabilitation

1. The Microsoft HoloLens Headset is used for ARROW-CP (**Figure 1**). Game development was made with Unity 2019.4.8f1 and Mixed Reality Toolkit (MRTK). MRTK-Unity is a Microsoft-driven project that provides a set of components and features, used to accelerate cross-platform MR app development in Unity.

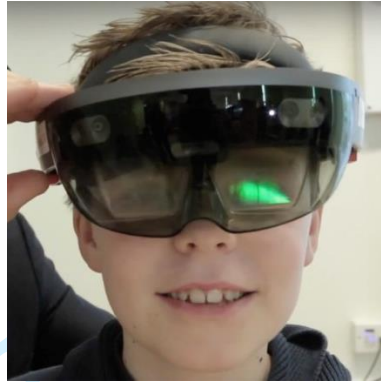


Figure 1. Microsoft HoloLens Augmented reality headset.

2. The player is immersed in a samurai world. He meets the chief of the village that can no longer protect its population. The natural elements are unleashed, causing famine and various damages. The player's role is to develop his energy through ninja training to build a protective totem for the village's inhabitants (trailer: <https://youtu.be/BbmniijuaA>).

The software architecture is presented in **Figure 2**.

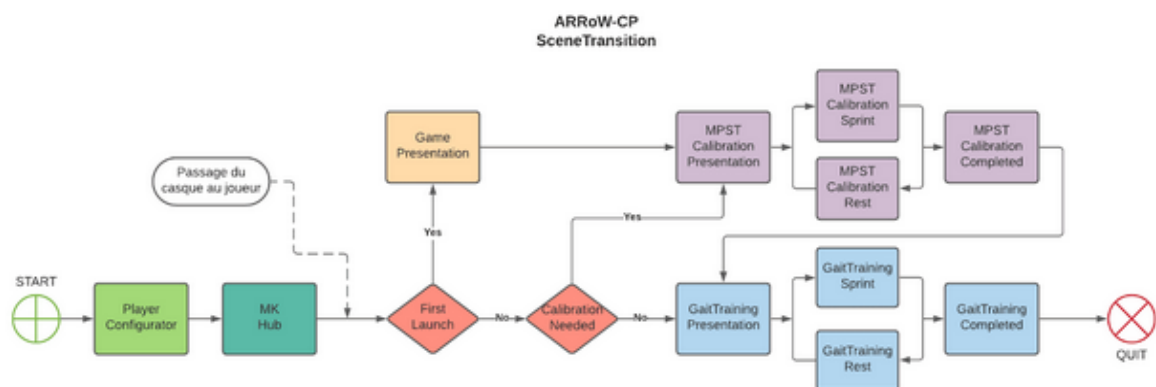


Figure 2. Game architecture of the ARROW CP game. When the game starts, the AR headset is worn by the therapist. He creates the user profile of the player by entering his name, first name, age, height, and weight during session 1 week 1. Next session, he loads the existing user profile. The therapist then accesses the "MK Hub", which contains information about the performance of previous sessions and the number of sessions

3. The mechanism of feedback provided during sprints and rest time is detailed in **Figure 3**.

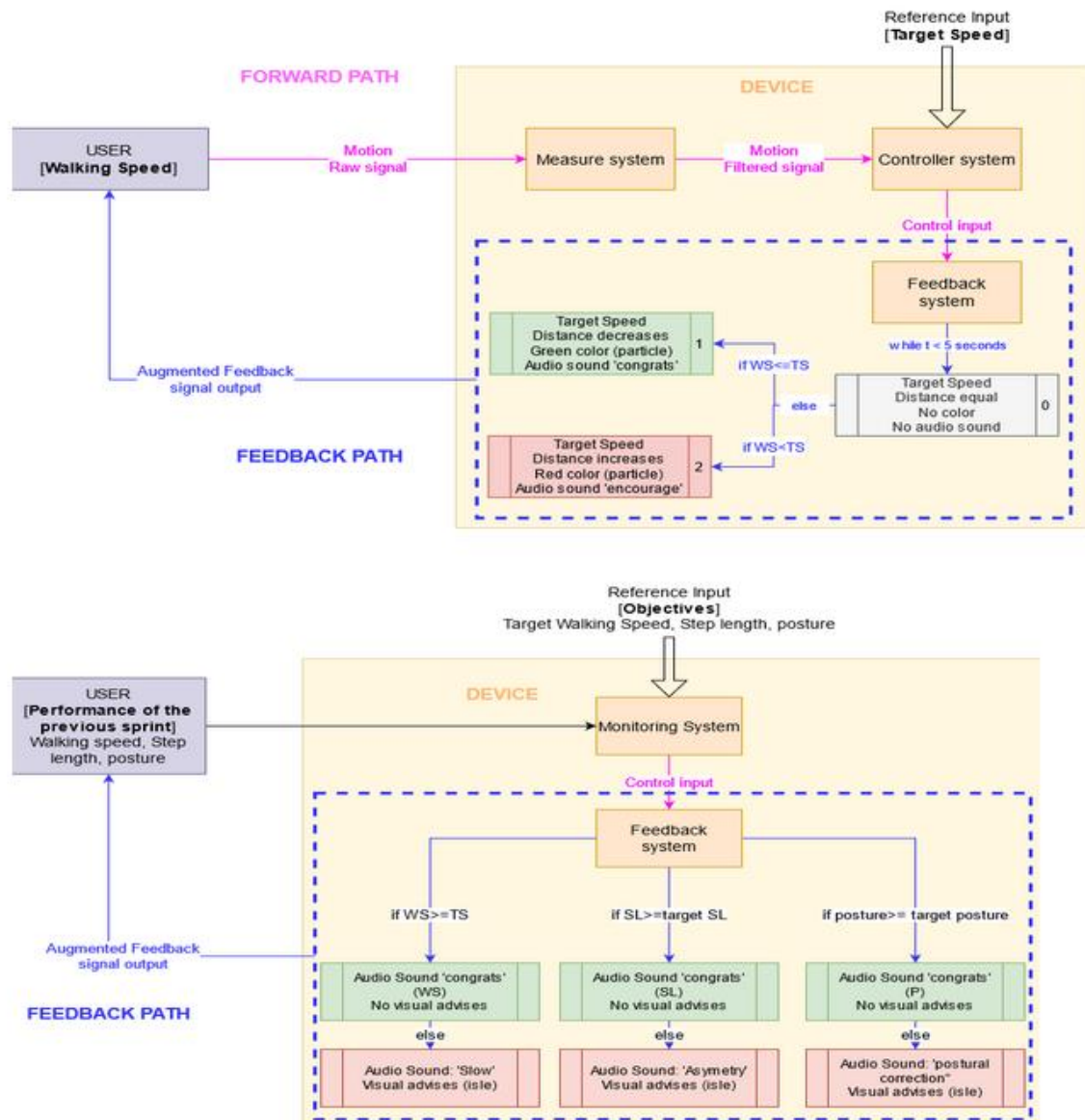


Figure 3. Feedback mechanism during sprints (A) and rest period (B).

At the beginning of each session, through the "Physio HUB", therapists know the previous performance of their patient and they can adjust their advice.

At the end of each session, feedback with delay is proposed to the child: they can choose to see their actual performance through the game scoreboard and totem construction (feedback on demand). These feedbacks were based on knowledge of results.

Test name	Instructions
<i>The 6 minutes walk test (6MWT)</i>	To summarize, patients are instructed to walk, not run, as far as they could along a 20-m level surface track during a 6-minute period. This shorter distance has been validated for children in order to be more focused on the task. They could use their usual walking aids. After each minute, participants are told the elapsed time and standardized encouragement is provided. Patients are allowed to stop and rest during the test but are instructed to resume walking as soon as they feel able to do so. The stopwatch is not stopped during this time. The 6MWT distance (in meters) is registered. Measured 6MWT distance could be compared with normative values for children with CP. It is recommended to monitor heart rate during the 6MWT.
<i>Muscle power sprint test (MPST)</i>	The 15-m distance is marked by 2 lines taped to the floor. Cones are placed at the end of each of the lines. Participants are instructed to walk as fast as possible from one line to the other, and to be sure to cross each line. Between each run, participants are allowed to rest for 10 seconds before turning around to allow them to prepare for the following sprint. Children should be encouraged to give maximal effort. The following variables are calculated for each of the 6 sprints: velocity (m/s) = distance/time, acceleration (m/s ²) = velocity/time, force (kg/s ²) = body mass × acceleration, and power (watts) = force × velocity. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints.
10-meters Shuttle Run Test (SRT)	Description of the test is available here : “The course is 10 metres long; the end is marked with 2 cones and measuring tape. Subjects should wear regular sports clothing and shoes, and orthoses, if applicable. Each child should also wear a heart rate monitor. Children walk or run between the 2 markers at a set incremental speed. These runs are synchronised with a pre-recorded sound. (...) As the test proceeds, the interval between each successive beep reduces, forcing the child to increase speed over the course of the test, until it is impossible to keep in sync with the recording.” We have developed a mobile application that beeps at regular intervals, indicates the time spent and allows the assessor to increment the number of shuttles made by the child.
Physical Activity Enjoyment Scale (PACES)	This is a 5-point Likert scale (from 1- I totally disagree to 5- I totally agree). A translation procedure from English to French language has been made using guidelines (figure).

Validity
<p>In population of children with CP, test/retest reliability is excellent for distance output (ICC=0.98).</p> <p>The 6MWT is poorly related to VO₂ peak in ambulatory adolescents and young adults with CP. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.</p>
<p>The MPST is a valid test to assess the anaerobic performance in children with CP, significant correlations between the performance on these tests for both PP and MP were found. (PP: $r = 0.731$; MP: $r = 0.903$).</p> <p>Standard error of measurement (SEM), minimal detectable change (MDC) and normative data are available in Verschuren et al. The children with CP had impaired anaerobic performance as it was lower than that of their peers.</p>
<p>The SRT is a valid and reliable test. Test-retest is excellent (ICC=0.99) and high correlations were found for the relationship between data for both shuttle run tests and data for the treadmill test ($r=0.96$).</p>
<p>The PACES is a valid and reliable measure of physical activity enjoyment.</p>



1
2
3
4 **Global Aim**

5
6
7
8
9 **Operational objectives**

10 *describe the needs in general*
11
12
13
14
15
16
17
18
19
20

21 **Restrictions**

22 *detail economical, technical,*
23 *operational, legal restrictions*
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38

39 **Stakeholders**

40 *identify customers, special needs and*
41 *required functionality ;*
42 *define experts and representatives end*
43 *users*
44
45
46
47
48
49
50
51
52
53
54

55 **Therapy Selection**
56
57
58
59
60

Project Initiation

to develop a walking rehabilitation serious game for children with motor disabilities and particularly cerebral palsy

to be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun.

The development of the game must correspond to the duration of a 3-year thesis; grants are limited and predefined; the agreement of the ethics committee and written consents from participants are required before any test on humans ; all technical solution could be explored.

Customers :

- Children with cerebral palsy, 12-18 years old, GMFCS I-III, with cognitive skills to understand and follow simple instructions == END USERS
- Physiotherapists, occupational therapists, physiotherapist assistants, rehabilitation therapists == EXPERTS

Special needs and required functionalities :

- The serious game must include the principles of motor learning, which are task-specific practice, variable practice, high practice intensity, progressive difficulty, augmented feedback, and adaptability to user abilities.
- The serious game should allow the inclusion of motivational elements to increase engagement.
- Children must be free to move in the global environment, without restriction of movement.
- Children must be able to use their usual walking aids (crutches or posterior walker).
- Therapists should have access to the previous and global performance of their patient through the game
- The solution should be "ready to use" easily both for children and therapists

The team's members agreed on making walking speed the main variable input of the serious game. Meaningful reason is that intensive gait training focused on walking speed has shown their clinical efficacy.^{12,39} The therapy to transfer into the serious game should include walking sprints.

Interaction Mechanism

Aim of this phase

To select the interaction system and to capture the therapy into this system.

Device selection

Device: Microsoft HoloLens AR headset version 1 was selected because its technical characteristics matched all identified specifications.

Tools : - Unity software (version 2019.4.8f1) -
Microsoft Visual Studio 2019 - Mixed Reality Toolkit for Unity (MRTK version 4.2.3)

Gait parameters detection *development and evaluation*

Algorithm development: HoloStep measuring the real-time gait parameters with the AR headset system⁴³

Evaluation :

- The accuracy of the AR headset's sensors was sufficiently high to evaluate the position of the user without time drift in the global environment⁴²
- HoloStep was reliable for measuring and calculating walking speed, cadence, step length and global distance travelled in comparison to a reference motion analysis tracking system⁴³

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Aim of this phase

Feedback reflexion

Game selection & Universe

For peer review only

Interaction Elements

To design the interaction elements that force patients to perform the therapy correctly

After a debate between team development members, the choice was made to develop the game around the 'do not escape' scenario using body-locked hologram to follow. Main reasons were technical constraints (Microsoft Azure credits were required to build fixed and high-quality world-locked holograms) and experts point of view (physiotherapists judged that the world-locked holograms that disappeared over the time decreased the quality of walking). Feedback with delay was also chosen (game scoreboard). During rest periods, team members agreed to provide advice through animation.

The choice of the game universe (Samurai world) and reward panel were unanimously validated by experts and end users. All packages used to design the game were available in the Unity Asset Store: Polygon Samurai low poly 3D Art by Synty, Tiny Dragon by Suriyun, the GUI Kit - The Stone, and the Particle FX. Voice of game characters from volunteers were recorded in a professional radio studio (HandiFM – France 107.3 FM).

BMJ Open

Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery : Protocol for a Randomized Controlled Trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-061580.R1
Article Type:	Protocol
Date Submitted by the Author:	01-Jul-2022
Complete List of Authors:	Guinet, Anne-Laure; Universite Paris-Saclay, IBISC Laboratory; Fondation Ellen Poidatz, Pôle Recherche&Innovation Bams, Michel; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Payan-Terral, Sandrine; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Khouri, Neijib; Hôpital universitaire Necker-Enfants malades Otmame, Samir; Universite Paris-Saclay, IBISC Laboratory Bouyer, Guillaume; Universite Paris-Saclay, IBISC Laboratory Desailly, Eric; Fondation Ellen Poidatz, Pôle Recherche & Innovation
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Paediatrics, Sports and exercise medicine
Keywords:	Paediatric orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric neurology < NEUROLOGY, Developmental neurology & neurodisability < PAEDIATRICS, REHABILITATION MEDICINE, Clinical trials < THERAPEUTICS

SCHOLARONE™
Manuscripts

OPEN ACCESS PROTOCOL**Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery: Protocol for a Randomized Controlled Trial**

Anne-Laure Guinet^{1,2*†}, Michel Bams¹, Sandrine Payan-Terral¹, Neijib Khouri³, Samir Otmane², Guillaume Bouyer² and Eric Desailly^{1†}

Abstract

Introduction: In paediatric rehabilitation, fun and motivation are also critical keys to successful therapy. A variety of interventions have shown positive effects, high level of interest, compliance and engagement with active video game (AVG).

This seems to be an interesting approach for the postoperative gait rehabilitation of children with CP. In this study, we will investigate if an overground gait training (GT) delivered through an AVG can improve walking capacity and anaerobic performance.

Methods and analysis: This study is a randomized clinical controlled trial. A total of 14 children and adolescents in the age of 12–18 years with CP will be included. The minimum time between surgery and inclusion will be 7 weeks. The test group will participate in the GT program with ARRoW-CP AVG (Augmented Reality Rehabilitation of Walking-Cerebral Palsy), control group will receive GT on a treadmill. The primary outcome is the 6-Minutes Walk Test assessing walking capacity; secondary outcomes are the Muscle Power Sprint Test for anaerobic performance and Shuttle Run Test for physical fitness level. Satisfaction is tested with the Physical Activity Enjoyment Scale. This study has been registered in ClinicalTrials.gov (NCT04837105). The findings will be disseminated by publications in peer-reviewed journals and conferences.

Keywords: cerebral palsy; surgery; active video game; augmented reality; gait performance

1
2
3
4 *Correspondence: anne-laure.guinet@fondationpoidatz.com

5 1 Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, FR

6 2 IBISC Lab, University Paris-Saclay, Paris, FR

7 3 Hôpital Universitaire Necker-Enfants Malades, Paris, FR

8
9
10 Full list of author information is available at the end of the article

11
12 †Equal contributor

13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Strengths and limitations of this study

- This is the first randomized clinical trial to compare traditional rehabilitation and technology-delivered gait performance training in children with cerebral palsy after surgery.
- The control group receives treadmill therapy to counterbalance the additional dose effect of active video game use in the experimental group.
- The active video game intervention being investigated have been tailored to the needs of children with cerebral palsy based on feedback from patient and public involvement and expert review groups conducted during the first phase of this project.
- Patients and patient's physiotherapist cannot be blinded; however, the professional caregiver administering outcome measures and the trial statistician will remain blinded to group allocation until the database has been locked.
- The interventions require participants to have no visual, cognitive or auditory impairment that would interfere with playing the game.

Introduction

Cerebral palsy is commonly defined as a “group of permanent disorders of the development of movement and posture, causing activity limitation”[1]. The overall prevalence of CP remains constant (2.11 per 1000 births) [2] with an estimated prevalence of 17 million people worldwide.[3] Individuals with CP present various clinical symptoms including a non-exhaustive list of neurological, orthopaedic, movement, cognitive, vision/hearing, aero digestive disorders.

Musculoskeletal disorders are considered as a secondary impairment contributing to restricted mobility in childhood and adulthood.[4, 5, 6] Since 1985, therapeutic interventions to correct orthopaedic disorders include single-event multilevel surgery (SEMLS). This surgery proposes, during one operative period, to realign the musculoskeletal system, practicing tendon transfer, muscle lengthening, derotation and/or deflexion osteotomy and joint stabilization. Novak *et al.* classified SEMLS as effective intervention for children with CP for improving both Gross Motor, walking speed and walking capacity but also contracture and alignment deformities [7]. To date, systematic reviews on the effect of SEMLS reported improvement in passive range of motion, kinematics and kinematics gait parameters, overall gait index and energy efficiency [8, 9]. Results were more disputed about the long-term effect on spatio-temporal gait parameters, gross motor function and the activity and participation domain [10].

A recent literature review has proposed a model in five steps that could guide clinicians during the post-operative rehabilitation [11]. The authors suggested that the fourth phase, which included more intensive exercises, functional gait training and resistive muscle strengthening should be optimized to improve the gross motor function and walking speed after surgery. Functional gait training has been defined as ‘actively practice the task of walking, to improve walking ability [12]. Intervention could be overground gait training (OGT), or treadmill gait training (TT), with or without body support.

Previously, Grecco *et al.* demonstrated the efficacy of treadmill gait training program including both on functional mobility and gross motor function on children with CP after SEMLS [13]. Recently, a systematic review showed that gait training was a safe and effective intervention to improve walking capacity in children with CP, outside postoperative context [12]. In particular, the minimal clinically important difference (MCID) for increase in walking speed (0.1m/s) was achieved after intervention in 12 studies/14 (studies level between II and III). Authors discussed two points: OGT could provide greater effect on locomotor abilities than TT because OGT is more representative of the natural walking, and the addition of feedback could enhance the patient outcomes. These points were important to consider after SEMLS, because the overall gait pattern of children was modified by the bone and muscle gestures. Novak *et al.* highlighted the importance of the context focused therapy and goal-directed training

1
2
3
4 for children with CP [7]. Functional gait training should therefore take into account
5 those recommendations and involve motor learning strategies: task-specific, variable
6 practice, high intensity, augmented feedback during therapy sessions and motivation of
7 the patient [14].

8 In recent years, new technologies have been introduced in rehabilitation practice, both
9 for upper and lower limbs therapy. These systems include a large type of technology
10 ranging from fully immersive virtual reality (VR) or augmented reality (AR) using
11 commercially available head-mounted displays (HMD) (e.g., Oculus Quest; HTC VIVE,
12 Microsoft HoloLens), Cave Automatic Virtual Environment where video is projected on
13 the walls and floor to video game console on television screen (e.g., Nintendo Switch,
14 PlayStation).

15 To 'actively practice the task of walking', systems combining treadmill training and active
16 video game (AVG) delivered through a screen in a semi-immersive environment have been
17 tested with good results [15]. However, motor learning principles are not always fully
18 integrated into VR/AR systems because of the lack of knowledge about which feedback
19 modality and which intensity level should be provided in the rehabilitation settings [16].

20 To our knowledge, even if OGT was recommended for functional gait training, no AR
21 system with AVG exists to provide high-intensity, with progressive difficulty, and
22 variable modalities including feedback. To this end, we have developed the active video
23 game ARRoW-CP (Augmented Reality Rehabilitation of Walking-Cerebral Palsy)
24 combining OGT based on previous results [12] and literature [17] and motor learning
25 theory [14]. ARRoW-CP active video game has been developed for Microsoft HoloLens
26 headset (mixed reality headset). The team used the game development framework
27 PROGame and all stakeholders have been involved through the process (children with
28 CP, researchers, engineers, therapists)[18]. In most studies, even if feedback is effective
29 to improve motor activities, the characteristics applied during interventions were
30 generally inconsistent with motor control feedback theory. Authors suggest that timing,
31 frequency and autonomy should be adjusted to optimize long-term effect [19]. A
32 strategy that provides feedback to the user on demand promotes learning. Then, by
33 reducing the frequency and timing of the feedback, the user can develop a sense of self-
34 regulation. In this AVG, continuous feedback as well as terminal feedback, both with
35 different audio and visual modalities, are combined following the recommendations of the
36 literature [20, 16]. The general principle for defining the feedback to be used is primarily
37 defined by the results from a previous study that the team lead (article under review).
38 Specific recommendations from this previous study included using feedback moving on in
39 front of the player at the target speed to create a more challenging task that motivates
40 participants to excel. In addition, our results highlighted that the temporary modification
41 of visual aspect according to the performance (red light/too slow; green light/good speed)
42 helped to improve walking speed creating a playful challenge. The feedback attached to
43 the player seemed to be better to minimize visual discomfort and, by extension, fatigue.
44 More details of ARRoW-CP game, architecture, framework development and feedback
45 characteristics, are available in the Supplementary Files 1 and 3.

