Meta-Analysis

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Robotic Assistance in Percutaneous Liver Ablation Therapies

A Systematic Review and Meta-Analysis

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Objective: The aim of this systematic review and meta-analysis is to identify current robotic assistance systems for percutaneous liver ablations, compare approaches, and determine how to achieve standardization of procedural concepts for optimized ablation outcomes.

Background: Image-guided surgical approaches are increasingly common. Assistance by navigation and robotic systems allows to optimize procedural accuracy, with the aim to consistently obtain adequate ablation volumes.

Methods: Several databases (PubMed/MEDLINE, ProQuest, Science Direct, Research Rabbit, and IEEE Xplore) were systematically searched for robotic preclinical and clinical percutaneous liver ablation studies, and relevant original manuscripts were included according to the Preferred Reporting items for Systematic Reviews and Meta-Analyses guidelines. The endpoints were the type of device, insertion technique (freehand or robotic), planning, execution, and confirmation of the procedure. A meta-analysis was performed, including comparative studies of freehand and robotic techniques in terms of radiation dose, accuracy, and Euclidean error.

Results: The inclusion criteria were met by 33/755 studies. There were 24 robotic devices reported for percutaneous liver surgery. The most used were the MAXIO robot (8/33; 24.2%), Zerobot, and AcuBot (each 2/33, 6.1%). The most common tracking system was optical (25/33, 75.8%). In the meta-analysis, the robotic approach was superior to the freehand technique in terms of individual radiation (0.5582, 95% confidence interval [CI] = 0.0167–1.0996, dose-length product range 79–2216 mGy.cm), accuracy (0.6260, 95% CI = 0.1423–1.1097), and Euclidean error (0.8189, 95% CI = –0.1020 to 1.7399).

Conclusions: Robotic assistance in percutaneous ablation for liver tumors achieves superior results and reduces errors compared with manual applicator insertion. Standardization of concepts and reporting is necessary and suggested to facilitate the comparison of the different parameters used to measure liver ablation results. The increasing use of image-guided surgery has encouraged robotic assistance for percutaneous liver ablations. This systematic review analyzed 33 studies and identified 24 robotic devices, with optical tracking prevailing. The meta-analysis favored robotic assessment, showing increased accuracy and reduced errors compared with freehand technique, emphasizing the need for conceptual standardization.

Keywords: accuracy, Euclidean error, minimally invasive liver ablation, navigation systems, robotic percutaneous liver ablation

INTRODUCTION

Image-guided techniques have revolutionized the treatment of liver tumors. Minimally invasive percutaneous applicator-based[1] procedures are increasingly common among interventional radiologists and surgeons. Ablation therapies have the advantages of repeatability and rapid recovery, they spare liver parenchyma and are mainly used for tumors measuring less than 3 cm. Procedural success depends on accurate planning and precise applicator placement to ensure adequate coverage of the tumor volume, including for larger tumors. The postprocedural confirmation should show an ablated margin of peritumoral liver tissue.[2–5]

There are several ablation modalities, including radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (Cryo),

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The data used to support the findings of this systematic review and meta-analysis are included in the article. Further information and reprints are available upon request. Please contact the corresponding author.

The research and analysis plan were not preregistered in any independent, institutional registry.

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and irreversible electroporation (IRE). The most commonly used for liver tumors are RFA and MWA.[2,6] Conventional (freehand) applicator insertion techniques require a long learning curve, and the outcomes depend on the physician's expertise and experience.[7] Consequently, navigation and robotic assistance systems were developed to enhance the planning and execution of applicator placement to reduce the need for readjustments. Strategies to improve tumor targeting include the use of advanced imaging and rigid or elastic fusion of different imaging modalities, including two-dimensional (2D) ultrasound (US), multiplanar computed tomography (CT), magnetic resonance imaging (MRI), and three-dimensional (3D) image reconstructions. Depending on the tumor location, challenges arise that may require oblique (out-of-plane) access and trajectory readjustments to minimize targeting errors, which are categorized as longitudinal, lateral, angular, and Euclidean errors.[8–10]

When compared with manual applicator insertion, robotic assistance has the potential to optimize procedural accuracy, resulting in adequate ablation volumes and optimal oncologic outcomes, while reducing the training period to reach proficiency.[3,8] A classification of 6 levels of autonomy was proposed for medical robotics, from no autonomy (level 0) to full automation where the robot performs a procedure (level 5).[11–13] Current robotic surgical systems have either no autonomy, or correspond to manual control with robotic assistance (level 1) or operator-initiated task autonomy (level 2), such as automatic suturing.[14] Telemanipulation, mechanical guidance, and task autonomy are not yet at the level of automation but already provide valuable assistance.

The purpose of the present systematic review is to identify available robotic devices and key parameters for standardized reporting of approaches, ablation margins, and results. In the meta-analysis, robotic and freehand approaches are compared in terms of radiation dose, procedural accuracy, and Euclidean error.

METHODS

Eligibility Criteria

All articles in the medical/surgical and engineering literature reporting robotic assistance with or without the use of a navigation system for percutaneous liver ablation were considered for inclusion. Inclusion criteria were original research articles published in peer-reviewed journals in English, excluded were review articles, case reports, and conference abstracts, as well as articles on organs other than the liver. This systematic review and meta-analysis was completed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] For the systematic review, original preclinical/clinical articles reporting the use of a percutaneous robotic approach for liver ablations were included. Inclusion in the meta-analysis required that articles report the comparison of robotic and freehand percutaneous liver ablation techniques and at least one of the following endpoints: dose-length product (DLP) in patients, accuracy, and Euclidean error.

