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A Review on the Applications of Virtual Reality, Augmented Reality and Mixed Reality in Surgical Simulation: An Extension to Different Kinds of Surgery

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ABSTRACT

Background: Research proves that the apprenticeship model, which is the gold standard for training surgical residents, is obsolete. For that reason, there is a continuing effort towards the development of high-fidelity surgical simulators to replace the apprenticeship model. Applying Virtual Reality Augmented Reality (AR) and Mixed Reality (MR) in surgical simulators increases the fidelity, level of immersion and overall experience of these simulators.

Areas Covered: The objective of this review is to provide a comprehensive overview of the application of VR, AR and MR for distinct surgical disciplines, including maxillofacial surgery and neurosurgery. The current developments in these areas, as well as potential future directions, are discussed.

Expert Opinion: The key components for incorporating VR into surgical simulators are visual and haptic rendering. These components ensure that the user is completely immersed in the virtual environment and can interact in the same way as in the physical world. The key components for the application of AR and MR into surgical simulators include the tracking system as well as the visual rendering. The advantages of these surgical simulators are the ability to perform user evaluations and increase the training frequency of surgical residents.

KEYWORDS: Virtual Reality (VR), Augmented Reality (AR), Mixed Reality (MR), Surgical Simulation, Surgical Training

1. Introduction

The dynamic nature of many surgical procedures demands careful judgment, professional know-how and high levels of attention. In the apprenticeship model, surgeons are extensively and broadly educated under the supervision of an experienced surgeon to acquaint these skills. However, the apprenticeship model, which is the gold standard for training surgical residents, is outdated for several reasons, including the impact on the patient's comfort, the procedural duration, the time and cost of the operation and the possibility of complications [1]. In addition, surgical residents need more training time to learn increasingly complex surgical skills, such as minimally invasive surgery. A possibility to overcome these obstacles is by incorporating surgical simulators, for example, based on VR, into the resident's curricula as it provides them with greater flexibility and practice without an experienced surgeon's supervision. Additional benefits include the opportunity to fail at any given time without consequences, objective performance assessment, the creation of unusual surgical procedures and repeated practice. Agha et al. [2] also emphasize that simulators allow trainees to develop more sequentially their skillset at a rate that is individually tailored, which would not necessarily be possible with a real patient.

Furthermore, simulators are also useful to teach new techniques to experts. Finally, simulators can also help develop non-technical competencies, including teamwork and communication. In recent years, the field of surgical simulation has made a lot of progress. Today, not only VR surgical simulators but also surgical simulators based on AR and MR have been developed. Sophisticated techniques and algorithms have allowed surgeons to conduct correct surgical procedures, intraoperative control and postoperative tracking. AR is beneficial for preoperative surgical preparation, providing useful outcome predictions and intraoperative navigation to minimize possible risks. MR has enabled three-dimensional (3D) imagery to be more comprehensive and accurate, hence improving surgical navigation and pre-processing. Literature shows that VR, AR and MR technologies have all been utilized in surgical workflows. However, for surgical planning and intraoperative guidance there is a clear preference towards AR and MR. On the other hand, VR is used for its immersive character and is, therefore, more suited for training purposes. The relationship between VR, AR and MR is that all three technologies rely on the use of virtual data to alter the physical world around the user. AR technology changes the physical world by overlaying information onto the physical world. MR technology anchors virtual data into the physical world. Finally, VR replaces the physical world with an entire virtual world. This review's objective is to provide an overview of the underlying key technologies and highlight VR, AR and MR applications extending to various forms of surgery, as present reviews focus solely on one particular surgical discipline. The key technologies described for VR, AR and MR are the current standards regarding visual rendering, haptic rendering, tracking and image registration. However, there may be several competing key technologies, such as optical and electromagnetic tracking for AR. One technology is not simply better than the other because each technology has different strengths and weaknesses. The choice of which technology to apply depends on the scope of the application.

2. Virtual reality

Virtual reality is an immersive experience where a virtual world replaces the physical world. With input devices such as hand-held controllers, haptic feedback devices and haptic gloves, the user can interact with this virtual world. The position of these devices is measured by optical tracking, laser tracking or by rotary encoders. When the user moves the input device in the physical world, its translation and rotation are tracked and applied to the virtual surgical instrument. This ensures a one-on-one relationship between a translation and rotation in the physical world and the virtual world. Two key technologies used to realize high fidelity VR experiences are visual rendering and haptic rendering. **Figure 1** shows a virtual surgical simulator, with haptic feedback and related components, capable of simulating maxilla-cutting.

2.1 Visual rendering

A surgical simulator [3] renders an immersive 3D environment to mimic the real surgical scene. To realize the rendering of the surgical environment, developers use 3D graphical application programming interfaces (APIs). The most common are Direct3D (Microsoft Corporation, US), a Windows dedicated graphics API, OpenGL (Open Graphics Library, the Khronos Group Inc., US), a cross-language, cross-platform graphics API and the more recently introduced Vulkan (The Khronos Group Inc., US), a cross-platform graphics API. Nowadays, there are game engines such as Unreal Engine (Epic Games, US) and Unity (Unity Technologies, US) that support VR application development and operate on top of these graphics APIs. These engines make the creation and deployment of 3D scenes easier and have gained more attention in the build process of surgical simulators, especially Unity [3, 4, 5, 6]. When creating a scene based on a 3D graphics API, the developers need to start from scratch, which gives a lot of flexibility and control. Since only the features necessary for the application will be implemented, it is often more lightweight. However, due to its low-level nature, there is a steep learning curve and it is also time-consuming as the developer needs to start from scratch. On the other hand, game engines already include all the features necessary to create 3D scenes. They often have a graphical user interface (GUI) and are easier to learn since the developer does not have to engage in the low-level work involved with the 3D graphical APIs. Consequently, this comes at the cost of being less flexible, having less control and using an integrated development environment (IDE) with many unused features. The technical specifications for making 3D scenes rely on the nature of the scenario (e.g., number of objects, object details, etc.). Hence dedicated workstations with powerful graphics processing units (GPUs) to accelerate virtual scene computations to comply with the update frequency of 30Hz-120Hz are used. After rendering, the scene will be shown to the user. The interface to view the created scene can be a monitor [7], but the use of a head-mounted display (HMD) to completely immerse the user in the virtual world is also possible [5]. Commercially available display systems for virtual surgical simulation include the HTC Vive (HTC Corporation, Taiwan and Valve Corporation, US) [5] [8], the Display 300 (Sense Graphics, Sweden) [9] and the Oculus Rift (Oculus VR, US) [10]. The advantage of using an HMD over a monitor for displaying the surgical scene lies in the degree of immersion that can be realized. When an HMD is worn, the user will be completely immersed in the created virtual environment.

However, based on the intended application, this is not always desirable. When a surgical simulator for minimally invasive surgery is developed, for example, then it can be more useful for the surgical resident to look at a monitor since this resembles the actual conditions in the operation theater where the surgeon looks at a monitor while steering the surgical equipment through the patient's body.

2.2 Haptic rendering

Haptic technology enables the interaction with virtual environments and can be implemented into surgical simulators to improve their fidelity. The haptic sensory information itself can be divided into two categories: tactile and proprioceptive information. The tactile information is obtained from tactile sensors embedded in the skin and sense pressure, vibration, temperature differences, etc. In contrast, the proprioceptive information is received from proprioceptive receptors generally embedded in the joints and muscle fibers and sense the position and motion of limbs as well as the forces exerted on them [11]. For surgical simulators, the emphasis lies on the proprioceptive feedback that the haptic feedback device applies to the user. This device consists of several actuators that measure the user's position and block the user's movement when necessary, which gives the impression of force feedback. The workspace, force range, resolution, stiffness and degrees-of-freedom (DOF) characterize these devices. The haptic feedback system exerts a force output based on the result of the haptic rendering algorithm. Due to the 1 kHz bandwidth of the haptic sensory information, accurate haptic rendering algorithms with low latency are necessary. These algorithms detect collisions in the virtual environment and resolve these collisions by providing proper force feedback, which happens in two stages. First, there is the collision detection. In the field of collision detection, there are a variety of object representations to enable fast collision detection. These object representations include the Voxmap-PointShell method [12], point clouds [13, 14], Axis Aligned Bounding Boxes (AABB), Oriented Bounding Boxes (OBB), k-DOPs and spheres [14]. Data structures created from these object representations are implicit surfaces [13] and tree structures [14]. After the collision detection, it is time to resolve the collision by calculating the appropriate force feedback. The term 3-DOF force feedback applies when the haptic feedback system exerts only translational forces. When the haptic feedback system exerts rotational forces and translational forces, then this is referred to as 6-DOF force feedback. There are two main categories among force feedback methods, which are penalty-based [15] and constraint-based methods [16]. Nowadays, several haptic software development kits and haptic application programming interfaces are available to accelerate the integration of haptics into software applications. These include the Haptic SDK (Force Dimension, Switzerland), the Open Haptics Toolkit (3D Systems, US), CHAI3D, SOFA (Simulation Open-Framework Architecture) and the H3D API (Sense Graphics, Sweden).

Fig 1: A VR surgical simulator during the simulation of maxilla-cutting composed of a 6-DOF haptic feedback device (Omega 6), a 3D immersive workbench (Display 300), a 2D LCD Monitor and 3D glasses. ***(SHANGHAI JIAO TONG UNIVERSITY, CHINA)***

3. Augmented Reality

Augmented reality is a technology to enhance the physical world with virtual data by superimposing visual information onto the user's field of view [17]. The realization of a high-fidelity AR experience is based on three key technologies: visual rendering, tracking and image registration.

3.1 Visual rendering

There are several application programming interfaces (APIs), software development kits (SDKs), game engines and commercially available software packages currently used to enhance the surgeon's field of view with patient-specific information. When discussing the use of AR to overlay additional information over the physical world, it is important to differentiate between two-dimensional (2D) data and 3D data that are incorporated into the user's field of view. For the 2D data visualization

CrowdOptic (CrowdOptic Inc., US) [18], OpenCV (Open Source Computer Vision Library) [19, 20] and VitalVideo (Vital Enterprises Inc., US) [21] have been used. On the other hand VTK (Visualization Toolkit, Kitware Inc., US) [22, 23, 24, 25], CTK (Common Toolkit) [22, 23], ITK (Insight Segmentation and Registration Toolkit, Insight Software Consortium) [22, 23, 24], IGSTK (Image-Guided Surgery Toolkit, Insight Software Consortium) [22, 23], QT (The Qt Company, Finland) [22, 23, 24] and OpenCV [24, 25] are common libraries used for 3D data visualization. Unity3D is used to visualize 3D data on the Microsoft HoloLens (Microsoft Corporation, US) [26]. The arguments given for VR regarding the advantages and drawbacks of using graphical libraries or game engines to develop virtual scenes are also applicable for AR. AR display types can be classified as Video-See-Through (VST), Optical See-Through (OST), or projection-based [27]. In the case of VST, a camera captures the physical scene, and the augmented data is fused into the captured image, and then the fused image is shown to the user. VST displays occur in the form of HMDs [28], hand-held devices [29] as well as ordinary monitors [24]. OST displays enable the user to view the physical world directly and overlay its direct view with augmented data. To achieve this, optical combiners are used, which superimpose rendered images onto the physical world, seen by the user, with the aid of a spatial light modulator (SLM) [30]. In addition to the frequently used OST HMDs, which include the Google Glass (Google LLC, US) [18, 19, 20, 21, 31] and the HoloLens [26], there are also less known devices such as the Moverio BT-200 (Seiko Epson Corporation, Japan) [32], the nVisor ST60 (NVIS In, US) [22, 23] and the Vuzix (Vuzix, US) [33]. Finally, projection-based displays project the virtual data on top of the real scene and are often used to cover larger areas. Integral videography (IV), which is based on integral photography (IP), is a method used to achieve projection-based AR for medical applications [34, 35]. This technique uses a flat display with a convex lens hexagonal array placed in front of the display. The rays from the pixels on the flat display are transmitted through the convex lenses and converge in a 3D space point. The observer views the 3D image through a half-silvered mirror, which acts as the optical combiner in this system. The advantage of a VST AR display system is that a camera can capture the environment, and the virtual data can be superimposed onto the captured frames. This is a lot easier than overlaying the virtual data directly onto the physical world, which is the case with OST AR displays. In OST AR displays, the user's view is still natural and the virtual data needs to be added to this view as opposed to VST AR displays where the user's view is no longer natural as the captured frames replace it and the user looks at a screen which shows the physical world. A disadvantage of OST AR displays is the intensity by which images can be shown [30]. Finally, projection-based AR displays can be used to project the virtual data onto the physical world. However, in this case there needs to be an object onto which the virtual data can be projected. It is also more suited to cover larger areas and has thus a greater FOV compared to OST AR displays.

