Virtual Reality During Brain Mapping for Awake-Patient Brain Tumor Surgery: Proposed Tasks and Domains to Test

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■ BACKGROUND: **Virtual reality (VR) use in health care has increased over the past few decades, with its utility expanding from a teaching tool to a highly reliable neuro-technology adjunct in multiple fields including neurosurgery. Generally, brain tumor surgery with the patient awake has only been performed for mapping of language and motor areas. With the rise of VR and advancing surgical techniques, neurosurgical teams are developing an increased understanding of patients' anatomo-functional connectivity. Consequently, more specific cognitive tasks are being required for the mapping and preservation of deeper layers of cognition.**

■ METHODS: **An extensive literature review was conducted with the inclusion criteria of manuscripts that described the use of VR during awake neurosurgery mapping.**

■ RESULTS: **We identified 3 recent articles that met our inclusion criteria, yet none of them addressed the specific use of VR for cognition mapping. Consequently, a cognitive task phase was performed to search and craft the tasks and domains that better filled the spotted niche of this need inside the operating room. A proposed protocol was developed with 5 potential uses of VR for brain mapping during awake neurosurgery, each of them with a specific proposed example of use.**

■ CONCLUSIONS: **The authors advocate for the use of a VR protocol as a feasible functional tool in awake-patient brain tumor surgery by using it as a complement during cognitive screening in addition to language testing.**

Virtual reality technology allows the user to become completely immersed in a fully computer-generated and synthetic environment, one that can potentially mimic and simulate a particular environment of choice. It has been used for more than 2 decades to supplement medical training, improve clinical interventions, provide objective assessments, and to promote health and wellness. Until recently, the cost of virtual reality technology has been a barrier to acceptance outside of the university setting. Now, however, the reduced cost and increased availability of virtual reality systems have made clinical virtual environments practical for everyday use. As a result, virtual reality technology has expanded from university and surgical training centers to other sectors of medicine. Publications have documented the use of virtual reality in multiple fields, including cognitive neuroscience and neuropsychology,[1] psychiatry,[2] physical medicine and rehabilitation,[3,4] neurology,[4,5] palliative medicine,[6,7] gastroenterology,[8] emergency medicine,[9] disaster medicine,[10] telemedicine,[11] oral and maxillofacial surgery,[12,13] plastic surgery,[14] obstetrics and gynecology,[15] hepatic surgery,[16] orthopedic surgery,[17] and neurosurgery,[18-22] among others. Within neurosurgery, virtual reality has been used both as a training tool for resident education as well as clinical care, both in cranial and spine pathologies.

In virtual reality, real environmental situations are virtually generated by computers and software. As such, virtual reality is becoming increasingly used for simulation and training in neurosurgical care.[21,23] It provides a risk-free environment for clinical training for surgeons, aimed at reducing the learning curve, improving conceptual understanding of complex anatomy, and enhancing visuospatial skills. These training opportunities are unconstrained, independent of patient or cadaver accessibility. In addition to surgical training, virtual reality provides a method for

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- Awake surgery
- Brain mapping
- Cognitive monitoring
- Functional mapping
- Neuro-oncology
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objective assessments and opportunities to assess trainees' progress via various competence metrics. Various virtual reality programs are being developing that provide trainees with simulation in ventricular drain placement, endoscopy, open cranial, transsphenoidal, skull base, spinal, endovascular, and peripheral nerve surgery.[21-24]

In additional to surgical training and assessment, virtual reality can be used at several time points during a patient's clinical care continuum: 1) preoperatively for surgical planning, baseline testing, and to improve patient's understanding of the procedure; 2) intraoperatively; and 3) postoperatively for objective clinical assessments as well as cognitive and physical rehabilitation. The objective of this review is to summarize and review the use of virtual reality intraoperatively, specifically as it relates to awake brain tumor surgery. Furthermore, the authors propose a protocol to improve upon existing paradigms, suggesting various intraoperative VR tasks and the respective domains that can be tested.