Search Strategy

A systematic literature search was conducted in the medical/surgical and engineering literature from database inception to January 18, 2023. Detailed search terms and databases are listed in Supplementary Table 1, http://links.lww.com/AOSO/A299. References of published studies were searched to ensure the identification of all relevant articles.

Study Selection

Two authors (A.K.U.R. and B.S.) independently reviewed the eligibility of each publication by reviewing titles, abstracts, and full text as specified in the PRISMA flowchart (Fig. 1). Discrepancies during title/abstract screening were resolved at the full-text stage by consensus between the two reviewers.

Data Extraction and Risk of Bias Assessment

To address the key points for the systematic review and meta-analysis, the relevant technical and clinical parameters were extracted and grouped into tables to facilitate comparison among studies and standardization of definitions related to needle placement and accuracy. If reported, quantitative data regarding the number of targets, errors, and readjustments were extracted according to the technique and needle type used.

The risk of bias in individual studies was assessed using the QUADAS-2[16] tool, classifying each study into low, high, or unclear risk of bias, and applicability problems in 4 domains: patient selection, index test, reference standard, and flow and timelines. Risk categories have to be defined according to the target study. Consequently, in the first domain (patient selection), we classified as high risk the use of phantom models, ex vivo models, live models with insufficient details of the setting, and clinical case reports with inadequate information about the inclusion and exclusion criteria. Applicability problems in this domain were related to reproducibility in a clinical setting. For the second domain (index test: robotic equipment), a high risk was determined when device descriptions lacked adequate technical detail, tests were performed without clear methodology, prototype devices were used outside of clinical trials, and when extensive engineering support was required that could limit their applicability. The third domain (reference standard: freehand technique) was based on adequate specifications of the study results in the context of the current state of the art, and concerns about its applicability focused on assessing the relevance and utility of the results in the clinical setting. In the last domain (flow and timelines), the assessment considered technical issues and decision-making timelines that could impact the accuracy of the results. Supplementary Table 2, http://links.lww.com/AOSO/A300 provides a structured and detailed assessment of these aspects for the included studies.

Definitions

To foster agreement on terminology and thus standardization and comparability between studies, a summary of relevant nomenclature is proposed with key points in the description of robotic equipment and its function/benefit in the setting of liver ablations (Table 1).

Meta-analysis

Subgroup meta-analysis was performed to compare the freehand and robotic techniques in terms of individual radiation (DLP), ablation accuracy, and Euclidean error, as well as for a comparison of studies that used the same device. The presence or absence of heterogeneity was assessed with the Q-statistic (χ^2) of homogeneity, and the extent of heterogeneity of effects among studies was quantified with the I^2 index (an I^2 >60% representing high heterogeneity). Sensitivity analysis was performed by comparing the results of the subgroup analyses against the overall results and the random-effects analyses against the fixed-effects analyses. Egger's test was used to assess potential publication bias (P value <0.05 is the cutoff point related to the possible publication bias). The R 4.3.1 meta-package was used for all meta-analyses and graphics design. Statistical significance was set with a P value <0.05.

RESULTS

Among the 755 references retrieved, 33 preclinical and clinical trials met the inclusion criteria for the systematic review

