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Overview: Virtual Reality in Medicine

Pensieri Claudio & Pennacchini Maddalena
Institute of Philosophy of Scientific and Technological Activity,
Campus Bio-Medico University of Rome, Italy

Abstract

Background: Virtual Reality (VR) was defined as a collection of technological devices: "a computer capable of interactive 3D visualization, a head-mounted display and data gloves equipped with one or more position trackers". Today, lots of scientists define VR as a simulation of the real world based on computer graphics, a three dimensional world in which communities of real people interact, create content, items and services, producing real economic value through e-Commerce.

Objective: To report the results of a systematic review of articles and reviews published about the theme: "Virtual Reality in Medicine".

Methods: We used the search query string: "Virtual Reality", "Metaverse", "Second Life", "Virtual World", "Virtual Life" in order to find out how many articles were written about these themes. For the "Meta-review" we used only "Virtual Reality" AND "Review". We searched the following databases: Psycinfo, Journal of Medical Internet Research, Isiknowledge till September 2011 and Pubmed till February 2012. We included any source published in either print format or on the Internet, available in all languages, and containing texts that define or attempt to define VR in explicit terms.

Results: We retrieved 3,443 articles on Pubmed in 2012 and 8,237 on Isiknowledge in 2011. This large number of articles covered a wide range of themes, but showed no clear consensus about VR. We identified 4 general uses of VR in Medicine, and searched for the existing reviews about them. We found 364 reviews in 2011, although only 197 were pertinent to our aims: 1. Communication Interface (11 Reviews); 2. Medical Education (49 reviews); 3. Surgical Simulation (49 Reviews) and 4. Psychotherapy (88 Reviews).

Conclusion: We found a large number of articles, but no clear consensus about the meaning of the term VR in Medicine. We found numerous articles published on these topics and many of them have been reviewed. We decided to group these reviews in 4 areas in order to provide a systematic overview of the subject matter, and to enable those interested to learn more about these particular topics.

1. Introduction

In recent years, Virtual Reality (VR) generated both excitement and confusion. The first healthcare applications of VR started in the early '90s due to the need of medical staff to visualize complex medical data, particularly during surgery and for surgery planning (Chinnock, 1994). These factors are evident in the extensive material published in both scientific and popular press, and in the possibly unrealistic expectations held by healthcare professionals (Riva, 2002).

Since 1986, when Jaron Lanier (1987) used the term for the first time, VR has been usually described as a collection of technological devices: a computer capable of interactive 3D visualization, a head-mounted display and data gloves equipped with one or more position trackers. The trackers sense the position and orientation of the user and report that information to the computer which updates (in real time) the images for display.

Rubino (2002), McCloy and Stone (2001), Székely and Satava (1999) in their reviews share the same vision of VR: "*a collection of technologies that allow people to interact efficiently with 3D computerized databases in real time using their natural senses and skills*".

Typically, a VR system is composed of (Burdea, 2003; Brooks, 1999):

- A database construction and virtual object modeling software
- An input tool (trackers, gloves or user interface)
- A graphic rendering system
- An output tool (visual, aural and haptic): actually, less than 20% of VR healthcare applications in medicine are using any immersive equipment
- A VR sensory stimuli delivery: using various forms of visual display technology that integrate real-time computer graphics and/or photographic images/video with a variety of other sensory (audio, force-feedback haptic/touch sensations and even olfactory) output devices. Other methods employ 3D displays that project on a single wall or on a multiple wall space (multi-wall projection rooms are known as CAVES) (Rizzo, 2011). Other gadgets are: a helmet or head-mounted display in high-resolution, 3D sights and sounds, head and/or limb-tracking hardware, and specialized software to reproduce an interactive virtual environment.

It is also possible to describe VR in terms of human experience as "*a real or simulated environment in which a perceiver experiences telepresence*", where telepresence can be described as the "*experience of 'Presence'* (Riva, 2003; Steuer, 1992) *in an environment by means of a communication medium*".

In behavioural sciences, where immersive devices are used by more than 50% of the applications, VR is described as "an advanced form of human-computer interface that allows the user to interact with and become immersed in a computer-generated environment in a naturalistic fashion" (Schultheis, 2001). During the exposing, patients can thus experience the feeling of "being there". For Bellani and Fornasari (2011) VR is only a simulation of the real world based on computer graphics.

For Heim (1998), VR is "an immersive, interactive system based on computable information… an experience that describes many life activities in the information age". In particular, he describes the VR experience according to its "three I's":

1. Immersion

2. Interactivity

3. Information intensity.

Developing this position, Bricken (1990) identifies the core characteristic of VR in the inclusive relationship between the participant and the virtual environment, where the direct experience of the immersive environment constitutes communication. According to this point of view VR is described as "*an advanced form of human-computer interface that allows the user to interact with and become immersed in a computer-generated environment in a naturalistic fashion*" (Schultheis, 2001).

All these definitions underline two different focuses of VR in medicine: VR as a simulation tool and VR as an interaction tool. For physicians and surgeons, the simulation focus of VR prevails over the interaction one: the ultimate goal of VR is the presentation of virtual objects to every human sense in a way identical to their natural counterpart (Székely, 1999).

For Riva et al. (Gorini, Riva, 2008) VR is an interaction tool: 3D virtual worlds can be considered as 3D social networks, where people can collaborate to create and edit objects (like a collaborative 3D wiki space) also meeting each other and interacting with existing objects. For Kamel Boulos (2009) "*comparing the World Wide Web (also known as 2D, two-dimensional Web or flat Web) to three-dimensional (3D) multi-user, immersive virtual worlds can be tricky, and some might consider it similar to comparing apples with oranges or comparing the experience of reading an online health information leaflet to that of having a face-to-face meeting with a clinician*". According to Boulos "*the affordances of both media are different; they are also not mutually exclusive nor a substitute for one another. They are rather complementary and synergistic in many ways*".

Beside this description of VR, it is necessary to underline that there are some potential distinctions between VR and Virtual World (VW). A VW may be considered a form of VR with some unique features, such as the possibility to meet other people, interact with them, create objects, sell/trade them, etc. instead of a VR that might be inhabited only by the patient (e.g. VR for psychology).

VR offers new ways to develop social skills, socialize and interact with other people via customizable, realistic, 3D, fully textured and animated avatars. The user can attend and participate in live events like lectures and conferences, build communities – including learners' communities and patient support groups – relax and visit new places, browse document collections in 3D virtual libraries.

The growing interest in medical applications of VR is also highlighted by the increasing number of scientific articles published every year on this topic: in 2003 Riva found 951 papers on MEDLINE and 708 on Psycinfo with the search term "Virtual Reality" (Riva, 2003).

In 2006, searching Medline with the keyword "virtual reality", the total number of publications increased from 45 in 1995 to 951 in 2003 (Gorini, 2005) and to 3,203 in 2010 (Riva, 2011).

There are currently a large number of articles about VR. In February 2012, the authors found 3,443 articles about "Virtual Reality" on Pubmed. The aim was to make an overview of the reviews (meta-Review), in order to limit the research to four areas (1. Communication Interface; 2. Medical Education; 3. Surgical Simulation; and 4. Therapy), given the large number of publications.

2. Methods

2.1   Keyterms Search on Pubmed and Psycinfo

Reviewers searched (Table 1) for the term "Virtual Reality" on Pubmed, Psycinfo, JMIR (Journal of Medical Internet Research) and Isiknowledge and noted that in 2010 a search for VR in Pubmed resulted in 2,960 articles, which increased to 3,290 in 2011, (+ 330 articles) and 3,443 in February 2012. On Psycinfo the number of articles found using the same term increased from 29 in 2010 to 114 in 2011 (+ 85 articles) and on Isiknowledge from 6,213 to 8,237 (+ 2,024 articles).

