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The HoloLens in medicine: A systematic review and taxonomy

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ABSTRACT

The HoloLens (Microsoft Corp., Redmond, WA), a head-worn, optically see-through augmented reality (AR) display, is the main player in the recent boost in medical AR research. In this systematic review, we provide a comprehensive overview of the usage of the first-generation HoloLens within the medical domain, from its release in March 2016, until the year of 2021. We identified 217 relevant publications through a systematic search of the PubMed, Scopus, IEEE Xplore and SpringerLink databases. We propose a new taxonomy including use case, technical methodology for registration and tracking, data sources, visualization as well as validation and evaluation, and analyze the retrieved publications accordingly. We find that the bulk of research focuses on supporting physicians during interventions, where the HoloLens is promising for procedures usually performed without image guidance. However, the consensus is that accuracy and reliability are still too low to replace conventional guidance systems. Medical students are the second most common target group, where AR-enhanced medical simulators emerge as a promising technology. While concerns about human-computer interactions, usability and perception are frequently mentioned, hardly any concepts to overcome these issues have been proposed. Instead, registration and tracking lie at the core of most reviewed publications, nevertheless only few of them propose innovative concepts in this direction. Finally, we find that the validation of HoloLens applications suffers from a lack of standardized and rigorous evaluation protocols. We hope that this review can advance medical AR research by identifying gaps in the current literature, to pave the way for novel, innovative directions and translation into the medical routine.

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1. Introduction

Augmented Reality (AR) enhances the users' perception of the environment, by expanding the reality with virtual content, and allows the user to see and interact with both the physical world and digital content at the same time. While it can target all human senses, e.g., hearing, tactile perception or even taste,

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most recent AR research focuses on vision. This is likely connected to the fact that recent consumer-oriented developments made visual AR devices accessible to the general public. As a result, the AR field saw a strong growth in various domains, such as industry and entertainment. A main player in this new development was the HoloLens (Microsoft Corp., Redmond, WA), released in 2016. The HoloLens was originally marketed for applications in gaming, communication and 3D modeling; nevertheless, it quickly drew the attention from the medical domain. This development is unsurprising – after all, one can hardly imagine a professional domain in which AR could have a more significant impact than in medicine. For example, AR has the potential to grant physicians the ability to see critical structures within the patient through obstructive anatomy, without making a single incision. Wearable devices, such as the HoloLens, can make critical patient information permanently and readily available, and show them directly in the vision of the physicians. In open interventions with direct view of the patient anatomy, this approach may allow them to keep their focus on the patient only. For minimally invasive procedures, on the other hand, it could reduce clutter by monitors. Immersing remote experts for assistance and monitoring into the mixed reality environment via telemedicine is another promising scenario, which would permit more and more patients to benefit from their expertise, in particular in disadvantaged areas, where medical care is more sparse (Huang et al. (2019a)). Using AR, Patients could be monitored and guided through various treatment and rehabilitation stages, and AR could help them understand their conditions and treatment options, providing visual aids and explanations in an interactive and engaging way. Medical students, on the other hand, could improve their skills in critical interventions in a safe, virtually enhanced setting or immerse themselves in 3D anatomy. Overall, AR can improve the quality and accessibility of healthcare. The HoloLens 1, as the first wearable, fully untethered and self-localizing AR device, was certainly an important step towards the future of AR in medicine. But how much could it contribute, and how far are we in making the aforementioned scenarios a reality?

In this systematic review, we provide a comprehensive overview of works that reported the usage of the first-generation HoloLens in the medical domain from 2016 to 2021. We identified 217 relevant publications through a systematic search of the PubMed, Scopus, IEEE Xplore and Springer Link databases. We introduce a new taxonomy consisting of intended use case, technical methodology concerning registration and tracking, data sources and data visualization, as well as evaluation and validation, and analyze the retrieved publications accordingly. Throughout our review, we highlight principal findings which include:

- Supporting physicians during interventions is, by far, the most common application of the HoloLens, although it has the highest technical demands. Applications in lower risk scenarios, such as educational systems for medical students or AR-supported therapies for patients are far less common.
- The high demands in accuracy and reliability of procedures prohibit the application of the HoloLens as a surrogate for conventional image-guided interventions. However, the HoloLens is promising for interventions usually performed without guidance, due to its ergonomic advantages over conventional image guidance systems.
- Hybrid medical simulators, enhanced with HoloLens guidance, emerge as a promising technology, which has been shown to consistently improve the skill gain of medical students during training.

We further identify gaps and discuss challenges and limitations, such as:

- A lack of standardized, rigorous evaluation protocols impedes the validation and comparability of medical HoloLens applications. This can be a major factor hindering the translation of research prototypes into medical routine.
- Although many studies evaluate their AR systems in terms of human-computer interaction, usability and perception of virtual content, and mention severe concerns in these areas, novel concepts or technologies to overcome them are hardly ever proposed.
- Although registration and tracking lie at the core of most reviewed publications, only few of them propose innovative technologies. Many works apply variants of the same registration and tracking methods to different interventions, with limited methodological innovations.

This review outlines the impact the first generation HoloLens had in the medical area. By analyzing works proposed for a common platform, we hope to enable a fair, unprejudiced comparison between the introduced systems and technologies, and a more indepth analysis of challenges and limitations. The capabilities of the HoloLens, such as environmental understanding and optical see-through 3D visualization, have certainly set a new standard for medical AR devices, overcoming previous problems, such as self-localization. Although novel hardware is already setting foot in medical AR, we think that our principal findings will remain relevant and continue to challenge researchers in the future. Our taxonomy can be applied to past and future medical AR research using other devices as well, to extract information in a structured and organized way. We hope that this will help researchers in identifying patterns, trends and gaps in the literature and promote a more consistent communication of contributions.

2. Background

2.1. Augmented reality

One of the most common definitions of AR stems from the virtuality continuum definition by Milgram and Kishino (1994), who describe AR as a mixed reality (MR), which contains mainly real elements, enhanced with virtual content. Azuma (1997) further characterizes AR environments as combining reality and virtuality by registration in 3D, while being interactive in real-time. Although this definition makes clear that AR can appeal to all senses, it is mostly concerned with visual data. In the medical field, where digital imaging techniques provide rich information, AR has huge potential. Unsurprisingly, once technology was advanced enough to consider real-world AR applications, it quickly drew the attention from the medical domain.

AR displays. Generally, visual AR displays can be categorized into video see-through (VST), optical see-through (OST) and spatial displays (Schmalstieg and Hollerer (2016)). VST displays observe the scene through a camera, and the camera images can be combined digitally with virtual information. OST displays, on the other hand, directly overlay the reality with virtual objects using optical combiners, such as half-transparent lenses.

Spatial displays directly cast imagery onto real objects. The first medical AR systems were introduced as early as the late 1980s, with Roberts et al. (1986) describing the first system, an operating microscope augmented with segmented computed tomography (CT) images. A head-mounted displays (HMD) continued to be a popular display choice in early medical AR systems, as, for example, demonstrated by the works in the 1990s (State et al. (1996); Fuchs et al. (1996)) and in the early 2000 by Sauer et al. (2001), who developed a VST HMD for medical applications. An HMD is a natural choice for medicine, as it is mobile, can intuitively align the head gaze of the wearer with the viewpoint of the content, and allows a permanent anchoring of content to the users' view. Furthermore, it keeps the hands of the wearer free. However, early HMD designs could not easily fulfill the high demands of medical AR systems in terms of performance, latency and accuracy, which require powerful computational infrastructure. Usually, this challenge resulted in bulky form factors, with wired connections between HMD and sufficiently capable computing and tracking infrastructure, making these systems difficult to implement in real clinical scenarios. Still, head-locked microscopes found their way not only into research (Drouin et al. (2017)) but also into clinical practice, e.g., the Zeiss Kinevo (Carl Zeiss AG, Oberkochen, Germany) or the Leica ARveo (Leica Camera AG, Wetzlar, Germany), and OST (Chaballout et al. (2016); Markovic et al. (2017)) and VST (Boschmann et al. (2016); Chen et al. (2015)) displays also continued to be relevant in research. In the years between 2011 and 2017, we see a shift towards world-localized displays, such as stationary monitors or projector systems (Eckert et al. (2019)). The release of the HoloLens 1, which was the first self-contained, mobile AR-HMD, subsequently caused research attention to shift towards OST displays again (Gsaxner et al. (2021a)).

Registration and tracking. Alignment between reality and virtuality is a fundamental concept of AR, which is realized via registration. In a medical context, registration is mostly desired between medical data, often volumetric imaging such as CT or magnetic resonance imaging (MRI), and the patient. To maintain registration and synchronization of the viewpoint in the user's perspective, the position and orientation of the AR viewing camera with respect to the environment need to be tracked. Thus, tracking for self-localization is integral in any AR system.

For tracking and registration, two paradigms can be distinguished: *outside-in* and *inside-out*. Outside-in (or extrinsic) tracking refers to strategies where external sensors (e.g., cameras) are stationed around the user and thus, observe the movement of the device from the outside. Such methods can be very accurate, but require many components and only work in a limited space. In inside-out (or intrinsic) tracking, the sensors are integrated within the AR device itself, and, thus, the device can self-locate within an unprepared environment. Although diverse types of sensors can be used for tracking, vision-based methods, relying on visible light, infrared (IR) cameras or depth sensors, have dominated the field for many years (Zhou et al. (2008)). For vision-based tracking, observable features need to be visible to the tracking cameras. Typically, these features can be divided into artificial features for *marker-based* tracking, and natural features for marker-less tracking.

Marker-based tracking relies on indicators of pre-defined pattern and size, whose location in relation to the real world is precisely known. These indicators can, for example, be fiducial markers visible to standard RGB cameras, or IR emitters (either active or passive), which are more robust to variable lighting conditions. Medical technology has appropriated this principle years ago: IR emitting markers are well-established in surgical navigation systems, where they are anchored in rigid tissue, such as the patients' bones, and on surgical instruments, while being tracked with stereo IR cameras. This approach allows a computation of the relative position of tools in relation to critical anatomy.

Marker-less systems do not require artificial objects and, instead, rely on naturally observable features. Simultaneous localization and mapping (SLAM) (Durrant-Whyte and Bailey (2006)) and its variants are the most common markerless tracking techniques for self-localization. SLAM is a method used by robots and other autonomous devices to build a map of their environment and to determine their own location within that map. This is typically done by fusing a combination of sensors, e.g., visible light, depth and GPS, as well as algorithms that allow the device to understand its surroundings. This allows devices to navigate or reason about their environment and perform tasks without relying on pre-existing maps or external localization systems. Consequently, a solution to the SLAM problem results in the orientation and position of the AR device with respect to some world frame, and a 3D map of regions already observed by the device. Virtual content can then be placed manually or with the aid of markers into the mapped world. Other markerless tracking approaches involve models or templates of known, stationary real-world objects, which are fitted to their real counterparts, either through 2D-3D (in case of visible light cameras) or 3D-3D (if 3D information of the scene is available) matching. Since 3D models of the patient's skin surface are typically available from medical imaging, such methods are well-suited for medical applications.

2.2. The HoloLens

The first generation HoloLens is wearable computer glass (often also referred to as "smartglass"), which delivers augmented reality experiences through a 3D optical see-through head-mounted display (OST-HMD). It was developed by Microsoft and rolled out in 2016. The HoloLens was marketed as the first AR device to run fully untethered, meaning that it requires no connections to external infrastructure. Earlier HMDs, such as the Moverio (Epson, Suwa, Japan), already ran independently of stationary infrastructure, but still required a wired connection to a body-worn device. Contrary to other mixed or virtual reality headsets, a distinct capability of the HoloLens is its ability to self-localize in an unprepared environment, without external tracking infrastructure or markers, making it completely self-contained (Zeller et al. (2019)).

The HoloLens features a set of built-in sensors, including an inertial measurement unit (IMU), four side-facing visible light cameras for capturing the environment, a time-of-flight (ToF) depth sensor, an ambient light sensor, four microphones and a front-facing, high definition photo/video camera. Only microphone and photo/video camera were accessible to developers in the beginning. In mid 2018, however, the so-called Research Mode enabled access to ToF and environmental understanding cameras for research purposes (Ferrone and Coulter (2020)). Stereoscopic virtual content is displayed on two semitransparent combiner lenses in front of the user's eyes for 3D vision, combined with the real environment. The equivalent of two 720p displays with four color fields, one in front of each eye, allows a diagonal field of view (FOV) of 34 degrees, with a resolution of 47 pixels per degree (Goode (2019)). The displays refresh at a rate of 240 Hz per color field, resulting in rendering at 60 frames per second. The displays are fixed to an optical focus distance of 2 m from the user. It is recommended to place virtual objects close to this virtual plane for ideal user comfort and image quality. Sound is delivered via built-in speakers. The HoloLens is equipped with an Intel Atom x5 32-bit central processing unit (CPU) with 1 GB of random access memory (RAM), and has 64 GB of storage. Its active battery life is specified at 2-3 hours.

A custom, dedicated hardware accelerator, the so-called "Holographic Processing Unit" with 1 GB of additional RAM, enables efficient processing of the sensor data in parallel to processes running on the HoloLens' CPU. This custom chip facilitates a set of on-board capabilities to understand the users actions, as well as the environment around the device. A proprietary SLAM algorithm continuously constructs and refines a spatial map of the environment, and locates the device within it, resulting in on-board, marker-less inside-out tracking of the HoloLens (Klein (2017)). Determination of the users' head gaze direction is supported via tracking their head movement. Users can interact with virtual content via hand gestures or voice commands, both of which are automatically recognized. Additional input devices can be connected to the device via Bluetooth 4.1 LE, for example, the included clicker, a gamepad or an external keyboard. Connections can further be established wireless via Wi-Fi 802.11ac, or wired via Micro USB 2.0. The detailed hardware specifications of the device are listed in the appendix, Table A.8.

Commercial usage of the HoloLens in healthcare. While we focus on research about medical applications of the HoloLens in this review, several commercial products based on the HoloLens (first and second generation) have been proposed or are in development by healthcare companies. For example, SonoEyes (Incremed AG, Zurich, Switzerland), integrates video outputs of imaging systems (such as ultrasound) with the HoloLens. The MediView platforms (MediView, Cleveland, USA) also support ultrasound guidance, together with see-through visualization of anatomical structures. OpenSight (Novarad, Provo, UT, USA) is a surgical navigation system which supports seethrough visualizations with the HoloLens. Siemens Healthineers (Erlangen, Germany) has demonstrated that the HoloLens can be used for photo-realistic Cinematic Rendering of CT and MRI. CAE healthcare (CAE Inc., Montreal, Canada) provides several HoloLens-supported medical simulators, e.g. for ultrasound examinations, childbirth and emergency care training. VSI HoloMedicine by apoQlar (Hamburg, Germany) proposes

a comprehensive platform for the entire clinical workflow, including intervention planning and support, patient education and resident training. We believe that this increased interest from industry will accelerate research and development of both software and hardware.

Hardware limitations of the HoloLens. It is important to remember that the HoloLens was not designed for high-precision medicine, and several hardware limitations are confining clinical usability for many interesting medical tasks. For example, it has been shown by Hübner et al. (2020) that the HoloLens SLAM and depth sensor is afflicted by noise and its accuracy drifts over time. To avoid spatio-temporal dissonance between virtual and real world, tracking, registration and rendering need to run in real time (Ferrari et al. (2019)). This prohibits expensive computations running on the device directly, and remote solutions come with additional latency. Another limitation is the focus plane of the HoloLens, which is fixed at 2 m, while medical procedures are typically carried out at arm's length. Condino et al. (2019) show that this limits the usability of the HoloLens for high-precision manual tasks, such as surgery. An issue especially for applications with high accuracy demands is display calibration: Since in OST-HMDs, no direct knowledge about the view of the user is available, a user-dependent calibration is necessary for a precise alignment of virtual objects with the user's view (Azimi et al. (2017)). The HoloLens performs this calibration in a rather simplistic manner, based on the interpupillary distance of users, which is subobtimal (Hu et al. (2020)) and may lead to a substantial perceived offset in the view of the user, even in cases of otherwise perfect registration. Furthermore, the active battery life of 2-3 hours is too short for many interventions, and the small field of view of 30° limits the amount of virtual content available to the user.

