



## Application of virtual reality in neurosurgery: Patient missing. A systematic review



Pia Vayssiere<sup>a,b,\*</sup>, Paul E. Constanthin<sup>a</sup>, Bruno Herbelin<sup>c</sup>, Olaf Blanke<sup>b,c</sup>, Karl Schaller<sup>a,b</sup>, Philippe Bijlenga<sup>a,b</sup>

<sup>a</sup> Department of Neurosurgery, Hôpitaux Universitaires de Genève (HUG), Geneva, Switzerland

<sup>b</sup> Faculty of Medicine, Université de Genève (UNIGE), Geneva, Switzerland

<sup>c</sup> Laboratory of Cognitive Neuroscience, Center for Neuroprosthetics & Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne (EPFL), Geneva, Switzerland

### ARTICLE INFO

#### Article history:

Received 12 May 2021

Accepted 26 November 2021

#### Keywords:

Virtual reality

Neurosurgery

Applications

Patients

### ABSTRACT

Virtual reality (VR) technology had its earliest developments in the 1970s in the U.S. Air Force and has since evolved into a budding area of scientific research with many practical medical purposes. VR shows a high potential to benefit to learners and trainees and improve surgery through enhanced preoperative planning and efficiency in the operating room. Neurosurgery is a field of medicine in which VR has been accepted early on as a useful and promising tool for neuro-navigation planning. Through recent technological developments, VR further increased its level of immersion, accessibility and intuitive use for surgeons and students and now reveals a therapeutic potential for patients.

In this paper, we systematically reviewed the neurosurgery literature regarding the use of VR as an assistance for surgery or a tool centered on patients' care. A literature search conducted according to PRISMA guidelines resulted in the screening of 125 abstracts and final inclusion of 100 original publications reviewed.

The review shows that neurosurgeons are now relatively familiar with VR technologies (N = 95 articles) for their training and practice. VR technologies are useful for education, pain management and rehabilitation in neurosurgical patients. Nevertheless, the current patient-oriented use of VR remains limited (N = 5 articles).

Successful surgery does not only depend on the surgeon's skills and preparation, but also on patients' education, comfort, empowerment and care. Therefore further clinical research is needed to promote the direct use of VR technologies by patients in neurosurgery.

© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Since its early developments, Virtual Reality (VR) has been constantly improving, with an exponential acceleration in the recent years [1].

Early VR developments were based on concepts from cybernetics: an artificial system which would be capable of emulating sensory inputs, thus removing the person from his/her true environment and placing him/her into an artificial one [2]. This view initiated the quest for fully immersive systems, which could entirely surround the human body and its senses. Immersion is

the entry point for VR; putting in place the conditions for the cognitive processes to occur, it is defined as the ability of a VR system to induce the experience of the displacement of a person inside what is called an immersive virtual environment [3]. The high-level immersion of the subject in VR is made possible by multi-sensory integration [4], and its underlying neurocognitive mechanisms are still being investigated in engineering and cognitive sciences cross-studies [5,6].

Applications of VR in neurosurgery are developing rapidly. Some examples are training in dexterity and technical skills, teaching of neuroanatomy and planning of surgical procedures. Education and Training seem to be the predominant fields of application for VR. Neurosurgery requires a long training and the acquisition of extensive knowledge; the anatomy of the central nervous system must be mastered, going beyond the classical 2D representations found in textbooks. Indeed, in order to navigate

Abbreviations: VR, Virtual Reality; OR, Operative Room.

\* Corresponding author at: Service de Neurochirurgie, Hôpitaux Universitaires de Genève, Rue Gabriel-Perret-Gentil 5, 1205 Genève, Switzerland.

E-mail address: [pia.vayssiere@gmail.com](mailto:pia.vayssiere@gmail.com) (P. Vayssiere).

during surgery, neurosurgeons need to have a 3D representation or “map” of the different anatomical structures.

This challenge has been made easier by access to precise, detailed 3D representations of the human brain and spine, resulting in the possibility to examine anatomical and functional relationships and of to study variations of pathologies, as well as exploring surgical alternatives. VR allows precise 3D anatomical training, as well as the acquisition of common surgical pathways and the testing of new surgical strategies.

VR could also be used more directly to the benefit of neurosurgical patients. In the current way of thinking, surgical success is too often centered on the surgeons and on their ability to perform a procedure. However, beyond the procedure itself, the way patients react to the procedure will also affect the postoperative outcome. Patient’s perception is an integral part of care success. When a patient becomes an active and involved partner in his or her care, he or she develops a feeling of autonomy and self-determination, which helps with the maintenance or promotion of the patient’s self-management resources [7]. Neurosurgery is a surgical specialty that is particularly distressing for patients because of its possible consequences in terms of postoperative complications that can be particularly disabling [8].

The goal of this work is to report the current state of the art regarding the use of VR in neurosurgery oriented towards its specific use by either surgeons or patients.

## 2. Material & methods

### 2.1. Search strategy and study selection

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P) 2015 guidelines [9]. No registration was required for this study. On February 1st 2021, a literature search was performed in PubMed and Google Scholar. The following terms were used: “virtual reality AND Neurosurgery”, resulting in a list of 125 articles.

A total of 116 original articles were retained after abstract review and 16 were subsequently excluded after full-text analysis. Works were excluded if data were previously reported in other original articles or publications were not written in English (Fig. 1). A total of 100 articles published between 1995 and 2021 were included for final analysis (Table 1).

### 2.2. Data collection and analysis

The following data items were recorded: first author; year of publication and journal/book.

Studies were grouped by “Target Population” according to the population studied either “Surgeons” or “Patients”. The aim was to categorize the population who is using the VR set. Was the individual who put the helmet a surgeon or a patient?

Studies were further categorised according to a “Study Domain” being one of: “Training”, “Education”, “Therapeutic”, “Safety”.

“Training” applies to all articles in which VR was used for planning or simulating steps of surgical procedures. “Training” domain can be used by the surgeon to repeat a procedure in order to memorize all the step of the surgery. But it can also be used (with a different program but following the same concept) by a patient to see how a surgery is organized and what will happen around them when they are under sedation. In doing so, it becomes a way to avoid added stress linked to the unknown.

“Education” applies to teaching tools to acquire knowledge such as anatomy or pathophysiology.

“Therapeutic” applies to VR developments aiming at relieving symptoms or improving the patients’ condition.