3.2 Tracking

There are different techniques applied for tracking in AR applications. First, there is a distinction between marker-less and marker-based tracking. It is possible to achieve marker-less tracking with a stereo camera setup where 3D matching algorithms are applied to estimate the pose of the tracked object [34, 36, 37]. Another approach is to use a single camera and a 3D-2D shape matching method into a 2D tracking-learning-detection framework [38]. The advantage of marker-less tracking is the ease of use since no markers need to be attached to the patient. Therefore, there is also less preparation time for the surgeon. However, the drawback is that there is a larger computational burden compared to marker-based tracking due to the computer vision algorithms that need to extract features used for tracking directly from the captured camera frames. Another drawback is that it is not possible to use electromagnetic tracking for marker-less tracking. On the other hand, there is marker-based tracking where the marker types and the tracking technique classify the kind of marker-based tracking. Two common marker types are fiducial markers [19, 20, 26] and spherical markers [22, 23, 24]. A spherical marker that is often used is the passive retro-reflective IR marker. This marker reflects incident IR light, which is emitted by the optical tracking system. The reflected IR light will then be detected by the IR cameras of the optical tracking system. As a result, this technique can be used in dimly lit places. A drawback is that these markers are consumables and need to be replaced when their reflecting coating is contaminated with blood from the operation. Fiducial markers, on the other hand, are cheaper, as they can be printed onto paper sheets. However, they are less accurate than the spherical markers. For marker-based tracking, more preparation time is needed since the markers need to be attached to the patient and surgical instruments. However, due to their distinct shape, the markers are easy to detect in the 3D space, and there is no need for heavy post-processing to extract their coordinates from 3D space. It is also possible to categorize the technology that is used for the tracking devices. They are generally optical trackers, electromagnetic trackers, or a combination of the two known as hybrid trackers. The optical trackers are based on the use of infrared (IR) cameras [24], colored (RGB) cameras, or monochromatic cameras [19, 20]. The drawback of optical trackers is that the user can obstruct the line of sight and can, therefore, interfere with the tracking. In addition, optical trackers also introduce technical complexity into the surgical workflow. However, for electromagnetic trackers to achieve the same precision as optical trackers, they need to be placed closer to the region of interest as their reliability and accuracy drop in the presence of ferromagnetic materials, conductive materials or both. The key benefit of electromagnetic trackers is the tracking of hidden structures. A combination of both technologies in the form of a hybrid tracking system in which the user can switch between the two tracking approaches for a specific task can be a solution to overcome the drawbacks that both systems face individually [27].

3.3 Image registration

Image registration is required to align the virtual data accurately with the physical scene. In [19, 20], a multi-step co-registration strategy has been adopted in which four fiducial markers are placed around the surgical site. During navigation, these markers track the tumor margin that needs to be resected. To register the virtual coordinate system to that of the physical coordinate system, Wang et al. [23] adopted a point-to-point registration method. For the extraction of the fiducial landmark coordinates in the virtual coordinate system, image processing is applied. The fiducial landmark coordinates have been obtained using a positioning probe in the physical coordinate system. Liu et al. [24] adopted a similar point-based registration approach. To improve the registration accuracy, Chen et al. [22] combine fiducial point-based registration with surface-based registration. These registration methods are based upon visible markers. However, there are also marker-less methods that can be used for image registration. It has been demonstrated that the SIFT, SURF, BRISK and ORB algorithms can be used in fluorescence-to-color image registration for intraoperative AR [39]. It is also possible to use anatomical landmarks to perform image registration. Wang et al. [34] use patient tracking in combination with 3D contour matching of the teeth to obtain automatic marker-free patient-image registration. Similar approaches have been used by Suenaga et al. [36] and Wang et al. [37, 38].

4. Mixed reality

The distinction between AR and MR is not always clear. Although both technologies use virtual data to enhance the physical world, the difference lies in the way the data is represented and incorporated into the physical world. Sauer et al. [17] define AR as the superimposing of visual information onto the user's field of view, and MR as the merging of images with a scene or object behind the display. In other words, AR overlays data onto the real world where MR anchors the virtual data into the physical world. AR is thus the technology where information is superimposed onto the real world. The information is independent of the user's head movement and will always appear in the same region of the user's field of view. While for MR the head movement of the user will be tracked and when rotating away from a virtual object, the object will move in the opposite direction. Google Glass is an AR device since it overlays information onto the physical world. On the other hand, Microsoft HoloLens is an MR device capable of overlaying information, like Google Glass, but can also integrate virtual objects into the physical world. In addition to the Microsoft HoloLens, there are also other MR HMDs such as the Magic Leap One (Magic Leap Inc., US) and the Avegant Light Field Display (Avegant Corp, US). Since there is no unified description of the term MR, things become very confusing. Therefore it occurs that the names MR and AR are used interchangeably, which is the case in the work of Perkins et al. [40]. The key technologies described for AR regarding visualization, tracking and image registration also apply to MR due to the overlap between AR and MR. When discussing the applications of MR in the field of surgical simulation, it is not guaranteed that the applications comply with the definition of MR given above because it is the author's interpretation that resulted in the application being labeled as MR. Among the three technologies, MR is the most recent one regarding commercially available hardware and the most difficult to accomplish regarding visual rendering. However, since it allows the physical world to merge with the virtual world, it has a considerable advantage regarding haptic cues. As discussed earlier, haptic rendering introduces a computational burden onto a simulation besides the computational workload already present from the visual rendering. In MR, physical models can partially replace these haptic cues to introduce passive haptic feedback, which allows for high-fidelity low-cost haptic feedback.

5. Evaluation Metrics

5.1 Data acquisition

The data acquisition for virtual reality surgical simulators depends primarily on the haptic feedback device's positional sensors, which return the translation and rotation based on the 3D position of the haptic device handler. When the haptic device handler's pose is known, the mapping from the physical space to the virtual space can be performed. Once the position of the haptic device handler in the virtual space is known, it can be calculated which force should be set, what the cutting angle is, if healthy tissue has been cut and so on. The acquired raw data is the position of the haptic device handler. It is up to the developers to interpret these values correctly and derive the metric values from them.

5.2 Evaluation metric design

The design of adequate evaluation metrics involves close collaboration between engineers and surgeons. The expertise and practical know-how of the surgeons need to be translated into valuable evaluation metrics. Besides this interaction, the developers themselves need to acquire basic knowledge about the surgical procedure for which the surgical simulator will be developed. Mirchi et al. [41] describe a total of three different approaches to generate performance metrics. First, there is the option to collaborate with medical experts to mimic metrics currently used to measure expertise. The second option would be to consult the literature on surgical simulators and use the metrics described in those publications. Finally, there is the option to develop novel metrics to distinguish between different levels of expertise. Of course, it is also possible to use a combination of the approaches mentioned above. Pperformance metrics can also be grouped based on the task that needs to be evaluated, which is the case for the iDental [42], a dental simulator. In total, three procedures can be trained with the iDental. The first task is the pocket probing check. During this task, the pocket depth, maximum contact force and probing angulation are recorded. These metrics can be obtained from the haptic feedback device. The second task is calculus detection, where the metrics are the number of identified calculus and the reported value of position and size of the calculus. For the final task, calculus removal, the number of removed calculus, the damage to the neighboring gingiva and the operation angle of the probe are measured. Choudhury et al. [43] constructed evaluation metrics for basic to advanced neurosurgical skills for five different tasks. These tasks include the correct insertion of a ventricular catheter, locating and identifying the sphenoid ostium, tumor debulking, performing hemostasis and arachnoid dissection to remove convexity meningiomas. The performance metrics that are implemented are divided into three categories: outcome, efficiency and errors. The outcome performance metrics include catheter tip placement in the ventricular system, sphenoid ostium localization, percentage of tumor that is resected, hemostasis achieved or not and percentage of bands cut. The efficiency metrics include the angle of perforation at the surface, the time it took to complete the task, the travelled distance to reach the ostium, the time taken to reach the ostium, the path length, the volume of blood loss and the tool tip path length. For the error performance metrics, it is checked if the burr hole lays outside an acceptable region or not, the number of times an excessive force was applied, the percentage of healthy tissue that has been removed, the number of bands torn, the deviation from the expert tool tip path length and the volume of healthy tissue damaged. Finally, Azarnoush et al. [44] proposed a number of metrics for brain tumor resection. These metrics are the percentage of brain tumor resected, the volume of simulated normal brain tissue removed, the instrument tip path length, the duration of time taken for the resection of the brain tumor, the pedal activation frequency, the sum of applied forces and finally the force bandwidth.

5.3 Evaluation metric generation

Evaluation metrics for surgical simulators can be divided into two categories: qualitative and quantitative evaluation metrics. For a surgical simulator to be considered acceptable, its key components need to be evaluated positively. Chen et al. [45] define these components as visual and haptic feedback fidelity, stability, real-time performance and user-friendliness. A common approach for evaluating the surgical simulator regarding these components is to perform a qualitative evaluation. In such an assessment, a user group composed of novices with limited surgical experience and surgical experts is formed. The user group gets time to familiarize themselves with the surgical simulator and perform the surgical procedure when they are accustomed to the simulator. Afterward, they fill out a questionnaire to score every question according to a Likert scale. Currently, there is no unified approach towards the subjects that should be included in the questionnaire or the scope of the questions. As a result, qualitative validation studies vary regarding the number of questions, the scope of the questions, the Likert scale range, the number of participants, the share of medical experts, trainees, etc. [3, 46, 47]. As opposed to the qualitative metrics, there are also quantitative metrics. These metrics are measurable and can vary from an improvement score derived from pre- and post-tests [48] to operation time, blood vessel injury, rib injury, pelvicalyceal system perforations, infundibular injury and number of needle punctures [6]. These metrics can be used to assess both the surgical simulator and the trainee's progress and vary depending on the targeted surgical procedure. For the quantitative method, it is essential to rely on identifying critical parameters from the target task and the specification of quantified metrics for these parameters, as demonstrated in [42]. Finally, a simulator's performance can also be assessed by carrying out a comparative study between the developed simulator and commercially available simulators [6]. Compared to VR simulators, there are additional metrics for AR and MR simulators regarding image registration and tracking accuracy. According to Hussain et al. [49], the fiducial registration error (FRE), fiducial localization error (FLE), target registration error (TRE), overlay error (OR) and tool error (OR) are crucial characteristics of an AR system and need to be taken into account when evaluating AR systems. Due to the close similarity between AR and MR systems, these metrics can also be used for assessing MR systems.

