

Article

Augmented Reality in Surgery: A Scoping Review

Eleonora Barcali ^{1,2} , Ernesto Iadanza ^{3,*} , Leonardo Manetti ⁴, Piergiorgio Francia ¹ , Cosimo Nardi ²  and Leonardo Bocchi ¹ 

- ¹ Department of Information Engineering, University of Florence, 50139 Florence, Italy; eleonora.barcali@unifi.it (E.B.); piergiorgiofrancia5@gmail.com (P.F.); leonardo.bocchi@unifi.it (L.B.)
² Department of Biomedical Experimental and Clinical Sciences “Mario Serio”, University of Florence, 50139 Florence, Italy; cosimo.nardi@unifi.it
³ Department of Medical Biotechnologies, University of Siena, 53100 Siena, Italy
⁴ Epica Imaginalis, 50019 Sesto Fiorentino, Italy; l.manetti@imaginalis.it
* Correspondence: ernesto.iadanza@unisi.it

Abstract: Augmented reality (AR) is an innovative system that enhances the real world by superimposing virtual objects on reality. The aim of this study was to analyze the application of AR in medicine and which of its technical solutions are the most used. We carried out a scoping review of the articles published between 2019 and February 2022. The initial search yielded a total of 2649 articles. After applying filters, removing duplicates and screening, we included 34 articles in our analysis. The analysis of the articles highlighted that AR has been traditionally and mainly used in orthopedics in addition to maxillofacial surgery and oncology. Regarding the display application in AR, the Microsoft HoloLens Optical Viewer is the most used method. Moreover, for the tracking and registration phases, the marker-based method with a rigid registration remains the most used system. Overall, the results of this study suggested that AR is an innovative technology with numerous advantages, finding applications in several new surgery domains. Considering the available data, it is not possible to clearly identify all the fields of application and the best technologies regarding AR.

Keywords: augmented reality; image guided surgery; surgery



Citation: Barcali, E.; Iadanza, E.; Manetti, L.; Francia, P.; Nardi, C.; Bocchi, L. Augmented Reality in Surgery: A Scoping Review. *Appl. Sci.* **2022**, *12*, 6890. <https://doi.org/10.3390/app12146890>

Academic Editors:
João M. F. Rodrigues
and Dimitris Mourtzis

Received: 5 May 2022
Accepted: 4 July 2022
Published: 7 July 2022

Publisher’s Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Imaging is known to play an increasingly important role in many surgery domains [1]. Its origin can be dated back to 1895 when W. C. Roentgen discovered the existence of X-rays [2]. While in the course of the twentieth century, X-rays have found increasing application, in more recent years, other techniques have been developed and acquiring data from the internal structures of the human body has become more and more useful [1,3–5]. All this facilitated an increasing use of images to guide surgeons during interventions, leading to the affirmation of image-guided surgery (IGS) [6]. In this sense, the need for reducing surgery evasiveness, by supporting physicians in the diagnosis and preoperative phases as well as during surgeries themselves, led to the use of different solutions such as the 3D visualization of anatomical parts and the application of augmented reality (AR) in surgery [1,3,4]. Augmented reality consists in merging the real world with virtual objects (VOs) generated by computer graphic systems, creating a world for the user that is augmented with VOs. The first application of AR in medicine dates back to 1968 when Sutherland created the first head-mounted display [7]. The term AR is often used in conjunction with virtual reality (VR). The difference between them is that VR creates a digital artificial environment by stimulating the senses of the user and simulating the external world through computer graphic systems [8], while AR overlays computer-generated images onto the real world, increasing the user perception and showing something that would otherwise not be perceptible as reported by Park et al. in [1] and Desselle et al. in [9].

The application of AR in IGS can be an increasingly important opportunity for the treatment of patients. In particular, AR allows one to see 3D images projected directly

onto patients thanks to the use of special displays. All this can facilitate the perception of the reality examined and lighten the task of the operators themselves compared to the traditional approach consisting in 2D preoperative images displayed on 2D monitors [1,5].

In this way, doctors can directly see 3D images projected onto patients using special displays, described in the next paragraph, instead of using 2D preoperative images displayed on 2D monitors that require the doctor to mentally transform them into 3D objects as well as remove the sight from the patient [1,5].

The purpose of this review is providing an overview of AR by describing which medical applications it can be used in and which aspects characterize this technology to provide doctors with information on this emerging tool. We would like it to be a starting point for more in-depth research and applications in the clinical field. In order to better understand AR application, this review started by describing some key technological aspects such as: tracking, registration and displays.

2. Theoretical Background

This section describes the main aspects leading to the visualization of the VOs superimposed on the real world. The workflow of augmented-reality-enabled systems is shown in Figure 1. This Figure 1 shows that once the virtual model has been rendered, tracking and recording are the two basic steps. In this sense, tracking and registration provide the correct spatial positioning of the VOs with respect to the real world [10]. This result is possible because, with monitoring, the spatial characteristics of an object are detected and measured. Specifically, with regard to AR, tracking indicates the operations necessary to determine the device's six degrees of freedom, 3D location and orientation within the environment, necessary to calculate the real time user's point of view. Tracking can be performed outdoors and indoors. We focused on the latter. Two methods of indoor tracking are then distinguishable: outside-in and inside-out. In the outside-in method, the sensors are placed in a stationary place in the environment and sense the device location, often resorting to marker-based systems [11]. In the inside-out method, the camera or the sensors are placed on the actual device whose spatial features are to be tracked in the environment. In this case, the device aims to determine how its position changes in relation to the environment, as for the head-mounted displays (HMDs). The inside-out tracking can be marker-based or marker-less. The marker-based vision technique, making use of optical sensors, measures the device pose starting from the recognition of some fiducial markers placed in the environment. This method can also hyperlink physical objects to web-based content using graphic tags or automatic identification technologies such as radio-frequency-identification (RFID) systems [12]. The marker-less method, conversely, does not require fiducial markers. It bases its measures on the recognition of distinct characteristics, present in the environment, that in turn are used to localize the position of the device in combination with computer vision and image-processing techniques. Registration involves the matching and alignment of tracked spatial features obtained from the real world (RW) with the corresponding points of the VOs to reach an optimal overlapping between them [1]. The accuracy of this process allows an accurate representation of the virtual reality over the real world and determines the natural appearance of an augmented image [13]. The registration phase is connected to the tracking one. Based on the ways these two are accomplished, the process is defined as manual, fully automatic or semiautomatic. The manual one refers to manual registration and manual tracking. It consists in finding landmarks both on the model and the patient and consequently manually orienting and resizing of the obtained preoperative 3D model displayed on the operative monitor to make it match real images. The fully automatic process is the most complex one, especially with soft tissues. Since real world objects change their shapes with time, the same deformation needs to be applied to the VOs to address the fact that any deformation during surgery, due to events such as respiration, can result in an inaccurate real-time registration, subsequently causing an imprecise overlapping between 3D VOs and ROs. Finally, the semiautomatic process associates the automatic tracking with the manual registration. The identification of

landmark structures, both on the obtained 3D model and on the real structures, occurs automatically, while its overlay on the model, and its orienting and resizing, occurs manually. This aspect is what differentiates the automatic process from the semiautomatic one. The latter provides the overlay of the AR images on real life statically and manually, while the former makes the 3D virtual models dynamically match the actual structures [1,14–16]. For the visualization of the VOs onto the real world, several AR display technologies exist, usually classified in head, body and world devices, depending on the place where they are located [7,17]. World devices are located in a fixed place. This category includes desktop displays used as AR displays, and projector-based displays. The former are equipped with a webcam, a virtual mirror showing the scene framed by the camera and a virtual showcase, allowing the user to see the scene, alongside additional information. Projector-based displays cast virtual objects directly onto the corresponding real-world objects' surfaces. With body devices, we usually refer to handheld Android-based platforms, such as tablets or mobile phones. These devices use the camera for capturing the actual scenes in real time, while some sensors (e.g., gyroscopes and accelerometers and magnetometer) can determine their rotation. These devices usually resort to fiducial image targets for the tracking-registration phase [18]. Finally, the HMDs are near eye displays, wearable devices consisting in sort of glasses that have the advantage of leaving the hands free to perform other tasks. HMDs are mainly of two types: video see-through and optical see-through. The first ones refer to special lenses that let the user see the external real world through a camera whose frames are in turn combined with VOs. In this way, the external environment is recorded in real time and the final images overlaying the VOs are produced directly over the user's lenses. Differently, the optical see-through devices consist of an optical combiner or holographic waveguides, the lenses, that enable the overlay of images transmitted by a projector over the same lenses through which a normal visualization of the real world is allowed. In this way the user visualizes directly the reality augmented with the VOs overlaid onto it [7,19]. Figure 2 shows an example of HMD.