46
47 The current study, denoted as the ARRoW-CP study, will investigate whether a gait
48 training protocol through an active video game in AR can:

- 49 1. Increase the walking capacity
- 50 2. Increase anaerobic performance & physical fitness level
- 51 3. Improve the level of satisfaction during therapy

52
53 Our hypothesis is that the AVG ARRoW-CP is at least as effective as treadmill training to
54 improve walking performance and more enjoyable for children with CP following surgery.
55
56
57
58
59
60

Methods and analysis

Study Design

This study is a randomized control trial with two groups: OGT using the AVG ARRoW-CP in AR (OGT-AR) and Treadmill Training control group (TT). All children and adolescents participate in a four-week gait training intervention to improve their walking function in one of this two groups. During this period, children continue their usual physical therapy program (5 weekly 45-minutes session). This postoperative protocol has been standardized following a 5-step framework [11]. These usual rehabilitation sessions include muscle stretching exercises, muscle strengthening exercises (active resistance exercises), functional exercises (sit-to-stand, transfer, balance, walk, stairs). The study is planned to start in April 2021 and end in December 2023.

Description of the two gait training interventions

To standardize the session content as much as possible, the therapists involved in the study participate in the training sessions before the start of the study. During these sessions, a member of the project team presents them the process and objectives of this study, as well as the gait training protocol proposed for the two groups. A session is dedicated to the familiarization with Microsoft HoloLens and the ARRoW-CP game via a tutorial application.

ARRoW-CP: Overground Gait Training in AR

Intervention group receives the OGT-AR protocol through the AVG ARRoW-CP using the Microsoft HoloLens headset (Figure 1). ARRoW-CP sessions are monitored by physiotherapist, assistant physiotherapist, or research assistant.

The intervention consists of 4 weeks of OGT (3 sessions per week), including a series of walking sprints. These sessions are always performed indoors, along the same flat and straight 30m in length hallway with a hard surface that is seldom traveled. The starting point is marked with a round floor sticker ARRoW-CP. Children can see the real environment because of transparency of holograms and use of augmented reality (that is different from virtual reality), but some safety measures are taken to avoid collision with other people: the caregiver signals to others that a session is in progress, checking before starting the game that there are no obstacles in the hallway. This protocol is an adaptation from Zwinkels *et al.* [17]. Every training session consists of a prescribed intensity, volume and time (Table I).

Before the first session of each week, the target velocity is calculated during a Muscle Power Sprint Test (MPST) [21]. This test is made through the ARRoW-CP game and is presented as a “calibration” to the participant. During this test, no feedback is presented to the player. The target velocity is defined as the highest velocity of 6 sprints. This test is repeated every week to adapt the difficulty of the game to the child’s progress.

Treadmill Gait Training

The control group protocol consists of 4 weeks of GT on a treadmill (3 sessions per week), with a maximal duration of 30 minutes. This protocol is an adaptation from Grecco *et al.*[13]

Before the first session, the target velocity is estimated during a treadmill speed test: participants are instructed to walk on a treadmill with increasing speed (initially 0.5 km/h and increased 0.5 km/h each minute). Each minute, children are asked about shortness of breath and the subjective responses are classified using the 1-10 Borg Rating of Perceived Exertion Scale. The test is stopped if the score is higher than 5. The target velocity is defined as 80% of the maximum speed achieved during the test.

The first 5 minutes is a warm-up time, the speed is gradually increased until reaching the target velocity. The child walks for a maximal 20 minutes at their target velocity. Then, the treadmill speed is gradually diminished over the final 5 minutes. Training could be interrupted at any time at the child’s request or physical therapist judgement. Treadmill sessions are monitored by physiotherapist, assistant-physiotherapist, or a member of the research staff.

Randomization Procedure

After baseline measures, eligible participants are randomized to the intervention or control group based on a computerized randomization program. Blocks randomization are calculated in block sizes of fours and six. The randomization procedure is only available to an independent researcher who will not be involved in the delivery of the interventions or the performance of the measurements. Due to small sample size required, the randomization lists were not stratified.

Participants

All participants are recruited from the Poidatz Rehabilitation Centre. The children are operated in several hospitals in Paris: Necker Enfants Malades University Hospital, Trousseau University Hospital or Robert Debré University Hospital. Ethics approval is granted by the French Ethical Committee Sud-Est VI (Clermont-Ferrand). Additionally, all parents, and participants from 10 years of age, should provide informed consent prior to study initiation. All participants should have a cooling off period prior to the inclusion (minimum 15 days between information and consent). Confidentiality and data access are guaranteed by the National Commission of Informatic (CNIL). A Data Protection Officer has been designated for all research studies conducted in this rehabilitation centre. He guarantees that the data protection and the rights of the subject are respected according to the General Data Protection Regulation (EU) 2016/679 (GDPR). The study has been registered in ClinicalTrials.gov (Identifier: NCT04837105).

Inclusion criteria are children with CP admitted for inpatient rehabilitation following SEMLS, 10–18 years of age, functioning preoperatively at GMFCS I–III. The minimum time between surgery and inclusion in the study is 7 weeks (step 4 of post-SEMLS rehabilitation process), they should have a Functional Mobility Scale 50 meters rating superior or equal to 2 (ability to walk on 50m using a walker or frame without help from another person).

All children should be able to cooperate, understand and follow simple instructions in French to practice the game. Only voluntary patients whose parents give their consent for their child's participation in the study and patient affiliated to the French social security system are included. Criteria for exclusion include a diagnosis of photosensitive epilepsy in the medical record and/or patient's case history mentioning seizures that occurred while playing a video game, visual, cognitive or auditory impairment that would interfere with playing the game. The patient must have normal or corrected vision and hearing. During the 4-weeks, children can wear their orthotic device and their assistive device as prescribed by medical staff. In cases of evolution regarding the level of support (a patient going from walking with crutches to no walking aid, for example), the medical staff decides if patient is able to practice series of walking sprints safely and efficiently according to the main objective of the study, then they inform the research staff. This change should only be made during the first session of the week to proceed with the new weekly calibration and thus adapt the objective walking speed to the child's abilities.

Patient and Public Involvement

Patient involved as described above. All patients meeting the study criteria were approached directly in the rehabilitation center when they were in the phase of walking recovery after surgery. Information about the study was given to them orally. They are given time to reflect. If they are interested, a physiotherapist contacts the family by phone to give them information about the study. Written consent is obtained after a further period of reflection. No public involved.

Outcomes

Outcome measures take place at baseline (T0), immediately after four weeks of GT (T1), and six months later (T2). The professional caregiver administering outcome measures remains blinded to group allocation. See Supplementary File 2 for outcomes details and criterion validity.

Primary outcome : The 6 minutes walk test (6MWT) The 6MWT is increasingly used in paediatrics, in clinics to monitor patients' abilities or in research as a criterion for evaluating the effectiveness of a rehabilitation protocol [22]. The 6MWT assesses distance walked over 6 minutes as a submaximal test of aerobic capacity/endurance. The reference guideline detailing the recommendations and instructions has been updated in 2013 [23, 24]. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP [25, 26]. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness. This primary outcome is relative to the primary objective i.e. improve walking capacity.

Secondary outcome : Muscle power sprint test (MPST)

The MPST evaluates anaerobic performance of youth with CP over a 6x15 meters at their maximal speed [21]. Velocity (m/s), acceleration (m/s²), force (kg/s²) and power (watts) are calculated. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power

(MP) is the average over 6 sprints. This secondary outcome is relative to the secondary objective i.e. improve anaerobic performance.

Secondary outcome : Shuttle Run Test (SRT)

The 10-meters shuttle run test is an adapted version of the 20-metre shuttle run test to accommodate children with cerebral palsy (CP) classified at Level I or Level II on the Gross Motor Function Classification System (GMFCS) [27]. This test evaluates cardiovascular endurance. In this study, the SRT-II will be used because of postoperative context. The SRT-II starts at 2 km/h. Speed is increased 0.25 km/h every level (minute). The test is over when the child cannot go to the next cone in time. This secondary outcome is relative to the secondary objective i.e. improve physical fitness level.

Secondary outcome : Questionnaire (PACES)

To assess enjoyment for both control and test group, the 16-items of the Physical Activity Enjoyment Scale (PACES) will be used. The PACES is a valid and reliable measure of physical activity enjoyment. It has been used in many studies assessing the effectiveness of VR therapy [28]. This questionnaire will be presented to the participant at the end of the last session. This secondary outcome is relative to the secondary objective i.e. improve satisfaction during therapy.

Sample size and statistical analysis

According to a study of Grecco et al. an average augmentation of 83% (range 80-85%) in 6MWT was calculated after following 12-weeks of treadmill training in postoperative context [13]. The distance travelled during the 6MWT increases from before: 166.4 ± 39.1 m to after: 304.7 ± 75.8 m. The effect size was calculated: $d = 2.29$. In this previous study, the mean number of training sessions throughout the 12-week period was 11.1 (around 1-session per week) i.e. total dose of 6h/12-weeks. It has been hypothesized that participants following a more intensive protocol (3 sessions/week i.e. total dose of 6h/4-weeks) will show the same effect on the 6MWT.

With an alpha = 0.05 and beta = 0.20 (power = 0.80), a sample size of 6 subjects per group will be required. When taking a failure rate of 10% into account, 14 subjects should be included.

The required sample size was calculated with G Power 3.1.9.7. Parameter was t-tests – Means; difference between two independent means (two groups) with a priori analysis.

The effect of the GT protocol will be analyzed using a multivariate repeated measures

1
2
3
4 ANOVA. The possible differences between and within T0, T1 and T2 for the intervention
5 group and control group will be calculated with a statistical significance level of $p = 0.05$. If
6 there is a significant difference, a post-hoc test will be executed to further investigate
7 group differences. Quantitative descriptive statistics will be used to present patient
8 characteristics and global results. Data from PACES questionnaire will be analyzed using
9 normality test (deciding to use parametric / non-parametric statistics), descriptive
10 statistics, reliability test (Cronbach Alpha / Composite Reliability), Pearson / Spearman
11 correlational test. All statistical analyses will be performed using R with a statistical
12 significance level of $p = 0.05$. Moreover, the trial statistician will remain blinded to group
13 allocation until the database has been locked.

14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Discussion

This approach has evolved from two directions: interest to improve walking capacity after SEMLS for children with CP, and from concern that the usual post-operative rehabilitation approach has not produced sustainable improvements in participation and activity in daily life for these children [8].

AVG development framework

This work followed the AVG development framework PROGame, proposed by Amenguai Alcover *et al.* [18]. A participate process including both professional healthcare and patients has been conducted. The first step was the project initiation. The team identified the need for a AVG, the stakeholders, and user categories (users and experts). They also clarified the game functionality and constraints. They selected the therapy to transfer into the AVG. The operational objectives were to be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun. These identifications were based upon prior experience and literature review [12, 29]. The team used communication tools like oral presentation of preliminary results, open debates, surveys and meeting reports. The aim was to support incremental development between team's members (that has their own specialty) and to share knowledge. At this stage, the project proposed a general description. The second step was the interaction mechanism, all technical solutions were explored and an algorithm for gait parameters detection was developed and tested [30, 31]. During the third step, the interactive elements, the team investigated actual commercial or AVGs to get inspired. Team exploration and discussion conducted to games like Pokemon Go or Zelda, in which the gamer must explore the world and accomplish missions. These games appear very popular with the younger generation. The development team was composed of therapists (3 physiotherapists), researchers (2 in computer science, 1 in rehabilitation science, 1 in movement science) and a software engineer. These steps occurred between January 2020 and June 2021. All details are available in Supplementary File 3.

The aim was to think together about the best solution for improving postoperative results, especially walking capacity. New technologies were young people's preferred solution. These solutions seem to be a very promising tools for rehabilitation purposes, allowing to manipulate the environment, to offer interaction, to optimize feedback and many other potentialities [19, 32]

Feedback, a key point for motor learning

Feedback retraining paradigm is based on the conversion, the supplementation and augmentation of sensory information that are usually accessible only by an internal focus of attention, to accessible information [32, 33]. In this paradigm, augmented feedback is defined as augmented sensory information provided by an external resource (therapist or display) to the patient [34]. The information provided to the user could be relative to the movement's pattern or result on the environment or the outcome of a movement with respect to the goal. Sensory channels used to deliver information are visual, auditory, or haptic, linked to the proprioception properties of humans. The timing of feedback delivery is critical. Concurrent feedback is delivered while the skill is being performed, terminal feedback is delivered after the skill is performed with or without delay [35]. In our previous study, we have confirmed that children with CP can adapt their walking speed, and they can positively respond to the real-time AR feedback (article under review). However, we have observed that not all patients performed equally well with the scenarios. When we have looked at the individual responses of each participant for each scenario, we have observed some essential differences. Some people did not perform better with the feedback; others were helped by a particular feedback but disturbed with another. Some authors highlighted these inter-individual differences. Recently, Liu *et al.* have underscored different patient profiles: "non-responders" and "responders" to the feedback [19]. In their study, patients were people after stroke. They were instructed to walk on a treadmill while visualizing an avatar replicating their exact walking pattern in real-time on a large screen. Overall, patients improved step length and walking speed when the avatar was displayed on a side view. But results were not the same

for all participants; the authors distinguished non-responders and responders to the feedback. They hypothesized that the initial step length ratio could influence the result because patients with a larger paretic step length better responded. This study has shown that specific populations are more sensitive to the virtual environment.

Serious aspect of ARRoW-CP game

ARRoW-CP AVG combines many of the motor learning theories: context focused therapy and goal-directed training, task-specific, variable practice, high intensity, augmented feedback during therapy sessions and motivation of the patient [16]. To find the best feedback modalities for our AVG, we have conducted preliminary studies exploring the impact of feedback modalities on walking speed, both in healthy adults and in children with CP. Study on healthy adults showed that certain feedback helped to increase walking speed, provided that the game instruction was clear. Typically, feedback combining a focus of attention with knowledge of results, a spatial representation with world-locked holograms and a method of presentation with rich holographic content (like animation, colour changes) increased walking speed in healthy subject [36]. This step allowed us to modify and adapt feedback modalities.

A second study has occurred with children with CP. Results showed that scenarios combining world-locked holograms that disappeared over the time helped children with CP to reach their target speed. On the other hand, a body-locked hologram that advances in front of the user at the target speed was better able to control the walking speed of the patient[37].

ARRoW-CP is an adaptation of the validated protocol from Zwinkels et al. The original protocol consists of 8 weeks, twice a week [17]. Every training session consisted of a 30s walking sprints following the pre-scribed intensity, volume, and time: Week 1 to week 2: 8 sprints, work/rest ratio 1:4; Week 3 to week 4: 10 sprints, work/rest ratio 1:4; Week 5 to week 8: 12 sprints, work/rest ratio 1:3. Because of post-operative context, the intensity should be reduced. At the beginning of the fourth step of rehabilitation process, even if gait training is recommended, children did not recover to their pre-operative level, specifically some children needed crutches or k-walkers. Moreover, a further aspect not to be underestimated: fatigue and pain [38]. The choice of intensity, volume and time in the ARRoW CP protocol is based on practical experience from expert clinician and from literature [12, 17].

Limitations

The limited sample size limit the ability to balance the two groups according the gender, age, GMFCS level and type of surgery. The randomization lists were not stratified. But the next step in the ARRoW-CP project is to modify the game based on our initial results and to conduct a new RCT including more centers (and more children) worldwide. Using AR for therapy is not suitable for all children. We excluded patients with cognitive trouble and with patients high risks of fall based on medical recommendations.

Conclusion

This article presents in detail the gait training protocol tested through a RCT. Both control group and experimental group have an evidence-based physical therapy training. This article also presents the game development framework of the ARRoW-CP AVG. This game is based on the most recent motor learning approach. This is the first study assessing the efficacy of postoperative gait rehabilitation using an active video game. If our hypothesis is validated, ARRoW-CP game will make possible to intensify gait training. This innovative strategy will have significant clinical impact by improving walking capacity for children after SEMLS. Publishing study protocol of the RCT offers the opportunity to collaborate with other teams and to give more details about the study. Results will be available in 2023.

Tables

Table 1 Details of the gait training protocol deployed in the active video game ARRoW-CP

	WEEK 1	WEEK 2	WEEK 3	WEEK 4
Session Number per week	3	3	3	3
Sprint Time (s)	30	30	30	30
Rest Time (min:s)	2:00	2:00	1:30	1:30
Sprint Number	4	6	8	10
Total time of the session	10	15	18	22

Figure 1. Image capture from ARRoW-CP active video game. On the left, this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle, an adult (not a patient) wearing the Microsoft HoloLens AR headset to see holograms. On the right, game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard).

Supplementary Files

Supplementary file 1 — ARRoW-CP Active Video Game

Supplementary file 2 — Main Outcomes details and criterion validity. Additional file 3 — Active Video game development framework

Competing interests

Not applicable.

Author's contributions

ALG, GB, SO and ED conceived the study, participated in its design and helped to draft the manuscript. SPT, NK and MB participated in the acquisition and coordination of the study. All authors read, revisit it critically and approved the final manuscript.

Author details

¹Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, FR.

²IBISC Lab, University Paris-Saclay, Paris, FR.

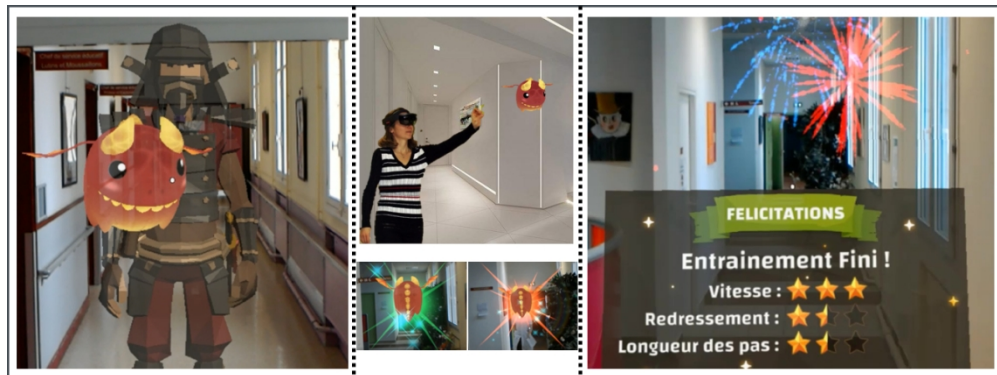
References

- Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M., Damiano, D., Dan, B., Jacobsson, B.: A report: the definition and classification of cerebral palsy april 2006. *Developmental Medicine and Child Neurology* **109**, 8–14 (2007). doi:10.1111/j.1469-8749.2007.tb12610.x
- Oskoui, M., Coutinho, F., Dykeman, J., Jett'e, N., Pringsheim, T.: An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology* **55(6)**, 509–519 (2013). doi:10.1111/dmcn.12080
- Graham, H.K., Rosenbaum, P., Paneth, N., Dan, B., Lieber, R.L.: Cerebral palsy. *Nat Rev Dis Primers* **2(1)**, 15082 (2016). doi:10.1038/nrdp.2015.82

4. Park, E.: Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. *Health and Quality of Life Outcomes* **16(1)**, 383–390 (2018). doi:10.1186/s12955-018-0891-1
5. Himuro, N., Mishima, R., Seshimo, T.: Change in mobility function and its causes in adults with cerebral palsy by gross motor function classification system level: A cross-sectional questionnaire study. *NeuroRehabilitation* **42(4)**, 383–390 (2018). doi:10.3233/NRE-172340
6. Benner, J., Hilberink, S., Roebroek, M.: Long-term deterioration of perceived health and functioning in adults with cerebral palsy. *Arch Phys Med Rehabil.* **98(11)**, 2196–2205 (2017). doi:10.1016/j.apmr.2017.03.013
7. Novak, I., Morgan, C., Badawi, N.: State of the evidence traffic lights 2019: Systematic review of interventions for preventing and treating children with cerebral palsy. *Curr Neurol Neurosci Rep* **20(2)**, 3–24 (2020). doi:10.1007/s11910-020-1022-z
8. McGinley, J.L., Dobson, F., Ganeshalingam, R., Graham, H.K.: Single-event multilevel surgery for children with cerebral palsy: a systematic review. *Dev Med Child Neurol* **54(2)**, 117–128 (2012). doi:10.1111/j.1469-8749.2011.04143.x
9. Lamberts, R.P., Burger, M., Langerak, N.G.: A systematic review of the effects of single-event multilevel surgery on gait parameters in children with spastic cerebral palsy. *PLoS ONE* **11(10)**, 0164686 (2016). doi:10.1371/journal.pone.0164686
10. Amichai, T., Harries, N., Dvir, Z., Patish, H., Copeliovitch, L.: The effects of femoral derotation osteotomy in children with cerebral palsy: an evaluation using energy cost and functional mobility. *J Pediatr Orthop* **29**, 68–72 (2009). doi:10.1097/BPO.0b013e3181924331
11. Guinet, A., Khouri, N., Desailly, E.: Rehabilitation after single-event multilevel surgery for children and young adults with cerebral palsy: A systematic review. *American Journal of Physical Medicine & Rehabilitation* **21**, 2697 (2021). doi:10.1097/PHM.0000000000001864
12. Booth, A., Buizer, A., Meyns, P., Van der Krogt, M.: The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine and Child Neurology* **60(9)**, 866–83 (2018). doi:10.1111/dmcn.13708
13. Grecco, L., De Freitas, T., Satie, J., Bagne, E., Oliveira, C., De Souza, D.: Treadmill training following orthopedic surgery in lower limbs of children with cerebral palsy. *Pediatr Phys Ther* **25(2)**, 187–192 (2013). doi:10.3109/17453674.2014.960141
14. Cano-de-la-Cuerda, R.: Theories and control models and motor learning: Clinical applications in neurorehabilitation. *Neurología* **30(1)**, 32–41 (2021). doi:10.1016/j.nrleng.2011.12.012
15. Cho, C., Hwang, W., Hwang, S., Chung, Y.: Treadmill training with virtual reality improves gait, balance, and muscle strength in children with cerebral palsy. *The Tohoku Journal of Experimental Medicine* **238(3)**, 213–8 (2016). doi:10.1620/tjem.238.213
16. Demers, M., Fung, K., Subramanian, S., Lemay, M., Robert, M.: Do virtual interventions in individuals with cerebral palsy make use of motor learning principles?: A systematic review (preprint). *JMIR Serious Games* **XX**, (2020). doi:10.2196/23822
17. Zwinkels, M., Verschuren, O., De Groot, J.: Effects of high-intensity interval training on fitness and health in youth with physical disabilities. *Pediatric Physical Therapy* **31(1)**, 84–93 (2019). doi:10.1097/PEP.0000000000000560
18. Amengual-Alcover, E., Jaume-i-Capó, A., Moyà-Alcover, B., Martinuzzi, A.: Progame: A process framework for serious game development for motor rehabilitation therapy. *PLOS ONE* **13(5)**, 0197383 (2018). doi:10.1371/journal.pone.0197383
19. Liu, L., Sangani, S., Lamontagne, A.: Real-time avatar-based feedback to enhance the symmetry