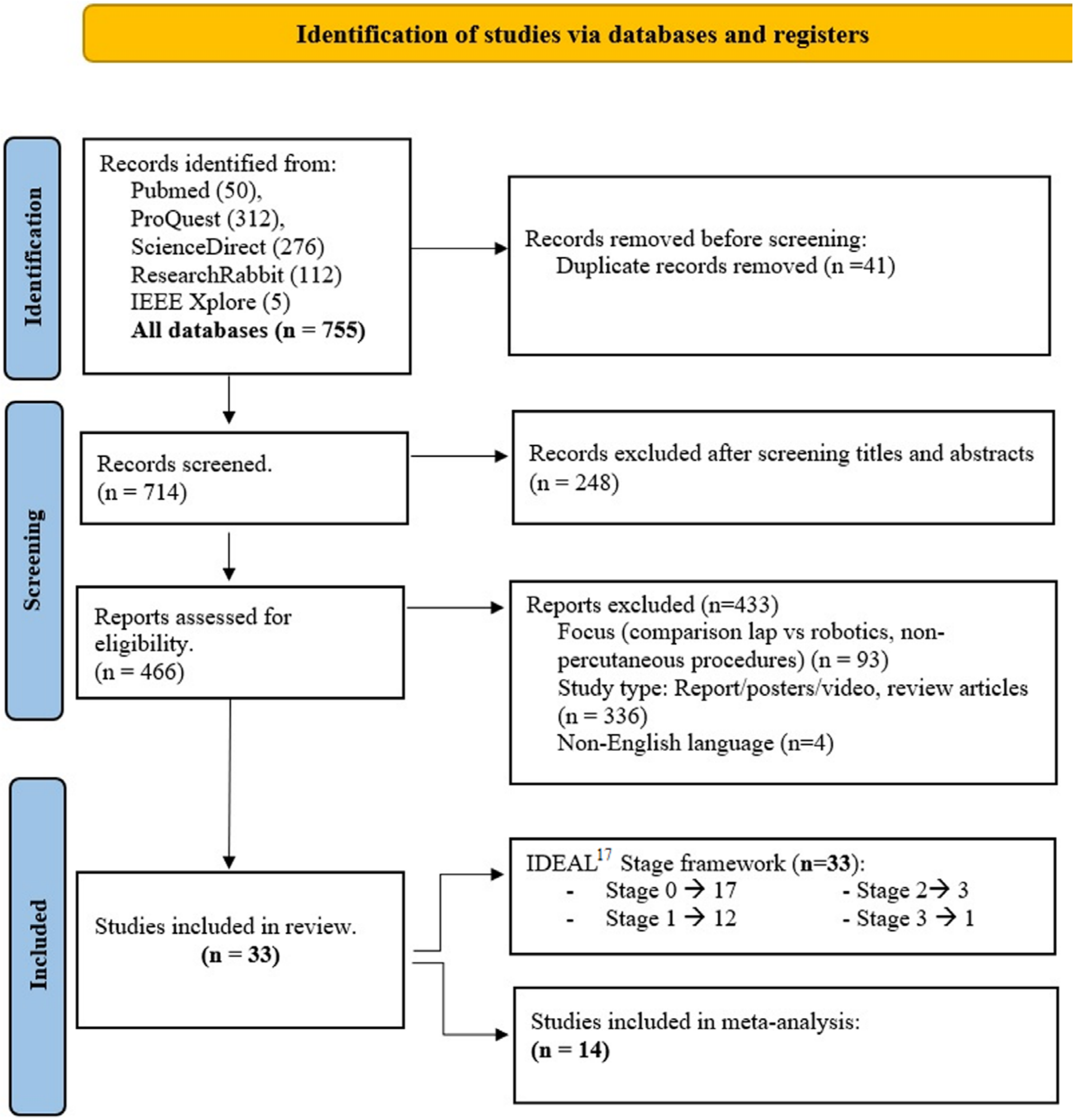


FIGURE 1. PRISMA flow chart.[15]

and 14/33 for the meta-analysis. The PRISMA flowchart of the study selection process is presented in Figure 1, and the selected references are listed in Supplementary Table 3,[23–29] http://links.lww.com/AOSO/A301. An overview of the characteristics of different studies regarding the device used and the ablation workflow phases is listed in Supplementary Table 4, http://links.lww.com/AOSO/A302.

Systematic Review

The QUADAS-2 tool was used to assess all 33 articles included in the systematic review. It revealed varying degrees of risk of bias and concerns regarding applicability in the different domains, as listed in Supplementary Table 2, http://links.lww.com/AOSO/A300. The first domain (patient selection) showed 11 studies with low risk (33.3%), 21 with high risk (63.7%), and 1 with unclear risk (3%). The second domain (index test) revealed 29 studies classified as low risk (87.9%) and 4 as high risk (12.1%). The third domain (reference standard) showed 27 studies with low risk (81.8%), 5 with high risk (15.2%), and 1 with unclear risk (3%). The fourth domain (flow and time) revealed 29 studies with low risk (87.9%), 3 with high risk (9.1%), and 1 with unclear risk (3%). In terms of concerns for clinical applicability, in patient selection, 21 studies showed a low risk of bias (63.6%), 9 high risk (27.3%), and 3 unclear risk (9.1%). In the index test, 27 studies showed low risk (81.8%) and 6 high risk (18.2%). In the reference standard, 28 studies showed low risk (84.9%), 4 high-risk (12.1%), and 1 unclear risk (3%). In 3 of the 4 risk of bias domains and in all domains relevant for clinical applicability, the majority of included studies presented a low risk.

There were 27 prospective and 6 retrospective studies included (81.8 and 18.2%, respectively). Among the 13 clinical trials involving 482 patients, 7 were led by interventional

TABLE 1.

Concept Summary Based on the Systematic Review and Meta-analysis

Concept	Description	References
Applicator	Generic term for energy-based devices (needles, probes, antennas, etc.).	1
Planning	Refers to the set of imaging techniques used (such as US, CT, MRI, or PET-CT) to assess the suitability of the procedure for the patient. These imaging modalities provide critical information about the size, shape, location, and number of tumors in the tissue and their relationship to blood vessels and adjacent structures.	1
Execution		1,17
Targeting	The step in which an applicator is placed within the tumor to be treated. Image-guided targeting techniques (US, CT, among others) allow for precise localization and delineation of the tumor and surrounding anatomy. Clear visualization, multiplanar capability, and interactive image functions are necessary. Transtumoral: applicators pass through the tumor to reach the target point. Peritumoral: applicators are arranged around the tumor to cover the target area.	
Monitoring	The process of observing and evaluating the treatment effects during the procedure under different imaging techniques.	
Intraprocedural modification	Refers to the tools and techniques used during the procedure that allow to assess the need for real-time modification of the ablation site by repositioning the applicator until the appropriate safety margin is obtained. Repositioning: reentry of the applicator through the organ capsule Readjustment (s): Withdrawal and/or advancement of the applicator without exiting the organ capsule.	
Confirmation	Immediate evaluation of the treatment response using imaging studies upon completion of the procedure. This evaluation aims to assess the efficacy and confirm whether the final objective has been achieved, demonstrating that the ablation zone covers the target tumor, with an adequate safety halo.	1
Target plane		8,18
Axial	The target is in the same axial plane as the applicator insertion point.	
Oblique	The target is in a different axial plane than the applicator insertion point.	
Image fusion	Imaging technique that combines information from several images (US, CT, MRI, PET-CT) of the same scene into a single image that ideally contains all the important features of each original image (e.g., sensor coils, internal references, anatomical landmarks).	19,20,21
Rigid	Fusion of 2 data sets in a predefined region of interest. One of the images is used as a reference to the geometric transformation that is applied in the other images (source images) and is linked to static anatomic structures.	
Elastic	Can fuse 2 data sets accurately over. Thereby compensate for different patient positioning in the preoperative and the intraoperative setting, with a median error below 1.34 mm.	
Accuracy	Refers to how closely a set of measurements aligns with their true value. It is assessed by measuring the error between the predicted "optimal" applicator position and the "actual" final position of the applicator. Ideally, the error should be as close as possible to zero, which indicates that the current location of the applicator is aligned with the intended position.	10,22
Precision	Refers to the closeness of measurements to each other (consistency or reproducibility) at the same target site during repeated procedures under similar conditions. It measures the ability of the procedure to consistently achieve the same target with a high level of accuracy.	10
Error		8–10
Longitudinal	Depth error. The applicator is in the correct axis and has to be advanced or retracted on the same axis.	
Lateral	Lateral distance of the target measured at a 90° angle to the insertion line.	
Euclidean	Also known as total error, is the physical distance between the applicator tip and the target, in a 3D space.	
Angular	Deviation between planned trajectory and the applicator axis.	

