This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

Date of publication xxxx 00, 0000, date of current version xxxx 00, 0000.

Digital Object Identifier 10.1109/ACCESS.2017.Doi Number

Virtual Reality for Pain Management in Cancer: A Comprehensive Review

MELPO PITTARA[1,3], MARIA MATSANGIDOU[2], KYRIAKOS STYLIANIDES[4], NICOLAI PETKOV[1], AND COSTANTINOS S. PATTICHIS[2,3]

[1] Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligent, University of Groningen
[2] Research Centre on Interactive Media, Smart Systems and Emerging Technologies RISE
[3] Department of Computer Science, University of Cyprus
[4] Cyprus Association of Cancer Patients and Friends PASYKAF

Corresponding author: Melpo Pittara (e-mail: m.pittara@rug.nl).

ABSTRACT Virtual Reality is a computer-simulated 3-Dimensional technology in which the user interacts via different senses: visual, auditory, tactile, and/or olfactory. In the past decades, it has been argued that Virtual Reality as a technique could be applied in the clinical environment to successfully manage pain. This article provides a systematic review of research on Virtual Reality and pain management for patients who are suffering from cancer. More specifically, this article focuses on all types of Virtual Reality technologies (Non-Immersive, Semi-Immersive, Fully-Immersive) which has been developed and released to manage the pain which evokes from the treatment of cancer. An exhaustive search identified 23 relevant studies from 2010 to 2020. Overall, the identified studies indicated that Virtual Reality can improve the experience of pain for patients who are suffering from cancer. It was also found that, if Virtual Reality is appropriately designed, the pain which is arising from cancer treatments can be reduced. Even though some positive outcomes have been reported, overall, the results are inconclusive and studies that examine specifically the treatment of pain in cancer patients are limited. Further research needs to be conducted, to articulate clearly, under what circumstances Virtual Reality is an effective tool for cancer patients, and under what factors Virtual Reality can be the solution to the pain patients are experiencing.

INDEX TERMS Virtual Reality; Cancer; Pain; Interactive Devices.

I. INTRODUCTION

Pain has been characterised as a multidimensional and complex phenomenon that refers to a negative sensation, related to a sense of self-danger that arise at the brain, and can be caused via an injury, illness or any invasive medical process [1], [2], [3], [4], [5]. A variety of pharmacological analgesics have been used to treat pain, with unwanted side effects. To overcome this issue several psychological methods (e.g., distraction techniques such as deep breathing and mindfulness training) have been used as an alternative and effective solution [2]. This is because Virtual Reality (VR) can offer an advance alternative solution to traditional psychological practices since it distracts the patients from the painfully sensory signals and draws their attention to the virtual experience [6], [7]. Based on Ma and Zheng (2011) [8] there are three types of VR systems: (a) Non-Immersive; (b) Semi-Immersive; and (c) Fully-Immersive. A Non-Immersive VR system is a desktop computer-based 3D graphical system which allows the user to navigate the Virtual Environment (VE) through keyboard, mouse and a small computer screen. A Semi-Immersive system is an improved system; where the graphical display is projected on a large screen, and there may be some forms of gesture recognition system for natural interactions. Finally, a Fully-Immersive is a Head-Mounted Display (HMD) system where users' vision is fully enveloped, creating a sense of full immersion and the interactions with the system are based on natural gesture recognition processes. In the past years, low-cost immersive VR systems have been developed and released providing a feasible and accessible solution that can implement in real-words clinical settings. In particular, during the past two decades, there is an exponential increase in the use of VR technology to treat the mental and physical health with the results to indicate that the use of VR into the medical field can enhance the treatment outcomes and their long-term effects. For the mental health, it has been found that VR exposure therapy can be a conceivable solution for anxiety and post-traumatic stress disorders [9], [10], [11], it can also enhance the treatment of psychosis, delivering cognitive rehabilitation, social skills training interventions and VR-assisted therapies, eating disorders, autism, and smoking addiction [12], [13], [14], [15], [16], [17]. For the treatment of physical health research in the field of VR has examined its use to manage procedural pain during several invasive medical processes (e.g., wound debridement, phlebotomy, dental examination, etc) or to ameliorate pain for chronic conditions (e.g., burn-injured patients) [2]. Cancer is a neoplastic disease [18], where "normal cells evolve progressively to a neoplastic state, they acquire a succession of these hallmark capabilities, and that the multistep process of human tumour pathogenesis could be rationalized by the need of incipient cancer cells to acquire the traits that enable them to become tumorigenic and ultimately malignant" [19]. People who are suffering from cancer undergo through painful medical processes including medical examinations, surgeries, biopsies, chemotherapies, and others. VR has been used to treat the procedural pain cancer patients are dealing with, reporting positive results [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [42]. This study presents a review of research, for the last 10 years (2010–19) and examines the use of VR technology for cancer patients who undergo painful medical processes. Evidence from empirical, experimental studies that included several types of pain and cancer was systematically reviewed to address the following research questions:

- Is VR an effective solution for pain management for cancer patients?
- Which are the commonest VR contents used for pain management in cancer patients?
- How feasible is VR for real-world deployment?
- What are the current limitations of VR technologies?
- What are the future directions of VR technologies?

II. METHOD

The review was conducted based on Bargas-Avila and Hornbæk (2011) and Cochrane methodology [43], [44], [45], consisted of 5 phases:

A) PROCEDURE

1) Phase 1: Detailed evaluation of publications

Electronic Libraries: We searched seven electronic libraries, which cover a balanced range of disciplines, including computer science/engineering, medical research and multidisciplinary sources. The libraries which included in the review were:

1. ACM Digital Library (ACM)
2. Google Scholar
3. IEEE Xplore (IEEE)
4. MEDLINE
5. PubMed
6. Sage
7. ScienceDirect (SD)
8. Scopus
9. Web of Science

We restricted the search to a timeframe of ten years (2010 to 2020).

Search terms: We used the exact three queries to all the libraries since we are aiming to cover any type of VR technology on pain management in cancer disease.

— Virtual Reality AND Cancer
— Virtual Reality AND Pain
— Virtual Reality AND Pain AND Cancer

Search procedure: The search term used to search the publication's title, abstract and/or keywords.

Search results: The total search that returned in phase 1 can be seen in Table I.

2) Phase 2: Publications retrieved for detailed evaluation

First exclusion: All search results from phase 1 imported into a drive folder. Then, we exclude manually possible entries with wrong years. We removed 1648 wrong year entries. This narrowed down our findings to 3290 papers.

Second exclusion: Duplicate publications *between* each library (e.g., different libraries produce the same result) and *within* each library (e.g., different terms produce the same result into the same library) were removed. We removed 430 duplicate publications *between* each library.

As a result, we end up with 2860 different papers. Then we searched for duplicates *within* each library.

	ACM	Google Scholar	IEEE	MEDLINE	PubMed	Sage	SD	Scopus	Web of Science
VR & Cancer	27	90	128	295	380	143	199	291	352
VR & Pain	62	115	115	373	464	193	267	175	260
VR & Pain & Cancer	9	154	6	233	33	213	300	30	31
Total Findings from Each Library	98	359	249	901	877	549	766	496	643
Total Findings					4,938				

TABLE I. Findings per library and in Total

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

The duplicate articles that were provided by different terms were 59. The total outcome of this phase was 2801 different papers.

Third exclusion: We narrowed the entries down to the original full papers that are written in English. We excluded papers that we did not have access to the full length and papers that are not original full paper such as workshops, posters, speeches, reviews, magazine articles and generally grey literature without formal peer-review. As a result, we excluded 1664 papers. The 1137 remaining papers were: 934 Journal Articles and Conference papers, 203 book chapters.

3) Phase 3: Publications to be included in the analysis

Final exclusion: Since the focus on this review is on VR technologies as a complementary treatment to cancer, we excluded studies which used other types of technologies not related to VR, nor to cancer. We also excluded studies which were only related to pain management and general conditions and not to cancer disease. Based on these criteria, in this phase, we excluded any irrelevant papers that appeared in the first phase and were not excluded through the second phase filtering. These papers may appear in our findings because they contain relevant words to the one that we searched but did not match to the specific technical content. Based on these restrictions, we removed 909 irrelevant publications to VR, 162 irrelevant publications to pain and 43 irrelevant publications to cancer. As a result, we ended up with 23 relevant papers (20 Journal Articles and, 3 Conference papers, 0 Book Chapters), presented in Fig. 1. At the end of this phase, all papers were downloaded for the analysis to be conducted.

4) Phase 4: Data Gathering

At this phase, we extracted all the relevant information from the papers for the analysis to be conducted. In an excel file, we extracted information from each study: the type of pain, type of cancer disease, the VR type, the VR content, VR feasibility, the sample size of the population studied, the methodology, the instruments, the key findings, the current VR limitations and the future directions of VR.