- of spatiotemporal parameters after stroke: Instantaneous effects of different avatar views. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* **28(4)**, 878–887 (2020). doi:10.1109/TNSRE.2020.2979830
20. MacIntosh, A., Desailly, E., Biddiss, E.: A biofeedback-enhanced therapeutic exercise video game intervention for young people with cerebral palsy: A randomized single-case experimental design feasibility study. *PLoS One* **15(6)**, (2020). doi:10.1371/journal.pone.0234767
21. Verschuren, O., Bongers, B., Obeid, J., Ruyten, T., Takken, T.: Validity of the muscle power sprint test in ambulatory youth with cerebral palsy. *Pediatric Physical Therapy* **25(1)**, 25–28 (2013). doi:10.1097/PEP.0b013e3182791459
22. Gillett, J., Lichtwark, G., Boyd, R., Carty, C., Barber, L.: The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy. *Gait & Posture*. **70**, 323–329 (2019). doi:10.1016/j.gaitpost.2019.03.023
23. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, .: Ats statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111–117 (2002). doi:10.1164/ajrccm.166.1.at1102.
24. Shirley Ryan Ability Lab, .: The 6 minute walk test: Instrument details (2021). <https://sralab.org/rehabilitation-measures/6-minute-walk-test>
25. Slaman, J., Dallmeijer, A., Van Den Berg-Emons, R.: The six-minute walk test cannot predict peak cardiopulmonary fitness in ambulatory adolescents and young adults with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **94(11)**, 2227–2233 (2013). doi:10.1016/j.apmr.2013.05.023
26. Maltais, D., Robitaille, N., Dumas, F., Boucher, N., Richards, C.: Measuring steady-state oxygen uptake during the 6-min walk test in adults with cerebral palsy: feasibility and construct validity. *Int J Rehabil Res* **35(2)**, 181–183 (2012). doi:10.1097/MRR.0b013e3283527792
27. Verschuren, O., Takken, T., Ketelaar, M., Gorter, J., Helders, P.: Reliability and validity of data for 2 newly developed shuttle run tests in children with cerebral palsy. *Physical therapy* **86(8)**, 1107–1117 (1988). doi:10.1080/02640418808729800
28. Motl, R., Dishman, R., Saunders, R., Dowda, M., Pate, R.: Measuring enjoyment of physical activity in adolescent girls. *Am J Prev Med* **21**, 110–117 (2001). doi:10.1016/S0749-3797(01)00326-9
29. Fehlings, D., Switzer, L., Findlay, B., Knights, S.: Interactive computer play as ”motor therapy” for individuals with cerebral palsy. *Semin Pediatr Neurol* **20(2)**, 127–38 (2013). doi:10.1016/j.spen.2013.06.003
30. Guinet, A., Bouyer, G., Otmame, S., Desailly, E.: Reliability of the head tracking measured by microsoft hololens during different walking conditions. *Comput Methods Biomech Biomed Engin* **xx**, 159–161 (2019). doi:10.1080/10255842.2020.1714228
31. Guinet, A., Bouyer, G., Otmame, S., Desailly, E.: Validity of hololens augmented reality head mounted display for measuring gait parameters in healthy adults and children with cerebral palsy. *Sensors* **21**, 2697 (2021). doi:10.3390/s21082697
32. Levin, M.F.: *Feedback and Virtual Environments for Motor Learning and Rehabilitation* vol. 2(1), pp. 19–36 (2010)
33. Booth, A.T., Buizer, A.I., Harlaar, F.: Immediate effects of immersive biofeedback on gait in children with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **100(4)**, 598–605

- 1
2
3
4 (2019). doi:10.1016/j.apmr.2018.10.013
- 5
6 34. Durkin, M.S., Maenner, M.J., Benedict, R.E., Yeargin-Allsopp, M.: The role of socio-
7 economic status and perinatal factors in racial disparities in the risk of cerebral palsy. *Dev Med*
8 *Child Neurol* **57(9)**, 835–843 (2015). doi:10.1111/dmcn.12746
- 9
10 35. MacIntosh, A., Lam, E., Vigneron, V., Vignais, N., Biddiss, E.: Biofeedback interventions for
11 individuals with cerebral palsy: a systematic review. *Disability and Rehabilitation* **41(20)**,
12 2369–2391 (2019). doi:10.1080/09638288.2018.1468933
- 13
14 36. Guinet, A., Khouri, N., Desailly, E.: Clinical gait analysis and physical examination don't
15 correlate with physical activity of children with cerebral palsy. cross-sectional study. *International*
16 *Biomechanics* **7(1)**, 88–96 (2020). doi:10.1080/23335432.2020.1812429
- 17
18 37. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Towards an ar game for walking rehabilitation:
19 Preliminary study of the impact of augmented feedback modalities on walking speed. *IEEE*
20 *International Symposium on Mixed and Augmented Reality Adjunct* **1**, 264–268 (2020). Doi:
21 10.1109/ISMAR-Adjunct51615.2020.00075
- 22
23 38. Hoiness, P., Capjon, H., B, L.: Pain and
24 rehabilitation problems after single- event
25 multilevel surgery including bony foot
26 surgery in cerebral palsy. a series of 7
27 children. *Acta Orthop* **85(6)**, 646–651
28 (2014).
29 doi:10.1097/PEP.0b013e3182888495
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Caption : Figure 1. Image capture from ARRoW-CP active video game. On the left, this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle, an adult (not a patient) wearing the Microsoft HoloLens AR headset to see holograms. On the right, game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard)

577x216mm (59 x 59 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ARROW-CP Serious game for gait rehabilitation

1. The Microsoft HoloLens Headset is used for ARROW-CP (**Figure 1**). Game development was made with Unity 2019.4.8f1 and Mixed Reality Toolkit (MRTK). MRTK-Unity is a Microsoft-driven project that provides a set of components and features, used to accelerate cross-platform MR app development in Unity.



Figure 1. Microsoft HoloLens Augmented reality headset.

2. The player is immersed in a samurai world. He meets the chief of the village that can no longer protect its population. The natural elements are unleashed, causing famine and various damages. The player's role is to develop his energy through ninja training to build a protective totem for the village's inhabitants (trailer: <https://youtu.be/BbmiiiiJuaA>).

The software architecture is presented in **Figure 2**.

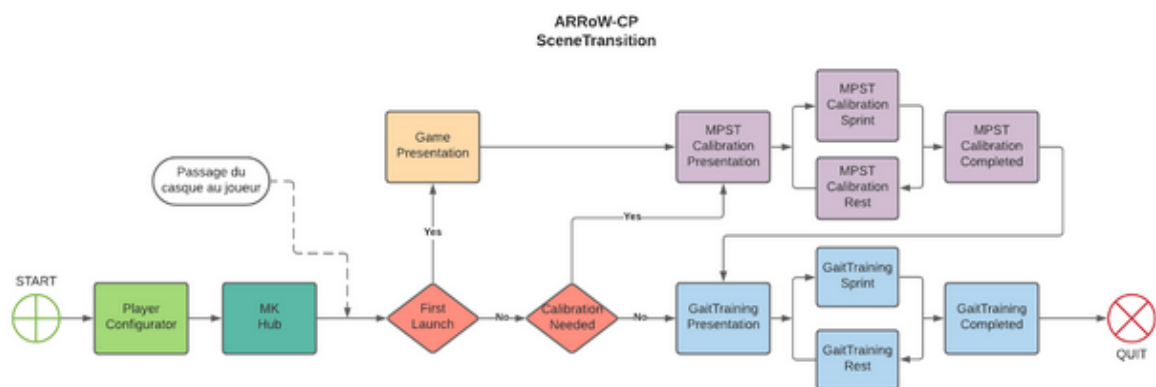


Figure 2. Game architecture of the ARROW CP game. When the game starts, the AR headset is worn by the therapist. He creates the user profile of the player by entering his name, first name, age, height, and weight during session 1 week 1. Next session, he loads the existing user profile. The therapist then accesses the “MK Hub”, which contains information about the performance of previous sessions and the number of sessions

3. The mechanism of feedback provided during sprints and rest time is detailed in **Figure 3**.

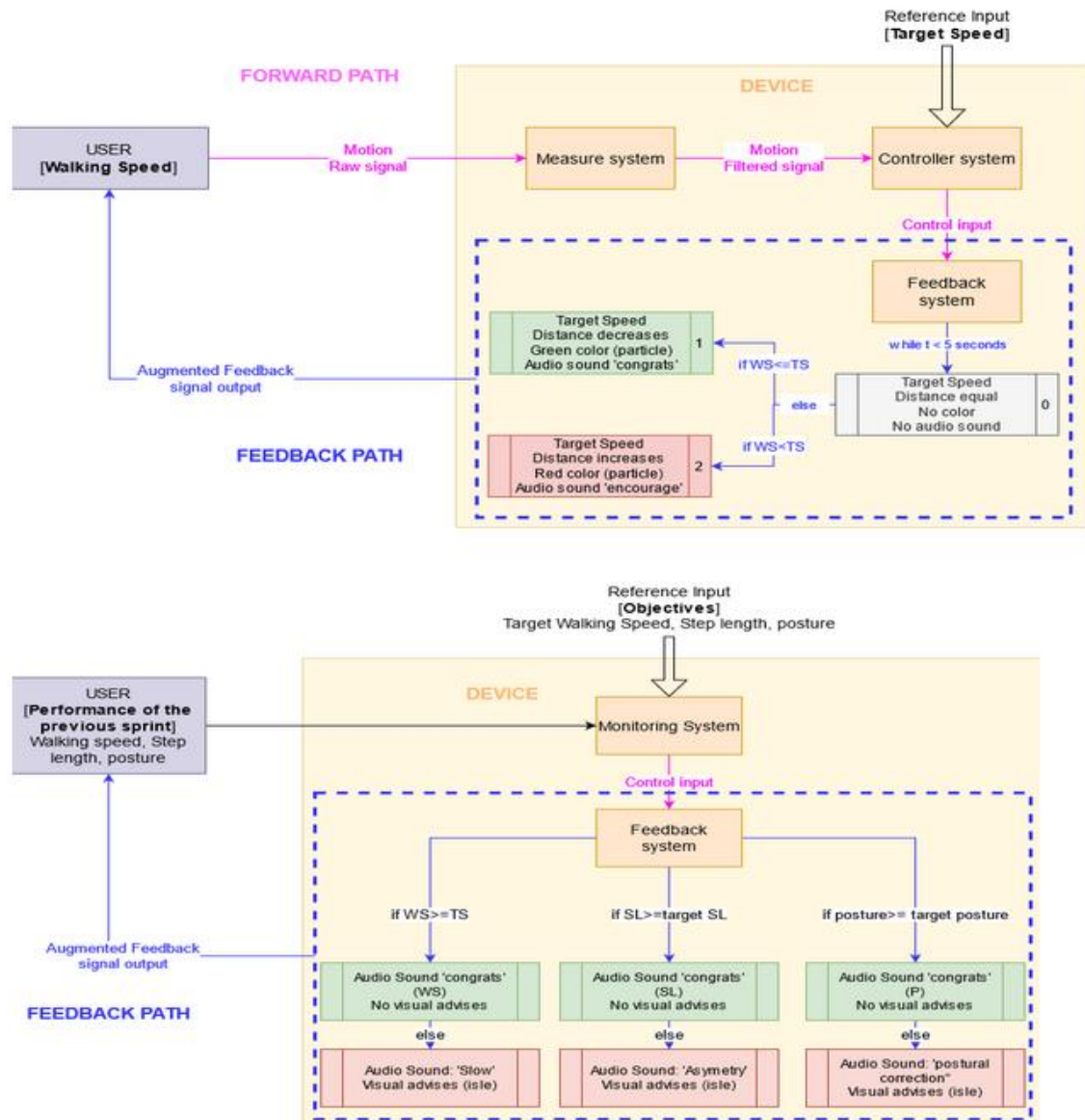


Figure 3. Feedback mechanism during sprints (A) and rest period (B).

At the beginning of each session, through the “Physio HUB”, therapists know the previous performance of their patient and they can adjust their advice.

At the end of each session, feedback with delay is proposed to the child: they can choose to see their actual performance through the game scoreboard and totem construction (feedback on demand). These feedbacks were based on knowledge of results.

Test name	Instructions	Validity
<p>[PRIMARY OUTCOME]</p> <p>The 6 minutes walk test (6MWT)</p>	<p>To summarize, patients are instructed to walk, not run, as far as they could along a 20-m level surface track during a 6-minute period. This shorter distance has been validated for children in order to be more focused on the task. They could use their usual walking aids. After each minute, participants are told the elapsed time and standardized encouragement is provided. Patients are allowed to stop and rest during the test but are instructed to resume walking as soon as they feel able to do so. The stopwatch is not stopped during this time. The 6MWT distance (in meters) is registered. Measured 6MWT distance could be compared with normative values for children with CP. It is recommended to monitor heart rate during the 6MWT.</p>	<p>In population of children with CP, test/retest reliability is excellent for distance output (ICC=0.98). The 6MWT is poorly related to VO2 peak in ambulatory adolescents and young adults with CP. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.</p>
<p>[SECONDARY OUTCOME]</p> <p>Muscle power sprint test (MPST)</p>	<p>The 15-m distance is marked by 2 lines taped to the floor. Cones are placed at the end of each of the lines. Participants are instructed to walk as fast as possible from one line to the other, and to be sure to cross each line. Between each run, participants are allowed to rest for 10 seconds before turning around to allow them to prepare for the following sprint. Children should be encouraged to give maximal effort. The following variables are calculated for each of the 6 sprints: velocity (m/s) = distance/time, acceleration (m/s²) = velocity/time, force (kg/s²) = body mass × acceleration, and power (watts) = force × velocity. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints.</p>	<p>The MPST is a valid test to assess the anaerobic performance in children with CP, significant correlations between the performance on these tests for both PP and MP were found. (PP: r = 0.731 ; MP: r = 0.903). Standard error of measurement (SEM), minimal detectable change (MDC) and normative data are available in Verschuren et al. The children with CP had impaired anaerobic performance as it was lower than that of their peers.</p>
<p>[SECONDARY OUTCOME]</p> <p>10-meters Shuttle Run Test (SRT)</p>	<p>Description of the test is available here : "The course is 10 metres long; the end is marked with 2 cones and measuring tape. Subjects should wear regular sports clothing and shoes, and orthoses, if applicable. Each child should also wear a heart rate monitor. Children walk or run between the 2 markers at a set incremental speed. These runs are synchronised with a pre-recorded sound. (...) As the test proceeds, the interval between each successive beep reduces, forcing the child to increase speed over the course of the test, until it is impossible to keep in sync with the recording." We have developed a mobile application that beeps at regular intervals, indicates the time spent and allows the assessor to increment the number of shuttles made by the child.</p>	<p>The SRT is a valid and reliable test. Test-retest is excellent (ICC=0.99) and high correlations were found for the relationship between data for both shuttle run tests and data for the treadmill test (r=0.96).</p>
<p>[SECONDARY OUTCOME]</p> <p>Physical Activity Enjoyment Scale (PACES)</p>	<p>This is a 5-point Likert scale (from 1- I totally disagree to 5- I totally agree). A translation procedure from English to French language has been made using guidelines (figure).</p>	<p>The PACES is a valid and reliable measure of physical activity enjoyment.</p>

Project Initiation

Interaction Mechanism

Interaction Elements

7	Global Aim	to develop an active video game for gait rehabilitation for children with motor disabilities and particularly cerebral palsy
10	Operational objectives	To be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun.
16	Restrictions	The development of the game must correspond to the duration of a 3-year thesis; grants are limited and predefined; the agreement of the ethics committee and written consents from participants are required before any test on humans ; all technical solution could be explored.
27	Stakeholders	Customers : Children with cerebral palsy, 10-18 years old, GMFCS I-III, with cognitive skills to understand and follow simple instructions == END USERS Physiotherapists, occupational therapists, physiotherapist assistants, rehabilitation therapists == EXPERTS Special needs and required functionalities : The active video game must include the principles of motor learning, which are task-specific practice, variable practice, high practice intensity, progressive difficulty, augmented feedback, and adaptability to user abilities. The active video game should allow the inclusion of motivational elements to increase engagement. Children must be free to move in the global environment, without restriction of movement. Children must be able to use their usual walking aids (crutches or posterior walker). Therapists should have access to the previous and global performance of their patient through the game The solution should be "ready to use" easily both for children and therapists
39	Therapy Selection	The team's members agreed on making walking speed the main variable input of the serious game. Meaningful reason is that intensive gait training focused on walking speed has shown their clinical efficacy. ^{12,39} The therapy to transfer into the serious game should include walking sprints.

7	Aim of this phase	To select the interaction system and to capture the therapy into the system.
14	Device selection	Device: Microsoft Hololens AR headset version 1 was selected because its technical characteristics matched all identified specifications. Tools : - Unity software (version 2019.4.8f1) -Microsoft Visual Studio 2019 - Mixed Reality Toolkit for Unity (MRTK version 4.2.3)
27	Gait parameters detection development and evaluation	Algorithm development: HoloStep measuring the real-time gait parameters with the AR headset system ⁴³ Evaluation : - The accuracy of the AR headset's sensors was sufficiently high to evaluate the position of the user without time drift in the global environment ⁴² - HoloStep was reliable for measuring and calculating walking speed, cadence, step length and global distance travelled in comparison to reference motion analysis tracking system ⁴³

7	Aim of this phase	To design the interaction elements that force patients to perform the therapy correctly.
14	Feedback reflexion	We have proposed a model of feedback in Augmented Reality (AR) for Motor Rehabilitation (article not published yet). Indeed, AR feedback can be displayed to the user through different characteristics. This theoretical work was necessary before designing feedback and testing specific characteristics of the model. The final aim was to optimize the augmented information provided to the patient. To carry out this work, we extended and adapted the biofeedback model described by Macintosh et al., and the qualitative model from Martinez et al., to the AR context. Our descriptive model of feedback in AR application helped us design an AR application, called Best-Of ARRoW. We have tested with this app, the impact of different virtual feedback characteristics on walking speed of children with CP. The results of this first study will be published soon (article under review). This help us to better design the feedback used in ARRoW-CP AVG.
39	Game selection & Universe	The choice of the game universe (Samurai world) and reward panel were unanimously validated by experts and end users. All packages used to design the game were available in the Unity Asset Store: Polygon Samurai low poly 3D Art by Synty, Tiny Dragon by Suriyun, the GUI Kit - The Stone, and the Particle FX. Voice of game characters from volunteers were recorded in a professional radio studio (HandiFM – France 107.3 FM).



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	na
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	7
	5b	Name and contact information for the trial sponsor	na
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	na
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1-3
	6b	Explanation for choice of comparators	1-3
Objectives	7	Specific objectives or hypotheses	3
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	3

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	3
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	2-3
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	na
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	na
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	na
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	4-5
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	4
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	5
---------------------	-----	--	---

1				
2	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central	na
3	concealment		telephone; sequentially numbered, opaque, sealed envelopes),	
4	mechanism		describing any steps to conceal the sequence until interventions are	
5			assigned	
6				
7	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,	4-5
8			and who will assign participants to interventions	
9				
10	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial	4-5
11	(masking)		participants, care providers, outcome assessors, data analysts), and	
12			how	
13				
14				
15		17b	If blinded, circumstances under which unblinding is permissible, and	4-5
16			procedure for revealing a participant's allocated intervention during	
17			the trial	
18				
19				

Methods: Data collection, management, and analysis

20				
21				
22	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other	5
23	methods		trial data, including any related processes to promote data quality (eg,	
24			duplicate measurements, training of assessors) and a description of	
25			study instruments (eg, questionnaires, laboratory tests) along with	
26			their reliability and validity, if known. Reference to where data	
27			collection forms can be found, if not in the protocol	
28				
29				
30		18b	Plans to promote participant retention and complete follow-up,	5
31			including list of any outcome data to be collected for participants who	
32			discontinue or deviate from intervention protocols	
33				
34	Data	19	Plans for data entry, coding, security, and storage, including any	5
35	management		related processes to promote data quality (eg, double data entry;	
36			range checks for data values). Reference to where details of data	
37			management procedures can be found, if not in the protocol	
38				
39				
40	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.	5
41	methods		Reference to where other details of the statistical analysis plan can be	
42			found, if not in the protocol	
43				
44		20b	Methods for any additional analyses (eg, subgroup and adjusted	5
45			analyses)	
46				
47		20c	Definition of analysis population relating to protocol non-adherence	5
48			(eg, as randomised analysis), and any statistical methods to handle	
49			missing data (eg, multiple imputation)	
50				
51				

Methods: Monitoring

52				
53				
54	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role	na
55			and reporting structure; statement of whether it is independent from	
56			the sponsor and competing interests; and reference to where further	
57			details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1				
2		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	na
3				
4				
5				
6	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
7				
8				
9				
10				
11	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	na
12				
13				
14				
15				
16	Ethics and dissemination			
17	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	1
18				
19				
20	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	na
21				
22				
23				
24				
25				
26	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
27				
28				
29				
30		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	na
31				
32				
33	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	na
34				
35				
36				
37	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	7
38				
39				
40	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	na
41				
42				
43				
44				
45	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	na
46				
47				
48	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	na
49				
50				
51				
52				
53				
54		31b	Authorship eligibility guidelines and any intended use of professional writers	na
55				
56				
57		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	na
58				
59				
60				

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	na
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	na

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

For peer review only

BMJ Open

Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery : Protocol for a Randomized Controlled Trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-061580.R2
Article Type:	Protocol
Date Submitted by the Author:	24-Aug-2022
Complete List of Authors:	Guinet, Anne-Laure; Universite Paris-Saclay, IBISC Laboratory; Fondation Ellen Poidatz, Pôle Recherche&Innovation Bams, Michel; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Payan-Terral, Sandrine; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Khouri, Neijib; Hôpital universitaire Necker-Enfants malades Otmame, Samir; Universite Paris-Saclay, IBISC Laboratory Bouyer, Guillaume; Universite Paris-Saclay, IBISC Laboratory Desailly, Eric; Fondation Ellen Poidatz, Pôle Recherche & Innovation
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Paediatrics, Sports and exercise medicine
Keywords:	Paediatric orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric neurology < NEUROLOGY, Developmental neurology & neurodisability < PAEDIATRICS, REHABILITATION MEDICINE, Clinical trials < THERAPEUTICS

SCHOLARONE™
Manuscripts

OPEN ACCESS PROTOCOL**Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery : Protocol for a Randomized Controlled Trial**

Anne-Laure Guinet^{1,2*†}, Michel Bams¹, Sandrine Payan-Terral¹, Neijib Khouri³, Samir Otmane², Guillaume Bouyer² and Eric Desailly^{1†}

Abstract

Introduction: In paediatric rehabilitation, fun and motivation are also critical keys to successful therapy. A variety of interventions have shown positive effects, high level of interest, compliance and engagement with active video game (AVG).