AWAKE-PATIENT BRAIN TUMOR SURGERY

Background

Brain tumor surgery performed with the patient awake—instead of intubated and sedated—has several advantages. The main purpose of surgery performed with the patient awake is to maximize the extent of tumor resection while minimizing morbidity, and it is used in particular cases depending on the location and nature of the lesion. This is particular true for malignant brain tumors as a safe, maximal, and perhaps even supramaximal surgical resection is shown to improve overall mortality in these patients.[25] Various surgical adjuncts or techniques help increase extent of resection as well as overall and progression-free survival: fiber tracking, neuronavigation, ultrasonography, intraoperative imaging, fluorescence, cortical and subcortical mapping, and awake surgery.[26-29] An awake surgery, in particular, allows for intraoperative, real-time neurofunctional monitoring with a participatory patient. Such neuromonitoring or brain mapping allows the identification and preservation of eloquent neural tissue involving motor and language networks, all with the goal of improving the patient's morbidity and accelerating the patient's full reinsertion back into society, normal life, and the workforce.

Brain mapping via direct electrical stimulation involves the neurosurgeon directly stimulating the cortex while the patient performs certain tasks. In assessing speech, the patient is asked to name images presented by a neuropsychologist or to state certain phrases. If language fluency is perturbed or language arrest occurs, it suggests a network or subnetwork has been identified that must be tagged and preserved during surgery. The same method can be applied to the mapping of motor networks while having the patient perform motor tasks. This process can be performed either by a negative or positive mapping approaches.[29] The former works to validate that the preplanned trajectory to the tumor does not involve cortical and subcortical brain tissue involved in eloquent networks. The latter involves a much wider exposure of the brain to fully identify these eloquent areas and validate that the preplanned surgical approach is safe in an effort to not interrupt these networks.

Classically, awake brain tumor surgery was performed with merely the mapping of language in the dominant hemisphere (usually left) as well as motor regions. Recently, with the rise of technology and advancement of surgical techniques, neurosurgical teams are able to learn the anatomo-functional connectivity of patients more than ever. Preventing aphasia or hemiplegia is now the minimum requirement; the preservation of cognition and emotion can further maintain the patient's behavior, personality, and desired quality of life.

More complex tasks are being used to map and preserve deeper layers of cognition and emotion, including frontal executive function, optic pathway function (e.g., optic radiations), nondominant (usually right) hemispheric cognitive functions such as visuospatial and social cognitions (e.g., nonverbal language, empathy, and theory of mind), complex movement control, emotional regulation, and conscious awareness.[20,30-32] Ideally, an awake brain tumor surgery would incorporate a cognitive prescreening, intraoperative language and cognition mapping, and postsurgical cognitive assessment and rehabilitation.

Incorporation of Virtual Reality

As neurofunctional advancements evolve, one immersive technology is starting to be incorporated as a complementary mapping tool in the operating room: virtual reality. Recent reports—although limited—describe the feasibility of using virtual reality inside the operating room during brain mapping procedures. Mazerand et al.[19] described the use of virtual reality in combination with direct stimulation as a method to perform intraoperative visual field assessment and mapping of the optic radiations during awake surgery. Such mapping of optic radiations is classically rarely performed due to difficulty of testing intraoperatively. Through a multidisciplinary approach involving an orthoptist, patients responded to luminous stimuli on the screen of the virtual reality headset while the neurosurgeon performed direct cortical or subcortical electrostimulation, with the goal of preserving permanent visual function. Bernard et al.[18] explored the use of virtual reality to map social cognition during awake craniotomy. The authors sought to assess perioperative mapping of nonverbal language (including facial emotion recognition and emotional prosody), empathy, and theory of mind by assessing the patient's interaction with the neuropsychologist's avatar in virtual reality. Lastly, Delion et al.[20] described the use of virtual reality for language mapping during awake surgery. The authors performed the classic DO 80 naming task in virtual conditions while performing direct cortical electrical stimulation. Similar to Bernard et al., Delion et al. demonstrated the possibility of immersing an awake craniotomy patient in a virtual environment and having the patient interact with the environment and an avatar (e.g., neuropsychologist). In addition to facilitating with functional mapping, such intraoperative virtual reality experiences for the awake-surgery patient may help alleviate pain and anxiety.[6,7,20]

