Systematic Review: Applications of Intraoperative Ultrasonography in Spinal Surgery

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■ BACKGROUND: **As a result of increased practicality and decreased costs and radiation, interest has increased in intraoperative ultrasonography (iUS) in spinal surgery applications; however, few studies have provided a robust overview of its use in spinal surgery. We synthesize findings of existing literature on use of iUS in navigation, pedicle screw placement, and identification of anatomy during spinal interventions.**

■ METHODS: **PRISMA guidelines were used in this systematic review. Studies were identified through PubMed, Scopus, and Google Scholar databases using the search string. Abstracts mentioning iUS in spine applications were included. On full-text review, exclusion criteria were implemented, including outdated studies or those with weak topic relevance or statistical power. On elimination of duplicates, multireviewer screening for eligibility, and citation search, 44 articles were analyzed.**

■ RESULTS: **Navigation using iUS is safe, effective, and economical. iUS registration accuracy and success are within clinically acceptable limits for image-guided navigation. Pedicle screw instrumentation with iUS is precise, with a favorable safety profile. Anatomic landmarks are reliably identified with iUS, and surgeons are overwhelmingly successful in neural or vascular tissue identification with iUS modalities, including standard B mode, Doppler, and contrast-enhanced ultrasonography. iUS use in traumatic reduction of fractures properly identifies anatomic structures, intervertebral disc space, and vasculature.**

■ CONCLUSIONS: **iUS eliminates radiation, decreases costs, and provides sufficient accuracy and reliability in identification of anatomic and neurovascular structures in various spinal surgery settings.**

INTRODUCTION

With advancements in spinal technology in recent years, image-guided surgery (IGS) has been increasingly used because of its impressive accuracy and safety profile in providing a three-dimensional (3D) multiplanar spatial visualization of spinal anatomy.[1-5] IGS is routinely performed by registration of preoperative imaging onto intraoperative modalities such as computed tomography (CT), fluoroscopy, magnetic resonance imaging (MRI), ultrasonography (US), or alternatively via co-use of C-arm fluoroscopy with computer-assisted navigation (CAN) to allow CT navigation without requiring surgeon-dependent patient registration.[2,6] IGS registration with preoperative imaging is often completed manually by identifying fiducial/anatomic landmarks on preoperative imaging (often CT or MRI) and the patient.[7] Intraoperative CT and MRI have been considered as the gold standard for image-guided spinal navigation because of their ability to rapidly visualize normal and pathologic anatomy and provide real-time surgical monitoring.[8,9] However, both modalities have setbacks. Both techniques come

Key words
- Intraoperative ultrasonography
- Navigation
- Spine surgery
- Systematic review

Abbreviations and Acronyms
3D: Three-dimensional
AI: Artificial intelligence
CAN: Computer-assisted navigation
CE-US: Contrast-enhanced ultrasonography
CT: Computed tomography
GI: Gastrointestinal
IGS: Image-guided surgery
iUS: intraoperative ultrasonography
IV: Intervertebral
LLIF: Lateral lumbar interbody fusion
MRI: Magnetic resonance imaging
PSI: Pedicle screw instrumentation
TRE: Target registration error
US: Ultrasonography

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with high costs and low availability, rendering it difficult for medical facilities to afford or accommodate them.[9] Furthermore, CT exposes patients to significant levels of radiation, whereas MRI is even costlier and ferromagnetically incompatible with many surgical instruments.[8] Intraoperative US (iUS) mitigates many of these concerns and thus provides a plausible alternative to traditional CT-based or MRI-based spinal navigation.[8-11] A major challenge in integration of iUS is its registration with preoperative imaging modalities (i.e., CT or MRI) of differing inherent properties.[12] In addition, iUS use is subject to a variety of challenges, including high user dependency, limited field of view, nonstrict image plane viewing, difficulty of identification because of varying echogenicity, and varying image quality because of its patient-dependent nature.[12] Nevertheless, iUS has been shown to reduce radiation exposure and minimize organ damage and represents a lower-cost, more convenient alternative to intraoperative CT-based or MRI-based navigation.[4,13] Because of these advantages, which allow for better safety and practicality, iUS has gained popularity in spinal intervention during recent decades.[11]

One spine discipline that has shown robust use of iUS is oncologic surgery.[14-16] Primary spinal tumors represent 4%—8% of all central nervous system tumors and can originate from the spinal cord, nerve roots, meninges, or cauda equina.[17] Tumors of the spine are generally classified into extradural, intradural extramedullary, and intradural intramedullary based on their origin.[17] Although the standard of care for spinal tumors is surgery, this carries a substantial risk for neurologic impairment, with up to 40% of patients undergoing intradural tumor interventions experiencing neurologic damage as a result of their operation.[17] This situation is likely caused by the difficult nature of detecting spinal tumors, especially within the spinal canal.[13] Iatrogenic trauma during tumor intervention can even lead to complications of vascular damage, cerebrospinal fluid leakage, or contamination.[18] iUS has been extensively studied in oncologic intervention and shown to mitigate such challenges. Prada et al.[16] showed that iUS can be used to identify many spinal lesions and aid in oncologic surgical planning via identification of bony landmarks, nerves, and vasculature close to the mass. Toktas et al.[13] determined that iUS was valuable in providing surgical orientation and minimizing iatrogenic spinal cord injury. iUS has shown adeptness in localization of both extramedullary and intramedullary tumors, including meningiomas, neurinomas, ependymomas, and schwannomas.[15,18,19]

A better understanding of regional anatomy via iUS can greatly improve the quality of pedicle screw instrumentation (PSI) during spinal surgery. Lou et al.[20] described the high precision of 3D iUS in vertebral pedicle localization during navigation surgery for scoliosis. Kantelhardt et al.[21,22] have reported multiple studies evaluating the efficacy of iUS for pedicle screw insertion (PSI) trajectory monitoring during lumbar and cervical interbody fusions. These investigators highlighted the high efficiency and accuracy of iUS in real-time tracking of PSI, suggesting that its use may significantly reduce postsurgical complications caused by inaccurate screw placement.