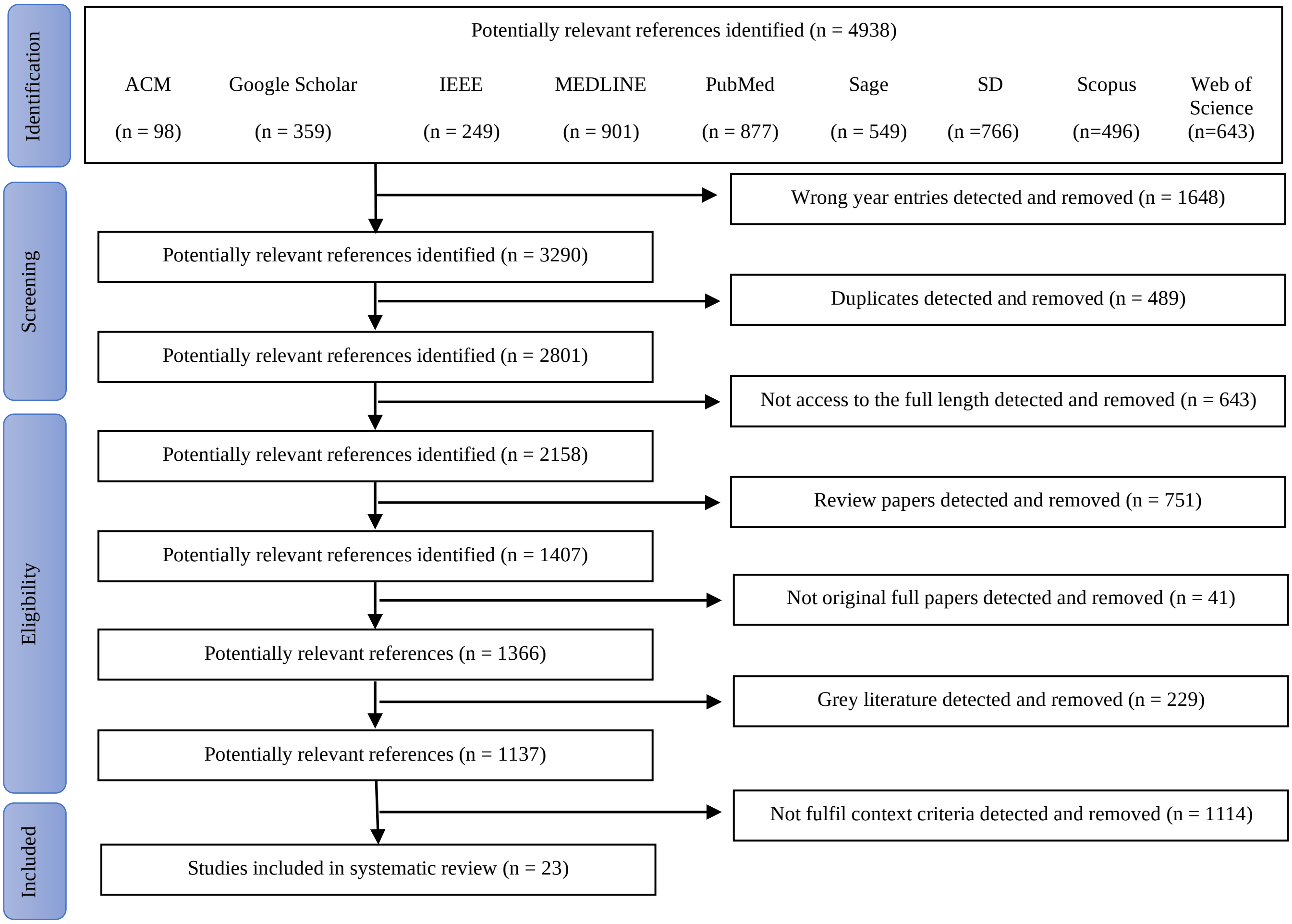

FIGURE 1. **Identification and selection of studies**

IEEE Access
Multidisciplinary | Rapid Review | Open Access Journal

Moreover, we labelled each study, based on the result as positive (+), negative (-) or neutral ( ).

5) Phase 5: Data Analysis

The data, collected in phase 4, analysed through descriptive statistics. Then we reviewed the literature to support and enhance the additional knowledge that this paper provides. Thematic analysis was used as an extra methodology to categorize our findings based on the themes. The themes we used included the types of VR, the type of VE content, the VR effectiveness, the VR feasibility, the VR design strategies, the VR limitations, and the VR future directions. Intercoder reliability was carried out between the researcher, and the research assistant. Cohen's Kappa formula was used to calculate the similarity between researcher and research assistant. The similarity was 0.83.

III. RESULTS

All studies (23/23) examined the applicability of VR in cancer. However, the type of cancer in each study differs considerably, as shown in Table II. Approximately, 23% of the papers were focused on breast cancer treatments [22], [23], [26], [27], [28], [31], [35], [37], [39], [41] followed by blood cancer (e.g., leukaemia, lymphoblastic, etc.) (12%) [21], [25], [33], [36],[38], bone cancer (12%) [25], [29], [33], [38], [40], and brain cancer (12%) [25], [32], [33], [38], [40]. Various studies examined lymphoma cancer (9%) [25], [33], [38], [39] and lung cancer (7%) [20], [30], [35] while some studies focused on sarcoma (5%) [32], [40], and germ cell tumors (5%) [33], [38]. A few studies assessed the

Study	Sample	Type of Cancer	Pain Type
1.Ayala et al., 2011 [22]	38 Females, Ages: 30 – 65	Breast	Side Effects of Pain: Neurocognitive issues
2.Atef et al., 2020 [41]	30 Females, Ages: 40 – 65	Breast	Acute - Procedural
3.Bani et al., 2019 [23]	80 Females, Ages: 18 – 70	Breast	Not Reported
4.Camargo et al., 2013 [26]	1 Female, Age: 30	Breast	Acute - Procedural
5.Camargo et al., 2013 [27]	2 Females, Ages: 40, 53	Breast	Acute - Procedural
6.Duivon et al., 2018 [28]	75 Females, Ages:>70	Breast	Side Effects of Pain: Issues related to Prospective Memory
7.Feyzioğlu et al., 2020 [37]	40 Females, Ages: 30 – 60	Breast	Acute - Procedural
8.House et al., 2016 [31]	12 Females, Ages: 22 – 78	Breast	Chronic
9.Garret et al., 2020 [39]	7 Males / 5 Females, Ages: 37 – 73	Breast, Abdominal, Non-Hodgkin's Lymphoma, Throat	Chronic and Neuropathic
10.Schneider et al., 2011 [35]	137 Males / Females (sex not reported), Ages: ≥18	Breast, Lung, Colon	Side Effects of Pain: Fatigue and Anxiety
11.Abushakra et al., 2014 [20]	Not Applicable	Lung	Not Applicable
12.Hoffman et al., 2016 [30]	Sex and number of participants not reported, Ages: ≈ 60	Lung	Side Effects of Pain: Fatigue
13.Atzori et al., 2018 [21]	10 Males / 5 Females, Ages: 7 – 17	Blood	Acute – Procedural
14.Glennon et al., 2018 [29]	52 Males / 45 Females, Ages: 19 – 70	Bone Marrow	Acute – Procedural
15.Tsuda et al., 2016 [36]	10 Males / 6 Females, Ages: 60 – 76	Hematologic Malignancies	Acute – Procedural
16.Birnie et al., 2018 [25]	12 Males / 5 Females, Ages: 8 – 18	Lymphoblastic, Leukemia, Lymphoma, Brain Tumor and Ewing's Sarcoma	Acute – Procedural
17.Høybye et al., 2018 [32]	6 Males / 4 Females, Ages: 16 – 27	Sarcoma and Brain Tumors	Not Applicable
18.Li et al., 2011 [33]	65 Males / 57 Females, Ages: 8 – 16	Leukaemia, Lymphoma, Osteosarcoma, Brain and Germ-cell Tumors	Side Effects of Pain: Stress and Depression
19.Sharifpour et al., 2020 [40]	30 Males and Females (sex not reported), Ages: 14 – 18	Osteosarcoma, Ewing's Sarcoma, Brain Tumors, Ovarian Cancer, and Skeletal Muscle Cancer	Pain Intensity, Anxiety, Catastrophising, Self-Efficacy
20. Tennant et al., 2020 [38]	50 Males / 40 Females, Ages: 7 – 19	Leukemia, Lymphoma, Brain Tumor, Bone, Melanoma, Germ-cell Tumors	Side Effects of Pain: Cancer-related psychophysiological distress
21.Baños et al., 2013 [24]	10 Males / 9 Females, Ages: 29 – 85	Metastatic	Acute – Procedural and Chronic
22.Li et al., 2016 [34]	3 Males / 7 Females Ages: not reported	Not Reported	Side Effects of Pain: Stress
23.Scates et al., 2020 [42]	50 Males / Females (sex not reported), Ages: >18	Not Reported	Acute-Procedural, Side Effects of Pain: Anxiety and Stress

TABLE II. **Sample Size, Type of Cancer and Pain of the Reviewed Studies.**

IEEE Access
Multidisciplinary ⋮ Rapid Review ⋮ Open Access Journal

VR impact on cancer related to ovaries [40], melanoma [38], abdominal [39], throat [39], and metastatic [24] types of cancer (2% each). Finally, two of the reviewed studies, did not report the specific type of cancer type (5%) [34], [42].

Further to the type of cancer, almost half of the studies examined the effectiveness of VR in accordance to pain (65%). Most focused on Acute-Procedural Pain (38%) [21], [24], [25], [26], [27], [29], [36], [37], [41], [42]. The pain was induced via venipuncture, surgery and biopsies, while the remaining 15% cases of pain, as a result of chronic conditions [24], [31], [39], [40]. Finally, 12% of papers did not report the type of pain [20], [23], [32]. Some of the reviewed studies were not related directly to pain (35%), meaning that they, examined closely side effects such as fatigue, anxiety, depression, emotional distress, neurocognitive problems, prospective memory issues, and other issues that cancer patients are usually dealing with because of the procedural pain caused by the medical processes, [22], [28], [30], [33], [34], [35], [38], [40], [42].