“Safety” encompassed articles in which VR was used to simulate specific dangers during a procedure in order to anticipate them, allowing for control of the viability of a procedure or the operative room’s (OR) organisation around a procedure. “Safety” is another domain which can be found for both population (surgeon and patient). The duo “Patient” and “Safety” stands for the evaluation of the tolerance and safety of a virtual reality headset (VRH) and immersive virtual experiences in patients undergoing awake craniotomy [10].

### 2.3. Group attribution

The attribution of each article to a group and Domain was done by the first author and then controlled by the second author and one supervisor (PB).

## 3. Results

We included 100 articles for final analysis (Table 1). The Target Population of the VR applications were Surgeons in 95% of studies. Only 5 studies were targeting Patients as VR users (5%) (Fig. 2).

Regarding the classification according to Study Domain, the vast majority of VR applications targeting Surgeons were classified as focused on Training (N = 73 (76,8%)) or Education (N = 20 (21.0%)). Studies on VR applications targeting Patients were focused on Therapeutic (N = 4 (80%)) or Safety (N = 1 (20%)) (Fig. 3 and Table 2).

Regarding the evolution of the number of publications across years, we observed that VR research dedicated to patient appears to be quite new with the first paper published in 2017 (Fig. 4.1). “Training” represented the specific field with the greatest number of publications regarding VR and neurosurgeons in the last few years (2016 to 2021). Finally, “Education” of neurosurgeons with VR appeared to be the second most recent and important field of research (Fig. 4.2).

## 4. Discussion

### 4.1. Results description

Taken together, these results show that the vast majority of studies describing the use of VR in neurosurgery have, to this point, targeted surgeons and not patients. Regarding the domain of VR publications in neurosurgery, there is an increasing number of papers between 2016 and 2020 addressing specifically training, with the emergence of new domains of VR like education and safety. The use of VR targeting neurosurgical patients appears very recent with the first article published in 2017 and the number of publications remaining low compared to those targeting surgeons.

### 4.2. Training

One of the most important skill in neurosurgery is manual dexterity. Uncontrolled surgical maneuvers can indeed result in devastating injuries, potentially leading to long-term neurological deficits or the patient’s death. VR allows meticulous movements to be repeated and mastered in surgical simulators. Above all, VR allows aspiring and advanced neurosurgeons to practice wherever they are. This is in contrast with operating room training, where mistakes due to stress or inexperience can result in dramatic outcomes [11].

As a new approach, the introduction of VR has been met with popularity and holds exciting prospects for both surgical training and preoperative surgical planning of complex procedures because it allows for patient-specific safe environments in which surgeons

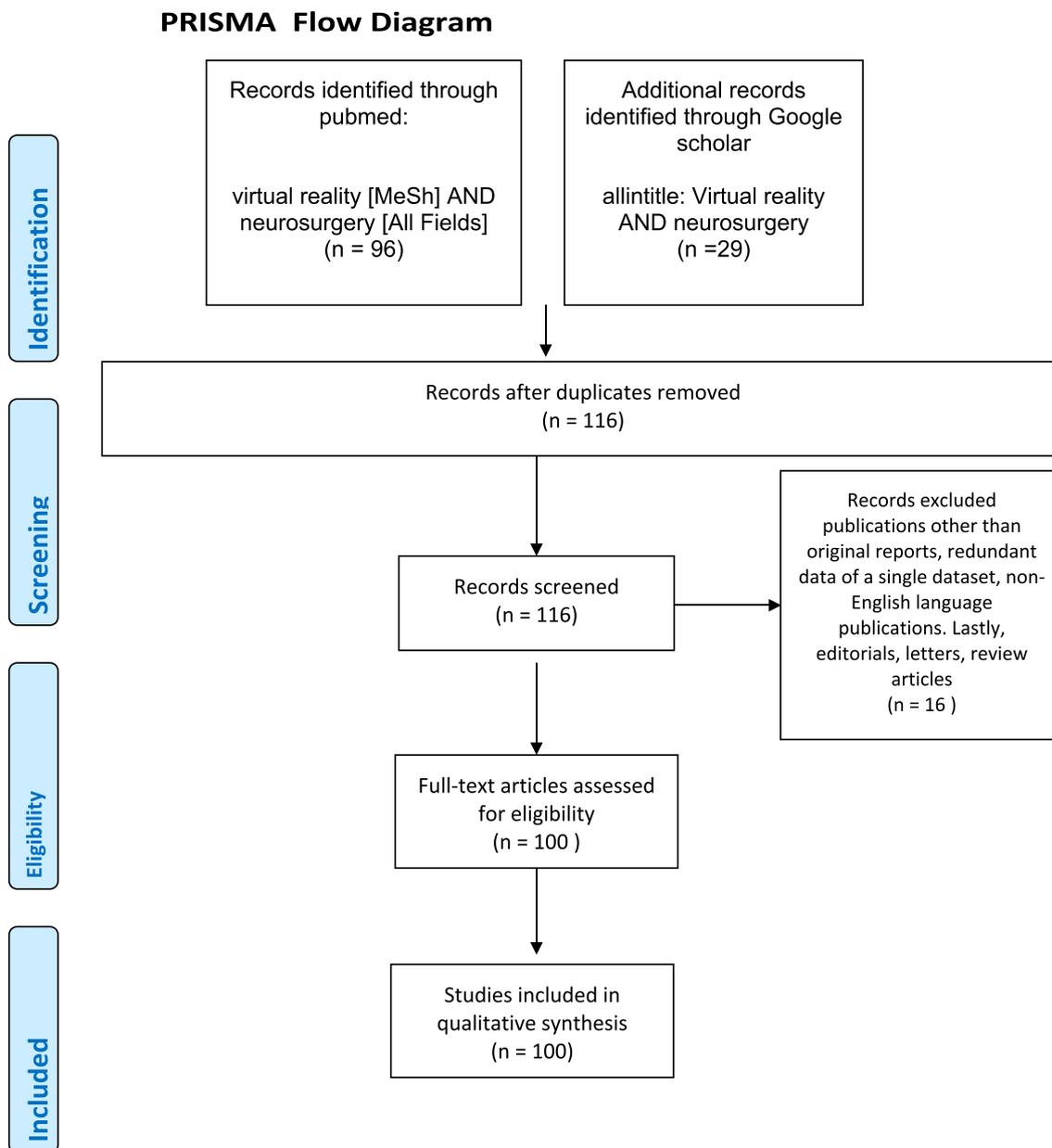


Fig. 1. PRISMA Flow Diagram.

may hone their skills without risking patient's safety [12,13]. Although the use of VR is already frequent for many surgical specialties [14], adaptation into neurosurgery has been slow and evidence that outlines its usefulness is scant.