Variations of US have also been evaluated for use in neurovascular identification during spinal surgery. Standard B mode, Doppler, and contrast-enhanced iUS have shown remarkable promise in avoidance of iatrogenic vascular injury, which is a rare but potentially devastating consequence of spinal intervention.[23-27] Vascular complications have been reported in a wide breadth of spinal procedures, including cervical, thoracic, and lumbar fusions.[27] Lofrese et al.[23] reported on the ability of Doppler iUS to prevent vertebral artery injury during Goel and Harms C1-C2 posterior arthrodesis. Nojiri et al.[4] showed the usefulness of iUS in visualizing and preventing damage to vertebral and lumbar arteries during lateral fusion. Similar to vascular injury, intraoperative nerve damage poses a considerable threat to spine surgeons.[28-31] Although rare, several nerve-related complications may occur after spine procedures: nerve palsies, meralgia paresthetica, Parsonage-Turner syndrome, Horner syndrome, and other forms of somatic and sympathetic nerve injury-related consequences such as urinary retention.[30,32,33] Kutteruf et al.[31] further discovered permanent disabling nerve damage to be significantly more likely in spine versus nonspinal surgeries. Carson et al.[34] analyzed an artificial intelligence (AI)-based iUS approach and determined its ability to adequately identify neural structures within the psoas muscle, which can pose significant ramifications in lateral lumbar interbody fusion (LLIF) procedures. Wessel et al.[36] and Kimura et al.[35] reported ability of iUS to localize neural tissue in thoracic and cervical surgery for patients with disc herniation and stenosis, respectively. Wang et al.[37] concluded that iUS showed satisfactory results in monitoring circumferential decompression to potentially decrease levels required among patients with thoracic spinal stenosis.

These studies show that the usefulness of iUS has been investigated in a multitude of scenarios to test its various capabilities; however, if any major decision is to be made over implementation of iUS within spinal practices, an overall consensus must be established. This systematic review aims to compile and synthesize results from peer-reviewed studies evaluating iUS use in spinal surgery.

METHODS

Literature Search

In accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, this systematic review was performed by using the following 3 databases: PubMed, Scopus, and Google Scholar. With the help of Rush University Medical Center library personnel, we collected pertinent articles with key words/phrases listed in **Table 1**. Google Chrome was used for both database searches and our search strategy consisted of the following string: ((“spinal” or “spine”) AND (“ultrasound” or “ultrasonic” or “ultrasonography”or “sonography”) AND (“intraoperative”)). After our initial search, 2410 articles were identified and incorporated into the Covidence platform for removal of duplicates (1103), resulting in 1307 articles available for title/abstract screening (**Figure 1**). A total of 251 full-length reports were critically evaluated for determination of inclusion based on predefined inclusion and exclusion criteria.

Eligibility Criteria

Titles and abstracts were independently screened within the Covidence platform by 2 researchers with the following inclusion criteria: 1) full-text English article was accessible, 2) studies used

Table 1. Key Words/Phrases

Database Search String
[Spinal] OR [Spine] AND
[Ultrasound] OR [Ultrasonography] OR [Ultrasonic] OR [Sonography] AND
[Intraoperative]

either human participants, animal or cadaveric specimens, or phantom models, and 3) studies reported outcomes pertaining to iUS use in spinal procedures. Conversely, studies were excluded if they 1) were irrelevant to iUS use, 2) examined nonspinal interventions, or 3) were limited case reports and/or technical reports. After literature search and duplicate removal, potentially eligible studies were reviewed in full text by both researchers for final inclusion. Any disagreements about study inclusion were resolved by consensus between the 2 reviewers or consultation from the senior author. The 2 reviewers completed a quality assessment of all included studies using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria.[38] Screeners disagreed on the clinical applicability and topic relevance of 60 studies during the quality assessment process (10 studies in title/abstract screening, 50 studies in full-text screening). On discussion of the advantages and disadvantages of the methodology and findings of each study, a decision for inclusion versus exclusion was made. Investigators also manually reviewed references provided by included studies to identify an additional 7 pertinent articles for inclusion. On review of implemented inclusion and exclusion criteria, joint investigator screening, and incorporation of manually reviewed references, 44 relevant articles were selected for inclusion (Figure 1).

Data Extraction

All eligible articles were searched for descriptive or quantitative outcomes on the usefulness of iUS in various components of spinal surgery such as navigation, accuracy of registration, PSI, tumor identification, anatomic and neurovascular identification, and applicability in traumatic spinal disease. Eight authors independently abstracted relevant study data from the final pool of included articles into an electronic spreadsheet.

RESULTS

We aimed to evaluate the current status of the usefulness of iUS in spine surgery. We conducted a comprehensive search methodology using the search terms as provided in Table 1. The initial search criteria provided 2410 studies. After evaluation by 2 independent reviewers, 44 studies were selected to evaluate the effectiveness of iUS in navigation, registration accuracy, pedicle screw placement, tumor removal, identification of anatomic and neurovascular structures, and traumatic applications (Figure 1).

iUS-Based Navigation and iUS Registration Accuracy

We discovered many studies evaluating varying spinal diseases and procedures that reported success and validity for use of iUS in spinal navigation. iUS-based spinal navigation is safe and practical and offers many benefits compared with conventional modalities. In a systematic review by Gueziri et al.,[11] the use of iUS-guided navigation was found to offer promise in accuracy, robustness, reliability, and usability. Accuracy in iUS-based registration was determined to vary by target registration error (TRE) of 4.20–0.62 mm (vs. our findings of 4.20–0.3 mm) and showed gradual improvements over the past 2 decades on evaluation of animal and cadaver studies (Table 2).[11] Furthermore, during surgery, iUS-guided navigation allowed for swift acquisition of images, with minimal disruption to workflow.[11] Although this is a clear advantage in the usability of iUS, further studies of time effectiveness, iUS imaging quality, and the learning curve of iUS use are necessary.[11] In the present review, Lou et al.[20] studied phantom tissue for thoracic vertebrae and demonstrated an exceptional accuracy of 0.3 mm (Table 2). Using navigation concomitant with iUS, Velho et al.[41] was able to successfully distinguish border between benign and malignant tissues during tumor surgery, Tian et al.[43] successfully identified anatomic landmarks during thoracic ossification of the posterior longitudinal ligament; Ungi et al.[42] reported a 100.0% success rate in identification of anatomic structures with a registration accuracy of 1.28 mm; Dekomien et al.[39] reported an accuracy in registration of 0.68 mm using iUS on lumbar plastic phantom tissue; and Lerch et al.[40] successfully identified anatomic structures in lumbar decompression surgery (Tables 2 and 3). A separate study by Gueziri et al.[8] further showed superior accuracy and efficiency compared with conventional CT navigation. Success rates for iUS-based registration were predominantly satisfactory, with a range from 59.75% to 100.0% and most studies >80% (Table 2). Although registration computation time varied significantly because of variance in methodologies of definition/measurement, many studies indicated times <1 minute (Table 2). Because of varied modalities used for iUS registration, including CT, MRI, and augmented reality, different registration approaches used (5 feature-based; 6 image-based), along with varied tissue types studied (i.e., phantom, sheep, human, and porcine), more controlled research is needed with more patients to strengthen applicability of navigation and iUS registration in spinal surgery (Table 2). Studies focused on accuracy, robustness, reliability, and usability of navigation with iUS specifically in a clinical setting also remain in their infancy, showing the need for future studies comparing these validation metrics among different methods of navigation.[11]