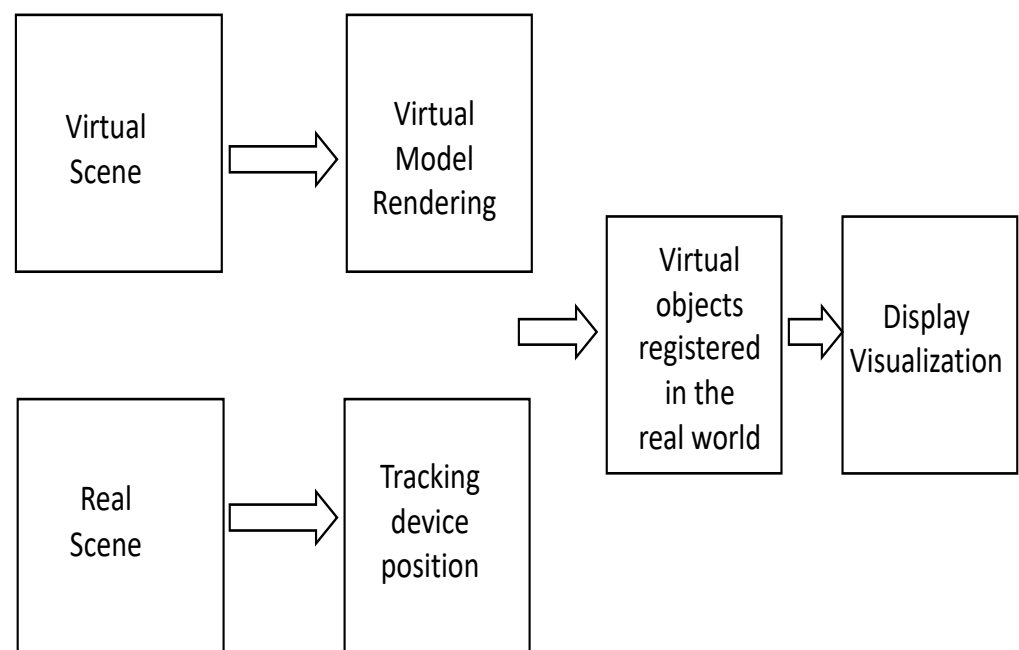


Figure 1. Workflow of augmented-reality-enabled systems.



Figure 2. Example of HMD, HoloLens 2 (Microsoft, WA, USA) .

The different techniques are summarized in Figure 3. The aim of this study was to describe the state of the art relating to the use of AR in the surgery domain. The description and analyses of the various procedures used to create the virtual images represented a further objective. This scoping review aims to provide a summary of the surgical fields in which this new technology finds its best application providing doctors with an overview of the key aspects behind viewing accurate virtual images superimposed on the real world. The research highlighted that the marker-based tracking and the rigid registration are currently the most used systems to acquire data, as reported in the following paragraphs.

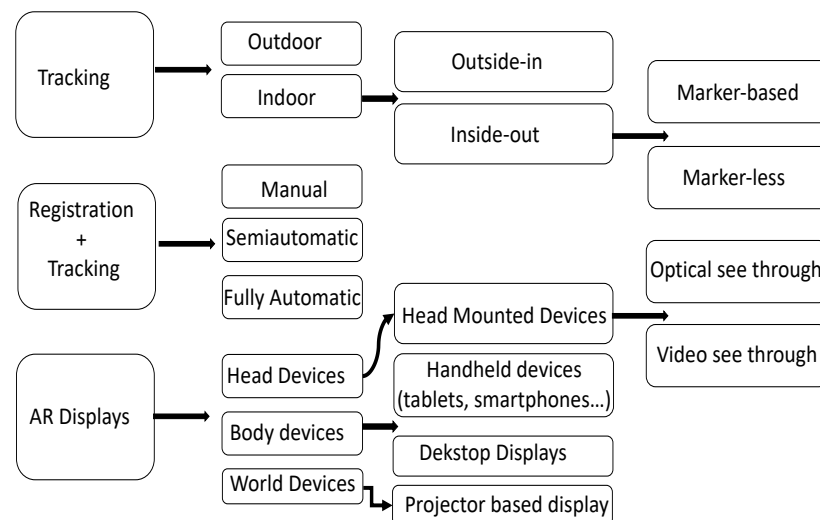


Figure 3. Summary of the techniques.

3. Materials and Methods

We followed the PRISMA Guidelines for scoping reviews [20]. The results are shown in Figure 4. The histogram in Figure 5 shows the trend of the number of publications from 1982 to 2021 present on Scopus searching English articles for “augmented reality in surgery”. Between 2020 and 2021, the number of publications increased by 40%. In 2022, at the time of writing, 50 articles have already been published and indexed on Scopus.

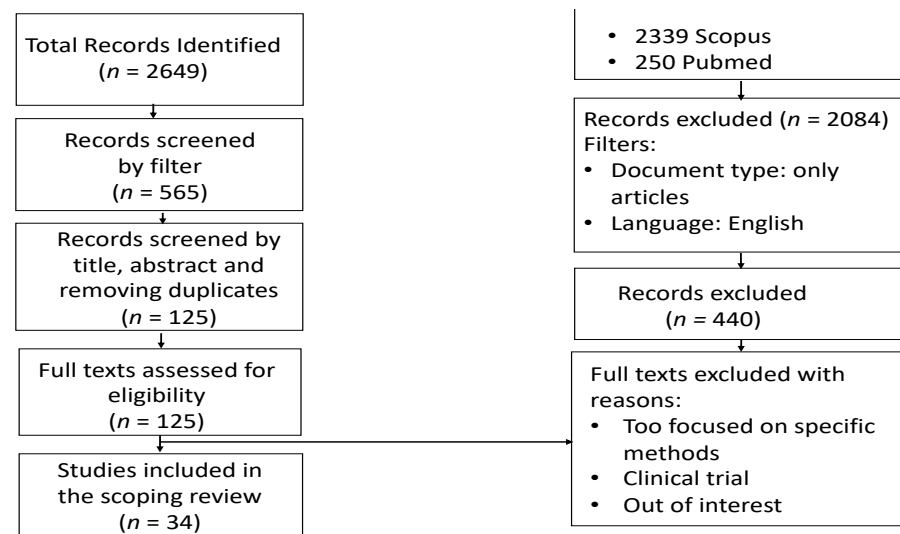


Figure 4. Criteria for the inclusion of articles.

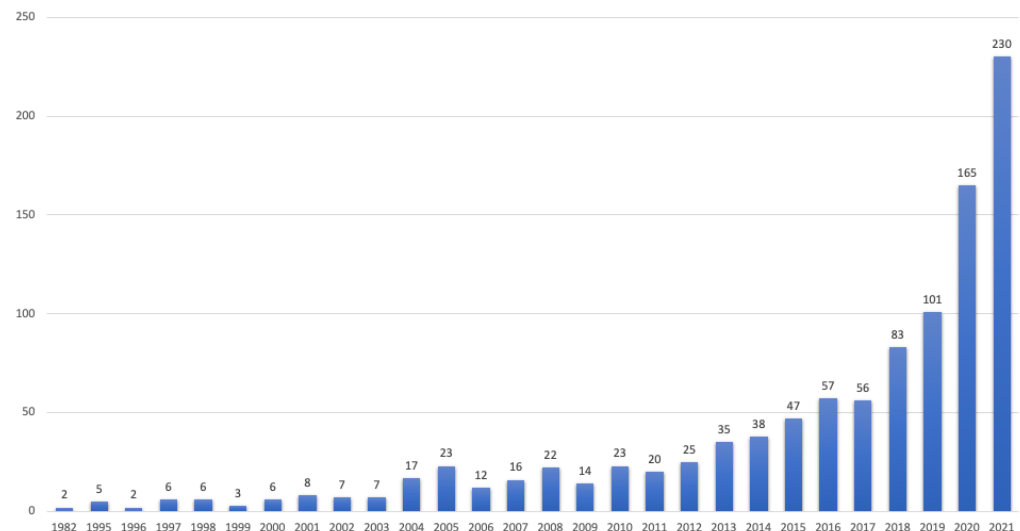


Figure 5. Trend of Publications on Augmented Reality in Surgery over the Years.

3.1. Inclusion Criteria

The studies included in the review need to be related to the main topic: augmented reality. We limited the selection by imposing restrictions on the document type (articles only) and on the language (English only). The query was limited to a relatively short period of time, (2019–February 2022) ensuring the attention was focused on the innovations introduced in the latest years. The queries we used during our searches were: “TITLE-ABS-KEY (“augmented reality” AND surgery) AND (LIMIT-TO (DOCTYPE, “ar”)) AND (LIMIT-TO (LANGUAGE, “English”)) AND (LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019))” for Scopus and Record on Pubmed.

