Three-dimensional Printed Drill Guides Versus Fluoroscopic-guided Freehand Technique for Pedicle Screw Placement

A Systematic Review and Meta-analysis of Radiographic, Operative, and Clinical Outcomes

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Study Design: A systematic review and meta-analysis.

Objective: The objective of this study was to compare surgical, clinical, and radiographic outcomes of 3-dimensional printed (3DP) drill guides to the fluoroscopic-guided, freehand placement of pedicle screws in the spine.

Summary of Background Data: 3DP is a budding technology in spine surgery and has recently been applied to patient-specific drill guides for pedicle screw placement. Several authors have reported the benefits of these drill guides, but no clear consensus exists on their utility.

Materials and Methods: A comprehensive search of the literature was conducted and independent reviewers assessed eligibility for included studies. Outcomes analyzed included: total operation time, estimated blood loss, screw accuracy, pain score, Japanese Orthopedic Association score, and postoperative complications. Weighted mean differences (WMD) and weighted risk differences were calculated using a random-effects model.

Results: Six studies with a total of 205 patients were included. There were significantly lower operation times [$\mathrm{WMD} = -32.32$ min, 95% confidence interval $(\mathrm{CI}) = -53.19$ to -11.45] and estimated blood loss ($\mathrm{WMD} = -51.42$ mL, 95% $\mathrm{CI} = -81.12$ to -21.72) in procedures performed with 3DP drill guides as compared with freehand technique. The probability of "excellent" screw placement was significantly higher in 3DP guides versus freehand (weighted risk difference $= -0.12$, 95% $\mathrm{CI} = -0.17$ to 0.07); however, no differences were observed in "poor" or "good" screw placement. There were no significant differences between groups in pain scores or Japanese Orthopedic Association scores. No difference in the rate of surgical complications was noted between the groups.

Conclusions: Pedicle screws placed with 3DP drill guides may result in shorter operative time, less blood loss, and a greater probability of excellent screw placement as compared with those placed with freehand techniques. We conclude that 3DP guides may potentially develop into an efficient and accurate option for pedicle screw placement. However, more prospective, randomized controlled trials are needed to strengthen the confidence of these conclusions.

Level of Evidence: Level III.

Key Words: 3-dimensional print, additive manufacturing, patient-specific, stereolithography, selective laser sintering, drill guide, pedicle screw, posterior spinal instrumentation

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Three-dimensional printing (3DP) is a burgeoning, new technology in the medical field and its usage has increased over the last decade. 3DP is a manufacturing method in which objects are made by fusing or depositing materials in layers to create 3-dimensional (D) objects. This process is alternatively referred to as rapid prototyping, stereolithography (SLA), additive manufacturing, or solid free-form technology.[1,2]

Charles Hull is credited as inventing 3DP technology in 1983 while experimenting with photopolymers and UV light. He went on to establish a rapid prototyping company, 3D Systems, which developed the world's first 3D printer.[2] Hull[3] coined the term "stereolithography" in 1986 with his US patent, "Apparatus for production of three-dimensional objects by sterolithography." In its simplest form, 3DP uses a digital 3D model sliced into 2D sections [akin to axial sections of computed tomography (CT) scan] to print an object. Each layer is laid onto the printer bed sequentially and fused together into a single, solid form. There are 3 commonly used methods of adding the material in layers: fused deposition modeling (FDM), selective laser sintering (SLS), and SLA. FDM extrudes a

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heat-softened polymer through a computer-navigated nozzle. SLS focuses lasers on a fine powder bed, melting, and fusing the powder simultaneously. SLA uses a light-curable resin in which layers of the liquid are selectively targeted by optical light as the print platform ascends from the liquid. Though FDM printers are fast, economical, and easy to use, SLS and SLA printers are the benchmark in medical instrumentation due to their higher precision, reproducibility, and ability to print material with higher melting points (ie, titanium, steel, ceramics).[2]

The first application of this technology in spine surgery was for biomodeling, used by D'Urso et al[4] for preoperative planning. Biomodels have proven useful for complex, atypical anatomy commonly resulting from severe scoliosis, traumatic deformity, and tumors.[4–13] This technology expanded to navigation systems for pedicle screw placement using patient-specific 3DP drill guides. These guides are reverse-engineered from preoperative CT scans and designed with congruent geometries to match the instrumented vertebral levels (Fig. 1). Standard contact points include the transverse process, lamina/pars region, or the inferior articular process. The guide is placed directly in contact with the bony landmarks and held in place by temporary fixation screws or pins. Navigation channels built into the guide will then direct drills and taps in the proper orientation and depth.

Several authors have reported the outcomes of these drill guides on operative, clinical, and radiographic metrics within the last few years, but no clear consensus exists on their utility.[14–19] The goal of this meta-analysis is to determine the benefits, if any, of 3DP drill guides when compared with conventional techniques of placing pedicle screws.

MATERIALS AND METHODS

Literature Search Strategy

A literature search of Embase, Ovid Medline, and Scopus was performed to identify relevant studies. The following terms and their combinations were used for title/abstract searches: three dimensional printing, additive manufacturing, drill guide, navigation, template, instrument, pedicle screw, spine. A manual search of reference lists was also implemented. See the Appendix (Supplemental Digital Content 1, http://links.lww.com/CLINSPINE/A142) for a detailed description of search strategies.