PSI

A pedicle screw was successfully placed with iUS guidance in all 7 PSI studies included in Table 2 and all 4 PSI studies included in Table 3. Insertion was largely feasible, accurate, and complication free using iUS. Several studies using varied nonhuman tissues (sheep, porcine, and phantom), along with Chen et al.[44] using in vivo humans with 82 patients, have reported successful pedicle screw placement using US during spinal surgeries (Table 2).[7,20,42,44-47] Ma et al.[46] used an augmented reality–based navigation model using iUS for PSI and reported results within an acceptable threshold of clinically desired targeting accuracy, along with substantially decreased radiation exposure. Ungi et al.[41] used tracked snapshots on ultrasound of phantom lumbar spines and determined iUS-navigated PSI was accurate in locating registration anatomic

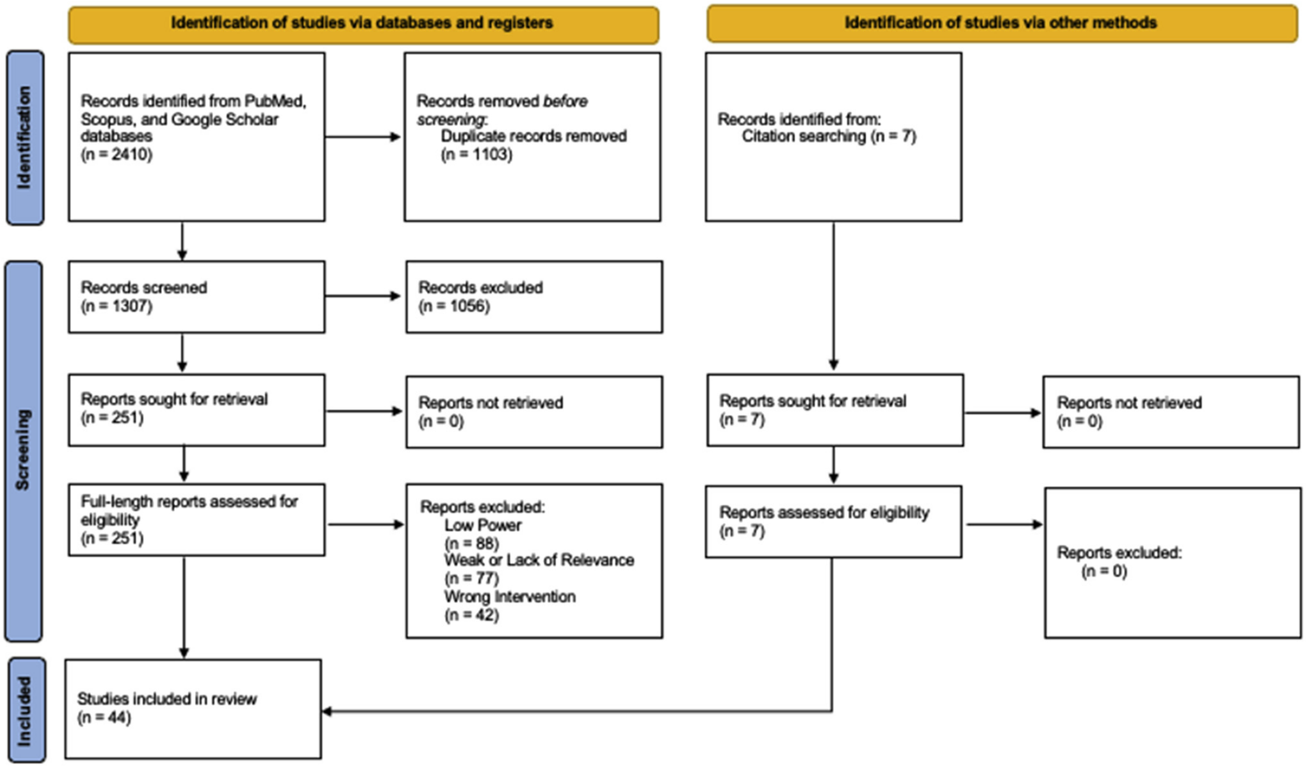

Figure 1. PRISMA flowchart on study selection.

markers. Schär et al.[49] and Seichi et al.[48] confirmed successful iUS-based PSI among patients with cervical myelopathy, whereas Tian et al.[43] and Lou et al.[20] successfully used iUS-based PSI in patients receiving thoracic surgery (Table 3).[20,43,48,49]

Tumor

All tumor studies ($n = 7$) adequately localized the lesion via iUS, which allowed for enhanced delineation of tumor borders, increased safety, reduced morbidity, and decreased costs (Table 3). B mode, Doppler, and contrast-enhanced iUS allowed for proper visualization of vasculature to help in tumor identification (Table 3). Ivanov et al.,[50] Moiyadi and Shetty[51] and Regelsberger et al.[52] confirmed successful intraoperative visualization of the surgical field using iUS for patients with spinal tumor (Table 3). Kaale et al.[9] showed adequate visualization of tumor borders and blood vessels using iUS among patients with cervical and thoracic tumor, along with Velho et al.,[41] who focused on intramedullary tumor surgery, while Han et al.[53] and Vetrano et al.[54] used contrast-enhanced US (CE-US) to accomplish this among patients with intramedullary spinal tumors (Table 3).

Anatomic/Neurovascular Identification

Intraoperative sonography allowed for robust identification of vertebral landmarks in all but 3 studies (33/36). Fourteen studies visualized the intervertebral (IV) disc space, 3 visualized muscle (of which 2 identified the psoas), and 1 reported identification of gastrointestinal (GI) organs (Table 3). All studies reporting on neural and vascular identification showed proficient capabilities with iUS ($n = 11$ and $n = 10$, respectively) (Table 3). Carson et al.[34] studied a porcine model to assess an AI-based method using Sonovision iUS (Sonovision, Letchworth Garden City, Hertfordshire, United Kingdom) during LLIF. This system identified neural structures, psoas tissue, and the vertebral body surface with satisfactory sensitivity and specificity, with a Dice coefficient score >80% among all tissue types detected. Nojiri et al.[4] used iUS with a transvaginal probe to identify vertebral landmarks, the IV disc space, psoas, GI organs, neural tissue, and vasculature. Wang et al.[37] identified anatomy and vasculature in detail during 360° circumferential decompression for patients with thoracic spinal stenosis, with iUS allowing for examination of dural sac pulsation and blood flow rate. Most studies reporting on whether or not anatomic structures could be identified with iUS showed successful identification, ranging from 96% to 100% (Table 3).

