

## RESEARCH ARTICLE

# Image-guided procedures in the hybrid operating room: A systematic scoping review

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## Abstract

### Background

The shift from open to minimally invasive procedures with growing complexity has increased the demand for advanced intraoperative medical technologies. The hybrid operating room (OR) combines the functionality of a standard OR with fixed advanced imaging systems to facilitate minimally invasive image-guided procedures.

### Objective

This systematic scoping review provides an overview of the use of the hybrid OR over the years, and reports on the encountered advantages and challenges.

### Methods

We conducted a systematic search in PubMed, Embase, Web of Science, and Cochrane library databases for studies that described procedures being performed with the aid of 3D imaging in the hybrid OR.

### Results

The search identified 123 studies that described 44 distinct procedures, divided over nine clinical disciplines. The number of studies increased from two in 2010 to 15 in the first five months of 2020. Ninety-nine (80%) of the studies described how 3D imaging was performed in the hybrid OR; 95 (96%) used cone-beam CT; four (4%) used multi-detector CT. Advantages and challenges of the hybrid OR were described in 94 (76%) and 34 (35%) studies, respectively. The most frequently reported advantage of using a hybrid OR is the achievement of more accurate treatment results, whereas elongation of the procedure time is the most important challenge, followed by an increase in radiation dose.

### OPEN ACCESS

**Citation:** Spenkelink IM, Heidkamp J, Fütterer JJ, Rovers MM (2022) Image-guided procedures in the hybrid operating room: A systematic scoping review. PLoS ONE 17(4): e0266341. <https://doi.org/10.1371/journal.pone.0266341>

**Editor:** Diego Raimondo, Dipartimento di Scienze Mediche e Chirurgiche (DIMEC), Orsola Hospital, ITALY

**Received:** July 22, 2021

**Accepted:** March 19, 2022

**Published:** April 1, 2022

**Peer Review History:** PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0266341>

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**Data Availability Statement:** All studies included in this manuscript can be found in the databases that were searched as mentioned in the methods section. The search strategy is described in [S1 File](#)

and URLs/DOIs of the included studies can be found in [S1 Table](#).

**Funding:** Siemens Healthineers paid money directly to the institute in the form of an unrestricted grant, from which the salaries for authors J. H. and I. S. are partly paid. The specific roles of these authors are articulated in the 'author contributions' section. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. No additional external funding was received for this study.

**Competing interests:** The authors have read the journal's policy and have the following competing interests: J. J. F. reports grants from Siemens Healthineers outside the submitted work. M. M. R. reports grants from Siemens Healthineers outside the submitted work. Siemens Healthineers provided an unrestricted grant, from which the salaries for authors J. H. and I. S. are partly paid. This does not alter our adherence to PLOS ONE policies on sharing data and materials. There are no patents, products in development, or marketed products associated with this research to declare.

## Conclusion

In conclusion, the growing number of clinical disciplines that uses the hybrid OR shows its wide functionality. To optimize its use, future comparative studies should be conducted to investigate which procedures really benefit from being performed in the hybrid OR.

## Introduction

Over the past decade, hybrid operating rooms (OR) have revolutionized the way image-guided procedures are performed. In a hybrid OR, the properties of an aseptic OR are combined with advanced imaging techniques like multidetector computed tomography (MDCT), cone-beam computed tomography (CBCT), fluorescence imaging, and magnetic resonance imaging (MRI). These properties of the hybrid OR allow the combination of open and percutaneous interventions, which avoids the need to perform multiple consecutive procedures or intraoperative patient transport. The advanced imaging techniques facilitate planning of the procedure based on the current intraoperative situation, real-time intraoperative guidance, and direct assessment of technical success at the end of the procedure [1, 2].

The first procedure that induced the development of the hybrid OR, was a cardiovascular procedure. Barstad et al. described a procedure that combined percutaneous transluminal coronary angioplasty and minimally invasive direct coronary artery bypass grafting in the same anesthetic setting [3]. This combination of procedures required imaging in the OR. In earlier days, imaging was mainly performed using mobile equipment. However, with an increase in complex and demanding procedures, a new type of OR was designed. Barstad et al. already mentioned a specially designed surgical-radiologic suite for their hybrid procedure [3]. Later on, the term 'hybrid operating room' was introduced for ORs that enabled specialists to perform procedures that require imaging in a sterile environment. Only recently, a definition of 'hybrid operating room' was established in an expert consensus meeting [4]. According to this definition, the OR should at least be equipped with a coordinate system-based imaging technique. In this review, we follow this definition and explore procedures in which intra-operative 3D imaging is performed within the OR.

Nowadays, cardiovascular surgeons are still major users of the hybrid OR, but due to improvements in imaging modalities, computer graphics, and surgical instruments, the use of hybrid ORs is no longer limited to cardiovascular procedures [5]. For example, orthopedic and neurosurgeons also perform minimally invasive image-guided procedures in the hybrid OR and other potential areas of application are still arising [6, 7].