The earliest Neurosurgery VR systems were developed in the late 2000s, including a ventriculostomy environment using ImmersiveTouch and a brain tumor resection environment using NeuroTouch (subsequently named NeuroVR) [15,16]. In preoperative planning, VR allows physicians to visualize 3D representations of surgical structures and design optimal patient-specific approaches, which has been shown to decrease complications and improve outcomes [17–19].

#### 4.3. Education

Neuroanatomy is one of the most challenging subjects in anatomy and students or novice surgeons often experience difficulty grasping the complex three-dimensional (3D) spatial relationships. In medical education, VR allows students to see anatomic structures in 3D and

thus better conceptualize relationships between structures, leading to superior training through improved attention, motivation, and learner satisfaction [20–23]. Immersive VR simulation provides learners with the opportunity to conceptualize complex 3D anatomic relationships rapidly. This technology is being employed at all levels of medical training and its adoption is likely to expand considerably [24]. Several studies have shown that 3D neuroanatomical learning is an effective strategy for increasing neuroanatomical knowledge, motivation and retention of neuroanatomy material [25–29]. Furthermore, participants improved in their knowledge of spatial relations when they were exposed to both physical [30] and virtual [31] 3D brain models. VR technology appears to be a logical next step for enhanced spatial and interactive learning.

#### 4.4. Safety

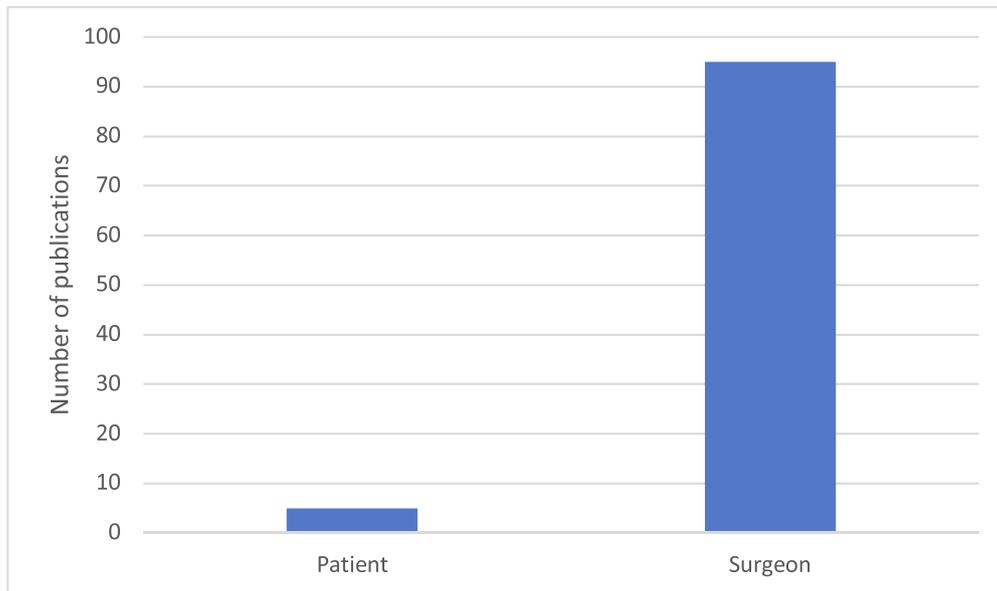
Hazards in real life can involve serious danger. This is why VR emerges as a potential medium for risk assessment and training, allowing users to operate, without risks, in a quasi-real environ-