Trauma/Fracture

We identified 6 studies commenting on the use of iUS in patients with spinal fracture (Table 3). Intraoperative use of US showed clear visualization of anatomic landmarks, IV disc space, and

Table 2. Registration Accuracy

Reference	Imaging Modality	Tissue Type	Patients/ Trials	Level/Vertebrae	Accuracy (Target Registration Error) (mm)	Success Rate (%)	Registration Computation Time	Registration Approach	Pedicle Screws
Talib et al., 2011[45]	CT-3D US	Plastic phantom	1 Trial	L4	1.29		<1 second per computer frame	Feature-based	X
Chen et al., 2016[42]	CT-US	Human (in vivo)	82	L2-L4	2.3	82	—	Image-based	X
Ma et al., 2017[46]	AR CT-iUS	Sheep	8	Lumbar	2.41	—	—	Feature-based	X
Drouin et al., 2016[47]	AR-US	Porcine	3	Lumbar	1.65	82.50	—	Feature-based	X
Ungi et al., 2013[42]	CT-US	Plastic phantom	4	Lumbar	1.28	93.30	—	Image-based	X
Dekomien et al., 2012[39]	Magnetic resonance imaging US	Phantom	100	—	0.68		—	Image-based	—
Gueziri et al., 2021[8]	CT-US	Porcine Cadaver	120	—	1.42–1.58	65–70	9.04 ± 1.58 seconds	Feature-based	—
Gueziri et al., 2020[11]	Varied	Varied	53 studies	—	0.62–4.20	59.75–100	<1 second–43 minutes	Image-based	—
Gueziri et al., 2020[97]	CT to iUS	Porcine	—	Lumbar	1.47	100	<8 seconds	Image-based	—
Lou et al., 2021[20]	3D-US	Phantom	—	T2-T8 and T7-T11	0.3	—	18.9 ± 3.1 seconds	Feature-based	X
Yan et al., 2011[7]	US-CT	Porcine, Phantom	2	Lumbar	0.89–1.59	92.6–97.3	2 minutes	Image-based	X

CT, computed tomography; 3D, three-dimensional; US, ultrasonography; AR, augmented reality, iUS, intraoperative ultrasonography.

vasculature with standard and Doppler modalities used in fracture reductions of the cervical, thoracic, and lumbar spine (**Table 3**). Degreif and Wenda[55] and Lofrese et al.[23] used iUS with Doppler mode and successfully identified vertebral landmarks and vasculature among patients with spinal fracture. Vincent et al.[56] focused on patients with thoracic fracture using standard iUS and identified vertebral landmarks and IV disc space, whereas Lerch et al.[40] and Lazennec et al.[57] in addition identified neural tissue. Eismont et al.[58] included 23 patients with thoracic fracture using standard iUS and identified vertebral landmarks with 100% success.

DISCUSSION

Although use of iUS has been reported in existing spine literature to show ease of use, accuracy, and effectiveness for identification and monitoring of anatomic structures, research on this low-cost radiation-free imaging modality remains in its infancy.[11,19] The aim of our study is to address this shortcoming in the literature through the presentation of a systematic review examining iUS applications in navigation, registration accuracy, PSI, tumor delineation, anatomic identification, and trauma surgery.

Navigation

With spinal surgery becoming more sophisticated, intraoperative image-based guidance has become increasingly popular because of its exceptional accuracy and safety profile.[6] In spinal IGS, instruments are positioned and traced by superimposition onto preoperative CT scans, intraoperative fluoroscopic images, or using a method that integrates C-arm fluoroscopy with CAN, enabling navigation with intraoperative CT without requiring surgeon-directed registration.[2,6] The added component of CAN in IGS has allowed spine providers to optimize surgical strategy, reduce errors/enhance precision in intraoperative hardware insertion, and limit radiation exposure in the operating room.[5] Helm et al.[59] reported a success rate of 96.8% among 12,622 pedicle screw placements using navigation in IGS. Since the early 2000s, use of iUS has been increasingly introduced in disciplines of navigational spine intervention for anatomic and neurovascular localization during preprocedural anesthetic injections, spinal tumor operations, and cervical, thoracic, or lumbar fusions.[11,53,60,61] In addition, with the advent of AI and machine learning, US-specific algorithms have evolved that may complement existing IGS technology, increasing its safety profile and surgical applicability by enhancing detection, segmentation, and classification of the vulnerable tissue types frequently encountered in spinal surgery.[34] This AI-trained US is a logical extension of the previously well-established benefits of iUS.

When successfully implemented, iUS-based navigation has shown satisfactory accuracy, robustness, reliability, and usability according to a systematic review by Gueziri et al.[11] A separate study by the same authors[8] showed better accuracy and efficiency using iUS versus conventional CT-based navigation. In a study that reported on intradural tumor identification via iUS, Vasudeva et al.[62] noted that a distinguishing characteristic of iUS is that it is the only intraoperative navigation technology capable of providing an accurate real-time depiction of soft tissue anatomy throughout a spinal operation. Carson et al.[34] noted that AI-enhanced US was capable of identifying and localizing nerves in the lumbar plexus that other imaging modalities failed to recognize, theoretically enabling surgeons to avoid common anatomic pitfalls in procedures such as LLIF, but with broader uses. It can thus be concluded that existing evidence overwhelmingly supports the application of iUS in navigation during spinal surgery, during percutaneous pedicle screw placement, tumor resection, fusion, decompression, and numerous other interventions.[11,20,39-43]

Registration Accuracy

To successfully implement iUS in spinal navigation, the surgeon registers preoperative CT or MRI with iUS images.[11] This registration process is complex and must provide accurate and reliable results in an efficient timeline.[11] In our evaluation of iUS registration, accuracy was measured by root-mean-square TRE. TRE was determined as the distance from the coordinates of the CT reconstruction combined with iUS compared with targeting placement because certain degrees of inherent error may exist.[63] The clinically acceptable TRE cutoff used by studies to characterize registration success varied from 2 to 3 mm.[63] A systematic review by Gueziri et al.[11] reported an iUS registration accuracy range from 4.20 mm to 0.62 mm, with most values being below the accepted range of 2—3 mm. Compared with these previous results found by Gueziri et al., our accuracy range was as low as 0.3 mm with several studies reporting values <2 mm.[7,20,39] Nevertheless, most studies using iUS show clinically acceptable accuracy with a TRE within 2—3 mm, with which our findings align, justifying its continued use in spinal surgery.[8,11,39,42,44-47,63] Computation time to registration varied significantly among experiments, suggesting discrepancies in methodological designs and a need for uniform registration practices based solely on studies with human participants. Still, several investigators reported times <1 minute, showing potential for acceptable feasibility and efficiency for iUS-based registration.[8,11,20,46,63] Our overall findings suggest excellent potential for iUS-based registration in applications of spinal navigation. We hope that our favorable results compel researchers and spine surgeons worldwide to develop a standardized protocol for evaluating and implementing iUS registration, characterizing the next step toward more appropriately assessing its effectiveness in a clinical setting.

