Image overlay surgery based on augmented reality: a systematic review

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**Abstract**

Augmented Reality (AR) applied to surgical guidance is gaining relevance in clinical practice. AR-based image overlay surgery (i.e. the accurate overlay of patient-specific virtual images onto the body surface) helps surgeons to transfer image data produced during the planning of the surgery (e.g. the correct resection margins of tissue flaps) to the operating room, thus increasing accuracy and reducing surgery times. We systematically reviewed 76 studies published between 2004 and August 2018 to explore which existing tracking and registration methods and technologies allow healthcare professionals and researchers to develop and implement these systems in-house. Most studies used non-invasive markers to automatically track a patient’s position, as well as customised algorithms, tracking libraries or software development kits (SDKs) to compute the registration between patient-specific 3D models and the patient’s body surface. Few studies combined the use of holographic headsets, SDKs and user-friendly game engines, and described portable and wearable systems that combine tracking, registration, hands-free navigation and direct visibility of the surgical site. Most accuracy tests included a low number of subjects and/or measurements and did not normally explore how these systems affect surgery times and success rates. We highlight the need for more procedure-specific experiments with a sufficient number of subjects and measurements and including data about surgical outcomes and patients’ recovery. Validation of systems combining the use of holographic headsets, SDKs and game engines is especially interesting as this approach allows to easily develop mobile AR applications, thus facilitating the implementation of AR-based image overlay surgery in clinical practice.

**Keywords**: Augmented Reality, Mixed Reality, Surgical Guidance, Surgical Navigation, Holographic Headsets, Head-Mounted Displays.

1. Introduction

AR-based image overlay surgery superimposes patient-specific digital data onto the patient’s body using Augmented Reality (AR), i.e. it augments the real surgical scene by means of computer graphics (Azuma, 1997). This approach helps to reduce surgery times, e.g. by preventing the need for surgeons to recall image data produced in the planning of the surgery or by facilitating the interpretation of 3D data during surgery (Hummelink et al., 2015, Jiang et al., 2018, Khor et al., 2016, Kim, Kim & Kim, 2017, Profeta, Schilling & McGurk, 2016, Vávra et al., 2017). It also has the potential to reduce intra- and post-operative complications, e.g. by indicating the exact location of high-risk anatomical structures adjacent to the surgical site that are not to be injured or facilitating the accurate placement of implants (Fritz et al., 2013, Liu et al., 2014). Typically, AR-based image overlay surgery consists of three major steps: 1) tracking, i.e. acquisition of positional information about the patient; 2) registration, i.e. scaling and alignment of the patient-specific imaging data with the previously acquired positional information and; 3) overlay, i.e. projection of the patient-specific digital data onto the patient’s body surface using a display device, e.g. a headset.

Tracking and registration methods determine key technical aspects of AR-based image overlay surgery systems, e.g. the level of technical skill required to implement and/or use these systems within a surgical setup. A recent review by Eckert et al. (Eckert, Volmerg & Friedrich, 2019) used a large sample of studies obtained from PubMed and Scopus to discuss tracking methods in AR-based medical training and treatment. However, their research does not provide a detailed analysis of the state-of-the-art of AR-based image overlay for surgical guidance. Another recent review by Fida et al. (2018) discussed AR-based image overlay in open surgery. The authors used a single database for their systematic search (PubMed) and excluded studies on neurosurgery, orthopaedics and maxillofacial surgery, which resulted in a fairly small sample of 13 studies. In addition, they did not include a critical reflection of the tracking and registration methods used in their reviewed studies.

Our systematic review focuses on AR-based surgical guidance where patient-specific digital data are overlaid onto the patient’s body surface (incl. the patient’s internal anatomy once exposed during open surgery) and in line with the surgeon’s view of the surgical site. In contrast to Eckert, Volmerg & Friedrich (2019), our narrower area of study allowed for a detailed analysis and discussion of the results across studies that share a particular aim: to guide surgeons by overlaying content on the patient’s body surface. For instance, we excluded surgical training, as well as studies on surgical guidance for minimally invasive surgery because this type of surgery presents different tracking and registration challenges than those in open surgery, e.g. tracking markers or anatomical landmarks inside the patient’s body using an endoscopic camera (Li et al., 2016). In addition, we included all types of open surgery in our search and used 8 databases, which resulted in a larger sample of studies than in Fida et al. (2018). Finally, we discussed the implications of different registration methods in terms of their application in clinical practice. Other reviews differ from ours in that they cover a particular surgical discipline (Joda et al., 2019, Bertolo et al., 2019, Sayadi et al., 2019, Bosc et al., 2019, Wong et al., 2018) or do not explore the technical aspects of the tracking and registration methods (Contreras López, Navarro & Crispin, 2019, Sayadi et al., 2019, Yoon et al., 2018, Kolodzey et al., 2017).

The aim of this review is to assess which existing tracking and registration methods and technologies allow healthcare professionals and researchers to develop and implement these systems in-house. As main objectives, we: a) identify the most commonly used tracking methods and the computational methods that are easiest to implement and; b) explore the registration accuracy of these systems and to what extent they improve surgical outcomes and reduce invasiveness for patients. This work is part of a larger research project which aims to create a methodological and technological framework for AR-based image overlay surgery within the context of reconstructive surgery.

1. Materials and Methods

This review follows the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009). The following scientific databases were used for the systematic search in August 2018: Ovid, Medline, Embase, Scopus, Web of Science, PubMed, IEEE (accessed via the University of Aberdeen) and Google Scholar. The search was performed using the following search terms: *Augmented Reality* AND *Image Guided Surgery* OR *Surgery* OR *Computer Assisted Surgery* AND *Tracking* OR *Registration* OR *Projection* OR *Head Mounted Display* OR *Heads up display* OR *Smart Glasses* OR *Autostereoscopic* OR *Microscopy* OR *Retinal Displays*. Specific and generic terminology as well as alternate spellings and plurals were considered in the search. The full systematic search strategy is provided in the appendix: [S1 Table](#S1Table).

We considered research on AR-based image overlay surgery published since 2004 when AR was implemented on a mobile device for the first time (Mohring, Lessig & Bimber, 2004). Outcomes were restricted to scientific journal and conference papers written in English and involving animals, humans (including cadaveric material and/or in vivo clinical data belonging to males and females of all ages) and phantom representations. A selection of the retrieved studies was done by one author (LP) through the screening of their titles and abstracts after all authors agreed on the eligibility criteria. The selected studies were classified according to the variables described in [Table 1](#Table1). The experiments conducted by the selected studies were classified according to the Fiducial Registration Error (FRE) and Target Registration Error (TRE) because they were the most common accuracy metrics considered across the reviewed studies.

To perform a risk of bias assessment we ranked the individual reviewed studies based on their quality of evidence following the GRADE guidelines (Guyatt et al., 2008): “high” for randomised control trials and “low” for observational studies. Then, an upgrade/downgrade of the resulting level of quality was done based on each study’s characteristics: inclusion of accuracy metrics, sample size and inclusion of information about the surgical outcomes. To assess the risk of bias across studies, we considered the uniformity of the tracking and registration methods and display technologies used across them. This research did not require the involvement of patients or members of the public.