The aim of this scoping review therefore is to provide an overview of the use of the hybrid OR over the years, and to report on the advantages and challenges that were encountered during procedures performed in the hybrid OR.

## Methods

This systematic scoping review was conducted following the Arksey and O'Malley framework and the revisions made by Levac et al. [8, 9] The results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR) guidelines [10].

## Literature search

PubMed, Embase, Web of Science, and Cochrane Library databases were systematically searched using the combined synonyms for the following search terms: hybrid, operating, operation, surgery, room, and theater ([S1 File](#)). No date or language limits were applied. The last search was performed in May 2020. Reference lists of included documents were reviewed to identify related and relevant studies.

## Study selection

After removal of duplicates, one author (IS) reviewed the retrieved citations for potential eligibility by screening the titles. Subsequently, two authors (IS, JH) independently reviewed a random sample of fifty citations for potential eligibility by screening the titles and abstracts. After an inter-rater agreement of more than 80% was achieved, one author (IS) reviewed the remaining citations [11]. Any cases of doubt were solved by independent assessment of, and discussion with, a second author (JH). The full-text was retrieved for all citations identified for potential inclusion. Studies were included if they described a procedure that used intra-operative 3D imaging techniques for planning, guidance or control in human patients, and that was carried out in a hybrid OR. Again, two authors (IS, JH) independently reviewed fifty randomly sampled full-texts for eligibility. After an inter-rater agreement of more than 80% was reached, one author (IS) reviewed the remaining studies. In case studies had overlapping patient cohorts, the most recent study was included.

## Data extraction and analysis

Using a pre-defined form, the following data were extracted: authors, year, country, clinical discipline, disease, intervention, number of patients, main imaging technique, additional technologies, advantages of the hybrid OR, and challenges of the hybrid OR. The data were summarized based on the use of 3D imaging techniques in the hybrid OR. Furthermore, the studies were grouped based on the procedure and categorized into main clinical discipline that performed the procedures. A descriptive analysis of the advantages and challenges was conducted within these groups.