3.2. Selection of Sources Criteria

The inclusion criteria were applied to filter the found articles. Additional documents were then added based on citations from excluded articles, deemed interesting for this review but not caught by the query because of the limitations that we decided to set. The team established two reviewers, E.B. and P.F. In both searches; they screened independently all the articles, starting from the abstracts and the titles, choosing the ones deemed

pertinent according to their own judgement. The articles chosen by both reviewers were directly integrated in the list of articles to be downloaded. The studies that were chosen from only one of the two reviewers were integrated in the list only after the agreement of a third reviewer, L.B., who took the final decision whether to include or discard the article from the final review. Starting from this list, full texts of these studies were downloaded and the process of choice was repeated based on the content of the studies found, thus obtaining the final list of articles to be included.

4. Results

The initial search yielded a total of 2649 articles. After applying filters, removing duplicates and screening the studies based on abstracts and titles, 125 studies remained, from which those included in the study were chosen. The final summary refers to a total of 34 articles. The reason for not including some articles is related to their content, in some cases deemed too specific, concerning clinical trials or topics outside the field of interest. The list of AR applications in the different surgery domains as reported in the selected articles is shown in Table 1. We decided to create Table 1, containing an overview of the AR applications in different areas and methods present in the chosen articles. The Table 1 is organized as follows: the first column shows the author (or authors) of the article, the second the application to which the article refers, the third the technology used for processing, the fourth the display used to view the virtual object merged with reality, the fifth the registration method used in the article, the sixth the error made in terms of approximations and the seventh the data set that was used in the article.

Evaluating all the selected articles, both in the filtered research and those added manually, we decided to summarize the main aspects of the AR applications in three schemes reported in Tables 2–4. The aspects we decided to analyze and report as percentage of application in the analyzed studies are the ones described in the section “Theoretical Background”. For what concerns the application of AR in different fields, the scheme in Table 2 shows that this technique has been traditionally mainly used in orthopedics. Lately, the innovation has been represented by its increasingly widespread application in maxillofacial surgery, in addition to oncology. However, the numerous areas in which AR is used confirm the important role that this technology may have in the future in the health field. The scheme in Table 3 shows how the projection over the patient is, at the moment, the least used method, while the Optical Viewer by Microsoft, HoloLens, is the most used one. The first model (HoloLens 1) together with the second one (HoloLens 2) amounts to 38% of the scheme in Table 3. For what concerns tracking and registration, reported in the scheme in Table 4, the marker-based method paired with rigid registration remains the most used system. Once we analyzed all the articles listed in Table 2, we decided to delve into the applications more recurrent in our research and which, in our opinion, seemed to have the most interesting clinical implications. The applications we decided to investigate are reported below.

Table 1. Most recent Augmented reality application for each field and method that resulted from the research.

Author	Application	Technology	Display	Registration	Error	Data Set
Schwam [21]	Lateral skull surgery	BrainLab Curve™, Surgical Theate and Zeiss OPMI PENTERO 900	Microscope-based HUD	Marker-less, rigid	Not reported	40 patients.
Coelho [22]	Antenatal Treatment of Myelomeningocele. Preoperative and post operative simulation to make it happen	Unity Engine, Google ARCore libraries, ray casting target object rendering	Application for smartphone and tablets	object placed based on the rendering,	Not reported	1 pregnant woman at 27 weeks of gestation.
Gouveia [23]	Left breast cancer: Oncology	Contrast-enhanced MRI Horos R software v2.4.0	HoloLens AR Headset	Marker-based, rigid,	Not reported	57 menopausal woman.
Chen [24]	Knee surgery arthroscopy	CT scanner, optical tracking system,	Glasses-free 3D display	Marker-based, rigid	Mean: 0.32 mm. Reduced error targets of 2.10 mm and 2.70 mm	Experiments: preclinical on knee phantom and in-vitro swine knee.
Golse [25]	Liver resection	3D segmentation. CT	Standard mobile external monitor	Real time Marker-less, non-rigid	7.9 mm root mean square error for internal landmark registration	In vivo: 5 patients, ex vivo: native tumor-free.
Gsaxner [26]	Head and neck Carcinoma: Training	CT, PET-CT and MRI scans. Instant calibration	HoloLens AR Headset	Marker-less, rigid	Between a few mm of up to 2 cm.	11 health care professionals.
Molina [27]	Spinal navigation	iCT scans. Gertzbein-Robbins (GS) scale	AR-HMD Xvision (Augmedics)	Marker-based, rigid	Linear deviation: 2.07 mm. Angular deviation: 2.41°.	78-yr-old female.
Ackermann [28]	Osteotomy cuts and reorientation of the acetabular fragment: navigation system	CT scan	Microsoft HoloLens	Marker-based, rigid	Osteotomy starting points: 10.8 mm. Osteotomy directions: 5.4. Reorientation errors: $x = 6.7^\circ$, $y = 7.0^\circ$, $z = 0.9^\circ$. LCE angle postoperative error: 4.5°	2 fresh-frozen human cadaverous hips.
Liu [29]	Medical training and telemonitored surgery	2 color digital cameras.	Microsoft HoloLens	Marker-based, rigid	The overall tracking one: less than 2.5 mm. The overall guidance one: less than 2.75 mm	Ex vivo arm phantom, in vivo rabbit model.

Table 1. Cont.

Author	Application	Technology	Display	Registration	Error	Data Set
Collins [30]	Uterus: Laparoscopy	MR or CT and monocular laparoscopes	Monitor	Marker-less, rigid	Distribution increase towards the cervix (2 mm for 15 views up to 8 mm for 2 views)	Phantom and videos recorded during laparoscopic surgery.
Arpaia [31]	Neurosurgery	Equipment of the brain computer interface.	Epson Moverio BT-350 glasses.	Not reported	Not reported	10 runs on the same patient.
Shrestha [32]	Bowel	CT scans and endoscope camera intraoperatively.	Monitor	Marker-based, rigid	The overlay error accuracy was 0.24777px. Performance was 44fps	People with three different ages: 15–25, 26–35, 35–60.
Wei [33]	Plastic surgery	Google Face API	Android display	Rigid, Marker-based	Not reported	4 benchmarks data set.
Lee [34]	thyroid surgery	CT. Semiautomatic registration	AR screen. Master surgical robot screen.	Marker-based, rigid	Mean \pm SD = 1.9 ± 1.5 mm	9 patients.
Hussain [35]	Ear surgery	Without tracking system, CT. Microscope 2D real time video	DDM. Bronchoscopy monitor	Marker-less, rigid	Surgical instrument tip position one: 0.3 ± 0.22 mm	6 artificial human temporal bone specimens.
Feufel [36]	Ultrasound guided needle placement	Reflective markers Ultrasound transducer	Microsoft HoloLens	Marker-based, rigid	Mean error of 7.4 mm	20 participants.
Carl [37]	Aneurysm surgery: indocyanine green (ICG) hagiography	CT, 3D rotational (DynaCT) or Time-of-flight magnetic resonance angiography. Automatic registration	Operating microscope HUD	Marker-based, rigid	Target registration one: 0.71 ± 0.21 mm	20 patients with 22 aneurysm.
Chan [38]	Transoral robotic surgery	CT	3D Surgeon's console	Marker-based, rigid	Not reported	2 cadavers.
Ferraguti [39]	Percutaneous Nephrolithotomy	Ct or MRI, 3 electrodes. Real time registration.	Microsoft HoloLens	Marker-based, rigid	Translation and orientation norm between 2 transformation matrices: 15.80 mm and 4.12°	11 samples.
Auloge [40]	Percutaneous vertebroplasty	Cone-beam CT	Monitor	Marker-based, rigid	Not reported	2 groups of 10 patients.
Libaw [41]	Inhaled induction of general anesthesia, pediatric	iPhone 7.	AR headset	Not reported	Not reported	3 patients: 8 an 10 years old.

Table 1. Cont.