This seems to be an interesting approach for the postoperative gait rehabilitation of children with CP. In this study, we will investigate if an overground gait training (GT) delivered through an AVG can improve walking capacity and anaerobic performance.

Methods and analysis: This study is a randomized clinical controlled trial. A total of 14 children and adolescents in the age of 10–18 years with CP will be included. The minimum time between surgery and inclusion will be 7 weeks. The test group will participate in the GT program with ARRoW-CP AVG (Augmented Reality Rehabilitation of Walking-Cerebral Palsy), control group will receive GT on a treadmill. The primary outcome is the 6-Minutes Walk Test assessing walking capacity; secondary outcomes are the Muscle Power Sprint Test for anaerobic performance and Shuttle Run Test for physical fitness level. Satisfaction is tested with the Physical Activity Enjoyment Scale. This study has been registered in ClinicalTrials.gov (NCT04837105).

The findings will be disseminated by publications in peer-reviewed journals and conferences.

Keywords: cerebral palsy; surgery; active video game; augmented reality; gait performance

1
2
3
4 *Correspondence: anne-laure.guinet@fondationpoidatz.com

5 1 Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, France

6 2 Université Paris-Saclay, Univ Evry, IBISC, 91020, Evry-Courcouronnes, France.

7 3 Hôpital Universitaire Necker-Enfants Malades, Paris, France

8 Full list of author information is available at the end of the article

9 †Equal contributor

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Strengths and limitations of this study

- This is the first randomized clinical trial to compare traditional rehabilitation and technology delivered gait performance training in children with cerebral palsy after surgery.
- The control group receives treadmill therapy to counterbalance the additional dose effect of active video game use in the experimental group.
- The active video game intervention being investigated have been tailored to the needs of children with cerebral palsy based on feedback from patient and public involvement and expert review groups conducted during the first phase of this project.
- Patients and patient's physiotherapist cannot be blinded; however, the professional caregiver administering outcome measures and the trial statistician will remain blinded to group allocation until the database has been locked.
- The interventions require participants to have no visual, cognitive or auditory impairment that would interfere with playing the game.

Introduction

Cerebral palsy is commonly defined as a “group of permanent disorders of the development of movement and posture, causing activity limitation”[1]. The overall prevalence of CP remains constant (2.11 per 1000 births) [2] with an estimated prevalence of 17 million people worldwide.[3] Individuals with CP present various clinical symptoms including a non-exhaustive list of neurological, orthopaedic, movement, cognitive, vision/hearing, aero digestive disorders.

Musculoskeletal disorders are considered as a secondary impairment contributing to restricted mobility in childhood and adulthood.[4, 5, 6] Since 1985, therapeutic interventions to correct orthopaedic disorders include single-event multilevel surgery (SEMLS). This surgery proposes, during one operative period, to realign the musculoskeletal system, practicing tendon transfer, muscle lengthening, derotation and/or deflexion osteotomy and joint stabilization. Novak *et al.* classified SEMLS as effective intervention for children with CP for improving both Gross Motor, walking speed and walking capacity but also contracture and alignment deformities [7]. To date, systematic reviews on the effect of SEMLS reported improvement in passive range of motion, kinematics and kinematics gait parameters, overall gait index and energy efficiency [8, 9]. Results were more disputed about the long-term effect on spatio-temporal gait parameters, gross motor function and the activity and participation domain [10].

A recent literature review has proposed a model in five steps that could guide clinicians during the post-operative rehabilitation [11]. The authors suggested that the fourth phase, which included more intensive exercises, functional gait training and resistive muscle strengthening should be optimized to improve the gross motor function and walking speed after surgery. Functional gait training has been defined as ‘actively practice the task of walking, to improve walking ability [12]. Intervention could be overground gait training (OGT), or treadmill gait training (TT), with or without body support.

Previously, Grecco *et al.* demonstrated the efficacy of treadmill gait training program including both on functional mobility and gross motor function on children with CP after SEMLS [13]. Recently, a systematic review showed that gait training was a safe and effective intervention to improve walking capacity in children with CP, outside postoperative context [12]. In particular, the minimal clinically important difference (MCID) for increase in walking speed (0.1m/s) was achieved after intervention in 12 studies/14 (studies level between II and III). Authors discussed two points: OGT could provide greater effect on locomotor abilities than TT because OGT is more representative of the natural walking, and the addition of feedback could enhance the patient outcomes. These points were important to consider after SEMLS, because the overall gait pattern of children was modified by the bone and muscle gestures. Novak *et al.* highlighted the importance of the context focused therapy and goal-directed training for children with CP [7]. Functional gait training should therefore take into account those recommendations and involve motor learning strategies: task-specific, variable practice, high intensity, augmented

1
2
3
4 feedback during therapy sessions and motivation of the patient [14].

5 In recent years, new technologies have been introduced in rehabilitation practice, both for
6 upper and lower limbs therapy. These systems include a large type of technology ranging
7 from fully immersive virtual reality (VR) or augmented reality (AR) using commercially
8 available head-mounted displays (HMD) (e.g., Oculus Quest; HTC VIVE, Microsoft
9 HoloLens), Cave Automatic Virtual Environment where video is projected on the walls
10 and floor²⁰ to video game console on television screen (e.g., Nintendo Switch,
11 PlayStation).

12 To 'actively practice the task of walking', systems combining treadmill training and active
13 video game (AVG) delivered through a screen in a semi-immersive environment have been
14 tested with good results [15]. However, motor learning principles are not always fully
15 integrated into VR/AR systems because of the lack of knowledge about which feedback
16 modality and which intensity level should be provided in the rehabilitation settings [16].
17

18
19 To our knowledge, even if OGT was recommended for functional gait training, no AR
20 system with AVG exists to provide high-intensity, with progressive difficulty, and variable
21 modalities including feedback. To this end, we have developed the active video game
22 ARRoW-CP (Augmented Reality Rehabilitation of Walking-Cerebral Palsy) combining
23 OGT based on previous results [12] and literature [17] and motor learning theory [14].
24 ARRoW-CP active video game has been developed for Microsoft HoloLens headset
25 (mixed reality headset). The team used the game development framework PROGame and
26 all stakeholders have been involved through the process (children with CP, researchers,
27 engineers, therapists)[18]. In most studies, even if feedback is effective to improve motor
28 activities, the characteristics applied during interventions were generally inconsistent with
29 motor control feedback theory. Authors suggest that timing, frequency and autonomy
30 should be adjusted to optimize long-term effect [19]. A strategy that provides feedback to
31 the user on demand promotes learning. Then, by reducing the frequency and timing of the
32 feedback, the user can develop a sense of self-regulation. In this AVG, continuous
33 feedback as well as terminal feedback, both with different audio and visual modalities,
34 are combined following the recommendations of the literature [20, 16]. The general principle
35 for defining the feedback to be used is primarily defined by the results from a previous
36 study that the team lead (article under review). Specific recommendations from this
37 previous study included using feedback moving on in front of the player at the target speed
38 to create a more challenging task that motivates participants to excel. In addition, our
39 results highlighted that the temporary modification of visual aspect according to the
40 performance (red light/too slow; green light/good speed) helped to improve walking speed
41 creating a playful challenge. The feedback attached to the player seemed to be better to
42 minimize visual discomfort and, by extension, fatigue. More details of ARRoW-CP game,
43 architecture, framework development and feedback characteristics, are available in the
44 Supplementary Files 1 and 2.

45
46 The current study, denoted as the ARRoW-CP study, will investigate whether a gait
47 training protocol through an active video game in AR can:

- 48 1. Increase the walking capacity
- 49 2. Increase anaerobic performance & physical fitness level
- 50 3. Improve the level of satisfaction during therapy

51
52 Our hypothesis is that the AVG ARRoW-CP is at least as effective as treadmill training to
53 improve walking performance and more enjoyable for children with CP following surgery.
54

55 **Methods and analysis**

56 **Study Design**

57
58 This study is a randomized control trial with two groups: OGT using the AVG ARRoW-
59 CP in AR (OGT-AR) and Treadmill Training control group (TT). All children and
60 adolescents participate in a four-week gait training intervention to improve their walking
function in one of this two groups. During this period, children continue their usual physical

1
2
3
4 therapy program (5 weekly 45-minutes session). This postoperative protocol has been
5 standardized following a 5-step framework [11]. These usual rehabilitation sessions include
6 muscle stretching exercises, muscle strengthening exercises (active resistance exercises),
7 functional exercises (sit-to-stand, transfer, balance, walk, stairs). The study is planned to
8 start in April 2021 and end in December 2023.
9

10 Description of the two gait training interventions

11 To standardize the session content as much as possible, the therapists involved in the study
12 participate in the training sessions before the start of the study. During these sessions, a
13 member of the project team presents them the process and objectives of this study, as well as
14 the gait training protocol proposed for the two groups. A session is dedicated to the
15 familiarization with Microsoft Hololens and the ARRoW-CP game via a tutorial
16 application.
17

18 *ARRoW-CP: Overground Gait Training in AR*

19 Intervention group receives the OGT-AR protocol through the AVG ARRoW-CP using
20 the Microsoft Hololens headset (Figures 1A-C). ARRoW-CP sessions are monitored by
21 physiotherapist, assistant physiotherapist, or research assistant.
22

23 The intervention consists of 4 weeks of OGT (3 sessions per week), including a series of
24 walking sprints. These sessions are always performed indoors, along the same flat and
25 straight 30m in length hallway with a hard surface that is seldom traveled. The starting
26 point is marked with a round floor sticker ARRoW- CP. Children can see the real
27 environment because of transparency of holograms and use of augmented reality (that is
28 different from virtual reality), but some safety measures are taken to avoid collision with
29 other people: the caregiver signals to others that a session is in progress, checking before
30 starting the game that there are no obstacles in the hallway. This protocol is an adaptation
31 from Zwinkels *et al.* [17]. Every training session consists of a prescribed intensity, volume
32 and time (Table I).
33

34 Before the first session of each week, the target velocity is calculated during a Muscle Power
35 Sprint Test (MPST) [21]. This test is made through the ARRoW- CP game and is presented
36 as a “calibration” to the participant. During this test, no feedback is presented to the player.
37 The target velocity is defined as the highest velocity of 6 sprints. This test is repeated every
38 week to adapt the difficulty of the game to the child’s progress.

39 *Treadmill Gait Training*

40 The control group protocol consists of 4 weeks of GT on a treadmill (3 sessions per week),
41 with a maximal duration of 30 minutes. This protocol is an adaptation from Grecco *et*
42 *al.* [13]

43 Before the first session, the target velocity is estimated during a treadmill speed test:
44 participants are instructed to walk on a treadmill with increasing speed (initially 0.5 km/h
45 and increased 0.5 km/h each minute). Each minute, children are asked about short- ness
46 of breath and the subjective responses are classified using the 1-10 Borg Rating of
47 Perceived Exertion Scale. The test is stopped if the score is higher than 5. The target
48 velocity is defined as 80% of the maximum speed achieved during the test.

49 The first 5 minutes is a warm-up time, the speed is gradually increased until reaching the
50 target velocity. The child walks for a maximal 20 minutes at their target velocity. Then, the
51 treadmill speed is gradually diminished over the final 5 minutes. Training could be interrupted
52 at any time at the child’s request or physical therapist judgement. Treadmill sessions are
53 monitored by physiotherapist, assistant-physiotherapist, or a member of the research staff.
54

55 Randomization Procedure

56 After baseline measures, eligible participants are randomized to the intervention or control
57 group based on a computerized randomization program. Blocks randomization are
58 calculated in block sizes of fours and six. The randomization procedure is only available
59 to an independent researcher who will not be involved in the delivery of the interventions
60 or the performance of the measurements. Due to small sample size required, the

randomization lists were not stratified.

Participants

All participants are recruited from the Poidatz Rehabilitation Centre. The children are operated in several hospitals in Paris: Necker Enfants Malades University Hospital, Trousseau University Hospital or Robert Debré University Hospital. Ethics approval is granted by the French Ethical Committee Sud-Est VI (Clermont-Ferrand). All patients meeting the study criteria were approached directly in the rehabilitation center when they were in the phase of walking recovery after surgery. Information about the study was given to them orally. They are given time to reflect. If they are interested, a physiotherapist contacts the family by phone to give them information about the study. Written consent is obtained after a further period of reflection. Additionally, all parents, and participants from 10 years of age, should provide informed consent prior to study initiation. All participants should have a cooling off period prior to the inclusion (minimum 15 days between information and consent). Confidentiality and data access are guaranteed by the National Commission of Informatic (CNIL). A Data Protection Officer has been designated for all research studies conducted in this rehabilitation centre. He guarantees that the data protection and the rights of the subject are respected according to the General Data Protection Regulation (EU) 2016/679 (GDPR). The study has been registered in ClinicalTrials.gov (Identifier: NCT04837105). Inclusion criteria are children with CP admitted for inpatient rehabilitation following SEMLS, 10–18 years of age, functioning preoperatively at GMFCS I–III. The minimum time between surgery and inclusion in the study is 7 weeks (step 4 of post-SEMLS rehabilitation process), they should have a Functional Mobility Scale 50 meters rating superior or equal to 2 (ability to walk on 50m using a walker or frame without help from another person).

All children should be able to cooperate, understand and follow simple instructions in French to practice the game. Only voluntary patients whose parents give their consent for their child's participation in the study and patient affiliated to the French social security system are included. Criteria for exclusion include a diagnosis of photosensitive epilepsy in the medical record and/or patient's case history mentioning seizures that occurred while playing a video game, visual, cognitive or auditory impairment that would interfere with playing the game. The patient must have normal or corrected vision and hearing. During the 4-weeks, children can wear their orthotic device and their assistive device as prescribed by medical staff. In cases of evolution regarding the level of support (a patient going from walking with crutches to no walking aid, for example), the medical staff decides if patient is able to practice series of walking sprints safely and efficiently according the main objective of the study, then they inform the research staff. This change should only be made during the first session of the week to proceed with the new weekly calibration and thus adapt the objective walking speed to the child's abilities.

Patient and Public Involvement

Patient involved as described above. Throughout the development phase of the ARRoW-CP active video game, test sessions were organized with some of the patients of the rehabilitation centre to collect their opinion on the game. The results of the RCT will be disseminated to the international community through the publication of articles and conference papers. It is also planned to spread these results to communicate them to parents, families, and children with motor disabilities (regional or national newspapers in French, social networks, patient associations).

Outcomes

Outcome measures take place at baseline (T0), immediately after four weeks of GT (T1), and six months later (T2). The professional caregiver administering outcome measures remains blinded to group allocation. See Supplementary File 3 for outcomes details and criterion validity.

Primary outcome : The 6 minutes walk test (6MWT) The 6MWT is increasingly used in paediatrics, in clinics to monitor patients' abilities or in research as a criterion for evaluating the effectiveness of a rehabilitation protocol [22]. The 6MWT assesses distance walked over 6 minutes as a submaximal test of aerobic capacity/endurance. The reference guideline detailing the recommendations and instructions has been updated in 2013 [23,

24]. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP [25, 26]. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness. This primary outcome is relative to the primary objective i.e. improve walking capacity.

Secondary outcome : Muscle power sprint test (MPST)

The MPST evaluates anaerobic performance of youth with CP over a 6x15 meters at their maximal speed [21]. Velocity (m/s), acceleration (m/s²), force (kg/s²) and power (watts) are calculated. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints. This secondary outcome is relative to the secondary objective i.e. improve anaerobic performance.

Secondary outcome : Shuttle Run Test (SRT)

The 10-meters shuttle run test is an adapted version of the 20-metre shuttle run test to accommodate children with cerebral palsy (CP) classified at Level I or Level II on the Gross Motor Function Classification System (GMFCS) [27]. This test evaluates cardiovascular endurance. In this study, the SRT-II will be used because of postoperative context. The SRT-II starts at 2 km/h. Speed is increased 0.25 km/h every level (minute). The test is over when the child cannot go to the next cone in time. This secondary outcome is relative to the secondary objective i.e. improve physical fitness level.

Secondary outcome : Questionnaire (PACES)

To assess enjoyment for both control and test group, the 16-items of the Physical Activity Enjoyment Scale (PACES) will be used. The PACES is a valid and reliable measure of physical activity enjoyment. It has been used in many studies assessing the effectiveness of VR therapy [28]. This questionnaire will be presented to the participant at the end of the last session. This secondary outcome is relative to the secondary objective i.e. improve satisfaction during therapy.

Sample size and statistical analysis

According to a study of Grecco et al. an average augmentation of 83% (range 80-85%) in 6MWT was calculated after following 12-weeks of treadmill training in postoperative context [13]. The distance travelled during the 6MWT increases from before: 166.4 ± 39.1 m to after: 304.7 ± 75.8 m. The effect size was calculated: $d = 2.29$. In this previous study, the mean number of training sessions throughout the 12-week period was 11.1 (around 1-session per week) i.e. total dose of 6h/12-weeks. It has been hypothesized that participants following a more intensive protocol (3 sessions/week i.e. total dose of 6h/4-weeks) will show the same effect on the 6MWT.

With an $\alpha = 0.05$ and $\beta = 0.20$ (power = 0.80), a sample size of 6 subjects per group will be required. When taking a failure rate of 10% into account, 14 subjects should be included.

The required sample size was calculated with G Power 3.1.9.7. Parameter was t-tests – Means; difference between two independent means (two groups) with a priori analysis.

The effect of the GT protocol will be analyzed using a multivariate repeated measures ANOVA. The possible differences between and within T0, T1 and T2 for the intervention group and control group will be calculated with a statistical significance level of $p = 0.05$. If there is a significant difference, a post-hoc test will be executed to further investigate group differences. Quantitative descriptive statistics will be used to present patient characteristics and global results. Data from PACES questionnaire will be analyzed using normality test (deciding to use parametric / non-parametric statistics), descriptive statistics, reliability test (Cronbach Alpha / Composite Reliability), Pearson / Spearman correlational test. All statistical analyses will be performed using R with a statistical significance level of $p = 0.05$. Moreover, the trial statistician will remain blinded to group allocation until the database has been locked.

Discussion

This approach has evolved from two directions: interest to improve walking capacity after SEMLS for children with CP, and from concern that the usual post-operative rehabilitation approach has not produced sustainable improvements in participation and activity in daily life for these children [8].

AVG development framework

This work followed the AVG development framework PROGame, proposed by Amenguai Alcover *et al.* [18]. A participate process including both professional healthcare and patients has been conducted. The first step was the project initiation. The team identified the need for a AVG, the stakeholders, and user categories (users and experts). They also clarified the game functionality and constraints. They selected the therapy to transfer into the AVG. The operational objectives were to be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun. These identifications were based upon prior experience and literature review [12, 29]. The team used communication tools like oral presentation of preliminary results, open debates, surveys and meeting reports. The aim was to support incremental development between team's members (that has their own specialty) and to share knowledge. At this stage, the project proposed a general description. The second step was the interaction mechanism, all technical solutions were explored and an algorithm for gait parameters detection was developed and tested [30, 31]. During the third step, the interactive elements, the team investigated actual commercial or AVGs to get inspired. Team exploration and discussion conducted to games like Pokemon Go or Zelda, in which the gamer must explore the world and accomplish missions. These games appear very popular with the younger generation. The development team was composed of therapists (3 physiotherapists), researchers (2 in computer science, 1 in rehabilitation science, 1 in movement science) and a software engineer. These steps occurred between January 2020 and June 2021. All details are available in Supplementary File 2.

The aim was to think together about the best solution for improving postoperative results, especially walking capacity. New technologies were young people's preferred solution. These solutions seem to be a very promising tools for rehabilitation purposes, allowing to manipulate the environment, to offer interaction, to optimize feedback and many other potentialities [19, 32]

Feedback, a key point for motor learning

Feedback retraining paradigm is based on the conversion, the supplementation and augmentation of sensory information that are usually accessible only by an internal focus of attention, to accessible information [32, 33]. In this paradigm, augmented feedback is defined as augmented sensory information provided by an external resource (therapist or display) to the patient [34]. The information provided to the user could be relative to the movement's pattern or result on the environment or the outcome of a movement with respect to the goal. Sensory channels used to deliver information are visual, auditory, or haptic, linked to the proprioception properties of humans. The timing of feedback delivery is critical. Concurrent feedback is delivered while the skill is being performed, terminal feedback is delivered after the skill is performed with or without delay [35]. In our previous study, we have confirmed that children with CP can adapt their walking speed, and they can positively respond to the real-time AR feedback (article under review). However, we have observed that not all patients performed equally well with the scenarios. When we have looked at the individual responses of each participant for each scenario, we have observed some essential differences. Some people did not perform better with the feedback; others were helped by a particular feedback but disturbed with another. Some authors highlighted these inter-individual differences. Recently, Liu *et al.* have underscored different patient profiles: "non-responders" and "responders" to the feedback [19]. In their study, patients were people after stroke. They were instructed to walk on a treadmill while visualizing an avatar replicating their exact walking pattern in real-time on a large screen. Overall, patients improved step length and walking speed when the avatar was displayed on a side view. But results were not the same for all participants; the authors distinguished non-responders and

1
2
3
4 responders to the feedback. They hypothesized that the initial step length ratio could
5 influence the result because patients with a larger paretic step length better responded.
6 This study has shown that specific populations are more sensitive to the virtual
7 environment.