However, VR was not the only term searched. Additional terms used on PUBMED included the words: "Metaverse" (2 articles), "Second Life" (69 in 2010, 103 in 2011), "Virtual World" (151 in 2010, 200 in 2011) and "Virtual Life" (7 in 2010, 10 in 2011). These words are not completely representative of the entire world of VR applications in healthcare, but they are the most used. We could also add: Virtual Environment, Augmented Reality, Multiverse, etc. It is also important, and a criticality of this study, that the four search engines taken into consideration are not enough to make this review completely exhaustive, as APA search engine and others have not been employed.

Table 1: Keyterms researched

	29/03/10	23/03/11	**28/09/11**	29/03/10	23/03/11	**28/09/11**	28/09/11	**20/02/12**	29/03/10	**23/03/11**
	Pub Med			**Psycinfo**			**JMIR**		**Isiknowledge**	
"Virtual Reality"	2,960	3,126	**3,290**	29	35	**114**	4	**4**	6,213	**237**
"Metaverse"	2	2	**2**	0	0	**0**	0	**0**	16	**21**
"Second Life"	69	92	**103**	1	1	**18**	54	**62**	256	**375**
"Virtual World"	151	191	**200**	2	2	**33**	4	**5**	711	**901**
"Virtual Life"	7	8	**10**	1	1	**1**	0	**0**	37	**45**

2.2   Four Areas Reviews

According to Riva's definition on *"Application of Virtual Environment in Medicine" (*Riva, 2003), the authors divided the findings into 4 main areas:

1. Communication Interface: Presence and Avatar.

2. Medical Educational: training.

3. Surgical Simulation: a) Neurosurgery), b) Laparoscopic & Endoscopic, c) Simulators, d) Other.

4. Therapy: a) Phobias, PTSD, Anxiety Disorders, b) Rehabilitation, c) Clinical & Pain Management.

The authors also completed a review of reviews (meta-review), and searched for articles including the words "Virtual Reality" or "Virtual Environment" in the titles or in the abstracts on Pubmed. The search for "Virtual Reality" [Title/Abstract] gave 364 results (03/10/2011). Only 197 had to do with VR, with the Augmented Reality or the Virtual Environment (VE).

3. Result

3.1   VR as a Communication Interface: Presence and Avatar

VR and Communication: According to Riva (2000), VR can be considered as the leading edge of a general evolution of present communication interfaces like television, computer and telephone (Riva, Mantovani, 2000; Riva, Davide, 2001). The main characteristic of this evolution is the full immersion of the human sensory motor channels into a vivid and global communication experience (Biocca, 1995). Most of the work in this area is trying to improve the effectiveness of a VE by providing a more "realistic" experience to the user, such as adding physical qualities to virtual objects or improving the graphic resolution.

VWs, VE and VR provide the remote patient with a feeling of embodiment that has the potential to facilitate the clinical communication process and positively influence group cohesiveness in group-based therapies (Gorini, 2007).

Further studies include using Collaborative Virtual Environments (CVEs) which support multiple simultaneous users, in particular the patient and the therapist, who can communicate with each other through their avatars. CVEs have been used to examine and investigate the ability of recognizing emotions (Moore, 2005) and also to improve social interaction, teaching students how to express their emotions and understand those of other people (Cheng, 2010). All these studies yielded encouraging results in identifying emotions and in the improvement of social performance after the intervention.

More than the richness of available images, the effectiveness of a virtual environment (VE) depends on the level of interaction/interactivity which actors have in both "real" and simulated environments. According to Sastry and Boyd (1998), a VE, particularly when it is used for real world applications, is effective when "the user is able to navigate, select, pick, move and manipulate an object much more naturally". In this sense, emphasis shifts from the quality of the image to the freedom of the interaction, from the graphic perfection of the system to the affordances provided to the users in the environment (Satava, 1994). Furthermore, as the underlying enabling technologies continue to evolve and allow us to design more useful and usable structural virtual environments, the next important challenge will involve populating these environments with virtual representations of humans (avatars) (Rizzo, 2001).

According to the International Organization for Standardization's ISO 13407 "*Human centered design for interactive systems*" requires (ISO/IEC 9126, 2001*)*: a) active involvement of users; b) clear understanding of use and task requirements; c) appropriate allocation of function; d) iteration of design solutions; e) multi-disciplinary design team; and f) it is to be based on the processes of understanding and specifying the context of use; specifying the user and organizational requirements; producing designs and prototypes; carrying out user-based assessment. One example of VE developed using the ISO 13407 guidelines is the IERAPSI surgical training system (John, 2001).

The key characteristic of VR, differentiating it from other media or communication systems, is the sense of *presence* (Riva, Davide, 2003; Ijsselsteijn, 2001).

"*Presence*" is defined as the "*sense of being there*", or as the "*feeling of being in a world that exists outside of the self*" (Riva, Waterworth, 2004). It is now widely acknowledged that presence can be considered as a neuropsychological phenomenon (Riva, Anguera, 2006). Different studies indicate a direct connection between the intensity of the emotions experienced in VR and the level of presence by which it is elicited (Riva, Mantovani, 2007).

In particular, Riva and Waterworth (2004) describe presence as a defining feature of the self, related to the evolution of a key feature of any central nervous system: the embedding of sensory-referred properties into an internal functional space.

VR and Avatar: The inhabitants of virtual environments can be classified as *bots* and *avatars*. A *bot* is an autonomous agent that pursues its own goals. On the contrary, an *avatar* — a representation of a human being — is under the direct control of that human being (Whalen, 2003). A typical humanoid avatar like those defined by the H-Anim Standard (ISO/IEC FCD 19774) contains more than four dozen joints (not including the additional joints in the spine which have limited mobility).

This example proves that the avatar's behaviour needs only represents human behaviour to a certain extent. It is impossible in practice for any representation to be exact — perfect faithfulness is impossible — but at any level of fidelity, a closer approximation could always be obtained. There are no absolute criteria – one must choose the level of faithfulness which is most cost-effective to meet the needs imposed by each application. People and their avatars have two classes of behaviours: *independent* and *interactive* (Yang, 2003).

Independent behaviours, such as waving a hand, are performed by the avatar alone; they can depend on other objects in the environment.

Interactive behaviours, like picking up a pen or shaking hands, require that the avatar locates other objects, possibly objects moving unpredictably in the environment, and moves in relation to those objects.

Another VR application used as a communication interface for physicians may be the 4D GIS (four-dimensional Geographic Information Systems comprising three-dimensional 3D GIS, plus the temporal/real-time dimension) which serves very well the classic public health Person-Place-Time Triad.

Kamel Boulos (2009) proposed to develop a 4D GIS collaborative and interactive platform which combines virtual globes or 3D mirror worlds and 3D virtual worlds and complements, and tightly integrates them with other key technologies, e.g., real-time, geo-tagged RSS-Really Simple Syndication feeds and geo-mash-ups. Such a platform would be much suited for emergency and disaster management in real-time, e.g., for managing an influenza pandemic and coordinating actions at global, regional and local levels. Another one is the Interactive 3D Earth globe for accessing web-based, geographically-indexed information (Kamel Boulos, Burden, 2007). This globe in Second Life offered access to web-based statistics and information about sexually transmitted infections (STIs)/HIV/AIDS from 53 European region countries. The globe is part of the University of Plymouth Sexual Health SIM in Second Life (Kamel Boulos, Wheeler, 2007). Starting from literature that documented the extent to which people are using the Internet to enquire about their real life health (Madden, 2006), in 2008 Gonzalez (2009) started a research in SL, expecting to observe a similar interest in personal health in Second Life. Yet while she visited numerous medical sites and clinics in SL, she found them all empty. Universities, clinics and other health organizations had made a considerable effort to set up elaborate architectural structures with placards and displays of health information, but not a single avatar was in sight. Gonzalez wandered these empty structures, looking for health-seeking behavior in SL, but in vain. The only clinic where she found avatars was a setting for sexual role play in which people enacted sexual fantasies between doctors and patients.