Author	Application	Technology	Display	Registration	Error	Data Set
Pietruski [42]	Fibula free flap harvest	7 markers. Actual, virtual registration. Sagittal surgical saw (GB129R) with a tracking adapter	HMD: Moverio BT-200 Smart Glasses, Epson	Marker-based, rigid	Not reported	756 osteotomies simulated.
Jiang [43]	Vascular localization system	CTA scan. No ionic contrast agent. Registration real time.	Microsoft HoloLens	Marker-based, rigid	Minimum 1.35 mm. Maximum 3.18 mm	7 operators.
Samei [44]	Laparoscopic radical prostatectomy	MRI. 3 transformations.	From Da Vinci to pc	Marker-based, rigid	Not reported	Agar prostate phantom ex vivo. 12 patients in vivo.
Rose [45]	Otolaryngology - head and neck surgery	CT, MeshLab and Unity.	Microsoft HoloLens	Marker-based, rigid	In measurement of accuracy: 2.47 ± 0.46 mm (1.99, 3.30)	A phantom.
Carl [46]	Transsphenoidal Surgery	C-arm radiographic fluoroscopy. Registration using iCT.	Operating microscopes HUD	Marker-based, rigid	Target registration error of 0.83 ± 0.44 mm	288 cases of transsphenoidal surgery.
Sharma [47]	Jaw surgery	Ct scan. Virtual scenes. Stereo views.	monitor	Marker-less, rigid	Alignment error 0.59 ± 0.62 mm	20 different samples after jaw surgery.
Abdel [48]	Foot sarcoma: Oncology	NDI Polaris. Smartphone AR application: FINO	Samsung galaxy	Marker-based, rigid	Not reported	A 39-year-old male patient.
Melero [49]	Rehabilitation: upper limbs	Myo armband. EMG data. Microsoft Kinect sensor	Monitor	Marker-less, rigid	Not reported	3 subjects, with 10 trials for each subject.
Tu [50]	Orthopedics	C++ application on pc. C# application in Unity. Connection via TCP/IP	HoloLens 2	Marker-based, rigid	Distance error: 1.61 ± 0.44 mm. 3D angle error: $1.46 \pm 0.46^\circ$	Phantom and cadaver experiment.
Cofano [51]	Spine Surgery	Ct, TeamViewer software and holosurgery	HoloLens 2	Marker-less, rigid	not reported	2 patients.
Heinrich [52]	Training	Not specified	HoloLens 1	Marker-based, rigid	Error rates ($p = 0.047$)	10 surgical trainees.

Table 2. Augmented Reality Applications.

Application	Percentage of Application
Telemonitoring	4%
Maxillofacial	23%
Liver Surgery	4%
Pediatric	4%
Orthopedics	27%
Oncology	19%
Training	8%
Puncture Surgery	7%
Bowel Surgery	4%

Table 3. Percentage of distribution of the displays of Augmented Reality used in medical applications evaluated in our study.

Type of Display	Percentage of Application
Smartphone	14%
Video see through Device	14%
Generic Head Mounted Display	17%
Unspecified Display	14%
Projected Directly over the Patient	3%
HoloLens 2	10%
HoloLens 1	28%

Table 4. Augmented Reality tracking and registration methods.

Tracking and Registration Methods	Percentage of Application
Marker based and Non-rigid Registration	4%
Markerless rigid Registration	20%
Markerless Non-rigid Registration	8%
Markerbased and rigid Registration	68%

4.1. Oncology

AR application is frequent in oncology, being used for osteosarcoma [53], mandibular [54], kidney and prostate cancer [55], meningioma [56], urological cancer, intracranial [57], neuro-oncological [58], and cancer of the liver [14]. Indeed, AR application ensures an accurate visualization of the tumor, identifying its edges and position during surgeries. The capability to visualize the real anatomical structures, such as convolutions, grooves, blood vessels and nervous tracts, allows control during their resection, and permits surgeons to try to eradicate the tumor while removing as little of the surrounding healthy tissue as possible [59–62]. Adequate planning also provides bone information that, together with information about the tumor, can lead to its successful removal [54]. Furthermore, the application of the AR to the innovative twin digital simulation technique can also be a medical support tool. In particular, this solution may allow oncologists to monitor and control the patient in addition to predicting the outcome of cancer through the development of appropriate simulation models and the creation of appropriate data sets [63].

4.2. Orthopedics

The application of AR in orthopedics [64–66] is relatively recent, dating back to the beginning of the 2000s [65]. The purpose of applying AR to orthopedic computer systems for computer-assisted surgery (CAS) is to increase the accuracy during surgeries, improving the possible outcomes and at the same time decreasing procedure-related complications. AR application can also contribute to the reduction of both surgery time and radiographic

doses for both patients and surgery teams. AR avoids the use of X-rays to see through the patients, reducing their exposure time [67].

4.3. Spinal Surgeries

AR is often used in spinal surgeries [68,69]. In this application, the accuracy is fundamental since an imprecision in the placement of an instrument can lead to spinal cord, nerve root or vascular injuries [70]. Open methods and direct visualization supporting the placement of the instrumentation, such as pedicle screw, have historically characterized this type of surgery [70]. The use of AR in spine surgery dates back to 1997 when Peuchot and his team developed a system for visualizing a vertebra during surgery [71]. For the past 20 years, Minimally Invasive Surgery (MIS) has been under investigation. Many articles have targeted study of Minimally Invasive Surgery (MIS) over the past 20 years. This has led to the introduction of new approaches such as the inoperative navigation that introduces several advantages to visualizing anatomy and precisely guiding surgeries. Furthermore, MIS ensures a higher level of accuracy, while minimizing possible damage to contiguous structures, providing access to deeper ones and improving dynamics and logistics in the operating room. The union of AR and MIS allows the surgeon to see more accurately inside the patient, possibly visualizing the preoperative planned drilling trajectory over the display, ensuring advantages in terms of accuracy, reduction of radiation exposure, blood loss and hospital stay. The drawbacks are mainly related to high costs and to the steepness of the learning curve, still too high [72].

4.4. Neurosurgery

The use of AR is quite frequent also in neurosurgery. Its application in this area has already been tackled in oncology, but it finds its maximum utility in neuronavigation [73]. It can help surgeons in reducing the consequences of the treatment, improving the quality of the surgery and reducing the operation time [74–77]. The first neuronavigation system (NNS) dates back to 1986. The advantage offered by AR associated to NSS consists in the mapping of the preoperative images directly onto the patient's visible surface, thus showing its anatomy on it [73,78].

4.5. Surgical Training and Medical Education

AR is assuming a fundamental and emerging role also for what concerns surgical training and medical education [79–83]. Its introduction results in providing students with a better anatomic conceptualization and allows surgical simulations to improve their performances [84]. AR ensures the possibility to practice surgeries without risks for the patient, saving the need of a supervisor and consequently reducing costs for the structures [85]. It also provides an increasing acquisition of skills such as speed, ability to multitask, accuracy, hand-eye coordination and bimanual operation. The evolution of this system has led to the use of telemonitoring, where experienced surgeons can train students remotely, and also to take part in consultations among experts located in different countries [86].

5. Discussion

Augmented reality is an innovative technology that presents several advantages, with new applications still in development. Knowing about this technology is every day becoming more important and can provide information to medical doctors and encourage new applications and deeper research. The reason for its increasing success is connected to the possibility it offers to visualize and interact with digital objects without having to lose view of the real world to watch the monitor displaying the medical imaging of the area of interest [1]. Moreover, research has shown its capacity to reduce the exposure to ionizing radiation. This aspect is important because it is well known that ionizing radiations can have harmful effects with possible effects on biomolecules such as DNA, lipids, proteins, and cancer risks [87–89]. One study [71] calculated the average of the staff radiation exposure using AR that, compared to the literature values, decreased to less than 0.01%. Moreover,

the absorbed dose of the patient exposition resulted in a decrease of its value up to 32% compared to the quantities due to conventional techniques [71]. All these aspects may allow the diffusion of AR and the possibility of assuming it as a systemic tool in medicine. The analysis of the studies considered showed that AR finds applications in many surgery domains and especially in the field of maxillofacial surgery, orthopedics and oncology. In particular, oncology is one of the areas of application particularly indicated. In this sense, AR finds a lot of applications in different kinds of cancer with the aim of facilitating and reducing the consequences of the treatment as well as improving outcomes [14,53–58]. Even with regard to orthopedics, the use of AR can be particularly recommended and is aimed at promoting the quality of surgical interventions, and therefore improving the outcomes as well as reducing the risk of complications [64–67]. In this sense, spinal surgeries represent an important area of application of AR where it can represent an important resource available to surgeons [68,69]. Regarding the available display technology, the results obtained show that the Optical Viewer by Microsoft, HoloLens, is the most used [36,39,90]. The marker-based method paired with the rigid registration was the most used solution in the context of AR tracking and registration methods [42–46]. In this regard, it is clear that the goal is to be able to reduce or eliminate the problems associated with tissue deformations. Unfortunately, the limited number of data available did not allow for more in-depth analyses on this issue. AR is a technology that is every day becoming more popular. Here we provided an idea of what it is, which technologies it is formed from and in which applications it is more popularly used. Unfortunately, some limitations still affect the application of AR in the surgical field. From our study, we noticed that the output is too much related to the accuracy of the registration and tracking systems that need to be as reliable as possible. Errors during those mentioned phases could lead to a misalignment of the VOs with the real world [91,92]. Mainly for the HMDs, the different field of view between human vision and visors represents an obstacle too [93,94]. Finally, one of the biggest issues that affects this technology is the vergence–accommodation conflict. In nature, the point where the eyes verge and focus is the same, while AR displays are featured by a fixed focal distance; consequently, the points of vergence and focus may be different. This causes discomfort, fatigue and different eye depth perception [95–97]. Some limitations characterize this study since the purpose of the review consisted in providing a contemporary view, but the results may exclude longitudinal trends. A potential problem in this study may also be the possible underrepresentation of documents about AR in surgery. Not all the studies published in the years analyzed may have been identified, despite trying to be as comprehensive as possible (according to the filters chosen). For our search, we used only those terms indicated in the Section 3, but others could have been chosen. Moreover, it is possible that some papers were excluded as they did not include those specific words, but their synonyms. Furthermore, our search was attempted using two multidisciplinary databases, Pubmed and Scopus, but others could have yielded additional studies. We decided to use only English terms and include only English articles. We did not reach out to experts on the topic for a consultation about additional studies that we may not have included.