8 Serious aspect of ARRoW-CP game

9 ARRoW-CP AVG combines many of the motor learning theories: context focused therapy
10 and goal-directed training, task-specific, variable practice, high intensity, augmented
11 feedback during therapy sessions and motivation of the patient [16]. To find the best
12 feedback modalities for our AVG, we have conducted preliminary studies exploring the
13 impact of feedback modalities on walking speed, both in healthy adults and in children
14 with CP. Study on healthy adults showed that certain feedback helped to increase walking
15 speed, provided that the game instruction was clear. Typically, feedback combining a
16 focus of attention with knowledge of results, a spatial representation with world-locked
17 holograms and a method of presentation with rich holographic content (like animation,
18 colour changes) increased walking speed in healthy subject [36]. This step allowed us
19 to modify and adapt feedback modalities (Figures 1A-C).

20
21
22 A second study has occurred with children with CP. Results showed that scenarios
23 combining world-locked holograms that disappeared over the time helped children with
24 CP to reach their target speed. On the other hand, a body-locked hologram that advances
25 in front of the user at the target speed was better able to control the walking speed of the
26 patient[37].

27 ARRoW-CP is an adaptation of the validated protocol from Zwinkels *et al.* The original
28 protocol consists of 8 weeks, twice a week [17]. Every training session consisted of a 30s
29 walking sprints following the pre-scribed intensity, volume, and time: Week 1 to week 2:
30 8 sprints, work/rest ratio 1:4; Week 3 to week 4: 10 sprints, work/rest ratio 1:4; Week 5
31 to week 8: 12 sprints, work/rest ratio 1:3. Because of post-operative context, the intensity
32 should be reduced. At the beginning of the fourth step of rehabilitation process, even if
33 gait training is recommended, children did not recover to their pre-operative level,
34 specifically some children needed crutches or k-walkers. Moreover, a further aspect not to
35 be underestimated: fatigue and pain [38]. The choice of intensity, volume and time in the
36 ARRoW CP protocol is based on practical experience from expert clinician and from
37 literature [12, 17].

38 Limitations

39 The limited sample size limit the ability to balance the two groups according the gender,
40 age, GMFCS level and type of surgery. The randomization lists were not stratified. But
41 the next step in the ARRoW-CP project is to modify the game based on our initial results
42 and to conduct a new RCT including more centers (and more children) worldwide. Using
43 AR for therapy is not suitable for all children. We excluded patients with cognitive trouble
44 and with patients high risks of fall based on medical recommendations.

46 Conclusion

47 This article presents in detail the gait training protocol tested through a RCT. Both control
48 group and experimental group have an evidence-based physical therapy training. This
49 article also presents the game development framework of the ARRoW-CP AVG. This
50 game is based on the most recent motor learning approach. This is the first study assessing
51 the efficacy of postoperative gait rehabilitation using an active video game. If our
52 hypothesis is validated, ARRoW-CP game will make possible to intensify gait training.
53 This innovative strategy will have significant clinical impact by improving walking
54 capacity for children after SEMLS. Publishing study protocol of the RCT offers the
55 opportunity to collaborate with other teams and to give more details about the study. Results
56 will be available in 2023.

Tables

Table 1 Details of the gait training protocol deployed in the active video game ARRoW-CP

	WEEK 1	WEEK 2	WEEK 3	WEEK 4
Session Number per week	3	3	3	3
Sprint Time (s)	30	30	30	30
Rest Time (min:s)	2:00	2:00	1:30	1:30
Sprint Number	4	6	8	10
Total time of the session	10	15	18	22

Figures 1A-C. Image capture from ARRoW-CP active video game. On the left (A), this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle (B), an adult (not a patient) wearing the Microsoft Hololens AR headset to see holograms. On the right (C), game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard).

Supplementary Files

Supplementary file 1 — ARRoW-CP Active Video Game

Supplementary file 2 — Active Video game development framework

Supplementary file 3 — Main Outcomes details and criterion validity.

Author details

¹ Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, France.

² Université Paris-Saclay, Univ Evry, IBISC, 91020, Evry-Courcouronnes, France.

a. Contributorship

ALG, GB, SO and ED conceived the study, participated in its design, and helped to draft the manuscript. SPT, NK and MB participated in the acquisition and coordination of the study. All authors read, revisit it critically and approved the final manuscript. All of them affirm that the manuscript is an honest, accurate, and transparent account of the study being reported.

b. Funding statement

This study is a part of the ARRoW CP project supported by the Association Nationale Recherche et Technologie (ANRT) ID CIFRE 2018/0973. This is a public sponsor that does not influence the study.

c. Competing interests

There are no competing interests for any author.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

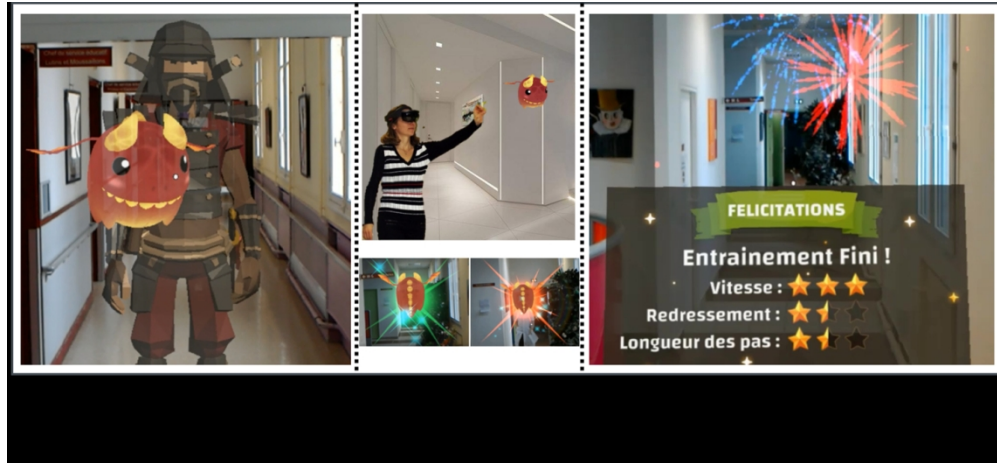
For peer review only

References

1. Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M., Damiano, D., Dan, B., Jacobsson, B.: A report: the definition and classification of cerebral palsy april 2006. *Developmental Medicine and Child Neurology* **109**, 8–14 (2007). doi:10.1111/j.1469-8749.2007.tb12610.x
2. Oskoui, M., Coutinho, F., Dykeman, J., Jett'e, N., Pringsheim, T.: An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology* **55(6)**, 509–519 (2013). doi:10.1111/dmcn.12080
3. Graham, H.K., Rosenbaum, P., Paneth, N., Dan, B., Lieber, R.L.: Cerebral palsy. *Nat Rev Dis Primers* **2(1)**, 15082 (2016). doi:10.1038/nrdp.2015.82
4. Park, E.: Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. *Health and Quality of Life Outcomes* **16(1)**, 383–390 (2018). doi:10.1186/s12955-018-0891-1
5. Himuro, N., Mishima, R., Seshimo, T.: Change in mobility function and its causes in adults with cerebral palsy by gross motor function classification system level: A cross-sectional questionnaire study. *NeuroRehabilitation* **42(4)**, 383–390 (2018). doi:10.3233/NRE-172340
6. Benner, J., Hilberink, S., Roebroek, M.: Long-term deterioration of perceived health and functioning in adults with cerebral palsy. *Arch Phys Med Rehabil.* **98(11)**, 2196–2205 (2017). doi:10.1016/j.apmr.2017.03.013
7. Novak, I., Morgan, C., Badawi, N.: State of the evidence traffic lights 2019: Systematic review of interventions for preventing and treating children with cerebral palsy. *Curr Neurol Neurosci Rep* **20(2)**, 3–24 (2020). doi:10.1007/s11910-020-1022-z
8. McGinley, J.L., Dobson, F., Ganeshalingam, R., Graham, H.K.: Single-event multilevel surgery for children with cerebral palsy: a systematic review. *Dev Med Child Neurol* **54(2)**, 117–128 (2012). doi:10.1111/j.1469-8749.2011.04143.x
9. Lamberts, R.P., Burger, M., Langerak, N.G.: A systematic review of the effects of single-event multilevel surgery on gait parameters in children with spastic cerebral palsy. *PLoS ONE* **11(10)**, 0164686 (2016). doi:10.1371/journal.pone.0164686
10. Amichai, T., Harries, N., Dvir, Z., Patish, H., Copeliovitch, L.: The effects of femoral derotation osteotomy in children with cerebral palsy: an evaluation using energy cost and functional mobility. *J Pediatr Orthop* **29**, 68–72 (2009). doi:10.1097/BPO.0b013e3181924331
11. Guinet, A., Khouri, N., Desailly, E.: Rehabilitation after single-event multilevel surgery for children and young adults with cerebral palsy: A systematic review. *American Journal of Physical Medicine & Rehabilitation* **21**, 2697 (2021). doi:10.1097/PHM.0000000000001864
12. Booth, A., Buizer, A., Meyns, P., Van der Krogt, M.: The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine and Child Neurology* **60(9)**, 866–83 (2018). doi:10.1111/dmcn.13708
13. Grecco, L., De Freitas, T., Satie, J., Bagne, E., Oliveira, C., De Souza, D.: Treadmill training following orthopedic surgery in lower limbs of children with cerebral palsy. *Pediatr Phys Ther* **25(2)**, 187–192 (2013). doi:10.3109/17453674.2014.960141
14. Cano-de-la-Cuerda, R.: Theories and control models and motor learning: Clinical applications in neurorehabilitation. *Neurología* **30(1)**, 32–41 (2021). doi:10.1016/j.nrleng.2011.12.012
15. Cho, C., Hwang, W., Hwang, S., Chung, Y.: Treadmill training with virtual reality improves gait, balance, and muscle strength in children with cerebral palsy. *The Tohoku Journal of Experimental Medicine* **238(3)**, 213–8 (2016). doi:10.1620/tjem.238.213

16. Demers, M., Fung, K., Subramanian, S., Lemay, M., Robert, M.: Do virtual interventions in individuals with cerebral palsy make use of motor learning principles?: A systematic review (preprint). *JMIR Serious Games* **XX**, (2020). doi:10.2196/23822
17. Zwinkels, M., Verschuren, O., De Groot, J.: Effects of high-intensity interval training on fitness and health in youth with physical disabilities. *Pediatric Physical Therapy* **31(1)**, 84–93 (2019). doi:10.1097/PEP.0000000000000560
18. Amengual-Alcover, E., Jaume-i-Cap'ó, A., Moy'a-Alcover, B., Martinuzzi, A.: Progame: A process framework for serious game development for motor rehabilitation therapy. *PLOS ONE* **13(5)**, 0197383 (2018). doi:10.1371/journal.pone.0197383
19. Liu, L., Sangani, S., Lamontagne, A.: Real-time avatar-based feedback to enhance the symmetry of spatiotemporal parameters after stroke: Instantaneous effects of different avatar views. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* **28(4)**, 878–887 (2020). doi:10.1109/TNSRE.2020.2979830
20. MacIntosh, A., Desailly, E., Biddiss, E.: A biofeedback-enhanced therapeutic exercise video game intervention for young people with cerebral palsy: A randomized single-case experimental design feasibility study. *PLoS One* **15(6)**, (2020). doi:10.1371/journal.pone.0234767
21. Verschuren, O., Bongers, B., Obeid, J., Ruyten, T., Takken, T.: Validity of the muscle power sprint test in ambulatory youth with cerebral palsy. *Pediatric Physical Therapy* **25(1)**, 25–28 (2013). doi:10.1097/PEP.0b013e3182791459
22. Gillett, J., Lichtwark, G., Boyd, R., Carty, C., Barber, L.: The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy. *Gait & Posture*. **70**, 323–329 (2019). doi:10.1016/j.gaitpost.2019.03.023
23. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, .: Ats statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111–117 (2002). doi:10.1164/ajrccm.166.1.at1102.
24. Shirley Ryan Ability Lab, .: The 6 minute walk test: Instrument details (2021). <https://sralab.org/rehabilitation-measures/6-minute-walk-test>
25. Slaman, J., Dallmeijer, A., Van Den Berg-Emons, R.: The six-minute walk test cannot predict peak cardiopulmonary fitness in ambulatory adolescents and young adults with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **94(11)**, 2227–2233 (2013). doi:10.1016/j.apmr.2013.05.023
26. Maltais, D., Robitaille, N., Dumas, F., Boucher, N., Richards, C.: Measuring steady-state oxygen uptake during the 6-min walk test in adults with cerebral palsy: feasibility and construct validity. *Int J Rehabil Res* **35(2)**, 181–183 (2012). doi:10.1097/MRR.0b013e3283527792
27. Verschuren, O., Takken, T., Ketelaar, M., Gorter, J., Helders, P.: Reliability and validity of data for 2 newly developed shuttle run tests in children with cerebral palsy. *Physical therapy* **86(8)**, 1107–1117 (1988). doi:10.1080/02640418808729800
28. Motl, R., Dishman, R., Saunders, R., Dowda, M., Pate, R.: Measuring enjoyment of physical activity in adolescent girls. *Am J Prev Med* **21**, 110–117 (2001). doi:10.1016/S0749-3797(01)00326-9
29. Fehlings, D., Switzer, L., Findlay, B., Knights, S.: Interactive computer play as "motor therapy" for individuals with cerebral palsy. *Semin Pediatr Neurol* **20(2)**, 127–38 (2013). doi:10.1016/j.spen.2013.06.003

- 1
2
3
4 30. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Reliability of the head tracking measured by
5 microsoft hololens during different walking conditions. *Comput Methods Biomech Biomed*
6 *Engin* **xx**, 159–161 (2019). doi:10.1080/10255842.2020.1714228
7
8 31. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Validity of hololens augmented reality head
9 mounted display for measuring gait parameters in healthy adults and children with cerebral
10 palsy. *Sensors* **21**, 2697 (2021). doi:10.3390/s21082697
11
12 32. Levin, M.F.: *Feedback and Virtual Environments for Motor Learning and Rehabilitation* vol.
13 2(1), pp. 19–36 (2010)
14
15 33. Booth, A.T., Buizer, A.I., Harlaar, F.: Immediate effects of immersive biofeedback on gait in
16 children with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **100(4)**, 598–605
17 (2019). doi:10.1016/j.apmr.2018.10.013
18
19 34. Durkin, M.S., Maenner, M.J., Benedict, R.E., Yeargin-Allsopp, M.: The role of socio-
20 economic status and perinatal factors in racial disparities in the risk of cerebral palsy. *Dev Med*
21 *Child Neurol* **57(9)**, 835–843 (2015). doi:10.1111/dmcn.12746
22
23 35. MacIntosh, A., Lam, E., Vigneron, V., Vignais, N., Biddiss, E.: Biofeedback interventions for
24 individuals with cerebral palsy: a systematic review. *Disability and Rehabilitation* **41(20)**,
25 2369–2391 (2019). doi:10.1080/09638288.2018.1468933
26
27 36. Guinet, A., Khouri, N., Desailly, E.: Clinical gait analysis and physical examination don't
28 correlate with physical activity of children with cerebral palsy. cross-sectional study. *International*
29 *Biomechanics* **7(1)**, 88–96 (2020). doi:10.1080/23335432.2020.1812429
30
31 37. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Towards an ar game for walking rehabilitation:
32 Preliminary study of the impact of augmented feedback modalities on walking speed. *IEEE*
33 *International Symposium on Mixed and Augmented Reality Adjunct* **1**, 264–268 (2020). Doi:
34 10.1109/ISMAR-Adjunct51615.2020.00075
35
36 38. Hoiness, P., Capjon, H., B, L.: Pain and
37 rehabilitation problems after single- event
38 multilevel surgery including bony foot
39 surgery in cerebral palsy. a series of 7
40 children. *Acta Orthop* **85(6)**, 646–651
41 (2014).
42 doi:10.1097/PEP.0b013e3182888495
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Figures 1A-C. Image capture from ARroW-CP active video game. On the left (A), this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle (B), an adult (not a patient) wearing the Microsoft HoloLens AR headset to see holograms. On the right (C), game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard)

289x134mm (130 x 130 DPI)

ARROW-CP Serious game for gait rehabilitation

1. The Microsoft HoloLens Headset is used for ARROW-CP (**Figure 1**). Game development was made with Unity 2019.4.8f1 and Mixed Reality Toolkit (MRTK). MRTK-Unity is a Microsoft-driven project that provides a set of components and features, used to accelerate cross-platform MR app development in Unity.



Figure 1. Microsoft HoloLens Augmented reality headset.

2. The player is immersed in a samurai world. He meets the chief of the village that can no longer protect its population. The natural elements are unleashed, causing famine and various damages. The player's role is to develop his energy through ninja training to build a protective totem for the village's inhabitants (trailer: <https://youtu.be/BbmniiiJuaA>).

The software architecture is presented in **Figure 2**.

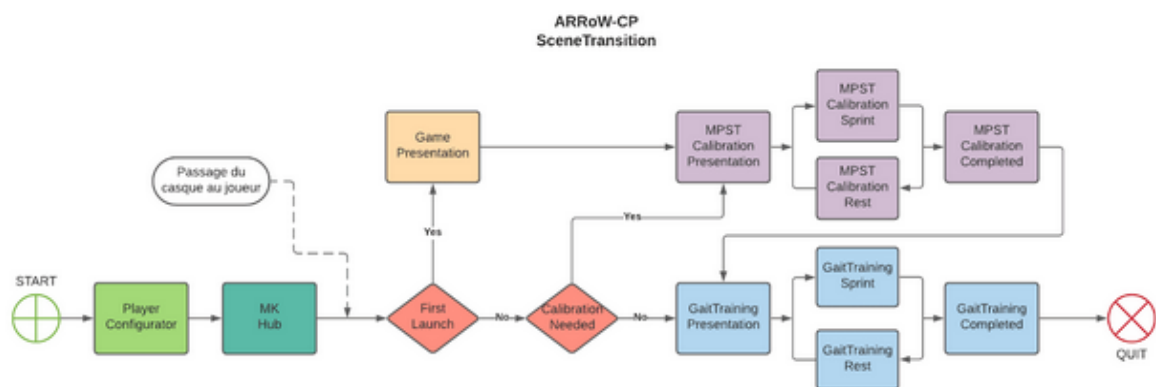


Figure 2. Game architecture of the ARROW CP game. When the game starts, the AR headset is worn by the therapist. He creates the user profile of the player by entering his name, first name, age, height, and weight during session 1 week 1. Next session, he loads the existing user profile. The therapist then accesses the “MK Hub”, which contains information about the performance of previous sessions and the number of sessions

3. The mechanism of feedback provided during sprints and rest time is detailed in **Figure 3**.

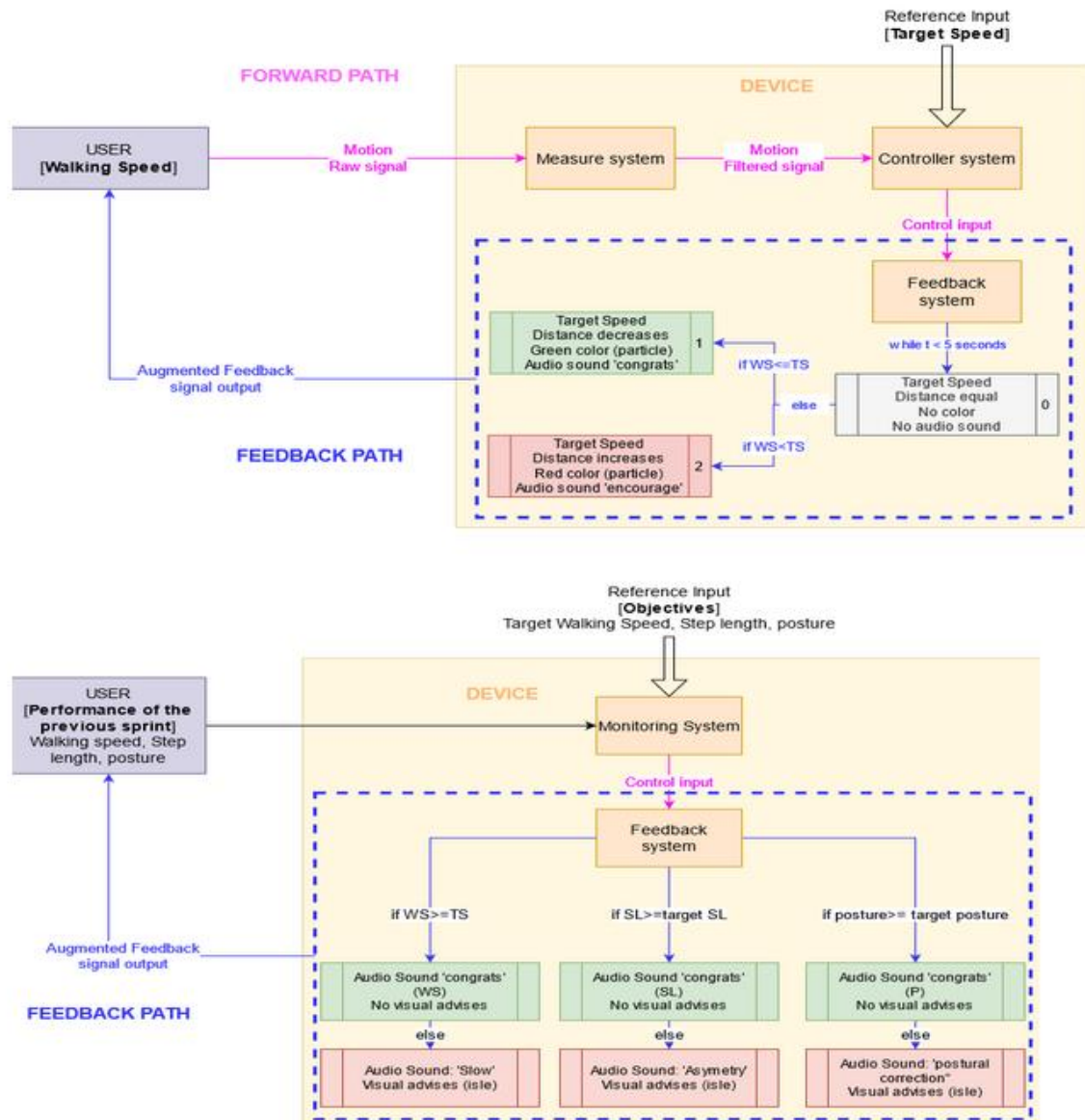


Figure 3. Feedback mechanism during sprints (A) and rest period (B).