3. Methodology

3.1. Search strategy and selection process

We conducted a systematic review of existing research about the HoloLens applied in medical scenarios. The review followed the Preferred Reporting Items on Systematic Reviews and Meta-Analysis (PRISMA) guidelines by Moher et al. (2009). A systematic literature search in the databases PubMed, Scopus, IEEE Xplore and SpringerLink was performed for the keyword [hololens], together with any of the terms [medicine], [surgery] or [healthcare] in March 2022. The publication period was restricted to the years 2016 to 2021. Duplicates were removed, then, an initial screening of titles and abstracts was performed. After the initial screening, full texts were retrieved and reviewed for eligibility. Criteria for inclusion in both phases of screening were: 1) studies with English full texts, 2) studies describing full original research by the authors, 3) studies which have been peer reviewed, and 4) studies describing the application of the HoloLens primarily for a human medical purpose. Consequently, exclusion criteria were: 1) studies without English full texts, 2) studies not describing full original research, such as reviews or book chapters 3) studies which have not been peer-reviewed, for example conference

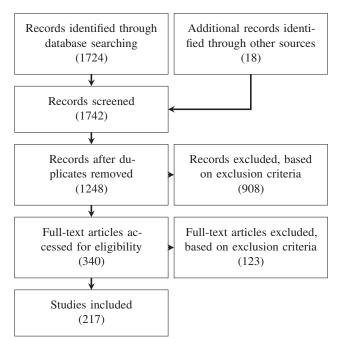


Fig. 1: Search strategy used in this systematic review. Adapted from the PRISMA flow diagram by Moher et al. (2009).

posters/abstracts or commentaries, 4) studies which do not use the HoloLens as the main AR device, but only mention it, and 5) studies which are not primarily focused on a human medical purpose, but on other applications such as industry or gaming, and only mention medicine as a possible field of application.

The systematic electronic search resulted in a total of 1724 records. 18 additional records previously known to the authors were also considered. After removal of duplicates and screening of titles, abstracts and full texts according to our inclusion criteria, 217 studies were selected for the final analysis (see Figure 1).

3.2. Data extraction and taxonomy

Each study was reviewed by one author. We extracted information about authors, year of publication and medical speciality from every publication. Medical specialities were determined as stated by the authors, by publication venue or targeted anatomy and grouped, where applicable, e.g., cranial and facial sub-specialities were combined as cranio-maxillofacial. Then, we extracted information about every publication according to our novel taxonomy, seen in Figure 2. For this structured search, the full texts of the studies were screened. In section 6, we classified each study by the main intended user of the HoloLens: 1) clinical systems, whose main purpose is the support of physicians and healthcare professionals in the clinical routine, 2) Educational works, which aid medical and healthcare students in their schooling and training, and 3) applications focused on treatment and rehabilitation, which aim at supporting patients during different stages of therapy and disease management. Further, we divided each main category into sub-categories, based on application areas. From every publication, we also extracted information about applied registration and tracking methodologies,

if any (see section 7), where we first categorized studies based on their tracking paradigm (manual vs. inside-out vs. outside-in), and further distinguished between marker-based and marker-less methods. Data and visualization techniques are reviewed in section 8, where we define categories based on data source (medical vs. non-medical), data type (2D, 3D and other), as well as acquisition time, and describe how they can be visualized. Finally, we analyzed how medical AR applications using the HoloLens have been evaluated, grouping studies according to their evaluation scenarios, and identified commonly used qualitative and quantitative measures in section 9.

We think that this taxonomy is generally applicable to works in medical AR, and can help readers to extract information in a more structured and organized way. Thus, is can be useful for future reviews, but also for helping researchers in identifying patterns, trends and gaps in the literature, or in putting work into context with the existing state-of-the-art. We hope that it can aid in determining areas which have not been as actively researched yet, and also in promoting a more effective and consistent communication of findings, to pave the way for even more innovative AR research in the future.

3.3. Related reviews

According to our exclusion criteria, review publications are not analyzed in this study. Still, we identified several related reviews during our literature search, which might be of interest for the reader.

Barsom et al. (2016) provide a systematic review about AR for medical training to the year of 2015, and found that, although promising results were achieved, full validation of training systems was lacking. Chen et al. (2017) analyze trends and challenges in medical AR found in over 1400 publications in the time period between 1995 and 2015. They identify powerful enabling technologies, human-computer-interaction and validation as major research challenges. Eckert et al. (2019) review medical AR applications described between the years of 2012 and 2017. In these years, a trend towards display technology research and medical treatment scenarios could be identified. Still, a lack of evidence in clinical studies was noted.

Several reviews about AR, specifically for surgical applications, have been published. Vávra et al. (2017) and Yoon et al. (2018) review articles published pre-HoloLens, between 2010 and 2016, as well as 1995 and 2017, respectively. In this time period, live streaming from endoscopy, followed by navigation and video recording, were the most popular applications. Rahman et al. (2020) focus specifically on HMD use in surgical scenarios up to the year of 2017. More recent reviews about surgical AR using OST-HMD come from Birlo et al. (2022) and Doughty et al. (2022) for the years between 2013 and 2020, and 2021 to March 2022, respectively. They clearly show that the Microsoft HoloLens was the major driving force in OST-HMD research for surgery in the past years. Even more specialized surgical reviews have been published for orthopedic surgery (Jud et al. (2020)), oral and cranio-maxillofacial surgery (Badiali et al. (2020); Gsaxner et al. (2021a)), neurosurgery (Meola et al. (2017); Guha et al. (2017); López et al. (2019)), laparoscopic surgery (Bernhardt et al. (2017)) and robotic surgery (Qian et al. (2019a)).

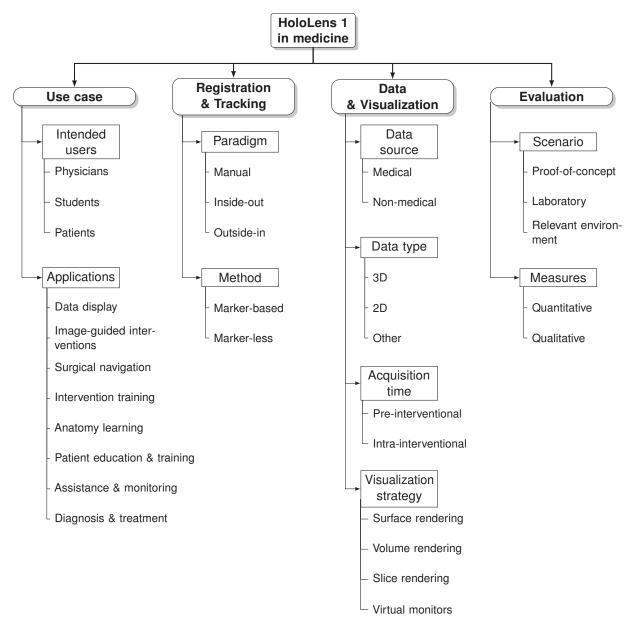


Fig. 2: Taxonomy employed in this review. Each publication is analyzed with regard to intended use case, registration and tracking principles, data sources and visualization, as well as evaluation and validation.

In all these reviews, the lack of clinical validation is the most re-occurring aspect, something we also identify in this study. Other commonly mentioned challenges include technical limitations in regards to device tracking and rendering, and limited usability due to complicated workflows. The HoloLens, with its self-tracking capabilities, good support for the development of user interfaces and interactions and improved rendering capabilities, makes some of these challenges obsolete. Therefore, in this review, we focus exclusively on aspects and challenges coming with this new generation of OST-HMD devices, which still bear significance for more recent hardware, such as the HoloLens 2 or Magic Leap 2 (Magic Leap, Plantation, FL). Thus, we hope that it is interesting for not only looking back, but in particular also for pointing future researchers towards directions in which increased efforts are required.

4. Publications per year

Figure 3 provides an overview of the number of papers published in each reviewed year, from 2016 to 2021. Although the HoloLens was available from March 2016 in North America and October 2016 worldwide, no publications reporting it's use in the medical domain were published in this year. After that, the number of publications in all categories shows a steady increase, with the highest number of research reported in 2020. In 2021, the number of papers decreases again – likely caused by the release of the HoloLens 2, which led many researchers to shift their attention towards the newer generation device. Furthermore, the COVID-19 pandemic impeded access to laboratories, the possibility to carry out user studies and made the evaluation of research prototypes in a clinical routine almost impossible in the years of 2020 and 2021, which may also contribute to the

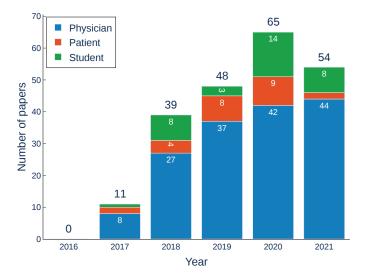
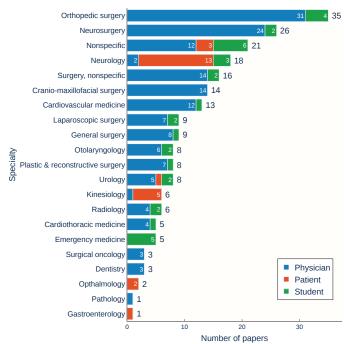


Fig. 3: Number of papers published per year between the years 2016 and 2021. We further distinguish between the intended user of the proposed systems (physicians, patients, or medical students).



decrease in publications.

5. Medical fields of application

As shown in Figure 4, the HoloLens saw applications in a large variety of medical areas, which we group into 21 fields. Surgical disciplines, in particular orthopedic surgery (35) and neurosurgery (26), were most frequently supported by AR applications, especially those targeted at physicians. Interestingly, in these most frequent disciplines, image-guided and navigated interventions are already particularly common, e.g., through surgical navigation systems or fluoroscopy. Hence, it can be assumed that, from the perspective of user acceptance and recognition, the translation of AR technology into clinical practice can be more successful in areas which already heavily rely on such technological assistance. However, relevant procedures have also highest demands in accuracy and safety, which makes the implementation of AR much more difficult from a technical standpoint. 22 publications do not indicate a specific medical field, and 16 target surgical procedures in general. These publications mostly introduce more general concepts not targeted at specific medical procedures - thus, they could be used in more than one specialty. Patient-focused applications are rather situated in speciality areas, where patient cooperation and motivation has a large impact on treatment outcome, such as neurology and kinesiology.

6. Use cases

We first categorize publications by their intended users, and further by the supported application. An overview of the identified categories and number of associated publications is given in Figure 5. Physicians and healthcare professionals working within the clinical routine have been, by far, the most popular target audience of proposed HoloLens-based AR systems. 158 out of 217 studies, almost 75%, describe an application of the

Fig. 4: Frequency of papers in each of the 21 identified medical fields. "Nonspecific" refers to applications where authors did not indicate a specific area, which means they could be used in several disciplines.

device for supporting healthcare professionals in tasks such as diagnosis, treatment planning and treatment execution. Medical students come second, with 34 works dedicated to anatomy learning or training of interventional procedures. Lastly, 25 studies targeted an application for patients, either for patient education, monitoring and guidance, or diagnosis.

6.1. Physician-centered applications of the HoloLens

We group research within this category based on application, ranked by technological complexity: 1) Data visualization applications, where the HoloLens primarily serves as a display, are relatively simple to implement. 2) Image-guided interventions demand a registration between virtual content and the patient and are, consequently, more challenging. 3) Surgical navigation applications require tracking of medical tools in addition to the patient and the HoloLens, and have the highest demands in accuracy and reliability, which makes them the most complex. Table 1 shows all studies targeted at physicians and other healthcare professionals, including their applications.

6.1.1. Data display

In its simplest form, the HoloLens can be used as an immersive display for pre-interventionally acquired medical data, such as 2D/3D imaging or healthcare records (see Figure 6 (a) and (b)). Pure data display applications do not need to establish a correspondence between the physical space and the shown data – content can simply be anchored to a fixed position according to the display itself, to be always visible for the wearer. Since the HoloLens self-locates within its environment, virtual objects can further be anchored to a stationary position within the real world without additional expenditure, to be naturally examined from

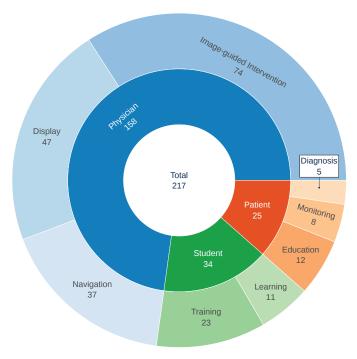


Fig. 5: Overview of the number of papers identified in each of our three main categories (defined by targeted users) and sub-categories (defined by application area).

different perspectives. This ability can have several advantages for clinicians. Access to medical data can be detached from stationary infrastructure and brought to treatment rooms, operating theaters and the bedside of the patient. For 3D data, such as volumetric medical imaging, stereoscopic visualization through the HoloLens may lead to an improved perception of 3D relations. Furthermore, the possibility of touch-less interaction with data is ideal for scenarios where sterility is important. Finally, by synchronizing several headsets, visualizations may be more easily shared between users. These factors could make inspection of interaction with medical data during diagnosis, intervention planning and procedures more intuitive and less cumbersome. We identified 47 publications in this category. Most of them describe workflows for visualizing pre-interventionally acquired, 3D volumetric imaging data, such as CT, MRI or positron emission tomography (PET), but also healthcare records and other documents.

A second category of works focuses on streaming live imaging data to the HoloLens, to enhance traditional image-guided procedures such as laparoscopy, endoscopy, fluoroscopy or ultrasound. It has been shown that monitor placement during such interventions plays an important role – a misalignment of the visual-motor axis can increase fatigue and decrease orientation and hand-eye coordination of the operator, and, consequently, increase the risk of intervention-induced injuries (El Shallaly and Cuschieri (2006)). By anchoring the virtual 2D "monitor" to a convenient physical location or the head gaze of the user, ergonomics and subjective workload may be improved. These applications require methods to deliver live medical data to the HoloLens in real-time. While most frameworks could support a variety of imaging sources, studies specifically evaluate intraoperative X-ray (Deib et al. (2018); Al Janabi et al. (2020)), endoscopy (Al Janabi et al. (2020)), ultrasound (Cartucho et al. (2020)), electro-anatomic mapping (Southworth et al. (2020)) and MRI (Velazco-Garcia et al. (2021b)). An example is shown in Figure 6 (c).

A smaller group of works explores telemedicine, where remote monitoring and assistance are important concepts. A remote expert can assist local staff in carrying out critical interventions, which is particularly useful in rural or disadvantaged areas, with limited funding and staff. The HoloLens features video conferencing capabilities, which enable the real-time transmission and visualization of the viewpoint of an interventionist to a remote expert/observers, and, vice versa, expert guidance via voice, video or annotations, without having to look away from the patient or using an external computer. Sirilak and Muneesawang (2018) developed an e-consulting platform to connect specialized physicians with rural and remote hospitals. The feasibility of video and voice communication during intervention or surgery has further been explored by Mitsuno et al. (2019a) and Glick et al. (2020). Proniewska et al. (2020) developed a strategy for digitizing the operating room, allowing tele-monitoring from different perspectives with the HoloLens.