**Table 1**  
List of articles included (sorted by date of occurrence).

Author	Journal/Book	Publication Year	DOMAIN	TARGET POPULATION
Doyle	Study in health technology and informatics	1995	Training	Surgeon
Kelly	Bulletin of the American College of surgeons	1996	Training	Surgeon
Kockro et al	Neurosurgery	2000	Training	Surgeon
Kockro et Seera	Comprehensive Healthcare Simulation: Neurosurgery	2000	Training	Surgeon
Spicer et Apuzzo	Neurosurgery	2003	Training	Surgeon
Spicer et al	Neurosurgery	2004	Training	Surgeon
Prasad	Medical Science Monitor	2005	Education	Surgeon
Wang et al	Comput Methods Programs Biomed	2005	Training	Surgeon
Goha	Conf Proc IEEE Eng Med Biol Soc	2006	Education	Surgeon
Wang et al	Comput Methods Programs Biomed	2006	Training	Surgeon
Liu et Wang	International Conference on Artificial Reality and Telexistence	2006	Training	Surgeon
Zhnag et al	Chinese Journal of Microsurgery	2006	Training	Surgeon
Cy et al	Annu Int Conf IEEE Eng Med Biol Soc	2007	Training	Surgeon
Toimofeev et al	SPIIRAS Proceedings	2008	Education	Surgeon
Chen et al	Journal of Clinical Neurosurgery	2008	Training	Surgeon
Stadie et al	Journal of Neurosurgery	2008	Training	Surgeon
Lemole et al	Neurological Research	2009	Training	Surgeon
Alaraj et al	Surgical Neurology International	2011	Training	Surgeon
Patel et al	World neurosurgery	2013	Training	Surgeon
Choudhury et al	World neurosurgery	2013	Training	Surgeon
Roitberg et al	Neurosurgery	2013	Training	Surgeon
Cohen et al	Child's Nervous System	2013	Training	Surgeon
Suri et al	Journal of neurological surgery	2014	Training	Surgeon
Natekar et al,	International Conference on Intelligent Informatics and BioMedical Sciences	2015	Training	Surgeon
Roitberg et al	Journal of surgical Education	2015	Training	Surgeon
Vilanilam et al	Neurology India	2016	Education	Surgeon
de Faria et al	Journal of Neurosurgery	2016	Training	Surgeon
Stepan et al	International Forum of Allergy and Rhinology	2017	Education	Surgeon
Kin et al	Neurologia Medico Chirurgicala	2017	Education	Surgeon
Pelargos et al	Journal of Clinical Neuroscience	2017	Education	Surgeon
Tadic	Neurosurgery	2017	Safety	Surgeon
Bajunaid et al	Journal of Neurosurgery	2017	Therapeutic	Patient
Breimer et al	Operative Neurosurgery	2017	Training	Surgeon
Azarnoush et al	Journal of Neurosurgery	2017	Training	Surgeon
Lafage et al	Spine	2017	Training	Surgeon
Bernardo	World Neurosurgery	2017	Training	Surgeon
Incekara et al	World Neurosurgery	2018	Education	Surgeon
Hendricks et al	Operative Neurosurgery	2018	Education	Surgeon
Qian et al	Journal of Craniofacial Surgery	2018	Education	Surgeon
Sawaya et al	Operative Neurosurgery	2018	Education	Surgeon
Cano Porras et al	Neurology	2018	Therapeutic	Patient
Bernard et al	Journal of Medical Internet Research	2018	Therapeutic	Patient
Chen et al	Zhonghua Yi Xue Za Zhi	2018	Training	Surgeon
Zhang et al	Zhonghua Wai Ke Za Zhi	2018	Training	Surgeon
Hendricks et al	Operative Neurosurgery	2018	Training	Surgeon
Dimitrov et al	Neurology India	2018	Training	Surgeon
Won et al	Int Forum Allergy Rhinol	2018	Training	Surgeon
Perin et al	Acta Neurochirurgica	2018	Training	Surgeon
Shono et al	Oper Neurosurg (Hagerstown)	2018	Training	Surgeon
Yao et al	World Neurosurgery	2018	Training	Surgeon
Tucker et al	Operative Neurosurgery	2018	Training	Surgeon
Raabe et al	Journal of Neurosurgery	2018	Training	Surgeon
Sah Perez et al	J-Global	2018	Training	Surgeon
Liu et al	Clinical Neurology and Neurosurgery	2018	Training	Surgeon
Choque-Velasquez et al	World Neurosurgery	2018	Training	Surgeon
Mazur et al	World Neurosurgery	2018	Training	Surgeon
Jean et al	Acta Neurochirurgica	2019	Education	Surgeon
Winkler-Schwartz et al	Journal of Surgical Education	2019	Education	Surgeon
Benjamin et al	Operative Neurosurgery	2019	Education	Surgeon
Tomlinson et al	World Neurosurgery	2019	Education	Surgeon
Bairamian et al	Neurosurgery	2019	Education	Surgeon
Zawy Alsofy et al	Br J Neurosurg	2019	Safety	Surgeon
Denmark et al	Neuropsychological Rehabilitation	2019	Therapeutic	Patient
Bernard et al	Neurosurgery	2019	Training	Surgeon
Chen et al	Beijing Da Xue Xue Bao Yi Xue Ban	2019	Training	Surgeon
Winkler-Schwartz et al	World Neurosurgery	2019	Training	Surgeon
Fiederer et al	Cornell University	2019	Training	Surgeon
Singh et al	World Neurosurg	2019	Training	Surgeon
Bissonnette et al	The Journal of Bone and Joint Surgery	2019	Training	Surgeon
Burström et al	Spine	2019	Training	Surgeon
Serrano et al	World Neurosurgery	2019	Training	Surgeon
Sah Perez et al	The Proceedings of JSME annual Conference on Robotics and Mechatronics	2019	Training	Surgeon
Bugdadi et al	Journal of Surgical Education	2019	Training	Surgeon
Bracq et al	Nurse Educ Today	2019	Training	Surgeon

**Table 1** (continued)

Author	Journal/Book	Publication Year	DOMAIN	TARGET POPULATION
Winkler-Schwartz et al	JAMA Netw Open	2019	Training	Surgeon
Bracq et al	Nurse Education Today	2019	Training	Surgeon
Mikhail et al	World Neurosurgery	2019	Training	Surgeon
Cagiltay et al	Surgical Innovation	2019	Training	Surgeon
Bernard et al	Neurosurgery	2019	Training	Surgeon
Kimura et al	Neurosurgical Review	2019	Training	Surgeon
Lee et Wong	Journal of Clinical Neuroscience	2019	Training	Surgeon
Heredia-Pérez et al	The International Journal of Medical Robotics	2019	Training	Surgeon
Zawy Alsofy et al	World Neurosurgery	2019	Training	Surgeon
Ros et al	Neurosurgery	2020	Education	Surgeon
Tsitsiklis et al	Current Biology	2020	Education	Surgeon
Shao et al	BMC Med Educ	2020	Education	Surgeon
Delion et al	World Neurosurg	2020	Safety	Patient
Teodoro-Vite et al	Simulation Healthcare	2020	Training	Surgeon
Baby et al	Neurosurgical Revue	2020	Training	Surgeon
Barber et al	Otolaryngol Head Neck Surgery	2020	Training	Surgeon
Coelho et al	World Neurosurg	2020	Training	Surgeon
Zawy Alsofy et al	Journal of Craniofacial Surgery	2020	Training	Surgeon
Rahman et al	Surgical Innovation	2020	Training	Surgeon
Jean et al	Journal of Clinical Neuroscience	2020	Training	Surgeon
Sabbagh et al	World Neurosurgery	2020	Training	Surgeon
Mirchi et al	PLoS One	2020	Training	Surgeon
Tayebi Meybodi et al	World Neurosurgery	2020	Training	Surgeon
Kim et al	Journal of Craniofacial Surgery	2020	Training	Surgeon
Iwanaga et al	Clinical Anatomy	2021	Education	Surgeon
Sugiyama et al	Operative Neurosurgery	2021	Training	Surgeon



**Fig. 2.** Distribution of publications on VR and neurosurgery per targeted population.

ment [32]. VR allows the exposure of a person to a risky situation and the activation of high-fidelity cognitive processes and behaviors due to the plausibility of the immersion. VR environments allow users to take part in an embodied learning experience, mainly through physical interactions [33]. Under this paradigm, embedding assessments in immersive virtual worlds is an innovative approach [34] that, in our view, is an improvement from the standpoint of better validity. Regarding physiological real-time measurement, VR provides interactive and multimodal sensorial stimuli that provide unique advantages over other methodologies in neuroscientific investigation [35]. VR is the most appropriate

medium for assessing attitudes to risk and risk perception, conditioning factors in the risk taking process, due to their immersive capabilities [36].