3D indicates three-dimensional; CT, computed tomography; MRI, magnetic resonance imaging; PET-CT, positron emission tomography–computed tomography, US, ultrasonography.

radiologists (53.8%), 3 by surgeons (23.1%), and 3 were interdisciplinary (23.1%).

The technical parameters of the included studies are detailed in Supplementary Table 5, http://links.lww.com/AOSO/A303. According to the IDEAL framework,[30] the devices were in preclinical (stage 0; 17 studies; 51.5%), first-in-human (stage I; 12 studies; 36.4%), prospective developmental (stage II; 3 studies; 9.1%), or larger randomized controlled or equivalent (stage III; 1 study; 3%) stages, and none was a long-term monitoring and registry (stage IV). According to the 6 levels of autonomy for medical robotics,[11] the devices had either no autonomy (level 0; 30 studies; 90.9%) or provided robotic assistance during continuous control by the physicians (level 1; 2 studies, 6.1%) or task autonomy during discrete control by the physicians (level 2; 1 study; 3%). None of the reported devices had conditional or high autonomy or provided full automation. The tracking systems were mainly optical (25/33, 75.8%), electromagnetic (4/33, 12.1%), or not specified (4/33, 12.1%). Overall, the use of 24 robotic devices was reported. The most common were the MAXIO robot (8/33; 24.2%), Zerobot and AcuBot (each 2/33, 6.1%), and prototypes (13/33; 39.4%) and other robots (8/33, one different robot per study; 3% each).

The ablation workflow and clinical parameters of the included studies are detailed in Supplementary Table 6, http://links.lww.com/AOSO/A304. In all studies, rigid image fusion was used for planning and execution; the use of elastic fusion was not reported. Imaging for planning and final confirmation was predominantly achieved via multiplanar CT scan (20/33; 60.6%, and 22/33; 66.7%, respectively). Image planning was performed either via multiplanar CT scan alone (20/33; 60.6%) or combined 3D-CT and 3D-CT with 2D-US (4/33; 12.1% each) and much less with 3D-US alone (2/33; 6.1%). The use of MRI and MRI-3D reconstructions was rare (1/33; 3% each). During the execution phase, multiple applicators were used in most trials (23/33; 69.7%). The applicator was inserted by physicians in 29/33 (87.9%) or by a robotic arm in 1/33 (3%); insertion was not specified in 3/33 (9.1%). The publication by Chang et al,[31] despite being categorized as a review, was included as the authors reported original data. The robot (Transcutaneous Robot-assisted Ablation-device Insertion Navigation System: TRAINS) was programmed to execute the applicator insertion in an ex vivo model.

By definition, the applicator trajectory is either axial, with the target in the same axial plane as the insertion point (in-plane), or oblique, with the target in a different axial plane than the insertion point (out-of-plane). Only 1 study reported the insertion angle relative to the CT scan acquisition planes.[8]

The data to assess overall ablation accuracy and accuracy relative to technique, model, targets, learning curve, and follow-up are summarized in Supplementary Table 7, http://links.lww.com/AOSO/A305. RFA was the most common ablation modality, either alone (14/33; 42.4%) or combined with MWA (2/33;

6.1%), or with MWA and Cryo (1/33; 3%) with a total of 4 different applicator types used.[32] To a lesser extent, MWA (7/33; 21.2%) or IRE (1/33; 3%) alone and not specified data (8/33; 24.2%) were reported.

Three studies compared the accuracy results with the robotic approach between experts and novices. The number of operators involved in the studies reporting operator experience ranged between 1 and 6. No statistically significant difference in the accuracy of ablations was found in relation to the physician's experience ($P < 0.01$,[33] $P = 0.41$,[34] and $P = 0.44$[35]).

A total of 6 studies reported follow-up data, 3 with 6-week follow-up and 3 with 6-month follow-up. Five studies focused on lesion outcomes, while 1 evaluated lesion and patient outcomes, indicating an overall survival of 90% and a disease-free survival of 83.3%. Four studies reported technical success rates (76–100%) for the freehand and robotic approaches (88–100%). These success rates were considered the "primary efficacy of the technique" as determined by CT and MRI studies.

Meta-analysis

The meta-analysis included 14 comparative studies of freehand and robotic techniques and assessed individual radiation, accuracy, and Euclidean error. For each study, the sample size (n), effect size (d), and 95% confidence interval (95% CI) are presented in Table 2 with the corresponding forest plots expressed in standard deviation units. For a subgroup meta-analysis of studies using the same commercially available device, the MAXIO was chosen as the most reported one (Table 3).

Dose-length product

Nine out of the 14 included studies assessed the individual radiation measured as DLP, the ranges were 68–7025 *versus* 79–2216 mGy.cm for freehand and robotic evaluation, respectively. The DerSimonian and Laird procedure yielded a Q-statistic (χ^2) value of 55.5155, $P < 0.05$, and I^2 of 85.58%, demonstrating a significant heterogeneity. The coefficient of variation of 1.9626 indicated a high variability between the studies. Consequently, the random pooled effects model was used and showed a random effect of 0.5582 in favor of the robotic technique (95% CI = 0.0167–1.0996). Egger's test showed no evidence of publication bias ($P = 0.1666$).