Table 2: Communication Interface

	Communication Interface		
Wann JP, Rushton S, Mon-Williams M.	Natural problems for stereoscopic depth perception in Virtual Environments.	Vision Res. Oct;35(19):2731-6.	1995
Steffin M.	Virtual reality therapy of multiple sclerosis and spinal cord injury: design consideration for a haptic-visual interface.	Stud Health Technol Inform.;44:185-208.	1997
Rushton SK, Riddell PM.	Developing visual systems and exposure to virtual reality and stereo displays: some concerns and speculations about the demands on accommodation and vergence	Appl Ergon. Feb;30(1):69-78.	1999
Wilson JR.	Virtual environments applications and applied ergonomics	Appl Ergon. Feb;30(1):3-9.	1999
Haase J.	Neuronavigation	Childs Nerv Syst. Nov;15(11-12):755-7.	1999
Marsh A.	The integration of virtual reality into a Web-based telemedical information society	Stud Health Technol Inform.; 79:305-25.	2000
Anderson PL, Rothbaum BO, Hodges L.	Virtual reality: using the virtual world to improve quality of life in the real world.	Bull Menninger Clin. Winter;65(1):78-91.	2001
Evett L, Tan YK.	Talk your way round--a speech interface to a virtual museum	Disabil Rehabil. Jul 20-Aug 15;24(11-12):607-12. Review.	2002
Sanchez-Vives MV, Slater M.	From presence to consciousness through virtual reality	Nat Rev Neurosci. Apr;6(4):332-9.	2005
Erren-Wolters CV, van Dijk H, de Kort AC, Ijzerman MJ, Jannink MJ.	Virtual reality for mobility devices: training applications and clinical results: a review	Int J Rehabil Res. Jun;30(2):91-6.	2007
Davis RL.	Exploring possibilities: virtual reality in nursing research	Res Theory Nurs Pract. ;23(2):133-47.	2009

3.2   Medical Education and Training

Virtual worlds are an exciting area offering opportunities in clinical teaching and interventions. Clinicians and academics may approach these emerging opportunities with enthusiasm or scepticism (Kashani, 2009).Through 3D visualization of massive volumes of information and databases, clinicians and students can understand important physiological principles or basic anatomy (Alcañiz, 2000). For instance, VR can be used to explore the organs by "flying" around, behind, or even inside them. In this sense VEs can be used both as didactic and experiential educational tools, allowing a deeper understanding of the interrelationship of anatomical structures that cannot be achieved by any other means, including cadaveric dissection.

Apart from anatomical training, VR has been used for teaching the skill of performing different tasks like a 12-lead ECG (Jeffries, 2003). In all these cases, VR simulators allowed the acquisition of the necessary technical skills required for the procedure.

In some cases, VWs were also used for prevention and to provide healthcare information, educate and improve patients' healthcare knowledge (Kamel Boulos, Toth-Cohen, 2009), i.e. the University of Plymouth has tested a Sexual Health SIM in Second Life. The sexual health project in Second Life was aimed to provide education about sexually transmitted infections, prevention of unintended pregnancy and promotion of equalitarian sexual relationships. The University of Plymouth Sexual Health SIM provides a wide variety of educational experiences, including opportunities to test knowledge of sexual health through quizzes and games, web resources integrated within the virtual context and live seminars

on sexual health topics. Between 12nd July 2007 and 12th May 2008, the SIM received more than 3,350 visitors/avatars.

Other uses of VW (Second Life) for medical and healthcare education (Douglas, Procter, 2009) have been documented in different articles (Beard, Wilson, 2009; Kamel Boulos, Hetherington, 2007; Kamel Boulos, Ramloll, 2008; Gorini, Gaggiolo, 2008; Hansen, 2008).

Second Life has been used for disaster simulation, nursing training (Skiba, 2009), nutrition education, etc., much of which is referenced by one of the primary in-world sources of healthcare information (HealthInfo Island funded by the National Library of Medicine) (Perryman, 2009). Virtual Worlds like Second Life were also used for consumer health and higher education. Thot-Cohen describes the development and evaluation of public exhibits on health and wellness at the Jefferson occupational therapy education center in Second Life (Toth-Cohen, 2009).

Table 3: Medical Education & Training

	Medical Education & Training		
Kaltenborn KF, Rienhoff O.	Virtual reality in medicine	Methods Inf Med. Nov;32(5):407-17.	1993
Lefrançois L, Puddington L.	Extrathymic intestinal T-cell development: virtual reality?	Immunol Today. Jan;16(1):16-21.	1995
Völter S, Krämer KL.	Virtual reality in medicine	Radiologe. Sep;35(9):563-8.	1995
Sakurai K.	A survey of virtual reality research: From technology to psychology	Shinrigaku Kenkyu. Oct;66(4):296-309.	1995
Marran L, Schor C.	Multiaccommodative stimuli in VR systems: problems & solutions	Hum Factors. Sep;39(3):382-8.	1997
Ahmed M, Meech JF, Timoney A.	Virtual reality in medicine	Br J Urol. Nov;80 Suppl 3:46-52.	1997
Kaufman DM, Bell W.	Teaching and assessing clinical skills using virtual reality	Stud Health Technol Inform.;39:467-72.	1997
Moline J.	Virtual reality for health care: a survey	Stud Health Technol Inform.; 44:3-34.	1997
Riva G.	Virtual reality as assessment tool in psychology	Stud Health Technol Inform.;44:71-9.	1997
Riva G.	Virtual reality in neuroscience: a survey	Stud Health Technol Inform.;58:191-9.	1998
Gobbetti E, Scateni R.	Virtual reality: past, present and future	Stud Health Technol Inform.;58:3-20.	1998
Botella C, Perpiñá C, Baños RM, et. Al.	Virtual reality: a new clinical setting lab	Stud Health Technol Inform.;58:73-81.	1998
Blonde L, Cook JL, Dey J.	Internet use by endocrinologists	Recent Prog Horm Res.;54:1-29; discussion 29-31.	1999
Dzhafarova OA, Donskaia OG, Zubkov AA, et. Al	Virtual reality technology and physiological functions	Vestn Ross Akad Med Nauk.;(10):26-30.	1999
Parham P.	Virtual reality in the MHC	Immunol Rev. Feb;167:5-15.	1999
Lum LG.	T cell-based immunotherapy for cancer: a virtual reality?	CA Cancer J Clin. Mar-Apr;49(2):74-100, 65.	1999
Marescaux J, Mutter D, Soler L, Vix M, Leroy J.	The Virtual University applied to telesurgery: from tele-education to tele-manipulation	Bull Acad Natl Med.;183(3):509-21; discussion 521-2.	1999
Riva G, Bacchetta M, Baruffi M, et. Al.	The use of PC based VR in clinical medicine: the VREPAR projects	Technol Health Care.;7(4):261-9.	1999
Stenzl A, Kölle D, Eder R, Stöger A, et. Al.	Virtual reality of the lower urinary tract in women	Int Urogynecol J Pelvic Floor Dysfunct.;10(4):248-53.	1999