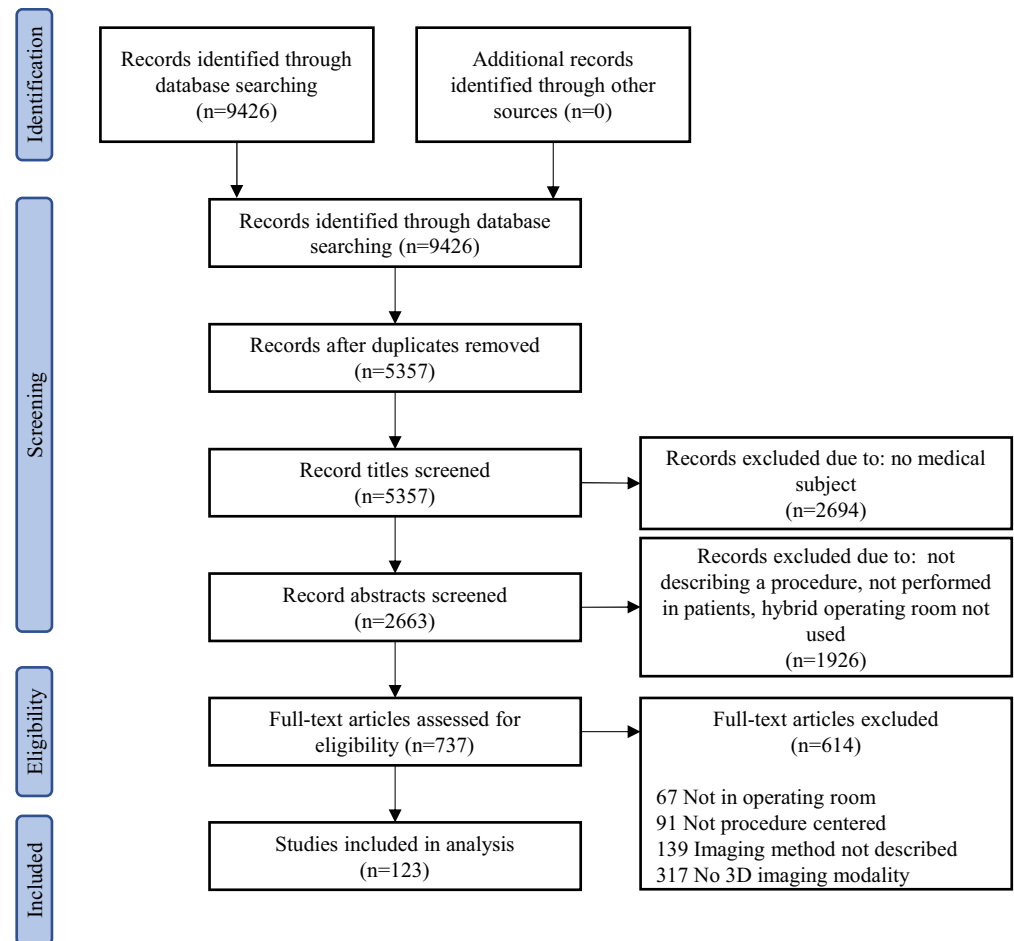
## Results

### Literature search

A total of 9426 records were identified of which 5357 unique studies were screened based on title, abstract and full text. Inter-rater agreements of 92% (kappa: 0.81, 95% CI: 0.63–0.99) and 90% (kappa: 0.74, 95% CI: 0.55–0.95) were reached for the abstract and full-text screening, respectively. Finally, 123 studies did fulfill the inclusion criteria for this scoping review. A flow-chart of this literature search can be found in [Fig 1](#), and an overview of the included studies can be found in [S1 Table](#).

### Study characteristics

The number of studies increased over the years, from two in 2010 to fifteen in the first five months of 2020, as has the number of clinical disciplines that use the hybrid OR. ([Fig 2](#)). In 2010, the hybrid OR was only used by the cardiac surgeons, whereas there were nine different disciplines using the hybrid OR in 2020: Thoracic surgery (n = 42), Neurosurgery (n = 37), Vascular surgery (n = 21), Cardiac surgery (n = 8), Urology (n = 6), Orthopedic surgery (n = 6), Ophthalmology (n = 1), Oral and maxillofacial surgery (n = 1), and Otolaryngology/cervicofacial surgery (n = 1). The studies were performed in 21 different countries. Most of



**Fig 1. PRISMA flowchart of the study selection process.**

<https://doi.org/10.1371/journal.pone.0266341.g001>

them originated from Europe ( $n = 38$ , 31%), followed by the USA ( $n = 26$ , 21%), Taiwan ( $n = 23$ , 18%), and Japan ( $n = 17$ , 14%). The median number of included patients was 15 (range 1–1027). Fifty-one studies (41%) enrolled 10 or fewer patients. Furthermore, only 15 studies (12%) compared the outcomes of a patient group treated in the hybrid OR with those of a patient group treated in a standard procedure room.

## Use of the hybrid operating room

**3D imaging in the hybrid OR.** Ninety-nine (80%) of the included studies described how 3D imaging in the hybrid OR was performed. Ninety-five (96%) of these studies used CBCT as a coordinate-based imaging system, while four studies (4%) used MDCT.

We identified three stages in which 3D imaging was performed: at the start of the procedure, during the procedure, and at the end of the procedure. 3D imaging was performed at the start of the procedure in 68/99 (69%) studies. In this stage, imaging was used to acquire insight into the patient's anatomy in surgical position; to translate a pre-operative procedure plan to the intraoperative situation; or to make a procedure plan. The procedure plan was made either using the software of the 3D imaging modality itself, or by using other navigation technology. 3D imaging was performed during the procedure in 41/99 (41%) studies. In this stage, the images were used to acquire an updated view of the anatomy; to update the navigation; to

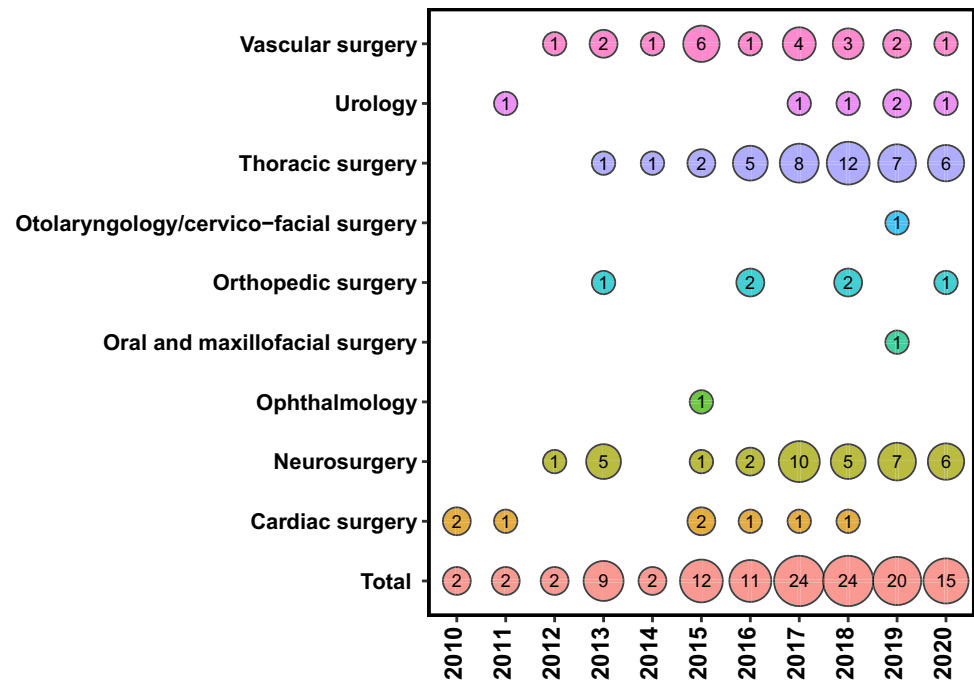


Fig 2. Number of studies per clinical discipline per year.