A) EFFECTIVENESS OF VR ON PAIN MANAGEMENT AND CANCER

Regarding the effectiveness of VR on pain management and cancer, most of the studies outcomes were positive (83%) [20], [21], [22], [23], [24], [25], [26], [27], [32] , [30], [31], [33], [36], [37], [38], [39], [40], [41], [42] and less than quarter neutral (17%) [28], [29], [34], [35], while negative results were not reported. To illustrate this, it was found that the use of VR can reduce pain [21], [24], [25], [26], [27], [29], [37], [39], [40] improve emotional wellbeing [21], [23], [24], [29], [32], [33], [34], [35], [38], [39], [40], [42] enhance the rehabilitation training [20], [26], [27], [30], [31], [36], [37], [41] and be an assistive technology for clinicians, during the medical evaluation process at [22], of the studies as shown in Table III. In particular, the reviewed studies reported that VR can improve and enhance the rehabilitation training, by minimizing the sensation of pain the patients are feeling during their trainings [26], [27], [37] and maximizing the patients' range of movements and functional abilities [31], [36], [37], [41]. VR can also reduce pain during venipuncture in children and teenagers suffering from cancer [21], [25], [38]. Also, a case study revealed that VR can minimize the post-surgical pain in breast cancer patients [26], [27], [37], [41] while is also able to improve analgesia impact when combined with pharmacological analgesics [23]. Additionally, a recent study showed that VR can reduce pain intensity, and at the same time increase the levels of self-efficacy among adolescents with cancer during chemotherapy [40].

A particularly promising finding was reported by Abushakra and colleague (2014) [20], who designed a VR breathing therapy tool to improve the immune system of lung cancer patients through a series of breathing exercises. The VR application was found to have an accuracy greater than 85% on lung capacity estimation and breathing movements classification [20].

It was further corroborated that VR can be used as a tool to treat side effects arising from pain and improve the emotional wellbeing of cancer patients. Specifically, VR can eliminate negative emotions, such as anxiety and depression and produce positive emotions, such as positive mood and calmness [24], [33], [38], [42]. This was done through a VR platform which hosted cancer patients able to communicate their experiences with other patients [32]. In addition, a study used nature scenes to induce positive emotions such as pleasantness, happiness and peacefulness to cancer patients during the chemotherapy procedure [42]. Finally, a study suggested that VR can assist the medical evaluation of cancer patients. This was validated through the use of a VR application that helped to evaluate the performance of visuospatial memory in women with breast cancer who were undergoing through long-term chemotherapy or radiotherapy treatments [22].

B) EQUIPMENT AND APPARATUS

As aforementioned, based on Ma and Zheng (2011) [8], there are three types of immersive VR systems: a Non-Immersive, a Semi-Immersive, and a Fully-Immersive. Our review suggested that most of the reviewed studies used Semi-Immersive and Fully- Immersive VR systems (19/23), while only two (2/23) studies explored the use of Non-Immersive VR for clinical purposes related to cancer. One study did not report on the type of VR system. Approximately, 57% (13/23) of the reviewed studies required some sort of interactivity (e.g., sports, puzzles, darts, bowling) while 43% (10/23) of the studies exposed the patient only visually to the VR environment (Table IV). More explicitly:

1) NON-IMMERSIVE

Only two out of seventeen studies used a Non-Immersive VR technology for the treatment of cancer (9%) [32], [33]. The first study examined the use of VR as a communication system running on patients' personal computer. The patients were residing at the hospital, and the study asked them to connect into a virtual space using a weblink. Patients had to log in to the system and create a personalized avatar. Once this process was completed all patients were asked to communicate their feelings with other patients who were also logged in to the system and were undergoing similar cancer treatment, [32] (Fig. 2). On the other hand, the second study focused on minimizing the depressing episodes of children with cancer were dealing with. This was done via the PlayMotion[1] system and the software created by the researchers which allowed the patients to alter the room's surroundings and convert them into fun environments (e.g., a playground, a city space with a blue sky, a football and/or

[a] http://www.playmotion.com/legacy/corelib1.html

IEEE Access
Multidisciplinary ⋮ Rapid Review ⋮ Open Access Journal

Study	Objective	Feasibility	Findings	Label
1.Ayala et al., 2011 [22]	Evaluate the radiation and chemotherapy effects on memory	Visuospatial learning and memory assessment	VR can assess the cognitive effects of chemotherapy on visuospatial memory	(+)
2.Atef et al., 2020 [41]	Identify the advantages of VR in postmastectomy lymphedema	Reduce postmastectomy lymphedema	VR can improve upper limb function and excessive arm volume	(+)
3.Bani et al., 2019 [23]	Manage pain during hospitalized	Reduce pain and anxiety	VR can enhance morphine's analgesia	(+)
4.Camargo et al., 2013 [26]	Cure secondary pain to breast cancer patients	Reduce breast surgery pain and improve rehabilitation	VR can decrease pain up to 43%	(+)
5.Camargo et al., 2013 [27]	Reduce surgery breast pain	Reduce breast surgery pain and improve rehabilitation	VR can decrease pain up to 85%	(+)
6.Duivon et al., 2018 [28]	Assess prospective and retrospective memory	Not applicable	The paper is research in progress. No findings reported	( )
7.Feyzioğlu et al., 2020 [37]	Identify the effects of postoperative VR therapy on breast cancer patients	Reduce breast surgery pain and improve rehabilitation	VR can decrease pain, and increase range of motion, muscle strength, and functionality	(+)
8.House et al., 2016 [31]	Enhance rehabilitation of cancer survivors with upper body chronic pain	Physical rehabilitation	VR can improve patients' cognition, shoulder range, strength, function, and emotional health	(+)
9.Garrett et al., 2020 [39]	Manage chronic pain	Pain management	VR can improve sleep quality, mobility, and mental health	(+)
10.Schneider et al., 2011 [35]	Reduce distress	Reduce anxiety	VR can reduce time perception	( )
11.Abushakra et al., 2014 [20]	Monitor breathing movements	Accurately perform breathing therapy	VR has 85% accuracy on lung capacity estimation and breathing movement classification	(+)
12.Hoffman et al., 2016 [30]	Enhance emotional health and improve the quality of rehabilitation at home	Home-based use	VR can be used as a home-based therapy	(+)
13.Atzori et al., 2018 [21]	Manage pain during venepuncture	Distraction	VR – Distraction can reduce pain	(+)
14.Glennon et al., 2018 [29]	Management pain during bone marrow aspiration and biopsy procedure	Distraction	VR does not affect significantly pain and anxiety	( )
15.Tsuda et al., 2016 [36]	Enhance physical rehabilitation	Improve rehabilitation	VR can improve mental and physical health	(+)
16.Birnie et al., 2018 [25]	Management pain in children with cancer undergoing Implantable Venous Access Device (IVAD)	Distraction	VR is an enjoyable and fun way to manage pain	(+)
17.Høybye et al., 2018 [32]	Facilitate social interaction in hospitalized teenagers' patients	Social interaction	(1) VR can facilitate social interactions in hospitalization; (2) User-centred designed should be used	(+)
18.Li et al., 2011 [33]	Maximize the effects of therapeutic paly in children with cancer	Enhance emotional health	VR can reduce depression	(+)
19.Sharifpour et al., 2020 [40]	Investigate the effects of VR on pain during chemotherapy	Reduce pain	VR can decrease chemotherapy's side effects	(+)
20. Tennant et al., 2020 [38]	Investigate the effects of VR on psychophysiology	Enhance physical and emotional health	VR can reduce negative symptoms	(+)
21.Baños et al., 2013 [24]	Improve emotional health in hospitalized patients with metastatic settings cancer	(1) Reduce pain and anxiety (2) Implementation in real hospital metastatic settings cancer	VR can improve the patients' emotional well-being	(+)
22.Li et al., 2016 [34]	Alleviate symptoms of physical pain and psychological distress via a low-cost solution	Distraction	Usability feedback suggested that a future study need to re-design and re-evaluate the VR system	( )
23.Scates et al., 2020 [42]	Determine if VR nature simulation can reduce pain and stress	Distraction	VR can increase relaxation, feelings of peace, and positive distractions	(+)

TABLE III. Summary of the Reviewed studies, Objectives, and Findings.

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

volleyball arenas). To do so the patients were required to move their arms, which were projected onto the walls as shadows, and the system was responding to their movements via analysing the motion signals [33].