5.4 Automated feedback platforms

Nowadays, research has evolved beyond metric generation towards automated feedback platforms. Such automated feedback platforms for virtual reality surgical simulators have been introduced in [41]. The authors use supervised machine learning algorithms to train the system to distinguish between novices and experts in the field of neurosurgery based on pre-selected metrics. They trained a linear Support Vector Machine (SVM) on a database of 50 participants. Each participant was assigned to one of two categories, i.e. novice or expert. The expert group consisted of 28 participants, the novice group of the remaining 22 participants. Four metrics were extracted from the recorded data and used for the classification. These metrics have been selected by combining forward and backward feature selection. The incorporation of artificial intelligence in assessing the performance metrics of virtual reality surgical simulators and the classification of its users according to their performance has also been addressed in a number of recent studies. Virtual reality surgical simulators are at the crossroad of medicine, science and education. Winkler-Schwartz et al. [50] introduced the Machine Learning to Assess Surgical Expertise (MLASE) checklist to streamline the reporting of research on virtual reality surgical simulation and artificial intelligence across these disciplines. Winkler-Schwartz et al. [51] used the MLASE checklist for their research on the identification of surgical and operative metrics selected by machine learning algorithms to obtain an accurate classification of virtual reality surgical simulation practitioners by their level of expertise. In their study, 50 participants (i.e. 14 neurosurgeons, 4 fellows, 10 senior residents, 10 junior residents and 12 medical students) were divided among four levels of expertise (i.e. expert, seniors, juniors and medical students). Each participant performed a neurosurgical tumor resection in virtual reality and repeated the presented scenario five times. Four different machine learning algorithms have been used: the K-nearest neighbor algorithm, the naïve Bayes algorithm, the discriminant analysis algorithm and the support vector machine algorithm. The K-nearest neighbor algorithm reached, with 90% and six performance metrics, the highest accuracy. In a research study from Bissonnette et al. [52], 41 participants were involved in a study where they performed spine surgery on a virtual reality surgical simulator. The study aimed to uncover new surgical performance metrics that aid in the classification between two groups of different training levels and verify if different machine learning algorithms can classify an individual's surgical training level as senior or junior. In total, twelve metrics were selected to classify senior and junior participants. Since these metrics were obtained by employing a support vector machine, these metrics likely work best for support vector machines. Therefore, that four other algorithms (i.e. linear discriminant analysis, K-nearest neighbors, naïve Bayes and decision tree) have been trained on these metrics. From those algorithms, the linear discriminant and K-nearest neighbors displayed acceptable accuracies. Finally, Mirchi et al. [53] used an artificial neural network to classify users based on their performance of the anterior cervical discectomy and fusion procedure on a virtual reality surgical simulator. In total, there were 21 participants divided into three groups: post-resident, senior and junior. The metrics used to train the neural network were obtained by consulting surgical experts from published work involving lumbar discectomy. Finally, the authors constructed novel metrics based on different surgical skill components. In total, sixteen metrics were used. Their artificial neural network can classify participants into one of three groups (i.e. post-resident, senior and junior) with an accuracy of 83.3%.

6. Clinical Applications

VR proves to be the most widely applied technology in surgical simulation, hence been most utilized in surgical training platforms. AR and MR are incorporated and widely used in real surgical settings, especially in preoperative planning and intraoperative guidance. This section highlights some relevant examples of studies utilizing VR, AR and MR in different surgical procedures. Table 1, Table 2 and

Table 3 gives a summary of these studies for neurosurgery, maxillofacial and general surgery (open and laparoscopic), respectively.

6.1 Neurosurgery

Advanced techniques and algorithms in the field of VR, AR and MR give neurosurgeons the ability to perform accurate surgical planning, intraoperative control and postoperative tracking. As a result, several interactive 3D VR applications have been developed to simulate surgical procedures (**Figure 2)** [1, 54]. VR simulation has been applied in distinct medical fields such as endoscopic neurosurgery [55] [56] and cranial tumor surgery [44] [57]. Clinical applications have emerged regarding bone dissection [58], clipping of cerebral aneurysm [59, 60], microvascular decompression [61] and placement of pedicle screws [62]. AR has been helpful in neuro-oncological procedures to identify lesions, direct the resection and schedule the craniotomy as well as skin incision before surgery [63]. Kersten M. et al. [64] presented an AR neuronavigation image-guided system for vascular surgery. Yoon J.W. et al. [65] evaluated applications related to external ventricular drain placement. Watanebe E. et al. [66] created a navigation system based on AR with full-space tracking in tumor-related procedures. Other applications have emerged in the areas of cerebral aneurysms [67], spinal surgery [68, 69], tumor resection [70], intracranial meningioma [71] and craniosynostosis surgery [72].

Fig 2: Surgical simulation laboratory at The Weill Cornell Skills Acquisition & Innovation Lab (USA). A-C: Simulation equipment D: Residents have a fully immersive experience inside the practical physical environments *(Bernardo A. Virtual Reality and Simulation in Neurosurgical Training. World Neurosurgery. 2017* **[1]***)*

In the field of neurosurgery, MR has enabled 3D imagery to be more comprehensive and accurate, hence improving surgical navigation and pre-processing. Zhang Z. et al. [73] present three case studies among eight patients to demonstrate the application of MR in the field of neurosurgery. They reconstructed a 3D holographic image of the brain tissue and the intracranial nerves based on patient-specific data. McJunkin J. et al. [74] designed an MR headset for lateral skull base anatomy to enable 3D rendering of immersive holograms anchored to different points in the physical space. Incekara F. et al. [75] conducted a clinical study to assess the HoloLens's therapeutic viability in the pre-planning of a brain tumor procedure. MR has also been applied in thoracic surgery [76], orthopedics [77] and pediatric surgeries [78].

6.2 Maxillofacial Surgery

Oral and Maxillofacial Surgery (OMS) refers to a clinical specialty that involves surgical procedures in the area of the mouth, neck, face and jaws [45]. Following the advancements in simulation-based surgery technology, the field of OMS has adopted the use of surgical simulators and the benefits of VR, AR and MR for simulating surgical procedures, as illustrated in **Figure 3** [79]**.** VR has been applied in dental implantology [80, 81], orthognathic surgery [82, 83] and for mandibular reconstruction [84]. Literature encompassing drilling and cutting for VR-based simulated procedures are discussed in [45, 81]. Hanken H. et al. [85] assessed the degree of similarity between the simulated plans and the actual results from performing the maxillofacial procedures. Virtual surgical planning and hardware manufacturing for open reduction and internal fixation of atrophic edentulous mandibular fractures have also been demonstrated in a series of case reports [86, 87]. Matsuo A. et al. [88] used VR in endoscopic implant surgery for maxillofacial based applications. AR in maxillofacial surgery is beneficial for preoperative planning to provide practical outcome forecasts and intraoperative navigation to minimize possible risks [89]. AR has also been applied in dental implantology [90, 91]. In a pilot-clinical analysis of two patients, the feasibility of using a virtual display for dynamic navigation during dental implantology has been evaluated to determine whether the usage of AR technology may affect the accuracy of dynamic navigation [92]. In the field of orthognathic surgery, the use of AR has also been demonstrated [93]. Other applications include the work performed by Zhu M. et al. [94] on a novel AR device, which has been used to view the alveolar nerve bundles in maxillofacial surgery. Karner et al. offer an implementation of AR operating on a regular mobile or tablet device, offering visualizations of patient-overlaid diagnostic image details in a video see-through mode [95]. MR systems such as the Microsoft's HoloLens have been employed in operating rooms to help surgeons improve their decision-making and improve the operational flow [96]. Furthermore, MR has been used for surgical telepresence and visualization [97, 98]. In orthognathic surgery, a system for mandibular motion tracking was developed and assessed by Fushima K. et al. [99]. Most MR clinical applications use manual registration. As a result, a marker-less implementation of MR for maxillofacial oncological surgery was developed and tested by Pepe A et al. [100], which was later extended to CT [101] [102].

Fig 3: A surgeon interacts with a 3D maxillofacial anatomic model (*Pulijala et al. Immersive VR for Surgical Training. J Oral Maxillofacial Surg 2018* [79]*)*

6.3 General Surgery

Apart from the applications discussed in the fields of neurosurgery and maxillofacial surgery, applications extend to other surgical procedures, such as open surgery, laparoscopic and endoscopic surgery. Benish F. et al. [103] subdivided the AR applications in open surgery into pancreatic [104] and hepatobiliary surgery [105]. AR for these surgical procedures has been reported mainly for recognizing lesions and safe dissection. Navigation with AR has been used to enhance the protection for surgical dissection in pancreaticoduodenectomy (PD) [106]. Onda S. et al. examined the pancreaticoduodenal artery (IPDA) with an AR navigation system [107]. Other studies include hilar cholangiocarcinoma (HCAC) [108], open urological surgery, [109] and open liver surgery [110]. Researchers have also utilized hybrid surgical guidance concepts to fluorescence guidance, as illustrated by Kleinjan G. et al. for sentinel lymph nodes biopsy in penile cancer during open surgery [111]. Van Oosterom et al. have done a similar study on both penile cancers for open surgery and prostate cancer for laparoscopic surgery [112]. Weidert S. et al. have also applied video augmented fluoroscopy for distal interlocking on intramedullary nails [113]. MR ultrasound guidance systems have been proposed, as shown by Ameri.G. et al. [114]. The authors describe and critically analyze implementation recommendations in the sense of a mixed reality ultrasound guidance system through a case study. In addition, an MR system using a HMD to visualize anatomical constructs in specific visceral-surgical procedures during open surgery has been described by Sauer M. et al. [17]. During open hepatic surgery, the surgeon's field of view was superimposed by a 3D representation of the patient's complex liver structures and shown on an MR-HMD. Unlike open surgery, laparoscopic surgery requires a different skillset and is sometimes more complicated than open surgery. A reduced number of working hours, fewer training sessions and patient safety issues result in the acquisition of these skills outside the operating room. Hence both VR and AR modelling has been leveraged [115]. **Figure 4** depicts a Laparoscopic VR training set up during the laparoscopic salpingectomy procedure [116]. Bernhardt S. et al. [117] give an overview of the applications of AR in the field of laparoscopic surgery as of 2016. Laparoscopic liver surgery has been one of the major applications of VR and AR, as shown by Lau L. et al. [118] and Prevost G. et al. [119]. VR and AR have also been applied in distal laparoscopic pancreatectomy [120] and gynecological laparoscopic surgery, as indicated by Akladios C. et al. [121], for the detection of ureters during surgery.

Fig 4: External view of two residents in an immersive and conventional VR session with LapSim Surgical Simulator (Frederiksen J et al. Cognitive load and performance in immersive virtual reality versus conventional virtual reality simulation training of laparoscopic surgery: a randomized trial. *Surgical Endoscopy. 2020* [116])

7. Expert Opinion

7.1 Challenges for virtual reality

The challenge for VR is to represent the rendered scene as realistic as possible while still guaranteeing real-time interactivity. However, currently, a trade-off needs to be made between realism and real-time interactivity. This trade-off needs to be made on several aspects, including the visual rendering and haptic rendering. Besides these aspects, there is also the challenge of implementing fluid simulation and using haptic feedback devices that mimic the look and feel of actual surgical instruments.