	Medical Education & Training		
Hoffman HM.	Teaching and learning with virtual reality	Stud Health Technol Inform.;79:285-91.	2000
Riva G, Gamberini L.	Virtual reality as telemedicine tool: technology, ergonomics and actual applications	Technol Health Care.;8(2):113-27.	2000
Riva G, Gamberini L.	Virtual reality in telemedicine	Telemed J E Health. Fall;6(3):327-40.	2000
Reznek M, Harter P, Krummel T.	Virtual reality and simulation: training the future emergency physician	Acad Emerg Med. Jan;9(1):78-87.	2002
Nichols S, Patel H.	Health and safety implications of virtual reality: a review of empirical evidence	Appl Ergon. May;33(3):251-71.	2002
Riva G.	Virtual reality for health care: the status of research	Cyberpsychol Behav. Jun;5(3):219-25.	2002
Letterie GS.	How virtual reality may enhance training in obstetrics and gynecology	Am J Obstet Gynecol. Sep;187(3 Suppl):S37-40.	2002
Schultheis MT, Himelstein J, Rizzo AA.	Virtual reality and neuropsychology: upgrading the current tools	J Head Trauma Rehabil. Oct;17(5):378-94.	2002
Tarr MJ, Warren WH.	Virtual reality in behavioral neuroscience and beyond	Nat Neurosci. Nov;5 Suppl:1089-92.	2002
Riva G.	Applications of virtual environments in medicine	Methods Inf Med.;42(5):524-34.	2003
Mantovani F, Castelnuovo G, Gaggioli A, Riva G.	Virtual reality training for health-care professionals	Cyberpsychol Behav. Aug;6(4):389-95.	2003
Beutler LE, Harwood TM.	Virtual reality in psychotherapy training	J Clin Psychol. Mar;60(3):317-30.	2004
Dankelman J, Wentink M, Grimbergen CA, Stassen HG, Reekers J.	Does virtual reality training make sense in interventional radiology? Training skill-, rule- and knowledge-based behavior	Cardiovasc Intervent Radiol. Sep-Oct;27(5):417-21. Epub 2004 Aug 12.	2004
Choi KS, Sun H, Heng PA.	An efficient and scalable deformable model for virtual reality-based medical applications	Artif Intell Med. Sep;32(1):51-69.	2004
Xiao J, Zhang HX, Liu L.	Application of virtual reality technique in forensic pathology	Fa Yi Xue Za Zhi. May;21(2):146-8.	2005
Lum LG, Padbury JF, Davol PA, Lee RJ.	Virtual reality of stem cell transplantation to repair injured myocardium	J Cell Biochem. Aug 1;95(5):869-74.	2005
Khalifa YM, Bogorad D, Gibson V, et al.	Virtual reality in ophthalmology training	Surv Ophthalmol. May-Jun;51(3):259-73.	2006
Hilty DM, Alverson DC, Alpert JE, Tong L, et al.	Virtual reality, telemedicine, web and data processing innovations in medical and psychiatric education and clinical care	Acad Psychiatry. Nov-Dec;30(6):528-33.	2006
Mohan A, Proctor M.	Virtual reality--a 'play station' of the future. A review of virtual reality and orthopaedics	Acta Orthop Belg. Dec;72(6):659-63.	2006
Chan C, Kepler TB.	Computational immunology--from bench to virtual reality	Ann Acad Med Singapore. Feb;36(2):123-7.	2007
Stetz MC, Thomas ML, Russo MB, Stetz TA, et al.	Stress, mental health, and cognition: a brief review of relationships and countermeasures.	Aviat Space Environ Med. May;78(5 Suppl):B252-60.	2007
Liu W, Wang S, Zhang J, Li D.	Application of virtual reality in medicine	Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. Aug;24(4):946-9.	2007
Banerjee PP, Luciano CJ, Rizzi S.	Virtual reality simulations	Anesthesiol Clin. Jun;25(2):337-48. Review. Erratum in: Anesthesiol Clin. 2007 Sep;25(3):687.	2007
Jiang HP, Feng H, Dong FP.	The influence of virtual reality both on biology experiment and teaching	Yi Chuan. Dec;29(12):1529-32.	2007
Thorley-Lawson DA, Duca KA, Shapiro M.	Epstein-Barr virus: a paradigm for persistent infection - for real and in virtual reality	Trends Immunol. Apr; 29(4):195-201. Epub 2008 Mar 6.	2008
Schmidt B, Stewart S.	Implementing the virtual reality learning environment: Second	Nurse Educ. Jul-Aug; 34(4):152-5.	2009

	Medical Education & Training		
	Life		
Adamovich SV, Fluet GG, Tunik E, Merians AS.	Sensorimotor training in virtual reality: a review.	NeuroRehabilitation.;25(1):29-44.	2009
Desender LM, Van Herzeele I, Aggarwal R, et al.	Training with simulation versus operative room attendance	J Cardiovasc Surg (Torino). Feb;52(1):17-37.	2011
Galvin J, Levac D.,	Facilitating clinical decision-making about the use of virtual reality within paediatric motor rehabilitation: describing and classifying virtual reality systems	Dev Neurorehabil.; 14(2):112-22.	2011
Levac DE, Galvin J.	Facilitating clinical decision-making about the use of virtual reality within paediatric motor rehabilitation: application of a classification framework	Dev Neurorehabil.;14(3):177-84.	2011

3.3   The Surgical Simulation: Neurosurgery, Laparoscopic & Endoscopic, Simulators

In 1995, Whalley (1995) stated that complex operative techniques can be taught in a virtual reality machine – it is already feasible to use the results of clinical investigations (for example MRI scans) to construct a precise virtual reality model of all or part of a patient. Supercomputers now allow the integration of quite massive databases derived from structural imaging of diseased organs and their simultaneous functional mapping that can be used to give the surgeon the opportunity to rehearse a potentially complex surgical procedure in virtual reality before attempting this with a patient.

3.4   VR & AR Surgery, Previous Review

Mabrey's (2010) previous literature review including "virtual reality'' AND ''surgery'' yielded 1,025 citations spanning from 1992 to 2009. This subset, VR+Surgery, was then searched using ''orthopaedic'' OR ''orthopedic'' OR ''fracture'' OR ''spine'' OR ''hip'' OR ''knee'' OR ''shoulder'', yielding 232 articles from 1994 to 2009.

Among the 48 relevant orthopaedic articles from 1995 to 2009 found in the informal literature review, only 23 dealt with specific simulators, with the rest being more general reviews of the topic.

Only 16 of these 23 articles dealt with specific simulators with the rest covering principles of VR training as it related to orthopaedics. They broke down into 9 papers about knee arthroscopy simulators (1995–2006), four involving shoulder simulators (1999–2008), and three fractures (2007–2008.) On the other hand, there were 246 citations of laparoscopic virtual reality simulation out of the original 1,025 citations (1992–2009).

Gurusamy et al. (2008) reviewed 23 randomized control trials of VR laparoscopic simulators that included 612 participants. They reported that VR laparoscopic training decreased the time for task completion and increased overall accuracy in comparison with the controlled subjects who had not undergone VR training. VR technology, when applied to the education of residents in general surgery programs, had a positive impact on their training (Aggarwal, 2007; Ahlberg, 2007; Grantcharov, 2003; Larsen, 2009; Stefanidis, 2005; Verdaasdonk, 2008).

The number of papers specific to orthopaedics and VR is limited (Mabrey, 2010). VR is used effectively in other specialties, especially general surgery. VR simulators are readily available for shoulder and knee arthroscopy but not as well incorporated into training curricula.

One limitation is that VR laparoscopic simulators assess performance, but lack realistic haptic feedback. Augmented Reality (AR) combines a VR setting with real physical materials, instruments, and

feedback. Botden and Jakimowicz (2009) present the current developments in Augmented Reality laparoscopic simulation.

The different kinds of simulators used for training purposes are: traditional box trainers, virtual reality (VR), and Augmented Reality (AR) simulators.

- Traditional box trainers have realistic haptic feedback during procedures, but an expert observer must be at disposal to assess the performance.
- VR simulators provide explanations of the tasks to be practised and objective assessment of the performance; however, they lack realistic haptic feedback.
- AR simulators retain realistic haptic feedback and provide objective assessment of the performance of the trainee.