FIGURE 2. **An example of a Non-Immersive VR system from Høybye *et al.,* 2018 [32]. The depicted avatars represent researchers during system testing and evaluation.**

2) SEMI-IMMERSIVE

Several Semi-Immersive VR applications were developed to enhance the treatment of cancer patients (39%) [24], [26], [27], [28], [30], [31], [36], [37], [41]. In particular, most of the Semi-Immersive VR systems aimed to reduce pain and improve the rehabilitation and physical training of cancer patients [26], [27], [30], [31], [36], [37], [41]. To do so, four studies used existing Semi-Immersive VR applications offered by the Nintendo Wii Fit[2] [36], the Nintendo Wii Fit Plus[3] [30], the Nintendo Wii[4] [41] and Xbox 360 Kinect[5] [37]. Apart from the existing solutions, three studies created VR applications to help women who were undergoing breast cancer to perform their rehabilitation exercises to improve the functional abilities of the affected area and to increase the lymph fluid flow through their body. More specifically, two out of three studies used a VR system where red and green marks were presented on the screen to position the patient into the right posture. To achieve that, an infrared laser projector with a monochrome CMOS sensor[6] was placed in three meters distance from the patient. Once the software tracked the patients' motion, real-time feedback with visual and auditory commands returned on the screen, to illustrate the correct performance of the task (Fig. 3) [26], [27]. Finally, the third VR rehabilitation system for breast cancer called BrightArm Duo[7] was created using a low-friction robotic rehabilitation table, a computerized forearm supports (robotic arms which were connected to the rehabilitation table, to able the patients' rehabilitation moves), a large monitor display and a laptop (Fig. 3). The system incorporated nine rehabilitation games: Breakout 3D, Card Island, Remember the Card, Musical Drums, Xylophone, Pick & Place, Arm Slalom, Avalanche and Treasure Hunt. To play the games, the patients were asked to move their arms assisted by the computerized forearms. The system adopted on the patients' performance by increasing gradually the level of difficulty. All game movements were related to traditional rehabilitation training [31]. The rest of the studies developed VR environments, to improve emotional health and memory. The first study used mindfulness techniques to promote positive emotions. To do so, a virtual city park and forest enhanced with relaxing music were projected on a 32-inches screen. The patients were instructed to navigate into the virtual space using the mouse and the keyboard [24]. The second study used a VE of the Memorial Museum in Caen-France to assess memory in breast cancer patients. The Memorial Museum was presented to the patients through a Cave Automatic VE(CAVE)[8]. The CAVE consisted of four wide screens - 3D stereoscopic projection: two laterals (9 m × 3 m), one facial (4.80 m × 3 m), and one on the floor (9 m × 4.80 m). Besides, the patients wore stereoscopic glasses with position sensors able to compute perspective in real-time. A joystick was used to allow the patients to project elements of the Memorial Museum (e.g., fictional time, map) [28].

3) FULLY- IMMERSIVE

Several studies used Fully-Immersive VR technology to enhance cancer patients therapy (48%) [20], [21], [23], [25], [29], [34], [35], [38], [39], [40], [42]. Most of the studies did so using natural habitat scenes (90%). Examples of the above are given by: (a)Four studies which aimed to distract children [21], [25], [40], and adults [42] during painful medical processes such as venepuncture and chemotherapy (b) Three studies which tried to reduce the emotional inclemency arising from the complexity of the condition [23], [34], [38], (c) A study intended to soothe the procedural pain arising from bone marrow aspiration and biopsy procedures [29] (d) A study targeted to chronic pain management [39]. All the above studies used HMDs to immerse the patients into the VE and distract them from perceiving nociceptive signals, pain, and anxiety. In particular, the first study [21] used the Sony HMZ T-2 3d HMD[9], along with latex-free headphones, and a mouse. The study used a pre-existing VE, SnowWorld[10] [24], [46], [47], which was found to be an

[2] https://www.nintendo.com/wiifit/launch/
[3] https://www.nintendo.com/wiifit/launch/wiifitplus/
[4] https://www.engadget.com/products/nintendo/wii/console
[5] https://www.cnet.com/products/microsoft-xbox-360-special-edition-4gb-kinect-family-bundle-game-console-glossy-white-with-kinect/
[6] CMOS sensor is an electronic chip that converts photons to electrons for digital processing. These sensors are used to create images in digital camera, digital video cameras and digital CCTV cameras.
[7] http://brightcloudint.com/
[8] https://www.antycipsimulation.com/projects/vr-cave-caen/personal-3d-viewer/hmz-t2/specifications
[9] https://www.sony.co.uk/electronics/support/televisions-projectors-
[10] http://www.vrpain.com

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

FIGURE 3. An example of a Semi-Immersive VR system. To the top [26], [27]: Subject training on breast cancer rehabilitation training. To the bottom [31]: Subject training on BrightArm Duo Rehabilitation System and Screen images of nine bimanual games (a) Breakout 3D, (b) Card Island, (c) Remember that Card, (d) Musical Drums, (e) Xylophone, (f) Pick & Place, (g) Arm Slalom, (h) Avalanche, and (i) Treasure Hunt.

advance distractive environment (i.e., use ice-features to offer a cooling effect to the patients). The patients played ice-war with other animals and characters who were found to be living into the virtual SnowWorld [21]. Similarly, three studies used the Samsung Gear VR[11][25], [38], [40], and Samsung smartphones (Galaxy S6[12], Galaxy S7[13], and Note 8[14] respectively). The first one used it along with noise-cancelling headphones SonyMDR 10R[15] and a wireless Bluetooth controller Moga Pro Power[16], to distract the patients from the procedural pain arising from venepuncture. The patients were immersed into a calm submarine environment with corals and sea animals, as scuba divers in. The patients were able to aim and shoot the sea animals. When a sea animal got shot by the patients, it turned into bright colours [25]. Finally, the other two studies used VR to represent nature (e.g., national parks), animals (e.g., zoos), and travel (e.g., tourist spots) to distract patients and reduced the perceived pain during chemotherapy [38], [40]. Similarly, distraction was utilized by a study with nature-inspired VR simulations of water features and animals, and local parks. The patient exposed to nature via VR One Glasses by Zeiss[17]. [42]. Another study used an HMD ezVision X4[18] to immerse the patients into natural environments (e.g., undersea diving, palm trees, babbling brooks, etc). This was further enhanced by soft/relaxing music to reduce discomforted and time perception for patients going through bone marrow aspiration and biopsy procedures [29]. Also, two of the studies used natural environments to improve patients' emotional wellbeing. An unspecified low-cost HMD where headphones were used to immersed breast cancer patients into a deep-sea diving and other beach environments. The aim was for the patients to use the HMD at their own homes to overcome stress and anxiety [23]. The second study also examined the home-based use of VR in cancer patients to reduce fatigue, anxiety and depressive feelings. This was done via the least expensive VR HMD solution, which was powered by Google Cardboard VR[19] and could be paired with any smartphone.

[11] https://www.samsung.com/global/galaxy/gear-vr/#gear-vr
[12] https://www.samsung.com/global/galaxy/galaxys6/galaxy-s6/
[13] https://www.gsmarena.com/samsung_galaxy_s7-7821.php
[14] https://www.gsmarena.com/samsung_galaxy_note8-8505.php
[15] https://www.sony.ca/en/electronics/headband-headphones/mdr-10r
[16] https://www.powera.com/us/moga/

[17] https://www.zeiss.com/content/dam/virtual-reality/english/downloads/pdf/vr_one_plus_spec.pdf
[18] https://www.cnet.com/products/ezgear-ezvision-x4-head-mounted-display/
[19] https://arvr.google.com/cardboard/

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

The patients were immersed into a virtual beach with a colourful sky [34]. Another study used HTC Vive[20] to enhance pain management, via mindfulness (e.g., forest walk enhanced with relaxing music, sky flying), and cognitive (e.g., puzzle-based interventions) training. The first category included [39]. Lastly, a Fully Immersive VR system was developed to enhance respiratory training for patients suffering from lung cancer. The system used a HMD and a smartphone to present to the patients' features which imitated the lung and blood cells movement when performing a breathing exercise in real-time. To capture and detect the patients' breathing intensity (lung capacity at each breathing cycle) the smartphone's microphone was used. The patients were asked to regulate the inhalation and exhalation on a specific pace until the blood cells will disappear from the lung organ. The smartphone was connected to the HMD to provide visual feedback to the patients (Fig. 4) [20].

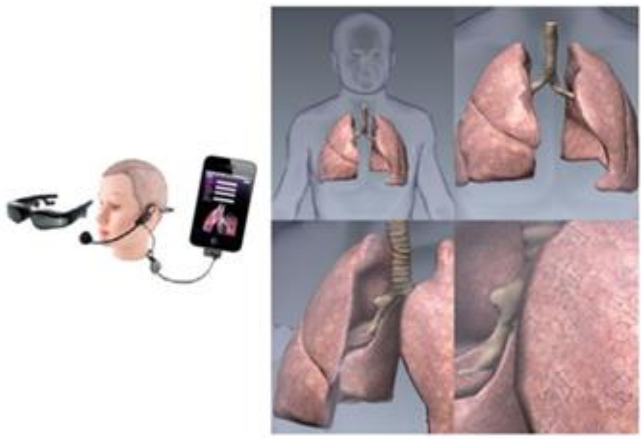

FIGURE 4. Smart-phone application for breathing exercises in lung cancer patients [20].

C) VR THERAPEUTIC INTERVENTIONS EVALUATION

Reviewed papers were based their research in 3 different types of study. Controlled study experiments where performed by 57% of the reviewed papers [21], [22], [23], [28], [29], [33], [34], [37], [38], [39], [40], [41], [42] equally to non-controlled experiments (30%) [24], [25], [30], [31], [32], [35], [36]. Only two were case studies (9%) [26], [27]. One paper prevented the architecture and the technical aspect of the developed VR system. The VR system was not testing on participants (4%) [20]. All the reviewed studies collected patients' demographic information (e.g., age, sex, ethnicity, educational level, type cancer, type of treatment, etc.).

As aforementioned most of the studies examined the effectiveness of VR in accordance to pain (25%) [21], [23], [24], [25], [26], [27], [29], [31], [37], [38], [39], [40]. To do so, studies used several instruments, which are presented in Table V. In particular, quantitative, and qualitative measurements with scale questionnaires, and biosignals were preferred over other types of data.

The scale questionnaire were: Visual Analog Scale (VAS) [21], [23], [24], [25], [37], [38] and Numerical Pain Scale (NPS) [26], [27], [29], [31], were used equally from the reviewed studies. Both VAS and NPS are subjective ten-point Likert scales ranging from 0 (no pain) to 10 (worst pain) [49], [50]. In addition to the above, McGill pain questionnaire (MPQ) [40] was also administered by a study to measure the quality and intensity of their pain through sensory, affective, and evaluative sessions [51]. Finally, pain perception of the patients related to the time the patients spent on thinking about pain was also assessed [21].