<https://doi.org/10.1371/journal.pone.0266341.g002>

assess the presence of accidental tissue damage; or to assess the position of a needle/probe/catheter after which the next stage of the procedure started. In 40/99 (40%) studies 3D imaging was performed at the end of the procedure to assess the results of the treatment and to continue the procedure to make adjustments if necessary. In five studies, some patients received a repeated confirmation scan after the adjustments.

**Procedures performed in the hybrid OR without using 3D imaging.** Twenty-four (20%) of the included studies described the presence of a coordinate-based imaging system in the hybrid OR, but they did not report the use of 3D imaging during the procedure. In 20/24 (83%) studies, the use of 2D imaging, that is, mainly fluoroscopy or 2D angiography, was described. Three of 24 (13%) studies did not describe performing imaging at all, and 1/24 (4%) studies used the imaging facilities of the hybrid OR but performed surgery in the standard OR. Most of the studies (16/24, 67%) described a vascular procedure performed by vascular surgeons ( $n = 10$ , 42%) or neurosurgeons ( $n = 6$ , 25%).

**Additional medical technologies in the hybrid OR.** In addition to 3D imaging, other medical technologies were used in the hybrid OR, namely surgical navigation and fluorescence imaging. Infrared- and electromagnetic tracking-based surgical navigation was used in 12/123 (10%) and 6/123 (5%) studies, respectively. Infrared-based navigation was mainly used by thoracic, orthopedic, and neurosurgeons, while electromagnetic tracking was used by thoracic surgeons only. Fluorescence imaging was performed in 8/123 (7%) studies, in which a near-infrared camera is used to image the administered indocyanine green (ICG). It was mainly used in thoracic and neurovascular interventions. In thoracic surgery, tumors were marked with an ICG-dye for minimally invasive localization of non-palpable small pulmonary nodules. In the neurovascular procedures, ICG video angiography was used to visualize the patency of blood vessels.

## Clinical disciplines in the hybrid operating room

**Thoracic surgery.** We identified four different thoracic surgical procedures that were performed in the hybrid OR; image-guided video-assisted thoracoscopic surgery (iVATS), lung biopsy, pulmonary tumor ablation, and rib tumor resection. The reasons to perform these procedures in the hybrid OR were: to enable the localization and resection in one setting for the iVATS procedure; to improve needle positioning and by that the tumor yield of the lung biopsy; to use image-guidance for planning and positioning of the probe to improve tumor targeting during the ablation procedure; and to minimize tissue damage and evaluate the completeness of the resection of non-palpable rib tumors.

**Neurosurgery.** We identified twelve types of neurosurgical procedures, of which seven were cerebrovascular procedures: clipping of aneurysms, vessel embolization, aspiration of hematomas and abscesses, excision of arteriovenous malformations (AVM), angioplasties, vessel coiling, and endarterectomies. The reason to perform these procedures in the hybrid OR was the availability of real-time feedback regarding the angioarchitecture to directly assess the treatment result, which improves patient safety as well as the accuracy of the treatment results. This in turn helps preventing hemorrhages and detecting iatrogenic traumas. In clipping of aneurysm, vessel embolization, and endarterectomy procedures, ICG fluorescence and infra-red-based neuronavigational techniques were used in addition to 3D imaging.

The other five neurosurgical procedures were: tumor resection, shunt placement, odontoidectomy, lead positioning, and percutaneous sclerotization and vertebroplasty combined with surgical decompression. Tumor resection and odontoidectomy procedures were performed in the hybrid OR to avoid complications and improve resection completeness. This was realized by using infra-red-based navigation and assessed by intra-operative 3D imaging. For all other neurosurgical procedures, the reason to perform the procedure in the hybrid OR was to assess treatment results using 3D imaging to improve accuracy. Furthermore, in shunt placement, the burr hole and catheter positions were planned using 3D imaging to improve patient safety.

**Vascular surgery.** Within vascular surgery, five procedures were identified: endovascular aortic repair (EVAR), embolization procedures, stenting procedures, removal of a catheter remnant, and detection and treatment of pulmonary embolism in hemodynamically unstable patients. The reason to perform EVARs, embolization, and stenting procedures in the hybrid OR was to limit the contrast and radiation doses by using image fusion possibilities or by performing an intraoperative control CBCT instead of a control computed tomography angiography at discharge. Removal of a catheter remnant was performed in the hybrid OR because 3D imaging enabled surgeons to perform the operation minimally invasively. The procedure involving pulmonary embolisms was the only procedure in which patients were brought to the hybrid OR for a diagnosis, in order to immediately perform a treatment if necessary.