Virtual Reality Protocol

In light of the advances of virtual reality and the recent feasibility of the use of virtual reality during awake patient brain surgeries, we recommend a "virtual reality protocol" to be used at various time points in a patient's care. Table 1 provides a summary of classical tasks used intraoperatively in awake patient brain surgery with potential advances with virtual reality. Table 2 further elaborates

Table 1. Traditional Versus Virtual Reality—Assisted Tasks Used in Awake Patient Brain Surgery

Task Domain	Classical Brain Mapping Use	Limitations	Authors' Recommendation with Virtual Reality Use
Naming	Showing pictures using physical cards or a computer.	Nonimmersive. Possibility of habituation/learning of images.	Immersive environment with preprogrammed set of images shown with varying pace and in different contexts.
Emotional	Role playing or facial emotional recognition cards.	Nonimmersive environment.	Immersive experience with emotional recognition tasks using avatars.
Praxis	Asking patient to perform motor movements.	Nonimmersive and rarely performed in operating room.	A gamified experience with an avatar.
Gnosias	Familiar faces are shown on a screen.	Static, nonimmersive tasks.	A familiar or famous face can be presented in a more immersive way.

on the proposed intraoperative tasks using virtual reality and the respective domains that the tasks would assess.

First, patients undergoing awake brain surgery should participate in a basic introductory session using virtual reality in the ambulatory setting; this will immerse them in the virtual reality environment, together with the neurosurgeon and the multidisciplinary team that will be participating in surgery (e.g., neuropsychologist, speech therapist, anesthesiologist). This protocol will serve many purposes. The patient's pathology, anatomy, and proposed surgery can be illustrated and demonstrated with 3-dimensional modeling in virtual reality, helping the patient to understand the planned testing during surgery. Together with the neuropsychologist, patients can be told and shown what will be asked of them intraoperatively so they are prepared and comfortable. Various immersive virtual assessments and neuropsychological test batteries may be created depending on the need and anatomical area of the brain that is to be tested.[1]

Second, intraoperatively, we recommend using a virtual naming test in situations in which detection of speech areas is necessary. Classically, neuropsychologists have used a digital black and white image naming test. We recommend a more immersive naming test catered to patient's background and education level. The neuropsychologists could then program the images including the categories, quantity, duration of time spent per image, and transition length between images, all which are key during surgery. Similarly, an auditory association naming test may be utilized; an audio file can be played that details a physical description of an animal followed by a question regarding what animal was described (i.e., the audio file would state "a yellow animal with brown dots and long neck, what animal is this?" with an expected answer of "giraffe").

Third, we recommend the use of virtual reality applications for social cognition and emotion recognition. This would be particular useful in patients with insular gliomas; the neurosurgeon would intraoperatively stimulate insular tracts while the neuropsychologist assesses preservation of emotions such as empathy. Instead of role playing or empathy paper and pencil tests, virtual reality (e.g., an avatar emotional recognition task) would allow a

Table 2. Proposed Tasks and the Respective Domains Tested Using Virtual Reality During Awake Patient Brain Mapping