6. Conclusions

AR is a technology that is increasingly being applied in surgery. This is due to the numerous advantages it offers although it is still an evolving technology. Since AR allows an accurate visualization of the anatomical structures and a good control of the activities performed during surgical resections, the fields in which it is most commonly used are orthopedics and oncology. For what concerns the displays, Microsoft HoloLens Viewer is the most used method. Likewise, the marker-based system combined with rigid registration is the most common solution for tracking and registration. The need for high accuracy of registration and tracking systems, as well as VOs misalignment problems and the possible vergence–accommodation conflict are important limitations. The latter can hinder the use of AR in surgery. The results of this study, as well as presenting the technological solutions used, show that AR can be applied in different fields of surgery. All of this can favor the

realization of further studies aimed at overcoming the current limitations on AR in the clinical setting as well as promoting its application. Considering the significant role that AR can play within the treatment of a large numbers of patients, further studies are needed to better define all possible fields of application of AR and the best technological solutions to be used.

Author Contributions: E.B., L.M., E.I. and L.B. designed the study. E.B., P.F. and L.B. performed the bibliographic research and organized the results. E.I., P.F., C.N. and L.M. aided in interpreting the results and wrote the final version of the manuscript with the support of all authors. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by Fondazione Cassa di Risparmio di Firenze, Florence, Italy (grant number 2020.1515). The authors thank Ian Webster PGCE for revising the English content.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Park, B.J.; Hunt, S.J.; Martin, C., III; Nadolski, G.J.; Wood, B.; Gade, T.P. Augmented and Mixed Reality: Technologies for Enhancing the Future of IR. *J. Vasc. Interv. Radiol.* **2020**, *31*, 1074–1082. <https://doi.org/10.1016/j.jvir.2019.09.020>.
2. Villarraga-Gómez, H.; Herazo, E.L.; Smith, S.T. X-ray computed tomography: From medical imaging to dimensional metrology. *Precis. Eng.* **2019**, *60*, 544–569. <https://doi.org/10.1016/j.precisioneng.2019.06.007>.
3. Cutolo, F. Augmented Reality in Image-Guided Surgery. In *Encyclopedia of Computer Graphics and Games*; Lee, N., Ed.; Springer International Publishing: Cham, Switzerland, 2017; pp. 1–11. https://doi.org/10.1007/978-3-319-08234-9_78-1.
4. Allison, B.; Ye, X.; Janan, F. *MIXR: A Standard Architecture for Medical Image Analysis in Augmented and Mixed Reality*; IEEE Computer Society: Washington, DC, USA, 2020; pp. 252–257. <https://doi.org/10.1109/AIVR50618.2020.00053>.
5. Marmulla, R.; Hoppe, H.; Mühling, J.; Eggers, G. An augmented reality system for image-guided surgery: This article is derived from a previous article published in the journal International Congress Series. *Int. J. Oral Maxillofac. Surg.* **2005**, *34*, 594–596. <https://doi.org/10.1016/j.ijom.2005.05.004>.
6. Peters, T.M. Image-guidance for surgical procedures. *Phys. Med. Biol.* **2006**, *51*, R505–R540. <https://doi.org/10.1088/0031-9155/51/14/r01>.
7. Eckert, M.; Volmerg, J.S.; Friedrich, C.M. Augmented Reality in Medicine: Systematic and Bibliographic Review. *JMIR Publ.* **2019**, *7*, e10967. <https://doi.org/10.2196/10967>.
8. Kim, Y.; Kim, H.; Kim, Y.O. Virtual Reality and Augmented Reality in Plastic Surgery: A Review. *Arch. Plast. Surg.* **2017**, *44*, 179–187. <https://doi.org/10.5999/aps.2017.44.3.179>.
9. Desselle, M.R.; Brown, R.A.; James, A.R.; Midwinter, M.J.; Powell, S.K.; Woodruff, M.A. Augmented and Virtual Reality in Surgery. *Comput. Sci. Eng.* **2020**, *22*, 18–26. <https://doi.org/10.1109/MCSE.2020.2972822>.
10. Pérez-Pachón, L.; Poyade, M.; Lowe, T.; Gröning, F. Image Overlay Surgery Based on Augmented Reality: A Systematic Review. In *Biomedical Visualisation. Advances in Experimental Medicine and Biology*; Springer International Publishing: Cham, Switzerland, 2020; Volume 1260, pp. 175–195. https://doi.org/10.1007/978-3-030-47483-6_10.
11. Zafari, F.; Gkelias, A.; Leung, K.K. A Survey of Indoor Localization Systems and Technologies. *IEEE Commun. Surv. Tutor.* **2019**, *21*, 2568–2599. <https://doi.org/10.1109/COMST.2019.2911558>.
12. Cheng, J.; Chen, K.; Chen, W. Comparison of marker-based AR and markerless AR: A case study on indoor decoration system. In Proceedings of the Lean and Computing in Construction Congress (LC3): Proceedings of the Joint Conference on Computing in Construction (JC3), Heraklion, Greece, 4–7 July 2017; pp. 483–490. <https://doi.org/10.24928/JC3-2017/0231>.
13. Thangarajah, A.; Wu, J.; Madon, B.; Chowdhury, A.K. Vision-based registration for augmented reality—a short survey. In Proceedings of the 2015 IEEE International Conference on Signal and Image Processing Applications (ICSIPA), Kuala Lumpur, Malaysia, 19–21 October 2015; pp. 463–468. <https://doi.org/10.1109/ICSIPA.2015.7412236>.
14. Quero, G.; Lapergola, A.; Soler, L.; Shahbaz, M.; Hostettler, A.; Collins, T.; Marescaux, J.; Mutter, D.; Diana, M.; Pessaux, P. Virtual and Augmented Reality in Oncologic Liver Surgery. *Surg. Oncol. Clin. N. Am.* **2019**, *28*, 31–44. <https://doi.org/10.1016/j.soc.2018.08.002>.
15. Tuceryan, M.; Greer, D.S.; Whitaker, R.T.; Breen, D.E.; Crampton, C.; Rose, E.; Ahlers, H.K. Calibration requirements and procedures for a monitor-based augmented reality system. *IEEE Trans. Vis. Comput. Graph.* **1995**, *1*, 255–273. <https://doi.org/10.1109/2945.466720>.
16. Maybody, M.; Stevenson, C.; Solomon, S.B. Overview of Navigation Systems in Image-Guided Interventions. *Tech. Vasc. Interv. Radiol.* **2013**, *16*, 136–143. <https://doi.org/10.1053/j.tvir.2013.02.008>.