**4.5. Therapeutics**

A growing body of literature recognizes the advantages of VR-based rehabilitation in neurological conditions [37,38]. Such advantages stem from the capacity of VR to increase motivation and enhance motor learning [39,40]. For instance, VR has the ability to provide real-time intrinsic and extrinsic multisensory feed-

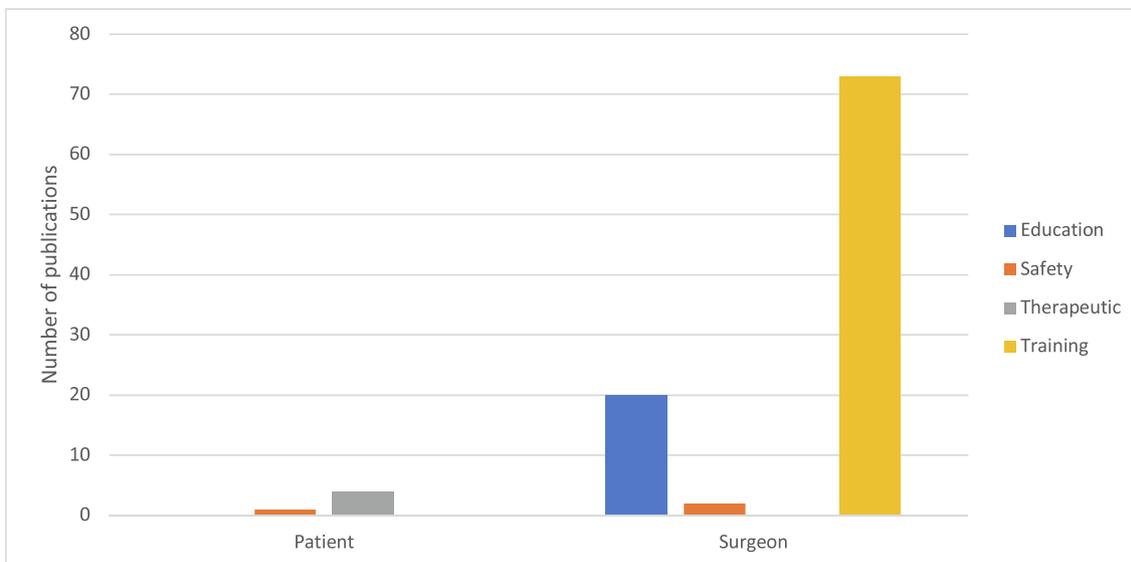


Fig. 3. Distribution of publications on VR and neurosurgery per targeted population.

Table 2  
Repartition of publications between domains and target populations.

Number of Publications	Education	Safety	Therapeutic	Training	Total
Patients	20	1	4	0	5
Surgeons	0	2	0	73	95
<b>Total</b>	<b>20</b>	<b>3</b>	<b>4</b>	<b>73</b>	<b>100</b>

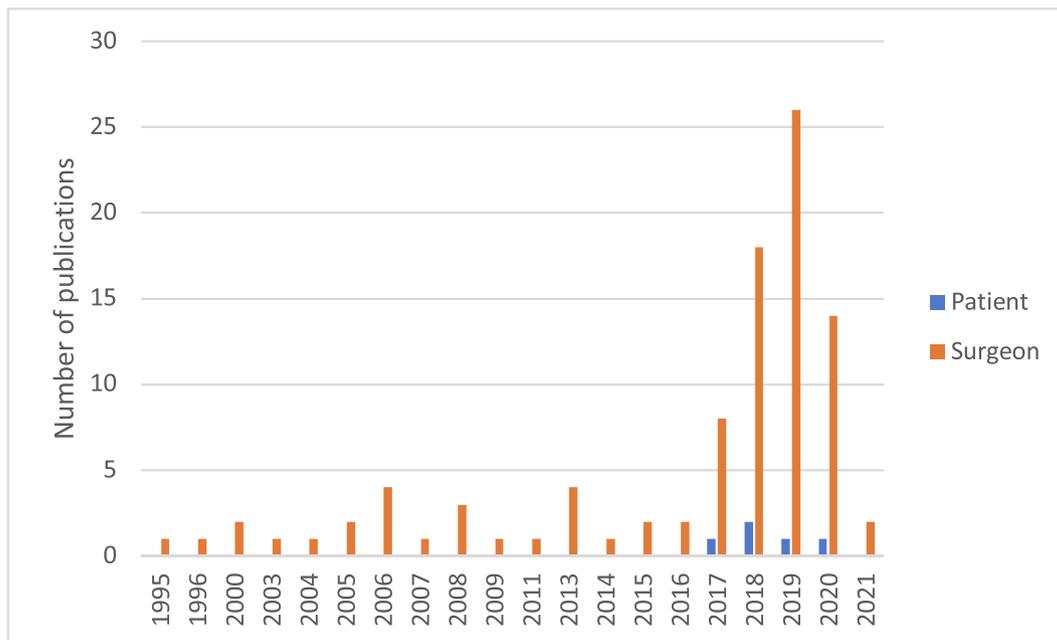


Fig. 4.1. Distribution of publications on VR and neurosurgery per target population across years.

back, and facilitates task variation through the application of various virtual environments that simulate real and daily life tasks [39,40]. VR can also be used to measure and detect impairments in executive functions in individuals with frontal lobe lesions [41].

VR has been used in numerous clinical settings to help treat anxiety disorders, to control pain, to support physical rehabilitation and to distract patients during wound care [42,43]. For exam-

ple, VR coupled with medication is effective in decreasing pain during bandage changes for severe burns [44–47]. Similarly, VR reduces pain and provides positive distraction during routine procedures such as intravenous line placements [48] and dental procedures [49–51]. Other studies revealed that VR helps in managing chronic pain conditions such as complex regional pain syndrome [51,52] and chronic neck pain [53]. By stimulating the visual and