Domain	Task	Description
Auditory association	Auditory naming test by sound	Patient hears an animal sound and then is asked to name the animal.
Auditory Association	Auditory naming test by description	Patient hears characteristics of an animal and then is asked to name the animal.
Calculus/attention	Digits backwards	Patient is presented with three series of numbers: first series consists of 3 numbers, second series consists of 5 numbers, and the third series consists of 7 numbers. The patient is asked to recite them backwards.
Calculus/working memory/attention	Subtract 3 from the number presented on the screen	Random 3-digit numbers appear on screen and the patient has to subtract 3. Example: 343; expected answer: 340.
Praxis	Gesture production by hearing command	Patient is asked to "gesture how you brush your teeth."
Praxis	Gesture production by reading command	Patient reads a screen that states "gesture how you brush your teeth."
Gnosias	Recognition of familiar faces	Patient is presented with 10 familiar/famous faces.
Gnosias	Recognition of familiar sounds	Patient is presented with familiar sounds (e.g., bus horn, train locomotion, keys opening a door, a person walking).
Emotional recognition	Emotional recognition task (reading facial emotions)	Actors appear on screen and ask the patient: "how do you think I am feeling right now?"

more immersive setting and one that could potentially evoke a stronger emotional reaction. For example, a virtual immersive environment can incorporate actors portraying various facial emotions and asking the patient what emotion they are feeling. As the patient is thinking or choosing between different answer options, the neurosurgeon can be stimulating the brain cortex.

Fourth, we recommend having the patient perform arithmetic tasks using virtual reality. Numeric tasks and digits can be presented in more immersive ways to the patients. For instance, the patient can be asked to subtract 3 from a random number that appears on the screen, all while the neurosurgeon stimulates the cortex. Instead of digits on a screen, the patient can be also asked to count or perform calculating tasks using objects in virtual reality.

Fifth, we recommend virtual reality tasks for praxis (gesture imitation) and gnosias (recognition). Inside the operating room, the neuropsychologist can ask the patient to imitate and act as if he/she is brushing their teeth. Familiar faces or sounds can also be used in the virtual reality setting to test recognition, and can be potentially selected preoperatively to be specifically tailored to that individual patient.

Last, we recommend incorporating virtual reality to perform intraoperative visual field assessment and mapping of the optic radiations for patients with tumors adjacent to the optic radiations.[19] Similar to the study by Mazerand et al., stimuli introduced in the virtual reality headset while the neurosurgeon performs direct cortical or subcortical electro stimulation can allow for identification of the visual fibers, protection of the fibers, and subsequent preservation of vision.

Protocol Limitations

Although we recommend the use of virtual reality in awake-patient brain surgery, this technology should be used as a complement and not as a substitution of common and standardized regular tests. Furthermore, we recommend that neurosurgical teams analyze on a case-by-case scenario the suitability of each patient for the use of virtual reality since cases of evoked seizures have been documented. Duffau[32] described "a la carte" mapping in brain tumor patients, one that evolves from the "standardized protocol" only aiming to avoid aphasia and hemiplegia, to a "high-fashion" philosophy that aims to take into account the patient as a complete, complex human being with unique cognitive and emotional neural networks. Perhaps one day a patient will choose in virtual reality what neurocognitive monitoring he/she desires, setting up a protocolized pathway that assesses these unique networks preoperatively for baseline metrics, intraoperatively for preservation, and postoperatively for reassessment and rehabilitation.

CONCLUSIONS

Virtual reality offers the opportunity to have more immersive environments that generate more complex emotional reactions and output performances. Initial studies display the promise of incorporating this technology and the potential benefits of generating a formalized, multidisciplinary protocol, particularly in awake brain surgery. A protocol using virtual reality can assist the treatment team in the presurgical phase as a screening tool and for baseline testing. In addition, virtual reality can be used intraoperatively as a more robust and precise tool for language and emotional mapping. Virtual reality has been tested against conventional and computer-based tests and has been shown to generate more precise diagnostics in which the clinician can observe a patient's errors in situ. Therefore, we recommend the generation of a virtual reality protocol for oncologic patients scheduled for awake-patient brain surgery. In combination with standardized tests, such a protocol incorporating virtual reality could assist the clinician to go deeper into the consciousness activation of these patients.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Gennadiy A. Katsevman: Data curation, Formal analysis, Investigation, Methodology, Validation, Writing - original draft, Writing - review & editing. **Walter Greenleaf:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Writing - review & editing. **Ricardo García-García:** Data curation, Formal analysis, Investigation, Validation, Writing - review & editing. **Maria Victoria Perea:** Data curation, Formal analysis, Investigation, Validation, Writing - review & editing. **Valentina Ladera:** Data curation, Formal analysis, Investigation, Validation, Writing - review & editing. **Jonathan H. Sherman:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. **Gabriel Rodríguez:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing.