**Table 1. Variables used to classify the reviewed studies.**

|  |  |
| --- | --- |
| **VARIABLE** | **Description** |
| Surgical task | Surgical step for which the system provided guidance |
| Surgery type | Surgical procedure for which the system provided guidance |
| Tracking method | Method used to obtain positional information about the patient |
| Non-invasive for patients | The system does not require the use of invasive markers attached to the patient’s body (yes/no). |
| Registration method | Method used to compute the registration between the patient-specific digital data and the patient’s body surface |
| Compact | The system integrates the tracking, registration and display capabilities in a single device (yes/no). |
| Wireless | The system does not require the use of cables within the operating room (yes/no). |
| Surgical site directly visible | The system components do not occlude the surgeon’s direct view of the surgical site (yes/no). |
| Hands-free tracking | The surgical team does not need to manipulate the system throughout surgery (yes/no). |
| Stand-alone application | The system is presented as a portable program which does not rely on an operating system (yes/no). |
| Type of display | Type of device used by the system to project the patient-specific digital data on the patient’s body surface |
| Includes accuracy metrics | The study includes experiments to measure the registration accuracy of their system (yes/no). |
| N accuracy experiments | Number of accuracy experiments extracted from each reviewed study |
| Fiducial and target registration errors (FRE and TRE, respectively) | Distance between corresponding real and digital points after registration of the patient-specific digital data with the patient’s body. Typically, the FRE is measured at points used to set the registration, while the TRE is measured at points other than those used for registration (Fitzpatrick and West, 2001). |
| Experimental approach | Subject on which the FRE and TRE were measured |
| N subjects | Number of subjects per experiment |
| N measurements | Number of measurements per experiment |
| Success rate reported | The study includes information about the post-operative outcomes (yes/no). |
| Surgery time reported | The study includes information about the time required to perform the surgery (yes/no). |
| Long-term study | The study includes monitoring data about the patient’s recovery and surgical outcomes (yes/no). |
| Type of study | Type of study design (randomised control trial or observational study) |
| Evidence quality | Quality of the evidence provided by the reviewed studies according to GRADE guidelines [21]. |

1. Results

The systematic search yielded 1352 publications, 724 after removing duplicates ([Fig 1](#Fig1)). Publications were selected using the following eligibility criteria: 1) the patient-specific digital data were displayed on the patient’s body surface (incl. the patient’s internal anatomy once exposed during open surgery) either directly (e.g. using conventional projection) or indirectly (e.g. on live images of the patient seen through a tablet) and; 2) the visualisation was in line with the surgeon’s view of the surgical site. Therefore, we excluded studies presenting systems which overlaid the patient-specific digital data onto digital scans or images of the patient’s internal anatomy (e.g. as in endoscopic procedures), as well as those requiring the surgeon to look away from the surgical site in order to see the digital images (e.g. on a monitor). Among studies on minimally invasive surgery, we included only those in which the tracked features were part of the patient’s external anatomy or environment and the patient-specific digital data were overlaid onto the patient’s body surface. In total, we selected 76 publications and generated a database (electronic supplementary material: [S1 Appendix](#Appendix)). These studies covered a variety of surgical tasks ([Table 2](#Table2)) and procedures (appendix: [S2 Table](#S2Table)) showing that some clinical applications had much wider representation within our sample than others.

**Fig 1. Flow diagram showing the systematic search strategy used for this review.**

**Table 2. Classification of reviewed AR-based image overlay surgery studies according to surgical tasks.**

|  |  |  |
| --- | --- | --- |
| **SURGICAL TASK** | **Studies** | **Articles** |
| **%** | **N** |  |
| Locate internal anatomical structures, tumours and haematomas | 36.84 | 28 | (Maruyama et al., 2018, Zhang, Chen and Liao, 2017, Jiang et al., 2017, Wen, Chng and Chui, 2017, Yang et al., 2018, Sun et al., 2017, Scolozzi and Bijlenga, 2017, Drouin S. et al., 2017, Hou et al., 2016, Cabrilo, Schaller and Bijlenga, 2015, Wang et al., 2015, Zhang X., Chen and Liao, 2015, Pauly et al., 2015, Suenaga et al., 2015, Yoshino et al., 2015, Kramers et al., 2014, Wang et al., 2014, Deng et al., 2014, Wen et al., 2014, Parrini et al., 2014, Han et al., 2013, Mahvash and Tabrizi, 2013, Müller M. et al., 2013, Kersten-Oertel et al., 2012, Volonte et al., 2011, Tran et al., 2011, Sugimoto et al., 2010, Giraldez et al., 2007) |
| Indicate correct entry points and trajectories of surgical instruments | 31.58 | 24 | (Andress et al., 2018, Cutolo et al., 2016, Eftekhar, 2016, Fichtinger et al., 2005, Gavaghan et al., 2012, Gibby et al., 2019, Khan et al., 2006, Krempien et al., 2008, Lee J.-D. et al., 2010, Liang et al., 2012, Liao et al., 2010, Ma et al., 2018, Ma et al., 2017, Martins et al., 2016, Rodriguez et al., 2012, Shamir et al., 2011, Si et al., 2018, Suenaga et al., 2013, Vogt, Khamene and Sauer, 2006, Wacker et al., 2005, Wang et al., 2016, Wen et al., 2013, Wesarg et al., 2004, Wu et al., 2014) |
| Indicate correct soft tissue resection margins and osteotomy lines | 21.05 | 16 | (Badiali et al., 2014, Besharati Tabrizi and Mahvash, 2015, Kosterhon et al., 2017, Lin et al., 2016, Lin et al., 2015, Marmulla et al., 2005, Mischkowski et al., 2006, Mondal et al., 2015, Pessaux et al., 2015, Qu et al., 2015, Shao et al., 2014, Sun et al., 2016, Tang et al., 2017, Wang et al., 2017, Zhu et al., 2016, Zhu et al., 2011) |
| Indicate correct position of implants | 3.95 | 3 | (Ma et al., 2019, Mahmoud et al., 2017, Zeng et al., 2017) |
| Assist more than one surgical task | 3.95 | 3 | (He, Liu and Wang, 2016, Hu, Wang and Song, 2013, Wu et al., 2018) |
| Indicate anatomical asymmetry | 2.63 | 2 | (Huang et al., 2012, Mezzana, Scarinci and Marabottini, 2011) |