Accuracy

Eight studies reported the accuracy, comparing the techniques. There was statistical evidence for significant heterogeneity (Q-statistic (χ^2) value of 33.3511, $P < 0.05$, and I^2 of 79.01%) and high variability between studies (coefficient of variation of 0.9061). A significant and positive effect on accuracy was found overall for the robotic technique (0.6260, 95% CI = 0.1423–1.1097). Egger's test indicated no evidence of publication bias ($P = 0.7007$).

In the subgroup analysis of the 5 studies reporting the accuracy when using the MAXIO device and comparing the robotic and freehand techniques, the random-effects model demonstrated a significant and positive effect on overall accuracy in favor of the robotic technique (1.60, 95% CI = 0.42–2.77) (**Table 3**).

Euclidean Error

Five studies reported the Euclidean error when comparing both techniques. There was high heterogeneity among studies (Q-statistic (χ^2) value of 51.3554, $P < 0.05$, and I^2 of 92.21%), and high variability was identified between studies (coefficient of variation of 1.4541). The combined positive effect of the robotic approach was statistically significant; the random pooled effects model was used and showed an effect of 0.8189 (95% CI = −0.1020 to 1.7399). Egger's test indicated no evidence of publication bias ($P = 0.4115$).

DISCUSSION

The systematic review and meta-analysis has revealed evidence that robotic-assisted percutaneous liver ablation is superior to the freehand approach in terms of individual radiation (such as DLP), accuracy, and Euclidean error. However, these results should be interpreted with caution, as heterogeneity between studies leads to greater uncertainty regarding the magnitude and direction of the observed effects. Despite the superiority of robotic assistance for these technical intraprocedural criteria, follow-up is crucial to assess the efficacy of each technique. Although the number of studies reporting follow-up is limited, the clinical results are also in favor of robotic assistance. Furthermore, robotic assistance is promising to lead the way for future therapeutic strategies by enhancing the learning curve aiming at reduced inter-operator variability and increased accuracy of image-guided liver ablations.

In one systematic review and meta-analysis of liver ablation techniques, 34 studies were included that used laparoscopic and/or percutaneous approaches.[9] The comparison of their efficacy with the manual technique demonstrated a significant improvement in treatment accuracy with stereotactic and/or robotic guidance, achieving 94% efficacy and low complication rates. It is important to emphasize that the study pooled both minimally invasive techniques, including 6 studies with robotic guidance, whereas our analysis focuses exclusively on the comparison between the robotic approach and the manual technique.

To facilitate agreement on terminology, standardization, and comparability between studies, a summary of the relevant nomenclature is proposed in Table 1. Overall, the number of studies comparing both approaches was low, and further comparative studies are anticipated. Among the 33 studies included in the systematic review, the most frequently reported device was the MAXIO system, which has stereotactic spatial positioning and includes software that registers current images with preoperative images; visualizes and edits estimated ablation volumes, includes a respiratory gating system, and verifies applicator placement by adapting the procedure according to the image recordings.[48]

Many of the devices used were in the prototype stage (13/33; 39.4%), with a majority of studies (29/33; 87.9%) reporting devices in the IDEAL innovation stages 0 (preclinical) and I (first-in-human).[30] In this context, it comes as no surprise that most of the 24 different devices used had no autonomy (90.9% of studies) or low autonomy with continuous or discrete physician control. Another key point of the present study is to provide definitions and concepts focusing exclusively on the robotic approach.

In a minimally invasive setting, precise placement of an ablation applicator is challenging. This includes involuntary operator movements,[49,50] breathing movements,[18] complex lesion management (e.g., small lesions, deep location, poor visibility, proximity to adjacent organs, and anatomical changes in the liver), and imaging studies for guidance, such as CT or MRI. Although MRI shows greater precision and target orientation, its use is limited by the nonferromagnetic materials or sensors required.[51]

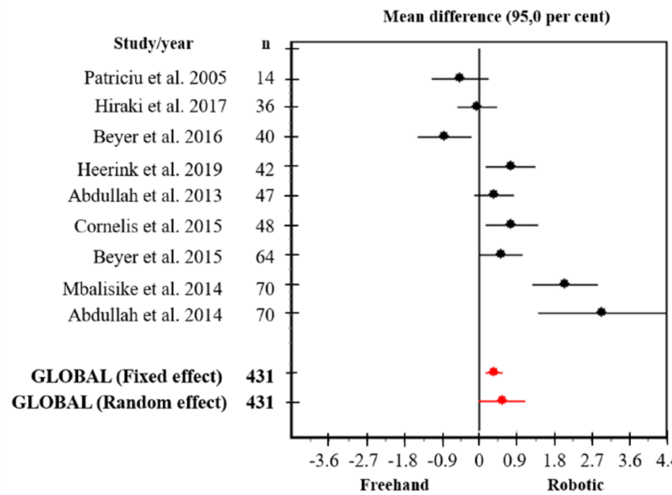
The applicator insertion techniques can be conventional (freehand technique, most widely used) and hybrid (navigation guidance system with or without a robotic arm). Most complex cases require experience to improve accuracy,[9,52] the freehand technique may increase the number of readjustments or repositionings and thus complication rates.[53] The aim of local control is to completely ablate the target with a sufficient safety halo (distance

TABLE 2.

s-analysis and Forest Plot Comparison of Freehand *versus* Robotic Targeting for Individual Radiation (Dose-length Product), Accuracy and Euclidean Error