The bio signals were measurements of physiological changes (20%) [20], [26], [27], [28], [29], [30], [31], [36], [37], [38]. In particular, the studies used Electromyography (EMG) [26], [27], [31], [36] to record the electrical activity produced by the muscles and Dynamometer to evaluate the changes in muscles strength after the rehabilitation session [26], [27], [31], [37]. This was followed by some studies [20], [28], [29], which used acoustic signal of respiration to assess the performance of the immune system of lung cancer patients during a series of breathing exercises. A couple of studies collected Electrocardiography (ECG) and blood pressure signals [29], [31] while additional physiological signals were collected in response to oxygen saturation using Oximeter devices through a finger pulse [28], [29], [38] and sleep functionality through a Polysomnography (PSG) [28].

Further, some of the reviewed studies examined the use of VR to treat side effects (e.g., fatigue, nausea, anxiety, depression, emotional distress, neurocognitive problems, cognition, mobility etc.) (23%) [22], [23], [25], [28], [31], [33], [34], [35], [36], [37], [41]. To begin with, several instruments were used by the researchers to reflect on the cognitive level of the patients, the most common were: (1)Continuous Performance Test (CPT) [22]; (2) Grooved Pegboard Test (GPT) [22]; and (3) Paper-based tests such as – Montreal Cognitive test [28] and Wechsier Adult Intelligence Scale (WAIS) [22]. CPT [52] evaluates attention deficiencies. It is projected on a computer screen and the patients' response using the keyboard [22]. Simple tasks are administrated for the test to run, for example, letters are presented to the screen and the patients are requested to press the space bar for all the letters except the letter X. to assess the patients' performance, the system records the response time, the changes in response time, consistency, omission, and errors are documented by the system. The GPT [53], reflects on the patients' cognitive level. GPT [54] is a square metal surface with holes in various orientations. The task requires for the subjects to match the groove of the pegs with the groove of the board working left to right when using their right hand and working right to left when using the left hand. The test lasts up to five minutes or it ends once all holes are filled. To assess the patients' performance, the researcher records the duration, which is required to perform each trial,

[20] https://www.vive.com/us/product/vive-cosmos/specs/

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

Study	VR Type	Interaction	Virtual Environment	Equipment
1.Ayala et al., 2011 [22]	NC	Yes	Virtual island with water flowing, birds singing and hidden treasures. The patients search for red flags to find the treasures	Headphones, joystick
2. Atef et al., 2020 [41]	SI	Yes	Tennis, triceps extension, and rhythmic boxing tasks	Nintendo Wii®
4.Bani et al., 2019 [23]	FI	No	Relaxing nature scenes: 1) Under-Water world , 2)Beach	Unspecified low-cost HMD, headphones
4&5. Camargo et al., 2013 a, b [26] [27]	SI	Yes	Imitation of traditional rehabilitation training through red marks on the screen. The patients were instructed to reach the marks who turned green once the exercise was performed correctly	Infrared-based motion capture device with a laser projector and a monochrome CMOS sensor
6.Duivon et al., 2018 [28]	SI	No	A virtual reproduction of the Memorial Museum in Caen, Italy	CAVE, stereoscopic glasses, joystick, MotionWatch 8
7.Feyzioğlu et al., 2020 [37]	SI	Yes	7 games: 1) Darts, 2) Bowling, 3) Boxing, 4) Beach volleyball, 5) Table tennis, 6) Dance Central 3: Macarena, 7) Fruit Ninja	Xbox 360 Kinect
8.House et al., 2016 [31]	SI	Yes	9 games: 1) Breakout 3D, 2) Card Island, 3) Remember the Card, 4) Musical Drums, 5) Xylophone, 6) Pick & Place, 7) Arm Slalom, 8) Avalanche 9) Treasure Hunt	Rehabilitation table, laptop, monitor
9.Garrett et al., 2020 [39]	FI	Yes	4 games: 1) Forest walk, 2) Wild-flowers, 3) Puzzle carpe lucem, 4) Puzzle obduction	HTC VIVE
10.Schneider et al., 2011 [35]	FI	No	3 scenes which were reported in a previous study [48]: 1) Oceans discovering, 2) A World of Art, 3) Titanic ship discovering	Unspecified HMD
11.Abushakra et al., 2014 [20]	FI	Yes	Human upper body with lung breathing interactivity. Patients perform inhale and exhale tasks to remove blood cells from the lung organ	Smartphone, Unspecified HMD
12.Hoffman et al., 2016 [30]	SI	Yes	Walking and balance exercise activities	Nintendo Wii Fit Plus, Wii balance board
13.Atzori et al., 2018 [21]	FI	Yes	SnowWorld - An icy 3D canyon and other ice-features, where the user can fight other ice-creatures	Sony HMZ T-2 HMD, laptop, latex-free earphones, mouse
14.Glennon et al., 2018 [29]	FI	No	3 scenes: 1) Babbling brooks, 2) Swaying palm trees, 3) Undersea life	ezVision X4 HMD
15.Tsuda et al., 2016 [36]	SI	Yes	Hula hoop and the basic steps exercises	Nintendo Wii fit, Wii balance board
16.Birnie et al., 2018 [25]	FI	Yes	Underwater world with corals, sea animals and a hidden treasure	Galaxy S6™, Samsung GearVR™ HMD, Sony MDR 10R Headphones, MOGA PRO™ POWER controller
17.Høybye et al., 2018 [32]	NI	No	Real-time communication with other patients in a forest, through a personalized avatar	Laptop
18.Li et al., 2011 [33]	NI	Yes	4 games: 1) Flying over a city, 2) Create trance-like waves, 3) Football, 4) Volleyball	PlayMotion system
19.Sharifpour et al., 2020 [40]	FI	No	A walk by the beach at sunset time and ocean diving	Samsung Gear VR, Samsung Note 8
20. Tennant et al., 2020 [38]	FI	No	3 different scenes: 1) National parks, 2) Zoos, 3) City tourist spots	Samsung Gear VR, Samsung Galaxy S7
21.Baños et al., 2013 [24]	SI	No	2 scenes: 1) City park, 2) Forest	32-inch LCD television, computer, keyboard, mouse, headphones
22.Li et al., 2016 [34]	FI	No	A beach with colourful sky and moving clouds	Google Cardboard VR HMD, smartphone
23.Scates et al., 2020 [42]	FI	No	Local scenes of trees, water features, creeks, animals, and local parks	Zeiss VR One Glasses by

Note: FI= Fully-Immersive, SI= Semi-Immersive, NI= Non-Immersive, NC=Not clarify

TABLE IV. **Equipment and Apparatus.**

IEEE Access
Multidisciplinary ⋮ Rapid Review ⋮ Open Access Journal

the drops of a peg which might occur, and the number of pegs which are placed correctly in the holes of the surface. Cognitive impairment was also measured by MoCA [55]. MoCA is a paper-based instrument which is consisted of 30 items assessing: short-term memory via recall task; visuospatial abilities via clock drawing, and a cube copy task; executive abilities via clock drawing, and a cube copy task; executive functioning via an adaptation. In similar logic with MoCA, the WAIS was used by a study [22] to assess the patients' intelligence and cognitive ability. WAIS assess Verbal and Performance IQ. Verbal IQ is assessed by Verbal related to Perceptual Organization (e.g., Block Design, Matrix Reasoning, Picture Completion), and Processing Speed (e.g., Digit Symbol-Coding, Symbol Search). Verbal IQ is assessed by Verbal Comprehension tasks (e.g., vocabulary, similarities, information) and Working Memory tasks (e.g., Arithmetic, Digit Span), while the Performance IQ examines features related to Perceptual Organization (e.g., Block Design, Matrix Reasoning, Picture Completion), and Processing Speed (e.g., Digit Symbol-Coding, Symbol Search). Lastly, the Disability of Arm, Shoulder and Hand questionnaire (DASH [37] & QuickDASH-9 [41]) were used to measure breast cancer patients' ability to perform specific movements.

The emotional well-being was also assessed from several studies, with most of the studies focusing on anxiety and depression (18%) [23], [28], [31], [33], [34], [35], [36], [38], [40]. Anxiety was mostly measured by State Anxiety Inventory (STAI) [23], [28], [33], [35], [36], which is a 4-point Likert scale and consists of 40 questions on a self-report basis. The STAI measures two types of anxiety – state anxiety, or anxiety about an event, and trait anxiety, or anxiety level as a personal characteristic [56]. Higher scores are positively correlated with higher levels of anxiety [57]. Depression was mostly measured using the Beck Depression Inventory (BDI) [28], [31]. The BDI is a multiple-choice scale and consists of 21 questions on a self-report basis [58].

Lastly, VR experience was measured by 14% of the studies [21], [24], [25], [28], [34], [38] , [42] through self-reported scales which relates to: (1) Usability; (2) Enjoyment; and (3) motion sickness. Usability was measured [25], [34], through the three techniques of the Discount Usability Engineering testing (scenarios, simplified think-aloud, and heuristic evaluation) [59]. Enjoyment was measured through VAS [21], [24], [25], [28], and motion sickness [21], [25], [34], [38] was assessed by the Simulator Sickness Questionnaire (SSQ) [60], the Motion Susceptibility Questionnaire (MSSQ) [61], and Child Simulation Sickness Questionnaire (CSSQ)[62].