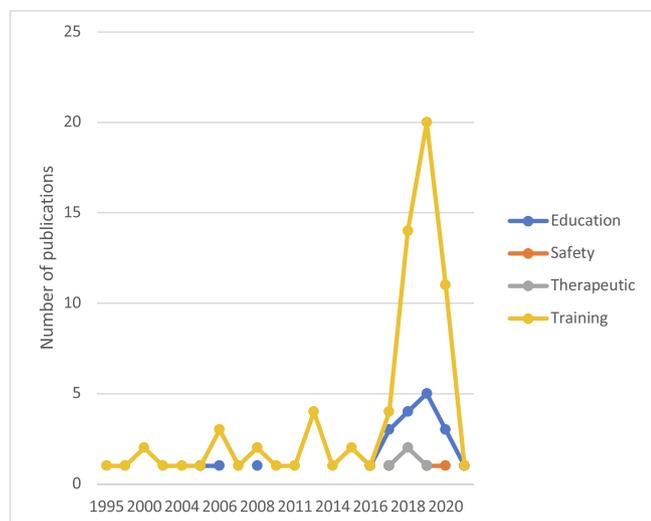


Fig. 4.2. Distribution of publications on VR and neurosurgery per domains of application across years.

auditory senses [54], VR acts as a distraction to limit the user's processing of nociceptive stimuli [55]. Another successful medical implementation of VR has been the demonstration of its ability to reduce phantom pain in amputees and paraplegics [56].

Another promising use resides in the support of functional therapy in the context of loss of motor skills. VR has indeed been hypothesized to allow for increased level of reintegration in the case of neurodegenerative or acute pathologies (such as strokes and traumas) [57,58]. In this case, the virtual scenario increases sensory feedbacks to the central nervous system, resulting in changes in synaptic plasticity and therefore reinforcing learning of motor skills and reeducation [59,60]. Platforms dedicated to rehabilitation of impaired cognitive functions or to recovery after head trauma have been established recently [61].

#### 4.6. Change in paradigm: surgery is a joined effort between the operator and the patient

Evaluation of the success of a surgical procedure has gone beyond the sole ability of the surgeon, with the patient's perception of such surgery being now considered an integral part of this success.

When the patient becomes an active and involved partner in his or her care, he or she has the feeling of autonomy and self-determination, which helps with the maintenance or promotion of the patient's self-management resources [7].

VR provides healthcare professionals with the possibility to involve patients in every step that precedes, composes and follows a surgery. Management of stress and pain [21,62–64] would be ideal candidates as these two parameters have a potentially significant impact on the overall success of a surgical procedure. As described above, VR has been reported to be effective in helping patients to manage both these parameters, either by decreasing situation-related anxiety or by training the mind to modulate the perception of pain [65–67]. As neurosurgery is stressful, potentially debilitating (requiring long rehabilitation periods) and painful for patients, VR-based preparation (through simulation of the clinical management or the cognitive aspects of VR in pain and stress management) might positively influence patient's pain and stress management, comfort and rehabilitation. This might, in turn, result in better surgical outcomes through patients' empowerment. Recently, the use of VR in awake surgery to test functions such as verbal and non-verbal language in a reconstructed environment

[10] demonstrated its utility during the neurosurgical procedure. To be able to collaborate with the patient during the surgical procedure itself by allowing them to remain active and to become an actor of the surgery is essential. In spite of all the intra-operative monitoring technologies, only the patient himself can show or "tell" better than anyone else what is happening when something changes. VR allows to open the discussion on a new mode of intra-operative monitoring and such new paradigm warrants further research.

## 5. Conclusion

Until now, the vast majority of VR applications in neurosurgery target neurosurgeons mostly in the field of training (76.8%) and education (21%). Little effort so far has targeted patients and focused on the use of VR for therapeutics. A change of paradigm is needed by acknowledging the patient's capabilities to empower the care provider – patient partnership. This study points out the need to use this powerful technology to address the complex management of neurosurgical patients: anxiety and pain, the intraoperative test functions such as verbal and non-verbal language but also motor rehabilitation and neuropsychological testing.

VR applications developed for patient's care exist in other fields and should be adopted, adapted or should inspire the neurosurgical community. Further research is therefore warranted to validate the potential of VR for neurosurgical patients and aim for its implementation in the coming years.

### CRedit authorship contribution statement

**Pia Vayssiere:** Project draft, literature review, data extraction/analysis and manuscript writing. **Paul E. Constanthin:** Manuscript correction. **Bruno Herbelin:** Supervision. **Olaf Blanke:** Supervision. **Karl Schaller:** Supervision. **Philippe Bijlenga:** Supervision.

### Declaration of Competing Interest

OB is member of the board and shareholder at Mindmaze SA and co-founder and shareholder at Metaphysiks Engineering SA.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

### References

- [1] Cipresso P, Giglioli IAC, Raya MA, Riva G. The Past, Present, and Future of Virtual and Augmented Reality Research: A Network and Cluster Analysis of the Literature. *Front Psychol* 2018;9:2086.
- [2] Herbelin B. SA, Salomon R. and Blanke O. . Neural mechanisms of bodily self-consciousness and the experience of presence in virtual reality. . 2016;Human Computer Confluence, Riva G. Ed., De Gruyter Publisher, Chapter 3.
- [3] Slater M. A note on Presence terminology. *Presence-Connect*, 3(1) Jan 2003 Online: <http://presencecsuclacuk/presenceconnect/>, 2003.
- [4] Randy Pausch1 DP, George Williams2. Quantifying immersion in virtual reality. SIGGRAPH '97: Proceedings of the 24th annual conference on Computer graphics and interactive techniques. 1997.
- [5] Barrett LF. The theory of constructed emotion: an active inference account of interoception and categorization. *Soc Cogn Affect Neurosci* 2017;12(11):1833.
- [6] Riva G, Wiederhold BK, Mantovani F. Neuroscience of Virtual Reality: From Virtual Exposure to Embodied Medicine. *Cyberpsychol Behav Soc Netw* 2019;22(1):82–96.
- [7] Nestler N. Nursing care and outcome in surgical patients – why do we have to care? *Innovative Surgical Sciences* 2019;4(4):139–43.
- [8] Fugate JE. Complications of Neurosurgery:.. CONTINUUM: Lifelong Learning in Neurology 2015;21:1425–44.
- [9] Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4(1). <https://doi.org/10.1186/2046-4053-4-1>.
- [10] Delion M, Klinger E, Bernard F, Aubin G, Minassian AT, Menei P. Immersing Patients in a Virtual Reality Environment for Brain Mapping During Awake Surgery: Safety Study. *World Neurosurg* 2020;134:e937–43.