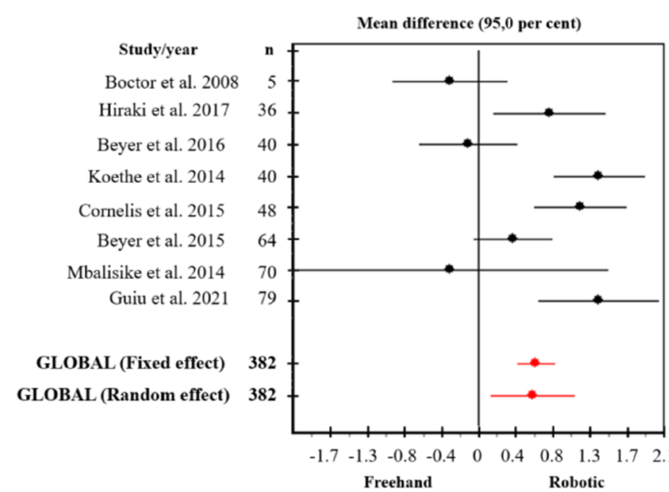
	Sample Size (n)	Effect Size (d)	CI (95%)	
DLP				
Patriciu et al, 2005[36]	14	−0.4406	−1.1018	0.2206
Abdullah et al, 2013[37]	47	0.3722	−0.1052	0.8496
Abdullah et al, 2014[38]	70	2.9318	1.4229	4.4407
Mbalisike et al, 2014[39]	70	2.0531	1.2866	2.8195
Beyer et al, 2015[40]	64	0.5402	0.0404	1.0400
Cornelis et al, 2015[41]	48	0.7828	0.1672	1.3985
Beyer et al, 2016[42]	40	−0.8075	−1.4365	−0.1784
Hiraki et al, 2017[43]	36	−0.0312	0.5046	0.4422
Heerink et al, 2019[8]	42	0.7679	0.1816	1.3542
Random effect	431	0.5582	0.0167	1.0996

Heterogeneity test (χ^2) = 55.5155; $P < 0.05$.
$I^2 = 85.58\%$.
Egger test = 1.5438; $P = 0.1666$.



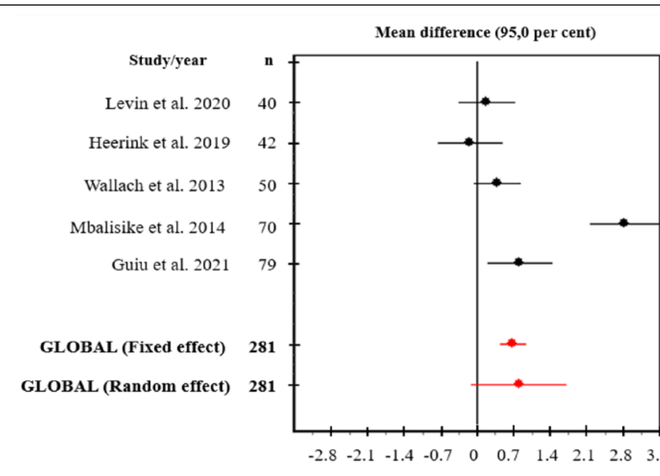
Accuracy	n	d	CI	(95%)
Boctor et al, 2008[44]	5	−0.3162	−0.9736	0.3412
Koethe et al, 2014[3]	40	1.3849	0.8589	1.9110
Mbalisike et al, 2014[39]	70	−0.3157	−2.1155	1.4842
Beyer et al, 2015[40]	64	0.4012	−0.0460	0.8484
Cornelis et al, 2015[41]	48	1.1740	0.6426	1.7054
Beyer et al, 2016[45]	40	−0.1131	−0.6794	0.4531
Hiraki et al, 2017[43]	36	0.8187	0.1727	1.4647
Guiu et al, 2021[35]	79	1.3796	0.6900	2.0691
Random effect	382	0.6260	0.1423	1.1097

Heterogeneity test (χ^2) = 33.3511; $P < 0.05$.
$I^2 = 79.01\%$.
Egger test = −0.4033; $P = 0.7007$.



Euclidean error	n	d	CI	(95%)
Wallach et al, 2013[46]	50	0.4012	−0.0406	0.8484
Mbalisike et al, 2014[39]	70	2.8445	2.1766	3.5124
Heerink et al, 2019[8]	42	−0.1219	−0.7423	0.4984
Levin et al, 2020[47]	40	0.1982	−0.3575	0.7540
Guiu et al, 2021[35]	79	0.8313	0.2009	1.4618
Random effect	281	0.8189	−0.1020	1.7399

Heterogeneity test (χ^2) = 51.3554; $P < 0.05$.
$I^2 = 92.21\%$.
Egger test = 0.9515; $P = 0.4115$.



between the tumor margin and the ablation volume surface). To compensate for the inaccuracy of the ablation applicator (which differs between 5 and 10 mm)[1,54] and the irregular shape of the tumors, the halo should measure 10 mm of safety margin during ablation; in contrast, during surgical resection, a safety margin of 1 mm is adequate in the absence of these limitations.

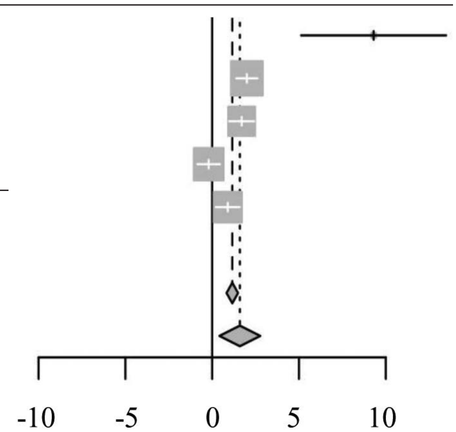
With tracking systems (optical, electromagnetic, and laser),[2,3,55] the information on location-position-orientation of

TABLE 3.