* 1. Tracking Methods

We classified the reviewed studies into the following categories: electromagnetic tracking, optical marker-less tracking and optical marker-based tracking with complex or simple set-up ([Fig 2](#Fig2)). Most studies used marker-based optical tracking (64%) ([Fig 3](#Fig3)), e.g. a system which uses a camera to detect the position of a marker fixed to a patient’s teeth and, based on this position, projects osteotomy lines onto the patient’s skull (Zhu et al., 2016). From these, infrared cameras that detect retro-reflective markers were the most commonly used tracking device (41%) (Ma et al., 2019, Maruyama et al., 2018, Si et al., 2018), followed by RGB cameras (20%) to detect 2D images with easily recognisable features (Jiang et al., 2017, Lin et al., 2015, Zhu et al., 2016)or simple shape objects (Cutolo et al., 2016, Sun et al., 2017, Wang et al., 2015). A few studies used marker-less optical tracking (12%) (Gibby et al., 2019, Wu et al., 2018, Zeng et al., 2017),e.g. a camera to detect the contour of the patient’s dentition which is matched with its corresponding points on video images of the patient (Wang et al., 2017).Some studies used electromagnetic tracking (3%) (Ma et al., 2018, Martins et al., 2016)or a manual approach (10%) (Eftekhar, 2016, Hou et al., 2016, Pessaux et al., 2015)to detect the patient’s position. The remaining studies used alternative methods (Andress et al., 2018, Mahmoud et al., 2017, Scolozzi and Bijlenga, 2017)or did not specify their tracking method (Rodriguez et al., 2012, Sun et al., 2016).A complete list of the reviewed studies classified based on these categories is available in the appendix: [S3 Table](#S3Table). Henceforth, the data analysis focuses on the studies using automatic optical tracking (58 studies).

**Fig 2. Main tracking methods identified in this review: electromagnetic, optical marker-less and optical marker-based with complex or simple set-up.** The diagram also shows the devices used for tracking (yellow), registration (green), overlay (orange) or tracking, registration and overlay using a single device (holographic headset).

**Fig 3. Reviewed studies organised according to their tracking method.** Marker-based tracking, use of cameras to detect objects attached to the patient’s body; marker-less tracking, superficial body features or a stripy pattern projected onto the patient’s body surface; electromagnetic tracking, use of an electromagnetic transmitter to detect sensors placed on a surgical instrument’s tip; manual registration, freehand alignment of the patient-specific digital data onto the patient’s body surface. EM - electromagnetic; RGB - Red, Green, Blue; RGB-D - Red, Green, Blue and Depth.

* 1. Registration Methods

Most reviewed studies used custom algorithms to align patient-specific digital data with the patient’s position (Ma et al., 2019, Maruyama et al., 2018, Si et al., 2018) ([Table 3](#Table3)), e.g. matching two sets of 3D points corresponding to the position of markers on the patient’s body and their corresponding points on the patient’s scans (Ma et al., 2019). Some studies used computer tracking libraries and/or Software Development Kits (SDKs) (Cutolo et al., 2016, Wang et al., 2016, Zeng et al., 2017), such as OpenCV (Shao et al., 2014), ARToolkit (<http://www.hitl.washington.edu/artoolkit/>) (Lin et al., 2016, Qu et al., 2015, Zhu et al., 2016) or Vuforia SDK (<https://www.vuforia.com/>) (Kramers et al., 2014, Wen, Chng and Chui, 2017). Both ARToolkit and Vuforia SDK provide algorithms to track 2D and 3D feature points on images and define a shared coordinate system between the digital data and the real world (e.g. the patient). They are sometimes used in combination with game engines (e.g. Unity, <https://unity3d.com/> or Unreal, <https://www.unrealengine.com/en-US/>) and capture devices such as conventional webcams or other RGB/-D camera systems (Jiang et al., 2017, Wu et al., 2018). Game engines with embedded computer tracking libraries and Software Development Kits (SDKs) (e.g. Vuforia SDK) are user-friendly tools that allow to easily develop mobile AR applications which automatically register digital data with real world features. For instance, Wu et al. (2018) used the Vuforia SDK and Unity to deploy the tracking of an image marker placed in the surgical scene.However, their registration strategy also required custom calculations that detect the patient’s position. In contrast, Jiang et al. (2017) used ARToolkit and Unity to deploy both the tracking of an image marker and the registration of the patient-specific digital data with the patient’s body surface without relying on custom calculations. Only 16% of the reviewed studies used fully integrated platforms (Drouin et al., 2017, Gibby et al., 2019, Sun et al., 2017), e.g. the Brainlab neuronavigation system (Brainlab, Germany).

**Table 3. Reviewed studies organised according to the computation method used for automatic optical tracking and registration. Some studies using fully integrated platforms, tracking libraries/SDKs and game engines also developed custom calculation algorithms.**

|  |  |  |
| --- | --- | --- |
| **REGISTRATION METHOD** | **Studies** | **Articles** |
| **%** | **N** |
| Custom algorithms | 56.90 | 33 | (Badiali et al., 2014, Deng et al., 2014, Giraldez et al., 2007, He, Liu and Wang, 2016, Hu, Wang and Song, 2013, Krempien et al., 2008, Lee et al., 2010, Liang et al., 2012, Liao et al., 2010, Lin et al., 2015, Ma et al., 2019, Ma et al., 2017, Maruyama et al., 2018, Müller et al., 2013, Pauly et al., 2015, Shamir et al., 2011, Si et al., 2018, Suenaga et al., 2013, Suenaga et al., 2015, Tang et al., 2017, Tran et al., 2011, Vogt, Khamene and Sauer, 2006, Wacker et al., 2005, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Wen et al., 2013, Wen et al., 2014, Wu et al., 2014, Yang et al., 2018, Yoshino et al., 2015, Zhang, Chen and Liao, 2017, Zhang, Chen and Liao, 2015) |
| Fully integrated platforms | 15.52 | 9 | (Cabrilo, Schaller and Bijlenga, 2015, Drouin et al., 2017, Gibby et al., 2019, Khan et al., 2006, Kosterhon et al., 2017, Mischkowski et al., 2006, Sun et al., 2017, Wesarg et al., 2004, Cutolo et al., 2016) |
| Tracking libraries/SDKs | 20.69 | 12 | (Gavaghan et al., 2012, Huang et al., 2012, Kersten-Oertel et al., 2012, Kramers et al., 2014, Lin et al., 2016, Qu et al., 2015, Shao et al., 2014, Wang et al., 2016, Wen, Chng and Chui, 2017, Zeng et al., 2017, Zhu et al., 2016, Zhu et al., 2011) |
| Tracking libraries/SDKs and game engines | 3.45 | 2 | (Jiang et al., 2017, Wu et al., 2018) |
| Not specified | 3.45 | 2 | (Marmulla et al., 2005, Parrini et al., 2014) |

* 1. Key Aspects of Augmented-Reality-Based Image Overlay Systems
		1. Ease of use

Most reviewed studies required the set-up of separate pieces of equipment in the operating room (83%), while a minority used compact systems (12%), e.g. those using headsets, smartphones or a microscope with an integrated tracking device (Gibby et al., 2019, Jiang et al., 2017, Sun et al., 2017)([Fig 4](#Fig4)). Headsets can be video see-through or optical see-through and display digital data on a screen or on transparent lenses in front of the surgeon’s view, respectively. In most cases, the display device occluded the surgeon’s view of the surgical site (66%), except for those studies which used optical see-through headsets, smart glasses or projectors (28%) (Gibby et al., 2019, Maruyama et al., 2018, Wu et al., 2018). A minority of studies used hands-free tracking (33%) (Gibby et al., 2019, Ma et al., 2017, Yang et al., 2018), while most required the manipulation of tracking devices (66%). For instance, some systems required the use of a navigation pointer to localise predefined registration landmarks on the patient’s body during surgery (Kosterhon et al., 2017). Only a few studies presented their systems as stand-alone applications (7%), combined with smart glasses (Maruyama et al., 2018), smartphones (Kramers et al., 2014) or holographic headsets (i.e. optical see-through AR headsets that integrate tracking, registration and display capabilities and recognise voice and gesture commands) (Gibby et al., 2019, Wu et al., 2018) (appendix: [S4 Table](#S4Table)). In addition, most studies relied on hardware with wired connections (84%), while only a few studies used wireless technology such as holographic headsets, smartphones or tablets (Gibby et al., 2019, Sun et al., 2017, Wu et al., 2018). A classification of the reviewed studies according to the display device used is shown in the appendix: [S5 Table](#S3Table).