There are 2 well-accepted methodologies to registration: feature based and image based.[11] Feature-based registration using point-based or surface-based concepts involves capturing multiple spatial point locations among preoperative CT/MRI and iUS images from the following regions: spinous apical processes, laminae, posterior transverse and inferior articular processes, and posterior vertebral surfaces. Landmark-based feature-based registration is used more when 2 congruent regions are known on both imaging devices.[11] Image-based registration uses the following shared similar metrics pertaining to image intensity to register preoperative and intraoperative films accurately: sum of squared differences and cross-correlation for monomodal image registration and mutual or gradient information in multimodal image registration.[11] Although both registration techniques may be used, there are complex advantages and disadvantages to each based on factors such as surgeon skill in interpreting US and capacity to acquire shared corresponding points among preoperative and intraoperative images.[11] Nevertheless, our review indicates acceptable registration accuracy among both techniques among studies included (**Table 2**). Future clinical research on in-field human application of both feature-based and image-based approaches should be pursued to further explore benefits and drawbacks of each registration approach.

PSI

Many spinal surgeries require vertebral stabilization via pedicle screw implantation. The widespread use of pedicle screws necessitated enhanced navigation modalities to avoid disturbing the surrounding anatomy.[44] Previous tissue-sparing techniques relied on time-intensive preoperative CT. However, novel methods to create CT-to-patient mapping from iUS acquisition followed by iUS-CT registration have shown promise as a means of safely expediting surgical navigation.[44] A recent systematic review and meta-analysis by Lener et al.[64] reported the widespread use of the following techniques among transforaminal lumbar interbody fusion surgeons: paramedian incisions, tubular retractors for complete facetectomy, decompression, and intraoperative imaging for percutaneous implantation of the pedicle screw. Numerous separate studies have reported on the practice of unilateral or bilateral percutaneous PSI during fusion procedures, with literature reporting an acceptable efficacy and safety profile of this technique with no additional adverse influence on fusion rate, functional recovery, or infection risk.[5,65-73] In a retrospective cohort study by Chen et al.,[65] percutaneous PSI advantageously reduced operative blood loss. It also improved early postoperative pain to a significantly greater extent compared with non—minimally invasive surgery anterior debridement and interbody fusion with open posterior PSI and percutaneous PSI and transforaminal lumbar interbody fusion with open posterior PSI. Most surgeons who use percutaneous PSI (representing 79% of 75 included studies in the report by Lener et al.) use standard fluoroscopy for intraoperative imaging.[64] Surgeons seldom report use of more advanced imaging technologies of 3D fluoroscopy or intraoperative CT with CAN.[64] Although the literature has assessed use of iUS in spine intervention, iUS is similarly rarely used for open or percutaneous PSI in a clinical setting, perhaps because of the lack of standardized methods for evaluation of accuracy, robustness, reliability, and usability of intraoperative CT/MRI-to-iUS registration.[11] In our comprehensive review, we examined 11 studies using iUS for PSI, all of which reported favorable results with no complications. Lou et al.[20] assessed intraoperative 3D US use in pedicle screw placement for patients with severe adolescent idiopathic scoliosis. These investigators concluded high precision, feasibility, and repeatability with sonography based navigation during PSI. Ungi et al.[42] compiled pedicle screw plans from tracked US snapshots into an intraoperative coordinate system based on anatomic landmarks. These investigators reported an error of <1.28 ± 1.37 mm across all directions and an angle difference <1.92° ± 1.95° per all axes relative to CT-based positions of intended pedicle screw location. Tian et al.[43] similarly successfully used iUS with 3D navigation for successful insertion of pedicle screws. Several

Table 3. Anatomic and Neurovascular Identification

Reference	Tissue Type	Patient/ Trials	Imaging Modality	Disease	Vertebral Level	Vertebral Landmarks	Intervertebral Disc space	Muscle	Gastrointestinal Organs	Nervous Tissue	Tumor	Vasculature	Lesions	Intraoperative Surgical Outcome Measure by US	Pedicle Screw	Positive US ID of Anatomic Structures (%)
Carson et al., 2020[34]	Porcine	50	SonoVision, Tissue Differentiation Intelligence	—	Lumbar	X	X	Psoas	—	X	—	X	—	—	—	100.00
Degreif and Wenda, 1998[55]	Human	60	US, Doppler mode	Fracture	Multiple	X	—	—	—	—	—	X	—	Intraoperative surgical field visualization	—	100
Nojiri et al., 2019[4]	Human	100	Transvaginal probe	Multiple	Multiple	X	X	Psoas	X	X		X	—	Intraoperative surgical field visualization	—	100
Ungi et al., 2013[42]	Human	10	US	—	Multiple	X	—	—	—	—	—	—	—	Intraoperative surgical field visualization	X	100
Moiyadi and Shetty, 2011[51]	Human	8	iUS	Tumor	Multiple	X	—	—	—	—	X	—	100%	Intraoperative surgical field visualization	—	96
Tian et al., 2013[43]	Human	18	iUS	Thoracic ossification of the posterior longitudinal ligament	Thoracic	X	—	—	—	—	—	—	—	Intraoperative surgical field visualization	X	X
Seichi et al., 2010[48]	Human	40	iUS	Cervical ossification of the posterior longitudinal ligament	Cervical	X	—	—	—	—	—	—	—	Evaluation of posterior shift of spinal cord after decompression	X	X
Velho et al., 2020[41]	Human	1250	iUS, CT, MRI	Lesions	Multiple	X	—	—	—	—	X	X	—	Delimitation of border between health and tumor tissues	—	X
Schär et al., 2019[49]	Human	3	iUS	Degenerative cervical myelopathy	Cervical	X	X	—	—	X	—	—	—	Evaluation of of posterior shift of spinal cord after decompression	X	X
Regelsberger et al., 2005[52]	Human	78	iUS	Tumor	Cervical, thoracic	X	—	X	—	—	X	—	—	Intraoperative surgical field visualization	—	X
Vetrano et al., 2021[54]	Human	12	CE-US	Tumor	Multiple	X	—	—	—	—	X	X	—	Intraoperative surgical field visualization	—	X
Pollard and Little, 2002[85]	Human	15	Duplex US	Degenerative cervical myelopathy	Cervical	X	—	—	—	—	—	—	—	—	—	—
Vincent et al., 1989[56]	Human	31	iUS	Vertebral Fractures	Thoracic	X	X	—	—	—	—	—	—	Analysis of spinal canal compromise against CT imaging	—	X

US, ultrasonography; iUS, intraoperative ultrasonography; CT, computed tomography; MRI, magnetic resonance imaging; CE-US, contrast-enhanced ultrasonography.