**Urology.** Four procedures were reported in urology: percutaneous nephrolithotomies, retrograde intrarenal surgery with lithotripsy, super-selective tumoral embolization, and laparoscopic thermal ablation. The procedures regarding kidney stones were performed in the hybrid OR because it was expected that 3D imaging would improve patient safety in complex cases and increased effectiveness in finding residual stones were expected when 3D imaging was used compared to using fluoroscopic or endoscopic techniques. The super-selective tumoral embolization combined with a partial nephrectomy was performed in the hybrid OR because intraoperative 3D imaging of the vasculature facilitated performing the procedure in a clampless fashion. The reason to perform the laparoscopic thermal ablation procedure in the hybrid OR was that the procedure could then be performed minimally invasively. 3D imaging was used for tumor targeting, verification of the position of the probe, and evaluation of the ablation zone.



**Orthopedic surgery.** Within orthopedic surgery, fixation of ankle bones and intralesional curettage of bone tumors were reported. In the fixation of ankle fractures, 3D imaging was used to assess the syndesmotic reduction by comparing both ankles to prevent malreduction after fixation, which could occur when fluoroscopy alone would have been used. The reason to perform the intralesional curettage procedure in the hybrid OR was to facilitate surgical navigation based on the current anatomical situation and to have the possibility of assessing the resection results.

**Cardiac surgery.** The hybrid OR was used by cardiac surgeons for performing a transapical aortic valve implantation, a ventricular pseudoaneurysm repair, placement of a stent graft in an atrial septal defect, and for object removal from a ventricle. In all procedures, the 3D imaging possibilities in the hybrid OR were used for image fusion. This transformed the pre-operative plan to the current anatomical situation, which increased patient safety.

**Neurosurgery and orthopedic surgery.** Placement of spinal screws is a procedure that was performed by neurosurgeons and orthopedic surgeons, in seven and three studies, respectively. This procedure was performed in the hybrid OR because 3D imaging allowed surgical navigation based on the current intraoperative situation. It was expected that this improved the accuracy and lowered the complication risks and radiation dose.

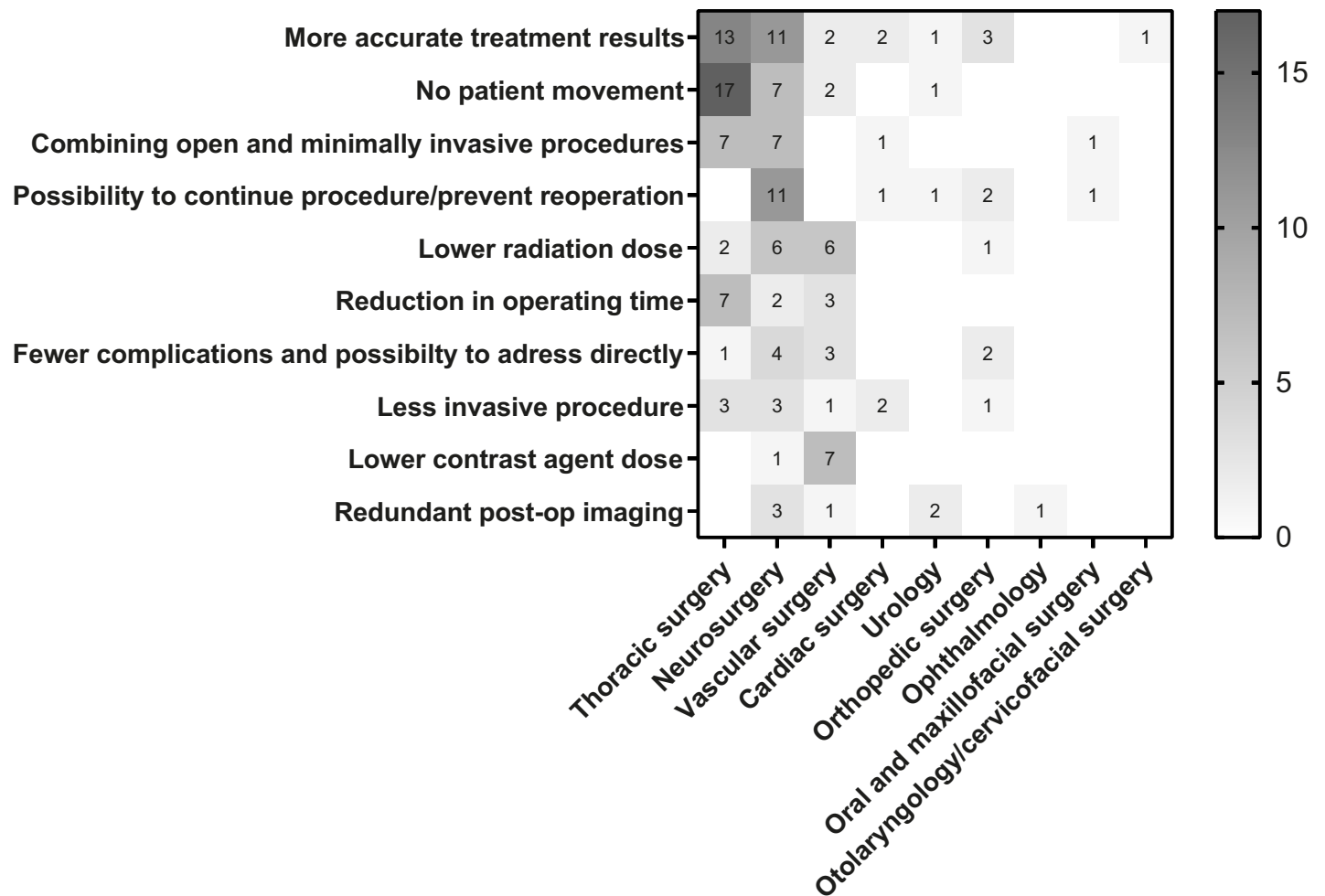
**Miscellaneous.** Procedures performed by other clinical disciplines were also found, e.g. by ophthalmology, oral and maxillofacial surgery, otolaryngology/cervicofacial surgery. These are described in [S1 Table](#).