Botden and Jakimowicz (2009) identify four augmented reality laparoscopic simulators: 1. ProMIS: that combines the virtual and real worlds in the same system: users learn, practice and measure their proficiency with real instruments on physical and virtual models. 2. CELTS (The computer-enhanced laparoscopic training system): that is a prototype laparoscopic surgery simulator that uses real instruments, real video display and laparoscopic light sources with synthetic skin and task trays to permit highly realistic practice of basic surgical skills. 3. LTS3-e: that is a relatively low-cost augmented reality simulator capable of training and assessing technical laparoscopic skills of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Fundamentals of Laparoscopy (FLS) program. 4. The Blue DRAGON: that is a system for acquiring the kinematics and the dynamics of two endoscopic tools along with the visual view of the surgical scene. The AR laparoscopic simulator's major advantage over the VR simulator is that it allows the trainee to use the same instruments that are currently used in the operating room. The simulator provides realistic haptic feedback because of the hybrid mannequin environment in which the trainee is working, which is absent in VR systems. This simulator offers a physically realistic training environment that is based on real instruments interacting with real objects.

Table 4: Surgical Simulators

	1. Neurosurgery		Date
Satava RM.	Emerging medical applications of virtual reality: a surgeon's perspective	Artif Intell Med. Aug;6(4):281-8.	1994
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Lange T, Indelicato DJ, Rosen JM.,	Virtual reality in surgical training	Surg Oncol Clin N Am. Jan;9(1):61-79, vii.	2000
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Tronnier VM, Staubert A, Bonsanto MM, Wirtz CR, Kunze S.	Virtual reality in neurosurgery	Radiologe. Mar;40(3):211-7.	2000
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Satava RM.	Surgical education and surgical simulation	World J Surg. Nov;25(11):1484-9.	2001
Jackson A, John NW, Thacker NA, Ramsden RT, Gillespie JE, et al.	Developing a virtual reality environment in petrous bone surgery: a state-of-the-art review	Otol Neurotol. Mar;23(2):111-21.	2002
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Spicer MA, Apuzzo ML.	Virtual reality surgery: neurosurgery and the contemporary landscape	Neurosurgery. Mar;52(3):489-97; discussion 496-7.	2003
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Wang P, Becker AA, Jones IA, et al.	A virtual reality surgery simulation of cutting and retraction in neurosurgery with force-feedback	Comput Methods Programs Biomed. 2006 Oct;84(1):11-8. Epub 2006 Aug 30.	2006
Albani JM, Lee DI.	Virtual reality-assisted robotic surgery simulation	J Endourol. Mar;21(3):285-7.	2007
Fried MP, Uribe JI, Sadoughi B.	The role of virtual reality in surgical training in otorhinolaryngology	Curr Opin Otolaryngol Head Neck Surg. Jun;15(3):163-9.	2007
Lemole GM Jr, Banerjee PP, Luciano C, Neckrysh S, Charbel FT.,	Virtual reality in neurosurgical education: part-task ventriculostomy simulation with dynamic visual and haptic feedback	Neurosurgery. Jul;61(1):142-8; discussion 148-9.	2007
Van der Meijden OA, Schijven MP.	The value of haptic feedback in conventional and robot-assisted minimal invasive surgery and virtual reality training: a current review	Surg Endosc. Jun;23(6):1180-90. Epub 2009 Jan 1.	2009
Abdelwahab MG, Cavalcanti DD, Preul MC.	Role of computer technology in neurosurgery	Minerva Chir. Aug;65(4):409-28.	2010
Malone HR, Syed ON, Downes MS, et al.	Simulation in neurosurgery: a review of computer-based simulation environments and their surgical applications	Neurosurgery. Oct;67(4):1105-16.	2010
Palter VN, Grantcharov TP.,	Virtual reality in surgical skills training	Surg Clin North Am. Jun;90(3):605-17.	2010
Lendvay TS.	Surgical simulation in pediatric urologic education	Curr Urol Rep. Apr;12(2):137-43.	2011
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Coleman J, Nduka CC, Darzi A.	Virtual reality and laparoscopic surgery	Br J Surg. Dec;81(12):1709-11.	1994
Hart R, Karthigasu K.	The benefits of virtual reality simulator training for laparoscopic surgery	Curr Opin Obstet Gynecol. Aug;19(4):297-302.	2007
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Botden SM, Jakimowicz JJ.	What is going on in augmented reality simulation in laparoscopic surgery?	Surg Endosc. Aug;23(8):1693-700. Epub 2008 Sep 24.	2009
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Carter FJ, Schijven MP, Aggarwal R, et al.	Consensus guidelines for validation of virtual reality surgical simulators	Surg Endosc. 2005 Dec;19(12):1523-32. Epub 2005 Oct 26.	2005
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Fairhurst K, Strickland A, Maddern G.	The LapSim virtual reality simulator: promising but not yet proven	Surg Endosc. 2011 Feb;25(2):343-55. Epub 2010 Jul 8.	2010
	4. Other		
Suramo I, Talala T, Karhula V, et al.	Virtual reality in radiology	Duodecim.;113(21):2151-6.	1997
Merril JR.	Using emerging technologies such as virtual reality and the World Wide Web to contribute to a richer understanding of the brain	Ann N Y Acad Sci. May 30;820:229-33.	1997
Shah J, Mackay S, Vale J, Darzi A.	Simulation in urology--a role for virtual reality?	BJU Int. Nov;88(7):661-5.	2001
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Dawson DL.	Virtual reality training for carotid intervention	Nat Clin Pract Neurol. Aug;3(8):470-1.	2007
Neequaye SK, Aggarwal R, Van Herzeele I, et al.	Endovascular skills training and assessment	J Vasc Surg. Nov;46(5):1055-64.	2007
Tsang JS, Naughton PA, Leong S, et al.	Virtual reality simulation in endovascular surgical training	Surgeon. Aug;6(4):214-20.	2008
Onuki T.	Virtual reality in video-assisted thoracoscopic lung segmentectomy	Kyobu Geka. Jul;62(8 Suppl):733-8.	2009
Mabrey JD, Reinig KD, Cannon WD.	Virtual reality in orthopaedics: is it a reality?	Clin Orthop Relat Res. Oct;468(10):2586-91.	2010

3.5   Therapy: a) Phobias, PTSD, Anxiety Disorders, etc., b) Rehabilitation, c) Clinical & Pain Management

In the psychotherapeutic field, VR can also be described as an advanced imaginary system: an experiential form of imagery that is as effective as reality in inducing emotional responses (North, 1997; Vincelli, 2001) – indeed in psychotherapy, the change may come through an intense focus on a particular instance or experience (Wolfe, 2002). As outlined by Baños et al. (1999) the VR experience can help the course of the therapy for "its capability of reducing the distinction between the computer's reality and the conventional reality". What is more, "VR can be used for experiencing different identities and… even other forms of self, as well". The feeling of "presence" that patients experience in these environments, involving all the sensory motor channels, enables them to really "live" the experience in a more vivid and realistic manner than they could do through their own imagination (Vincelli, 1998). This should mean fewer treatment sessions, and, therefore, lower costs for the treatment (Wiederhold, Gevirtz, 1998; Wiederhold 1998). The first commercial version of a VR system was developed by Morton Heilig in 1956 (Heilig, 1962).

Phobias, PTSD, Anxiety disorders: VR was verified in the treatment of six psychological disorders: acrophobia (Emmelkamp, 2001; Rothbaum, Hodges, 1995), spider phobia (Garcia-Palacios, 2002), panic disorders with agoraphobia (Vincelli, Anolli, 2003), body image disturbances (Riva, Bacchetta, 2001), binge eating disorders (Riva, Bacchetta, 2002; Riva, Bacchetta, 2003), and fear of flying (Rothbaum, Hodges, 2000; Wiederhold, Jang, 2002).