17. Zhanat, M.; Vslor, H.A. Augmented Reality for Robotics: A Review. *Robotics* **2020**, *9*, 21. <https://doi.org/10.3390/robotics9020021>.
18. Mourtzis, D.; Angelopoulos, J.; Panopoulos, N. Intelligent Predictive Maintenance and Remote Monitoring Framework for Industrial Equipment Based on Mixed Reality. *Front. Mech. Eng.* **2020**, *6*, 578379. <https://doi.org/10.3389/fmech.2020.578379>.
19. Bruce, T.H. A Survey of Visual, Mixed, and Augmented Reality Gaming. *Assoc. Comput. Mach.* **2012**, *10*, 1. <https://doi.org/10.1145/2381876.2381879>.
20. Tricco, A.C.; Lillie, E.; Zarin, W.; O'Brien, K.K.; Colquhoun, H.; Levac, D.; Moher, D.; Peters, M.D.; Horsley, T.; Weeks, L.; et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann. Intern. Med.* **2018**, *169*, 467–473. <https://doi.org/10.7326/M18-0850>.
21. Schwam, Z.G.; Kaul, V.F.; Bu, D.D.; Iloreta, A.M.C.; Bederson, J.B.; Perez, E.; Cosetti, M.K.; Wanna, G.B. The utility of augmented reality in lateral skull base surgery: A preliminary report. *Am. J. Otolaryngol.* **2021**, *42*, 102942. <https://doi.org/10.1016/j.amjoto.2021.102942>.
22. Coelho, G.; Trigo, L.; Faig, F.; Vieira, E.V.; da Silva, H.P.G.; Acácio, G.; Zagatto, G.; Teles, S.; Gasparetto, T.P.D.; Freitas, L.F.; et al. The Potential Applications of Augmented Reality in Fetoscopic Surgery for Antenatal Treatment of Myelomeningocele. *World Neurosurg.* **2022**, *159*, 27–32. <https://doi.org/10.1016/j.wneu.2021.11.133>.
23. Gouveia, P.F.; Costa, J.; Morgado, P.; Kates, R.; Pinto, D.; Mavioso, C.; Anacleto, J.; Martinho, M.; Lopes, D.S.; Ferreira, A.R.; et al. Breast cancer surgery with augmented reality. *Breast* **2021**, *56*, 14–17. <https://doi.org/10.1016/j.breast.2021.01.004>.
24. Chen, F.; Cui, X.; Han, B.; Liu, J.; Zhang, X.; Liao, H. Augmented reality navigation for minimally invasive knee surgery using enhanced arthroscopy. *Comput. Methods Programs Biomed.* **2021**, *201*, 105952. <https://doi.org/10.1016/j.cmpb.2021.105952>.
25. Golse, N.; Petit, A.; Lewin, M.; Vibert, E.; Cotin, S. Augmented Reality during Open Liver Surgery Using a Markerless Non-rigid Registration System. *J. Gastrointest. Surg.* **2021**, *25*, 662–671. <https://doi.org/10.1007/s11605-020-04519-4>.
26. Gsaxner, C.; Pepe, A.; Li, J.; Ibrahimipasic, U.; Wallner, J.; Schmalstieg, D.; Egger, J. Augmented Reality for Head and Neck Carcinoma Imaging: Description and Feasibility of an Instant Calibration, Markerless Approach. *Comput. Methods Programs Biomed.* **2020**, *200*, 105854. <https://doi.org/10.1016/j.cmpb.2020.105854>.
27. Molina, C.; Sciubba, D.; Greenberg, J.; Khan, M.; Withamm, T. Clinical Accuracy, Technical Precision, and Workflow of the First in Human Use of an Augmented-Reality Head-Mounted Display Stereotactic Navigation System for Spine Surgery. *Oper. Neurosurg.* **2021**, *20*, 300–309. <https://doi.org/10.1093/ons/opaa398>.
28. Ackermann, J.; Florentin, L.; Armando, H.; Jess, S.; Mazda, F.; Stefan, R.; Patrick, Z.; Furnstahl, P. Augmented Reality Based Surgical Navigation of Complex Pelvic Osteotomies—A Feasibility Study on Cadavers. *Appl. Sci.* **2021**, *11*, 1228. <https://doi.org/10.3390/app11031228>.
29. Peng, L.; Chenmeng, L.; Changlin, X.; Zeshu, Z.; Junqi, M.; Jian, G.; Pengfei, S.; Ian, V.; M., P.T.; Chengbiao, D.; et al. A Wearable Augmented Reality Navigation System for Surgical Telementoring Based on Microsoft HoloLens. *Ann. Biomed. Eng.* **2021**, *49*, 287–298. <https://doi.org/10.1007/s10439-020-02538-5>.
30. Collins, T.; Pizarro, D.; Gasparini, S.; Bourdel, N.; Chauvet, P.; Canis, M.; Calvet, L.; Bartoli, A. Augmented Reality Guided Laparoscopic Surgery of the Uterus. *IEEE Trans. Med. Imaging* **2021**, *40*, 371–380. <https://doi.org/10.1109/TMI.2020.3027442>.
31. Arpaia, P.; Benedetto, E.D.; Duraccio, L. Design, implementation, and metrological characterization of a wearable, integrated AR-BCI hands-free system for health 4.0 monitoring. *Measurement* **2021**, *177*, 109280. <https://doi.org/10.1016/j.measurement.2021.109280>.
32. Shrestha, G.; Alsadoon, A.; P.W.C, P.; Al-Dala'in, T.; Alrubaie, A. A novel enhanced energy function using augmented reality for a bowel: Modified region and weighted factor. *Multimed. Tools Appl.* **2021**, *80*, 17893–17922. <https://doi.org/10.1007/s11042-021-10606-8>.
33. Wei, W.; Ho, E.; McCay, K.; Damasevicius, R.; Maskeliunas, R.; Esposito, A. Assessing Facial Symmetry and Attractiveness using Augmented Reality. *Pattern Anal. Appl.* **2021**, 1–17. <https://doi.org/10.1007/s10044-021-00975-z>.
34. Lee, D.; Yu, H.W.; Kim, S.; Yoon, J.; Lee, K.; Chai, Y.J.; Choi, J.Y.; Kong, H.J.; Lee, K.E.; Cho, H.S.; et al. Vision-based tracking system for augmented reality to localize recurrent laryngeal nerve during robotic thyroid surgery. *Sci. Rep.* **2020**, *10*, 8437. <https://doi.org/10.1038/s41598-020-65439-6>.
35. Hussain, R.; Lalande, A.; Marroquin, R.; Guigou, C.; Bozorg Grayeli, A. Video-based augmented reality combining CT-scan and instrument position data to microscope view in middle ear surgery. *Sci. Rep.* **2020**, *10*, 6767. <https://doi.org/10.1038/s41598-020-63839-2>.
36. Rüger, C.; Feufel, M.; Moosburner, S.; Özbek, C.; Pratschke, J.; Sauer, I. Ultrasound in augmented reality: A mixed-methods evaluation of head-mounted displays in image-guided interventions. *Int. J. Comput. Assist. Radiol. Surg.* **2020**, *15*, 1895–1905. <https://doi.org/10.1007/s11548-020-02236-6>.
37. Carl, B.; Bopp, M.H.A.; Benescu, A.; Saß, B.; Nimsky, C. Indocyanine green angiography visualized by augmented reality in aneurysm surgery. *World Neurosurg.* **2020**, *142*, e307–e315. <https://doi.org/10.1016/j.wneu.2020.06.219>.
38. Chan, J.Y.K.; Holsinger, F.C.; Liu, S.; Sorger, J.M.; Azizian, M.; Tsang, R.K.Y. Augmented reality for image guidance in transoral robotic surgery. *J. Robot. Surg.* **2019**, *14*, 579–583. <https://doi.org/10.1007/s11701-019-01030-0>.
39. Ferraguti, F.; Minelli, M.; Farsoni, S.; Bazzani, S.; Bonfè, M.; Vandanjon, A.; Puliatti, S.; Bianchi, G.; Secchi, C. Augmented Reality and Robotic-Assistance for Percutaneous Nephrolithotomy. *IEEE Robot. Autom. Lett.* **2020**, *5*, 4556–4563. <https://doi.org/10.1109/LRA.2020.3002216>.
40. Auloge, P.; Cazzato, R.; Ramamurthy, N.; De Marini, P.; Rousseau, C.; Garnon, J.; Charles, Y.; Steib, J.P.; Gangi, A. Augmented reality and artificial intelligence-based navigation during percutaneous vertebroplasty: a pilot randomised clinical trial. *Eur. Spine J.* **2020**, *29*, 1580–1589. <https://doi.org/10.1007/s00586-019-06054-6>.