A virtual scene will be created based on a graphics API such as OpenGL. These graphics APIs represent each object in the virtual scene as a collection of triangles, called a triangular mesh since it is more efficient to operate on a triangular mesh than on a group of individual triangles. With an increasing number of triangles, more details can be embedded into the virtual object, but this results in a higher computational cost while rendering the scene. Therefore, the complexity of the surgical scene created by the surgical simulator needs to be taken into consideration since it can compromise its real-time interactivity.

Haptic feedback is often implemented to increase the fidelity of the VR experience. The requirements for the haptic update frequency are even sterner than for the visuals. For realistic force feedback, collision detection and force rendering need to be resolved in less than one millisecond. As the human body exists out of a combination of soft and hard tissue, the surgical simulator needs to be able to mimic rigid-rigid and rigid-soft object interaction. Rigid-rigid object interaction is the easiest to accomplish. It is implemented in most surgical simulators, although to increase the simulator's fidelity, rigid-soft object interaction needs to be present whenever necessary. Acceptable results have already been obtained for rigid object interaction. However, the interaction between rigid and deformable objects requires data structures to be updated within the one millisecond time limit and mimic correct physical behavior. These are challenging requirements, but recent literature shows promising results in this field [122].

Besides deformable objects and level-of-detail, there is another aspect that should be incorporated into VR applications, which is fluid simulation. Although, this introduces another computational burden onto the system's hardware. On the one hand, there is the calculation of the fluid flow itself. On the other hand, there is the tool-fluid interaction. Fluid simulation can be incorporated into VR surgical simulators in the form of blood flow simulation.

Another aspect of VR is the commercially available haptic feedback devices, which target a broad range of applications. Therefore, their design is not tailored towards medical applications, and their physical end-effector does not resemble the medical instruments that are used during operations. To cope with this, it is possible to replace the end-effector of the haptic feedback device with a real surgical tool [6]. However, the workspace, force range, resolution and stiffness remain the same. A better solution would be to develop application-specific haptic feedback devices. Also, high-quality haptic feedback devices are expensive to purchase and increase the cost of surgical simulators drastically.

7.2 Challenges for augmented and mixed reality

For tracking, optical trackers or electromagnetic trackers are often opted. The first one has the drawback that when the line-of-sight is obstructed, the tracking is lost. On the other hand, the primary shortcoming of electromagnetic trackers is their workspace, which is somewhat limited compared to optical trackers. Also, the calibration is a tedious process that adds a layer of complexity. Marker-less tracking could be a solution for this problem, like the inside-out tracking used in the Microsoft HoloLens. However, its tracking technology needs to be improved before it is possible to precisely overlay computer-generated images onto organs as required for surgical simulators [17].

As a result of the vergence-accommodation effect, which applies to VR, AR and MR HMDs, developers need to take into consideration the focal plane of the HMD. For example, the Microsoft HoloLens has its focal plane two meters in front of the user, making it impossible to create focused holograms close to the user without conflicts between convergence and accommodation. A possible solution for this challenge is the use of light field technology, as demonstrated with the Avegant Light Field Display. Regarding the display fidelity for current AR and MR HMDs, there is another challenge. The existing AR and MR HMDs overlay the physical world with virtual objects with the aid of beam combiners. However, with this technique, mutual occlusion is not easily implemented, and as a result, virtual objects are semi-transparent, and therefore their realism is compromised. Recent research has introduced the use of a single digital micromirror device (DMD), which enables the merging of virtual objects with the physical world on a pixel-by-pixel basis to block incident light from the physical world. In contrast, light emitted from a light source can be modulated to render the virtual world [30].

7.3 Challenges for evaluation metrics

Finally, there are the challenges for evaluation metrics for the VR, AR and MR based surgical simulators. The majority of surgical simulators are assessed based on subjective questionnaires, which impairs the possibility of comparing different surgical simulators among distinct user studies. Therefore, there is a need for standardized, target-specific and objective evaluation metrics to streamline the simulator assessment.

7.4 Five Year Review

In the past, medical training has been performed onto cadavers, synthetic mockups and eventually on real patients under supervision. Nowadays, a shift is ongoing towards the application of VR, AR and MR in medical simulators and their implementation into the curriculum of residents. The success of this shift depends on the fidelity of the simulation. Although the field of VR, AR and MR has emerged a lot since the introduction of the first VR surgical simulator, there is still room for improvement. Currently, the implementation of soft tissue interaction lacks realism due to the increased computational burden. Also, the use of commercial haptic feedback devices compromises the simulator's fidelity. Custom haptic feedback devices are needed to resemble the surgical scene more closely. Haptic platforms such as CHAI3D implement rudimental haptic rendering algorithms that need to be tailored towards the intended application. Haptic libraries in which the current state-of-the-art haptic rendering algorithms for both rigid object interaction as well as deformable object interaction are implemented are necessary to accelerate the development of VR, AR and MR applications for surgical simulators. Marker-less tracking techniques need to be developed, which allows users to apply AR and MR into surgical simulators without the tedious image registration procedure. Finally, standardized application-specific surgical simulator evaluation metrics are needed, as this makes it possible for a fairer comparison between different simulators as well as to focus on the aspects that are truly important regarding the targeted application.

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Declaration of Interest

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Table 1: Summary of studies highlighting clinical applications in Neuro-Surgery

Author & Year	**Technology**	**Study Size**	**Surgical Procedure**	**Study Summary**
Azarnoush et al. 2015 [44]	VR	18 brain tumors	Tumor resection (simulation)	NeuroTouch-haptic feedback surgical simulator for psychomotor skill evaluation
Breimer et al. 2016 [56]	VR	23 residents/3 fellows	Endoscopic Ventriculostomy (simulation)	Virtual Endoscope simulator utilization for third ventriculostomy training
Locketz et al. 2017 [58]	VR	16 residents/17 CT data specimen	Bone Dissection (simulation)	CardinalSim with haptic Feedback for Prospective pre-and post-study of a modern framework for simulated surgical rehearsal.
Alaraji et al. 2015 [59]	VR	1 Patient specific CT model	Cerebral Aneurysm Clipping(simulation)	Haptic feedback ImmersiveTouch platform to build and determine the utility of a modern interactive haptic-based device for surgical training
Gmeiner et al. 2018 [60]	VR	18 surgeons/4 patients	Cerebral Aneurysm Clipping(simulation)	Self-developed simulator with haptic feedback for virtual aneurysm clipping simulation
Yao et al. 2017 [61]	VR	42 Patients	Microvascular (simulation)	VR image-based simulation for real microvascular surgical procedure decompression
Xin et al. 2018 [62]	VR	16 residents/ 8 Cadavers	Spinal pedicle screw placement(simulation)	Immersive VR simulation for interactive virtual surgical training in pedicle screw insertion
Kersten et al. 2015 [64]	AR	4 Patients	Neurovascular (intraoperative)	Volumetric CT data overlaid from the tracked video camera on the patient image, displayed on the external monitor
Yoon et al. 2017 [65]	AR	2 Patients	Ventricular Catheter Placement (intraoperative)	3D imaging via wearable head-up Display
Watanabe et al. 2016 [66]	AR	6 Patients/ 1 Phantom	Tumor resection (intraoperative)	MRI/CT intracranial images overlaid on patient data, via tracked PC tablet and displayed on tablet screen
Karmonic et al. 2018 [67]	AR	6 Patients	Cerebral Aneurysm (intraoperative)	Optical see-through head mounted Display with self-developed algorithm in constructing an AR setting for natural interaction with complex 3D data
Carl et al. 2019 [68]	AR	10 patients	Spine (intraoperative)	Head Up Displays for microscopic based AR intradural spinal tumor
Edström et al. 2020 [69]	AR	20 trial cases	Spine(intraoperative)	AR Hybrid solution with robotic ceiling mounted C-arm during operation
Alfonso-Garcia et al.2020 [70]	AR	2 Patients/3 case studies	Tumor(intraoperative)	Fluorescence lifetime imaging with surgical microscopes integration
Lave et al. 2020 [71]	AR	1 Case report & Literature survey	Intracranial Meningioma(preoperative)	Augmented Optics technology, AR images injected into the binocular microscope during surgery
Coelho et al .2020 [72]	AR	1 case	Metopic Craniosynostosis (simulation)	Use of a hybrid AR developed app for visualization of patient anatomic data
Zhang et al. 2019 [73]	MR	8 Patients	Tumor(intraoperative)	HoloLens CT/MRI reconstructed virtual model superimposed on the patient's neurosurgical site
McJunkin et al. 2018 [74]	MR	Temporal bone models	Skull Base Anatomy (simulation)	3D interactive holograms displayed on HoloLens Head mounted Display
Incekara et al. 2018 [75]	MR	25 Patients	Tumor(preoperative)	MRI based 3D holograms of patient's data projected on patient via MR Head Display HoloLens
Wu et al. 2018 [77]	MR	undefined	Orthopedics (intraoperative)	MR-developed navigation system (display, magnetic launcher, passenger sensor, and processor)
Coelho et al. 2019 [78]	MR	18 Participants	Craniosynostosis (Simulation)	3DS Max developed videos and Renier's "H" technique for craniosynostosis correction was applied during the simulation

Table 2: Summary of studies highlighting clinical applications in oral and maxillofacial surgery

Author & Year	**Technology**	**Study Size**	**Surgical Procedure**	**Study Summary**
Chen et al. 2018 [81]	VR	3 patients/30 novices	Dental Implant (simulation)	Development of a Dental implant surgical simulator with Omega 6-haptic feedback & immersive workbench (SenseGraphics)
Holzinger at al. 2018 [82]	VR	16 patients	Orthognathic (planning & simulation)	Self-developed software for soft tissue planning & simulation
Pulijala et al. 2018 [83]	VR	9 surgeons	Orthognathic (simulation)	Oculus Rift and Leap Motion devices for surgical training platform
Maloney et al. 2015 [84]	VR	2 Patients	Mandible reconstruction (planning & simulation)	Self-developed Virtual Surgical Planning system for atrophic edentulous mandible fractures
Nguyen et al. 2019 [86]	VR	1 patient	Facial reconstruction (planning & simulation)	Self-developed Virtual Surgical Planning system for facial fracture fixation
Drake et al. 2019 [87]	VR	10 patients	Facial reconstruction (planning & simulation)	Self-developed system & algorithm for facial reconstruction planning
Matsuo et al. 2018 [88]	VR	1 patient	Implant surgery (intraoperative)	Endoscopic assisted Virtual Reality with Head Mounted Display during implant surgery
Kati´c et al. 2015 [90]	AR	1 Pig cadaver	Dental Implant (intraoperative)	Head Mounted Display-AR system with optical tracking for implant placement
Lin et al. 2015 [91]	AR	2 Patients	Dental Implant (planning & simulation)	Commercially available HMD viewer (Sony HMZ-T1 personal 3D viewer, Tokyo, Japan) with a live view-through binocular organic light emitting diodes (OLED)
Zhu et al. 2017 [94]	AR	20 patients	Mandible placement (intraoperative)	Virtual 3D images superimposed on the patient via AR Toolkit to recognize the tracking marker
Pellegrino et al. 2019 [92]	AR	2 patients	Dental Implant (intraoperative)	Virtual data superimposed on the patient site. Use of Microsoft HoloLens
Gsaxner et al . 2019 [101]	AR	1 phantom	Head & Neck Surgery (intraoperative)	Visualization on a patient phantom. Use of a headset hardware & marker-less registration
Gsaxner et al . 2019 [102]	AR	12 3D printed models	Head & Neck Surgery (intraoperative)	Visualization of patient models and data collection
Ahnet al. 2020 [93]	AR	Patients scheduled	Orthorgnathic (intraoperative)	Self-developed stereo camera-based AR navigation system
Karner et al. 2020 [93]	AR	1 patient	Facial reconstruction (intraoperative)	Patient-overlaid diagnostic image visualisation through AR based mobile or tablet device
Fushima et al.2016 [99]	MR	2 case studies	Orthorgnathic (simulation)	Self-Developed Mandibular motion tracking system (ManMoS)
Venkata et al. 2019 [98]	MR	20 sample data	Jaw reconstruction (intraoperative)	Self-developed algorithm for overlay accuracy improvement
Pepe et al . 2020 [100]	MR	2 case studies	Head & Neck Surgery (intraoperative)	Development of a marker-less registration approach