6.1.2. Image-guided interventions

The majority of papers reviewed in this study describe an application in image-guided intervention (IGI). AR for IGI is mainly motivated by the desire to see critical structures through the obstructive anatomy of a patient, which can incorporate medical imaging data intuitively into interventional workflows by aligning patient anatomy, imaging data and the physician's viewpoint, as illustrated in Figure 6 (d). This type of virtual *see-through visualization* is accomplished in AR by superimposing virtual pre- or intra-operative images and planning data directly with the target anatomy of the patient, allowing the physician to see target structures through skin or obstructive anatomy (Ferrari et al. (2019)). It can, thus, either replace traditional image guidance, or provide guidance for interventions usually performed without.

Especially minimally-invasive interventions, which are performed without gaining direct access to the underlying anatomy, can benefit from see-through visualization. Examples include skull base surgery (McJunkin et al. (2018); Kalavakonda et al. (2019); Creighton et al. (2020)), arthroplasty (Agten et al. (2018); Wang et al. (2019)), percutaneous orthopedic screw placement (Gibby et al. (2019); Liu et al. (2019a); Wei et al. (2019); Dennler et al. (2020); Buch et al. (2021); Dennler et al. (2018); Nuang et al. (2019b); Azimi et al. (2020); Schneider et al. (2021)) or ablations (Ferraguti et al. (2020); Condino et al. (2021)).

But see-through visualization with the HoloLens has also been applied for procedures where the target anatomy is surgically exposed, such as tumor removal (Perkins et al. (2017); Incekara et al. (2018); Rose et al. (2019); Soulami et al. (2019); Huang et al. (2020); Saito et al. (2020); Ivan et al. (2021); Scherl et al. (2021a,b); Gouveia et al. (2021)), vessel surgery (Pratt et al. (2018); Katayama et al. (2020); Wesselius et al. (2021)), or

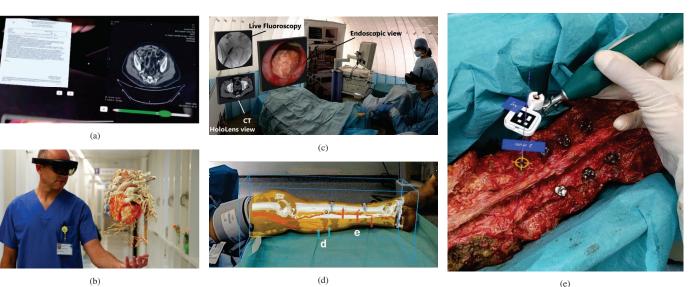


Fig. 6: Examples for physician-centered applications of the HoloLens. Left: Data display examples, showing immersive (a) 2D (Source: Galati et al. (2020), CC-BY) and (b) 3D patient data (Source: Gehrsitz et al. (2021), CC-BY), without a reference to the physical space. Middle: (c) Traditional image-guided interventions can be supported by visualizing live imaging on the HoloLens, instead of conventional monitors, (Source: Al Janabi et al. (2020), CC-BY). (d) AR image-guidance via see-through visualization needs to establish a correspondence between imaging and patient (Source: Pratt et al. (2018), CC-BY). Right: (e) example for a surgical navigation application, where tools are tracked in relation to the target anatomy (Source: Spirig et al. (2021), permission for re-print will be obtained after acceptance.)

cranio-maxillofacial surgeries (Koyachi et al. (2021); Sugahara et al. (2021); Meng et al. (2021)). In these scenarios, the visualization of critical anatomical structures, which are not directly or clearly visible on the surgical site, such as blood vessels and nerves, or important planning information; for example, tumor resection margins or osteotomy lines, have the potential to make interventions safer.

Aside from anatomical structure overlays, Takata et al. (2021) used the HoloLens for the visualization of radiation doses around patients, and Butaslac et al. (2020) visualized the 3D position of patients' joints during rehabilitation exercises.

For a convincing see-through visualization, an accurate overlay of imaging data with the patient is a prerequisite. Image-topatient-registration, relating virtual content with target anatomy, is the key component for such a system, but other factors, such as display calibration and stability of the HoloLens self-tracking, also play an important role. While many of the aforementioned works rely on a manual alignment of virtual content with the patient, several publications within this category focus on addressing these technical challenges. Mostly, they do not focus on specific medical applications, but develop new concepts for system calibration (Andress et al. (2018); Hajek et al. (2018); Fotouhi et al. (2019a,b)) or image-to-patient-registration (Wu et al. (2018); Chien et al. (2019); Pepe et al. (2018); Sylos Labini et al. (2019); Gsaxner et al. (2019)), which could be applied in various medical scenarios. Other works evaluate and compare selected technical aspects (Frantz et al. (2018); Mitsuno et al. (2019b); Van Doormaal et al. (2019); Li et al. (2020); Gu et al. (2021); Pérez-Pachón et al. (2021)). We will discuss image-to-patient registration and calibration methods in more detail in section 7

6.1.3. Surgical navigation

Surgical navigation systems (SNS) have been shown to make procedures more accurate, less invasive and faster, resulting in improved outcomes for the patient (Mezger et al. (2013)). Compared to conventional image guidance using intra-operative X-ray or CT, SNS do not burden operators and patients with additional radiation exposure, and, compared to ultrasound-based guidance, they are more accurate and work for every tissue type. Conventional SNS rely on visualizing navigation information on separate monitors, which leads to a *switching focus problem* for surgeons - they have to divide their attention between the surgical site and the navigation information. Such a division leads to issues of increased workload, disorientation and deteriorated hand-eye coordination (Hansen et al. (2013)), which AR could alleviate by fusing navigation information with the operating site. While IGI systems, as described above, can already provide a basic guidance based on images, precise surgical navigation requires real-time tracking of medical instruments and tools in relation to the patient anatomy, in addition to imageto-patient registration. In AR, navigation information can then be displayed in situ, fused with the target anatomy, as shown in Figure 6 (e).

Surgical navigation with the HoloLens has been explored as an alternative to commercial SNS in 37 publications. Mostly, AR navigation was studied in procedures where conventional SNS are already gold standard, such as neurosurgery (Carbone et al. (2018); Kunz et al. (2020); Van Gestel et al. (2021a,b)), orthopedic (in particular, spinal) surgery (El-Hariri et al. (2018); Liu et al. (2018); De Oliveira et al. (2019); Liebmann et al. (2019); Gibby et al. (2020); Kriechling et al. (2020); Müller et al. (2020); Kriechling et al. (2021); Teatini et al. (2021); Spirig et al. (2021)), general surgery (Meulstee et al. (2019)) or craniomaxillofacial surgery (Gao et al. (2019); Sun et al. (2020); Glas et al. (2021); Liu et al. (2021a,c)). AR SN can also provide an X-ray free alternative to interventions typically guided by intraoperative imaging, such as endovascular procedures (Kuhlemann et al. (2017); García-Vázquez et al. (2018); Liu et al. (2019b)) or tissue ablations (Kuzhagaliyev et al. (2018); Li et al. (2019)), or can be integrated into robotic surgery (Qian et al. (2017); Liu et al. (2018); Qian et al. (2018, 2020)).

These procedures have highest demands in accuracy and reliability of registration and tracking, with a high reference precision in a millimeter or sub-millimeter range. With the HoloLens hardware, it is difficult to meet these requirements. However, compared to conventional image guidance systems, the HoloLens is not bulky and can be easily moved around, which allows navigation for less critical procedures. Examples for such procedures include brain stimulation treatment (Leuze et al. (2018)) and US examinations (Farshad-Amacker et al. (2020); Rüger et al. (2020); Nguyen et al. (2022)).

Instrument tracking methods with the HoloLens will be reviewed in more detail in section 7.

6.2. Applications of the HoloLens for medical students

While the HoloLens 1 was originally not intended as a device for IGI or SN, its use as a tool for medical education was actively promoted. The CAE VimedixAR (CAE Healthcare, Montreal, Canada) app, an AR ultrasound training simulator, was amongst the first commercial applications available for the HoloLens 1, and tools for studying anatomy, such as HoloHuman by 3DMedical (Elsevier, Amsterdam, Netherlands) quickly followed. Probably due to the availability of commercial solutions, research in the area of medical education and training with the HoloLens is not as common as one might expect. We identified 34 publications in the area of HoloLens-based medical and healthcare student support, which we further categorize into 1) interventional and surgical training, and 2) anatomy learning. An overview is given in Table 2.

6.2.1. Interventional and surgical training

Simulation-based skill training has made its way into standard medical education, replacing or enhancing traditional teaching and training methods (Gaba (2004)). Aside from traditional simulators based on physical manikins, mixed reality technology has gained considerable popularity in this domain, either by enabling fully virtual environments, or by enhancing manikin-based training through virtual guidance and feedback (So et al. (2019)). 23 reviewed studies fall into this category.

The HoloLens 1 has been integrated into hybrid simulators, where it can be used to display additional guidance or even direct feedback to the user. Examples include the training of orthopedic surgery (Condino et al. (2018); Turini et al. (2018)), emergency medicine interventions (Azimi et al. (2018b); Kobayashi et al. (2018); Balian et al. (2019); Hong et al. (2020); Putnam et al. (2021)), laparoscopic or US examinations (Mahmood et al. (2018); Rewkowski et al. (2020); Heinrich et al. (2021)), neurological procedures (Azimi et al. (2018a); Liang et al. (2021)) or urological procedures (Muangpoon et al. (2020); Schoeb et al. (2020)). Another possibility is to build fully simulated, virtual training scenarios (Cecil et al. (2018); Aguilera-Canon et al. (2018); Brunzini et al. (2021)) or to include remote experts into the training sessions (Wang et al. (2017)).

6.2.2. Anatomy learning

A meta-survey by Yammine and Violato (2015) has shown that 3D visualization techniques are preferable over traditional methods for learning and teaching anatomy, both in terms of factual and spatial knowledge. Contrary to such visualizations on conventional monitors or in virtual reality (VR), AR could not only provide 3D visuals, but also annotate real, physical models or cadavers with digital information.

Out of the 11 studies reviewed in this category, most focus on displaying various anatomy models on the HoloLens for improved perception and understanding during learning (Stojanovska et al. (2019); Maniam et al. (2020); Antoniou et al. (2020b,a); Gnanasegaram et al. (2020); Ruthberg et al. (2020); Shao et al. (2020); Moro et al. (2021)). Robinson et al. (2020) further tested the HoloLens as a learning platform for studying microscopic anatomy.

6.3. Patient-focused applications of the HoloLens

25 publications describe HoloLens-based systems for assisting patients during rehabilitation and treatment. Designing AR applications for patients is challenging due to age demographics, varying affinity to novel technologies and general anxiety when it comes to medical treatments. The novelty of AR technology also provides opportunities, since it can make otherwise repetitive or dull activities significantly more engaging. We identify three main application areas in this domain: a) patient training and education, b) assistance and monitoring, and c) assessment and diagnosis. An overview over all studies, grouped by their application, is given in Table 3.

6.3.1. Patient training and education

It has been shown that immersive experiences can improve patient engagement and satisfaction during training tasks in rehabilitation (Tieri et al. (2018)) and pre-interventional patient education (Pandrangi et al. (2019)). Therefore, AR environments have the advantage of being potentially more intriguing for patients than conventional methods. At the same time, AR scenarios are safe and easy to control.

A series of studies has investigated the usage of the HoloLens to create virtual training environments for people with cognitive disorders, such as Alzheimer's disease (Aruanno et al. (2017); Garzotto et al. (2018); Aruanno and Garzotto (2019); Desai et al. (2020)), or mobility limitations (Karatsidis et al. (2018); Blomqvist et al. (2021)). Another training task, which has benefited from AR support through the HoloLens, is the control of functional prostheses (Sharma et al. (2018); Palermo et al. (2019)). In the context of patient education, the HoloLens has been used to provide a more comprehensible and imaginable explanation to patients before surgery (Wake et al. (2019); House et al. (2020); Rositi et al. (2021)).

6.3.2. Assistance and monitoring

AR, with its ability to enhance the reality around the users in real-time, without insulating them, could be ideal for compensating various impairments and overcoming difficulties during the daily lives of patients. Mobile health (mHealth) applications support such procedures through mobile devices, such

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Table 1: Studies reporting an application of the HoloLens for physicians and other health care professionals.

Application	Focus	Studies
Data display (47)	Medical Data Visualization (37)	Bucioli et al. (2017); Morales Mojica et al. (2017); Qian et al. (2017); Sauer et al. (2017); Fröhlich et al. (2018); Jang et al. (2018); Karmonik et al. (2018); Tan et al. (2018); Affolter et al. (2019); Brun et al. (2019); Checcucci et al. (2019); Cocco et al. (2019); Fink et al. (2019); Kobayashi et al. (2019); Kubben and Sinlae (2019); Moosburner et al. (2019); Soulami et al. (2019); Talaat et al. (2019); Witowski et al. (2019); Allison et al. (2020); Avari Silva et al. (2020); Bulliard et al. (2020); Cocco et al. (2020); Fitski et al. (2020); Galati et al. (2020); Kumar et al. (2020); Pelanis et al. (2020); Perkins et al. (2020); Yajima et al. (2020); Cofano et al. (2021); Dennler et al. (2021a); Gehrsitz et al. (2021); Iqbal et al. (2021a); Wake et al. (2021)
	Live imaging (6)	Cui et al. (2017); Deib et al. (2018); Al Janabi et al. (2020); Cartucho et al. (2020); Southworth et al. (2020); Velazco-Garcia et al. (2021b)
	Tele-medicine (5)	Sirilak and Muneesawang (2018); Mitsuno et al. (2019a); Glick et al. (2020); Proniewska et al. (2020); Cofano et al. (2021)
Image-guided interventions (74)	see-through vision: clinical focus (47)	Perkins et al. (2017); Agten et al. (2018); Hanna et al. (2018); Incekara et al. (2018); Li et al. (2018); McJunkin et al. (2018); Pratt et al. (2018); Rae et al. (2018); Amini and Kersten-Oertel (2019); Gibby et al. (2019); Huang et al. (2019b); Kalavakonda et al. (2019); Liu et al. (2019a); Lohou et al. (2019); Rose et al. (2019); Wang et al. (2019); Wei et al. (2019); Azimi et al. (2020); Butaslac et al. (2020); Dennler et al. (2020); Creighton et al. (2020); Ferraguti et al. (2020); Huang et al. (2020); Katayama et al. (2020); Kiarostami et al. (2020); Nuri et al. (2020); Saito et al. (2020); Tian et al. (2020); Viehöfer et al. (2020); Buch et al. (2021); Condino et al. (2021); Dennler et al. (2021); Fick et al. (2021); Gouveia et al. (2021); Lizuka et al. (2021); Ivan et al. (2021); Koyachi et al. (2021); Li et al. (2021b); Long et al. (2021); Meng et al. (2021); Qi et al. (2021); Wesselius et al. (2021)
	see-through vision: technical focus (27)	Xie et al. (2017); Andress et al. (2018); Frantz et al. (2018); Hajek et al. (2018); Moreta-Martinez et al. (2018); Pepe et al. (2018); Wu et al. (2018); Chien et al. (2019); Fotouhi et al. (2019a,b); Gsaxner et al. (2019); Mitsuno et al. (2019b); Pepe et al. (2019); Sylos Labini et al. (2019); Van Doormaal et al. (2019); Fischer et al. (2020); Jiang et al. (2020); Luzon et al. (2020); Nguyen et al. (2020b,a); Zuo et al. (2020); Castelan et al. (2021); Gsaxner et al. (2021c); Gu et al. (2021); Pérez-Pachón et al. (2021); Villani et al. (2021)
Surgical navigation (37)		Kuhlemann et al. (2017); Carbone et al. (2018); El-Hariri et al. (2018); García- Vázquez et al. (2018); Kuzhagaliyev et al. (2018); Leuze et al. (2018); Liu et al. (2018); Qian et al. (2018); Song et al. (2018); De Oliveira et al. (2019); Gao et al. (2019); Li et al. (2019); Liebmann et al. (2019); Liu et al. (2019b); Meulstee et al. (2019); Pellegrino et al. (2019); Qian et al. (2019b); Farshad- Amacker et al. (2020); Gibby et al. (2020); Kriechling et al. (2020); Kunz et al. (2020); Müller et al. (2020); Qian et al. (2020); Rüger et al. (2020); Sun et al. (2020); Glas et al. (2021); Kriechling et al. (2021); Li et al. (2021a); Liu et al. (2021b,a,c); Nguyen et al. (2022); Spirig et al. (2021); Teatini et al. (2021); Van Gestel et al. (2021a,b); Zhou et al. (2021)

as smartphones, smartwatches, or, in this case, the HoloLens, and are, consequently, fitting for scenarios outside of a clinical environment, e.g., in the homes of patients. vision impairments in navigating their surroundings (Yamashita et al. (2017); Angelopoulos et al. (2019)). Other applications include assisting patients with cognitive disorders in everyday activities (Rohrbach et al. (2019); Janssen et al. (2020)), helping

The HoloLens has been explored for aiding patients with



Fig. 7: Examples of HoloLens applications for medical students. (a): A hybrid simulator for training catheter insertion with AR guidance (Source: Schoeb et al. (2020), CC-BY). (b) Studying anatomy with the HoloLens (Source: Ruthberg et al. (2020), permission for re-print will be obtained after acceptance).