IV. LIMITATIONS AND FUTURE DIRECTIONS

Even though the effectiveness of VR for the treatment of cancer is well documented, however several limitations were identified in the reviewed studies. Firstly, previous research has suggested that several factors might affect the efficiency of VR. In particular, it was suggested that past experiences and knowledge of the medical process may affect negatively the effectiveness of VR and result in an increased level of pain. As aforementioned, pain has been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" [21], which suggests that pain has both a nociceptive and subjective element to its perception [63], and is affected by personal characteristics [64]. Therefore, the mental representation of the painfully medical process might shape the perception of pain felt by the patent, as in an anticipatory manner. As a result, it is expected that VR might have a greater impact on patients who are receiving the treatment for the first time in contrast to patients who have previously undergone through this medical process and are aware of the procedural pain arising from the treatment [25]. We suggest future research to validate the above statement through a between-subjects' experimental design study.

Further to the above, several studies also suggested that the effectiveness of VR technology on pain management for cancer patients has not been reliably assessed [23], [31], [34]. This is because VR's effectiveness on pain has been documented only via self-report scales (e.g., VAS, NPS) [23], [24], [31], [34], [42]. Even though self-report questionnaires have been validly used in the past by several psychological studies to assessed pain, it is suggested for future studies to triangulate the VR effectiveness on pain via self-reported scales, qualitative data (e.g., interviews) and physiological responses (e.g., ECG signals) [23], [24], [25].

Finally, it was also recommended that future studies should entail personalised instruments, based on each patient needs [35]. VR applications should offer both mindfulness and cognitive training to serve cancer patient needs. [39]. In particular, it has been argued that mobility issues occur for women, undergoing mastectomy recovery. The evaluation of the recovery process (i.e., Range of Movement – ROM) is nowadays assessed by a goniometer device[21]. Future studies should entail the technological solutions that will minimise the clinical time required for the evaluation process [24]. It was also noted that most of the studies did not take into consideration differences that might occur due to the disease procession or due to the medical history of the patients [31], [36]. Future studies should consider the neurological assessment of VR's effectiveness to identify the most crucial factors [39]. It is also suggested for future studies to do a thorough background of patient's history check to be able to study a more homogeneous sample size of the given population, which will increase the degree of variability in their findings [31], [36], [39]. In addition, it was further reported that most of the studies were limited in a short-term deployment of the VR system into clinical settings [33], [37],

[21] A device that enables healthcare professionals (e.g., physiotherapists, occupational therapists etc) to objectively measure the available range of motion at a joint

IEEE Access
Multidisciplinary | Rapid Review | Open Access Journal

Study	Study Duration	Instruments
1.Ayala et al., 2011 [22]	2 hours	Qualitative data: WAIS, Wechsler Memory Scale (WMS), Working Memory Index (WMI), Quantitative data: CPT-ii, GPT, COPE inventory
2.Bani et al., 2019 [23]	Not reported	Quantitative data: VAS, STAI, Mini-Mental State Examination (MMSE)
3&4.Camargo et al., 2013 a, b [26] [27]	30 minutes	Physiological Data: EMG, Dynamometer Quantitative data: NPS, Goniometer (shoulder joint)
5. Atef et al., 2020 [41]	8 sessions over 4 weeks. Each session lasted 30 minutes	Quantitative data: Excessive arm volume (EAV), QuickDASH-9 scale (4-point Likert scale)
6.Feyzioğlu et al., 2020 [37]	12 sessions over 6 weeks. Each session lasted 45 minutes.	Physiological Data: J Tech Commender Muscle Tester hand-held and Saehan hydraulic hand Dynamometer Quantitative data: VAS, Shoulder ROM, DASH, Tampa Kinesiophobia Scale (TKS)
7.Duivon et al., 2018 [28]	1 week	Physiological Data: PSG, Respiratory Airflow, Oxygen Saturation Quantitative data: WAIS, MoCA, VAS, Functional Assessment of Cancer Therapy Cognitive Scale (FACT-Cog), Prospective Retrospective Memory Questionnaire (PRMQ), STAI, BDI, Multidimensional Fatigue Inventory, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Karolinska Sleepiness Scale (KSS), Pittsburgh Sleep Quality Index (PSQI)
8.House et al., 2016 [31]	16 sessions over 8 weeks. Each session lasted 20 – 50 minutes	Physiological Data: ECG, Blood Pressure Quantitative data: NRS, Goniometer, Fulg–Meyer Assessment (FMA), Upper Extremity Section, Arm and Hand Activity Inventory-9 (CAHAI-9), BDI-II, Neuropsychological Assessment Battery (NAB), Attention Module (Orientation, Digit Span and Dots), Executive Functioning Module (EFM), Hopkins Verbal Learning Test, Revised (HVLT-R), Brief Visuospatial Memory Test-Revised (BVMT-R)
9.Schneider et al., 2011 [35]	Approximate time 63 minutes	Quantitative data: STAI
10.Garrett et al., 2020 [39]	24 sessions over 4 weeks. Each session lasted 30 minutes	Qualitative data: Semi-structured interview on: VR experience, Chronic Pain status, Cancer diagnosis status, Effectiveness of VR, Mode of Action, Usability, and Technical aspects
11.Abushakra et al., 2014 [20]	Not reported	Physiological Data: Deep Breathing, Lung Size, Lung Capacity, Total Lung Capacity in each breathing cycle
12.Hoffman et al., 2016 [30]	Not clarify	Quantitative data: Pedometer
13.Atzori et al., 2018 [21]	Not reported	Quantitative data: VAS, self-reported data on: VR experience, Nausea, Time Perception, Enjoyment (10-point liker scale)
14.Glennon et al., 2018 [29]	15 minutes	Physiological Data: Blood Pressure, Pulse, Respiration, Temperature, Oxygen Saturation Quantitative data: NPS
15.Tsuda et al., 2016 [36]	5 sessions over a week. Each session lasted 20 minutes	Qualitative data: Instrumental Activities of Daily Living (IADL) Quantitative data: Adherence Rate, Barthel Index for physical fitness, Grip Strength, one-leg standing time, Knee-extension Strength, Hospital Anxiety and Depression Scale (HADS)
16.Sharifpour et al., 2020 [40]	8-10 sessions over 2 months. Each session lasted 30 minutes	Qualitative data: MPQ Quantitative data: Pain Anxiety Symptoms Scale (PASS), Pain Catastrophizing Scale (PCS), 10-item self-report questionnaire (7-point Likert-type)
17.Birnie et al., 2018 [25]	25 minutes	Qualitative data: semi-structured interviews on: VR experience, Acceptability, Enjoyment Quantitative data: NPS for Pain, Anxiety, and Nausea
18.Li et al., 2011 [33]	30 minutes 5 days a week	Quantitative data: Chinese version of the State Anxiety Scale for Children (CSAS-C), Center for Epidemiologic Studies Depression Scale for Children (CES-DC)
19. Tennant et al., 2020 [38]	One session of 27 minutes	Physiological Data: Pulse Rate Quantitative data: VAS, Child-report Spence Children's Anxiety Scale (SCAS)– short form, Parent-proxy report Pediatric Quality of Life Inventory™ Cancer Module (PedsQL), Child-report Adapted version of the Total Immersion subscale of the Augmented Reality Immersion (ARI) questionnaire, CSSQ
20.Høybye et al., 2018 [32]	8 weeks	Qualitative data: medical adherence and diagnostics, VR experience
21.Baños et al., 2013 [24]	4 sessions over a week. Each session lasted 30 minutes	Qualitative data: open-ended questions on: VR experience, side effected, general comments of the exposure Quantitative data: VAS, self-reported data on: pre and post physical discomfort (6-point liker scale), satisfaction (7-point liker scale)
22.Li et al., 2016 [34]	30 minutes	Qualitative data: Discount Usability Engineering Quantitative data: MSSQ, NPS for anxiety
23.Scates et al., 2020 [42]	7 minutes loop	Quantitative data: Questionnaires about feelings, VR experience

TABLE V. Type of Study, Study Duration, and Instruments.

IEEE Access Multidisciplinary ⁞ Rapid Review ⁞ Open Access Journal

[38], [39] and a small sample size population [24], [25], [26], [27], [22], [31], [37], [39], [40], [41]. It is, therefore, suggested for future studies to run long-term experiments where the VR equipment will be deployed into the clinical settings for a longer period of time to validate the applicability of VR technology into the health care system [33], and to increase the sample size of the population to reduce the statistical errors [35]. It is also recommended for future studies to develop personalized solutions based on each patient's interests and needs [38], [42]. Apart from the methodological limitations and the future directions to those; several limitations based on the equipment were also reported. In particular, most of the reviewed studies used what is so-called as high-end VR technologies [23], [39]. This type of VR technology necessitates an expensive and not affordable solution to implement in real-world clinical setting. A relevant literature review which examines the effectiveness of low-cost VR equipment has suggested that moving to low-cost and accessible solutions can improve the use of VR in health care, and reduce the need of equipment maintenance, while it can still be an effective solution for pain management [2]. Therefore, it is suggested for future studies to evaluate the use of low-end VR solutions to offer more personalized and patient-centric VR medical applications.

To further corroborated the above, it was also reported the need for the development of a low-cost home-based VR tool which can be used by the patients without interrupting their daily activities [23]. Our review found only one study [30] which evaluated the used of VR from cancer patients at their personal spaces. Future studies need to be conducted to enhance our understanding of the requirements that are needed to develop an effective VR home-based solution for cancer patients [30], [39].