Table 3: Summary of studies highlighting clinical applications in General Surgery

Author & Year	**Technology**	**Study Size**	**Surgical Procedure**	**Study Summary**
Onda et al. 2013 [107]	AR	7 patients	Pancreaticoduodenectomy open surgery (intraoperative)	Preoperative computed tomography (CT) image fused in an operative field in real time after paired-point matching registration and shown on 3D monitor
Okamoto et al. 2018 [104]	AR	5 patients	Pancreatectomy open surgery (intraoperative)	The reconstructed images superimposed on the real organs & displayed on 3D monitor. Initial registration through optical location sensor
Ntouarakis et al. 2016 [105]	AR	3 Patients	Colorectal Liver Mestases-open (intraoperative)	Virtual model superimposed to the area of operation using an Exoscope. Manual registration via video mixer
Tang et al. 2017 [108]	AR	1 patient	hilar cholangiocarcinoma (HCAC) resection-open (intraoperative)	Using the IV overlay unit, patient's reconstructed 3D images of the biliary tree and hepatic vasculature superimposed on the 3D model
Borgmann et al. 2017 [109]	AR	31 case studies	Urological (survey)	AR assisted urological surgery with smart Google glass
Golse et al. 2020 [110]	AR	1 Patient	Liver resection-open (intraoperative)	Used Marker-less non-rigid registration system based on preoperative CT scanning 3-D segmentations, incorporating a liver elastic model
Kleinjan et al. 2016 [111]	AR	5 patients	Penile Cancer (intraoperative)	Hybrid surgical guidance to fluorescence camera
Van Oosterom et al. 2018 [112]	AR	4 phantoms /patients	Penile(open) & prostate(Laparoscopic) Cancer	Hybrid surgical guidance to fluorescence camera
Weidert et al. 2019 [113]	AR	7 cadaveric bones	Distal Interlocking (simulation/intraoperative)	Video-augmented fluoroscopy (VAF) procedure using the C□arm (CamC) handheld camera-augmentation
Sauer et al. 2017 [17]	MR	1 case study	Open hepatic surgery (intraoperative)	Surgeon's field of view superimposed by a 3D representation of the patient's complex liver structures and shown on an MR-HMD
Ameri et al. 2019 [114]	MR	1 phantom/25 surgeons	IJV Cannulation (simulation/intraoperative)	MR ultrasound guidance system-Scanner (SonixTouch,Ultrasonix, Analogic Corp., USA) and a magnetic tracking system (Aurora, Northern Digital, Canada)
Frederiksen et al. 2020 [116]	VR	31 resident surgeons	Laparoscopic surgery (simulation)	LapSim simulator, TeamSim & OculusRift for immersive training system
Aoki et al. 2020 [120]	VR	38 patients	Laparoscopic distal pancreatectomy (simulation)	Three-dimensional virtual endoscopy (SYNAPSE VINCENT: Fujifilm Medical, Tokyo, Japan)
Lau et al. 2018 [118]	AR	2 Liver Lesions	Laparoscopic Liver resection (intraoperative)	AR laparoscopic device combining laparoscopic ultrasonic (LUS) images and laparoscopic imagery in real time
Prevost et al. 2019 [119]	AR	18 Liver Lesions	Laparoscopic Liver resection (intraoperative)	3D laparoscope EV 3.0 and CAS-One AR system
Akladios et al. 2020 [121]	AR	3 pig cadavers	Gynecologic Laparoscopic (intraoperative)	Strasbourg experimental hybrid operating theatre

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

[1] A. Bernardo, “Virtual Reality and Simulation in Neurosurgical Training,” *World Neurosurgery,* vol. 106, pp. 1015-1029, 2017.

**** Important overview of the application of virtual reality and simulation in neurosurgical training.**

[2] R. A. Agha and A. J. Fowler, “The Role and Validity of Surgical Simulation,” *International Surgery,* vol. 100, no. 2, pp. 350-357, 2015.

[3] A. Gupta, J. Cecil, M. Pirela-Cruz and P. Ramanathan, “A Virtual Reality Enhanced Cyber-Human Framework for Orthopedic Surgical Training,” *IEEE Systems Journal,* vol. 13, no. 3, pp. 3501-3512, 2019.

*** Important, due to the introduction and application of the information centric systems engineering (ICSE) principles to design a simulator framework.**

[4] Y. Tai, L. Wei, H. Zhou, S. Nahavandi, J. Shi and Q. Li, “Integrating virtual reality and haptics for renal puncture surgical simulator,” in *International Conference on Computer and Communications (ICCC)*, Chengdu, 2016.

[5] M. Kaluschke, R. Weller, G. Zachmann, L. Pelliccia, M. Lorenz, P. Klimant, S. Knopp, J. P. Atze and F. Móckel, “HIPS - A Virtual Reality Hip Prosthesis Implantation Simulator,” in *IEEE Conference on Virtual Reality and 3D User Interfaces (VR)*, Reutlingen, 2018.

[6] Y. Tai, L. Wei, M. Xiao, H. Zhou, Q. Li, J. Shi and S. Nahavandi, “A High-Immersive Medical Training Platform Using Direct Intraoperative Data,” *IEEE Access,* vol. 6, pp. 69438 - 69452, 31 October 2018.

[7] Y. Tai, L. Wei, H. Zhou, J. Peng, J. Shi, Q. Li and S. Nahavandi, “Development of Haptic-Enabled Virtual Reality Simulator for Video-Assisted Thoracoscopic Right Upper Lobectomy,” in *IEEE International Conference on Systems, Man, and Cybernetics (SMC)*, Miyazaki, 2018.

[8] J. Egger, M. Gall, J. Wallner, P. Boechat, A. Hann, X. Li, X. Chen and D. Schmalstieg, “HTC Vive MeVisLab integration via OpenVR for medical applications,” *Plos One,* p. 12(3):e0173972, 2017.

[9] F. Wu, X. Chen, Y. Lin, C. Wang, X. Wang, G. Shen, J. Qin and P.-A. Heng, “A virtual training system for maxillofacial surgery using advanced haptic feedback and immersive workbench,” *The International Journal of Medical Robotics and Computer Assisted Surgery,* vol. 10, no. 1, pp. 78-87, March 2014.

[10] Y. Pulijala, M. Ma and A. Ayoub, “VR Surgery: Interactive Virtual Reality Application for Training Oral and Maxillofacial Surgeons using Oculus Rift and Leap Motion,” in *Serious Games and Edutainment Applications : Volume II*, Cham, Springer International Publishing, 2017, pp. 187-202.

[11] M. A. Srinivasan and C. Basdogan, “Haptics in virtual environments: Taxonomy, research status, and challenges,” *Computers & Graphics,* vol. 21, no. 4, pp. 393-404, 1997.

*** Important, due to the introduction and explanation of the terminology used for human**

and machine haptics.

[12] M. Sagardia, K. Hertkorn, T. Hulin, S. Schätzle, R. Wolff, J. Hummel, J. Dodiya and A. Gerndt, “VR-OOS: The DLR's virtual reality simulator for telerobotic on-orbit servicing with haptic feedback,” in *IEEE Aerospace Conference*, Big Sky, 2015.

[13] A. Leeper, S. Chan and K. Salisbury, “Point clouds can be represented as implicit surfaces for constraint-based haptic rendering,” in *IEEE International Conference on Robotics and Automation*, Saint Paul, 2012.

[14] M. Kaluschke, R. Weller and G. Zachmann, “A volumetric penetration measure for 6-DOF haptic rendering of streaming point clouds,” in *IEEE World Haptics Conference (WHC)*, Munich, 2017.

[15] H. Xu and J. Barbič, “Adaptive 6-DoF Haptic Contact Stiffness Using the Gauss Map,” *IEEE Transactions on Haptics,* vol. 9, no. 3, pp. 323-332, 2016.

[16] G. Yu, D. Wang, Y. Zhang and J. Xiao, “Simulating Sharp Geometric Features in Six Degrees-of-Freedom Haptic Rendering,” *IEEE Transactions on Haptics,* vol. 8, no. 1, pp. 67-78, 2015.

[17] I. M. Sauer, M. Queisner, P. Tang, S. Moosburner, O. Hoepfner, R. Horner, R. Lohmann and J. Pratschke, “Mixed Reality in Visceral Surgery: Development of a Suitable Workflow and Evaluation of Intraoperative Use-cases,” *Annals of Surgery,* vol. 266, no. 5, pp. 706-712, November 2017.

[18] Z. E. Brewer, H. C. Fann, W. D. Ogden, T. A. Burdon and A. Y. Sheikh, “Inheriting the Learner’s View: A Google Glass-Based Wearable Computing Platform for Improving Surgical Trainee Performance,” *Journal of Surgical Education,* vol. 73, no. 4, pp. 682-688, 2016.

[19] P. Shao, H. Ding, J. Wang, P. Liu, Q. Ling, J. Chen, J. Xu, S. Zhang and R. Xu, “Designing a Wearable Navigation System for Image-Guided Cancer Resection Surgery,” *Annals of Biomedical Engineering,* vol. 42, no. 11, pp. 2228-2237, 2014.

[20] Z. Zhang, J. Pei, D. Wang, Q. Gan, J. Ye, J. Yue, B. Wang, S. P. Povoski, E. W. Martin, C. L. Hitchcock, A. Yilmaz, M. F. Tweedle, P. Shao and R. X. Xu, “A Wearable Goggle Navigation System for Dual-Mode Optical and Ultrasound Localization of Suspicious Lesions: Validation Studies Using Tissue-Simulating Phantoms and an Ex Vivo Human Breast Tissue Model.,” *PloS one,* vol. 11, no. 7, 2016.

[21] C. A. Liebert, M. A. Zayed, O. Aalami, J. Tran and J. N. Lau, “Novel Use of Google Glass for Procedural Wireless Vital Sign Monitoring,” *Surgical Innovation,* vol. 23, no. 4, pp. 366-373, 2016.

[22] X. Chen, L. Xu, Y. Wang, H. Wang, F. Wang, X. Zeng, Q. Wang and J. Egger, “Development of a surgical navigation system based on augmented reality using an optical see-through head-mounted display,” *Journal of Biomedical Informatics,* vol. 55, pp. 124-131, 2015.

[23] H. Wang, F. Wang, A. P. Y. Leong, L. Xu, X. Chen and Q. Wang, “Precision insertion of percutaneous sacroiliac screws using a novel augmented reality-based navigation system: a pilot study,” *International Orthopaedics,* vol. 40, pp. 1941-1947, 2015.

[24] X. Liu, H. Bai, G. Song, Y. Zhao and J. Han, “Augmented Reality System Training for Minimally Invasive Spine Surgery,” in *International Conference on Robotics and Biomimetics*

(ROBIO), Macau, 2017.