Table 2: Studies reporting an	application of the HoloLens for medical stud	dents and residents in an educational context.

Main application	Studies
Interventional and surgical training (23)	Wang et al. (2017); Aguilera-Canon et al. (2018); Azimi et al. (2018a,b); Cecil et al. (2018); Condino et al. (2018); Kobayashi et al. (2018); Mahmood et al. (2018); Turini et al. (2018); Balian et al. (2019); Si et al. (2019); Guo et al. (2020); Hong et al. (2020); Lemke et al. (2020); Lu et al. (2020); Muangpoon et al. (2020); Rewkowski et al. (2020); Schoeb et al. (2020); Brunzini et al. (2021); Heinrich et al. (2021); Liang et al. (2021); Putnam et al. (2021); Suzuki et al. (2021)
Anatomy learning (11)	Stojanovska et al. (2019); Antoniou et al. (2020b,a); Gnanasegaram et al. (2020); Maniam et al. (2020); Robinson et al. (2020); Ruthberg et al. (2020); Shao et al. (2020); Bogomolova et al. (2021); Kumar et al. (2021); Moro et al. (2021)

outpatients to adhere to their care plans (Ingeson et al. (2018); Blusi and Nieves (2019); Boyd et al. (2020)) and text editing for people with motor disabilities (Guerrero et al. (2020)).

As mHealth applications are becoming more and more pervasive in our everyday lives, integrating them into augmented environments is a logical step, and the above-mentioned studies suggest promising applications of head-worn AR devices in mHealth. However, it should be noted that the HoloLens is not yet suitable for operation during everyday activities, as it is relatively expensive, and its short battery life and bulky form factor make it unfit for being worn and used for an extended period of time.

6.3.3. Assessment and diagnosis

The variety of built-in sensors, along with its self-tracking capabilities, unfold the possibility to utilize the HoloLens as a measurement device during patient assessments and diagnosis. At the same time, instructions and demonstrations, guiding patients through these tests, can be displayed immersively and interactively.

Sun et al. (2019) used the HoloLens for leading and tracking patient performance during functional mobility tests, by evaluating the inertial measurement unit (IMU) data recorded by the device. Geerse et al. (2020) and Koop et al. (2020) utilize motion data collected by the HoloLens to assess gait parameters (e.g., walking speed, step length, cadence) in patients with movement disorders, in particular Parkinson's disease. Martinez et al. (2019) apply the HoloLens as a tool to predict sensorimotor disorders, while Höhler et al. (2021) use it to examine distance and depth perception in stroke patients.

HoloLens-supported assessment and diagnosis is presumably closest to real clinical applicability in the domain of patientoriented applications, as all reviewed studies have shown reliability of the measurements derived from the HoloLens sensors. At the same time, the ability to simultaneously monitor clinical parameters, while providing instructions to the patient with a single device, has obvious benefits in terms of ergonomics and economics. Furthermore, using the HoloLens during the confined timespan of such screenings is feasible without undue discomfort for the patient.

7. Registration and object tracking with the HoloLens

The registration of virtual content to the physical situation is one of the fundamental concepts of medical AR. Registration permits see-through visualization for IGI or the localization of the patient's anatomy for surgical navigation, enables hybrid simulators or annotated anatomical specimens in educational settings.

General research in tracking for AR mostly focuses on the self-localization of the AR device. Since the HoloLens already provides SLAM for self-localization, applications in surgical

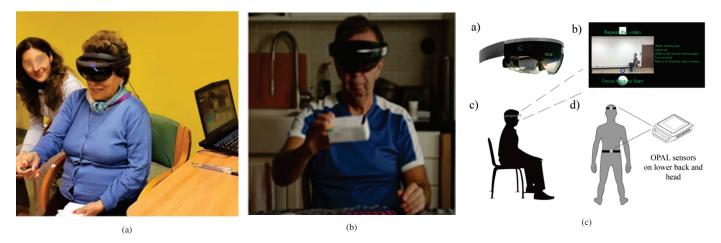


Fig. 8: Example applications for the patient. (a): The HoloLens is used during a training session for Alzheimer's patients (Source: Aruanno and Garzotto (2019), permission for re-print will be obtained after acceptance). (b) The HoloLens as an assistant and monitoring tool for medication adherence (Source: Blusi and Nieves (2019), CC-BY-NC). (c) A HoloLens-based system for functional mobility assessment (Source: Sun et al. (2019), CC-BY).

Table 3: Studies reporting a patient-focused application of the HoloLens.

Main application	Studies
Patient training and education (12)	Aruanno et al. (2017); Garzotto et al. (2018); Karatsidis et al. (2018); Sharma et al. (2018); Aruanno and Garzotto (2019); Palermo et al. (2019); Wake et al. (2019); Desai et al. (2020); House et al. (2020); Rositi et al. (2021); Thomos et al. (2020); Blomqvist et al. (2021)
Assistance and monitoring (8)	Yamashita et al. (2017); Ingeson et al. (2018); Angelopoulos et al. (2019); Blusi and Nieves (2019); Rohrbach et al. (2019); Boyd et al. (2020); Guerrero et al. (2020); Janssen et al. (2020)
Assessment and diagnosis (5)	Martinez et al. (2019); Sun et al. (2019); Geerse et al. (2020); Koop et al. (2020); Höhler et al. (2021)

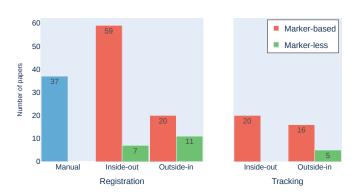


Fig. 9: Frequency of registration and tracking methods employed by the reviewed studies. Most works rely on inside-out, marker-based tracking, followed by manual alignment.

navigation or advanced medical simulators concern themselves with the tracking of additional non-stationary objects (i.e., medical tools and instruments) in relation to the device or the patient anatomy, ideally with high precision. SLAM gradually maps the static environment around the HoloLens and localizes the device within this map. Therefore, it is not suitable for this type of dynamic object tracking, and other tracking methods need to be implemented. Registration and tracking are usually closely related, as the same paradigms and methods can be applied to both tasks. Furthermore, for navigation applications, it is generally beneficial to combine patient registration and object tracking, so that their spatial relation can still be shown correctly in case of inaccuracies or drift in the SLAM. This is particularly important for applications with high accuracy demands.

In our analysis, we found 127 studies which describe one or more methods for registration between virtual and real content, which are listed in Table 4, grouped by registration paradigm and method. Since some studies compare various registration methods, they may appear several times. 45 studies further integrate methods for object tracking with their AR systems, which are shown in Table 5. Figure 9 visualizes the frequencies of identified paradigms and methods.

7.1. Manual registration

Due to the self-tracking capabilities of the HoloLens, registration between real and virtual content can be achieved simply by manually aligning position, orientation and scale of the virtual items to match their physical counterparts. Since registration is performed for the perspective of the user, factors hindering accurate perception, such as a poor display calibration, may be mitigated. 37 studies in this review adopt such a manual registration technique, mostly by using transformation of objects via on-board input methods (hand gestures and voice commands) or additional input devices, e.g., gamepads (Buch et al. (2021); Meng et al. (2021)) and keyboards (Nguyen et al. (2020b)).

Obviously, manual alignment of virtual content can be timeconsuming and ponderous, which affects applicability in clinical settings, where time and personnel are usually scarce. Landmarkbased methods can make manual alignment faster and less cumbersome. They involve the manual annotation of pre-defined anatomical landmarks in the spatial map of the real environment using gestures, which are matched with their virtual counterparts in pre-interventional imaging (Mitsuno et al. (2019b); Nguyen et al. (2020b,a)). However, due to the coarseness of the spatial map and the lack of haptic feedback when selecting landmarks, these approaches may not be reliable or accurate. All manual registration methods have the disadvantage of being static – if the patient moves, the registration has to be manually adapted accordingly.

7.2. Inside-out methods

The built-in sensors of the HoloLens offer several possibilities for inside-out registration and tracking. The advantages of insideout approaches in medical scenarios are evident: They work in unprepared and unrestricted environments and do not rely on expensive, specialized hardware, thus avoiding extra costs and further cluttering of already densely occupied spaces, such as operating rooms. However, it is still difficult to meet the high demands in accuracy and robustness of medical procedures using inside-out approaches (Sielhorst et al. (2008); Gsaxner et al. (2021a)).

Marker-based. Marker-based inside-out registration is the most common registration technique identified in this review, employed by 59 studies. Freely available AR fiducial libraries, such as Vuforia (PTC Inc, Boston, USA) or ArUco (Garrido-Jurado et al. (2014)), facilitate optimized, close to real-time detection and tracking of image fiducials via the HoloLens' front-facing RGB camera, which makes marker-based inside-out strategies easy to implement. The most straightforward method for registration, also employed by commercial SNS, is to anchor markers directly to rigid tissue of the patient, e.g., bones. For precisely relating the coordinate frame of the marker to the target anatomy, it is common practice to perform a pre-interventional scan, including the marker. However, attaching markers to patients is invasive and the additional imaging scan may lead to increased radiation exposure of the patient. Additive manufacturing offers an interesting alternative to this route, which allows the creation of patient-specific bone guides or occlusal splints for holding the markers (Moreta-Martinez et al. (2018); Gao et al. (2019); Koyachi et al. (2021)). In laboratory settings, 3D printing is also commonly used to create custom, marker-embedded phantoms for testing the registration method. Andress et al. (2018) even developed a multi-modal marker, allowing intra-interventional marker-based registration.

Alternatively, landmark-based approaches, where distinct anatomical landmarks are digitized in the coordinate frame of the HoloLens and matched to their virtual counterpart using point based registration, can be used. A marker-tracked pointing device is used for landmark selection in these studies (Van Doormaal et al. (2019); Liebmann et al. (2019); Azimi et al. (2020); Kriechling et al. (2020); Müller et al. (2020); Wesselius et al. (2021); Zhou et al. (2021); Liu et al. (2021a)). To adapt to movements of the patient, a rigidly attached marker is necessary, or the entire procedure has to be repeated.

It is straightforward to extend marker-based inside-out methods for medical instrument tracking by simply attaching markers to the tracked objects as well. 20 reviewed studies apply such a strategy, while Liu et al. (2021b) combine marker-based, insideout patient registration with outside-in tracking using stereo cameras.

A drawback of using planar image fiducial markers, which are, by far, most commonly used in this category, is a general lack of robustness and accuracy. It has been shown that the tracking error using common libraries can range from several millimeters to even centimeters (Brand et al. (2020); Cao et al. (2020)) and is highly dependent on viewing angles, distance, lighting conditions and movement patterns (Leuze et al. (2018); Jiang et al. (2020); Luzon et al. (2020); Zuo et al. (2020)). These issues make planar image targets ill-suited for highly precise, six degrees of freedom (6DoF) applications, as required in most medical scenarios. As an alternative, in proof-of-concept studies, Kunz et al. (2020) and Van Gestel et al. (2021a) have explored the possibility of tracking spherical, IR reflective markers in an inside-out paradigm using the IR sensor of the HoloLens, which appears to be a promising direction.

Marker-less. Ten studies explore the possibility of using the various on-board sensors of the HoloLens for inside-out, marker-less registration. An early work by Xie et al. (2017) explored the possibility of surface-based registration of a patient's skin surface with the spatial map created by the HoloLens SLAM. However, the spatial map accessible to developers is very coarse, resulting in insufficiently accurate natural features extractable from it. Hajek et al. (2018) also exploit the HoloLens SLAM by using two devices in a master-worker configuration, while Liu et al. (2019b) use image-based matching to align intra-operative X-ray with the patient anatomy.

Landmark-based registration approaches have been employed as well. For example, Pepe et al. (2018, 2019) use automatically detected facial landmarks for registration. From 2018 on, the *Research Mode* allowed access to the HoloLens' built in sensors aside from the RGB camera, opening new possibilities for insideout registration. Sylos Labini et al. (2019) used automatically detected facial landmarks as well, but showed that, by combining them with the ToF depth data, accuracy can be slightly improved. Gsaxner et al. (2019, 2021c) subsequently introduced a pipeline for fully automatic registration via point cloud matching, using 3D features from ToF depth alone. This method was later also employed by Gu et al. (2021), who compared surface-based registration with marker-based and outside-in methods.

7.3. Outside-in methods

31 reviewed publications use an outside-in paradigm for registration and tracking. Outside-in approaches rely on external infrastructure for registration and tracking. External infrastructure makes it possible to exploit highly precise, specialized hardware, such as commercial SNS. The high reference accuracy of such systems (usually $\leq 1 \text{ mm}$ and $\leq 1^{\circ}$) makes their integration into an AR environment promising. Using the HoloLens as an alternative to conventional monitors to display the navigation screen could already improve hand-eye coordination and ergonomics (El Shallaly and Cuschieri (2006)). For more advanced applications, however, especially for those providing see-through, in situ visualization, the integration of external systems requires the calibration of coordinate frames between the HoloLens and the navigation device. This procedure usually involves manual or semi-automatic steps, which can be cumbersome and disruptive to the clinical workflow, as well as error prone and highly subjective (De Oliveira et al. (2015)).

Marker-based. Most commercially available SNS track passively reflecting markers using stereoscopic IR cameras (Kral et al. (2013)). By attaching those markers to the patient, their relative localization in relation to pre-interventional imaging can be determined. The HoloLens can be integrated into such a setup, by affixing markers to the headset as well. Since SNS are designed not only for tracking patients, but, in particular, medical instruments, object tracking can be integrated easily with such systems, and all but one out of 20 reviewed studies in this category use this principle. Liu et al. (2021b) use stereo cameras and LED markers instead.

Such marker-based SNS have a high reference precision, often below one millimeter, however, in addition to potential complications resulting from system calibration, they require a constant line-of-sight between IR camera, patient and device, which may restrict movements.