**Fig 4. Classification of reviewed automatic optical tracking studies according to system's usability.**

* + 1. Registration Accuracy

A total of 38 studies on automatic optical tracking (66%) measured the registration accuracy of their system, while the remaining studies did not explore this or measured variables not considered in this review, e.g. the area of tumour successfully removed during AR-based image overlay surgery (Scolozzi and Bijlenga, 2017). In total, we extracted the mean FRE and/or TRE from 44 experiments ([Table 4](#Table4)). Most experiments measured the TRE, which has been described as the actual distance between matching real and digital points after registration as it includes all the errors which may occur during the registration process (Fitzpatrick and West, 2001, West et al., 2001). This review shows that many authors achieved TREs between 1-5 mm (52%), e.g. those using computer tracking libraries/SDKs and game engines (Jiang et al., 2017, Wu et al., 2018) and most studies using headsets (Badiali et al., 2014, Cutolo et al., 2016, Gibby et al., 2019, Jiang et al., 2017, Si et al., 2018, Wang et al., 2016, Wu et al., 2018). Some studies achieved a sub-millimetre accuracy (32%), e.g. a study which used a video see-through headset (Lin et al., 2015) and another one using a non-holographic optical see-through headset (Lin et al., 2016). Many reviewed studies included low numbers of subjects and/or measurements in their experiments and only a few were clinical studies (14%), while most measured the registration accuracy on phantoms. Large number of studies did not measure the accuracy of their systems.

**Table 4. Classification of experiments according to the registration accuracy and measurement approach. Some articles presented more than one experiment (Maruyama et al., 2018, Wu et al., 2018, Ma et al., 2017, Deng et al., 2014, Giraldez et al., 2007, Wacker et al., 2005). FRE - Fiducial Registration Error; TRE - Target Registration Error; AR - Augmented Reality.**

|  |  |  |
| --- | --- | --- |
| **REGISTRATION ACCURACY** | **Experiments** | **Articles** |
| **%**  | **N** |
| **FRE** | *<1 mm* | 11.36 | 5 | (Krempien et al., 2008, Ma et al., 2019, Wang et al., 2014, Wang et al., 2015, Zeng et al., 2017) |
| *1-5 mm* | 6.82 | 3 | (Maruyama et al., 2018, Yang et al., 2018, Zhang, Chen and Liao, 2017) |
| *>5 mm* | 0 | 0 | - |
| *Not specified* | 81.82 | 36 | (Badiali et al., 2014, Cutolo et al., 2016, Deng et al., 2014, Gibby et al., 2019, Giraldez et al., 2007, He, Liu and Wang, 2016, Jiang et al., 2017, Khan et al., 2006, Lee et al., 2010, Liang et al., 2012, Liao et al., 2010, Lin et al., 2016, Lin et al., 2015, Ma et al., 2017, Maruyama et al., 2018, Mischkowski et al., 2006, Qu et al., 2015, Si et al., 2018, Suenaga et al., 2013, Suenaga et al., 2015, Wacker et al., 2005, Wang et al., 2016, Wang et al., 2017, Wen et al., 2013, Wen et al., 2014, Wen, Chng and Chui, 2017, Wesarg et al., 2004, Wu et al., 2014, Wu et al., 2018, Yoshino et al., 2015, Zhu et al., 2016) |
| **TRE** | *<1 mm* | 31.82 | 14 | (Giraldez et al., 2007, He, Liu and Wang, 2016, Liao et al., 2010, Lin et al., 2016, Lin et al., 2015, Mischkowski et al., 2006, Suenaga et al., 2013, Suenaga et al., 2015, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Zeng et al., 2017, Zhang, Chen and Liao, 2017) |
| *1-5 mm* | 52.27 | 23 | (Badiali et al., 2014, Cutolo et al., 2016, Deng et al., 2014, Gibby et al., 2019, Jiang et al., 2017, Krempien et al., 2008, Lee et al., 2010, Liang et al., 2012, Ma et al., 2019, Ma et al., 2017, Maruyama et al., 2018, Qu et al., 2015, Si et al., 2018, Wang et al., 2016, Wen et al., 2013, Wen et al., 2014, Wen, Chng and Chui, 2017, Wu et al., 2018, Yoshino et al., 2015, Zhu et al., 2016) |
| *>5 mm* | 11.36 | 5 | (Khan et al., 2006, Wacker et al., 2005, Wesarg et al., 2004, Wu et al., 2014) |
| *Not specified* | 4.55 | 2 | (Maruyama et al., 2018, Yang et al., 2018) |
| **Experimental approach** | *Surgery performance*  | 13.64 | 6 | (Deng et al., 2014, Krempien et al., 2008, Maruyama et al., 2018, Mischkowski et al., 2006, Qu et al., 2015, Zhu et al., 2016) |
| *Surgery simulation on:* |   |  |  |
|  *Phantom* | 31.82 | 14 | (Cutolo et al., 2016, Gibby et al., 2019, He, Liu and Wang, 2016, Liang et al., 2012, Lin et al., 2016, Lin et al., 2015, Ma et al., 2019, Ma et al., 2017, Si et al., 2018, Wacker et al., 2005, Wen et al., 2013, Wen et al., 2014, Wen, Chng and Chui, 2017, Wesarg et al., 2004) |
|  *Animal* | 6.82 | 3 | (Ma et al., 2017, Wacker et al., 2005, Wu et al., 2014) |
|  *Cadaver* | 4.55 | 2 | (Khan et al., 2006, Wang et al., 2016) |
| *Only AR overlay on:* |   |  |  |
|  *Patient* | 2.27 | 1 | (Suenaga et al., 2015) |
|  *Phantom* | 38.64 | 17 | (Badiali et al., 2014, Deng et al., 2014, Giraldez et al., 2007, Jiang et al., 2017, Lee et al., 2010, Liao et al., 2010, Maruyama et al., 2018, Suenaga et al., 2013, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Wu et al., 2018, Yang et al., 2018, Yoshino et al., 2015, Zeng et al., 2017, Zhang, Chen and Liao, 2017) |
|  *Cadaver* | 2.27 | 1 | (Giraldez et al., 2007) |
| **N subjects per experiment** | *< 10* | 97.73 | 43 | (Badiali et al., 2014, Cutolo et al., 2016, Deng et al., 2014, Gibby et al., 2019, Giraldez et al., 2007, He, Liu and Wang, 2016, Jiang et al., 2017, Khan et al., 2006, Krempien et al., 2008, Lee et al., 2010, Liang et al., 2012, Liao et al., 2010, Lin et al., 2016, Lin et al., 2015, Ma et al., 2019, Ma et al., 2017, Maruyama et al., 2018, Mischkowski et al., 2006, Qu et al., 2015, Si et al., 2018, Suenaga et al., 2013, Suenaga et al., 2015, Wang et al., 2016, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Wen et al., 2013, Wen et al., 2014, Wen, Chng and Chui, 2017, Wesarg et al., 2004, Wu et al., 2014, Wu et al., 2018, Yang et al., 2018, Yoshino et al., 2015, Zeng et al., 2017, Zhang, Chen and Liao, 2017) |
| *10-50* | 2.27 | 1 | (Zhu et al., 2016) |
| *> 50* | 0.0 | 0 | - |
| **N measurements per experiment** | *< 10* | 50.00 | 22 | (Badiali et al., 2014, Giraldez et al., 2007, He, Liu and Wang, 2016, Jiang et al., 2017, Lee et al., 2010, Liang et al., 2012, Ma et al., 2019, Ma et al., 2017, Mischkowski et al., 2006, Qu et al., 2015, Si et al., 2018, Suenaga et al., 2013, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Wu et al., 2018, Yang et al., 2018, Yoshino et al., 2015, Zhang, Chen and Liao, 2017) |
| *10-50* | 34.09 | 15 | (Cutolo et al., 2016, Deng et al., 2014, Gibby et al., 2019, Khan et al., 2006, Krempien et al., 2008, Liao et al., 2010, Lin et al., 2015, Maruyama et al., 2018, Wang et al., 2016, Wen et al., 2014, Wen, Chng and Chui, 2017, Wesarg et al., 2004, Wu et al., 2014, Zeng et al., 2017, Zhu et al., 2016) |
| *> 50* | 15.91 | 7 | (Deng et al., 2014, Lin et al., 2016, Maruyama et al., 2018, Suenaga et al., 2015, Wacker et al., 2005, Wen et al., 2013) |