REFERENCES

1. Kourtesis P, Korre D, Collina S, Doumas LAA, MacPherson SE. Guidelines for the development of immersive virtual reality software for cognitive neuroscience and neuropsychology: the development of Virtual Reality Everyday Assessment Lab (VR-EAL), a neuropsychological test battery in immersive virtual reality. *Front Computer Sci*. 2020;1:1-24.
2. Park MJ, Kim DJ, Lee U, Na EJ, Jeon HJ. A literature overview of virtual reality (VR) in treatment of psychiatric disorders: recent advances and limitations. *Front Psychiatry*. 2019;10:1-9.
3. Darekar A, McFadyen BJ, Lamontagne A, Fung J. Efficacy of virtual reality-based intervention on balance and mobility disorders post-stroke: a scoping review. *J Neuroeng Rehabil*. 2015;12:1-14.
4. Thielbar K, Spencer N, Tsoupikova D, Ghassemi M, Kamper D. Utilizing multi-user virtual reality to bring clinical therapy into stroke survivors' homes. *J Hand Ther*. 2020;33:246-253.
5. Jütten LH, Mark RE, Maria Janssen BWJ, Rietsema J, Dröes RM, Sitskoorn MM. Testing the effectivity of the mixed virtual reality training Into D'mentia for informal caregivers of people with dementia: protocol for a longitudinal, quasi-experimental study. *BMJ Open*. 2017;7:1-10.
6. Konstantatos AH, Angliss M, Costello V, Cleland H, Stafrace S. Predicting the effectiveness of virtual reality relaxation on pain and anxiety when added to PCA morphine in patients having burns dressings changes. *Burns*. 2009;35:491-499.
7. Mallari B, Goh H, Boyd B, Spaeth E. Virtual reality as an analgesic for acute and chronic pain in adults. *J Pain Res*. 2019:2053-2085.
8. Hashimoto DA, Petrusa E, Phitayakorn R, Valle C, Casey B, Gee D. A proficiency-based virtual reality endoscopy curriculum improves performance on the fundamentals of endoscopic surgery examination. *Surg Endosc*. 2018;32:1397-1404.

9. McGrath JL, Taekman JM, Dev P, et al. Using virtual reality simulation environments to assess competence for emergency medicine learners. *Acad Emerg Med*. 2018;25:186-195.

10. Duan Y, Zhang J, Xie M, Feng X, Xu S, Ye Z. Application of virtual reality technology in disaster medicine. *Curr Med Sci*. 2019;39:690-693.

11. Mantovani E, Zucchella C, Bottiroli S, et al. Telemedicine and virtual reality for cognitive rehabilitation: a roadmap for the COVID-19 pandemic. *Front Neurol*. 2020;11:1-8.

12. Miki T, Iwai T, Kotani K, Dang J, Sawada H, Miyake M. Development of a virtual reality training system for endoscope-assisted submandibular gland removal. *J Craniomaxillofac Surg*. 2016;44:1800-1805.

13. Ayoub A, Pulijala Y. The application of virtual reality and augmented reality in Oral & Maxillofacial Surgery. *BMC Oral Health*. 2019;19:1-8.