Marker-less. Before the HoloLens Research Mode enabled access to the on-board ToF camera of the device, some works integrated external depth sensors with the HoloLens to enable a surface-based registration (Leuze et al. (2018); Liu et al. (2018); Wu et al. (2018); Chien et al. (2019); Wang et al. (2019)). As an alternative to capture the full surface of patients, again, a sub-set of points in the form of anatomical landmarks can be used, for example, digitized via external electromagnetic trackers (Kuhlemann et al. (2017); García-Vázquez et al. (2018); Muangpoon et al. (2020)). In these scenarios, the electromagnetic sensors have been used for instrument and tool tracking, as well. However, electromagnetic tracking is generally less popular than optical tracking, as it suffers from interference with metallic materials, commonly found in clinical spaces (Kral et al. (2013)). On the other hand, it can also be applied in scenarios where a direct line of sight of surgical tools is not available, such as minimally invasive (e.g., endovascular catheter) procedures.

8. Data and visualization

Various data were visualized in augmented environments through the HoloLens. We distinguish data based on its source (medical or non-medical) and dimensionality (2D, 3D, other). An overview of data source frequencies in the reviewed publications is given in Figure 10, and a list of all papers in each category is provided in Table 6. Note that most reviewed studies utilize more than one source and type of data – therefore, multiple mentions are possible.

8.1. Acquisition time

Regardless of the source and type, data can further be distinguished based on its acquisition time: Pre-interventional data is acquired offline, processed and uploaded to the HoloLens before the actual intervention. This method allows more complex workflows, including manual manipulations of data. With overall 206 examples, pre-interventional data makes up the majority of sources.

Intra-operative data is collected at run-time and streamed to the device for visualization. Obviously, intra-operative approaches are technically more complex, since they require a connection between the HoloLens and the raw data source, and necessary processing steps need to be performed automatically, in real-time. Overall, 58 intra-interventional data sources have been identified for this review.

8.2. Medical data

3D volumetric medical image data. For the majority (162) of reviewed papers, 3D medical images, acquired primarily through CT/CTA (112) and MRI (42), are a main source of data. They are represented as volumetric grids, where each voxel represents a specific value calculated by the imaging device. For visualization, they have to be rendered to present them on the HoloLens display.

Volumetric medical data is conventionally visualized in 2D on monitors in clinical practice, in the form of orthogonal slices through the image volume (mainly axial, sagittal and coronal planes or, sometimes, oblique reformats, so called multi-planar reformations). Since physicians are accustomed to this type of visualization, slice rendering of volumetric data has also been employed in 31 reviewed medical HoloLens systems. This technique has, of course, the drawback that data is only shown in selected planes. Given a stereoscopic AR display, true 3D visualization is becoming more widely used, mostly in the form of 3D surface renderings, which is computationally efficient and natively supported by all graphics engines compatible with the HoloLens. Furthermore, colors and opacities can easily be modified, enabling visualization techniques such as wire frames or outline visualizations. However, for surface rendering, tissue has to be segmented and converted to polygonal meshes prior to visualization, leading to more time intensive workflows and quantization inaccuracies. In contrast, direct volume rendering offers superior image quality (Kutter et al. (2008); Kilgus et al. (2015)) and does not require surface extraction before visualization. Instead, color and opacity are directly computed from the underlying voxel values using specialized transfer functions. Alas, performance requirements of volume rendering

Table 4: All studies applying registration between physical and virtual content, grouped by registration and tracking paradigm and method.

Paradigm	Method	Studies
Manual (37)		Agten et al. (2018); Frantz et al. (2018); Hanna et al. (2018); Incekara et al. (2018); Kobayashi et al. (2018); Li et al. (2018); McJunkin et al. (2018); Pratt et al. (2018); Rae et al. (2018); Gibby et al. (2019); Huang et al. (2019b); Liu et al. (2019a); Lohou et al. (2019); Mitsuno et al. (2019b); Wei et al. (2019); Creighton et al. (2020); Dennler et al. (2020); Fischer et al. (2020); Gibby et al. (2020); Katayama et al. (2020); Nguyen et al. (2020b,a); Nuri et al. (2020); Saito et al. (2020); Tian et al. (2020); Viehöfer et al. (2020); Buch et al. (2021); Gouveia et al. (2021); Gu et al. (2021); Iizuka et al. (2021); Ivan et al. (2021); Li et al. (2021b); Meng et al. (2021); Scherl et al. (2021a,b); Schneider et al. (2021); Sugahara et al. (2021)
Inside-out (66)	Marker-based (59)	Perkins et al. (2017); Aguilera-Canon et al. (2018); Andress et al. (2018); Azimi et al. (2018b,a); Carbone et al. (2018); Frantz et al. (2018); Mahmood et al. (2018); Moreta-Martinez et al. (2018); Qian et al. (2018); Song et al. (2018); Turini et al. (2018); Amini and Kersten-Oertel (2019); Fotouhi et al. (2019b); Gao et al. (2019); Huang et al. (2019b); Kalavakonda et al. (2019); Liebmann et al. (2019); Liu et al. (2019a); Qian et al. (2019b); Kalavakonda et al. (2019); Liebmann et al. (2019); Liu et al. (2019a); Qian et al. (2019b); Rose et al. (2019); Van Doormaal et al. (2019); Azimi et al. (2020); Ferraguti et al. (2020); Gibby et al. (2020); Huang et al. (2020); Jiang et al. (2020); Kiarostami et al. (2020); Kriechling et al. (2020); Kunz et al. (2020); Li et al. (2020); Luzon et al. (2020); Müller et al. (2020); Qian et al. (2020); Rewkowski et al. (2020); Zuo et al. (2020); Brunzini et al. (2021); Condino et al. (2021); Dennler et al. (2021b); Fick et al. (2021); Gu et al. (2021a); Liang et al. (2021); Liu et al. (2021); Kriechling et al. (2021); Liu et al. (2021); Schneider et al. (2021); Spirig et al. (2021); Suzuki et al. (2021); Takata et al. (2021); Van Gestel et al. (2021a); Villani et al. (2021); Wesselius et al. (2021); Zhou et al. (2021)
	Marker-less (7)	Xie et al. (2017); Pepe et al. (2018); Gsaxner et al. (2019); Pepe et al. (2019); Sy- los Labini et al. (2019); Gsaxner et al. (2021c); Gu et al. (2021)
Outside-in (31)	Marker-based (20)	Condino et al. (2018); El-Hariri et al. (2018); Kuzhagaliyev et al. (2018); Chien et al. (2019); De Oliveira et al. (2019); Fotouhi et al. (2019a,b); Li et al. (2019); Meulstee et al. (2019); Pellegrino et al. (2019); Si et al. (2019); Rewkowski et al. (2020); Rüger et al. (2020); Sun et al. (2020); Glas et al. (2021); Gu et al. (2021); Liu et al. (2021b,a); Teatini et al. (2021); Van Gestel et al. (2021b)
	Marker-less (11)	Kuhlemann et al. (2017); García-Vázquez et al. (2018); Leuze et al. (2018); Liu et al. (2018); Wu et al. (2018); Chien et al. (2019); Liu et al. (2019b); Wang et al. (2019); Muangpoon et al. (2020); Castelan et al. (2021); Gu et al. (2021)

cannot be easily addressed with mobile hardware, such as the HoloLens. Consequently, only seven reviewed studies attempt more advanced volume rendering on the HoloLens (Fröhlich et al. (2018); Fink et al. (2019); Witowski et al. (2019); House et al. (2020); Ivan et al. (2021); Gehrsitz et al. (2021); Allison et al. (2020)).

Since data acquisition and reconstruction of 3D volumetric data is relatively costly, only few applications with intraoperative acquisition times exist. Velazco-Garcia et al. (2021b) describe a framework for live interactions with MRI scanners. Qian et al. (2019b) stream 3D endoscopy data to the HoloLens in real time, while Southworth et al. (2020) and Avari Silva et al. (2020) display live 3D cardiac electrophysiology data with the HoloLens.

2D medical image data. 26 reviewed studies use 2D medical imaging as a data source. Common modalities include X- Ray/fluoroscopy scans (9), ultrasound (8) or endoscopic video (5). Contrary to 3D imaging, 2D modalities usually have short acquisition times (close to or even meeting real-time requirements) and are comparably easy to deploy, and are therefore popular for intra-interventional guidance of procedures. 19 publications in this category support intra-interventional data acquisition during the run-time of the HoloLens.

Analogous to the ordinary clinical practice, 2D imaging data in AR is often visualized on virtual (AR) monitors, which can be anchored to the head gaze of the HoloLens wearer. Another possibility is to position 2D images on 3D planes in the environment, which allows an in-situ visualization, if a registration between imaging data and patient is available.

Other data from medical sources. In many situations, it is beneficial to integrate other medical data not stemming from medical imaging into the workflow. Medical planning data is a par-

Table 5: All studies applying object tracking with the HoloLens, grouped by tracking paradigm and method.

Paradigm	Method	Studies
Inside-out (20)	Marker-based (20)	Carbone et al. (2018); Qian et al. (2018); Song et al. (2018); Gao et al. (2019); Liebmann et al. (2019); Qian et al. (2019b); Farshad-Amacker et al. (2020); Kiarostami et al. (2020); Kriechling et al. (2020); Kunz et al. (2020); Müller et al. (2020); Qian et al. (2020); Rewkowski et al. (2020); Kriechling et al. (2021); Li et al. (2021a); Liu et al. (2021c); Nguyen et al. (2022); Spirig et al. (2021); Van Gestel et al. (2021a); Zhou et al. (2021)
Outside-in (21)	Marker-based (16)	El-Hariri et al. (2018); Kuzhagaliyev et al. (2018); Leuze et al. (2018); Liu et al. (2018); De Oliveira et al. (2019); Li et al. (2019); Meulstee et al. (2019); Pellegrino et al. (2019); Rewkowski et al. (2020); Rüger et al. (2020); Sun et al. (2020); Glas et al. (2021); Liu et al. (2021b,a); Teatini et al. (2021); Van Gestel et al. (2021b)
	Marker-less (5)	Kuhlemann et al. (2017); Condino et al. (2018); García-Vázquez et al. (2018); Liu et al. (2019b); Muangpoon et al. (2020)

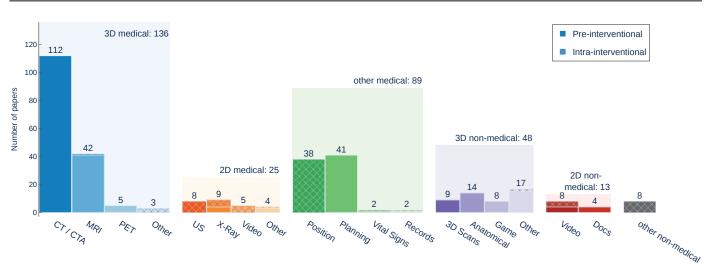


Fig. 10: Frequency of data sources used in the reviewed studies. 3D Medical imaging data is, by far, the most common source of data for a visualization in AR.

ticularly common example, with 41 publications integrating planning data into their workflows. This data is usually created manually and pre-operatively by medical professionals before an intervention on the basis of medical imaging. It can include access points, tool trajectories, cutting lines, resection margins and target positions of implants, amongst others. This type of data is usually translated into geometric primitives, which are displayed in relation to the target anatomy.

For intra-interventional data, the positional coordinates of medical tools (such as needles, wires, or screws) or other tracked objects (parts of the anatomy, imaging systems) obtained from outside-in or inside-out navigation systems are the most common data source (38). Mostly, these objects are represented by geometric primitives or 3D models, which are transformed according to the positional information. However, a simple numerical representation is also used in some studies (Gao et al. (2019); Liebmann et al. (2019); Liu et al. (2019b); Gibby et al. (2020); Kriechling et al. (2020, 2021); Van Gestel et al. (2021b,a); Zhou et al. (2021)).

Other medical data sources, which have been captured both pre- and intra-interventionally, include vital signs or other biosignals and patient records, which can be displayed on virtual monitors in AR.

8.3. Non-medical data

3D data. The inherent ability of the HoloLens for stereoscopic rendering make all sorts of 3D meshes an obvious choice of data source for AR visualizations.

Nine studies use 3D scans of patients, captured with depth or stereo cameras, instead of volumetric medical imaging, mostly for the purpose of image-to-patient registration. Contrary to medical 3D data, such scans can only capture the surface of patients and do not inform about the underlying anatomy. In particular in educational scenarios (targeting both patients and students), the visualization of anatomical models, created by medical artists, is common and used in 14 studies. Both of these data sources have exclusively been deployed pre-interventionally to the HoloLens.

In particular in the context of patient training or assessment, eight studies developed 3D AR games. Other non-medical 3D data are commonly used to produce virtual medical scenarios or procedure simulations (Wang et al. (2017); Cecil et al. (2018); Maniam et al. (2020); Rohrbach et al. (2019); Velazco-Garcia et al. (2021b)).

2D data. A small number of twelve studies visualize nonmedical two-dimensional data in the form of pre-recorded or live streamed videos or documents. As with 2D medical data, it is usually displayed on virtual monitors anchored to the display or environment. Table 6: All studies grouped by data source and type, data modality and acquisition time.

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3D medical (136)	CT & CTA (112)	Pre (112)	Bucioli et al. (2017); Kuhlemann et al. (2017); Sauer et al. (2017); Agten et al. (2018); Condino et al. (2018); El-Hariri et al. (2018); Frantz et al. (2018); Fröhlich et al. (2018); García-Vázquez et al. (2018); Hajek et al. (2018); Kobayashi et al. (2018); Li et al. (2018); Mahmood et al. (2018); McJunkin et al. (2018); Moreta-Martinez et al. (2018); Pratt et al. (2018); Rae et al. (2018); Tan et al. (2018); Turini et al. (2018); Wu et al. (2018); Affolter et al. (2019); Brun et al. (2019); Checcucci et al. (2019); Cocco et al. (2019); De Oliveira et al. (2019); Fink et al. (2019); Fotouhi et al. (2019b); Gao et al. (2019); Gibby et al. (2019); Gsaxner et al. (2019); Huang et al. (2019b); Kalavakonda et al. (2019); Kubben and Sinlae (2019); Li et al. (2019); Li et al. (2019); Li u et al. (2019); Li u et al. (2019); Kubben and Sinlae (2019); Li et al. (2019); Li bibmann et al. (2019); Li u et al. (2019); Lohou et al. (2019); Maniam et al. (2020); Mitsuno et al. (2019); Woosburner et al. (2019); Pellegrino et al. (2019); Wae et al. (2019); Sylos Labini et al. (2019); Van Doormaal et al. (2010); Allison et al. (2020); Azimi et al. (2020); Bulliard et al. (2020); Cartucho et al. (2020); Cocco et al. (2020); Creighton et al. (2020); Galati et al. (2020); Ferraguti et al. (2020); Fischer et al. (2020); Creighton et al. (2020); Galati et al. (2020); Gibby et al. (2020); Jiang et al. (2020); Katayama et al. (2020); Kiarostami et al. (2020); Kirechling et al. (2020); Sun et al. (2020); Tian et al. (2020); Viehöfer et al. (2020); Saito et al. (2020); Buch et al. (2021); Cofano et al. (2021); Condino et al. (2021); Gesaxner et al. (2021); Coci et al. (2021); Kriechling et al. (2021); Gehrsitz et al. (2021); Gias et al. (2021); Giasxner et al. (2021); Li et al. (2021); Birka et al. (2021); Korachi et al. (2021); Corachi et al. (2021); Cora
	MRI (42)	Pre (41)	Morales Mojica et al. (2017); Perkins et al. (2017); Xie et al. (2017); Carbone et al. (2018); Fröhlich et al. (2018); Incekara et al. (2018); Jang et al. (2018); Karmonik et al. (2018); Leuze et al. (2018); Gsaxner et al. (2019); Kubben and Sinlae (2019); Si et al. (2019); Soulami et al. (2019); Van Doormaal et al. (2019); Wake et al. (2019); Wei et al. (2019); Allison et al. (2020); Cartucho et al. (2020); Ferraguti et al. (2020); Galati et al. (2020); Gibby et al. (2020); Gnanasegaram et al. (2020); House et al. (2020); Kumar et al. (2020); Nguyen et al. (2020b,a); Pelanis et al. (2020); Tian et al. (2020); Condino et al. (2021); Fick et al. (2021); Gehrsitz et al. (2021); Gsaxner et al. (2021c); Iizuka et al. (2021); Ivan et al. (2021); Morales Mojica et al. (2021); Qi et al. (2021); Scherl et al. (2021a,b); Van Gestel et al. (2021a,b); Wake et al. (2021)
		Intra (1)	Velazco-Garcia et al. (2021b)
	PET (5)	Pre (5)	Fröhlich et al. (2018); Pepe et al. (2018, 2019); Gsaxner et al. (2021c); Galati et al. (2020)
	Other (3)	Intra (3)	Qian et al. (2019b); Avari Silva et al. (2020); Southworth et al. (2020)
2D medical (25)	US (8)	Intra (8)	El-Hariri et al. (2018); García-Vázquez et al. (2018); Kuzhagaliyev et al. (2018); Mahmood et al. (2018); Cartucho et al. (2020); Farshad-Amacker et al. (2020); Rüger et al. (2020); Nguyen et al. (2022)
	X-Ray	Pre (4)	Qian et al. (2017); Cocco et al. (2019, 2020); Galati et al. (2020)
2D	(9)	Intra (5)	Andress et al. (2018); Deib et al. (2018); Fotouhi et al. (2019a); Liu et al. (2019b); Al Janabi et al. (2020)
	Video (5)	Intra (5)	Qian et al. (2018); Kobayashi et al. (2019); Al Janabi et al. (2020); Qian et al. (2020); Yajima et al. (2020)
_	Other (4)	Pre (3)	Hanna et al. (2018); Huang et al. (2020); Robinson et al. (2020)