[25] R. M. Viglialoro, N. Esposito, S. Condino, F. Cutolo, S. Gaudagni, M. Gesi, M. Ferrari and V. Ferrari, “Augmented Reality to Improve Surgical Simulation: Lessons Learned Towards the Design of a Hybrid Laparoscopic Simulator for Cholecystectomy,” *IEEE Transactions on Biomedical Engineering,* vol. 66, no. 7, pp. 2091-2104, July 2019.

[26] N. Kalavakonda, L. Sekhar and B. Hannaford, “Augmented Reality Application for Aiding Tumor Resection in Skull-Base Surgery,” in *International Symposium on Medical Robotics (ISMR)*, Atlanta, 2019.

[27] G. Badiali, L. Cercenelli, S. Battaglia, E. Marcelli, C. Marchetti, V. Ferrari and F. Cutolo, “Review on Augmented Reality in Oral and Cranio-Maxillofacial Surgery: Toward “Surgery-Specific” Head-Up Displays,” *IEEE Access,* vol. 8, pp. 59015-59028, 11 February 2020.

[28] G. Badiali, V. Ferrari, F. Cutolo, C. Freschi, D. Caramella, A. Bianchi and C. Marchetti, “Augmented reality as an aid in maxillofacial surgery: Validation of a wearable system allowing maxillary repositioning,” *Journal of Cranio-Maxillofacial Surgery,* vol. 42, no. 8, pp. 1970-1976, December 2014.

[29] D. Andersen, C. Lin, V. Popescu, E. R. Muñoz, M. E. Cabrera, B. Mullis, B. Zarzaur, S. Marley and J. Wachs, “Augmented Visual Instruction for Surgical Practice and Training,” in *IEEE Workshop on Augmented and Virtual Realities for Good (VAR4Good)*, Reutlingen, 2018.

[30] B. Krajancich, N. Padmanaban and G. Wetzstein , “Factored Occlusion: Single Spatial Light Modulator Occlusion-capable Optical See-through Augmented Reality Display,” *IEEE Transactions on Visualization and Computer Graphics,* vol. 26, no. 5, pp. 1871-1879, 2020.

[31] T. S. Wu, C. J. Dameff and J. L. Tully, “Ultrasound-Guided Central Venous Access Using Google Glass,” *The Journal of Emergency Medicine,* vol. 47, no. 6, pp. 668-675, 2014.

[32] N. Kaneko, M. Sato, T. Takeshima, Y. Sehara and E. Watanabe, “Ultrasound-Guided Central Venous Catheterization Using an Optical See-Through Head-Mounted Display: A Pilot Study,” *Journal of Clinical Ultrasound,* vol. 44, no. 8, pp. 487-491, 2016.

[33] R. Przkora, W. McGrady, T. Vasilopoulos, N. Gravenstein and D. Solanki, “Evaluation of the Head-Mounted Display for Ultrasound-Guided Peripheral Nerve Blocks in Simulated Regional Anesthesia,” *Pain Medicine,* vol. 16, no. 11, pp. 2192-2194, 2015.

[34] J. Wang, H. Suenaga, K. Hoshi, L. Yang, E. Kobayashi, I. Sakuma and H. Liao, “Augmented Reality Navigation With Automatic Marker-Free Image Registration Using 3-D Image Overlay for Dental Surgery,” *IEEE Transactions on Biomedical Engineering,* vol. 61, no. 4, pp. 1295-1304, 17 January 2014.

[35] L. Ma, Z. Zhao, F. Chen, B. Zhang, L. Fu and H. Liao, “Augmented reality surgical navigation with ultrasound-assisted registration for pedicle screw placement: a pilot study,” *International Journal of Computer Assisted Radiology and Surgery,* vol. 12, no. 12, pp. 2205-2215, 2017.

[36] H. Suenaga, H. H. Tran, H. Liao, K. Masamune, T. Dohi, K. Hoshi and T. Takato, “Vision-based markerless registration using stereo vision and an augmented reality surgical navigation system: a pilot study,” *BMC Medical Imaging,* vol. 15, no. 1, 2 November 2015.

[37] J. Wang, Y. Shen and S. Yang, “A practical marker-less image registration method for augmented reality oral and maxillofacial surgery,” *International Journal of Computer Assisted Radiology and Surgery,* vol. 14, no. 5, pp. 763-773, 2019.

[38] J. Wang, H. Suenaga, L. Yang, E. Kobayashi and I. Sakuma, “Video see□through augmented reality for oral and maxillofacial surgery,” *The International Journal of Medical Robotics and Computer Assisted Surgery,* vol. 13, no. 2, 2016.

[39] T. Quang, M. Zhou, F. Papay and Y. Liu, “Fluorescence to color feature-based image registration for medical augmented reality,” in *2018 IEEE International Symposium on Signal Processing and Information Technology (ISSPIT)*, Louisville, 2018.

[40] S. L. Perkins, M. A. Lin, S. Srinivasan, A. J. Wheeler, B. A. Hargreaves and B. L. Daniel, “A Mixed-Reality System for Breast Surgical Planning,” in *International Symposium on Mixed and Augmented Reality (ISMAR-Adjunct)*, Nantes, 2017.

[41] N. Mirchi, V. Bissonnette, R. Yilmaz, N. Ledwos, A. Winkler-Schwartz and R. F. Del Maestro, “The Virtual Operative Assistant: An explainable artificial intelligence tool for simulation-based training in surgery and medicine,” *PLoS One,* vol. 15, no. 2, February 2020.

*** Important, due to the explanation of raw data acquisition and the steps to generate metrics for surgical simulators.**

[42] D. Wang, Y. Zhang, J. Hou, Y. Wang, P. Lv, Y. Chen and H. Zhao, “iDental: A Haptic-Based Dental Simulator and Its Preliminary User Evaluation,” *IEEE Transactions on Haptics,* vol. 5, no. 4, pp. 332-343, 2012.

[43] N. Choudhury, N. Gélinas-Phaneuf, S. Delorme and R. Del Maestro, “Fundamentals of Neurosurgery: Virtual Reality Tasks for Training and Evaluation of Technical Skills,” *World Neurosurgery,* vol. 80, no. 5, pp. e9-e19, November 2013.

[44] H. Azarnoush, G. Alzhrani, A. Winkler-Schwartz, F. Alotaibi, N. Gelinas-Phaneuf, V. Pazos, N. Choudhury, J. Fares, R. DiRaddo and R. F. Del Maestro, “Neurosurgical virtual reality simulation metrics to assess psychomotor skills during brain tumor resection,” *International Journal of Computer Assisted Radiology and Surgery,* vol. 10, no. 5, pp. 603-618, 1 May 2015.

[45] X. Chen and J. Hu, “A review of haptic simulator for oral and maxillofacial surgery based on virtual reality,” *Expert Review of Medical Devices,* vol. 15, no. 6, pp. 435-444, 2018.

[46] V. Chheang, P. Saalfeld, T. Huber, F. Huettl, W. Kneist, B. Preim and C. Hansen, “Collaborative Virtual Reality for Laparoscopic Liver Surgery Training,” in *IEEE International Conference on Artificial Intelligence and Virtual Reality (AIVR)*, San Diego, 2019.

[47] M. Peral-Boiza, T. Gómez-Fernández, P. Sánchez-González, B. Rodríguez-Vila, E. J. Gómez and Á. Gutiérrez, “Position Based Model of a Flexible Ureterorenoscope in a Virtual Reality Training Platform for a Minimally Invasive Surgical Robot,” *IEEE Access,* vol. 7, pp. 177414 - 177426, 2019.

[48] A. Gupta, J. Cecil, M. Pirela-Cruz and N. Ilidan, “Design of an Immersive Simulator for Orthopedic Surgical Training,” in *2018 IEEE International Conference on Systems, Man, and Cybernetics (SMC)*, Miyazaki, 2018.

[49] R. Hussain, A. Lalande, C. Guigou and A. Bozorg-Grayeli, “Contribution of Augmented

Reality to Minimally Invasive Computer-Assisted Cranial Base Surgery," *IEEE Journal of Biomedical and Health Informatics,* 18 November 2019.

**** Important, evaluation of the usefulness of augmented reality systems for neurosurgery and highlighting the challenges that current technology faces and their potential solutions.**

[50] A. Winkler-Schwartz, V. Bissonnette, N. Mirchi, N. Ponnudurai, R. Yilmaz, N. Ledwos, S. Siyar, H. Azarnoush, B. Karlik and R. F. Del Maestro, "Artificial Intelligence in Medical Education: Best Practices Using Machine Learning to Assess Surgical Expertise in Virtual Reality Simulation," *Journal of Surgical Education,* vol. 76, no. 6, pp. 1681-1690, 2019.

*** Important, introduction of the Machine Learning to Assess Surgical Expertise checklist.**

[51] A. Winkler-Schwartz, R. Yilmaz, N. Mirchi, V. Bissonnette, N. Ledwos, S. Siyar, H. Azarnoush, B. Karlik and R. Del Maestro, "Machine Learning Identification of Surgical and Operative Factors Associated With Surgical Expertise in Virtual Reality Simulation," *JAMA Network Open,* vol. 2, no. 8, pp. e198363-e198363, August 2019.

[52] V. Bissonnette, N. Mirchi, N. Ledwos, G. Alsidieri, A. Winkler-Schwartz and R. F. Del Maestro, "Artificial Intelligence Distinguishes Surgical Training Levels in a Virtual Reality Spinal Task," *The Journal of Bone and Joint Surgery,* vol. 101, no. 23, p. e127, 4 December 2019.

[53] N. Mirchi, V. Bissonnette, N. Ledwos, A. Winkler-Schwartz, R. Yilmaz, B. Karlik and R. F. Del Maestro, "Artificial Neural Networks to Assess Virtual Reality Anterior Cervical Discectomy Performance," *Operative Neurosurgery,* vol. 16, no. 1, pp. 65-75, 13 December 2019.

**** Important overview of immersive virtual reality application in surgical simulation.**

[54] S. Tomlinson , B. Hendricks and A. Cohen-Gadol , "Immersive Three-Dimensional Modeling and Virtual Reality for Enhanced Visualization of Operative Neurosurgical Anatomy," *World Neurosurg,* pp. 313-320, 2019.

**** Important overview of concepts of virtual reality application in endoscopic neurosurgery**

[55] A. Cohen , S. Lohani and S. Manjila , "Virtual reality simulation: basic concepts and use in endoscopic neurosurgery training," *Childs Nerv Syst(2013),* vol. 29, pp. 1235-1244, 2015.

[56] G. Breimer , F. Haji , V. Bodani, M. Cunningham , A. Lopez-Rios , A. Okrainec and J. Drake , "Simulation-based Education for Endoscopic Third Ventriculostomy: A Comparison Between Virtual and Physical Training Models," *Oper Neurosurg (Hagerstown),* vol. 13, no. 1, pp. 89-95, 2017.

**** Important systematic review of virtual reality based simulators in cranio tumor surgery.**

[57] T. Mazur, T. Mansour, l. Mugge and A. Medhkour, "Virtual Reality-Based Simulators for Cranial Tumor Surgery: A Systematic Review.," *World Neurosurg. 2018,* vol. 110, pp. 414-422, 2018.

*** Important literature on VR/AR/MR clinical applications in neurosurgical related procedures**

[58] G. Locketz, S. Chan and J. Lui , “Specific Virtual Reality Simulation in Temporal Bone Dissection: Perceived Utility and Impact on Surgeon Confidence,” *Otolaryngol Head Neck Surg,* vol. 156, no. 6, pp. 1142-1149, 2017.

[59] A. Alaraj , C. Luciano and D. Bailey , “ Virtual reality cerebral aneurysm clipping simulation with real-time haptic feedback,” *Neurosurgery.,* pp. 52-58, 2015.