41. Libaw, J.; Sinskey, J. Use of Augmented Reality During Inhaled Induction of General Anesthesia in 3 Pediatric Patients: A Case Report. *A&A Pract.* **2020**, *14*, e01219. <https://doi.org/10.1213/XAA.0000000000001219>.
42. Pietruski, P.; Majak, M.; Swiatek-Najwer, E.; Żuk, M.; Popek, M.; Jaworowski, J.; Mazurek, M. Supporting Fibula Free Flap Harvest With Augmented Reality: A Proof-of-Concept Study. *Laryngoscope* **2019**, *130*, 1173–1179. <https://doi.org/10.1002/lary.28090>.
43. Jiang, T.; Yu, D.; Wang, Y.; Zan, T.; Wang, S.; Li, Q. HoloLens-Based Vascular Localization System: Precision Evaluation Study With a Three-Dimensional Printed Model. *J. Med. Internet Res.* **2020**, *22*, e16852. <https://doi.org/10.2196/16852>.
44. Samei, G.; Tsang, K.; Kesch, C.; Lobo, J.; Hor, S.; Mohareri, O.; Chang, S.; Goldenberg, S.L.; Black, P.C.; Salcudean, S. A partial augmented reality system with live ultrasound and registered preoperative MRI for guiding robot-assisted radical prostatectomy. *Med. Image Anal.* **2020**, *60*, 101588. <https://doi.org/10.1016/j.media.2019.101588>.
45. Rose, A.; Kim, H.; Fuchs, H.; Frahm, J.M. Development of augmented-reality applications in otolaryngology-head and neck surgery: Augmented Reality Applications. *Laryngoscope* **2019**, *129*, S1–S11. <https://doi.org/10.1002/lary.28098>.
46. Carl, B.; Bopp, M.; Voellger, B.; Saß, B.; Nimsky, C. Augmented reality in transsphenoidal surgery. *World Neurosurg.* **2019**, *125*, e873–e883. <https://doi.org/10.1016/j.wneu.2019.01.202>.
47. Sharma, A.; Alsadoon, A.; P.W.C, P.; Al-Dala'in, T.; Haddad, S. A novel augmented reality visualization in jaw surgery: enhanced ICP based modified rotation invariant and modified correntropy. *Multimed. Tools Appl.* **2021**, *80*, 1–25. <https://doi.org/10.1007/s11042-021-10787-2>.
48. Abdel Al, S.; Abou Chaar, M.K.; Mustafa, A.; Al-Hussaini, M.; Barakat, F.; Asha, W. Innovative Surgical Planning in Resecting Soft Tissue Sarcoma of the Foot Using Augmented Reality With a Smartphone. *J. Foot Ankle Surg.* **2020**, *59*, 1092–1097. <https://doi.org/10.1053/j.jfas.2020.03.011>.
49. Melero, M.; Hou, A.; Cheng, E.; Tayade, A.; Lee, S.C.; Unberath, M.; Navab, N. Upbeat: Augmented Reality-Guided Dancing for Prosthetic Rehabilitation of Upper Limb Amputees. *J. Healthc. Eng.* **2019**, *2019*, 1–9. <https://doi.org/10.1155/2019/2163705>.
50. Tu, P.; Yao, G.; Lungu, A.; Li, D.; Wang, H.; Chen, X. Augmented Reality Based Navigation for Distal Interlocking of Intramedullary Nails Utilizing Microsoft HoloLens 2. *Comput. Biol. Med.* **2021**, *133*, 104402. <https://doi.org/10.1016/j.combiomed.2021.104402>.
51. Cofano, F.; Di Perna, G.; Bozzaro, M.; Longo, A.; Marengo, N.; Zenga, F.; Zullo, N.; Cavalieri, M.; Damiani, L.; Boges, D.; et al. Augmented Reality in Medical Practice: From Spine Surgery to Remote Assistance. *Front. Surg.* **2021**, *8*, 657901. <https://doi.org/10.3389/fsurg.2021.657901>.
52. Heinrich, F.; Huettl, F.; Schmidt, G.; Paschold, M.; Kneist, W.; Huber, T.; Hansen, C. HoloPointer: A virtual augmented reality pointer for laparoscopic surgery training. *Int. J. CARS* **2021**, *16*, 161–168. <https://doi.org/10.1007/s11548-020-02272-2>.
53. Brookes, M.J.; Chan, C.D.; Baljer, B.; Wimalagunaratna, S.; Crowley, T.P.; Ragbir, M.; Irwin, A.; Gamie, Z.; Beckingsale, T.; Ghosh, K.M.; et al. Surgical Advances in Osteosarcoma. *Cancers* **2021**, *13*, 388. <https://doi.org/10.3390/cancers13030388>.
54. Kraeima, J.; Glas, H.; Merema, B.; Vissink, A.; Spijkervet, F.; Witjes, M. Three-dimensional virtual surgical planning in the oncologic treatment of the mandible. *Oral Dis.* **2021**, *27*, 14–20. <https://doi.org/10.1111/odi.13631>.
55. Wake, N.; Nussbaum, J.E.; Elias, M.I.; Nikas, C.V.; Bjurlin, M.A. 3D Printing, Augmented Reality, and Virtual Reality for the Assessment and Management of Kidney and Prostate Cancer: A Systematic Review. *Urology* **2020**, *143*, 20–32. <https://doi.org/10.1016/j.urology.2020.03.066>.
56. Alexandre, L.; Torstein, M.; Karl, S.; Marco, C. Augmented reality in intracranial meningioma surgery: A case report and systematic review. *J. Neurosurg. Sci.* **2020**, *64*, 369–376. <https://doi.org/10.23736/S0390-5616.20.04945-0>.
57. Lee, C.; Wong, G.K.C. Virtual reality and augmented reality in the management of intracranial tumors: A review. *J. Clin. Neurosci.* **2019**, *62*, 14–20. <https://doi.org/10.1016/j.jocn.2018.12.036>.
58. Gerard, I.J.; Kersten-Oertel, M.; Petrecca, K.; Sirhan, D.; Hall, J.A.; Collins, D.L. Brain shift in neuronavigation of brain tumors: A review. *Med. Image Anal.* **2017**, *35*, 403–420. <https://doi.org/10.1016/j.media.2016.08.007>.
59. Inoue, D.; Cho, B.; Mori, M.; Kikkawa, Y.; Amano, T.; Nakamizo, A.; Yoshimoto, K.; Mizoguchi, M.; Tomikawa, M.; Hong, J.; et al. Preliminary study on the clinical application of augmented reality neuronavigation. *J. Neurol. Surg. Part A Cent. Eur. Neurosurg.* **2013**, *74*, 71–76. <https://doi.org/10.1055/s-0032-1333415>.
60. Besharati, T.L.; Mehran, M. Augmented reality-guided neurosurgery: accuracy and intraoperative application of an image projection technique. *J. Neurosurg.* **2015**, *123*, 206–211. <https://doi.org/10.3171/2014.9.JNS141001>.
61. Cabrilo, I.; Sarrafzadeh, A.; Bijlenga, P.; Landis, B.N.; Schaller, K. Augmented reality-assisted skull base surgery. *Neurochirurgie* **2014**, *60*, 304–306. <https://doi.org/10.1016/j.neuchi.2014.07.001>.
62. Contreras López, W.; Navarro, P.; Crispin, S. Intraoperative clinical application of augmented reality in neurosurgery: A systematic review. *Clin. Neurol. Neurosurg.* **2019**, *177*, 6–11. <https://doi.org/10.1016/j.clineuro.2018.11.018>.
63. Mourtzis, D.; Angelopoulos, J.; Panopoulos, N.; Kardamakis, D. A Smart IoT Platform for Oncology Patient Diagnosis based on AI: Towards the Human Digital Twin. *Procedia CIRP* **2021**, *104*, 1686–1691. <https://doi.org/10.1016/j.procir.2021.11.284>.
64. Casari, F.A.; Navab, N.; Hruby, L.A.; Philipp, K.; Ricardo, N.; Romero, T.; de Lourdes dos Santos Nunes Fatima.; C., Q.M.; Furnstahl, P.; Mazda, F. Augmented Reality in Orthopedic Surgery Is Emerging from Proof of Concept Towards Clinical Studies: a Literature Review Explaining the Technology and Current State of the Art. *Curr. Rev. Musculoskelet. Med.* **2021**, *14*, 192–203. <https://doi.org/10.1007/s12178-021-09699-3>.
65. Bagwe, S.; Singh, K.; Kashyap, A.; Arora, S.; Maini, L. Evolution of augmented reality applications in Orthopaedics: A systematic review. *J. Arthrosc. Jt. Surg.* **2021**, *8*, 84–90. <https://doi.org/10.1016/j.jajs.2021.02.006>.