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Source & Type	Modality	Acq. time	Studies
		Intra (1)	Cui et al. (2017)
other medical (89)	Position (38)	Intra (38)	Kuhlemann et al. (2017); Andress et al. (2018); Carbone et al. (2018); Condino et al. (2018); García-Vázquez et al. (2018); Hajek et al. (2018); Kuzhagaliyev et al. (2018); Liu et al. (2018); Qian et al. (2018); Song et al. (2018); Turini et al. (2018); Fotouhi et al. (2019b,a); Gao et al. (2019); Li et al. (2019); Liebmann et al. (2019); Liu et al. (2019a); Meulstee et al. (2019); Pellegrino et al. (2019); Qian et al. (2019b); Si et al. (2019); Guo et al. (2020); Kriechling et al. (2020); Muangpoon et al. (2020); Müller et al. (2020); Qian et al. (2020); Iqbal et al. (2021); Li et al. (2021a); Liu et al. (2021b,a,c); Spirig et al. (2021); Teatini et al. (2021); Van Gestel et al. (2021a,b); Velazco-Garcia et al. (2021a); Zhou et al. (2021)
other n	Planning (41)	Pre (41)	Azimi et al. (2018a); Carbone et al. (2018); Condino et al. (2018); Kobayashi et al. (2018); Li et al. (2018); Pratt et al. (2018); Song et al. (2018); Turini et al. (2018); Gibby et al. (2019); Li et al. (2019); Liebmann et al. (2019); Liu et al. (2019a); Lohou et al. (2019); Wang et al. (2019); Azimi et al. (2020); Ferraguti et al. (2020); Gibby et al. (2020); Kiarostami et al. (2020); Kriechling et al. (2020); Li et al. (2020); Maniam et al. (2020); Müller et al. (2020); Tian et al. (2020); Cofano et al. (2021); Condino et al. (2021); Dennler et al. (2021a); Glas et al. (2021); Li et al. (2021a); Spirig et al. (2021); Suzuki et al. (2021); Van Gestel et al. (2021a); Wesselius et al. (2021); Zhou et al. (2021)
	Vital	Pre (1)	Qian et al. (2017)
	Signs (2)	Intra (1)	Sirilak and Muneesawang (2018)
	Records	Pre (1)	Perkins et al. (2020)
	(2)	Intra (1)	Deib et al. (2018)
3D non-medical (48)	3D Scans (9)	Pre (9)	Hanna et al. (2018); Liu et al. (2018); Amini and Kersten-Oertel (2019); Chien et al. (2019); Talaat et al. (2019); Nuri et al. (2020); Proniewska et al. (2020); Kumar et al. (2021); Liu et al. (2021b)
	Anatomical model (14)	Pre (14)	Aguilera-Canon et al. (2018); Song et al. (2018); Balian et al. (2019); Stojanovska et al. (2019); Antoniou et al. (2020b,a); Robinson et al. (2020); Rositi et al. (2021); Ruthberg et al. (2020); Bogomolova et al. (2021); Brunzini et al. (2021); Castelan et al. (2021); Moro et al. (2021); Putnam et al. (2021)
3Г	Game (8)	Pre (8)	Aruanno et al. (2017); Garzotto et al. (2018); Aruanno and Garzotto (2019); Martinez et al. (2019); Desai et al. (2020); Guo et al. (2020); Thomos et al. (2020); Blomqvist et al. (2021)
	Other (17)	Pre (15)	Wang et al. (2017); Azimi et al. (2018b); Cecil et al. (2018); Sharma et al. (2018); Meulstee et al. (2019); Palermo et al. (2019); Rohrbach et al. (2019); Geerse et al. (2020); Janssen et al. (2020); Maniam et al. (2020); Rewkowski et al. (2020); Höhler et al. (2021); Liang et al. (2021); Velazco-Garcia et al. (2021a); Villani et al. (2021)
		Intra (2)	Angelopoulos et al. (2019); Butaslac et al. (2020)
2D non-	Video (8)	Pre (4)	Sun et al. (2019); Lemke et al. (2020); Lu et al. (2020); Schoeb et al. (2020)
medical (13)		Intra (4)	Sirilak and Muneesawang (2018); Mitsuno et al. (2019a); Glick et al. (2020); Cofano et al. (2021)
	Docs (4)	Pre (4)	Hanna et al. (2018); Sirilak and Muneesawang (2018); Galati et al. (2020); Rositi et al. (2021)

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Source & Type	Modality	Acq. time	Studies
other non- medical (8)	-	Intra (8)	Yamashita et al. (2017); Karatsidis et al. (2018); Sharma et al. (2018); Sun et al. (2019); Butaslac et al. (2020); Geerse et al. (2020); Koop et al. (2020); Heinrich et al. (2021)

Other data. Eight works have explored the possibility of integrating other data, in most cases coming from the HoloLens itself, into their applications. Three publications track the user wearing the HoloLens, to measure movement parameters (Butaslac et al. (2020); Geerse et al. (2020); Koop et al. (2020)) or guide the user (Yamashita et al. (2017); Karatsidis et al. (2018)). Two publications utilize the head gaze data from the HoloLens (Sun et al. (2019); Heinrich et al. (2021)). Only Sharma et al. (2018) use an external data source, namely IMU data, for training limb prosthesis control.

9. Evaluation of medical HoloLens applications

In general, an objective evaluation of AR applications is challenging, because each user has a different perception of augmented content, depending on individual anatomy (interpupillary distance, eye sight), familiarity with the technology, familiarity with 3D visualizations in general (Rosser et al. (2007)) and external influences, such as comfort while wearing the AR device.

In comparison to other areas of computer science, no benchmarks, datasets or standard protocols exist to evaluate AR systems, experiences and methodologies. Clinically, comparative clinical trials, measuring and comparing parameters about treatment outcomes, such as treatment time, number and severity of complications or survival rate, are considered gold standard. However, each AR application requires approval by a relevant agency or committee before it can be tested on cadavers, healthy human subjects or even patients. Depending on the executive research institution and national regulations, obtaining such an approval and the quantitative data that comes with it, can be very difficult for researchers. Therefore, in our reviewed studies, a large variety of evaluation metrics have been collected in distinct experimental scenarios, which are summarized in Table 7.

9.1. Evaluation scenario

We first analyze the reviewed publications with regard to the evaluation scenario. Inspired by the Technology Readiness Level (Mankins et al. (1995)), we group the studies according to their evaluation settings, also shown in Figure 11:

Proof of concept studies. Proof of concepts focus on reporting a medical problem, how AR could overcome it and describe their prototype workflows and applications. Sometimes, anecdotal or informal feedback from users or general observations are reported, but, in general, these studies do not follow a rigorous experimental protocol and do not collect quantitative or qualitative measurements. Therefore, it is difficult to draw general conclusions from them. With 42 papers, proof of concept studies are in the minority.

Laboratory studies. They typically focus on the technical aspects of their applications and report quantitative measurements, acquired by AR system designers. We identify 66 records in this category. Laboratory studies can be carried out using only hardware (e.g., the HoloLens), or on cadavers, animals or (healthy) humans. All but one study in this category target Most commonly, however, phantoms are used to collect measurements. Specialized medical phantoms, which include realistic anatomical structures and tissue characteristics, are commercially available, however, they are very expensive. Consequently, many researchers resort to additive manufacturing (i.e., 3D printing) to replicate the target anatomy or for building more abstract phantoms modeling certain procedures. Almost all reviewed publications in this category target an application for physicians. Studies carried out on humans focus on data display (2) or patient diagnosis (1), while animal and cadaver studies exclusively target image guided interventions or surgical navigation, similar to phantom studies, where only one reviewed publication aims at interventional training for students.

For a purely technical evaluation, all except one study, which deals with image-guided intervention, are targeted on data display.

Studies performed in a relevant environment. They evaluate their AR systems directly in the environment in which it should be implemented. Such an approach involves the usage of the system by one or more individuals of the intended target group - either clinicians, patients or medical students, in a clinically realistic setting (note that we do not require experiments performed on patients for studies to fall into this category). Most of the time, qualitative feedback in the form of questionnaires is collected from them, although quantitative measurements, for example measuring task performance, might also be taken. As seen in Figure 11, most of the reviewed studies (110) fall into this category, which indicates advanced research maturity. It is interesting to note that only 63 out of 158 (40 %) of physicianfocused studies were evaluated in a relevant environment, and only 40 thereof are related to IGI or surgical navigation, which are the applications with highest accuracy demands. Otherwise, 26 out of 34 (76 %) and 21 out of 25 (84 %) studies focused on students and patients, respectively, fall into this category. We further distinguish between non-comparative studies, where results acquired through AR are not compared to another method (for example, case series or uncontrolled cohort studies), and comparative studies, which provide comparisons to non-AR conditions. The latter are most conclusive about the possible advantages and implications of the HoloLens in their domain.

9.2. Quantitative metrics

Quantitative metrics are often focused on technical aspects of the AR system. Therefore, acquiring them does not require a large number of test subjects and, instead, can be done by individuals. However, they can also characterize the performance of individuals in carrying out certain tasks. In this case, quantitative measures are usually closely related to the application scenario.

Technical performance metrics. Several works, in particular in the area of data display, measure performance metrics of the HoloLens itself, such as hardware utilization, frame rate, power usage, execution time and latency. The studies come to the conclusion that the HoloLens is suitable for displaying pre- and intra-interventional medical data given an appropriate software framework, also within safety critical environments, such as the OR. A commonly reported limiting factor is battery life, which restricts device usage to around two hours, which is too short for many medical interventions.

The HoloLens was also compared to other OST-HMD devices for medical usage. Qian et al. (2017) evaluated the HoloLens, Epson Moverio BT-200 and ODG R-7 for displaying objectanchored 2D medical data, and concluded that the HoloLens is the best choice in terms of contrast, frame rate and perceived task load. Moosburner et al. (2019) compare the HoloLens to the

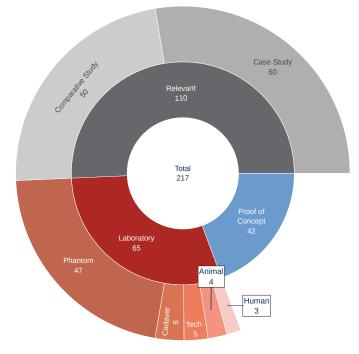


Fig. 11: Number of papers for each experimental setting (inner circle) and experimental level (outer circle).

Meta 2 (Meta Company, San Mateo, California, USA) and found that, albeit the HoloLens was criticized for having a comparably small FoV and being more complicated and difficult to operate, medical students preferred it over the competitor, as it does not rely on a wired connection to a powerful external computer and presented virtual models more stably.

Accuracy metrics. For registration and tracking, accuracy metrics, measuring the spatial distance between the virtual and real position of an object, are usually acquired. We would like to point out that most of these metrics are not well documented and standardized, and therefore, the studies included in this review use various techniques to measure and report them. Unfortunately, the measurement processes or formulas for metric computation are often not described entirely, which makes it very difficult to compare between studies. We hope that the metrics described hereafter can serve as a guiding principle for researchers looking to evaluate their systems.

While many different measures can be computed, the target registration error (TRE) is one of the most commonly and consistently used metrics for evaluating registration accuracy, and has been employed by 26 reviewed studies. Introduced by Maurer et al. (1997) for surgical navigation scenarios, TRE measures the end-to-end registration accuracy between the coordinate frame of pre-interventional imaging and the physical patient coordinate frame. Specifically, TRE computes the Euclidean distance between a set of 3D target points in the patient coordinate frame, \mathbf{t}^P , to their virtual counterparts in the imaging coordinate frame, \mathbf{t}^I , after they have been transformed by an estimated transformation *T*. It is defined by

$$TRE = \frac{1}{N_t} \sum_{n=1}^{N_t} ||\mathbf{t}_n^P - T(\mathbf{t}_n^I)||,$$
(1)

where N_t is the number of target points. Since the TRE was originally proposed for point-based registration, it is important to stress that \mathbf{t}^P and \mathbf{t}^I must not be used to estimate *T*. Commonly, points for TRE computation, both in the physical space and virtual model, are digitized using a tracked stylus, e.g., using outside-in optical (El-Hariri et al. (2018); Moreta-Martinez et al. (2018); Si et al. (2019); Wang et al. (2019); McJunkin et al. (2018); Fischer et al. (2020)), electromagnetic (Condino et al. (2018)) or inside-out (Liu et al. (2021c)) tracking. In the absence of an external system, the points can be selected directly in the vision of the user, in the AR environment, using the HoloLens' gesture input (Hajek et al. (2018); Gsaxner et al. (2019); Fotouhi et al. (2019b)).

Studies evaluating the TRE report averages of just above 1 mm and up to 40 mm. E.g., for a registration using outside-in tracking, El-Hariri et al. (2018) report a TRE of 36.9 mm, while Kuhlemann et al. (2017), Li et al. (2019), Si et al. (2019) and Sun et al. (2020) report much lower values of 4.3 mm, 2.2 mm, 2.1 mm and 1.3 mm, respectively. For manual registration, the reported error spectrum is also large, ranging between 20 mm (Buch et al. (2021)) and 3 mm (Tian et al. (2020)). Registration using image fiducials seems to be the most reliable in terms of TRE, with values in the 2 to 3 mm region (Condino et al. (2018); Moreta-Martinez et al. (2018); Liu et al. (2021c)), but several studies show that the achievable accuracy with image fiducials is highly dependent on lumination, viewing angle and movement (Jiang et al. (2020); Luzon et al. (2020); Zuo et al. (2020)). Whether the reported registration accuracies are acceptable is, of course, contingent upon the clinical scenario. However, most studies express the need to reduce the registration error before clinical usability. While TRE provides some comparability between registration methods, measuring it involves the selection or digitization of matching landmark points, which is itself a subjective, error-prone procedure, encumbered by a lack of haptic feedback, fine-grained input possibilities and depth perception. Therefore, the localization of a point always contains an error, which is referred to as target localization error (TLE) in the literature (Maurer et al. (1997)), and is highly variable depending on imaging modality and method for digitization. Unfortunately, this metric is not reported by any of the studies. These problems explain the large variability reported for this metric.