### Advantages of the hybrid operating room

Advantages of performing procedures in the hybrid OR were explicitly mentioned in 94 (76%) studies. The advantages that were most often described were the improved accuracy of treatment results and the improved patient safety (both mentioned by 33/94 (35%) studies). The improved patient safety is partly associated with the fact that the patient does not have to be transported to an imaging facility (27/94, 29%). Furthermore, 3D imaging for planning and the procedure itself can be performed without adjusting the patient position, which benefits the accuracy. Patient safety is further increased since accidental tissue trauma and complications can be visualized and treated instantaneously (10/94, 11%). Another often mentioned advantage is that the treatment result can be assessed before closing the patient. This allows continuation of the procedure if the result turns out to be unsatisfactory (16/94, 17%). As a result, the number of reinterventions might be reduced, as mentioned by 8/94 (9%) studies, and it could possibly eliminate the need for postoperative control imaging (7/94, 7%). Furthermore, 16/94 (17%) of the studies acknowledged that being able to combine minimally invasive and open procedures was an advantage of the hybrid OR. Other advantages are visualized in [Fig 3](#) and described per procedure in [S2](#) and [S3](#) Tables.

### Challenges of the hybrid operating room

Thirty-four of the 99 (35%) included studies that performed 3D imaging mentioned challenges of performing a procedure in the hybrid OR. A longer OR utilization time was mentioned in 11/34 (32%) studies. These studies described iVATS procedures (8/11, 73%), spinal screw positioning (2/11, 18%), and a navigational bronchoscopy procedure (1/11, 9%). The longer procedure times were mainly caused by a more complex patient positioning compared to the standard procedure and the extension of the anesthesia equipment, which were required for a CBCT-scan acquisition. Five of the studies that performed these procedures also mention the existence of a learning curve that is induced by the more complex patient positioning and preparation [[12–16](#)].



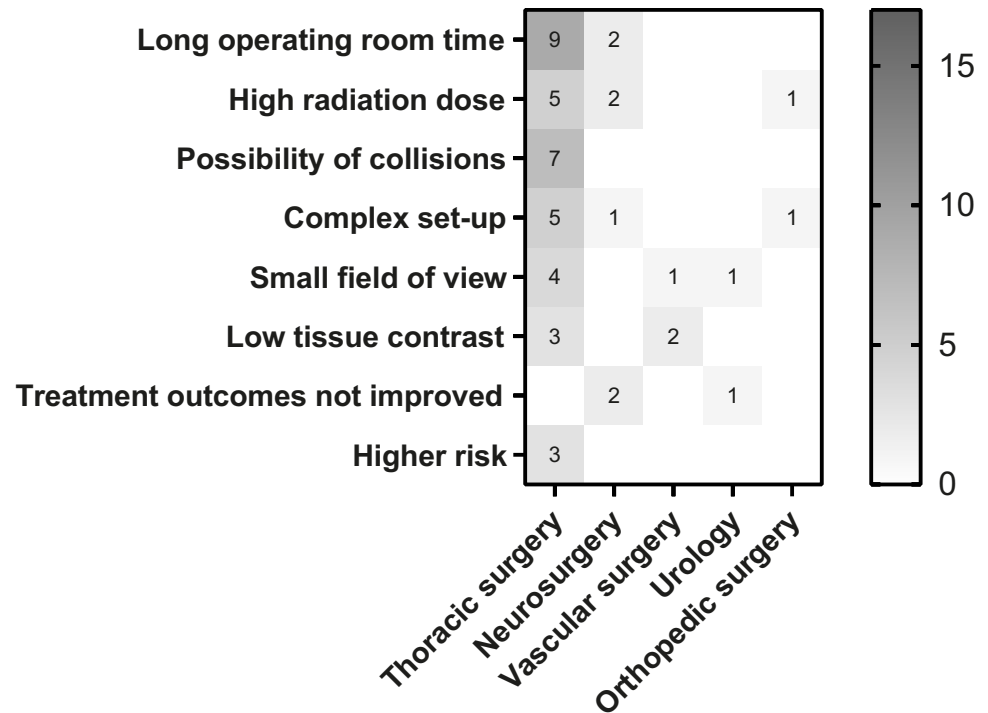
**Fig 3. Overview of the advantages mentioned by the studies per clinical discipline.** The numbers and grayscale indicate how many studies mentioned the advantage.