* + 1. Surgical Outcomes and Invasiveness for Patients

Only few studies compared the surgical success rates (Cutolo et al., 2016, Gibby et al., 2019, Huang et al., 2012, Liao et al., 2010, Lin et al., 2016, Ma et al., 2017, Qu et al., 2015, Si et al., 2018) and times (Khan et al., 2006, Liao et al., 2010, Mischkowski et al., 2006, [Mülle](https://www.ncbi.nlm.nih.gov/pubmed/?term=M%C3%BCller%20M%5BAuthor%5D&cauthor=true&cauthor_uid=23526436)r et al., 2013) with those achieved in conventional surgery. Similarly, only few authors performed long-term studies (Kosterhon et al., 2017). In terms of invasiveness, most marker-based optical tracking studies used non-invasive tracking markers (Giraldez et al., 2007, Huang et al., 2012, Kramers et al., 2014, Krempien et al., 2008, Lee et al., 2010, Maruyama et al., 2018, Wang et al., 2015, Wen et al., 2013, Wen et al., 2014). These markers were attached to the patient (Cutolo et al., 2016, Parrini et al., 2014, Si et al., 2018, Sun et al., 2017),a probe that digitises anatomical landmarks (i.e. superficial body features) (Hu, Wang and Song, 2013, Kosterhon et al., 2017, Ma et al., 2017, Tang et al., 2017), a surgical tool (He, Liu and Wang, 2016)or fiducial markers. Fiducial markers are easily identifiable landmarks fixed to the patient’s body surface at the time of scanning which allow preserving the spatial relationships between the patient-specific digital data obtained from the scans and the patient’s anatomy. Fiducial markers were attached to dental retainers (Ma et al., 2019, Qu et al., 2015, Suenaga et al., 2013, Tran et al., 2011, Yoshino et al., 2015, Zhu et al., 2016, Zhu et al., 2011), placed in the surgical scene (Shao P. et al., 2014), or non-invasively attached to the patient (Besharati Tabrizi and Mahvash, 2015, Cutolo et al., 2016, Deng et al., 2014, Drouin et al., 2017, Kersten-Oertel et al., 2012, Liao et al., 2010, Müller et al., 2013, Shamir et al., 2011, Tran et al., 2011, Wu et al., 2014, Yang et al., 2018, Zhang, Chen and Liao, 2017, Zhang, Chen & Liao, 2015, Zhu et al., 2016).

* 1. Risk of Bias

Most reviewed studies were case series and reports (Maruyama et al., 2018, Tang et al., 2017, Kosterhon et al., 2017, Sun et al., 2017, Zhu et al., 2016, Cabrilo, Schaller and Bijlenga, 2015, Deng et al., 2014, Zhu et al., 2011, Krempien et al., 2008, Giraldez et al., 2007, Mischkowski et al., 2006, Marmulla et al., 2005). Only one reviewed study was a randomised control trial (Qu et al., 2015). Due to their non-inclusion of accuracy metrics, the small sample size in their experiments and/or the lack of information about surgical outcomes, the reviewed case series and reports were downgraded to studies of “very low” quality of evidence, and the randomised control trial was downgraded to “moderate” quality of evidence (electronic supplementary material: [S1 Appendix](#Appendix)). In addition, a wide variety of tracking and registration methods and display technologies was found across the reviewed studies ([Table 3](#Table3) and appendix: [S3](#S3Table) and [S5 Tables](#S5Table)).

1. Discussion

To the authors’ knowledge, this is the first review that: a) identifies the most commonly used tracking and registration methods and technologies that overlay patient-specific digital data onto the patient’s body surface and in line with the surgeon’s view of the surgical site; b) evaluate the suitability of these methods for their in-house implementation by healthcare professionals and researchers without relying on advanced engineering and/or programming skills and; c) discusses the key challenges of AR-based image overlay surgery.

Our results show that the tracking method most commonly used among the reviewed studies is marker-based optical tracking, i.e. the use of markers with an easily recognisable pattern to establish a shared coordinate system between the real environment including the patient and the patient-specific 3D dataset ([Fig 3](#Fig3)). This is in line with the findings by Eckert et al. (Eckert, Volmerg and Friedrich, 2019) who explored a wider area of study: AR-based medical training and treatment. In addition, the registration between the patient-specific digital data and the patient’s body surface is normally achieved by using custom calculation algorithms, while the combination of tracking libraries/SDKs and game engines is very recent ([Table 3](#Table3)). This review also demonstrates that these systems, which have normally involved the use of several hardware components and cables, do not normally allow the surgeon’s direct view of the surgical site or hands-free tracking, and have rarely been presented as stand-alone applications ([Fig 4](#Fig4)). As key challenges for current AR-based image overlay surgery, we identified the need to validate these systems through more extensive accuracy metrics and to explore approaches that minimise invasiveness for patients.