As already mentioned, the interest points for TRE computation must not be used for estimating the transformation T. The fiducial registration error (FRE), on the other hand, computes the error in exactly these fiducial points \mathbf{f}^P and \mathbf{f}^I used in landmark-based registration:

$$FRE = \frac{1}{N_f} \sum_{n=1}^{N_f} ||\mathbf{f}_n^P - T(\mathbf{f}_n^I)||.$$
(2)

Five publications report FRE. For example, Van Doormaal et al. (2019) compared FRE achievable with marker-based inside-out registration using landmarks with a conventional SNS registration. They found that the AR system is less accurate and not yet suitable for clinical application. Fick et al. (2021) and Liu et al. (2021c) report FRE of 8.5 and 3.4 mm,

respectively. However, it has been shown that FRE does not correlate with the TRE and, thus, does not inform much about the actual registration accuracy (Fitzpatrick (2009)). Similar to TLE, fiducial localization error (FLE) gauges the accuracy with which fiducial points can be localized with the given setup.

Registration error, measured in four studies, calculates the deviation between the source-to-target transformation computed by the employed algorithm and a reference transformation obtained from a reference tracking system. Analogously, tracking error compares the pose of a tracked object to a ground truth, ideally in six degrees of freedom. Since the reference system and the HoloLens need to be calibrated, such experiments are complicated to set up. Therefore, many studies report a simplified tracking error, e.g., in 2D (Liu et al. (2019b)) or positional only (Kunz et al. (2020); Liu et al. (2021b)).

Another common measure, evaluated in 22 studies, is the target visualization error (TVE), which measures the re-projection error between physical and virtual objects as perceived by the user. Thus, it is similar to TRE or FRE in Equation 1 and Equation 2, respectively, depending on whether fiducial points or independent target points are used for computation, but is measured in 2D, i.e., the interest points are projected onto a plane. The error is either reported as the Euclidean distance (in 2D) between source and target points, or separately in x, y and z direction. Since TVE is measured from the perspective of the user, it is able to represent the display calibration error (resulting from insufficient calibration between the user's eyes and the display) and registration error together. Still, the manual measurement of TVE is, again, subject to operator bias. TVE Measurements can be taken using a ruler or similar scaling device (Pepe et al. (2018); Song et al. (2018); Sylos Labini et al. (2019); Nguyen et al. (2020a); Qi et al. (2021)) or a measurement grid (Frantz et al. (2018); Huang et al. (2020); Li et al. (2020); Pérez-Pachón et al. (2021); Teatini et al. (2021)). Some studies directly mark the virtual projection on the real counterpart for easier measurement (Perkins et al. (2017); Incekara et al. (2018)). Most studies report TVE values in the millimeter region. Four studies compare the TVE achieved using the HoloLens with a non-AR baseline: Ivan et al. (2021) found no significant difference to a commercial SNS in terms of TVE. Qi et al. (2021) state that AR could reach the reference precision in 80% of cases, while Incekara et al. (2018) determined that only in 38% of cases the reference could be met, and the mean deviation of 4 mm between HoloLens and SNS is too large for clinical applicability. Li et al. (2020) compare smartphone- and HoloLens-guided to freehand needle interventions, and show that AR guidance can reduce the placement error, although the smartphone performed better than the HoloLens.

In clinical interventions where pre-interventional planning data is available, the target deviation error (TDE), which measures the discrepancy between pre-operative plan and final location after intervention, can be determined. It is the most common amongst accuracy metrics defined here, with 34 studies measuring it. A typical scenario is the insertion of objects, such as needles, wires or screws, into a phantom, cadaver or patient under AR guidance. After insertion, all studies acquire postoperative imaging and compare it to the planning. This type of clinically specific evaluation is most informative about how an AR system can support the intervention in question, and takes display calibration and registration error into account. However, it is also heavily operator-biased, as an experienced operator might sub-consciously compensate for guidance errors and rely on their experience instead of the AR system. For point targets (e.g., the entry or destination point of an object), Euclidean distance between a pre-operatively planned target point $\mathbf{p}^{planned}$ and the final point after intervention \mathbf{p}^{final} is calculated:

$$TDE_p = \|\mathbf{p}^{planned} - \mathbf{p}^{final}\|.$$
(3)

For trajectories (e.g., needle or screw paths), the 3D angle between planned trajectory $\mathbf{v}^{planned}$ and executed trajectory \mathbf{v}^{final} may be obtained as

$$TDE_{v} = \arccos\left(\frac{\mathbf{v}^{planned} \ \mathbf{v}^{final}}{\|\mathbf{v}^{planned}\| \| \|\mathbf{v}^{final}\|}\right). \tag{4}$$

Several studies compare TDE of an AR-supported procedure to a non-AR control condition; however, results are inconclusive. For example, Agten et al. (2018); Andress et al. (2018); Liu et al. (2019a); Müller et al. (2020); Long et al. (2021) compare needle/wire placements under AR guidance with a conventional, flouroscopy-guided procedure. They found that placements in AR were slightly less accurate than in the reference condition, although AR guidance lead to faster task completion. Andress et al. (2018), Wei et al. (2019) and Long et al. (2021) further point out that, with AR, less radiation was required during imageguided procedures. Li et al. (2019), Rüger et al. (2020) and Glas et al. (2021), report favorable needle insertion accuracies in AR-guided procedures versus conventional image guided procedures. Compared to freehand, non-guided procedures, AR could improve both accuracy and number of successful task completions in placement tasks (Azimi et al. (2020); Ferraguti et al. (2020); Li et al. (2020); Dennler et al. (2021b); Van Gestel et al. (2021b)).

Task-specific scores. Studies using the HoloLens for supporting specific medical tasks usually report some quantification of task completion. The task completion time (TCT) is most commonly measured, namely in 38 reviewed studies. Most comparative studies report that AR guidance helped users in carrying out tasks faster (Agten et al. (2018); Al Janabi et al. (2020); Andress et al. (2018); Liu et al. (2019a); Wei et al. (2019); Galati et al. (2020); Farshad-Amacker et al. (2020); Müller et al. (2020); Long et al. (2021); Heinrich et al. (2021); Glas et al. (2021); Sharma et al. (2018); Ferraguti et al. (2020); Qian et al. (2020); Suzuki et al. (2021)), while others did not report significant differences (Wang et al. (2017); Azimi et al. (2018b); Deib et al. (2018)). Only Qi et al. (2021) and Rohrbach et al. (2019) report longer TCT for the AR condition, however, the latter application is targeted at Alzheimer's patients, who may have more difficulties in adapting to novel technology, such as AR and the HoloLens.

The number of successful task completions (NSC) is measured in 14 studies. Most studies report favorable outcomes of HoloLens usage in terms of NSC (Dennler et al. (2021b); Schneider et al. (2021); Sharma et al. (2018); Farshad-Amacker et al. (2020); Qian et al. (2020)). Only Agten et al. (2018) found that AR actually leads to less successful outcomes, compared to a conventional image-guided procedure.

The effectiveness of AR for learning in an educational scenario can be quantitatively measured by comparing exam scores between AR-supported learners and a control group. Seven studies perform such an evaluation. Most of them do not find a statistically significant knowledge improvement between students receiving AR lectures through the HoloLens versus students undergoing conventional anatomy courses (Stojanovska et al. (2019); Robinson et al. (2020); Ruthberg et al. (2020)). Only the study by Shao et al. (2020) measured significantly better outcomes of AR lectures over conventional ones. Robinson et al. (2020), however, highlight that students perceived the AR activity more favorably. Similar findings are described in comparison to other computerized learning methods by (Antoniou et al. (2020b); Gnanasegaram et al. (2020); Moro et al. (2021)) - while student engagement, motivation and excitement is typically higher for HoloLens-based education, the outcomes in terms of learning effect are not significantly different.

9.3. Qualitative metrics

We define qualitative metrics as parameters and data, which reflect the personal opinion of individuals, and can, therefore, not be objectively and repeatably measured. Usually, they are collected from application users by the means of questionnaires or interviews. Since AR experiences are highly individual, qualitative metrics can be considered equally if not more important than quantitative measures. After all, theoretical benefits of medical AR are negligible if the system that delivers them is deemed cumbersome or fails to meet the user's needs.

Commonly, questionnaires use a Likert scale, where respondents express their level of agreement or disagreement with certain statements. 49 reviewed publications use such questionnaires for evaluating various system aspects. Examples include general comfort, image quality and audio quality of the HoloLens and its suitability for medical applications (Condino et al. (2018); Jang et al. (2018); Sirilak and Muneesawang (2018); Moosburner et al. (2019); Galati et al. (2020); Kumar et al. (2020); Al Janabi et al. (2020); Scherl et al. (2021a); Dennler et al. (2021b)), the effectiveness of certain types of visualization (Brun et al. (2019); Wake et al. (2019); House et al. (2020); Gehrsitz et al. (2021)) or, most commonly, how well the proposed application can support a certain procedure.

Generally, the reported questionnaire outcomes are favorable towards the HoloLens and AR, and the common consensus is that AR can have a large impact in the medical domain. However, limitations of the device itself, such as the small field of view, short battery life and relative discomfort while wearing it are frequently mentioned. For IGI or navigation applications, users also frequently noticed a lack of registration accuracy or a drift of virtual content due to instabilities in the HoloLens SLAM, which negatively influenced user ratings. In these scenarios, issues of depth perception, where users perceived internal anatomy to be on top of, not within, the patient, were also frequently mentioned.

Some reviewed studies employed standardized questionnaires, with the NASA Task Load Index (NASA-TLX), a tool to assess

subjective workload, being the most common one, with 10 uses. A drawback of the NASA-TLX is that it is only fully descriptive in comparative studies, where it is measured for several conditions. A classification or interpretation of a single final score is, generally, not substantial. Unfortunately, only a few comparative studies measure the NASA-TLX – two of them report a reduced task load for AR-supported procedures (Ferraguti et al. (2020); Qian et al. (2020)), Rüger et al. (2020); Azimi et al. (2020, 2018b) found no significant difference in overall workload, although the latter study found that the participants' confidence was higher under the AR condition. Saito et al. (2020) measured an increased workload for participants using AR.

The System Usability Scale (SUS) by Brooke et al. (1996) was applied in six studies as a measure for application usability. Compared to the NASA-TLX, the advantage of SUS is that it is a fast way of classifying the ease of use of a system, even without a comparison. Generally, overall scores greater than 68 are considered above average; furthermore, an adjective rating scale has been proposed (Bangor et al. (2009)). Three reviewed studies compute the overall SUS, reporting above average usability with SUS values of 71.5 (Amini and Kersten-Oertel (2019)), 77.2 (Azimi et al. (2020)) and 74.8 (Gsaxner et al. (2021c)), indicating an above average usability of these systems. While these ratings are encouraging, they suggest that there is room for improvement.

10. Conclusion and outlook

With 217 original, peer reviewed works in the medical field, the HoloLens certainly had a large impact on medical AR already. In this systematic review, we found that, while various medical specialties and applications have been investigated, and a fair number of systems have been studied clinically, only few works have clinically demonstrated clear advantages of HoloLens-based systems over the current state-of-the-art. The acceptance of new technologies, such as AR, in the medical field is an ongoing challenge for researchers, medical professionals and patients alike. In this review, we identify that increased efforts in the areas of precision, reliability, usability, workflow and perception are necessary to establish AR in clinical practice.

We found that applications targeted at physicians and healthcare professionals are, by far, the most common. While the potential benefit for AR-supported image guidance and navigation is very high, those systems are also difficult to implement, mostly due to the high accuracy and reliability demands. The reviewed studies suggest that, for high precision applications, registration and tracking errors achieved with the HoloLens are generally too high, regardless of the employed technical paradigm and method. However, for procedures carried out without image guidance, for which sub-millimeter precision is not necessary (e.g., ablations (Ferraguti et al. (2020)), ventriculostomy (Li et al. (2018); Azimi et al. (2020); Van Gestel et al. (2021b); Schneider et al. (2021)) or certain orthopedic interventions (Dennler et al. (2021a))), the HoloLens is already a very promising tool. In these scenarios, the small form factor and low cost of the HoloLens in comparison to traditional image guidance systems could make navigation feasible for procedures which have not

benefited from it before. For this purpose, however, automatic and accurate inside-out registration and tracking is paramount to keep the setup and workflow manageable.

The second most common intended user group were students. In educational training scenarios, the HoloLens was shown to be an effective enhancement for medical simulators (Balian et al. (2019); Hong et al. (2020); Muangpoon et al. (2020); Schoeb et al. (2020); Suzuki et al. (2021); Heinrich et al. (2021)), in particular for providing visual feedback during training tasks. In anatomy learning, the effects of HoloLens learning compared to conventional learning using cadavers or other computerized methods seem to be small, although several studies report improved engagement and motivation of students, which could have positive effects in the long term. Anatomy learning studies in this review also usually feature relatively simple, conventional 3D models. More innovative visualizations, including interactive, dynamic content, which can not be easily delivered by regular computerized methods, have not been explored in depth yet.

Finally, patients were the least frequent target user. Unfortunately, many interesting assistance and monitoring applications are limited by the restricted possible usage time of the HoloLens, and it is not foreseeable that next-gen OST-HMD devices will overcome these limitations in the near future. However, for selected scenarios, such as guidance through therapy and diagnosis sessions, the HoloLens has already shown to be useful. Until now, only a small number of applications have been explored in this context – it will be interesting to see whether other disciplines can benefit from such paradigms as well.

In summary, we found that a large proportion of studies focuses on superimposing virtual data, most commonly preinterventional imaging or planning data, with real objects, usually the patient. Methods for patient registration and tracking lie at the core of these studies, however, only few reviewed works propose novel concepts in this direction, while the bulk of publications applies variations of the same methods to different medical scenarios with limited innovations. Inside-out approaches, in particular using image fiducials, are the most common. This observation is unsurprising - after all, such approaches are relatively easy to implement. Our analysis shows that they deliver a reliable accuracy in controlled settings, which is already acceptable for some medical applications which do not require sub-millimeter preciseness. Their disadvantages, such as line-of-sight constraints and susceptibility to different viewing positions, movement patterns and lighting conditions, however, likely impede clinical adoption. Spherical markers seem to be more robust and encouraging results have been reported (Kunz et al. (2020)), more recently also for the HoloLens 2 (Gsaxner et al. (2021b)). These markers have proven their value in commercial SNS, still, it remains to be seen whether they can be tracked with sufficient accuracy and reliability by AR devices in a real clinical setting. Innovative, marker-less, inside-out strategies have been reported for registration, but are still hampered by technical limitations. For instrument tracking, research in the direction of marker-less, inside-out methods based on deep learning is only recently gaining traction (Doughty and Ghugre (2022)), but will surely have a large impact in the field. It is important to point out that the perceived error by the user includes the display calibration error between HMD and the user's eyes, on top of the registration error, which is not considered by all common metrics, such as TRE. More recent hardware, including the HoloLens 2, features eye tracking capabilities (Ungureanu et al. (2020)), which enables more powerful, automatic display calibration to overcome this limitation.