Even if many different kinds of treatment are available for anxiety disorders (Gorini, Riva, 2008), such as behavioural treatments (relaxation, exposure, modelling and role play), cognitive therapies (thought stopping, mental distraction and thought recording), medication, psychodynamic therapy, support groups in VWs (Norris, 2009), family therapy and biofeedback, many studies have demonstrated that the exposure-based treatments are among the most effective (Deacon, Abramowitz, 2004; Kobak, Greist, 1998). Despite its effectiveness, exposure-based therapy presents significant limitations:

- Many patients are reticent to expose themselves to the real phobic stimulus or situation.
- *In vivo* exposure can never be fully controlled by the therapist and its intensity can be too strong for the patient.
- This technique often requires that therapists accompany patients into anxiety-provoking situations in the real world increasing the costs for the patient, and with great time expenditure for both therapist and patient (Gorini, Riva, 2008).

These are also the reasons why patients usually accept the use of VR very well. In a recent study, Garcia-Palacios et al. (2001) compared the acceptance of one-session and multisession *in vivo* exposure versus multi-session VR exposure therapy. More than 80% of the sample preferred VR to *in vivo* exposure.

In psychotherapy, repeated exposure leads patients to consider feared situations less and less threatening and to experience much less frequently feelings of anxiety – accordingly, patients are less inclined to avoid such situations. In the last few years, researchers and clinicians started using VR to carry out a specific form of exposure treatment (VR exposure therapy [VRET]). VRET has the potential to control, enhance and accelerate the treatment process offering several advantages over real exposure or imagination techniques.

Compared with the *in vivo* exposure, VRET is completely controlled: the quality, intensity and frequency of the exposure is entirely decided by the therapist in the office and can be stopped any time if the patient is unable to tolerate it. The flexibility of VEs also allows the patient to practice in situations often exaggerated and much worse than those that are likely to be encountered in real life (Kashani, Roberts, 2009).

The virtual experience is an "empowering environment" that the therapy provides for patients. As noted by Botella (1998), nothing the patients fear can "really" happen to them in VR. In the cognitive rehabilitation area different case studies and review papers suggest the use of VR in this area (Schultheis, Rizzo, 2001; Rizzo, Buckwalter, 1997; Riva, 1998; Riva, 1997) where there are no controlled clinical trials. A better situation can be found in the assessment of cognitive functions in persons with acquired brain injuries. In this area, VR assessment tools are effective and characterized by good psychometric properties (Zhang, Abreu, 2001; Piron, Cenni, 2001). A typical example of these applications is ARCANA. Using a standard tool (Wisconsin Card Sorting Test – WCST) of neuropsychological assessment as a model, Pugnetti and colleagues have created ARCANA: a virtual building in which the patient has to use environmental clues in the selection of appropriate choices (doorways) to move through the building.

For clinical psychologists and psychiatrists the interaction focus of VR prevails over the simulated one: they use VR to provide a new human–computer interaction paradigm in which users are no longer simply external observers of images on a computer screen but active participants within a computer-generated 3D virtual world (Riva, Rizzo, Alpini, 1999; Rizzo, Wiederhold, 1998). Starting from 1990, different companies have developed complete VR systems for the treatment of common anxiety disorders and specific phobias, such as: fear of heights, fear of flying, driving phobias, social phobia, fear of public speaking, fear of spiders, panic disorder and PTSD.

Clinical applications in Second Life include also an innovative form of group and personal therapy that uses the online world as a safe training environment for patients with social anxiety disorders and with autistic spectrum disorders, including Asperger syndrome (Biever, 2007). Patients can interact through their avatars in simulated social settings without fearing negative consequences in the real world (Huang, 2008).

Two meta-analyses (Powers, Emmelkamp, 2007; Parsons, Rizzo, 2007) deal with the effectiveness of VR in the psychotherapeutic field. The first demonstrates not only that VRET is more effective than no treatment, but also that it is slightly, but significantly, more effective than *in vivo* exposure. The other analysis, concerning the affective effects of VRET, suggests that it has a statistically significant effect on all affective domains and that these effects are of the magnitude described in the literature as large (Cohen, 1992).

As to PTSD, the University of Southern California (USC) Institute for Creative Technologies (ICT) created an immersive VRET system for combat-related PTSD. The treatment environment was initially based on recycling virtual assets that were built for the commercially successful X-Box game and tactical training simulation scenario, *Full Spectrum Warrior*. Over the years, other existing and newly created assets developed at the ICT have been integrated into this continually evolving application (Rizzo, Parsons, 2011).

The *Virtual Iraq* application (and the new *Virtual Afghanistan* scenario) consists of a series of virtual scenarios designed to represent relevant contexts for VR exposure therapy, including middle-eastern themed cities and desert road environments.

Another alternative therapy to typical imaginary exposure treatment for Vietnam combat veterans with PTSD is the VRE (Rothbaum, Hodges 1999). Rothbaum and colleagues (2001) exposed a sample of 10 combat veterans with PTSD to two environments: a virtual Huey helicopter flying over a virtual Vietnam and a clearing surrounded by the jungle. All the patients interviewed at the 6-month follow-up reported reductions in PTSD symptoms ranging from 15% to 67%.

Rehabilitation: A history of encouraging findings from the aviation simulation literature (Hays, Jacobs, 1992) has supported the concept that testing, training and treatment in highly proceduralized VR simulation environments would be a useful direction for psychology and rehabilitation to explore. As an aircraft simulator serves to test and practise piloting abilities under a variety of controlled conditions, VR can be used to create relevant simulated environments where assessment and treatment of cognitive, emotional and motor problems can take place.

In some cases, different authors showed that it is possible to use VR both to induce an illusory perception of a fake limb (Slater, Perez-Marcos, 2009) or a fake hand (Perez-Marcos, Slater, 2009). as part of our own body and to produce an out-of-body experience by altering the normal association between touch and its visual correlate. It is even possible to generate a body transfer illusion: Slater substituted the experience of male subjects' own bodies with a life-sized virtual human female body. It is also possible to use VR to improve body image (Riva, Melis, 1997; Riva, 1998) even in patients with eating disorders (Riva, Bacchetta, Baruffi, 2002; Perpiña, Botella, 1999) or obesity (Riva, Bacchetta, Baruffi, Molinari, 2001; Dean, Cook, 2009).

With patients living with "Autism spectrum disorders" (ASD), the realism of the simulated environment allows children to learn important skills, increasing the probability to transfer them into their everyday lives (Strickland, 1997; McComas, Pivik, 1998). The literature is increasingly recognising the potential benefits of VR in supporting the learning process, particularly related to social situations, in children with autism (Parsons, Mitchell, 2002; Goodwin, 2008; Ehrlich, 2009). Those researches analysed the ability of children with ASD in using VEs, and several studies, except one (Parsons, Mitchell, 2005), suggested that they successfully acquire new pieces of information from VEs. In particular, participants with ASDs learned how to use the equipment quickly and showed significant improvements in performance after a few trials in the VE (Parsons, Mitchell, 2004). Two studies, using desktop VEs as a habilitation tool, have recently been carried out to teach children how to behave in social domains and how to understand social conventions (Mitchell, Parsons, Leonard, 2007; Herrera, Alcantud, Jordan, 2008). The realism of the simulated environment allows children to learn important skills (Bellani, Fornasari, 2011), increasing the probability to transfer them into their everyday lives (Strickland, 1997; McComas, Pivik, 1998; Wang, Reid, 2010).