Continues

Table 3. Continued

Reference	Tissue Type	Patient/ Trials	Imaging Modality	Disease	Vertebral Level	Vertebral Landmarks	Intervertebral Disc space	Muscle	Gastrointestinal Organs	Nervous Tissue	Tumor	Vasculature	Lesions	Intraoperative Surgical Outcome Measure by US	Pedicle Screw	Positive US ID of Anatomic Structures (%)
Nishimura et al., 2014[86]	Human	16	iUS	Thoracic disc herniations	T2-3 to T12-L1	X	X	—	—	—	—	—	—	Intraoperative surgical field visualization	—	X
Naruse et al., 2009[87]	Human	101	iUS, MRI	Cervical myelopathy	C2-C7	—	—	—	—	—	—	—	—	Prediction of clinical outcome against MRI	—	X
Wang et al., 2011[37]	Human	13	iUS, MRI, CT	Thoracic spinal stenosis	Thoracic	X	X	—	—	—	—	X	—	Real-time analysis of spinal cord, dural sac pulsation, blood flow rate	—	X
Moses et al., 2010[88]	Human	24	iUS	Cervical spondylotic myelopathy and ossified posterior longitudinal ligament	Cervical	X	—	—	—	—	—	X	—	Correlation of iUS with postoperative CT imaging	—	X
Wei et al., 201[89]	Human	30	iUS	Cervical compressive myelopathy	Cervical	X	X	—	—	—	—	—	—	Spinal cord decompression analysis	—	X
Mihara et al., 2007[90]	Human	80	iUS	Cervical compressive myelopathy	Cervical	X	X	—	—	—	—	—	—	Spinal cord decompression analysis	—	X
Matsuyama et al., 2004[91]	Human	44	iUS, MRI	Cervical myelopathy	Cervical	X	X	—	—	—	—	—	—	Spinal cord decompression analysis	—	X
Wessell et al., 2019[36]	Human	10	iUS	Thoracic disc herniation	Thoracic	X	X	—	—	X	—	—	—	Intraoperative surgical field visualization	—	X
Löhr et al., 2005[92]	Human	27	iUS	Tumor	Lumbar	—	—	—	—	—	—	—	—	Identify hidden inflammatory masses	—	—
Winter et al., 2002[93]	Human		Three-dimensional US	—	Lumbar	X	—	—	—	—	—	—	—	Analysis of iUS from CT imaging	—	X
Lofrese et al., 2019[23]	Human	33	iUS Doppler	Vertebral fractures	Cervical	X	X	—	—	—	—	X	—	Analysis of mismatch error corrected by iUS	—	X
Lerch et al., 2002[40]	Human	22	iUS, CT	Retropulsed bony stenosis	—	X	X	—	—	X	—	—	—	iUS is an important tool to monitor the restoration of the spinal canal and decompression of the spinal cord in case of fracture	—	X
Lazennec et al., 1998[57]	Human	46	iUS	Fracture	Thoracic	X	X	—	—	X	—	—	—	Comparison of iUS and myelography	—	—
Kimura et al., 2012[94]	Human	85	iUS	Stenosis	Cervical	X	—	—	—	X	—	—	—	The recent development of high-resolution iUS allows real-time visualization of intraspinal abnormalities without dissection of the dura mater	—	—

Yan et al., 2011[7]	Porcine, phantom	—	US-CT	—	Lumbar	—	—	—	—	—	—	—	—	—	—	100
Jiang et al., 2012[95]	Human	10	iUS	Tumor	Thoracic	X	X	—	—	X	—	—	—	Visualization of the spinal cord	—	X
Ivanov et al., 2017[50]	Human	158	iUS	Tumor	Multiple	—	—	—	—	X	X	X	X	Intraoperative surgical field visualization	—	100
Han et al., 2020[53]	Human	14	CE-US	Tumor	Multiple	X	—	—	—	—	X	X	X	Delimitation of border between health and tumor tissues	—	100
Gao et al., 2020[96]	Human	24	iUS	Thoracic myelopathy	Thoracic	X	—	—	—	X	—	—	—	—	—	X
Eismont et al., 1984[58]	Human	23	iUS	Fracture	Thoracic, Lumbar	X	—	—	—	—	—	—	—	iUS correspondence with preoperative CT	—	100
Della Pepa et al., 2020[60]	Human	3	iUS, CE-US	Tumor, arteriovenous fistula	—	X	—	—	—	—	—	X	—	Intraoperative visualization tumor borders and vasculature	—	X
Chryssikos et al., 2021[81]	Human	3	iUS	Sagittal misalignment	Multiple	X	—	—	—	X	—	—	—	Confirm ventral decompression	—	—
Kaale et al., 2021[9]	—	7	iUS	Tumor	Cervical, thoracic	X	—	—	—	—	X	—	—	Intraoperative visualization tumor borders and vasculature	—	—

US, ultrasonography; iUS, intraoperative ultrasonography; CT, computed tomography; MRI, magnetic resonance imaging; CE-US, contrast-enhanced ultrasonography.

other studies have cited clinically acceptable TRE and success rates >80.0% in screw insertion.[44,46,47] Although further studies reporting comparisons in CT-guided versus iUS-guided PSI are needed, compiled evidence supports the ability of intraoperative sonography in correct pedicle screw placement.

Tumor

The recent adoption of iUS in spine surgery has seen manifold applications, ranging from aiding in the avoidance of key anatomic structures during approach to helping surgeons more accurately delineate and excise high-risk tumors, all of which translate to better patient outcomes.[41,52,54,62] Thus far, studies have documented the use of iUS in a wide range of intramedullary and extramedullary spinal cord tumors and lesions, including pilocytic astrocytomas, anaplastic astrocytomas, glioblastomas, subependymomas, ependymomas, hemangioblastomas, neurocytomas, and posttraumatic cysts.[54] All included oncologic studies reported successful identification of tumors ($n = 7$), with clear US visualization approaching 96%.[51] Velho et al.[41] performed a review including 1250 patients and reported successful delineation between healthy and tumor tissue. These investigators concluded iUS to be practical, economical, and efficient with reduced exploration and surgical time. Han et al.[53] commented on the reduction of invasiveness, delineation of tumor margins, and representation of perfusion features with intraoperative CE-US use. Vetrano et al.[54] further showed proficient vascular visualization using intraoperative CE-US. Regelsberger et al.[52] reported that iUS may decrease procedure-induced morbidity and concluded that it should be used as standard of care in surgical patients at high risk for adverse events.