Subgroup Meta-analysis and Forest Plot Comparison of Freehand *versus* Robotic Targeting for Accuracy in Advance-stage Device (MAXIO)

	Freehand			Robotic (MAXIO)				
	Total	Mean	SD	Total	Mean	SD	Mean Difference	95% CI
Study				20	6.50	2.5000	9.30	(5.12–13.48)
Koethe et al, 2014[3]	20	15.80	–1.1018					
Mbalisike et al, 2014[39]	40	4.10	–0.1052	30	2.10	0.7000	2.00	(1.39–2.61)
Beyer et al, 2015[40]	30	3.30	1.4229	34	1.60	1.3000	1.70	(0.98–2.42)
Cornelis et al, 2015[41]	24	4.50	0.1672	24	4.70	1.1000	–0.20	(–0.85–0.45)
Beyer et al, 2016[45]	19	3.10	–1.4365	21	2.20	1.0000	0.90	(0.21–1.59)
Random effect							1.60	(0.42–2.77)

Mean Difference (MD)



Heterogeneity test (χ^2) = 1.4194; $P < 0.05$.
$I^2 = 90\%$.

applicator-placement increases the accuracy of target management, and robotic navigation systems have increased the technical success[9,55,56] in association with ablation modalities (RFA, MWA, Cryo, and IRE) in the liver, reducing morbidity and mortality when compared with resection.[57] Furthermore, elastic image fusion creates an image of the organ, updating itself according to the data acquired in real-time, improving the evaluation, interpretation, and accuracy of the images. However, as shown in the present analysis, elastic image fusion was not used in any of the studies, and its worldwide diffusion is limited, which is probably related to the high costs of software development and the requirement of hybrid operating rooms.[19,20]

The "accuracy" is determined by the length of a special vector between the center of the target and the tip of the needle, using X-Y-Z coordinates, relevant for the different error types (Table 1, Figure 2).[8,18,43,46] The most important criterion for clinical success of tumor treatment with ablation is complete tissue destruction with a safety margin halo, a concept that goes beyond the multiple definitions described in the literature (conceived as "complete ablation without residual tumor",[40] "primary efficacy",[54] "treatment success",[45] and "hit rate",[44]) associated to image control.[40,44,45,54] However, this binary criterion lacks precision and does not allow the identification of weaknesses in applicator positioning systems. To gain insight into failed cases, it is useful to assess the percentage of tumor inclusion within the ablation zone. Clinicians can segment targets and the ablation zone, while specific software can calculate intersections and volumes. Furthermore, it is important to differentiate the tumor volume in the central ablation zone, the margin, and the outer area as 3 relevant criteria for the final result. One publication specifies the concepts of ablation coverage and overablation,[4] based on the ablation volume in relation to the tumor volume. Finally, secondary criteria are essential to evaluate the procedure in general: the number of adjustments (readjustments,[37] repositionings,[8] and invasiveness[44]), the number of applicators used, and the intervention time in relation to tumor parameters. Geometric criteria are no longer based on the actual ablation volume, but on the geometric position of the applicator relative to the target.[8] These criteria are often proposed in the literature and consist of measuring and calculating distances and residual angles. However, they must be performed on medical control images, and navigation systems alone do not guarantee a sufficient correlation with the quality of the final result.

Estimating the distance from the applicator tip to the tumor barycenter (Euclidean distance,[8,52] applicator deflection[39]) could be equivalent to the volumetric criterion if the 2 volumes were isotropic (spherical), but this is not the case. Geometric methods do not consider the delivered power or the environment that influences the shape and size of the ablation zone. To be comparable, it would be necessary to contemplate the sphere enclosing the tumor and the minimum sphere enclosed in the ablation zone, which is very conservative and would minimize real effectiveness, but in the other case, the assessment of real results would be too optimistic.

Another criterion is the alignment of the applicator with the axis from the entry point to the center of the target. Ideally, this axis should be aligned with the longitudinal axis of the ellipsoid encompassing the tumor, so this criterion indicates the ability of the system to follow the ideal plan. It is used as an indicator of the overall ability of the system (mechanical, software, and human) to perform the procedure correctly; however, on its own, it is insufficient to assess the quality of the result due to possible lateral and longitudinal errors. Nevertheless, drawing reasonable conclusions from these criteria or creating a single score is challenging due to differences in units and mathematical relations between them. Thus, the ultimate oncologic effectiveness of tumor ablation and the decrease in the ablation margin of normal parenchyma around the tumor will be related to addressing these considerations, with the aim of achieving greater accuracy in real-world applications and improving oncologic outcomes, while minimizing the need for overablation.

In this systematic review, a few individual studies reported important concepts such as applicator positioning accuracy. One study[58] showed a mean accuracy of 3.5 mm in an in-vivo model with robotically inserted applicators, while others reported a range of 2.7–10.2 mm,[18,22,32,35] indicating that an acceptable target error should be less than 5 mm in a 10-mm lesion. Applicator specifications (quantity, angles, and readjustments) were explored in several studies. In a randomized controlled trial[8] the accuracy of freehand *versus* robotic technique was compared, and robotic guidance eliminated the repositioning need. In addition, for oblique (out-of-plane) targets, lateral accuracy improved from 16.1 to 5.6mm. A study[32] comparing the applicator type energy device (RFA-MWA-Cryo) found a significant difference in target motion during insertion, and accuracy varied between the type and sharpness of the applicator. Several factors can influence the accuracy, such as procedural models, where insertion of the applicator into the target may move in in-vivo models, caused by several factors, like