Clinical: A short list of areas where Clinical VR has been usefully applied includes fear reduction in persons with simple phobias (Parsons, Rizzo, 2008; Powers, Emmelkamp, 2008), treatment for PTSD (Rothbaum, Hodges, 2001; Difede, Hoffman, 2002; Difede, Cukor, 2007; Rizzo, 2010; Rizzo, Difede, 2010), stress management in cancer patients (Schneider, Kisby, 2010), acute pain reduction during wound care and physical therapy with burn patients (Hoffman, Chambers, Meyer, 2011), body image disturbances in patients with eating disorders (Riva, 2005), navigation and spatial training in children and adults with motor impairments (Stanton, Foreman, 1998; Rizzo, Schultheis, Kerns, 2004), functional skill training and motor rehabilitation with patients having central nervous system dysfunction (e.g., stroke, TBI, SCI, cerebral palsy, multiple sclerosis) (Holden, 2005; Merians, Fluet, 2010), and for the assessment and rehabilitation of attention, memory, spatial skills and other cognitive functions in both clinical and unimpaired populations (Rose, Brooks, Rizzo, 2005; Rizzo, Klimchuk, Mitura, 2006; Parsons, Rizzo, 2008; Parsons, Rizzo, Rogers, 2009). To carry out these studies, VR scientists

constructed virtual airplanes, skyscrapers, spiders, battlefields, social settings, beaches, fantasy worlds and the mundane (but highly relevant) functional environments of schoolrooms, offices, homes, streets and supermarkets. In essence, clinicians can now create simulated environments that reproduce the outside world and use them in the clinical setting to immerse patients in simulations that support the aims and mechanics of a specific therapeutic approach (Rizzo, Parsons, Lange, 2011).

Optale et al. (1997; 1999) used immersive VR to improve the efficacy of a psychodynamic approach in treating male erectile disorders. In this VE experiment, four different expandable pathways open up through a forest, bringing the patients back into their childhood, adolescence, and teens, when they started to get interested in the opposite sex. Different situations were presented with obstacles that the patient had to overcome to proceed. VR environments were used as a form of controlled dreams allowing the patient to express in a non-verbal way transference reactions and free associations related to his sexual experience.

Pain Management: The first published report to document VR as an effective analgesic for burn wound care was authored by Hoffman (2000). After this original report, other groups have reported similar analgesic benefits when immersive VR (Chan, Chung, Wong, 2007; Maani, Hoffman, DeSocio, 2008) or 'augmented reality' distraction (Mott, Bucolo, 2008) is added to standard pharmacologic analgesia for portions of (as opposed to the entirety of) bedside wound care procedures, although generally with limited numbers of patients.

Numerous reports have also documented the potential analgesic benefit of immersive VR in medical settings ranging from cancer therapy (Gershon, Zimand, 2004; Windich-Biermeier, Sjoberg, 2007) to dental care (Hoffman, Garcia-Palacios, Patterson, 2001) to transurethral prostate ablation (Wright, Hoffman, Sweet, 2005).

The combination of multisensory inputs and interactivity makes the VR experience more immersive and realistic than conventional television or video games, and can successfully capture much of the user's conscious attention (Sharar, Miller, 2008).

Immersive virtual reality provides a particularly intense form of cognitive distraction during such brief, painful procedures, particularly well-adapted for use in children (Sharar, Miller, 2008).

Mechanistic investigations of VR analgesia in the setting of controlled, experimental pain suggest that the magnitude of analgesic effect is dependent upon the user's sense of 'presence' in the virtual environment (Hoffman, Sharar, Coda, 2004), that subjective VR analgesia is accompanied by simultaneous reductions in pain-related brain activity in the cerebral cortex and brainstem (Hoffman, Richards, Coda, 2004), and that VR analgesia is of similar magnitude to, and additive with, clinically relevant doses of concurrent systemic opioid analgesics (Hoffman, Richards, Van Oostrom, 2007).

A recent report by Sharar (2007) compiled results from three ongoing controlled studies to enhance statistical power and investigate such factors as gender, age and ethnicity. This report includes the largest number of subjects published to date – a total of 146 analgesic comparisons in 88 subjects ranging in age from 6 to 65 years – and found that subjective pain ratings were reduced by 20–37% with immersive VR during passive range of motion (ROM) therapy.

Furthermore, none of the pain improvements due to VR distraction varied with differences in gender, ethnicity, initial burn size or duration of the therapy session. Interestingly, the authors found that user assessments of both the realness of the virtual environment, as well as their sense of presence in the virtual environment, differed by age of subjects, with younger subjects (<19 years old) reporting significantly higher ratings for realness and presence than adult subjects (≥19 years old).

The current understanding of the mechanism(s) by which immersive VR reduces subjective pain is skeletal, and largely based on the assumption that multisensory VR experience is distracting to the user and thereby reduces the amount of conscious attention patients can employ to process and interpret nociceptive inputs arising from painful procedures.

Table 5: Psycotherapy

	Title		Date
	1. Psychotherapy: Phobias, PTSD, Anxiety disorders, ecc.		
Bloom RW.	Psychiatric therapeutic applications of virtual reality technology (VRT): research prospectus and phenomenological critique	Stud Health Technol Inform.;39:11-6.	1997
North MM, North SM, Coble JR.	Virtual reality therapy: an effective treatment for psychological disorders	Stud Health Technol Inform.;44:59-70.	1997
Strickland D.	Virtual reality for the treatment of autism	Stud Health Technol Inform.;44:81-6.	1997
Huang MP, Alessi NE.	Current limitations into the application of virtual reality to mental health research	Stud Health Technol Inform.;58:63-6.	1998
Vincelli F, Molinari E.	Virtual reality and imaginative techniques in clinical psychology	Stud Health Technol Inform.;58:67-72.	1998
Ohsuga M, Oyama H.	Possibility of virtual reality for mental care	Stud Health Technol Inform.;58:82-90.	1998
Bullinger AH, Roessler A, Mueller-Spahn F.	From toy to tool: the development of immersive virtual reality environments for psychotherapy of specific phobias	Stud Health Technol Inform.;58:103-11.	1998
North MM, North SM, Coble JR.	Virtual reality therapy: an effective treatment for phobias	Stud Health Technol Inform.;58:112-9.	1998
Rogers MB 2nd.	Virtual reality in psychotherapy: the MYTHSEEKER software	Stud Health Technol Inform.;58:170-9.	1998
Marks I.	Computer aids to mental health care	Can J Psychiatry. Aug;44(6):548-55.	1999
Rothbaum BO, Hodges LF.	The use of virtual reality exposure in the treatment of anxiety disorders	Behav Modif. Oct;23(4):507-25.	1999
Neziroglu F, Hsia C, Yaryura-Tobias JA.	Behavioral, cognitive, and family therapy for obsessive-compulsive and related disorders	Psychiatr Clin North Am. Sep;23(3):657-70.	2000
Davidson J, Smith M.	Bio-phobias/techno-philias: virtual reality exposure as treatment for phobias of 'nature'	Sociol Health Illn. Sep;25(6):644-61.	2003
Anderson P, Jacobs C, Rothbaum BO.	Computer-supported cognitive behavioral treatment of anxiety disorders	J Clin Psychol. Mar;60(3):253-67.	2004
Krijn M, Emmelkamp PM, Olafsson RP, Biemond R.	Virtual reality exposure therapy of anxiety disorders: a review	Clin Psychol Rev. Jul;24(3):259-81.	2004
Riva G.	Virtual reality in psychotherapy: review	Cyberpsychol Behav. Jun;8(3):220-30; discussion 231-40.	2005
Gregg L, Tarrier N.	Virtual reality in mental health : a review of the literature	Soc Psychiatry Psychiatr Epidemiol. May;42(5):343-54. Epub 2007 Mar 12.	2007
Gorini A, Riva G.	Virtual reality in anxiety disorders: the past and the future	Expert Rev Neurother. Feb;8(2):215-33.	2008
Freeman D.	Studying and treating schizophrenia using virtual reality: a new paradigm	Schizophr Bull. Jul;34(4):605-10. Epub 2008 Mar 28.	2008
Reger GM, Gahm GA.	Virtual reality exposure therapy for active duty soldiers	J Clin Psychol. Aug;64(8):940-6.	2008
da Costa RT, Sardinha A, Nardi AE.	Virtual reality exposure in the treatment of fear of flying	Aviat Space Environ Med. Sep;79(9):899-903.	2008