Future Challenges of VR in pain management	
1.	Reliable pain assessment through bio-signals, qualitative and quantitative data
2.	Personalised instruments and VEs based on each patient needs to properly assess the effectiveness of the developed technology
3.	Minimization of the time required for the patient's evaluation
4.	Long-term experiments to evaluate the efficiency and applicability of the VR technology in real-world clinical settings
5.	Evaluate the use of low-cost and accessible VR solutions to supply personalized VR medical applications for inpatients and outpatients
6.	Develop comfortable, flexible in set-up VR technology designs to reduce the patient's fatigue or discomfort

TABLE VI. Future Challenges of VR in pain management

Finally, some patients also reported that the use of a HMD in some cases was causing them discomfort [29]. We believe that future studies should take into consideration this factor for their design to reduce the risk of fatigue or discomfort that might be caused to the patients. This has been effectively done, by studies with people living with dementia. The aforementioned studies used a wireless mobile HMD which allowed flexibility in setting up the equipment quickly and unobtrusively in different familiar locations, allowing the caregivers to easily focus on introducing the equipment and supporting the person. To ensure comfortability the device incorporated soft padding and adjustable head striped to allow the comfortable use on the patients' head [65], [66].

V. CONCLUSIONS

Based on all the studies that were reviewed, it is suggested that VR can be an effective technology in clinical settings to ameliorate cancer patients' pain and improve the rehabilitation trainings the patients are receiving. This can result in minimizing the persistent disabilities the patients are dealing with, while it can also positively enhance their emotional well-being. Based on the reviewed studies, there are several characteristics and design strategies that a VR tool should incorporate in order develop and deliver an effective VR solution which depends on: (1) the patients' type of pain, medical history and demographics; (2) the patients' subjective experiences on medical processes; (3) the patients' interests and daily-living activities. Therefore, for an effective and feasible VR solution, the system should incorporate features relevant to: (1) distractive environments, with relaxation scenes; (2) real-time feedback; (3) personalized experiences based on each patient needs; (4) physiological responses; (5) comfortability; (6) affordable low-cost VR devices so the patients' will be able to use them from their personal spaces. We believe that if these criteria are met and VR applications are developed based on these criteria, these will result in an improved healthcare system, where patients will be able to manage successfully the procedural and chronic pain arising from cancer.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No 739578 and the Government of the Republic of Cyprus through the Directorate-General for European Programmes, Coordination and Development.

REFERENCES

[1] Arntz, and L. Claassens, "The meaning of pain influences its experienced intensity," *Pain*, vol.109, pp. 20–25, May 2004.

[2] M. Matsangidou, C. S. Ang, and M. Sakel, "Clinical utility of virtual reality in pain management: a comprehensive research review," *British Journal of Neuroscience Nursing*, vol.13, no. 3, pp. 133-143, 2017.

[3] H. Merskey, and N. Bogduk, "Classification of chronic pain," Seattle, USA, WA: IASP Press, 1994.

[4] G. L. Moseley, "A pain neuromatrix approach to patients with chronic pain," *Manual therapy*, vol. 8, no. 3, pp.130-140, Aug. 2003.

[5] D. Price, "Psychological mechanisms of pain and analgesia," Seattle, USA, WA: IASP Press, 1999.

[6] H. G. Hoffman et al., "Virtual reality as an adjunctive non-pharmacologic analgesic for acute burn pain during medical procedures," A*nnals of behavioral medicine*, vol. 41, no. 2, pp.183-191, Apr. 2011.

[7] H. G. Hoffman, T. L. Richards, B. Coda, A. R. Bills, D. Blough, A. L. Richards, and S. R. Sharar, "Modulation of thermal pain-related brain activity with virtual reality: evidence from fMRI," *Neuroreport*, vol. 15, no. 8, pp. 1245-1248, Jun. 2004.

[8] M. Ma, and H. Zheng, "Virtual reality and serious games in healthcare," in *Advanced Computational Intelligence Paradigms in Healthcare*, vol. 6, Virtual Reality in Psychotherapy, Rehabilitation, and Assessment, Springer, Berlin: Heidelberg, 2011, pp.169-192.

[9] T. E. Motraghi, R. W. Seim, E. C. Meyer, and S. B. Morissette, "Virtual reality exposure therapy for the treatment of posttraumatic stress disorder: a methodological review using CONSORT guidelines," *Journal of Clinical Psychology*, vol. 70, no. 3, pp. 197-208, Mar. 2014.

[10] B. Otkhmezuri et al., "Believing is seeing: a proof-of-concept semiexperimental study on using mobile virtual reality to boost the effects of interpretation bias modification for anxiety," *JMIR mental health*, vol. 6, no. 2, p115-117, Feb. 2019

[11] L. R. Valmaggia, L. Latif, M. J. Kempton, and M. Rus-Calafell, "Virtual reality in the psychological treatment for mental health problems: a systematic review of recent evidence," *Psychiatry research*, vol. 236, pp. 189-195, Jan. 2016.

[12] D. Freeman, S. Reeve, A. Robinson, A. Ehlers, D. Clark, B. Spanlang, and M. Slater, "Virtual reality in the assessment, understanding, and treatment of mental health disorders," *Psychological medicine*, vol. 47, no.14, pp. 2393-2400, Oct. 2017.

[13] O. Grynszpan, P. L.Weiss, F. Perez-Diaz, and E. Gal, "Innovative technology-based interventions for autism spectrum disorders: a meta-analysis," *Autism*, vol. 18, no. 4, pp. 346-361, Aug. 2014.

[14] J. L. Maples-Keller, B. E. Bunnell, S. J. Kim, and B. O. Rothbaum, "The Use of Virtual Reality Technology in the Treatment of Anxiety and Other Psychiatric Disorders," *Harvard review of psychiatry*, vol. 25, no. 3, pp. 103-113, Jun. 2017.

[15] M. Matsangidou, B. Otkhmezuri, C. S. Ang, M. Avraamides, G. Riva, A. Gaggioli, D. Iosif, and M. Karekla, "Now I Can See Me: A Virtual Representation of Self-image: Designing a Multi-User Virtual Reality Remote Psychotherapy for Body Shape and Size Concerns," *Journal of Human–Computer Interaction*, to be published

[16] M. Rus -Calafell, P. Garety, E. Sason, T. J. K. Craig, and L. R. Valmaggia, "Virtual reality in the assessment and treatment of psychosis: a systematic review of its utility, acceptability and effectiveness," *Psychological Medicine*, vol. 48, no. 3, pp. 362-391, Jul. 2017.

[17] W. Veling, S. Moritz, M. Van der Gaag, "Brave new worlds—Review and update on virtual reality assessment and treatment in psychosis," *Schizophrenia bulletin*, vol. 40, no. 6, pp. 1194-1197, Nov. 2014

[18] D. Hanahan, and R.A. Weinberg, "The hallmarks of cancer," *Cell*, vol. 100, no. 1, pp. 57-70, Jan 2000.

[19] D. Hanahan, D., and R. A. Weinberg, "Hallmarks of cancer: the next generation," *Cell*, vol. 144, no. 5, pp. 646-674, Mar. 2011.

[20] A. Abushakra and M. Faezipour, "Augmenting breath regulation using a mobile driven virtual reality therapy framework," *IEEE J. Biomed. Heal. Informatics*, vol. 18, no. 3, pp. 746–752, May 2014.

[21] B. Atzori et al., "Virtual reality analgesia during venipuncture in pediatric patients with onco-hematological diseases," *Front. Psychol.*, vol. 9, pp. 1–7, Dec. 2018.

[22] M. Ayala-Feliciano, J. J. Pons-Valerio, J. Pons-Madera, and S. F. Acevedo, "Breast Cancer: Basic and Clinical Research the Relationship between Visuospatial Memory and Coping Strategies in Breast Cancer Survivors," *Breast Cancer Basic Clin. Res.*, vol.5, pp. 117–130, Jun. 2011.

[23] E. B. Mohammad, "Virtual reality as a distraction technique for pain and anxiety among patients with breast cancer: A randomized control trial," *Palliative and Supportive Care,* vol. 17, no.1, pp. 29-34, Feb. 2019.

[24] R. M. Baños and M. Espinoza, "A positive psychological intervention using virtual reality for patients with advanced cancer in a hospital setting: a pilot study to assess feasibility," *Supporting Care in Cancer,* vol. 21, no.1, pp. 263–270, Jan. 2013.

[25] K. A. Birnie *et al.*, "Usability Testing of an Interactive Virtual Reality Distraction Intervention to Reduce Procedural Pain in Children and Adolescents with Cancer," *J. Pediatr. Oncol. Nurs.*, vol. 35, no. 6, pp. 406–416, Jun. 2018.

[26] C. Camargo *et al.*, "Protocols of Virtual Rehabilitation for Women in Post-Operative Breast Cancer Stage," *SBC Proceeding SBGames*, vol. 1, pp. 16–18, 2013.

[27] C. Camargo *et al.*, "Virtual rehabilitation in women with post breast cancer - A case study," *2013 Int. Conf. Virtual Rehabil. ICVR 2013*, pp. 188–189, 2013.

[28] M. Duivon *et al.*, "Impact of breast cancer on prospective memory functioning assessed by virtual reality and influence of sleep quality and hormonal therapy: PROSOM-K study," *BMC Cancer*, vol. 18, no. 1, pp. 1–10, Sep. 2018.

[29] C. Glennon *et al.*, "Use of virtual reality to distract from pain and anxiety," *Oncol. Nurs. Forum*, vol. 45, no. 4, pp. 545–552, Jul. 2018.

[30] A. J. Hoffman, R. A. Brintnall, and J. Cooper, "Merging technology and clinical research for optimized postsurgical rehabilitation of lung cancer patients," *Ann. Transl. Med.*, vol. 4, no. 2, pp. 1–7, Jan. 2016.