14. Kim Y, Kim H, Kim YO. Virtual reality and augmented reality in plastic surgery: a review. *Arch Plastic Surg*. 2017;44:179-187.

15. Letterie GS. How virtual reality may enhance training in obstetrics and gynecology. *Am J Obstet Gynecol*. 2002;187(3 suppl):37-40.

16. Quero G, Lapergola A, Soler L, Marescaux J, Mutter D, Pessaux P. Virtual and augmented reality in oncologic liver surgery. *Surg Oncol Clin North Am*. 2019;28:31-44.

17. Vaughan N, Dubey VN, Wainwright TW, Middleton RG. A review of virtual reality based training simulators for orthopaedic surgery. *Med Eng Phys*. 2016;38:59-71.

18. Bernard F, Lemée JM, Aubin G, Ter Minassian A, Menei P. Using a virtual reality social network during awake craniotomy to map social cognition: prospective trial. *J Med Internet Res*. 2018;20:e10332.

19. Mazerand E, Le Renard M, Hue S, Lemée JM, Klinger E, Menei P. Intraoperative subcortical electrical mapping of the optic tract in awake surgery using a virtual reality headset. *World Neurosurg*. 2017;97:424-430.

20. Delion M, Klinger E, Bernard F, Aubin G, Minassian A Ter, Menei P. Immersing patients in a virtual reality environment for brain mapping during awake surgery: safety study. *World Neurosurg*. 2020;134:e937-e943.

21. Bernardo A. Virtual reality and simulation in neurosurgical training. *World Neurosurg*. 2017;106:1015-1029.

22. Mikhail M, Mithani K, Ibrahim GM. Presurgical and intraoperative augmented reality in neuro-oncologic surgery: clinical experiences and limitations. *World Neurosurg*. 2019;128:268-276.

23. Pfandler M, Lazarovici M, Stefan P, Wucherer P, Weigl M. Virtual reality-based simulators for spine surgery: a systematic review. *Spine J*. 2017;17:1352-1363.

24. 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;141:291-298.

25. Dimou J, Beland B, Kelly J. Supramaximal resection: a systematic review of its safety, efficacy and feasibility in glioblastoma. *J Clin Neurosci*. 2020;72:328-334.

26. Certo F, Stummer W, Farah JO, et al. Supramarginal resection of glioblastoma: 5-ALA fluorescence, combined intraoperative strategies and correlation with survival. *J Neurosurg Sci*. 2019;63:625-632.

27. Zhang JJY, Lee KS, Voisin MR, Hervey-Jumper SL, Berger MS, Zadeh G. Awake craniotomy for resection of supratentorial glioblastoma: a systematic review and meta-analysis. *Neurooncol Adv*. 2020;2:vdaa111.

28. Katsevman GA, Turner RC, Urhie O, Voelker JL, Bhatia S. Utility of sodium fluorescein for achieving resection targets in glioblastoma: increased gross- or near-total resections and prolonged survival. *J Neurosurg*. 2020;132:914-920.

29. Almeida JP, Chaichana KL, Rincon-Torroella J, Quinones-Hinojosa A. The value of extent of resection of glioblastomas: clinical evidence and current approach. *Curr Neurol Neurosci Rep*. 2015;15:517.

30. Rodríguez A, Rey B, Clemente M, Wrzesien M, Alcañiz M. Assessing brain activations associated with emotional regulation during virtual reality mood induction procedures. *Exp Syst Appl*. 2015;42:1699-1709.

31. Lemée JM, Bernard F, Ter Minassian A, Menei P. Right hemisphere cognitive functions: from clinical and anatomical bases to brain mapping during awake craniotomy. Part II: neuropsychological tasks and brain mapping. *World Neurosurg*. 2018;118:360-367.

32. Duffau H. New philosophy, clinical pearls, and methods for intraoperative cognition mapping and monitoring "à la carte" in brain tumor patients. *Neurosurgery*. 2021;88:919-930.

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