<https://doi.org/10.1371/journal.pone.0266341.g003>

Another challenge of performing 3D imaging in the hybrid OR is a possible increase in radiation dose compared to the use of 2D fluoroscopy alone (mentioned by 8/34, 24% of the studies). The challenge of potential collisions between the C-arm and the surgical equipment, which could impede the procedure, was mentioned in 7/34 (21%) studies.

Furthermore, the use of 3D imaging to confirm the treatment results within the hybrid OR could lead to overtreatment. Lerisson et al. evaluated the influence of continuation of the treatment of anomalies that were detected by control CBCT on the long-term results in patients with abdominal aneurysms of the aorta [17]. These anomalies encompass endoleaks, bridging stent through the fenestration, and kinks. They found that immediate corrective treatment of endoleaks did not lead to a significant decrease in the number of reinterventions and number of late events compared to a patient group that was treated without an intra-operative 3D scan. This could be explained by possible spontaneous sealing of the endoleaks within a short period after the procedure, which suggests that not all intraoperatively found endoleaks require further treatment [17]. Other challenges are visualized in Fig 4, and described per procedure in S2 and S3 Tables. No challenges were mentioned by studies that performed the procedures in the hybrid OR without performing 3D imaging.





**Fig 4. Overview of the challenges mentioned by the studies per clinical discipline.** The numbers and grayscale indicate how many studies mentioned the challenge.

<https://doi.org/10.1371/journal.pone.0266341.g004>

## Discussion

This scoping review showed an increase in both the number of procedures performed in a hybrid OR and the number of clinical disciplines that have been using this infrastructure over the past ten years. The main coordinate-based imaging technique that was used was CBCT. Many studies discussed advantages of the hybrid OR, of which increased treatment accuracy and patient safety are the most important. The most often mentioned challenges comprise the longer procedure time and the increased radiation dose.

## Strengths and limitations

The major strength of our systematic scoping review is that, as far as we are aware, we are the first to provide an extensive overview of the clinical use of the hybrid OR. Prior studies have focused on the use and requirements of the hybrid OR within a certain clinical discipline, whereas our review provides a broad overview regarding the use of the hybrid OR by several disciplines [6, 18–21]. This can help hospitals to optimize the usage of the hybrid OR and inspire disciplines to exploit the room in new ways. The insight in the advantages of performing a procedure in the hybrid OR can aid in the transition from invasive open to minimally invasive image-guided surgery, since it indicates where the added value of the hybrid OR can be expected. Furthermore, by providing insight in the challenges, this review may guide research in improving the current set-up in the hybrid OR and the development of new techniques that could solve these issues.

Some possible limitations should also be discussed. First, despite a broad search, we may not have identified all studies that performed a procedure in a hybrid OR since there might be studies that performed a procedure in a hybrid OR without reporting this clearly. As a result,

there might be more procedures that are currently being performed in the hybrid OR than identified in this overview. Second, probably not all of the included studies reported on the advantages and challenges that were encountered while performing a procedure in the hybrid OR. In only one-third of the studies, challenges of performing the procedure in the hybrid OR were reported. Although this might give the impression that in many procedures no challenges were encountered, there could be additional challenges that might not have been identified by this review. Third, most of the reported studies were small feasibility studies and only a limited number of studies compared parameters of procedures performed in the hybrid OR with those performed in a standard OR or catheterization room. Therefore, there is no strong evidence that performing procedures in the hybrid OR is more effective than those performed in the standard OR or catheterization room.