iUS enables surgeons to identify tumor location and render apparent the vascular supply of the tumor and surrounding spinal cord without the limitation of image distortion caused by lesion-induced swelling.[54] This mapping of regional anatomy facilitates real-time visualization of deep-seated soft tissue structures that would otherwise require extensive dissection.[54,62] For example, Vetrano et al.[54] performed intraoperative CE-US in 12 patients with poorly defined boundaries or peritumoral cysts at preliminary intraoperative B-mode US and discovered that CE-US identified each patient's tumor. Many studies have reported the usefulness of iUS and intraoperative CE-US in determining tumor borders, minimizing the degree of dural opening and myelotomy, and identifying and protecting vasculature, resulting in decreased invasiveness and increased postoperative neurologic recovery.[53]

Used in conjunction with preexisting imaging technologies such as MRI and CT, iUS offers the capability of enhancing a surgeon's real-time anatomic assessment and minimizing the amount of patient exposure to ionizing radiation.[62] Given that imaging technology such as CT and MRI is necessary for the proper excision of a tumor, the lower radiation profile and thus carcinogenicity of iUS complements these modalities by decreasing the extent to which they must be used.[62] In keeping with the ability of iUS to identify soft tissue structures, in-field sonography has also been shown to be sensitive in delineating differences between solid or necrotic tumors and cystic areas.[41] Identifying between tumor and healthy tissue with iUS enables surgeons to decrease the likelihood of recurrence via more exact resection, yielding superior clinical results. Despite iUS remaining the only true real-time intraoperative imaging modality for soft tissue and its low-cost, high-availability perks, the image quality remains inferior to intraoperative MRI or high-quality CT.[41,62] Other obstacles in iUS for tumor removal that need to be overcome are a steep learning curve, lack of ease in maneuverability, slower interpretation of images on the US screen, and intraoperative bleeding and metal instruments distorting image quality.[41,54]

Anatomic and Neurovascular Identification

Conventional intraoperative spinal imaging includes radiography and C-arm fluoroscopic films. In addition, modern advancements have led to CT/MRI, 3D fluoroscopy, and cone-beam CT; cone-beam CT allows for greater neurovascular and anatomic accuracy and improved safety with decreased radiation.[74] For instance, cone-beam CT image reconstruction can be carried out in all planes near real time and offers greater anatomic clarity than do standard intraoperative imaging modalities.[74] Intraoperative CT combined with 3D CAN reduces reliance on K-wires, thereby reducing the risk of vascular damage secondary to misplacement of K-wires.[75] Furthermore, intraoperative use of O-arm CT has continued to improve surgical techniques, leading to improved postoperative outcomes such as decreased length of stay and decreased reoperation rates as a measure of long-term success.[76] The medical community has embraced the benefits that improved imaging allows; however, exposure to any radiation for the patient and the surgical team is a considerable drawback.[76] In addition, Gill et al[77] found an increase in operative time as a result of staff leaving the operative room to avoid radiation exposure and the hassle of correctly positioning imaging hardware.

Many practitioners turn to increased use of US to avoid radiation exposure and bulky imaging equipment, because other areas of spinal care have adopted use of iUS with great success. For instance, ultrasound-guided needle placement for epidurals, facet injections, and spinal tumor resection have proved advantageous as accuracy measures have significantly improved.[77,78] In the early 2000s, Furness et al.[79] found iUS to be useful in locating the IV space in the lumbar region, with correct identification just more than 60% of the time. Advancements in iUS software have since improved in vertebral identification with Nojiri et al.,[4] Ivanov et al.,[50] Han et al.,[53] and Ungi et al.[42] reporting 100% identification rates in identifying bony features, nervous tissue, tumors, and vasculature intraoperatively. All but 3 of 36 studies included in **Table 3** reported visualization of vertebral landmarks, whereas 14 visualized IV disc space, 3 visualized muscle (of which 2 identified the psoas), and 1 reported identification of GI organs. Advancing imaging technology with iUS is capable of improving surgical visualization and advancing open and minimally invasive procedures without added risk of harming patients or team members.[80] Although the benefits of integrating AI-enhanced US intraoperative imaging in spinal surgery are yet to be fully understood, a study by Carson et al.[34] shows how this technology is poised to revolutionize, augment, or replace commonly used imaging techniques for spinal procedures. Machine learning, which is being harnessed by companies such as Sonovision (Tissue Differentiation Intelligence, Delray Beach, Florida, USA), has the potential to decrease the navigation and anatomic identification burdens placed on both nascent and experienced spine surgeons, as shown by the ability of their AI-iUS to differentiate nerve, psoas muscle, vertebral body surface, and disc space with high sensitivity and specificity. This high sensitivity and specificity act as parameters for the stability of the algorithm. In alignment with the manner in which surgeons refine operative skills with repeated exposure to a surgical method, these algorithms use deep learning to heighten their discernment of both normal and aberrant anatomy, paving the way for patient relief in those struggling with complicated spinal disease. Carson et al.[34] contend that, with the aid of AI-enhanced US using Doppler color mode, spatial relationships between surgical instruments and vascular structures can be established in real time, circumventing unnecessary vascular and neural complications that not only affect patient quality of life but may increase health care costs. All of these advances may allow surgical specialists to identify targeted landmarks more accurately, enhancing surgical precision and results.[41] Our study summarizes the recent developments in intraoperative imaging and provides a foundation on which more information can be gathered to further this field of study.

iUS was shown to be proficient in all studies reporting on neural identification ($n = 11$). Carson et al.[34] found iUS with a transvaginal probe to effectively locate nervous tissue, the psoas muscle, vertebral body surface, disc space, and vascular structures in the lumbar region. This study further reported Dice identification scores >90% in bone, 85% in muscle, and 80% in nervous tissue; however, no data were provided for Dice identification in vasculature. Schär et al.[49] concluded that routine use of iUS in cervical decompression surgery could prevent neural element compression and benefit postoperative outcomes. Chryssikos et al.[81] similarly reported that iUS can be useful in neuromonitoring across cervical, thoracic, and lumbar vertebrae to avoid neural compromise. Lazennec et al.[57] compared iUS with intraoperative myelography in identification of neural tissue during thoracic fracture reduction surgery and reported better results with the former modality. Kimura et al.[35] discovered iUS adequately localized nerve tissue advantageously without dissection of dura. Ivanov et al.[50] identified tumors and vasculature along with nervous tissue and reported a fast learning curve for iUS with improved surgical accuracy and decreased procedure-related morbidity. The task of avoiding chronic morbidity, pain, and loss of function caused by iatrogenic nerve damage is challenging during open and even more so in minimal access procedures, with the limited visual field of a smaller incision.[82] Use of iUS allows surgeons to visualize what can no longer be seen in the operative field, sparing adverse iatrogenic events and positioning patients for improved short-term and long-term outcomes.