At the beginning of each session, through the “Physio HUB”, therapists know the previous performance of their patient and they can adjust their advice.

At the end of each session, feedback with delay is proposed to the child: they can choose to see their actual performance through the game scoreboard and totem construction (feedback on demand). These feedbacks were based on knowledge of results.

Project Initiation

Interaction Mechanism

Interaction Elements

2-061580 on 10 October 2022. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

7	Global Aim	to develop an active video game for gait rehabilitation for children with motor disabilities and particularly cerebral palsy
9	Operational objectives	To be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun.
11	<i>describe the needs in general</i>	
16	Restrictions	The development of the game must correspond to the duration of a 3-year thesis; grants are limited and predefined; the agreement of the ethics committee and written consents from participants are required before any test on humans ; all technical solution could be explored.
17	<i>detail economical, technical, operational, legal restrictions</i>	
24	Stakeholders	Customers : Children with cerebral palsy, 10-18 years old, GMFCS I-III, with cognitive skills to understand and follow simple instructions == END USERS Physiotherapists, occupational therapists, physiotherapist assistants, rehabilitation therapists == EXPERTS Special needs and required functionalities : The active video game must include the principles of motor learning, which are task-specific practice, variable practice, high practice intensity, progressive difficulty, augmented feedback, and adaptability to user abilities. The active video game should allow the inclusion of motivational elements to increase engagement.
28	<i>Identify customers, special needs and required functionality ; define experts and representatives end users</i>	Children must be free to move in the global environment, without restriction of movement. Children must be able to use their usual walking aids (crutches or posterior walker). Therapists should have access to the previous and global performance of their patient through the game The solution should be "ready to use" easily both for children and therapists
39	Therapy Selection	The team's members agreed on making walking speed the main variable input of the serious game. Meaningful reason is that intensive gait training focused on walking speed has shown their clinical efficacy. ^{12,39} The therapy to transfer into the serious game should include walking sprints.

	Aim of this phase	To select the interaction system and to capture the therapy into the system.
	Device selection	Device: Microsoft Hololens AR headset version 1 was selected because its technical characteristics matched all identified specifications. Tools : - Unity software (version 2019.4.8f1) -Microsoft Visual Studio 2019 - Mixed Reality Toolkit for Unity (MRTK version 4.2.3)
	Gait parameters detection development and evaluation	Algorithm development: HoloStep measuring the real-time gait parameters with the AR headset system ⁴³ Evaluation : - The accuracy of the AR headset's sensors was sufficiently high to evaluate the position of the user without time drift in the global environment ⁴² - HoloStep was reliable for measuring and calculating walking speed, cadence, step length and global distance travelled in comparison to reference motion analysis tracking system ⁴³

	Aim of this phase	To design the interaction elements that force patients to perform the therapy correctly.
	Feedback reflexion	We have proposed a model of feedback in Augmented Reality (AR) for Motor Rehabilitation (article not published yet). Indeed, AR feedback can be displayed to the user through different characteristics. This theoretical work was necessary before designing feedback and testing specific characteristics of the model. The final aim was to optimize the augmented information provided to the patient. To carry out this work, we extended and adapted the biofeedback model described by Macintosh et al., and the qualitative model from Martinez et al., to the AR context. Our descriptive model of feedback in AR application helped us design an AR application, called Best-Of ARRoW. We have tested with this app, the impact of different virtual feedback characteristics on walking speed of children with CP. The results of this first study will be published soon (article under review). This help us to better design the feedback used in ARRoW-CP AVG.
	Game selection & Universe	The choice of the game universe (Samurai world) and reward panel were unanimously validated by experts and end users. All packages used to design the game were available in the Unity Asset Store: Polygon Samurai low poly 3D Art by Synty, Tiny Dragon by Suriyun, the GUI Kit - The Stone, and the Particle FX. Voice of game characters from volunteers were recorded in a professional radio studio (HandiFM – France 107.3 FM).

Test name	Instructions	Validity
<p>[PRIMARY OUTCOME]</p> <p>The 6 minutes walk test (6MWT)</p>	<p>To summarize, patients are instructed to walk, not run, as far as they could along a 20-m level surface track during a 6-minute period. This shorter distance has been validated for children in order to be more focused on the task. They could use their usual walking aids. After each minute, participants are told the elapsed time and standardized encouragement is provided. Patients are allowed to stop and rest during the test but are instructed to resume walking as soon as they feel able to do so. The stopwatch is not stopped during this time. The 6MWT distance (in meters) is registered. Measured 6MWT distance could be compared with normative values for children with CP. It is recommended to monitor heart rate during the 6MWT.</p>	<p>In population of children with CP, test/retest reliability is excellent for distance output (ICC=0.98). The 6MWT is poorly related to VO₂ peak in ambulatory adolescents and young adults with CP. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.</p>
<p>[SECONDARY OUTCOME]</p> <p>Muscle power sprint test (MPST)</p>	<p>The 15-m distance is marked by 2 lines taped to the floor. Cones are placed at the end of each of the lines. Participants are instructed to walk as fast as possible from one line to the other, and to be sure to cross each line. Between each run, participants are allowed to rest for 10 seconds before turning around to allow them to prepare for the following sprint. Children should be encouraged to give maximal effort. The following variables are calculated for each of the 6 sprints: velocity (m/s) = distance/time, acceleration (m/s²) = velocity/time, force (kg/s²) = body mass × acceleration, and power (watts) = force × velocity. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints.</p>	<p>The MPST is a valid test to assess the anaerobic performance in children with CP, significant correlations between the performance on these tests for both PP and MP were found. (PP: r = 0.731 ; MP: r = 0.903). Standard error of measurement (SEM), minimal detectable change (MDC) and normative data are available in Verschuren et al. The children with CP had impaired anaerobic performance as it was lower than that of their peers.</p>
<p>[SECONDARY OUTCOME]</p> <p>10-meters Shuttle Run Test (SRT)</p>	<p>Description of the test is available here : "The course is 10 metres long; the end is marked with 2 cones and measuring tape. Subjects should wear regular sports clothing and shoes, and orthoses, if applicable. Each child should also wear a heart rate monitor. Children walk or run between the 2 markers at a set incremental speed. These runs are synchronised with a pre-recorded sound. (...) As the test proceeds, the interval between each successive beep reduces, forcing the child to increase speed over the course of the test, until it is impossible to keep in sync with the recording." We have developed a mobile application that beeps at regular intervals, indicates the time spent and allows the assessor to increment the number of shuttles made by the child.</p>	<p>The SRT is a valid and reliable test. Test-retest is excellent (ICC=0.99) and high correlations were found for the relationship between data for both shuttle run tests and data for the treadmill test (r=0.96).</p>
<p>[SECONDARY OUTCOME]</p> <p>Physical Activity Enjoyment Scale (PACES)</p>	<p>This is a 5-point Likert scale (from 1- I totally disagree to 5- I totally agree). A translation procedure from English to French language has been made using guidelines (figure).</p>	<p>The PACES is a valid and reliable measure of physical activity enjoyment.</p>



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	na
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	7
	5b	Name and contact information for the trial sponsor	na
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	na
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1-3
	6b	Explanation for choice of comparators	1-3
Objectives	7	Specific objectives or hypotheses	3
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	3

Methods: Participants, interventions, and outcomes

1				
2				
3				
4	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	3
5				
6				
7				
8	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4
9				
10				
11				
12				
13	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	2-3
14				
15				
16		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	na
17				
18				
19				
20				
21		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	na
22				
23				
24				
25		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	na
26				
27				
28	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	4-5
29				
30				
31				
32				
33				
34				
35				
36	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	4
37				
38				
39				
40				
41	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
42				
43				
44				
45	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
46				
47				

Methods: Assignment of interventions (for controlled trials)

Allocation:

51				
52				
53	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	5
54				
55				
56				
57				
58				
59				
60				

1				
2	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central	na
3	concealment		telephone; sequentially numbered, opaque, sealed envelopes),	
4	mechanism		describing any steps to conceal the sequence until interventions are	
5			assigned	
6				
7	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,	4-5
8			and who will assign participants to interventions	
9				
10	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial	4-5
11	(masking)		participants, care providers, outcome assessors, data analysts), and	
12			how	
13				
14				
15		17b	If blinded, circumstances under which unblinding is permissible, and	4-5
16			procedure for revealing a participant's allocated intervention during	
17			the trial	
18				
19				

Methods: Data collection, management, and analysis

20				
21				
22	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other	5
23	methods		trial data, including any related processes to promote data quality (eg,	
24			duplicate measurements, training of assessors) and a description of	
25			study instruments (eg, questionnaires, laboratory tests) along with	
26			their reliability and validity, if known. Reference to where data	
27			collection forms can be found, if not in the protocol	
28				
29				
30		18b	Plans to promote participant retention and complete follow-up,	5
31			including list of any outcome data to be collected for participants who	
32			discontinue or deviate from intervention protocols	
33				
34	Data	19	Plans for data entry, coding, security, and storage, including any	5
35	management		related processes to promote data quality (eg, double data entry;	
36			range checks for data values). Reference to where details of data	
37			management procedures can be found, if not in the protocol	
38				
39				
40	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.	5
41	methods		Reference to where other details of the statistical analysis plan can be	
42			found, if not in the protocol	
43				
44		20b	Methods for any additional analyses (eg, subgroup and adjusted	5
45			analyses)	
46				
47		20c	Definition of analysis population relating to protocol non-adherence	5
48			(eg, as randomised analysis), and any statistical methods to handle	
49			missing data (eg, multiple imputation)	
50				
51				

Methods: Monitoring

52				
53				
54	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role	na
55			and reporting structure; statement of whether it is independent from	
56			the sponsor and competing interests; and reference to where further	
57			details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1				
2		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	na
3				
4				
5				
6	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
7				
8				
9				
10				
11	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	na
12				
13				
14				

Ethics and dissemination

15				
16				
17	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	1
18				
19				
20				
21	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	na
22				
23				
24				
25				
26	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
27				
28				
29				
30		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	na
31				
32				
33	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	na
34				
35				
36				
37	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	7
38				
39				
40				
41	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	na
42				
43				
44				
45	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	na
46				
47				
48	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	na
49				
50				
51				
52				
53				
54		31b	Authorship eligibility guidelines and any intended use of professional writers	na
55				
56				
57		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	na
58				
59				
60				

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	na
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	na

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

For peer review only

BMJ Open

Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery : Protocol for a Randomized Controlled Trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-061580.R3
Article Type:	Protocol
Date Submitted by the Author:	29-Aug-2022
Complete List of Authors:	Guinet, Anne-Laure; Universite Paris-Saclay, IBISC Laboratory; Fondation Ellen Poidatz, Pôle Recherche&Innovation Bams, Michel; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Payan-Terral, Sandrine; Fondation Ellen Poidatz, Centre de Rééducation Fonctionnelle Khouri, Neijib; Hôpital universitaire Necker-Enfants malades Otmame, Samir; Universite Paris-Saclay, IBISC Laboratory Bouyer, Guillaume; Universite Paris-Saclay, IBISC Laboratory Desailly, Eric; Fondation Ellen Poidatz, Pôle Recherche & Innovation
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Paediatrics, Sports and exercise medicine
Keywords:	Paediatric orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric neurology < NEUROLOGY, Developmental neurology & neurodisability < PAEDIATRICS, REHABILITATION MEDICINE, Clinical trials < THERAPEUTICS

SCHOLARONE™
Manuscripts

OPEN ACCESS PROTOCOL**Effect of an Augmented Reality Active Video Game for Gait Training in Children with Cerebral Palsy following Single-Event Multilevel Surgery : Protocol for a Randomized Controlled Trial**

Anne-Laure Guinet^{1,2*†}, Michel Bams¹, Sandrine Payan-Terral¹, Neijib Khouri³, Samir Otmane², Guillaume Bouyer² and Eric Desailly^{1†}

Abstract

Introduction: In paediatric rehabilitation, fun and motivation are also critical keys to successful therapy. A variety of interventions have shown positive effects, high level of interest, compliance and engagement with active video game (AVG).

This seems to be an interesting approach for the postoperative gait rehabilitation of children with CP. In this study, we will investigate if an overground gait training (GT) delivered through an AVG can improve walking capacity and anaerobic performance.

Methods and analysis: This study is a randomized clinical controlled trial. A total of 14 children and adolescents in the age of 10–18 years with CP will be included. The minimum time between surgery and inclusion will be 7 weeks. The test group will participate in the GT program with ARRoW-CP AVG (Augmented Reality Rehabilitation of Walking-Cerebral Palsy), control group will receive GT on a treadmill. The primary outcome is the 6-Minutes Walk Test assessing walking capacity; secondary outcomes are the Muscle Power Sprint Test for anaerobic performance and Shuttle Run Test for physical fitness level. Satisfaction is tested with the Physical Activity Enjoyment Scale. This study has been registered in ClinicalTrials.gov (NCT04837105).

Ethics and dissemination: The findings will be disseminated by publications in peer-reviewed journals and conferences. This study received agreement from French ethic committee (Comité de Protection des Personnes Sud-Est VI – Number 2020-A02959-30)

Keywords: cerebral palsy; surgery; active video game; augmented reality; gait performance

1
2
3
4
5
6
7 *Correspondence: anne-laure.guinet@fondationpoidatz.com

8 1 Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, France

9 2 Université Paris-Saclay, Univ Evry, IBISC, 91020, Evry-Courcouronnes, France.

10 3 Hôpital Universitaire Necker-Enfants Malades, Paris, France

11 Full list of author information is available at the end of the article

12 †Equal contributor
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Strengths and limitations of this study

- This is the first randomized clinical trial to compare traditional rehabilitation and technology delivered gait performance training in children with cerebral palsy after surgery.
- The control group receives treadmill therapy to counterbalance the additional dose effect of active video game use in the experimental group.
- The active video game intervention being investigated have been tailored to the needs of children with cerebral palsy based on feedback from patient and public involvement and expert review groups conducted during the first phase of this project.
- Patients and patient's physiotherapist cannot be blinded; however, the professional caregiver administering outcome measures and the trial statistician will remain blinded to group allocation until the database has been locked.
- The interventions require participants to have no visual, cognitive or auditory impairment that would interfere with playing the game.

Introduction

Cerebral palsy is commonly defined as a “group of permanent disorders of the development of movement and posture, causing activity limitation”[1]. The overall prevalence of CP remains constant (2.11 per 1000 births) [2] with an estimated prevalence of 17 million people worldwide.[3] Individuals with CP present various clinical symptoms including a non-exhaustive list of neurological, orthopaedic, movement, cognitive, vision/hearing, aero digestive disorders.

Musculoskeletal disorders are considered as a secondary impairment contributing to restricted mobility in childhood and adulthood.[4, 5, 6] Since 1985, therapeutic interventions to correct orthopaedic disorders include single-event multilevel surgery (SEMLS). This surgery proposes, during one operative period, to realign the musculoskeletal system, practicing tendon transfer, muscle lengthening, derotation and/or deflexion osteotomy and joint stabilization. Novak *et al.* classified SEMLS as effective intervention for children with CP for improving both Gross Motor, walking speed and walking capacity but also contracture and alignment deformities [7]. To date, systematic reviews on the effect of SEMLS reported improvement in passive range of motion, kinematics and kinematics gait parameters, overall gait index and energy efficiency [8, 9]. Results were more disputed about the long-term effect on spatio-temporal gait parameters, gross motor function and the activity and participation domain [10].

A recent literature review has proposed a model in five steps that could guide clinicians during the post-operative rehabilitation [11]. The authors suggested that the fourth phase, which included more intensive exercises, functional gait training and resistive muscle strengthening should be optimized to improve the gross motor function and walking speed after surgery. Functional gait training has been defined as ‘actively practice the task of walking, to improve walking ability [12]. Intervention could be overground gait training (OGT), or treadmill gait training (TT), with or without body support.

Previously, Grecco *et al.* demonstrated the efficacy of treadmill gait training program including both on functional mobility and gross motor function on children with CP after SEMLS [13]. Recently, a systematic review showed that gait training was a safe and effective intervention to improve walking capacity in children with CP, outside postoperative context [12]. In particular, the minimal clinically important difference (MCID) for increase in walking speed (0.1m/s) was achieved after intervention in 12 studies/14 (studies level between II and III). Authors discussed two points: OGT could provide greater effect on locomotor abilities than TT because OGT is more representative of the natural walking, and the addition of feedback could enhance the patient outcomes. These points were important to consider after SEMLS, because the overall gait pattern of children was modified by the bone and muscle gestures. Novak *et al.* highlighted the importance of the context focused therapy and goal-directed training for children with CP [7]. Functional gait training should therefore take into account those recommendations and involve motor learning strategies: task-specific, variable practice, high intensity, augmented

1
2
3
4 feedback during therapy sessions and motivation of the patient [14].

5 In recent years, new technologies have been introduced in rehabilitation practice, both for
6 upper and lower limbs therapy. These systems include a large type of technology ranging
7 from fully immersive virtual reality (VR) or augmented reality (AR) using commercially
8 available head-mounted displays (HMD) (e.g., Oculus Quest; HTC VIVE, Microsoft
9 HoloLens), Cave Automatic Virtual Environment where video is projected on the walls
10 and floor²⁰ to video game console on television screen (e.g., Nintendo Switch,
11 PlayStation).

12 To ‘actively practice the task of walking’, systems combining treadmill training and active
13 video game (AVG) delivered through a screen in a semi-immersive environment have been
14 tested with good results [15]. However, motor learning principles are not always fully
15 integrated into VR/AR systems because of the lack of knowledge about which feedback
16 modality and which intensity level should be provided in the rehabilitation settings [16].

17
18 To our knowledge, even if OGT was recommended for functional gait training, no AR
19 system with AVG exists to provide high-intensity, with progressive difficulty, and variable
20 modalities including feedback. To this end, we have developed the active video game
21 ARRoW-CP (Augmented Reality Rehabilitation of Walking-Cerebral Palsy) combining
22 OGT based on previous results [12] and literature [17] and motor learning theory [14].
23 ARRoW-CP active video game has been developed for Microsoft HoloLens headset
24 (mixed reality headset). The team used the game development framework PROGame and
25 all stakeholders have been involved through the process (children with CP, researchers,
26 engineers, therapists)[18]. In most studies, even if feedback is effective to improve motor
27 activities, the characteristics applied during interventions were generally inconsistent with
28 motor control feedback theory. Authors suggest that timing, frequency and autonomy
29 should be adjusted to optimize long-term effect [19]. A strategy that provides feedback to
30 the user on demand promotes learning. Then, by reducing the frequency and timing of the
31 feedback, the user can develop a sense of self-regulation. In this AVG, continuous
32 feedback as well as terminal feedback, both with different audio and visual modalities,
33 are combined following the recommendations of the literature [20, 16]. The general principle
34 for defining the feedback to be used is primarily defined by the results from a previous
35 study that the team lead (article under review). Specific recommendations from this
36 previous study included using feedback moving on in front of the player at the target speed
37 to create a more challenging task that motivates participants to excel. In addition, our
38 results highlighted that the temporary modification of visual aspect according to the
39 performance (red light/too slow; green light/good speed) helped to improve walking speed
40 creating a playful challenge. The feedback attached to the player seemed to be better to
41 minimize visual discomfort and, by extension, fatigue. More details of ARRoW-CP game,
42 architecture, framework development and feedback characteristics, are available in the
43 Supplementary Files 1 and 2.

44
45
46 The current study, denoted as the ARRoW-CP study, will investigate whether a gait
47 training protocol through an active video game in AR can:

- 48 1. Increase the walking capacity
- 49 2. Increase anaerobic performance & physical fitness level
- 50 3. Improve the level of satisfaction during therapy

51
52 Our hypothesis is that the AVG ARRoW-CP is at least as effective as treadmill training to
53 improve walking performance and more enjoyable for children with CP following surgery.

54 55 **Methods and analysis**

56 **Study Design**

57
58 This study is a randomized control trial with two groups: OGT using the AVG ARRoW-
59 CP in AR (OGT-AR) and Treadmill Training control group (TT). All children and
60 adolescents participate in a four-week gait training intervention to improve their walking
function in one of this two groups. During this period, children continue their usual physical

therapy program (5 weekly 45-minutes session). This postoperative protocol has been standardized following a 5-step framework [11]. These usual rehabilitation sessions include muscle stretching exercises, muscle strengthening exercises (active resistance exercises), functional exercises (sit-to-stand, transfer, balance, walk, stairs). The study is planned to start in April 2021 and end in December 2023.

Description of the two gait training interventions

To standardize the session content as much as possible, the therapists involved in the study participate in the training sessions before the start of the study. During these sessions, a member of the project team presents them the process and objectives of this study, as well as the gait training protocol proposed for the two groups. A session is dedicated to the familiarization with Microsoft HoloLens and the ARRoW-CP game via a tutorial application.

ARRoW-CP: Overground Gait Training in AR

Intervention group receives the OGT-AR protocol through the AVG ARRoW-CP using the Microsoft HoloLens headset (Figures 1A-C). ARRoW-CP sessions are monitored by physiotherapist, assistant physiotherapist, or research assistant.

The intervention consists of 4 weeks of OGT (3 sessions per week), including a series of walking sprints. These sessions are always performed indoors, along the same flat and straight 30m in length hallway with a hard surface that is seldom traveled. The starting point is marked with a round floor sticker ARRoW-CP. Children can see the real environment because of transparency of holograms and use of augmented reality (that is different from virtual reality), but some safety measures are taken to avoid collision with other people: the caregiver signals to others that a session is in progress, checking before starting the game that there are no obstacles in the hallway. This protocol is an adaptation from Zwinkels *et al.* [17]. Every training session consists of a prescribed intensity, volume and time (Table I).