	Title		Date
Coelho CM, Waters AM, Hine TJ, Wallis G.	The use of virtual reality in acrophobia research and treatment	J Anxiety Disord. Jun;23(5):563-74. Epub 2009 Feb 10.	2009
Wiederhold BK, Wiederhold MD.	Virtual reality treatment of posttraumatic stress disorder due to motor vehicle accident	Cyberpsychol Behav Soc Netw. Feb;13(1):21-7.	2010
Riva G, Raspelli S, Algeri D, Pallavicini F, et al.	Interreality in practice: bridging virtual and real worlds in the treatment of posttraumatic stress disorders	Cyberpsychol Behav Soc Netw. Feb;13(1):55-65.	2010
De Carvalho MR, Freire RC, Nardi AE.	Virtual reality as a mechanism for exposure therapy	World J Biol Psychiatry. Mar;11(2 Pt 2):220-30.	2010
Gerardi M, Cukor J, Difede J, Rizzo A, Rothbaum BO.	Virtual reality exposure therapy for post-traumatic stress disorder and other anxiety disorders	Curr Psychiatry Rep. Aug;12(4):298-305.	2010
Meyerbröker K, Emmelkamp PM.	Virtual reality exposure therapy in anxiety disorders: a systematic review of process-and-outcome studies	Depress Anxiety. Oct;27(10):933-44.	2010
Spurgeon JA, Wright JH.	Computer-assisted cognitive-behavioral therapy	Curr Psychiatry Rep. Dec;12(6):547-52.	2010
Bouchard S.	Could virtual reality be effective in treating children with phobias?	Expert Rev Neurother. Feb;11(2):207-13.	2011
	2. Rehabilitation		
Brochard S, Robertson J, Médée B, Rémy-Néris O.	What's new in new technologies for upper extremity rehabilitation?	Curr Opin Neurol. Dec;23(6):683-7.	2010
Brooks BM, Rose FD.	The use of virtual reality in memory rehabilitation: current findings and future directions	NeuroRehabilitation.;18(2):147-57.	2003
Buckwalter JG, Rizzo AA.	Virtual reality and the neuropsychological assessment of persons with neurologically based cognitive impairments	Stud Health Technol Inform.;39:17-21.	1997
Burdea GC.	Virtual rehabilitation--benefits and challenges	Methods Inf Med.;42(5):519-23.	2003
Cameirão MS, Bermúdez I Badia S, et al.	The rehabilitation gaming system: a review	Stud Health Technol Inform.;145:65-83.	2009
Cherniack EP.	Not just fun and games: applications of virtual reality in the identification and rehabilitation of cognitive disorders of the elderly	Disabil Rehabil Assist Technol. 2011;6(4):283-9. Epub Dec 15.	2011
Crosbie JH, Lennon S, Basford JR, McDonough SM.	Virtual reality in stroke rehabilitation: still more virtual than real	Disabil Rehabil. Jul 30;29(14):1139-46; discussion 1147-52.	2007
D'Angelo M, Narayanan S, Reynolds DB, Kotowski S, Page S.	Application of virtual reality to the rehabilitation field to aid amputee rehabilitation: findings from a systematic review	Disabil Rehabil Assist Technol. Jan;5(2):136-42.	2010
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4. Discussion

Examining the available literature that we found in the 4 search engines considered, we may conclude that VR in medicine could be described as a communication interface based on interactive 3D visualization, able to collect and integrate different inputs and data sets in a single realistic experience.

VR for healthcare is different as to goals and applications from the "Real Virtual World" that is defined as a combination of 3D + 3C (communication, creation and commerce), that is to say a three dimensional world in which communities (Ikegami, 2008) of real people interact, creating content, objects and services and producing real economic value through e-Commerce (Martin, 2008).

All VR's definitions previously discussed underline two different points of view. For physicians and surgeons, the ultimate goal of VR is the presentation of virtual objects to all the human senses in a way identical to their natural counterpart (Székely, Satava, 1999). As noted by Satava and Jones (2002), as more and more of the medical technologies become information-based, it will be possible to represent a patient with such faithfulness that the image may become a surrogate for the patient – the *medical avatar*.

An effective VR system should offer real-like body parts or avatars that interact with external devices such as surgical instruments as near as possible to their real models.

For clinical psychologists and rehabilitation specialists the ultimate goal is radically different (Riva, Rizzo, Alpini, 1999; Rizzo, Wiederhold, Van Der Zaag, 1998). They use VR to provide a new human-computer interaction paradigm in which users are no longer simply external observers of images on a computer screen but active participants within a computer-generated 3D VW. According to Riva (2005) four barriers still remain in the VR application in Medicine. The first is the lack of standardization in VR devices and software. The PC-based systems, while cheap and easy-to-use, still suffer from a lack of flexibility and capabilities necessary to individualize environments for each patient (Riva, 1997). To date, very few of the various VR systems available are interoperable. This makes their use difficult in contexts other than those in which they are developed. The second is the lack of standardized protocols that can be shared by the community of researchers. Current searches of the two clinical databases used in this review yielded only five published clinical protocols: for the treatment of eating disorders (Riva, Bacchetta, Cesa, 2001), fear of flying (Klein, 1999; Rothbaum, Hodges, Smith, 1999), fear of public speaking (Botella, Baños, Villa, 2000), and panic disorders (Vincelli, Choi, Molinari, 2001). The third barrier is the cost required for the set-up of these protocols' trial.

Finally, the introduction of patients and clinicians to virtual environments raises particular safety and ethical issues (Durlach, Mavor, 1995). Despite developments in VR technology, some users still experience health and safety problems associated with VR use. It is however true that for a large proportion of VR users, these effects are mild and subside quickly (Nichols, Patel, 2002). According to Kennedy, Lane, Berbaum and Lilienthal (1993) the temporary side effects can be divided into three classes of symptoms related to the sensory conflicts and to the use of virtual reality equipment: (1) visual symptoms (eyestrains, blurred vision, headaches), (2) disorientation (vertigo, imbalance) and (3) nausea (vomiting, dizziness).

We also have to consider two critical aspects of this review: 1. We have taken into consideration only 4 search engines without considering other psychology search engines like APA (PsycINFO, PsycARTICLES, PsycBOOKS, PsycCRITIQUES, PsycEXTRA, PsycTHERAPY, PsycTESTS, etc.). 2. The key terms we selected are not completely descriptive for the entire world of virtual healthcare application.

But it is important to underline that Virtual worlds are an exciting area offering opportunities in every healthcare areas, from teaching to clinical interventions. We can assume this field of study will offer great opportunities in the world of e-learning and simulators. If we think about Augmented Reality application to glass, it is clear that it could be a very important tool in operating rooms or just for teaching. We may imagine that it could be useful for video sharing and storage – physicians could record medical visits and store them for future reference or share the footage with other doctors. Moreover, it could be employed for diagnostic reference: If glass is integrated with an electronic medical record (EMR), it could provide a real-time feed of the patient's vital signs.

We could also imagine other uses, such as:

- A textbook alternative: Rather than referring to a medical textbook, physicians can perform a search on the fly with their augmented reality glass.

- Emergency room/war zone care: dealing with wounded patients and right there in their field of vision, if they're trying to do any kind of procedure, they'll have step-by-step instructions walking them through it. In trauma situations, doctors need to keep their hands free.

- Helping medical students learn: a surgeon might live stream a live — and potentially rare — surgery to residents and students.

- Preventing medical errors: With an electronic medical record integration, a nurse can scan the medication to confirm whether the drug dose is correct and administered to the right patient.

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