Similarly, all 10 studies observing vasculature reported successful identification with iUS.[83,84] During an approach for LLIF passing through the psoas, Carson et al.[34] used transvaginal iUS to avoid psoas or neural compression and identified pertinent blood vessel flow in the insertion pathway using the Sonovision Doppler color mode. The study using the Doppler color mode by Nojiri et al.[4] took advantage of US assistance in avoiding GI organs and neurovasculature complications during various approaches of lumbar fusions. Nojiri et al.[4] and Ungi et al.[42] highlighted that intraoperative use of US could correctly identify nerves exiting the spinal cord along with specific lumbar arteries and the anterior spinal artery in the operative field to avoid damage to such structures. Beyond simply identifying vasculature in the operative field, Wang et al.[37] used US to observe the flow rate of blood and cerebrospinal fluid intraoperatively. Furthermore, numerous investigators have highlighted the simplicity and ease of use in vascular intraoperative identification, making it an invaluable tool to shorten a steep learning curve in spinal surgery and improve patient outcomes.[72,74] Reduction procedures for vertebral fractures also used iUS, which successfully identified blood vessels using Doppler US.[23] CE-US has also been used by several studies to determine tumor perfusion characteristics.[53,54,60] Lofrese et al.[23] reported on the likely potential of Doppler iUS in reducing risk of vertebral artery injury during Goel and Harms C1—C2 posterior fusion (**Table 3**). Our findings show that the use of iUS can allow for reliable and robust in-field identification of neighboring structures of neurovasculature in a variety of spine surgery applications to protect patients from vessel injury.

Trauma/Fracture

In response to the ability of iUS for rapid, real-time monitoring of surgical procedures, it has also been considered for spinal trauma. All studies within our report identified vertebral landmarks using iUS during spinal trauma surgery, and 3 studies located the IV disk space and 2 successfully identified blood vessels using iUS. These results show promise in use of iUS for monitoring and anatomic identification of structures during spinal fracture and trauma surgery. Lofrese et al.[23] found use in Doppler iUS during realignment of fractured thoracolumbar vertebrae, with high repeatability and ease of use and 100% success rates in identifying patients' anatomic structures and blood vessels. These investigators showed usefulness of iUS Doppler in providing information on blood flow velocity and preventing neurologic complications and vertebral artery injury, an adverse event that can occur after Goel and Harms C1-C2 posterior arthrodesis. Lerch et al.[40] evaluated iUS-based decompression among patients with trauma-induced spinal stenosis and showed that iUS provided important additional real-time insight in monitoring surgical repair and decompression of the stenosed cord after fracture. Vincent et al.[56] reported that iUS monitoring during reduction of thoracolumbar burst fractures showed favorable accuracy and safety, with no complications postoperatively. Lazennec et al.[57] also used iUS for patients with thoracolumbar fracture and highlighted its superiority compared with intraoperative myelography, commenting on the continued necessity of intraoperative radiography and precise CT scans, especially for complex surgeries. Degreif and Wenda[55] studied 116 spinal fractures and concluded iUS to be feasible with an advantage of ease of repeatability during posterior-based restoration of the spinal canal. These investigators further concluded iUS as a suitable monitoring system for fracture surgery and in addition mentioned its use in intraoperative visualization of the anterior spinal artery. Eismont et al.[58] studied iUS use in Harrington rod reduction and fusion surgeries and stated the potential for increased safety and effectiveness during reduction and posterolateral decompression of fractures using iUS. These studies highlight the general consensus that iUS is a safe and accurate neuronavigation method in evaluating reductions of cervical and thoracic burst fractures.[23,56-58] The literature has thus repeatedly shown considerable potential in use of iUS during both elective and emergency spinal procedures. However, because many spinal fracture and trauma studies using iUS date to the 1900s, more recent research in its usefulness is essential to determine if this intraoperative imaging modality may provide substantial clinical benefits to surgeons and patients alike.

Limitations

There are several limitations to this systematic review. Many studies provide qualitative outcomes, with no objective measure. This limitation may contribute significant variability and subjectivity in results because of lack of standardization in outcomes. Furthermore, several studies were excluded from review because of limitations posed in journals; however, these studies could have provided meaningful results. Eliminating those studies from review may have added skew to the overall conclusions of this study. Although studies generally report favorable results of iUS, few studies identified in this review directly compared qualitative and/or quantitative outcomes among other imaging modalities. This factor limits the external validity and generalizability of recommending use of iUS over conventional methods for spinal navigation and identification of anatomic structures. Only 3 total databases were used with a set search string, which may have eliminated relevant studies, potentially contributing selection bias to our conclusions.

CONCLUSIONS

The present systematic review shows the capability of iUS to safely and feasibly navigate spinal operations and identify bony anatomic landmarks, surrounding organs, IV disc space, muscle, nerves, and vasculature. iUS shows accuracy in registration for navigation and PSI. Its ability to identify anatomic and neurovascular structures is widely accepted in spinal oncologic surgery but extends to various types of spinal procedures, including fusions, decompressions, and fracture reductions. Because US provides more practicality, usability, and a decreased financial and radiation burden than does traditional IGS, a shift toward iUS use is warranted. Still, further comparative studies on its benefits and limitations versus conventional intraoperative imaging are necessary.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Madhav R. Patel: Conceptualization, Methodology, Visualization, Formal analysis, Software, Investigation, Writing — original draft, Writing — review & editing. **Kevin C. Jacob:** Conceptualization, Methodology, Visualization, Formal analysis, Software, Investigation, Writing — original draft, Writing — review & editing. **Alexander W. Parsons:** Writing — original draft, Writing — review & editing, Data curation, Writing — review & editing. **Frank A.**

Chavez: Writing — original draft, Writing — review & editing, Data curation, Writing — review & editing. **Max A. Ribot:** Writing — original draft, Writing — review & editing, Data curation, Writing — review & editing. **Mohammed A. Munim:** Writing — original draft, Writing — review & editing, Data curation, Writing — review & editing. **Nisheka N. Vanjani:** Project administration, Data curation, Investigation, Writing — review & editing. **Hanna Pawlowski:** Project administration, Data curation, Investigation, Writing — review & editing. **Michael C. Prabhu:** Project administration, Data curation, Investigation, Writing — review & editing. **Kern Singh:** Conceptualization, Methodology, Supervision, Resources, Investigation, Writing — review & editing, Final Approval.

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