[60] M. Gmeiner , J. Dirnberger and W. Fenz , “Virtual Cerebral Aneurysm Clipping with Real-Time Haptic Force Feedback in Neurosurgical Education,” *World Neurosurg,* 2018.

[61] S. Yao , J. Zhang J and Y. Zhao , “ Multimodal Image-Based Virtual Reality Presurgical Simulation and Evaluation for Trigeminal Neuralgia and Hemifacial Spasm,” *World Neurosurg,* 2018.

[62] B. Xin , Chen G and Wang Y, “The Efficacy of Immersive Virtual Reality Surgical Simulator Training for Pedicle Screw Placement: A Randomized Double-Blind Controlled Trial,” *World Neurosurg,* 2018.

[63] C. Lee C and G. Wong , “Virtual reality and augmented reality in the management of intracranial tumors: A review,” *J Clin Neurosci,* vol. 62, pp. 14-20, 2019.

[64] O. M. Kersten, I. Gerard and S. Drouin, “Augmented reality in neurovascular surgery: feasibility and first uses in the operating room,” *Int J CARS,* vol. 10, pp. 1823-1836, 2015.

[65] J. Yoon , R. Chen and K. ReFaey , “Technical feasibility and safety of image-guided parieto-occipital ventricular catheter placement with the assistance of a wearable head-up display,” *The International Journal of Medical Robotics + Computer Assisted Surgery : MRCAS,* 2017.

[66] E. Watanabe, M. Satoh M , T. Konno T , M. Hirai M and T. Yamaguchi , “The Trans-Visible Navigator: A See-Through Neuronavigation System Using Augmented Reality,” *World Neurosurgery,* vol. 87, pp. 399-405, 2016.

[67] C. Karmonik, S. Elias and J. Zhang , “Augmented Reality with Virtual Cerebral Aneurysms: A Feasibility Study,” *World Neurosurg.,* 2018.

[68] B. Carl , M. Bopp , B. Saß , M. Pojskic and C. Nimsky , “Augmented reality in intradural spinal tumor surgery,” *Acta Neurochir (Wien),* vol. 161, no. 10, p. 2181□2193, 2019.

[69] E. Edström , G. Burström , R. Nachabe , P. Gerdhem and T. A. Elmi, “A Novel Augmented-Reality-Based Surgical Navigation System for Spine Surgery in a Hybrid Operating Room: Design, Workflow, and Clinical Applications,” *Operative Neurosurgery (Hagerstown, Md.),* vol. 18, no. 5, pp. 496-502, 2020.

[70] A. G. Alfonso , J. Bec and S. . W. Sridharan , “Real-time augmented reality for delineation of surgical margins during neurosurgery using autofluorescence lifetime contrast,” *J Biophotonics,* vol. 13, no. 1, 2020.

[71] A. Lavé , T. Meling , K. Schaller and M. Corniola , “Augmented reality in intracranial meningioma surgery: a case report and systematic review,” *J Neurosurg Sci,* 2020.

[72] G. Coelho G, N. Rabelo NN and E. Vieira , “Augmented reality and physical hybrid model simulation for preoperative planning of metopic craniosynostosis surgery,” *Neurosurg Focus,* vol. 48, no. 3, 2020.

[73] Z. Zhang, W. Duan, R. Chen, F. Zhang and B. Yu, "Preliminary application of mxed reality in neurosurgery: Development Development and evaluation of a new intraoperative procedure," *Journal of Clinical Neuroscience,* vol. 67, pp. 234-238, 2019.

[74] J. McJunkin and P. Jiramongkolchai, "Development of a Mixed Reality Platform for Lateral Skull Base Anatomy," *Otol Neurotol,* vol. 39, no. 10, pp. e1137-e1142, 2018.

[75] F. Incekara, "Clinical Feasibility of a Wearable Mixed-Reality Device in Neurosurgery," *World Neurosurg,* vol. 118, pp. e422-e427, 2018.

[76] S. Heuts , P. N. Sardari and J. Maessen , "Preoperative planning of thoracic surgery with use of three-dimensional reconstruction, rapid prototyping, simulation and virtual navigation," *J Vis Surg,* vol. 77, no. 2, 2016.

[77] X. Wu , R. Liu and J. Yu , "Mixed Reality Technology-Assisted Orthopedics Surgery Navigation.," *Surg Innov,* vol. 25, no. 3, pp. 304-305, 2018.

[78] G. Coelho , E. Figueiredo , N. Rabelo and M. Teixeira , "Development and evaluation of a new pediatric mixed-reality model for neurosurgical training," *J Neurosurg Pediatr,* pp. 1-10, 2020.

[79] Y. Pulijala , M. Ma , M. Pears , D. Peebles and A. Ayoub , "Effectiveness of Immersive Virtual Reality in Surgical Training-A Randomized Control Trial," *J Oral Maxillofac Surg,* vol. 76, no. 5, pp. 1065-1072, 2018.

**** Important, systematic review of both virtual and augmented reality application in dental medicine.**

[80] T. Joda , G. Gallucci , D. Wismeijer and N. Zitzmann , "Augmented and virtual reality in dental medicine: A systematic review," *Comput Biol Med,* pp. 93-100, 2019.

*** Important literature on VR/AR/MR clinical applications in the field of oral and cranio-maxillofacial surgery**

[81] X. Chen , P. Sun and D. Liao , "A patient-specific haptic drilling simulator based on virtual reality for dental implant surgery," *Int J Comput Assist Radiol Surg,* vol. 13, no. 11, pp. 1861-1870, 2019.

[82] D. Holzinger , P. Juergens and K. Shahim, "Accuracy of soft tissue prediction in surgery-first treatment concept in orthognathic surgery: A prospective study.," *Journal of Cranio-maxillo-facial Surgery.,* vol. 46, no. 9, pp. 1455-1460, 2018.

[83] Y. Pulijala , M. Ma , M. Pears , D. Peebles and A. Ayoub , "An innovative virtual reality training tool for orthognathic surgery," *Int J Oral Maxillofac Surg,* vol. 47, no. 9, pp. 1199-1205, 2018.

[84] K. Maloney and T. Rutner, "Virtual Surgical Planning and Hardware Fabrication Prior to Open Reduction and Internal Fixation of Atrophic Edentulous Mandible Fractures," *Craniomaxillofacial Trauma & Reconstruction,* vol. 12, no. 2, pp. 156-162, 2019.

[85] H. Hanken, C. Schablowsky and R. Smeets, "Virtual planning of complex head and neck reconstruction results in satisfactory match between real outcomes and virtual models," *Clinical Oral Investigations,* vol. 19, no. 3, pp. 647-656, 2015.

[86] A. Nguyen, C. Vanderbeek, A. Herford and J. Thakker, “Use of Virtual Surgical Planning and Virtual Dataset With Intraoperative Navigation to Guide Revision of Complex Facial Fractures: A Case Report,” Journal of Oral and Maxillofacial Surgery. 2019.

[87] V. Drake, C. Rizzi, J. Greywoode and K. Vakharia, “Midface Fracture Simulation and Repair: A Computer-Based Algorithm,” *Craniomaxillofacial Trauma & Reconstruction,* vol. 12, no. 1, pp. 1-14, 2019.

[88] A. Matsuo , H. Hamada , H. Oba and K. Shibata , “Virtual reality head-mounted display for endoscopically-assisted implant surgery,” *Br J Oral Maxillofac Surg.,* vol. 56, no. 7, pp. 636-637, 2018.

[89] H. Kwon , Y. Park and J. Han, “Augmented reality in dentistry: a current perspective,” *Acta Odontologica Scandinavica,* vol. 76, pp. 497-503, 2018.

[90] D. Katić , P. Spengler and S. Bodenstedt , “system for context-aware intraoperative augmented reality in dental implant surgery,” *Int J Comput Assist Radiol Surg,* vol. 10, no. 1, pp. 101-108, 2015.

[91] Y. Lin , H. Yau , I. Wang , C. Zheng and K. Chung , “ A novel dental implant guided surgery based on integration of surgical template and augmented reality,” *Clin Implant Dent Relat Res,* vol. 17, no. 3, pp. 543-553, 2015.

[92] G. Pellegrino, C. Mangano and R. Mangano, “Augmented reality for dental implantology: a pilot clinical report of two cases,” *BMC Oral Health,* vol. 19, no. 1, 2019.

[93] J. Ahn , H. Choi and J. Hong , “Tracking Accuracy of a Stereo Camera-Based Augmented Reality Navigation System for Orthognathic Surgery,” *J Oral Maxillofac Surg,* vol. 77, no. 5, 2019.

[94] M. Zhu, F. Liu and G. Chai, “A novel augmented reality system for displaying inferior alveolar nerve bundles in maxillofacial surgery,” *Sci Rep,* 2017.

[95] F. Karner, C. Gsaxner, A. Pepe and et al., “Single-Shot Deep Volumetric Regression for Mobile Medical Augmented Reality,” in *10th International Workshop, ML-CDS, and 9th International Workshop CLIP, In Conjunction with MICCAI*, Peru, 2020.

[96] Tepper and M. Oren, “Mixed Reality With HoloLens: Where Virtual Reality Meets Augmented Reality in the Operating Room,” *Plast Reconstr Surg. 2017,* vol. 140, no. 5, pp. 1066-1070, 2017.

[97] S. Tuladhar, N. AlSallami and A. Alsadoon , “A recent review and a taxonomy for hard and soft tissue visualization-based mixed reality,” *Int J Med Robot,* 2019.

[98] H. Venkata , A. Alsadoon and P. Prasad , “A novel mixed reality in breast and constructive jaw surgical tele-presence,” *Comput Methods Programs Biomed,* vol. 177, pp. 253-268, 2019.

[99] K. Fushima and M. Kobayashi , “Mixed-reality simulation for orthognathic surgery,” *Maxillofac Plast Reconstr Surg,* vol. 38, no. 1, 2016.

[100] A. Pepe, G. Trotta and P. Mohr-Ziak, “A Marker-Less Registration Approach for Mixed Reality-Aided Maxillofacial Surgery: A Pilot Evaluation,” *Digit Imaging,* vol. 32, no. 6, pp. 1008-1018, 2019.

[101] C. Gsaxner, A. Pepe, J. Wallner, D. Schmalstieg and J. Egger, “Markerless Image-to-Face Registration for Untethered Augmented Reality in Head and Neck Surgery,” *Miccai,* pp. 236-244, 2019.

[102] C. Gsaxner, J. Wallner, X. Chen, W. Zemann and J. Egger, “Facial model collection for medical augmented reality in oncologic cranio-maxillofacial surgery,” *Scientific Data,* p. 6(1):310, 2019.

**** Important, review of augmented reality in open surgery.**

[103] F. Benish and C. Fabrizio, “Augmented reality in open surgery,” *Updates in Surgery,* 2018.

***Important Literature on VR/AR/MR clinical applications in open surgery.**

[104] T. Okamoto, S. Onda and J. Yasuda, “Navigation surgery using an augmented reality for pancreatectomy,” *Digestive Surgery,* vol. 32, no. 2, pp. 117-123, 2015.

[105] D. Ntourakis, R. Memeo and L. Soler, “Augmented Reality Guidance for the Resection of Missing Colorectal Liver Metastases: An Initial Experience,” *World J Surg 40,* vol. 440, pp. 419-426, 2016.

[106] R. Bell, H. McDermott and T. Fancher, “Impact of a randomized controlled educational trial to improve physician practice behaviors around screening for inherited breast cancer,” *Journal of General Internal Medicine,* vol. 30, no. 3, pp. 334-341, 2015.