When it comes to data and visualization, the majority of studies display pre-interventionally acquired 3D medical imaging data, primarily from CT or CTA, visualized through surface rendering. We expect this trend to continue. Although some preprocessing (i.e., segmentation and mesh extraction) is necessary, surface renderings are easy to create and modify. Compared to volume rendering, they are more efficient, and no clear advantage of volume rendering through the HoloLens has been shown so far. Perceptual issues, in particular depth perception, are a known problem in AR (Livingston et al. (2013)), and several works mention that incorrect depth perception negatively influenced the perceived accuracy of their application and impaired guidance through the HoloLens. Still, very few reports concern themselves with visualization strategies overcoming these limitations, and use very simple methods (e.g., wire frames (Fischer et al. (2020))). While many strategies exist to improve depth perception in medical AR (Gsaxner et al. (2021a)), most of them are difficult to apply with OST displays, such as the HoloLens, where only additive visual information is possible and the view of reality cannot be altered. Novel, innovative strategies will be necessary to overcome this limitation in the future.

It is paramount that medical AR applications are validated with the intended user in the loop, and it is encouraging to see that the majority of studies in this review evaluate their applications in a relevant setting. Unfortunately, studies in a relevant environment are most scarce in the areas which demand the highest amount of accuracy and reliability, i.e., image-guided interventions and navigated surgery. At the same time, the large variety in experimental setups and acquired measures, together with the lack of standardized protocols, makes it very difficult to clinically validate these methods.

The HoloLens 1 has caused a major boost in medical AR research. We can now see that the technical novelties of newer generation hardware, such as the HoloLens 2, open up new possibilities in medical AR (Palumbo (2022)). In particular, improved and more stable environmental understanding (Pose-Díez-de-la Lastra et al. (2022)) and automatic display calibration via eye tracking can reduce the perceived error in see-through visualization systems, while articulated hand tracking (Ungureanu et al. (2020)) and an increased field of view can enhance human-computer interactions (see Table A.8 in the appendix for details). With the recent increased interest of other leading tech companies in AR technologies, we expect this trend to continue. Furthermore, specialized medical OST-HMD devices, e.g., xvision (Augmedics Inc., Arlington Heights, IL) or VOSTARS (University of Pisa, Pisa, IT) (Carbone et al. (2022)), have the potential to address technical limitations in current, commercial devices. Improved hardware can also facilitate the use of deep learning models on the HMD itself, opening up countless possibilities in terms of recognition, tracking and scene underTable 7: Summary of evaluation strategies for medical HoloLens applications. Studies are grouped according to their evaluation setting and level. For each study, we report the acquired qualitative (Qual) and quantitative (Quant) measures.

Proof of Concept Studies (no measures reported)

Bucioli et al. (2017); Cui et al. (2017); Sauer et al. (2017); Xie et al. (2017); Aguilera-Canon et al. (2018); Azimi et al. (2018a); Carbone et al. (2018); Cecil et al. (2018); Garzotto et al. (2018); Hanna et al. (2018); Karmonik et al. (2018); Kobayashi et al. (2018); Kuzhagaliyev et al. (2018); Mahmood et al. (2018); Pratt et al. (2018); Tan et al. (2018); Affolter et al. (2019); Kalavakonda et al. (2019); Kubben and Sinlae (2019); Lohou et al. (2019); Mitsuno et al. (2019a); Soulami et al. (2019); Witowski et al. (2019); Allison et al. (2020); Boyd et al. (2020); Butaslac et al. (2020); Desai et al. (2020); Fitski et al. (2020); Katayama et al. (2020); Lu et al. (2020); Maniam et al. (2020); Perkins et al. (2020); Proniewska et al. (2020); Castelan et al. (2021); Gouveia et al. (2021); Iizuka et al. (2021); Li et al. (2021b); Morales Mojica et al. (2021); Saito et al. (2022); Sugahara et al. (2021); Wake et al. (2021); Wesselius et al. (2021)

	Laboratory Studies (Quantitative measures)					
Level	Study	Measures				
Technical	Morales Mojica et al. (2017) Fröhlich et al. (2018) Talaat et al. (2019) Velazco-Garcia et al. (2021b) Villani et al. (2021)	CPU usage, memory consumption, FPS CPU usage, GPU usage, memory consumption, FPS Distance between landmarks FPS, Latency FPS, RE				
	Agten et al. (2018) El-Hariri et al. (2018) Frantz et al. (2018) García-Vázquez et al. (2018) Hajek et al. (2018) Leuze et al. (2018) Liu et al. (2018) Moreta-Martinez et al. (2018)	Task completion time, Number of successful completions Target registration error Registration time, Target visualization error, content drift Latency Calibration error (hand-eye), Target registration error, Number of successful completions Tracking error, Registration error Target deviation error (drilled hole) Target registration error, Target deviation error (surgical guide)				
lom	Qian et al. (2018) Rae et al. (2018) Song et al. (2018) Wu et al. (2018) Chien et al. (2019) De Oliveira et al. (2019) Fink et al. (2019) Fotouhi et al. (2019a)	Target visualization error, Tracking error, FPS Target visualization error, Registration time Target visualization error Target registration error, Registration time Target registration error, Registration time SLAM accuracy, Latency, Target visualization error FPS, structural similarity index Calibration error (hand-eye), Tracking accuracy				
Phantom	Fotouhi et al. (2019b) Gibby et al. (2019) Gsaxner et al. (2019) Huang et al. (2019b) Liebmann et al. (2019) Liu et al. (2019b) Liu et al. (2019a)	Target registration error, Calibration error (hand-eye) Target deviation error (needle), Task completion time Target registration error, Registration error, Registration time Target visualization error, Task completion time Fiducial registration error, Registration time, Target deviation error (screw) Tracking error (2D) Target deviation error (screw)				
	Meulstee et al. (2019) Mitsuno et al. (2019b) Sylos Labini et al. (2019) Wang et al. (2019) Creighton et al. (2020) Dennler et al. (2020) Farshad-Amacker et al. (2020)	Calibration error (hand-eye), Target deviation error (model) Registration time, Target visualization error Target visualization error Target registration error, Registration time Target registration error Target deviation error (screw), performance metrics Task completion time, Number of successful completions				
	Huang et al. (2020) Jiang et al. (2020) Kiarostami et al. (2020) Kriechling et al. (2020) Kunz et al. (2020) Li et al. (2020)	Target visualization error Target registration error Target deviation error(osteotomy points) Target deviation error (k-wire) Tracking error (relative, position) Target visualization error, Target deviation error				
ntom	Luzon et al. (2020) Nguyen et al. (2020b) Rewkowski et al. (2020) Sun et al. (2020)	Target registration error Target visualization error Calibration error, Latency Target registration error, Registration time				

Level	Study	Measures		
	Spirig et al. (2021)	Target deviation error (k-wires)		
	Kobayashi et al. (2019)	Task completion time, performance metrics		
Human	Martinez et al. (2019)	Performance metrics, measurement accuracy		
Tumun	Yajima et al. (2020)	Voice recognition		
	Studies in a Releva	nt Environment (Quantitative and qualitative measures)		
	Aruanno et al. (2017)Quant: Number of successful completions			
	Kuhlemann et al. (2017)	Quant: Target registration error; Qual: Likert questionnaire		
	Perkins et al. (2017)	Quant: Target visualization error		
	Qian et al. (2017)	Quant: Latency; Qual: Image quality, NASA-TLX		
	Yamashita et al. (2017)	Quant: Number of successful completions		
	Condino et al. (2018)	Quant: Target registration error; Qual: NASA TLX, Likert questionnaire		
	Ingeson et al. (2018)	Qual: Likert questionnaire		
	Jang et al. (2018)	Quant: CPU usage, GPU usage, power usage, FPS; Qual: Likert questionnaire		
	Pepe et al. (2018) Sirilak and Munaesawang	Quant: Target visualization error; Qual: Likert questionnaire		
S	Sirilak and Muneesawang (2018)	Qual: System usability scale, Likert questionnaire		
ıdić	(2018) Turini et al. (2018)	Qual: Likert questionnaire		
s tl	Amini and Kersten-Oertel	Quant: Task completion time; Qual: Likert questionnaire, System usability scale		
Case studies	(2019)	Zaan zusk compresent unie, Zuur Erkert questionnune, System usuonny seate		
0	Aruanno and Garzotto (2019)	Quant: Number of successful completions, performance metrics; Qual: Likert		
		questionnaire		
	Balian et al. (2019)	Quant: Performance metrics; Qual: Likert questionnaire		
	Blusi and Nieves (2019)	Qual: Likert questionnaire		
	Brun et al. (2019)	Qual: Likert questionnaires, surgical plan		
	Checcucci et al. (2019)	Qual: Likert questionnaires, surgical plan		
	Gao et al. (2019) Moosburger et al. (2010)	Quant: Target deviation error (pointer), Task completion time		
	Moosburner et al. (2019) Pepe et al. (2019)	Qual: System usability scale, Likert questionnaire Quant: Target visualization error; Qual: Likert questionnaire		
	Qian et al. (2019)	Quant: Target visualization error, latency, Task completion time, Number of		
	Qian et al. (20190)	successful completions		
	Rose et al. (2019)	Quant: Target registration error, Task completion time; Qual: Likert questionnaire		
	Si et al. (2019)	Quant: Target registration error; Qual: Likert questionnaire		
	Sun et al. (2019)	Quant: Measurement accuracy, Task completion time		
	Bulliard et al. (2020)	Quant: Task completion time, number of interactions		
	Cartucho et al. (2020)	Qual: Likert questionnaires		
	Fischer et al. (2020)	Quant: Target registration error, Registration time; Qual: questionnaire		
	Gibby et al. (2020)	Quant: Target deviation error (needle)		
	Guerrero et al. (2020)	Qual: Likert questionnaire		
	Guo et al. (2020)	Quant: Tast completion time, Number of successful completions, performance		
	Hong et al. (2020)	metrics Quart: Performance metrics		
	Hong et al. (2020) Kumar et al. (2020)	Quant: Performance metrics Qual: Likert questionnaire		
	Kumar et al. (2020) Koop et al. (2020)	Quant: Measurement accuracy		
	Muangpoon et al. (2020)	Quant: Fiducial registration error; Qual: Likert questionnaire		
	Nguyen et al. (2020a)	Qual: preferences questionnaire		
	Nuri et al. (2020)	Quant: Target visualization error, Registration time		
	Pelanis et al. (2020)	Quant: Task completion time, Number of successful completions		
	Rositi et al. (2021)	Qual: Likert questionnaire		
ies	Southworth et al. (2020)	Quant: FPS, power usage, Latency; Qual: Image quality		
tud	Thomos et al. (2020)	Qual: System usability scale		
se s	Zuo et al. (2020)	Quant: Target registration error; Qual: NASA TLX		
Case studies	Zuo et al. (2020)	Quant: Target registration error; Qual: NASA TLX		
-	Buch et al. (2021)	Quant: Target registration error		
	Blomqvist et al. (2021)	Qual: Likert questionnaire		
	Bogomolova et al. (2021)	Qual: Likert questionnaire		
	Brunzini et al. (2021)	Qual: Likert questionnaire, questionnaire;		
	Brunzini et al. (2021) Cofano et al. (2021) Dennler et al. (2021b)	Qual: Likert questionnaire, questionnaire; Qual: System usability scale Qual: Likert questionnaire		

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Level	Study	Measures
	Saito et al. (2020)	Qual: NASA-TLX
	Schoeb et al. (2020)	Quant: Exam scores Qual: Self assessment, Likert questionnaires
	Shao et al. (2020)	Quant: Exam scores; Qual: Likert questionnaire
	Condino et al. (2021)	Qual: Likert questionnaire, planning
	Gehrsitz et al. (2021)	Quant: Task completion time; Qual: Likert questionnaire
	Glas et al. (2021)	Quant: Task completion time, Target deviation error (pointer); Qual: Question- naire
	Iqbal et al. (2021)	Quant: Task completion time; Qual: Likert questionnaire
	Ivan et al. (2021)	Quant: Target visualization error; Qual: Performance metrics,
	Long et al. (2021)	Quant: Target deviation error (needle), Task completion time, radiation
	Moro et al. (2021)	Quant: Exam scores; Qual: Likert questionnaire
	Nguyen et al. (2022)	Quant: FPS, Latency, marker tracking accuracy, Task completion time
	Putnam et al. (2021)	Qual: Likert questionnaire
	Qi et al. (2021)	Quant: Registration time, Target visualization error, Task completion time
	Scherl et al. (2021b)	Quant: Target registration error, Task completion time, number of complications
	Suzuki et al. (2021)	Quant: Task completion time, Performance metrics; Qual: Questionnaire
	Van Gestel et al. (2021b)	Quant: Target deviation error (drain); Qual: Performance metrics, Likert ques- tionnaire

standing. Still, it remains to be seen whether this novel hardware will be able to address concerns about accuracy and reliability sufficiently. Other current limitations, such as deficiencies in validation protocols or perceptual issues in AR cannot be addressed by hardware alone, and researchers will be challenged to overcome them with innovative concepts and applications. In conclusion, we think that, although the feasibility of using the HoloLens for various medical scenarios has been suggested, research in medical AR is still in its early stages, and abundant areas for future work remain.

We believe that this review can serve as a guideline to researchers, to help them in picking appropriate experimental protocols and measures for their scenario. We think that it is time for medical AR to step out of the comfort zone of controlled laboratory settings, and finally find its way into medical routine. To this end, close collaborations between researchers, universities, clinicians and patients, as well as comparative studies on a larger scale are necessary.

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Appendix A. Comparison between HoloLens 1 and HoloLens 2

In Table A.8, we compare the technical specifications of the HoloLens 1 and HoloLens 2.

Table A.8: Comparison of the specifications of the HoloLens 1 and HoloLens 2.

		HoloLens 1	HoloLens 2
	Release date	March 30, 2016	November 7, 2019
Compute	CPU Model	Intel Atom x5-Z8100P (1.04 GHz)	Qualcomm Snapdragon 850 (2.96 GHz)
	CPU Cores	4	8
	Architecture	32-bit x86	ARM
	RAM	1 GB	4 GB
	Storage	64 GB	64 GB
	Holographic processing unit	1st gen custom 1 GB memory	2nd gen custom memory not specified
	Battery Life	2-3 hours	2-3 hours
Connectivity	Wifi	802.11ac	Wifi 5 (802.11ac 2x2)
	Bluetooth	4.1	5.0
	USB	Micro USB	USB C
Sensors	photo / video reso- lution	2.4 MP (photo) 1280×720@30 FPS (video)	8 MP (photo) 1920×1080@60 FPS (video)
	ToF range	0.2 - 1 m (short mode) 1 - 5 m (long mode)	0.2 - 1 m (short mode) 1 - 5 m (long mode)
	ToF resolution	448×450@30 FPS (short) 448×450@1-5 FPS (long)	512×512@45 FPS (short) 320×288@1-5 FPS (long)
	VLC resolution	480×640@20-30 FPS	480×640@20-30 FPS
	Microphone	four-microphone array	five-microphone array
	IMU	no access	access (via Research Mode)
Display	Display resolution	1280×720 (per eye)	2048×1080 (per eye)
	FOV (horizontal)	30°	52°
Capabilities	6DOF device track- ing	\checkmark	1
	Voice recogniton	commands	commands, natural language (with internet)
	Biometric security	X	Iris scanning
	Eye tracking	X	✓
	Hand tracking	one hand, gesture & gaze based manip- ulation	both hands, fully articulated, direct ma nipulation
Ergonomics	Flip-up visor	X	✓
	Weight	579 g (1.28 lb)	566 g (1.25 lb)