* 1. Why is Marker-Based Tracking the Commonest Approach?

The use of markers to register patient-specific digital data with the patient’s body surface is very common ([Fig 3](#Fig3)). There are alternatives to using markers, e.g. marker-less optical tracking where anatomical features with well-defined borders (e.g. contour of the patient’s dentition) are detected (Suenaga et al., 2015, Wang et al., 2014, Wang et al., 2017). However, the application of marker-less optical tracking is limited as many surgeries do not necessarily involve the exposure of anatomical features with well-defined borders (e.g. soft tissue flap surgery). Similarly, electromagnetic tracking allows the detection of sensors even when they are not visible, e.g. because they are placed in a surgical instrument’s tip inside the patient’s body. However, this method may compromise surgical accuracy in operating theatres which include several metallic items as magnetic fields are usually affected by metallic artefacts (Poulin and Amiot, 2002). In the absence of anatomical features with well-defined borders or in environments with metallic items, marker-based optical tracking is a convenient tracking method. This might explain its high prevalence in our reviewed studies.

Two aspects must be considered to prevent an increased risk of intra- and post-operative complications when exploring the use of marker-based tracking: 1) to avoid occlusion of the surgeon’s view of the surgical site caused by the markers and; 2) to implement solutions which ensure both an optimal accuracy and low invasiveness for patients. This review shows that there is a variety of options that currently allow the efficient use of non-invasive markers attached to the patients’ body surface that minimise their discomfort and facilitate their recovery, e.g. 2D images detected by holographic headsets can be attached to dental splints (Qu et al., 2015, Zhu et al., 2016, Zhu et al., 2011). However, the use of other types of non-invasive markers (e.g. skin adhesives) can lead to a registration mismatch, e.g. due to changes in the soft tissue shape during resection (Jiang et al., 2017).

* 1. What Computational Method is Easiest to Implement?

Traditionally, the development of AR-based image overlay systems has required advanced engineering and programming skills. Fully integrated platforms are highly efficient and easy to implement in the operating room, but also expensive and not suitable for in-house adjustment to particular surgical needs (Drouin et al., 2017). The customisation of AR-based image overlay surgery systems often involves the development of tracking and registration algorithms (Badiali et al., 2014, Wen et al., 2013, Yang et al., 2018) and/or the use of computer tracking libraries and/or SDKs (e.g. OpenIGTLink) (Gavaghan et al., 2012, Huang et al., 2012, Kersten-Oertel et al., 2012, Kramers et al., 2014, Wang et al., 2016, Wen, Chng and Chui, 2017, Zeng et al., 2017). For this reason, this type of development is not available for a wide range of healthcare professionals and researchers. Some reviewed studies overcame this issue by combining computer tracking libraries (e.g. ARToolkits) or SDKs (e.g. Vuforia SDK) with game engines that can be used to create simple mobile AR applications (Andress et al., 2018, Jiang et al., 2017, Wu et al., 2018). In addition, game engines are increasingly becoming more popular due to their improved graphics performance. However, the number of studies using these tools is still relatively small ([Table 3](#Table3)).

* 1. What are the Benefits of Holographic Headsets?

Holographic headsets are compatible with the previously described tracking and registration methods. Game-based applications using tracking libraries and SDKs can be deployed not only on mobile devices such as smart phones, but also on more specialised displays such as holographic headsets (e.g. Microsoft HoloLens®, <https://www.microsoft.com/en-us/hololens>). In addition, these tools provide easy access to algorithms that detect markers (e.g. fiducial markers) on images and align patient-specific digital data with them, i.e. they are compatible with automatic optical tracking.

Holographic headsets integrate mobile hardware, a Holographic Processing Unit (HPU) and Depth (RGB-D) cameras (i.e. cameras able to capture both colour and depth information), allowing their use as tracking, registration and display device without relying on an external CPU. AR applications can be loaded into their HPU and used as stand-alone applications. Their RGB-D cameras can be easily set up for marker-based optical tracking by using game engines like Unity (Andress et al., 2018, Si et al., 2018, Wu et al., 2018) and computer tracking software like Vuforia SDK. In addition, their RGB-D cameras can be used to detect surface patterns in the environment (e.g. a patient’s body surface) and allow aligning patient-specific 3D models with the patient’s body in a fixed position regardless of the user’s movement around the room (Gibby et al., 2019). The digital data is overlaid on the headset’s transparent lenses without occluding the surgeon’s view of the surgical site. They recognise voice and gesture commands, eliminating the need to manipulate tracking devices and allowing hands-free interaction with the digital data (Andress et al., 2018, Jiang et al., 2017, Si et al., 2018, Wu et al., 2018).

In summary, the combination of holographic headsets, tracking libraries/SDKs and game-engines allows a wide range of healthcare professionals and researchers to develop simple AR-based image overlay systems in-house, without relying on engineering expertise or commercial providers of fully integrated platforms. In addition, while a wide variety of wearable technology including AR headsets shows promising results in several clinical areas (Kolodzey et al., 2017, Tepper et al., 2017, Keller, State and Fuchs, 2008), holographic headsets are better in facilitating the development of readily available, portable, and easy to set up AR-based image overlay surgery systems which do not alter the surgical workflow significantly (Kramers et al., 2014) ([Fig 4](#Fig4)). However, studies exploring suitable methodological frameworks for the use of holographic headsets and testing their registration accuracy are very scarce to date (appendix: [S5 Table](#Table3)). Part of the reason for this is their fairly recent release (e.g. Microsoft HoloLens® in 2016) and relatively high prices: e.g. Microsoft HoloLens® and Magic Leap® currently cost over $2000 (developer editions). For this reason and in spite of their advantages, assessing the potential of holographic headsets for their implementation in clinical practice remains a challenge.

* 1. Study Limitations

Outcomes from this systematic review show that the number of studies measuring the accuracy of AR-based image overlay surgery systems is low ([Table 4](#Table4)), especially if they are analysed separately based on specific characteristics of the system such as its tracking and registration method ([Table 3](#Table3) and appendix: [S3 Table](#S3Table)). Similarly, studies that compare the achieved surgical success rates and times with those of conventional surgery and that include data about the patient’s recovery and surgical outcomes in the long-term are scarce in this review. To validate surgical guidance systems that overlay patient-specific digital data onto the patient’s body surface ([Table 4](#Table4)), it is necessary to perform more clinical studies that include larger samples of subjects and accuracy measurements and that explore the aforementioned variables. For these reasons, most reviewed studies using automatic optical tracking were ranked as “very low” evidence quality (electronic supplementary material: [S1 Appendix](#Appendix)) and thus we considered that their accuracy estimates remain uncertain.