Before the first session of each week, the target velocity is calculated during a Muscle Power Sprint Test (MPST) [21]. This test is made through the ARRoW-CP game and is presented as a “calibration” to the participant. During this test, no feedback is presented to the player. The target velocity is defined as the highest velocity of 6 sprints. This test is repeated every week to adapt the difficulty of the game to the child’s progress.

Treadmill Gait Training

The control group protocol consists of 4 weeks of GT on a treadmill (3 sessions per week), with a maximal duration of 30 minutes. This protocol is an adaptation from Grecco *et al.* [13]

Before the first session, the target velocity is estimated during a treadmill speed test: participants are instructed to walk on a treadmill with increasing speed (initially 0.5 km/h and increased 0.5 km/h each minute). Each minute, children are asked about shortness of breath and the subjective responses are classified using the 1-10 Borg Rating of Perceived Exertion Scale. The test is stopped if the score is higher than 5. The target velocity is defined as 80% of the maximum speed achieved during the test.

The first 5 minutes is a warm-up time, the speed is gradually increased until reaching the target velocity. The child walks for a maximal 20 minutes at their target velocity. Then, the treadmill speed is gradually diminished over the final 5 minutes. Training could be interrupted at any time at the child’s request or physical therapist judgement. Treadmill sessions are monitored by physiotherapist, assistant-physiotherapist, or a member of the research staff.

Randomization Procedure

After baseline measures, eligible participants are randomized to the intervention or control group based on a computerized randomization program. Blocks randomization are calculated in block sizes of fours and six. The randomization procedure is only available to an independent researcher who will not be involved in the delivery of the interventions or the performance of the measurements. Due to small sample size required, the

randomization lists were not stratified.

Participants

All participants are recruited from the Poidatz Rehabilitation Centre. The children are operated in several hospitals in Paris: Necker Enfants Malades University Hospital, Trousseau University Hospital or Robert Debré University Hospital. Ethics approval is granted by the French Ethical Committee Sud-Est VI (Clermont-Ferrand). All patients meeting the study criteria were approached directly in the rehabilitation center when they were in the phase of walking recovery after surgery. Information about the study was given to them orally. They are given time to reflect. If they are interested, a physiotherapist contacts the family by phone to give them information about the study. Written consent is obtained after a further period of reflection. Additionally, all parents, and participants from 10 years of age, should provide informed consent prior to study initiation. All participants should have a cooling off period prior to the inclusion (minimum 15 days between information and consent). Confidentiality and data access are guaranteed by the National Commission of Informatic (CNIL). A Data Protection Officer has been designated for all research studies conducted in this rehabilitation centre. He guarantees that the data protection and the rights of the subject are respected according to the General Data Protection Regulation (EU) 2016/679 (GDPR). The study has been registered in ClinicalTrials.gov (Identifier: NCT04837105). Inclusion criteria are children with CP admitted for inpatient rehabilitation following SEMLS, 10–18 years of age, functioning preoperatively at GMFCS I–III. The minimum time between surgery and inclusion in the study is 7 weeks (step 4 of post-SEMLS rehabilitation process), they should have a Functional Mobility Scale 50 meters rating superior or equal to 2 (ability to walk on 50m using a walker or frame without help from another person).

All children should be able to cooperate, understand and follow simple instructions in French to practice the game. Only voluntary patients whose parents give their consent for their child's participation in the study and patient affiliated to the French social security system are included. Criteria for exclusion include a diagnosis of photosensitive epilepsy in the medical record and/or patient's case history mentioning seizures that occurred while playing a video game, visual, cognitive or auditory impairment that would interfere with playing the game. The patient must have normal or corrected vision and hearing. During the 4-weeks, children can wear their orthotic device and their assistive device as prescribed by medical staff. In cases of evolution regarding the level of support (a patient going from walking with crutches to no walking aid, for example), the medical staff decides if patient is able to practice series of walking sprints safely and efficiently according the main objective of the study, then they inform the research staff. This change should only be made during the first session of the week to proceed with the new weekly calibration and thus adapt the objective walking speed to the child's abilities.

Patient and Public Involvement

Patient involved as described above. Throughout the development phase of the ARRoW-CP active video game, test sessions were organized with some of the patients of the rehabilitation centre to collect their opinion on the game. The results of the RCT will be disseminated to the international community through the publication of articles and conference papers. It is also planned to spread these results to communicate them to parents, families, and children with motor disabilities (regional or national newspapers in French, social networks, patient associations).

Outcomes

Outcome measures take place at baseline (T0), immediately after four weeks of GT (T1), and six months later (T2). The professional caregiver administering outcome measures remains blinded to group allocation. See Supplementary File 3 for outcomes details and criterion validity.

Primary outcome : The 6 minutes walk test (6MWT) The 6MWT is increasingly used in paediatrics, in clinics to monitor patients' abilities or in research as a criterion for evaluating the effectiveness of a rehabilitation protocol [22]. The 6MWT assesses distance walked over 6 minutes as a submaximal test of aerobic capacity/endurance. The reference guideline detailing the recommendations and instructions has been updated in 2013 [23,

24]. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP [25, 26]. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness. This primary outcome is relative to the primary objective i.e. improve walking capacity.

Secondary outcome : Muscle power sprint test (MPST)

The MPST evaluates anaerobic performance of youth with CP over a 6x15 meters at their maximal speed [21]. Velocity (m/s), acceleration (m/s²), force (kg/s²) and power (watts) are calculated. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints. This secondary outcome is relative to the secondary objective i.e. improve anaerobic performance.

Secondary outcome : Shuttle Run Test (SRT)

The 10-meters shuttle run test is an adapted version of the 20-metre shuttle run test to accommodate children with cerebral palsy (CP) classified at Level I or Level II on the Gross Motor Function Classification System (GMFCS) [27]. This test evaluates cardiovascular endurance. In this study, the SRT-II will be used because of postoperative context. The SRT-II starts at 2 km/h. Speed is increased 0.25 km/h every level (minute). The test is over when the child cannot go to the next cone in time. This secondary outcome is relative to the secondary objective i.e. improve physical fitness level.

Secondary outcome : Questionnaire (PACES)

To assess enjoyment for both control and test group, the 16-items of the Physical Activity Enjoyment Scale (PACES) will be used. The PACES is a valid and reliable measure of physical activity enjoyment. It has been used in many studies assessing the effectiveness of VR therapy [28]. This questionnaire will be presented to the participant at the end of the last session. This secondary outcome is relative to the secondary objective i.e. improve satisfaction during therapy.

Sample size and statistical analysis

According to a study of Grecco et al. an average augmentation of 83% (range 80-85%) in 6MWT was calculated after following 12-weeks of treadmill training in postoperative context [13]. The distance travelled during the 6MWT increases from before: 166.4 ± 39.1 m to after: 304.7 ± 75.8 m. The effect size was calculated: $d = 2.29$. In this previous study, the mean number of training sessions throughout the 12-week period was 11.1 (around 1-session per week) i.e. total dose of 6h/12-weeks. It has been hypothesized that participants following a more intensive protocol (3 sessions/week i.e. total dose of 6h/4-weeks) will show the same effect on the 6MWT.

With an $\alpha = 0.05$ and $\beta = 0.20$ (power = 0.80), a sample size of 6 subjects per group will be required. When taking a failure rate of 10% into account, 14 subjects should be included.

The required sample size was calculated with G Power 3.1.9.7. Parameter was t-tests – Means; difference between two independent means (two groups) with a priori analysis.

The effect of the GT protocol will be analyzed using a multivariate repeated measures ANOVA. The possible differences between and within T0, T1 and T2 for the intervention group and control group will be calculated with a statistical significance level of $p = 0.05$. If there is a significant difference, a post-hoc test will be executed to further investigate group differences. Quantitative descriptive statistics will be used to present patient characteristics and global results. Data from PACES questionnaire will be analyzed using normality test (deciding to use parametric / non-parametric statistics), descriptive statistics, reliability test (Cronbach Alpha / Composite Reliability), Pearson / Spearman correlational test. All statistical analyses will be performed using R with a statistical significance level of $p = 0.05$. Moreover, the trial statistician will remain blinded to group allocation until the database has been locked.

Ethics and dissemination: The findings will be disseminated by publications in peer-reviewed journals and conferences. This study received agreement from French ethic committee (Comité de Protection des Personnes Sud-Est VI – Number 2020-A02959-30)

Discussion

This approach has evolved from two directions: interest to improve walking capacity after SEMLS for children with CP, and from concern that the usual post-operative rehabilitation approach has not produced sustainable improvements in participation and activity in daily life for these children [8].

AVG development framework

This work followed the AVG development framework PROGame, proposed by Amenguai Alcover *et al.* [18]. A participate process including both professional healthcare and patients has been conducted. The first step was the project initiation. The team identified the need for a AVG, the stakeholders, and user categories (users and experts). They also clarified the game functionality and constraints. They selected the therapy to transfer into the AVG. The operational objectives were to be safe; to provide efficient gait training; to improve walking speed; to motivate the patient; to be fun. These identifications were based upon prior experience and literature review [12, 29]. The team used communication tools like oral presentation of preliminary results, open debates, surveys and meeting reports. The aim was to support incremental development between team's members (that has their own specialty) and to share knowledge. At this stage, the project proposed a general description. The second step was the interaction mechanism, all technical solutions were explored and an algorithm for gait parameters detection was developed and tested [30, 31]. During the third step, the interactive elements, the team investigated actual commercial or AVGs to get inspired. Team exploration and discussion conducted to games like Pokemon Go or Zelda, in which the gamer must explore the world and accomplish missions. These games appear very popular with the younger generation. The development team was composed of therapists (3 physiotherapists), researchers (2 in computer science, 1 in rehabilitation science, 1 in movement science) and a software engineer. These steps occurred between January 2020 and June 2021. All details are available in Supplementary File 2.

The aim was to think together about the best solution for improving postoperative results, especially walking capacity. New technologies were young people's preferred solution. These solutions seem to be a very promising tools for rehabilitation purposes, allowing to manipulate the environment, to offer interaction, to optimize feedback and many other potentialities [19, 32]

Feedback, a key point for motor learning

Feedback retraining paradigm is based on the conversion, the supplementation and augmentation of sensory information that are usually accessible only by an internal focus of attention, to accessible information [32, 33]. In this paradigm, augmented feedback is defined as augmented sensory information provided by an external resource (therapist or display) to the patient [34]. The information provided to the user could be relative to the movement's pattern or result on the environment or the outcome of a movement with respect to the goal. Sensory channels used to deliver information are visual, auditory, or haptic, linked to the proprioception properties of humans. The timing of feedback delivery is critical. Concurrent feedback is delivered while the skill is being performed, terminal feedback is delivered after the skill is performed with or without delay [35]. In our previous study, we have confirmed that children with CP can adapt their walking speed, and they can positively respond to the real-time AR feedback (article under review). However, we have observed that not all patients performed equally well with the scenarios. When we have looked at the individual responses of each participant for each scenario, we have observed some essential differences. Some people did not perform better with the feedback; others were helped by a particular feedback but disturbed with another. Some authors highlighted these inter-individual differences. Recently, Liu *et al.* have underscored different patient

1
2
3
4 profiles: "non-responders" and "responders" to the feedback [19]. In their study, patients were
5 people after stroke. They were instructed to walk on a treadmill while visualizing an avatar
6 replicating their exact walking pattern in real-time on a large screen. Overall, patients
7 improved step length and walking speed when the avatar was displayed on a side view. But
8 results were not the same for all participants; the authors distinguished non-responders and
9 responders to the feedback. They hypothesized that the initial step length ratio could
10 influence the result because patients with a larger paretic step length better responded.
11 This study has shown that specific populations are more sensitive to the virtual
12 environment.

13 14 Serious aspect of ARRoW-CP game

15 ARRoW-CP AVG combines many of the motor learning theories: context focused therapy
16 and goal-directed training, task-specific, variable practice, high intensity, augmented
17 feedback during therapy sessions and motivation of the patient [16]. To find the best
18 feedback modalities for our AVG, we have conducted preliminary studies exploring the
19 impact of feedback modalities on walking speed, both in healthy adults and in children
20 with CP. Study on healthy adults showed that certain feedback helped to increase walking
21 speed, provided that the game instruction was clear. Typically, feedback combining a
22 focus of attention with knowledge of results, a spatial representation with world-locked
23 holograms and a method of presentation with rich holographic content (like animation,
24 colour changes) increased walking speed in healthy subject [36]. This step allowed us
25 to modify and adapt feedback modalities (Figures 1A-C).

26
27 A second study has occurred with children with CP. Results showed that scenarios
28 combining world-locked holograms that disappeared over the time helped children with
29 CP to reach their target speed. On the other hand, a body-locked hologram that advances
30 in front of the user at the target speed was better able to control the walking speed of the
31 patient[37].

32 ARRoW-CP is an adaptation of the validated protocol from Zwinkels et al. The original
33 protocol consists of 8 weeks, twice a week [17]. Every training session consisted of a 30s
34 walking sprints following the pre-scribed intensity, volume, and time: Week 1 to week 2:
35 8 sprints, work/rest ratio 1:4; Week 3 to week 4: 10 sprints, work/rest ratio 1:4; Week 5
36 to week 8: 12 sprints, work/rest ratio 1:3. Because of post-operative context, the intensity
37 should be reduced. At the beginning of the fourth step of rehabilitation process, even if
38 gait training is recommended, children did not recover to their pre-operative level,
39 specifically some children needed crutches or k-walkers. Moreover, a further aspect not to
40 be underestimated: fatigue and pain [38]. The choice of intensity, volume and time in the
41 ARRoW CP protocol is based on practical experience from expert clinician and from
42 literature [12, 17].

43
44 This article presents in detail the gait training protocol tested through a RCT. Both control
45 group and experimental group have an evidence-based physical therapy training. This
46 article also presents the game development framework of the ARRoW-CP AVG. This
47 game is based on the most recent motor learning approach. This is the first study assessing
48 the efficacy of postoperative gait rehabilitation using an active video game. If our
49 hypothesis is validated, ARRoW-CP game will make possible to intensify gait training.
50 This innovative strategy will have significant clinical impact by improving walking
51 capacity for children after SEMLS. Publishing study protocol of the RCT offers the
52 opportunity to collaborate with other teams and to give more details about the study. Results
53 will be available in 2023.

54 55 Limitations

56 The limited sample size limit the ability to balance the two groups according the gender,
57 age, GMFCS level and type of surgery. The randomization lists were not stratified. But
58 the next step in the ARRoW-CP project is to modify the game based on our initial results
59 and to conduct a new RCT including more centers (and more children) worldwide. Using
60

1
2
3
4 AR for therapy is not suitable for all children. We excluded patients with cognitive trouble
5 and with patients high risks of fall based on medical recommendations.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Tables

Table 1 Details of the gait training protocol deployed in the active video game ARRoW-CP

	WEEK 1	WEEK 2	WEEK 3	WEEK 4
Session Number per week	3	3	3	3
Sprint Time (s)	30	30	30	30
Rest Time (min:s)	2:00	2:00	1:30	1:30
Sprint Number	4	6	8	10
Total time of the session	10	15	18	22

Figures 1A-C. Image capture from ARRoW-CP active video game. On the left (A), this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle (B), an adult (not a patient) wearing the Microsoft Hololens AR headset to see holograms. On the right (C), game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard).

Supplementary Files

Supplementary file 1 — ARRoW-CP Active Video Game

Supplementary file 2 — Active Video game development framework

Supplementary file 3 — Main Outcomes details and criterion validity.

Author details

¹ Fondation Ellen Poidatz, Research&Innovation department, Saint Fargeau Ponthierry, France.

² Université Paris-Saclay, Univ Evry, IBISC, 91020, Evry-Courcouronnes, France.

a. Contributorship

ALG, GB, SO and ED conceived the study, participated in its design, and helped to draft the manuscript. SPT, NK and MB participated in the acquisition and coordination of the study. All authors read, revisit it critically and approved the final manuscript. All of them affirm that the manuscript is an honest, accurate, and transparent account of the study being reported.

b. Funding statement

This study is a part of the ARRoW CP project supported by the Association Nationale Recherche et Technologie (ANRT) ID CIFRE 2018/0973. This is a public sponsor that does not influence the study.

c. Competing interests

There are no competing interests for any author.

For peer review only

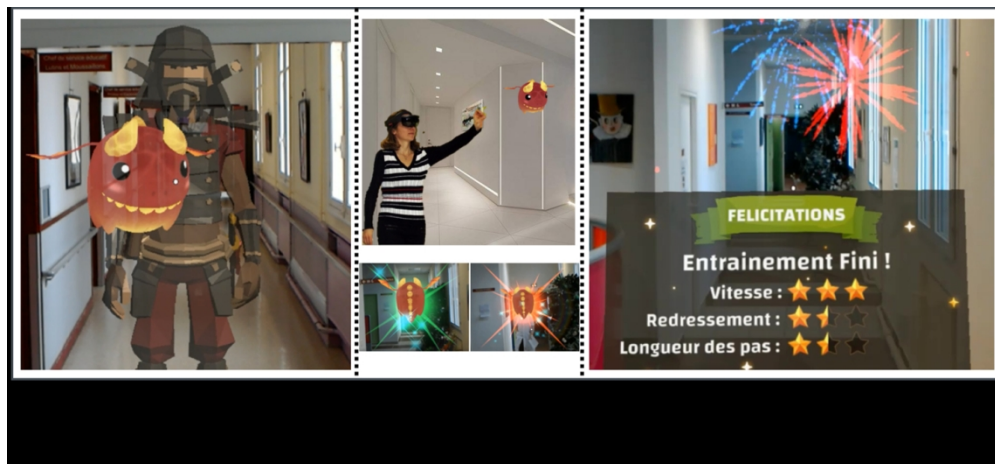
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M., Damiano, D., Dan, B., Jacobsson, B.: A report: the definition and classification of cerebral palsy april 2006. *Developmental Medicine and Child Neurology* **109**, 8–14 (2007). doi:10.1111/j.1469-8749.2007.tb12610.x
2. Oskoui, M., Coutinho, F., Dykeman, J., Jett'e, N., Pringsheim, T.: An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology* **55(6)**, 509–519 (2013). doi:10.1111/dmcn.12080
3. Graham, H.K., Rosenbaum, P., Paneth, N., Dan, B., Lieber, R.L.: Cerebral palsy. *Nat Rev Dis Primers* **2(1)**, 15082 (2016). doi:10.1038/nrdp.2015.82
4. Park, E.: Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. *Health and Quality of Life Outcomes* **16(1)**, 383–390 (2018). doi:10.1186/s12955-018-0891-1
5. Himuro, N., Mishima, R., Seshimo, T.: Change in mobility function and its causes in adults with cerebral palsy by gross motor function classification system level: A cross-sectional questionnaire study. *NeuroRehabilitation* **42(4)**, 383–390 (2018). doi:10.3233/NRE-172340
6. Benner, J., Hilberink, S., Roebroek, M.: Long-term deterioration of perceived health and functioning in adults with cerebral palsy. *Arch Phys Med Rehabil*. **98(11)**, 2196–2205 (2017). doi:10.1016/j.apmr.2017.03.013
7. Novak, I., Morgan, C., Badawi, N.: State of the evidence traffic lights 2019: Systematic review of interventions for preventing and treating children with cerebral palsy. *Curr Neurol Neurosci Rep* **20(2)**, 3–24 (2020). doi:10.1007/s11910-020-1022-z
8. McGinley, J.L., Dobson, F., Ganeshalingam, R., Graham, H.K.: Single-event multilevel surgery for children with cerebral palsy: a systematic review. *Dev Med Child Neurol* **54(2)**, 117–128 (2012). doi:10.1111/j.1469-8749.2011.04143.x
9. Lamberts, R.P., Burger, M., Langerak, N.G.: A systematic review of the effects of single-event multilevel surgery on gait parameters in children with spastic cerebral palsy. *PLoS ONE* **11(10)**, 0164686 (2016). doi:10.1371/journal.pone.0164686
10. Amichai, T., Harries, N., Dvir, Z., Patish, H., Copeliovitch, L.: The effects of femoral derotation osteotomy in children with cerebral palsy: an evaluation using energy cost and functional mobility. *J Pediatr Orthop* **29**, 68–72 (2009). doi:10.1097/BPO.0b013e3181924331
11. Guinet, A., Khouri, N., Desailly, E.: Rehabilitation after single-event multilevel surgery for children and young adults with cerebral palsy: A systematic review. *American Journal of Physical Medicine & Rehabilitation* **21**, 2697 (2021). doi:10.1097/PHM.0000000000001864
12. Booth, A., Buizer, A., Meyns, P., Van der Krogt, M.: The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis. *Developmental Medicine and Child Neurology* **60(9)**, 866–83 (2018). doi:10.1111/dmcn.13708
13. Grecco, L., De Freitas, T., Satie, J., Bagne, E., Oliveira, C., De Souza, D.: Treadmill training following orthopedic surgery in lower limbs of children with cerebral palsy. *Pediatr Phys Ther* **25(2)**, 187–192 (2013). doi:10.3109/17453674.2014.960141
14. Cano-de-la-Cuerda, R.: Theories and control models and motor learning: Clinical applications in neurorehabilitation. *Neurología* **30(1)**, 32–41 (2021). doi:10.1016/j.nrleng.2011.12.012
15. Cho, C., Hwang, W., Hwang, S., Chung, Y.: Treadmill training with virtual reality improves gait, balance, and muscle strength in children with cerebral palsy. *The Tohoku Journal of Experimental Medicine* **238(3)**, 213–8 (2016). doi:10.1620/tjem.238.213