[31] G. House *et al.*, "A feasibility study to determine the benefits of upper extremity virtual rehabilitation therapy for coping with chronic pain post-cancer surgery," *Br. J. Pain*, vol. 10, no. 4, pp. 186–197, Aug. 2016.

[32] M. T. Høybye, P. R. Olsen, H. E. Hansson, D. Spiegel, H. Bennetsen, and E. Cheslack-Postava, "Virtual environments in cancer care: Pilot-testing a three-dimensional web-based platform as a tool for support in young cancer patients," *Health Informatics J.*, vol. 24, no. 4, pp. 419–431, Dec. 2018.

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/ACCESS.2020.3044233, IEEE Access

[33] W. H. Li, J. O. Chung, and E. K. Ho, "The effectiveness of therapeutic play, using virtual reality computer games, in promoting the psychological well-being of children hospitalised with cancer," *J. Clin. Nurs.*, vol. 20, no. 15–16, pp. 2135–2143, 2011.

[34] X. Li, N. Jolani, T. T. Dao, and H. Jimison, "Serenity: A Low-Cost and Patient-Guided Mobile Virtual Reality Intervention for Cancer Coping," *Proc. - 2016 IEEE Int. Conf. Healthc. Informatics, ICHI 2016*, pp. 504–510, 2016.

[35] S. M. Schneider, C. K. Kisby, and E. P. Flint, "Effect of virtual reality on time perception in patients receiving chemotherapy," vol. 19, no. 4, pp. 555–564, Apr. 2011.

[36] K. Tsuda *et al.*, "A feasibility study of virtual reality exercise in elderly patients with hematologic malignancies receiving chemotherapy," *Intern. Med.*, vol. 55, no. 4, pp. 347–352, 2016.

[37] Ö. Feyzioğlu, S. Dinçer, A. Akan, and Z. C. Algun, "Is Xbox 360 Kinect-based virtual reality training as effective as standard physiotherapy in patients undergoing breast cancer surgery?," *Supportive Care in Cancer*, vol. 28, no. 9, pp. 4295-4303, Jan. 2020.

[38] M. Tennant, G. J. Youssef, J. McGillivray, T. Clark, L. McMillan, and M. C. McCarthy, "Exploring the use of Immersive Virtual Reality to enhance Psychological Well-Being in Pediatric Oncology: A pilot randomized controlled trial," *European Journal of Oncology Nursing*, vol.48, Jun. 2020.

[39] B. M. Garrett, G. Tao, T. Taverner, E. Gordingley, and C. Sun, "Patients perceptions of virtual reality therapy in the management of chronic cancer pain," *Heliyon*, vol. 6, no. 5, e03916, May 2020.

[40] S. Sharifpour, G. Manshaee, and I. Sajjadian, "Effects of virtual reality therapy on perceived pain intensity, anxiety, catastrophising and self-efficacy among adolescents with cancer," *Counselling and Psychotherapy Research*, pp. 1-9, Mar. 2020.

[41] D. Atef, M. M. Elkeblawy, A. El-Sebaie, and W. A. Abouelnaga, "A quasi-randomized clinical trial: virtual reality versus proprioceptive neuromuscular facilitation for postmastectomy lymphedema," *Journal of the Egyptian National Cancer Institute*, vol. 32, no. 1, Jun. 2020.

[42] D. Scates, J. I. Dickinson, K. Sullivan, H. Cline, and R. Balaraman, "Using Nature-Inspired Virtual Reality as a Distraction to Reduce Stress and Pain Among Cancer Patients," *Environment and Behavior*, vol. 52, no.8, pp. 895-918, May 2020.

[43] J. A. Bargas-Avila, and K. Hornbæk, "Old wine in new bottles or novel challenges: a critical analysis of empirical studies of user experience," in *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*, Vancouver BC, Canada, pp. 2689-2698, 2011.

[44] J. Deeks, J. Higgins, and D. G. Altman, "Analysing data and undertaking meta-analyses," Cochrane handbook for systematic reviews of interventions: Cochrane book series, pp. 243-296, 2008.

[45] K. S. Khan, G. Ter Riet, J. Glanville, A. J. Sowden, and J. Kleijnen, "Undertaking systematic reviews of research on effectiveness: CRD's guidance for carrying out or commissioning reviews," NHS Centre for Reviews and Dissemination, University of York, CRD Report, no. 4, 2001.

[46] H. G. Hoffman, D. R. Patterson, J. Magula, G. J. Carrougher, K. Zeltzer, S. Dagadakis, and S. R. Sharar, "Water-friendly virtual reality pain control during wound care," *Journal of clinical psychology*, vol. 60, no. 2, pp. 189-195, Feb. 2004.

[47] H. G. Hoffman et al., "Immersive virtual reality as an adjunctive non-opioid analgesic for predominantly Latin American children with large severe burn wounds during burn wound cleaning in the Intensive Care Unit: A pilot study," F*rontiers in human neuroscience*, vol. 13, pp. 262-273, Aug. 2019.

[48] S. M. Schneider, M. Ellis, W. T. CoombS, E. L. Shonkwiler, and L. C. Folsom, "Virtual reality intervention for older women with breast cancer," *Cyberpsychol Behav*, vol. 6, no. 3, pp. 301–307, Jun. 2003.

[49] D. A. Delgado, B. S. Lambert, N. Boutris, P. C. McCulloch, A. B. Robbins, M. R. Moreno, and J. D. Harris, "Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults," *Journal of the American Academy of Orthopaedic Surgeons. Global research & reviews*, vol. 2, no.3, Mar. 2018.

[50] J. T. Farrar, J. P. Young, L. LaMoreaux, J. L. Werth, R. M. Poole, "Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale," *Pain*, vol.94, no. 2, pp. 149-158, Nov. 2001.

[51] R. Melzack, "The McGill Pain Questionnaire: Major Properties and scoring methods," *Pain*, vol.1, no. 3, pp. 277-299, Sep. 1975.

[52] C. K. Conners, M. H. S. Staff, V. Connelly, S. Campbell, M. MacLean, and J. Barnes, "Conners' continuous performance Test II (CPT II)," *Multi-Health Syst Inc*, vol. 29, pp. 175-96, 2000.

[53] B. Merker, and K. Podell, "Grooved Pegboard Test," in *Encyclopedia of Clinical Neuropsychology*, J. S. Kreutzer, J. DeLuca, B. Caplan, Springer, New York, NY.

[54] P. J. Bryden, and E. A. Roy, "A new method of administering the Grooved Pegboard Test: performance as a function of handedness and sex," *Brain Cogn*., vol. 58, pp. 258–268, 2005

[55] Z. S. Nasreddine, N. A. Phillips, V. Bédirian, S. Charbonneau, V. Whitehead, I. Collin, J. L. Cummings, and H. Chertkow, "The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment," *J Am Geriatr Soc*, vol. 53, no. 4, pp 695–699, Apr. 2005.

[56] S. R. Tilton, "Review of the state-trait anxiety inventory (STAI)," *News Notes*, vol. 48, no. 2, pp. 1–3, 2008.

[57] C. D. Spielberger, "State-Trait anxiety inventory," *The Corsini encyclopedia of psychology*, Wiley Online Library, pp. 1-14, Jan. 2010.

[58] A. Beck, C.Ward, M. Mendelson, J. Mock, and J.Erbaugh J, "An inventory for measuring depression," *Arch Gen Psychiatry*, vol. 4, pp. 561-571, 1961.

[59] J. Nielsen, "Applying discount usability engineering," *Software*, IEEE, vol. 12, pp. 98-100, Jan. 1995.

[60] R. S. Kennedy, N. E. Lane, K. S. Berbaum, and M. G. Lilienthal, "Simulator sickness questionnaire: an enhanced method for quantifying simulator sickness," *Int J Aviat Psychol*., vol. 3, pp. 203-220, 1993.

[61] J. F. Golding, "Motion sickness susceptibility questionnaire revised and its relationship to other forms of sickness," *Brain research bulletin*, vol. 47, pp. 507-516, 1998.

[62] R. M. Hoeft, J. Vogel, and C. A. Bowers, “Kids get sick too: a proposed child simulator sickness questionnaire,” in *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, Sage Publication, Los Angeles, CA, 2003.

[63] M. Matsangidou, C. S. Ang, A. R. Mauger, B. Otkhmezuri, and L. Tabbaa, “How Real Is Unreal?”, *IFIP Conference on Human-Computer Interaction*, vol. 10516, pp. 273-288, Sep. 2017.

[64] M. Matsangidou, C. Siang, A. R. Mauger, J. Intarasirisawat, B. Otkhmezuri, and M. N. Avraamides, “Psychology of Sport & Exercise Is your virtual self as sensational as your real? Virtual Reality: The effect of body consciousness on the experience of exercise sensations,” *Psychology of Sport & Exercise*, vol. 41, pp. 218–224, Jul. 2019.

[65] V. Rose, I. Stewart, K. G. Jenkins, L. Tabbaa, C. S. Ang, and M. Matsangidou, “Bringing the outside in: The feasibility of virtual reality with people with dementia in an inpatient psychiatric care setting,” *Dementia*, Sep. 2019.

[66] L. Tabbaa, C. S. Ang, V. Rose, P. Siriaraya, I. Stewart, K. G. Jenkins, and M. Matsangidou, “Bring the Outside In: Providing Accessible Experiences Through VR for People with Dementia in Locked Psychiatric Hospitals,” in *Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems* , Glasgow, Scotland, UK, May 4-9, 2019.