In spite of our restricted eligibility criteria and even though we downsized our sample to automatic optical tracking for the analysis, there was a lack of methodological homogeneity between studies, e.g. due to the wide variety of approaches within each tracking method (appendix: [S3 Table](#S3Table)), which affects the risk of bias across the reviewed studies. This has also been reported in other reviews with different eligibility criteria, e.g. those reviews focusing on a specific type of surgical procedure (Contreras López, Navarro and Crispin, 2019, Joda et al., 2019) or on wearable technology (Kolodzey et al., 2017). This lack of homogeneity and the low number of studies using common methodological and technological frameworks ([Table 4](#Table4)) impeded statistical comparisons between the categories defined in our classifications. Such a statistical analysis would have allowed us to explore potential correlations between registration accuracy and tracking and registration methods and thus make more specific recommendations for improving registration accuracy in future studies. This contrasts with some AR-based guidance tools for minimally invasive surgery such as those for laparoscopy where Eckert et al. (Eckert, Volmerg and Friedrich, 2019) found a high level of research maturity, i.e. they were considered as successfully validated.

Incomplete retrieval of relevant publications must also be considered as our search was limited to publications in English. The search, selection and classification of studies was done by the first author only and our qualitative assessments may be biased due to their subjective nature. Finally, research published after August 2018 is not included in our review.

1. Conclusions

AR-based image overlay surgery is becoming more available to healthcare professionals and researchers by combining holographic headsets, computer tracking libraries and/or SDKs and game engines. However, manufacturers and researchers are facing key challenges for the implementation of these systems in clinical practice, such as the need for validation. Current research on AR-based image overlay surgery struggles to provide a sufficient level of registration accuracy for their use in clinical practice. There is also the need for more clinical studies that include larger numbers of subjects and measurements as well as data about patients’ recovery and surgical outcomes. In addition, further research must explore to what extent these systems improve surgery times and success rates and minimise invasiveness for patients. This knowledge would allow manufacturers and researchers to optimise these technologies based on the surgical needs and perform statistical comparisons that facilitate the design of highly efficient systems. Finally, finding a balance between the cost of holographic headsets and their suitability for implementation in clinical practice is important as these novel devices show key benefits: they are portable and wearable, integrate tracking and registration and hands-free navigation and offer direct visibility of the surgical site.

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1. Appendix

**S1 Table. Search strategy in MEDLINE.**

|  |  |  |
| --- | --- | --- |
| **Search** | **Search term/s** | **N publications** |
| 1 | Surgery, Computer-Assisted/ or Tomography, X-Ray Computed/ or augmented reality.mp. or Endoscopy/ or Laparoscopy/ | 483962 |
| 2 | image guided surg$.mp. or Surgery, Computer-Assisted/ | 15684 |
| 3 | 1 and 2 | 15367 |
| 4 | track$.tw. | 100868 |
| 5 | registration.tw. | 74110 |
| 6 | fiducial$.tw. | 2519 |
| 7 | projector.tw. | 847 |
| 8 | projection.tw. | 41826 |
| 9 | head mounted display$.tw. | 446 |
| 10 | head mounted display$.mp. or Surgery, Computer-Assisted/ | 15617 |
| 11 | head$ up display$.tw. | 100 |
| 12 | "Head and Neck Neoplasms"/ or Carcinoma, Squamous Cell/ or head$ up display$.mp. | 156219 |
| 13 | autostereoscop$.tw. | 56 |
| 14 | microscop$.tw. | 537608 |
| 15 | smart glasses.tw. | 26 |
| 16 | retinal display$.tw. | 14 |
| 17 | 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 | 909270 |
| 18 | 3 and 17 | 15251 |
| 19 | augmented reality.tw. | 839 |
| 20 | 18 and 19 | 263 |

**S2 Table. Reviewed studies organised according to surgical procedure.**

|  |  |  |
| --- | --- | --- |
| **SURGERY TYPE** | **Studies** | **Articles** |
| **%** | **N** |
| Neurosurgery | 26.32 | 20 | (Cabrilo, Schaller and Bijlenga, 2015, Deng et al., 2014, Drouin et al., 2017, Eftekhar, 2016, Hou et al., 2016, Huang et al., 2012, Kersten-Oertel et al., 2012, Kramers et al., 2014, Krempien et al., 2008, Liao et al., 2010, Mahvash and Tabrizi, 2013, Maruyama et al., 2018, Shamir et al., 2011, Sun et al., 2017, Sun et al., 2016, Besharati Tabrizi and Mahvash, 2015, Yang et al., 2018, Yoshino et al., 2015, Zeng et al., 2017, Zhang, Chen and Liao, 2015) |
| Dental, craniomaxillofacial and oral | 22.37 | 17 | (Badiali et al., 2014, Lee et al., 2010, Lin et al., 2016, Lin et al., 2015, Ma et al., 2019, Marmulla et al., 2005, Mezzana, Scarinci and Marabottini, 2011, Mischkowski et al., 2006, Qu et al., 2015, Suenaga et al., 2013, Suenaga et al., 2015, Tran et al., 2011, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Zhu et al., 2011, Zhu et al., 2016) |
| Assist several surgical procedures | 21.05 | 16 | (Cutolo et al., 2016, Fichtinger et al., 2005, Gavaghan et al., 2012, Giraldez et al., 2007, Han et al., 2013, He, Liu and Wang, 2016, Hu, Wang and Song, 2013, Khan et al., 2006, Martins et al., 2016, Mondal et al., 2015, Shao et al., 2014, Vogt, Khamene and Sauer, 2006, Wacker et al., 2005, Wen, Chng and Chui, 2017, Zhang, Chen and Liao, 2017, Wu et al., 2018) |
| Abdominal | 13.16 | 10 | (Mahmoud et al., 2017, Müller et al., 2013, Pessaux et al., 2015, Si et al., 2018, Sugimoto et al., 2010, Tang et al., 2017, Volonte et al., 2011, Wen et al., 2013, Wen et al., 2014, Wesarg et al., 2004) |
| Orthopaedic | 11.84 | 9 | (Andress et al., 2018, Gibby et al., 2019, Kosterhon et al., 2017, Liang et al., 2012, Ma et al., 2018, Ma et al., 2017, Pauly et al., 2015, Wang et al., 2016, Wu et al., 2014) |
| Eye | 2.63 | 2 | (Rodriguez et al., 2012, Scolozzi and Bijlenga, 2017) |
| Endovascular | 1.32 | 1 | (Parrini et al., 2014) |
| Perforator flap | 1.32 | 1 | (Jiang et al., 2017) |