16. Demers, M., Fung, K., Subramanian, S., Lemay, M., Robert, M.: Do virtual interventions in individuals with cerebral palsy make use of motor learning principles?: A systematic review (preprint). *JMIR Serious Games* **XX**, (2020). doi:10.2196/23822
17. Zwinkels, M., Verschuren, O., De Groot, J.: Effects of high-intensity interval training on fitness and health in youth with physical disabilities. *Pediatric Physical Therapy* **31(1)**, 84–93 (2019). doi:10.1097/PEP.0000000000000560
18. Amengual-Alcover, E., Jaume-i-Cap'ó, A., Moy'a-Alcover, B., Martinuzzi, A.: Progame: A process framework for serious game development for motor rehabilitation therapy. *PLOS ONE* **13(5)**, 0197383 (2018). doi:10.1371/journal.pone.0197383
19. Liu, L., Sangani, S., Lamontagne, A.: Real-time avatar-based feedback to enhance the symmetry of spatiotemporal parameters after stroke: Instantaneous effects of different avatar views. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* **28(4)**, 878–887 (2020). doi:10.1109/TNSRE.2020.2979830
20. MacIntosh, A., Desailly, E., Biddiss, E.: A biofeedback-enhanced therapeutic exercise video game intervention for young people with cerebral palsy: A randomized single-case experimental design feasibility study. *PLoS One* **15(6)**, (2020). doi:10.1371/journal.pone.0234767
21. Verschuren, O., Bongers, B., Obeid, J., Ruyten, T., Takken, T.: Validity of the muscle power sprint test in ambulatory youth with cerebral palsy. *Pediatric Physical Therapy* **25(1)**, 25–28 (2013). doi:10.1097/PEP.0b013e3182791459
22. Gillett, J., Lichtwark, G., Boyd, R., Carty, C., Barber, L.: The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy. *Gait & Posture*. **70**, 323–329 (2019). doi:10.1016/j.gaitpost.2019.03.023
23. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, .: Ats statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111–117 (2002). doi:10.1164/ajrccm.166.1.at1102.
24. Shirley Ryan Ability Lab, .: The 6 minute walk test: Instrument details (2021). <https://sralab.org/rehabilitation-measures/6-minute-walk-test>
25. Slaman, J., Dallmeijer, A., Van Den Berg-Emons, R.: The six-minute walk test cannot predict peak cardiopulmonary fitness in ambulatory adolescents and young adults with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **94(11)**, 2227–2233 (2013). doi:10.1016/j.apmr.2013.05.023
26. Maltais, D., Robitaille, N., Dumas, F., Boucher, N., Richards, C.: Measuring steady-state oxygen uptake during the 6-min walk test in adults with cerebral palsy: feasibility and construct validity. *Int J Rehabil Res* **35(2)**, 181–183 (2012). doi:10.1097/MRR.0b013e3283527792
27. Verschuren, O., Takken, T., Ketelaar, M., Gorter, J., Helders, P.: Reliability and validity of data for 2 newly developed shuttle run tests in children with cerebral palsy. *Physical therapy* **86(8)**, 1107–1117 (1988). doi:10.1080/02640418808729800
28. Motl, R., Dishman, R., Saunders, R., Dowda, M., Pate, R.: Measuring enjoyment of physical activity in adolescent girls. *Am J Prev Med* **21**, 110–117 (2001). doi:10.1016/S0749-3797(01)00326-9
29. Fehlings, D., Switzer, L., Findlay, B., Knights, S.: Interactive computer play as "motor therapy" for individuals with cerebral palsy. *Semin Pediatr Neurol* **20(2)**, 127–38 (2013). doi:10.1016/j.spen.2013.06.003

- 1
2
3
4 30. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Reliability of the head tracking measured by
5 microsoft hololens during different walking conditions. *Comput Methods Biomech Biomed*
6 *Engin* **xx**, 159–161 (2019). doi:10.1080/10255842.2020.1714228
7
8 31. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Validity of hololens augmented reality head
9 mounted display for measuring gait parameters in healthy adults and children with cerebral
10 palsy. *Sensors* **21**, 2697 (2021). doi:10.3390/s21082697
11
12 32. Levin, M.F.: *Feedback and Virtual Environments for Motor Learning and Rehabilitation* vol.
13 2(1), pp. 19–36 (2010)
14
15 33. Booth, A.T., Buizer, A.I., Harlaar, F.: Immediate effects of immersive biofeedback on gait in
16 children with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* **100(4)**, 598–605
17 (2019). doi:10.1016/j.apmr.2018.10.013
18
19 34. Durkin, M.S., Maenner, M.J., Benedict, R.E., Yeargin-Allsopp, M.: The role of socio-
20 economic status and perinatal factors in racial disparities in the risk of cerebral palsy. *Dev Med*
21 *Child Neurol* **57(9)**, 835–843 (2015). doi:10.1111/dmcn.12746
22
23 35. MacIntosh, A., Lam, E., Vigneron, V., Vignais, N., Biddiss, E.: Biofeedback interventions for
24 individuals with cerebral palsy: a systematic review. *Disability and Rehabilitation* **41(20)**,
25 2369–2391 (2019). doi:10.1080/09638288.2018.1468933
26
27 36. Guinet, A., Khouri, N., Desailly, E.: Clinical gait analysis and physical examination don't
28 correlate with physical activity of children with cerebral palsy. cross-sectional study. *International*
29 *Biomechanics* **7(1)**, 88–96 (2020). doi:10.1080/23335432.2020.1812429
30
31 37. Guinet, A., Bouyer, G., Otmane, S., Desailly, E.: Towards an ar game for walking rehabilitation:
32 Preliminary study of the impact of augmented feedback modalities on walking speed. *IEEE*
33 *International Symposium on Mixed and Augmented Reality Adjunct* **1**, 264–268 (2020). Doi:
34 10.1109/ISMAR-Adjunct51615.2020.00075
35
36 38. Hoiness, P., Capjon, H., B, L.: Pain and
37 rehabilitation problems after single- event
38 multilevel surgery including bony foot
39 surgery in cerebral palsy. a series of 7
40 children. *Acta Orthop* **85(6)**, 646–651
41 (2014).
42 doi:10.1097/PEP.0b013e3182888495
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Figures 1A-C. Image capture from ARroW-CP active video game. On the left (A), this is Yuki, the little dragon that children must follow during walking sprints, and Master Keito, who oversees providing Ninja gait training. On the middle (B), an adult (not a patient) wearing the Microsoft HoloLens AR headset to see holograms. On the right (C), game elements encourage participants, increase motivation and improve adherence to the therapy (game scoreboard)

289x134mm (130 x 130 DPI)

ARROW-CP Serious game for gait rehabilitation

1. The Microsoft HoloLens Headset is used for ARROW-CP (**Figure 1**). Game development was made with Unity 2019.4.8f1 and Mixed Reality Toolkit (MRTK). MRTK-Unity is a Microsoft-driven project that provides a set of components and features, used to accelerate cross-platform MR app development in Unity.



Figure 1. Microsoft HoloLens Augmented reality headset.

2. The player is immersed in a samurai world. He meets the chief of the village that can no longer protect its population. The natural elements are unleashed, causing famine and various damages. The player's role is to develop his energy through ninja training to build a protective totem for the village's inhabitants (trailer: <https://youtu.be/BbmiiiiJuaA>).

The software architecture is presented in **Figure 2**.

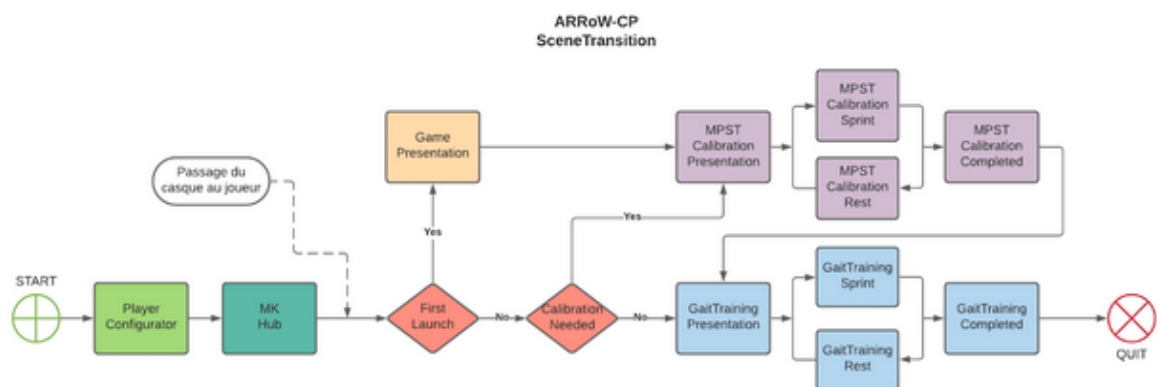


Figure 2. Game architecture of the ARROW CP game. When the game starts, the AR headset is worn by the therapist. He creates the user profile of the player by entering his name, first name, age, height, and weight during session 1 week 1. Next session, he loads the existing user profile. The therapist then accesses the “MK Hub”, which contains information about the performance of previous sessions and the number of sessions

3. The mechanism of feedback provided during sprints and rest time is detailed in **Figure 3**.

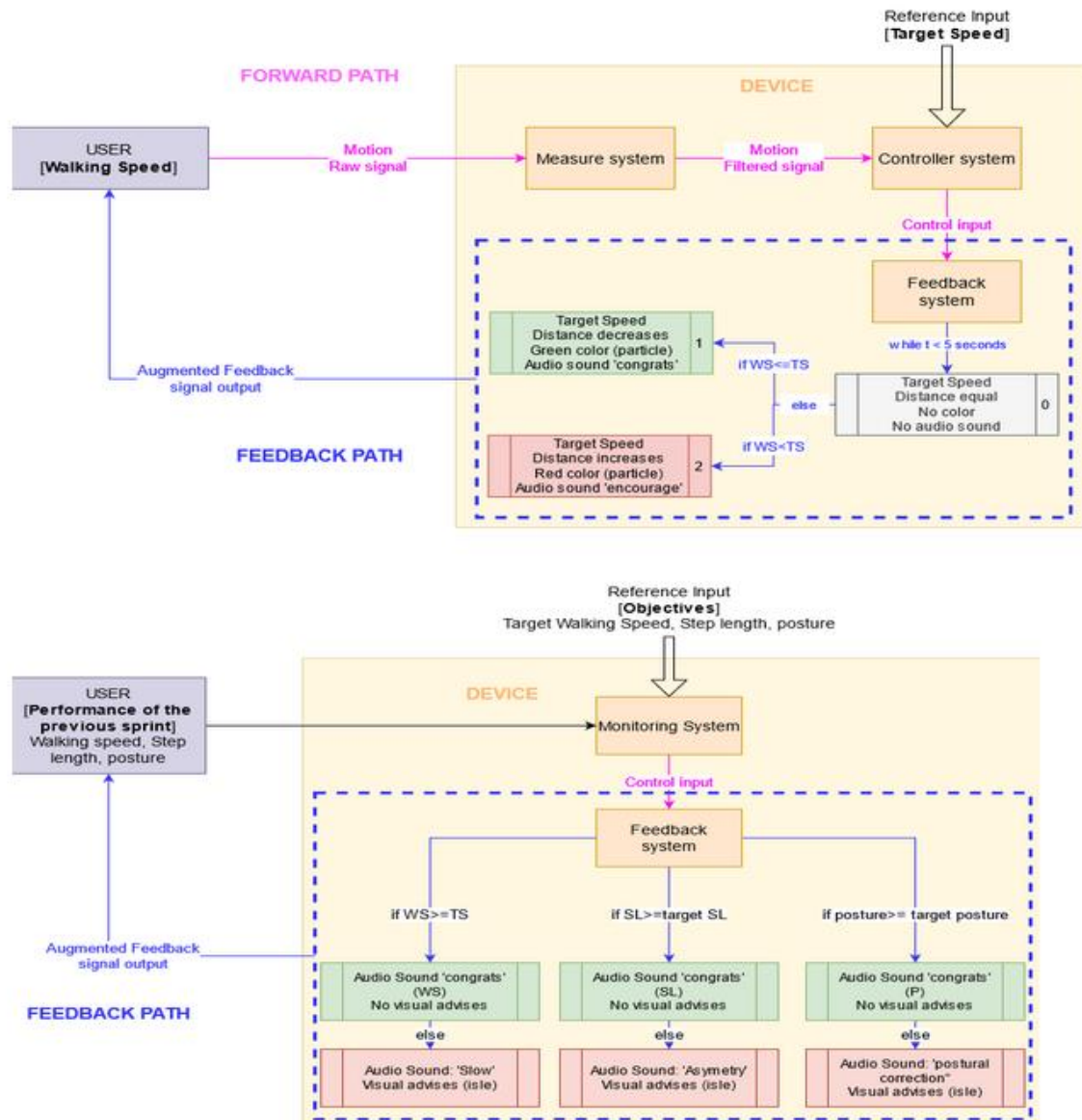


Figure 3. Feedback mechanism during sprints (A) and rest period (B).

At the beginning of each session, through the "Physio HUB", therapists know the previous performance of their patient and they can adjust their advice.

At the end of each session, feedback with delay is proposed to the child: they can choose to see their actual performance through the game scoreboard and totem construction (feedback on demand). These feedbacks were based on knowledge of results.

Project Initiation

Interaction Mechanism

Interaction Elements

2-061580 on 10 October 2022. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

7	Global Aim	to develop an active video game for gait rehabilitation for children with motor disabilities and particularly cerebral palsy
8		
9	Operational objectives	To be safe;
10		to provide efficient gait training;
11		to improve walking speed;
12	<i>describe the needs in general</i>	to motivate the patient;
13		to be fun.
14		
15		
16	Restrictions	The development of the game must correspond to the duration of a 3-year thesis; grants are limited and predefined; the agreement of the ethics committee and written consents from participants are required before any test on humans ; all technical solution could be explored.
17	<i>detail economical, technical, operational, legal restrictions</i>	
18		
19		
20		
21		
22		
23		
24		Customers :
25		Children with cerebral palsy, 10-18 years old, GMFCS I-III, with cognitive skills to understand and follow simple instructions == END USERS
26		Physiotherapists, occupational therapists, physiotherapist assistants, rehabilitation therapists == EXPERTS
27	Stakeholders	Special needs and required functionalities :
28	<i>Identify customers, special needs and required functionality ; define experts and representatives end users</i>	The active video game must include the principles of motor learning, which are task-specific practice, variable practice, high practice intensity, progressive difficulty, augmented feedback, and adaptability to user abilities.
29		The active video game should allow the inclusion of motivational elements to increase engagement.
30		Children must be free to move in the global environment, without restriction of movement.
31		Children must be able to use their usual walking aids (crutches or posterior walker).
32		Therapists should have access to the previous and global performance of their patient through the game
33		The solution should be "ready to use" easily both for children and therapists
34		
35		
36		
37		
38		
39	Therapy Selection	The team's members agreed on making walking speed the main variable input of the serious game. Meaningful reason is that intensive gait training focused on walking speed has shown their clinical efficacy. ^{12,39} The therapy to transfer into the serious game should include walking sprints.
40		
41		

7	Aim of this phase	To select the interaction system and to capture the therapy into the system.
8		
9		
10		
11		
12		
13		
14		Device: Microsoft Hololens AR headset version 1 was selected because its technical characteristics matched all identified specifications.
15	Device selection	Tools : - Unity software (version 2019.4.8f1) -Microsoft Visual Studio 2019 - Mixed Reality Toolkit for Unity (MRTK version 4.2.3)
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		
29		
30		
31		
32		
33		
34		
35		
36		
37		
38		
39		
40		
41		

7	Aim of this phase	To design the interaction elements that force patients to perform the therapy correctly.
8		
9		
10		
11		
12		
13		
14		We have proposed a model of feedback in Augmented Reality (AR) for Motor Rehabilitation (article not published yet). Indeed, AR feedback can be displayed to the user through different characteristics. This theoretical work was necessary before designing feedback and testing specific characteristics of the model. The final aim was to optimize the augmented information provided to the patient. To carry out this work, we extended and adapted the biofeedback model described by Macintosh et al., and the qualitative model from Martinez et al., to the AR context. Our descriptive model of feedback in AR application helped us design an AR application, called Best-Of ARRoW.
15	Feedback reflexion	We have tested with this app, the impact of different virtual feedback characteristics on walking speed of children with CP. The results of this first study will be published soon (article under review). This help us to better design the feedback used in ARRoW-CP AVG.
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		
29		
30		
31		
32		
33		
34		
35		
36		
37		
38		
39		
40		
41		

Test name	Instructions	Validity
<p>[PRIMARY OUTCOME]</p> <p><i>The 6 minutes walk test (6MWT)</i></p>	<p>To summarize, patients are instructed to walk, not run, as far as they could along a 20-m level surface track during a 6-minute period. This shorter distance has been validated for children in order to be more focused on the task. They could use their usual walking aids. After each minute, participants are told the elapsed time and standardized encouragement is provided. Patients are allowed to stop and rest during the test but are instructed to resume walking as soon as they feel able to do so. The stopwatch is not stopped during this time. The 6MWT distance (in meters) is registered. Measured 6MWT distance could be compared with normative values for children with CP. It is recommended to monitor heart rate during the 6MWT.</p>	<p>In population of children with CP, test/retest reliability is excellent for distance output (ICC=0.98). The 6MWT is poorly related to VO2 peak in ambulatory adolescents and young adults with CP. The 6MWT is a more suitable measure of walking capacity than peak cardiopulmonary fitness in children with CP. The 6MWT outcome appears to be more strongly influenced by potential limits to walking speed rather than cardiopulmonary fitness.</p>
<p>[SECONDARY OUTCOME]</p> <p><i>Muscle power sprint test (MPST)</i></p>	<p>The 15-m distance is marked by 2 lines taped to the floor. Cones are placed at the end of each of the lines. Participants are instructed to walk as fast as possible from one line to the other, and to be sure to cross each line. Between each run, participants are allowed to rest for 10 seconds before turning around to allow them to prepare for the following sprint. Children should be encouraged to give maximal effort. The following variables are calculated for each of the 6 sprints: velocity (m/s) = distance/time, acceleration (m/s²) = velocity/time, force (kg/s²) = body mass × acceleration, and power (watts) = force × velocity. Anaerobic performance is defined as peak and mean power. Peak power (PP) is the highest power of 6 sprints and mean power (MP) is the average over 6 sprints.</p>	<p>The MPST is a valid test to assess the anaerobic performance in children with CP, significant correlations between the performance on these tests for both PP and MP were found. (PP: r = 0.731 ; MP: r = 0.903). Standard error of measurement (SEM), minimal detectable change (MDC) and normative data are available in Verschuren et al. The children with CP had impaired anaerobic performance as it was lower than that of their peers.</p>
<p>[SECONDARY OUTCOME]</p> <p><i>10-meters Shuttle Run Test (SRT)</i></p>	<p>Description of the test is available here : “The course is 10 metres long; the end is marked with 2 cones and measuring tape. Subjects should wear regular sports clothing and shoes, and orthoses, if applicable. Each child should also wear a heart rate monitor. Children walk or run between the 2 markers at a set incremental speed. These runs are synchronised with a pre-recorded sound. (...) As the test proceeds, the interval between each successive beep reduces, forcing the child to increase speed over the course of the test, until it is impossible to keep in sync with the recording.” We have developed a mobile application that beeps at regular intervals, indicates the time spent and allows the assessor to increment the number of shuttles made by the child.</p>	<p>The SRT is a valid and reliable test. Test-retest is excellent (ICC=0.99) and high correlations were found for the relationship between data for both shuttle run tests and data for the treadmill test (r=0.96).</p>
<p>[SECONDARY OUTCOME]</p> <p><i>Physical Activity Enjoyment Scale (PACES)</i></p>	<p>This is a 5-point Likert scale (from 1- I totally disagree to 5- I totally agree). A translation procedure from English to French language has been made using guidelines (figure).</p>	<p>The PACES is a valid and reliable measure of physical activity enjoyment.</p>

BMJ Open: first published as 10.1136/bmjopen-2022-025180 on 10 October 2022. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	na
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	7
	5b	Name and contact information for the trial sponsor	na
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	na
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1-3
	6b	Explanation for choice of comparators	1-3
Objectives	7	Specific objectives or hypotheses	3
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	3

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	3
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	2-3
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	na
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	na
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	na
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	4-5
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	4
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	5
---------------------	-----	--	---

1				
2	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central	na
3	concealment		telephone; sequentially numbered, opaque, sealed envelopes),	
4	mechanism		describing any steps to conceal the sequence until interventions are	
5			assigned	
6				
7	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,	4-5
8			and who will assign participants to interventions	
9				
10	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial	4-5
11	(masking)		participants, care providers, outcome assessors, data analysts), and	
12			how	
13				
14				
15		17b	If blinded, circumstances under which unblinding is permissible, and	4-5
16			procedure for revealing a participant's allocated intervention during	
17			the trial	
18				
19				

Methods: Data collection, management, and analysis

20				
21				
22	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other	5
23	methods		trial data, including any related processes to promote data quality (eg,	
24			duplicate measurements, training of assessors) and a description of	
25			study instruments (eg, questionnaires, laboratory tests) along with	
26			their reliability and validity, if known. Reference to where data	
27			collection forms can be found, if not in the protocol	
28				
29				
30		18b	Plans to promote participant retention and complete follow-up,	5
31			including list of any outcome data to be collected for participants who	
32			discontinue or deviate from intervention protocols	
33				
34	Data	19	Plans for data entry, coding, security, and storage, including any	5
35	management		related processes to promote data quality (eg, double data entry;	
36			range checks for data values). Reference to where details of data	
37			management procedures can be found, if not in the protocol	
38				
39				
40	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.	5
41	methods		Reference to where other details of the statistical analysis plan can be	
42			found, if not in the protocol	
43				
44		20b	Methods for any additional analyses (eg, subgroup and adjusted	5
45			analyses)	
46				
47		20c	Definition of analysis population relating to protocol non-adherence	5
48			(eg, as randomised analysis), and any statistical methods to handle	
49			missing data (eg, multiple imputation)	
50				
51				

Methods: Monitoring

52				
53				
54	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role	na
55			and reporting structure; statement of whether it is independent from	
56			the sponsor and competing interests; and reference to where further	
57			details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	na
2				
3				
4				
5				
6	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	5
7				
8				
9				
10				
11	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	na
12				
13				
14				

Ethics and dissemination

15				
16				
17	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	1
18				
19				
20				
21	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	na
22				
23				
24				
25				
26	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
27				
28				
29				
30		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	na
31				
32				
33	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	na
34				
35				
36				
37	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	7
38				
39				
40				
41	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	na
42				
43				
44				
45	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	na
46				
47				
48	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	na
49				
50				
51				
52				
53				
54		31b	Authorship eligibility guidelines and any intended use of professional writers	na
55				
56				
57		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	na
58				
59				
60				

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	na
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	na

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

For peer review only