66. Negrillo-Cardenas, J.; Jimenez-Perez, J.R.; Feito, F.R. The role of virtual and augmented reality in orthopedic trauma surgery: From diagnosis to rehabilitation. *Comput. Methods Programs Biomed.* **2020**, *191*, 105407. <https://doi.org/10.1016/j.cmpb.2020.105407>.
67. Jud, L.; Fotouhi, J.; Andronic, O.; Aichmair, A.; Osgood, G.; Navab, N.; Farshad, M. Applicability of augmented reality in orthopedic surgery—A systematic review. *BMC Musculoskelet. Disord.* **2020**, *21*, 103. <https://doi.org/10.1186/s12891-020-3110-2>.
68. Molina, C.A.; Phillips, F.M.; Poelstra, K.A.; Colman, M.; Khoo, L.T. 151. A cadaveric precision and accuracy analysis of augmented reality mediated percutaneous pedicle implant insertion. *Spine J.* **2020**, *20*, S74. <https://doi.org/10.3171/2020.6.SPINE20370>.
69. Burstrom, G.; Persson, O.; Edstrom, E.; Elmi-Terander, A. Augmented reality navigation in spine surgery: a systematic review. *Acta Neurochir.* **2021**, *163*, 843–852. <https://doi.org/10.1007/s00701-021-04708-3>.
70. Frank, Y.; Georgios, M.; Kosuke, S.; Jeremy, S. Current innovation in virtual and augmented reality in spine surgery. *Ann. Transl. Med.* **2021**, *9*, 94–94. <https://doi.org/10.21037/atm-20-1132>.
71. D.Sakai.; Joyce, K.; Sugimoto, M.; N. Horikita, A.H.; Sato, M.; Devitt, A.; Watanabe, M. Augmented, virtual and mixed reality in spinal surgery: A real-world experience. *J. Vasc. Intervent Radiol.* **2020**, *3*, 28. <https://doi.org/10.1177/2309499020952698>.
72. Vadalà, G.; Salvatore, S.D.; Ambrosio, L.; F. R.; R. P.; V., D. Robotic Spine Surgery and Augmented Reality Systems: A State of the Art. *Neurospine* **2020**, *17*, 88–100. <https://doi.org/10.14245/ns.2040060.030>.
73. Liu, T.; Yonghang, T.; Chengming, Z.; Lei, W.; Jun, Z.; Junjun, P.; Shi, J. Augmented reality in neurosurgical navigation: A survey. *Int. J. Med Robot. Comput. Assist. Surg. MRCAS* **2020**, *16*, e2160. <https://doi.org/10.1002/rcs.2160>.
74. Deng, W.; Li, F.; Wang, M.; Song, Z. Easy-to-Use Augmented Reality Neuronavigation Using a Wireless Tablet PC. *Stereotact. Funct. Neurosurg.* **2014**, *92*, 17–24. <https://doi.org/10.1159/000354816>.
75. Gumprecht, H.K.; Widenka, D.C.; Lumenta, C.B. BrainLab VectorVision Neuronavigation System: Technology and clinical experiences in 131 cases. *Neurosurgery* **1999**, *44*, 97–104. <https://doi.org/10.1097/00006123-199901000-00056>.
76. Grunert, P.; Darabi, K.; Espinosa, J.; Filippi, R. Computer-aided navigation in neurosurgery. *Neurosurg. Rev.* **2003**, *26*, 73–99. <https://doi.org/10.1007/s10143-003-0262-0>.
77. Cleary, K.; Peters, T.M. Image-Guided Interventions: Technology Review and Clinical Applications. *Annu. Rev. Biomed. Eng.* **2010**, *12*, 119–142. <https://doi.org/10.1146/annurev-bioeng-070909-105249>.
78. Incekara, F.; Smits, M.; Dirven, C.; Vincent, A. Clinical Feasibility of a Wearable Mixed-Reality Device in Neurosurgery. *World Neurosurg.* **2018**, *118*, e422–e427. <https://doi.org/10.1016/j.wneu.2018.06.208>.
79. Moro, C.; Phelps, C.; Redmond, P.; Stromberga, Z. HoloLens and mobile augmented reality in medical and health science education: A randomised controlled trial. *Br. J. Educ. Technol.* **2020**, *52*, 680–694. <https://doi.org/10.1111/bjet.13049>.
80. Kumar, N.; Pandey, S.; Rahman, E. A Novel Three-Dimensional Interactive Virtual Face to Facilitate Facial Anatomy Teaching Using Microsoft HoloLens. *Aesthetic Plast. Surg.* **2021**, *45*, 1005–1011. <https://doi.org/10.1007/s00266-020-02110-5>.
81. Moro, C.; Phelps, C.; Jones, D.; Stromberga, Z. Using Holograms to Enhance Learning in Health Sciences and Medicine. *Med. Sci. Educ.* **2020**, *30*, 1351–1352. <https://doi.org/10.1007/s40670-020-01051-7>.
82. Parsons, D.; Mac Callum, K. Current Perspectives on Augmented Reality in Medical Education: Applications, Affordances and Limitations. *Adv. Med Educ. Pract.* **2021**, *12*, 77–91. <https://doi.org/10.2147/AMEP.S249891>.
83. Williams, M.A.; McVeigh, J.; Handa, A.I.; Regent, L. Augmented reality in surgical training: A systematic review. *Postgrad. Med. J.* **2020**, *96*, 537–542. <https://doi.org/10.1136/postgradmedj-2020-137600>.
84. Cao, C.; Cerfolio, R.J. Virtual or Augmented Reality to Enhance Surgical Education and Surgical Planning. *Thorac. Surg. Clin.* **2019**, *29*, 329–337. <https://doi.org/10.1016/j.thorsurg.2019.03.010>.
85. Yeung, A.W.K.; Tosevska, A.; Klager, E.; Eibensteiner, F.; Laxar, D.; Jivko, S.; Marija, G.; Sebastian, Z.; Stefan, K.; Rik, C.; et al. Virtual and Augmented Reality Applications in Medicine: Analysis of the Scientific Literature. *J. Med Internet Res.* **2021**, *23*, e25499. <https://doi.org/10.2196/25499>.
86. McKnight, R.R.; Pean, C.A.; Buck, J.S.; Hwang, J.S.; Hsu, J.R.; Pierrie, S.N. Virtual Reality and Augmented Reality—Translating Surgical Training into Surgical Technique. *Curr. Rev. Musculoskelet. Med.* **2020**, *13*, 663–674. <https://doi.org/10.1007/s12178-020-09667-3>.
87. Fazel, R.; Krumholz, H.M.; Wang, Y.; Ross, J.S.; Chen, J.; Ting, H.H.; Shah, N.D.; Nasir, K.; Einstein, A.J.; Nallamothu, B.K. Exposure to low-dose ionizing radiation from medical imaging procedures. *N. Engl. J. Med.* **2009**, *361*, 849–857. <https://doi.org/10.1056/NEJMoa0901249>.
88. Hong, J.Y.; Han, K.; Jung, J.H.; Kim, J.S. Association of exposure to diagnostic low-dose ionizing radiation with risk of cancer among youths in South Korea. *JAMA Netw. Open* **2019**, *2*, e1910584. <https://doi.org/10.1001/jamanetworkopen.2019.10584>.
89. Reisz, J.; Bansal, N.; Qian, J.; Zhao, W.; Furdui, C. Effects of ionizing radiation on biological molecules—mechanisms of damage and emerging methods of detection. *Antioxidants Redox Signal.* **2014**, *21*, 260–292. <https://doi.org/10.1089/ars.2013.5489>.
90. Peng, H.; Ding, C. Minimum redundancy and maximum relevance feature selection and recent advances in cancer classification. *Feature Sel. Data Min.* **2005**, *3*, 185–205. <https://doi.org/10.1142/S0219720005001004>.
91. Singh, V.K.; Ali, A.; Nair, P.S. A Report on Registration Problems in Augmented Reality. *Int. J. Eng. Res. Technol.* **2014**, *3*, 819–821.
92. Chen, Y.; Wang, Q.; Chen, H.; Song, X.; Tang, H.; Tian, M. An overview of augmented reality technology. *J. Phys. Conf. Ser.* **2019**, *1237*, 022082. <https://doi.org/10.1088/1742-6596/1237/2/022082>.
93. Lee, Y.H.; Zhan, T.; Wu, S.T. Prospects and challenges in augmented reality displays. *Virtual Real. Intell. Hardw.* **2019**, *1*, 10–20. <https://doi.org/10.3724/SP.J.2096-5796.2018.0009>.
94. Ren, D.; Goldschwendt, T.; Chang, Y.; Höllerer, T. Evaluating wide-field-of-view augmented reality with mixed reality simulation. In Proceedings of the 2016 IEEE Virtual Reality (VR), Greenville, SC, USA, 19–23 March 2016; pp. 93–102. <https://doi.org/10.1109/VR.2016.7504692>.

-
95. Zhou, Y.; Zhang, J.; Fang, F. Vergence-accommodation conflict in optical see-through display: Review and prospect. *Results Opt.* **2021**, *5*, 100160. <https://doi.org/10.1016/j.rio.2021.100160>.
 96. Erkelens, I.M.; MacKenzie, K.J. 19-2: Vergence-Accommodation Conflicts in Augmented Reality: Impacts on Perceived Image Quality. *SID Symp. Dig. Tech. Pap.* **2020**, *51*, 265–268. <https://doi.org/10.1002/sdtp.13855>.
 97. Kim, J.; Kane, D.; Banks, M.S. The rate of change of vergence–Accommodation conflict affects visual discomfort. *Vis. Res.* **2014**, *105*, 159–165. <https://doi.org/10.1016/j.visres.2014.10.021>.