**S3 Table. Classification of reviewed automatic optical tracking studies according to tracking method.**

|  |  |  |
| --- | --- | --- |
| **TRACKING METHOD** | **Studies** | **Articles** |
| **%** | **N** |
| Marker-based using: |  |  |  |
|  Infrared camera | 40.79 | 31 | (Cabrilo, Schaller and Bijlenga, 2015, Deng et al., 2014, Drouin et al., 2017, Gavaghan et al., 2012, Giraldez et al., 2007, He, Liu and Wang, 2016, Hu, Wang and Song, 2013, Huang et al., 2012, Kersten-Oertel et al., 2012, Khan et al., 2006, Kosterhon et al., 2017, Lee et al., 2010, Liang et al., 2012, Liao et al., 2010, Lin et al., 2016, Ma et al., 2019, Ma et al., 2017, Maruyama et al., 2018, Shamir et al., 2011, Si et al., 2018, Suenaga et al., 2013, Tang et al., 2017, Tran et al., 2011, Vogt, Khamene and Sauer, 2006, Wacker et al., 2005, Wang et al., 2016, Wesarg et al., 2004, Yang et al., 2018, Yoshino et al., 2015, Zhang, Chen and Liao, 2017, Zhang, Chen and Liao, 2015) |
|  RGB camera | 19.74 | 15 | (Badiali et al., 2014, Cutolo et al., 2016, Jiang et al., 2017, Kramers et al., 2014, Lin et al., 2015, Mischkowski et al., 2006, Müller et al., 2013, Parrini et al., 2014, Qu et al., 2015, Shao et al., 2014, Sun et al., 2017, Wang et al., 2015, Wu et al., 2014, Zhu et al., 2016, Zhu et al., 2011) |
|  RGB-D camera | 1.32 | 1 | (Wen et al., 2014) |
|  Projector and RGB camera | 2.63 | 2 | (Krempien et al., 2008, Wen et al., 2013) |
| Marker-less using: |  |  |  |
|  RGB camera | 3.95 | 3 | (Suenaga et al., 2015, Wang et al., 2014, Wang et al., 2017) |
|  RGB-D camera | 6.58 | 5 | (Gibby et al., 2019, Marmulla et al., 2005, Pauly et al., 2015, Wen, Chng and Chui, 2017, Wu et al., 2018) |
|  Projector and RGB camera | 1.32 | 1 | (Zeng et al., 2017) |
| Electromagnetic | 2.63 | 2 | (Ma et al., 2018, Martins et al., 2016) |
| Manual | 10.53 | 8 | (Eftekhar, 2016, Hou et al., 2016, Mahvash and Tabrizi, 2013, Mezzana, Scarinci and Marabottini, 2011, Pessaux et al., 2015, Sugimoto et al., 2010, Besharati Tabrizi and Mahvash, 2015, Volonte et al., 2011) |
| Other | 10.53 | 8 | (Andress et al., 2018, Fichtinger et al., 2005, Han et al., 2013, Mahmoud et al., 2017, Mondal et al., 2015, Rodriguez et al., 2012, Scolozzi and Bijlenga, 2017, Sun et al., 2016) |

**S4 Table. Reviewed studies organised according to the system’s usability.**

|  |  |  |
| --- | --- | --- |
| **USABILITY** | **Studies** | **Articles** |
| **%** | **N** |
| Compact | 12.07 | 7 | (Cutolo et al., 2016, Gibby et al., 2019, Giraldez et al., 2007, Jiang et al., 2017, Kramers et al., 2014, Parrini et al., 2014, Sun et al., 2017) |
| Wireless | 8.62 | 5 | (Gibby et al., 2019, Kramers et al., 2014, Müller et al., 2013, Sun et al., 2017, Wu et al., 2018) |
| Surgical site directly visible | 27.59 | 16 | (Gavaghan et al., 2012, Gibby et al., 2019, Jiang et al., 2017, Krempien et al., 2008, Liang et al., 2012, Lin et al., 2016, Marmulla et al., 2005, Maruyama et al., 2018, Shao et al., 2014, Si et al., 2018, Wang et al., 2016, Wen et al., 2013, Wen et al., 2014, Wu et al., 2014, Wu et al., 2018, Zeng et al., 2017) |
| Hands-free tracking | 32.76 | 19 | (Badiali et al., 2014, Cabrilo, Schaller and Bijlenga, 2015, Cutolo et al., 2016, Gibby et al., 2019, Krempien et al., 2008, Lee et al., 2010, Liang et al., 2012, Ma et al., 2017, Marmulla et al., 2005, Pauly et al., 2015, Suenaga et al., 2013, Suenaga et al., 2015, Tran et al., 2011, Wang et al., 2014, Wang et al., 2015, Wang et al., 2017, Wen et al., 2013, Yang et al., 2018, Yoshino et al., 2015) |
| Stand-alone application | 6.90 | 4 | (Gibby et al., 2019, Kramers et al., 2014, Maruyama et al., 2018, Wu et al., 2018) |

**S5 Table. Classification of reviewed automatic optical tracking studies according to display device.**

|  |  |  |
| --- | --- | --- |
| **DISPLAY** | **Studies** | **Articles** |
| **%** | **N** |  |
| Headset |  |  |  |
|  Video see-through | 15.52 | 9 | (Badiali et al., 2014, Cutolo et al., 2016, Hu, Wang and Song, 2013, Huang et al., 2012, Lin et al., 2015, Parrini et al., 2014, Shamir et al., 2011, Vogt, Khamene and Sauer, 2006, Wacker et al., 2005) |
|  Optical see-through (non-holographic) | 5.17 | 3 | (Jiang et al., 2017, Lin et al., 2016, Wang et al., 2016) |
|  Optical see-through (holographic) | 5.17 | 3 | (Gibby et al., 2019, Si et al., 2018, Wu et al., 2018) |
| Half-silvered mirror | 22.41 | 13 | (He, Liu and Wang, 2016, Liao et al., 2010, Ma et al., 2019, Ma et al., 2017, Pauly et al., 2015, Suenaga et al., 2013, Suenaga et al., 2015, Tran et al., 2011, Wang et al., 2014, Wang et al., 2015, Yang et al., 2018, Zhang, Chen and Liao, 2017, Zhang, Chen and Liao, 2015) |
| Projector | 15.52 | 9 | (Gavaghan et al., 2012, Krempien et al., 2008, Lee et al., 2010, Liang et al., 2012, Marmulla et al., 2005, Wen et al., 2013, Wen et al., 2014, Wu et al., 2014, Zeng et al., 2017) |
| Microscope | 8.62 | 5 | (Cabrilo, Schaller and Bijlenga, 2015, Drouin et al., 2017, Giraldez et al., 2007, Kosterhon et al., 2017, Yoshino et al., 2015) |
| Tablet | 8.62 | 5 | (Deng et al., 2014, Mischkowski et al., 2006, Müller et al., 2013, Tang et al., 2017, Wen, Chng and Chui, 2017) |
| Semi-transparent screen | 3.45 | 2 | (Khan et al., 2006, Wesarg et al., 2004) |
| Smartphone | 3.45 | 2 | (Kramers et al., 2014, Sun et al., 2017) |
| Smart glasses | 3.45 | 2 | (Maruyama et al., 2018, Shao et al., 2014) |
| Video camera screen | 1.72 | 1 | (Kersten-Oertel et al., 2012) |
| Not specified | 6.90 | 4 | (Qu et al., 2015, Wang et al., 2017, Zhu et al., 2016, Zhu et al., 2011) |

1. Supporting information

**S1 Appendix. Database of reviewed studies categorised according to the variables considered in this review.**