### Clinical implications

While the hybrid OR was originally developed for cardiovascular surgery, our results demonstrated that it is now used by many other clinical disciplines. The shift from invasive open surgery to minimally invasive surgery is still ongoing in most surgical disciplines, which may result in less tissue damage, faster recovery times, and lower morbidity and mortality rates. Inherent to this is the limited visualization of the surgical field [22]. Additionally, the procedures nowadays are performed in an ageing population with more co-morbidities [23]. As a result, procedures become more complex, which makes intra-operative imaging increasingly important. We therefore believe that the role of the hybrid OR in the minimally invasive surgical landscape will grow. Since the benefits of the hybrid OR become more apparent, we expect that new procedures that require intraoperative 3D imaging will be developed not only within the disciplines that already use the hybrid OR, but also in other disciplines.

In this study, we have classified the procedures in the hybrid OR based on the main clinical discipline that performed the procedure. However, there already are procedures in which the main discipline is assisted by interventional radiologists. Additionally, we believe that further multidisciplinary collaboration within the hybrid OR will emerge in the future, so multiple procedures can be combined within a single anesthetic. A first impression of this can be seen in the hybrid emergency resuscitation rooms, which are resuscitation rooms equipped with imaging facilities, where trauma surgeons perform a thoracotomy, while neurosurgeons perform intracranial surgery simultaneously [24].

To further optimize the use of the hybrid OR and patient care, it is necessary to carefully study whether it is beneficial to perform a procedure in this location. For example, Liao et al. concluded that 67.7% - 80.2% of the cerebrovascular procedures performed in the hybrid OR could also be performed in the standard OR without any compromise [25]. More comparative studies should therefore be performed to identify which procedures should be carried out in the hybrid OR and which type of patients would benefit most of being treated there.

Multiple studies from different clinical disciplines reported the same challenges, in particular the elongation of the procedure time and the increase in radiation dose. The increased operating time, which was most frequently mentioned, is an important parameter since it has implications on both the costs as well as the clinical results. An increase in preparation time could for example include a longer time under general anesthesia, which adversely affects patient safety. This increased preparation time can partly be explained by the more complex set-up. Since the CBCT-scanner requires more free space, a well-thought-out patient positioning is required to avoid collisions of the C-arm with the operating table. Additionally, often more medical-technical equipment is placed around the patient compared to a set-up in the

standard operating or catheterization room. Clinical disciplines could benefit from each other's experience on how to set up the equipment in the hybrid OR to avoid running into the same challenges. Additionally, there are studies that describe the existence of a learning curve [12–14, 16, 26–28]. This emphasizes the need of an optimized training, followed by a mock-up procedure when new procedures or techniques are applied in the hybrid OR, and the need of performing the procedures on a regular base. Therefore, the number of procedures should be high enough to overcome the learning curve. Since the courses of these learning curves are still largely unknown, more insight is warranted.

Patient safety can also be compromised by an increase in radiation dose. Although some studies found a reduction in total radiation dose, others reported significantly higher radiation doses. Keeping the radiation dose as low as reasonably possible is important for all procedures, which can be achieved by optimization of the scanning protocol and technical improvement of the imaging modalities. Furthermore, combining 3D imaging with image fusion or navigation technologies might also reduce the radiation dose, as was done in multiple studies [29, 30]. We believe, the clinical disciplines could also learn from each other about how to apply these techniques. In some procedures, the intraoperative 3D control scan obviates the need of post-operative control scans. This possibility should be considered in order to not further increase the radiation exposure beyond what is necessary.

## Conclusion

In conclusion, the increase in the number of clinical disciplines shows the wide functionality of the hybrid OR. The most reported advantage of using a hybrid OR is achievement of more accurate treatment results, whereas elongation of the procedure time is the most important challenge faced in the hybrid OR, followed by an increased radiation dose. To optimize the use of the hybrid OR, comparative studies should be performed in order to identify which procedures benefit of being performed in this facility.

## Supporting information

**S1 Checklist. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.**

(DOCX)

**S1 File. Search strategy.** Search query and number of results per database.

(DOCX)

**S1 Table. Study characteristics.** Information about the included studies regarding number of patients, disease, and procedure.

(DOCX)

**S2 Table. Procedural data of studies reporting on 3D imaging technique.** Overview of how 3D imaging is used in the hybrid OR per clinical discipline and information about its advantages and challenges.

(DOCX)

**S3 Table. Procedural data of studies without clear report of 3D imaging.** Overview of how the hybrid OR is used per clinical discipline and information about its advantages and challenges.

(DOCX)

## Author Contributions

**Conceptualization:** Ilse M. Spenkelink, Jan Heidkamp, Jurgen J. Fütterer, Maroeska M. Rovers.

**Data curation:** Ilse M. Spenkelink.

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**Validation:** Jan Heidkamp.

**Visualization:** Ilse M. Spenkelink.

**Writing – original draft:** Ilse M. Spenkelink.

**Writing – review & editing:** Ilse M. Spenkelink, Jan Heidkamp, Jurgen J. Fütterer, Maroeska M. Rovers.

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