[107] S. Onda, T. Okamoto and M. Kanehira, “Identification of inferior pancreaticoduodenal artery during pancreaticoduodenectomy using augmented reality-based navigation system,” *Journal of Hepato-biliary-pancreatic Sciences,* vol. 21, no. 4, pp. 281-287, 2014.

[108] R. Tang, L. Ma and C. Xiang, “Augmented reality navigation in open surgery for hilar cholangiocarcinoma resection with hemihepatectomy using video-based in situ three-dimensional anatomical modeling: A case report,” *Medicine. 2017,* vol. 96, 2017.

[109] H. Borgmann, S. Rodriguez and J. Salem, “Feasibility and safety of augmented reality-assisted urological surgery using smartglass,” *World J Urol,* vol. 35, pp. 967-972, 2017.

[110] N. Golse , A. Petit , M. Lewin , E. Vibert and S. Cotin , “Augmented Reality during Open Liver Surgery Using a Markerless Non-rigid Registration System,” *J Gastrointest Surg,* 2020.

[111] G. Kleinjan, N. Van den Berg and M. Van Oosterom, “Toward (Hybrid) Navigation of a Fluorescence Camera in an Open Surgery Setting,” *Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine,* vol. 57, no. 19, pp. 1650-1653, 2016.

[112] M. Van Oosterom, P. Meershoek and G. Kleinjan, “Navigation of Fluorescence Cameras during Soft Tissue Surgery-Is it Possible to Use a Single Navigation Setup for Various Open and Laparoscopic Urological Surgery Applications?,” *The Journal of Urology,* vol. 199, no. 4, pp. 1061-1068, 2018.

[113] S. Weidert , L. Wang , J. Landes , P. Sandner and et al., “Video-augmented fluoroscopy for distal interlocking of intramedullary nails decreased radiation exposure and surgical time in a bovine cadaveric setting,” *Int J Med Robo,* vol. 15, no. 4, 2019.

[114] G. Ameri , J. Baxter , D. Bainbridge , T. Peters and E. Chen, “Mixed reality ultrasound guidance system: a case study in system development and a cautionary tale,” *Int J Comput*

Assist Radiol Surg, vol. 13, no. 4, pp. 495-505, 2018 .

**** Important virtual reality Laparoscopic surgical training systems overview for both immersive and conventional simulation**

[115] M. Alaker, G. Wynn and T. Arulamalam, “Virtual reality training in laparoscopic,” *International Journal of Surgery,* 2016.

[116] J. Frederiksen , S. Sørensen , L. Konge and et al, “Cognitive load and performance in immersive virtual reality versus conventional virtual reality simulation training of laparoscopic surgery: a randomized trial,” *Surgical Endoscopy,* vol. 34, no. 3, pp. 1244-1252, 2020.

**** Important review of augmented reality in Laparoscopic surgery to give an update status as of 2016**

[117] S. Bernhardt , S. Nicolau, L. Soler and C. Doignon , “The status of augmented reality in laparoscopic surgery as of 2016,” *Medical Image Analysis,* vol. 37, pp. 66-90, 2017 .

***Important highlight of VR/AR/MR clinical applications in Laparoscopic surgery.**

[118] L. Lau , X. Liu , W. Plishker , K. Sharma, R. Shekha and T. Kane, “ Laparoscopic Liver Resection with Augmented Reality: A Preclinical Experience,” *Journal of laparoendoscopic & advanced surgical techniques.,* 2018.

[119] G. Prevost , B. Eigl and I. Paolucci, “Efficiency, Accuracy and Clinical Applicability of a New Image-Guided Surgery System in 3D Laparoscopic Liver Surgery,” *J Gastrointest Surg,* 2019.

[120] T. Aoki , T. Koizumi , D. Mansour and et al., “Virtual reality with three-dimensional image guidance of individual patients' vessel anatomy in laparoscopic distal pancreatectomy,” *Langenbeck's Archives of Surgery,* vol. 405, no. 3, pp. 381-389, 2020 .

[121] C. Akladios , V. Gabriele , V. Agnus and et al, “Augmented reality in gynecologic laparoscopic surgery: development, evaluation of accuracy and clinical relevance of a device useful to identify ureters during surgery,” *Surgical Endoscopy,* vol. 34, no. 3, pp. 1077-1087, 2020 .

***Important method for real time haptic interaction between rigid and deformable objects.**

[122] S. P. Byeon and D. Y. Lee, “Method for real-time simulation of haptic interaction with deformable objects using GPU-based parallel computing and homogeneous hexahedral elements,” *Computational Mechanics,* vol. 65, no. 5, pp. 1205-1218, 2020.

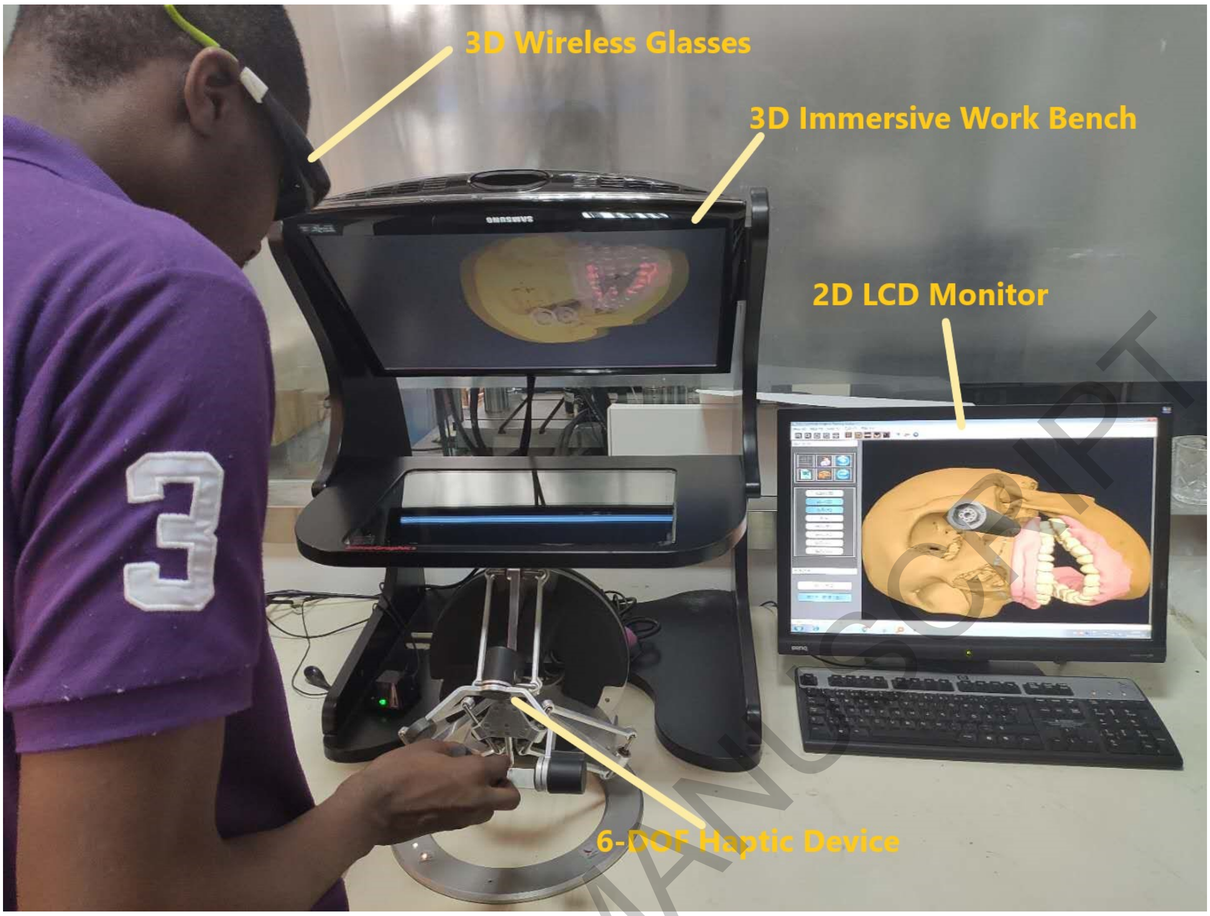
3D Wireless Glasses
3D Immersive Work Bench
2D LCD Monitor
6-DOF Haptic Device

Fig 1

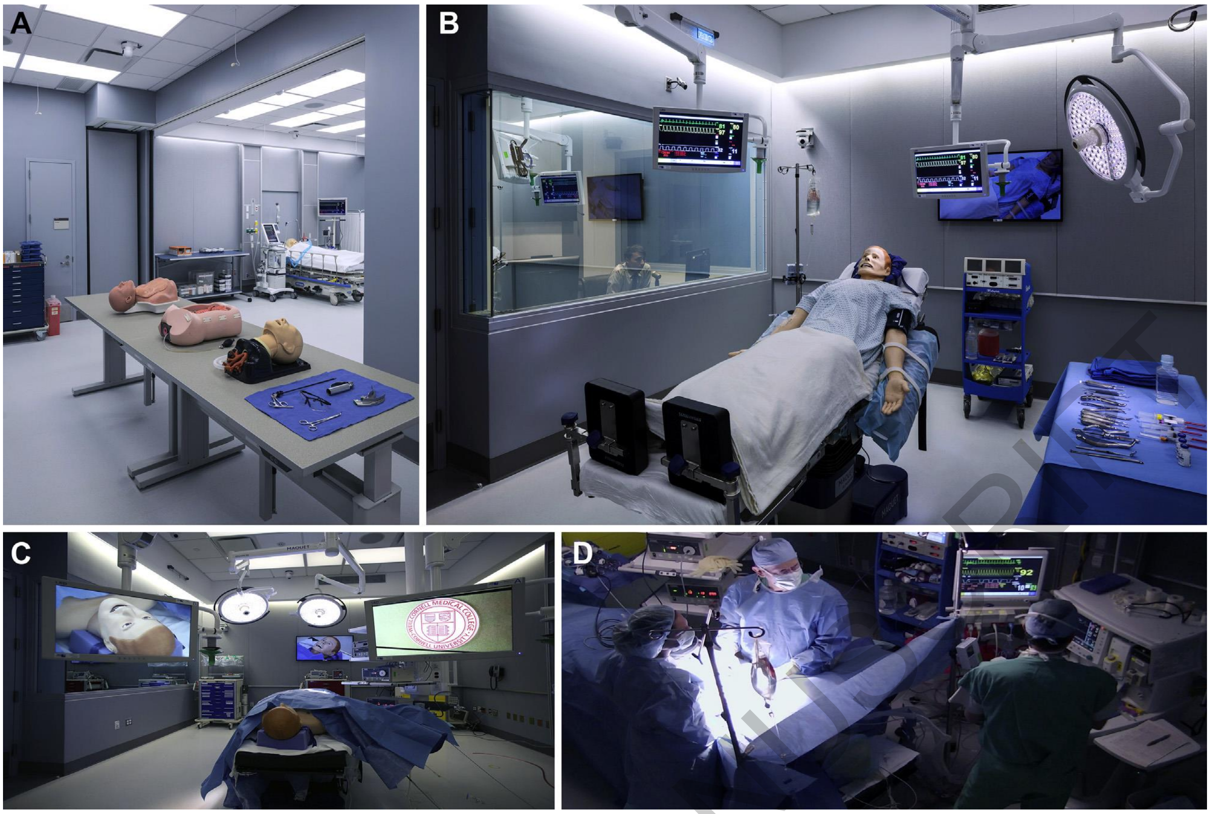

Fig 2

Fig 3

‘Fig 4