- [11] Alaraj A, Lemole M, Finkle J, Yudkowsky R, Wallace A, Luciano C, et al. Virtual reality training in neurosurgery: Review of current status and future applications. *Surg Neurol Int* 2011;2(1):52. <https://doi.org/10.4103/2152-7806.80117>.
- [12] Clark AD, Barone DG, Candy N, Guilfoyle M, Budohoski K, Hofmann R, et al. The Effect of 3-Dimensional Simulation on Neurosurgical Skill Acquisition and Surgical Performance: A Review of the Literature. *J Surg Educ* 2017;74(5):828–36.
- [13] Suri A, Patra DP, Meena RK. Simulation in neurosurgery: Past, present, and future. *Neurol India* 2016;64(3):387–95.
- [14] Pfandler M, Lazarovici M, Stefan P, Wucherer P, Weigl M. Virtual reality-based simulators for spine surgery: a systematic review. *Spine J* 2017;17(9):1352–63.
- [15] Clarke DB, D'Arcy RCN, Delorme S, Laroche D, Godin G, Hajra SG, et al. Virtual reality simulator: demonstrated use in neurosurgical oncology. *Surg Innov* 2013;20(2):190–7.
- [16] Fiani B, De Stefano F, Kondilis A, Covarrubias C, Reier L, Sarhadi K. Virtual Reality in Neurosurgery: "Can You See It?"—A Review of the Current Applications and Future Potential. *World Neurosurg* 2020;141:291–8.
- [17] Aggarwal R, Black SA, Hance JR, Darzi A, Cheshire NJW. Virtual reality simulation training can improve inexperienced surgeons' endovascular skills. *Eur J Vasc Endovasc Surg* 2006;31(6):588–93.
- [18] Willaert WIM, Aggarwal R, Nestel DF, Gaines PA, Vermassen FE, Darzi AW, et al. Patient-specific simulation for endovascular procedures: qualitative evaluation of the development process. *Int J Med Robot* 2010;6(2):202–10.
- [19] McCloy R, Stone R. Science, medicine, and the future. *Virtual reality in surgery BMJ* 2001;323(7318):912–5.
- [20] Konakondla S, Fong R, Schirmer CM. Simulation training in neurosurgery: advances in education and practice. *Adv Med Educ Pract* 2017;8:465–73.
- [21] Stepan K, Zeiger J, Hanchuk S, Del Signore A, Shrivastava R, Govindaraj S, et al. Immersive virtual reality as a teaching tool for neuroanatomy. *Int Forum Allergy Rhinol* 2017;7(10):1006–13.
- [22] Pelargos PE, Nagasawa DT, Lagman C, Tenn S, Demos JV, Lee SJ, et al. Utilizing virtual and augmented reality for educational and clinical enhancements in neurosurgery. *J Clin Neurosci* 2017;35:1–4.
- [23] de Faria JWV, Teixeira MJ, de Moura Sousa Júnior L, Otoch JP, Figueiredo EG. Virtual and stereoscopic anatomy: when virtual reality meets medical education. *J Neurosurg* 2016;125(5):1105–11.
- [24] Fried MP, Uribe JI, Sadoughi B. The role of virtual reality in surgical training in otorhinolaryngology. *Curr Opin Otolaryngol Head Neck Surg* 2007;15(3):163–9.
- [25] Allen LK, Bhattacharyya S, Wilson TD. Development of an interactive anatomical three-dimensional eye model. *Anat Sci Educ* 2015;8(3):275–82.
- [26] Ferdig R, Blank J, Kratoski A, Clements R. Using stereoscopy to teach complex biological concepts. *Adv Physiol Educ* 2015;39(3):205–8.
- [27] Küçük S, Kapakin S, Göktaş Yüksel. Learning anatomy via mobile augmented reality: Effects on achievement and cognitive load. *Anat Sci Educ* 2016;9(5):411–21.
- [28] Gould DJ, Terrell MA, Fleming J. A usability study of users' perceptions toward a multimedia computer-assisted learning tool for neuroanatomy. *Anat Sci Educ* 2008;1(4):175–83.
- [29] Brewer DN, Wilson TD, Eagleson R, de Ribaupierre S. Evaluation of neuroanatomical training using a 3D visual reality model. *Stud Health Technol Inform* 2012;173:85–91.
- [30] Estevez ME, Lindgren KA, Bergethon PR. A novel three-dimensional tool for teaching human neuroanatomy. *Anat Sci Educ* 2010;3(6):309–17.
- [31] Allen LK, Eagleson R, de Ribaupierre S. Evaluation of an online three-dimensional interactive resource for undergraduate neuroanatomy education. *Anat Sci Educ* 2016;9(5):431–9.
- [32] Amokrane K, Lourdeaux D, Burkhardt JM. HERA: learner tracking in a virtual environment. *IJVR* 2008;7:23–30.
- [33] Kiltner K, Groten R, Slater M. The sense of embodiment in virtual reality. *Presence Teleoperators Virtual Environ* 2012;21:373–87.
- [34] Shute VJ, Hansen EG, Almond RG. You can't fatten a hog by weighing it—or can you? evaluating an assessment for learning system called ACED. *Int J Artif Intell Educ* 2008;18:289–316.
- [35] Bohil CJ, Alicea B, Biocca FA. Virtual reality in neuroscience research and therapy. *Nat Rev Neurosci* 2011;12(12):752–62.
- [36] de-Juan-Ripoll C, Soler-Domínguez JL, Guixeres J, Contero M, Álvarez Gutiérrez N, Alcañiz M. Virtual Reality as a New Approach for Risk Taking Assessment. *Front Psychol* 2018;9(9):2532. <https://doi.org/10.3389/fpsyg.2018.02532>.
- [37] Perez-Marcos D, Bieler-Aeschlimann M, Serino A. Virtual Reality as a Vehicle to Empower Motor-Cognitive Neurorehabilitation. *Front Psychol* 2018;9:2120.
- [38] Cano Porras D, Sharon H, Inzelberg R, Ziv-Ner Y, Zeilig G, Plotnik M. Advanced virtual reality-based rehabilitation of balance and gait in clinical practice. *Ther Adv Chronic Dis* 2019;10. <https://doi.org/10.1177/2040622319868379>.
- [39] Keshner EA, Fung J. The quest to apply VR technology to rehabilitation: tribulations and treasures. *J Vestib Res* 2017;27(1):1–5.
- [40] Levin MF, Weiss PL, Keshner EA. Emergence of virtual reality as a tool for upper limb rehabilitation: incorporation of motor control and motor learning principles. *Phys Ther* 2015;95(3):415–25.