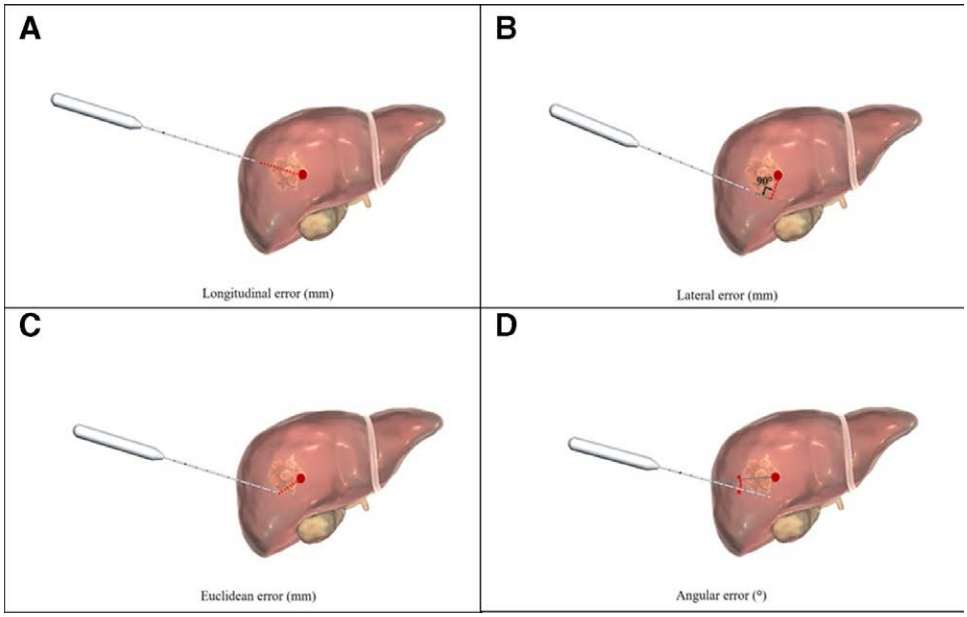


FIGURE 2. Classification of errors and their illustration. Red dot: Indicates the target needle tip position from which the deviating distances and angles are measured. Target needle tip: The position is not in the center of the lesion, as its location depends on the size of the lesion, the number of applicators used, the ablation area, and the desired safety halo to obtain a complete ablation. A, Longitudinal error, measured in millimeters. B, Lateral error, measured in millimeters. C, Euclidean error, measured in millimeters. D, Angular error, measured in degrees. This image represents a 2D environment; for oblique/out-of-plane targets, a 3D error measure is required.

respiratory movement, displacement, and deformation of the tissue during puncture. Precision can be improved when these procedures are performed under general anesthesia, allowing respiratory motion to be controlled by several techniques (temporary disconnection of the endotracheal tube and high-frequency jet ventilation).[43,55,59]

Error concepts[8,9] are fundamental to understanding the 3D space in which the targets are located. Regarding radiation exposure, most of the procedures were performed under CT guidance. One study,[22] compared the need for confirmatory CT scans after applicator placement between freehand (requiring 6–7 scans) and robotic assistance (requiring 1–2 scans).

The findings demonstrated the advantages of robotics over the freehand technique, as synthesized by the present meta-analysis.

Currently, percutaneous robotic approaches and navigation systems are based on optical tracking. EM tracking uses magnetic fields, with promising results in various surgical fields, such as flexible and ultrasound-guided endoscopy. However, its accuracy in percutaneous robotic arms has not yet been investigated. Advantages over optical tracking features (e.g., not susceptible to line-of-sight obstructions, and simultaneous tracking of multiple applicators) would improve surgical workflow and efficiency, especially for the multiapplicator approach. In training programs, the neurosurgical[58] domain has shown that the use of robotic devices with navigation considerably shortened the learning curve, and further studies are required to quantify the training effect in liver ablation therapies.

Although robotic percutaneous ablation is an emerging technique, the current data are in favor of the robotic approach. While this overall analysis of the literature is limited by still low cohort sizes and heterogeneity of study populations, more randomized comparative studies will provide stronger evidence. When considering that most of the devices used are prototypes and studies focused on the feasibility of their use, further studies on accuracy and recognition of the error types and models used as influencing factors are eagerly awaited.

The percentage of studies classified as high risk in the domains of patient selection and index test underscores potential limitations that may affect the validity of the results. Meanwhile, studies with low risk in the domains of reference standard and flow and timing suggest a more robust methodological approach in these aspects. Thus, applicability issues have to be anticipated in future study designs to ensure reproducibility in larger clinical cohorts and before potentially changing the current gold standard in favor of robotic assistance.

In conclusion, percutaneous robotic approaches enable a more precise management of liver tumors. In a minimally invasive setting, they decrease errors when compared with traditional techniques. Standardization of concepts and error reporting are necessary to ensure the comparability of results obtained with these systems. Error types are influenced by the study model (phantom, ex vivo or in-vivo model, static or dynamic model); the number and type of applicators, location of the target(s) (axial/in-plane or oblique/out-of-plane), the organ (respiratory motion of the liver), and the anesthesiologic management.

As a large number of devices are in a prototype stage, the present systematic review and meta-analysis can provide guidance for key points to address to enhance measurements and comparability of technical and future clinical results.

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Authors contribution

Conceptualization, formal analysis and writing—original draft preparation: A.K.U.R., B.S., M.E.G.; methodology A.K.U.R., B.S., L.G., M.E.G.; data curation and investigation: A.K.U.R., B.S., A.G.V.; writing—review and editing: A.K.U.R., B.S., L.G., A.G.V., D.M., M.E.G.; visualization: A.K.U.R., B.S.; supervision: D.M., M.E.G.; funding acquisition: A.K.U.R., B.S., D.M., M.E.G.. All authors have read and agreed to the final version of the article.

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