- [41] Denmark T, Fish J, Jansari A, Tailor J, Ashkan K, Morris R. Using Virtual Reality to investigate multitasking ability in individuals with frontal lobe lesions. *Neuropsychol Rehabil* 2019;29(5):767–88.
- [42] Malloy KM, Milling LS. The effectiveness of virtual reality distraction for pain reduction: a systematic review. *Clin Psychol Rev* 2010;30(8):1011–8.
- [43] Morris LD, Louw QA, Crous LC. Feasibility and potential effect of a low-cost virtual reality system on reducing pain and anxiety in adult burn injury patients during physiotherapy in a developing country. *Burns* 2010;36(5):659–64.
- [44] Carrougher GJ, Hoffman HG, Nakamura D, Lezotte D, Soltani M, Leahy L, et al. The effect of virtual reality on pain and range of motion in adults with burn injuries. *J Burn Care Res* 2009;30(5):785–91.
- [45] Hoffman HG, Doctor JN, Patterson DR, Carrougher GJ, Furness 3rd TA. Virtual reality as an adjunctive pain control during burn wound care in adolescent patients. *Pain* 2000;85(1–2):305–9.
- [46] Hoffman HG, Patterson DR, Carrougher GJ. Use of virtual reality for adjunctive treatment of adult burn pain during physical therapy: a controlled study. *Clin J Pain* 2000;16(3):244–50.
- [47] Hoffman HG, Patterson DR, Seibel E, Soltani M, Jewett-Leahy L, Sharar SR. Virtual reality pain control during burn wound debridement in the hydrotank. *Clin J Pain* 2008;24(4):299–304.
- [48] Gold JI, Kim SH, Kant AJ, Joseph MH, Rizzo A. Effectiveness of virtual reality for pediatric pain distraction during i.v. placement. *Cyberpsychol Behav* 2006;9(2):207–12.
- [49] Furman E, Jasinevicius TR, Bissada NF, Victoroff KZ, Skillicorn R, Buchner M. Virtual reality distraction for pain control during periodontal scaling and root planing procedures. *J Am Dent Assoc* 2009;140(12):1508–16.
- [50] Hoffman HG, Patterson DR, Carrougher GJ, Sharar SR. Effectiveness of virtual reality-based pain control with multiple treatments. *Clin J Pain* 2001;17(3):229–35.
- [51] Sato K, Fukumori S, Matsusaki T, Maruo T, Ishikawa S, Nishie H, et al. Nonimmersive virtual reality mirror visual feedback therapy and its application for the treatment of complex regional pain syndrome: an open-label pilot study. *Pain Med* 2010;11(4):622–9.
- [52] Solcà M, Ronchi R, Bello-Ruiz J, Schmidlin T, Herbelin B, Luthi F, et al. Heartbeat-enhanced immersive virtual reality to treat complex regional pain syndrome. *Neurology* 2018;91(5):e479–89.
- [53] Sarig-Bahat H, Weiss PL, Laufer Y. Neck Pain Assessment in a Virtual Environment. *Spine* 2010;35(4):E105–12.
- [54] Pozeg P, Palluel E, Ronchi R, Solcà M, Al-Khodayry A-W, Jordan X, et al. Virtual reality improves embodiment and neuropathic pain caused by spinal cord injury. *Neurology* 2017;89(18):1894–903.
- [55] Li A, Montañó Z, Chen VJ, Gold JI. Virtual reality and pain management: current trends and future directions. *Pain Manag* 2011;1(2):147–57.
- [56] Dunn J, Yeo E, Moghaddampour P, Chau B, Humbert S. Virtual and augmented reality in the treatment of phantom limb pain: A literature review. *NeuroRehabilitation* 2017;40(4):595–601.
- [57] Maresca G, Maggio MG, Buda A, La Rosa G, Manuli A, Bramanti P, et al. A novel use of virtual reality in the treatment of cognitive and motor deficit in spinal cord injury: A case report. *Medicine (Baltimore)* 2018;97(50):e13559. <https://doi.org/10.1097/MD.00000000000013559>.
- [58] Keshner EA. Virtual reality and physical rehabilitation: a new toy or a new research and rehabilitation tool? *J Neuroeng Rehabil* 2004;1(1):8.
- [59] Mikuni T, Uchigashima M. Methodological approaches to understand the molecular mechanism of structural plasticity of dendritic spines. *Eur J Neurosci* 2021;54(8):6902–11.
- [60] Lopatina OL, Morgun AV, Gorina YV, Salmin VV, Salmina AB. Current approaches to modeling the virtual reality in rodents for the assessment of brain plasticity and behavior. *J Neurosci Methods* 2020;335:108616. <https://doi.org/10.1016/j.jneumeth.2020.108616>.
- [61] B.Chen TRCSNK. Immersion of virtual reality for rehabilitation. *Applied Ergonomics*. May 2018;69:153–161.
- [62] Bernardo A. Virtual Reality and Simulation in Neurosurgical Training. *World Neurosurg* 2017;106:1015–29.
- [63] Ekstrand C, Jamal A, Nguyen R, Kudryk A, Mann J, Mendez I. Immersive and interactive virtual reality to improve learning and retention of neuroanatomy in medical students: a randomized controlled study. *CMAJ Open* 2018;6(1):E103–9.
- [64] Muller W, Grosskopf S, Hildebrand A, Malkewitz R, Ziegler R. Virtual reality in the operating room of the future. *Stud Health Technol Inform* 1997;39:224–31.
- [65] Morris LD, Louw QA, Grimmer-Somers K. The effectiveness of virtual reality on reducing pain and anxiety in burn injury patients: a systematic review. *Clin J Pain* 2009;25(9):815–26.
- [66] Glennon C, McElroy S, Connolly L, Mische Lawson L, Bretches A, Gard A, et al. Use of Virtual Reality to Distract From Pain and Anxiety. *Oncol Nurs Forum* 2018;45(4):545–52.
- [67] Eijlers R, Utens E, Staals LM, de Nijs PFA, Berghmans JM, Wijnen RMH, et al. Systematic Review and Meta-analysis of Virtual Reality in Pediatrics: Effects on Pain and Anxiety. *Anesth Analg* 2019;129(5):1344–53.