Inclusion and Exclusion Criteria

During the title and abstract screening, the following inclusion criteria were used: (1) levels 1, 2, and 3 evidence studies; (2) pedicle screw placement using 3DP drill guides compared with fluoroscopically-guided, freehand methods; (3) provided surgical, clinical, or radiographic outcomes of each group. Exclusion criteria included: (1) editorials, case reports, review articles, and studies without control group comparison; (2) cadaveric or animal studies; (3) manuscripts published in a language other than English; (4) manuscripts lacking desired outcome measures. Levels of evidence were assigned to the studies according to the criteria described in *Clinical Orthopedics and Related Research*.[20,21]

Search Result Screening

Two review authors (N.W., B.B.B.) independently reviewed all titles and/or abstracts with the senior author being available to resolve a dispute if a consensus agreement was not reached after discussion. All irrelevant titles were excluded and full-text papers were obtained when titles were deemed relevant or where eligibility was unclear. Two review authors independently assessed these full-text papers. A record of reasons for excluding studies was maintained for reference.

Data Extraction

Outcome data and study characteristics were extracted in duplicate. Two authors independently extracted data from the eligible studies. Missing information on the methods and missing statistics (means, SDs, clinical/radiographic outcomes, etc.) were encountered during data

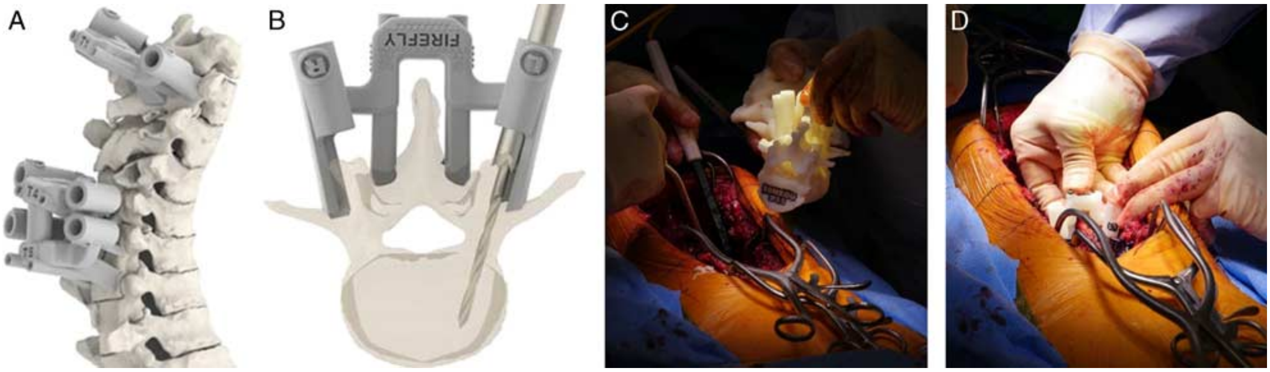


FIGURE 1. Image of 3-dimensional printed drill guides matched to congruent spine levels (A), diagram of a guide directing a drill into the pedicle (B), image of intraoperative comparison between patient anatomy and bone model (C), intraoperative placement of drill guide onto a patient's spine (D). Images adapted and reproduced with permission from Mighty Oak Medical. Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation. full color online

extraction. Attempts were made to collect the missing data by contacting study authors.

The following data was extracted from eligible studies: (1) study identifiers (authors, publication year, title); (2) study characteristics (design, region, sample sizes, sex, age, level of instrumentation, spine pathology, software, printer type, printed material); (3) clinical outcomes at baseline and 1 year (pain score, Japanese Orthopedic Association score); (4) radiographic outcomes (screw accuracy base on CT imaging); (5) surgical data [estimated blood loss (EBL), surgical time]; and (6) surgical complications. Of note, screw accuracy was graded into 3 categories (poor, good, excellent) based on the scale first published by Gertzbein et al.[22] An "excellent" grade was given to screws positioned in the pedicle without any cortex violation. "Good" grade was given to screws with a <4 mm cortical violation. "Poor" grade was given to screws with >4 mm cortical violation and posed a threat to surrounding neurovascular structures.[14,22] For statistical analysis, the gradings were then consolidated into dichotomous data to calculate the weighted risk difference (WRD) using the Mantel-Haenszel method. This was repeated twice: first to compare rates of poor screw placement and second to compare rates of excellent screw placement.

Quality Assessment

A systematic assessment of bias was performed using the Cochrane Risk of Bias tool and Minors criteria.[23,24] The items used for the assessment of each study were divided into the following sources of bias: selection (randomized sequence and allocation concealment), blinding, detection, attrition and management of drop out, selective outcome reporting and other potential sources of bias. Minors score was calculated using the 12 categories scoring 0–2 for a maximum score of 24. Two authors reviewed included studies and independently assessed quality.

Statistical Analysis

All meta-analyses were performed using Review Manager 5.3 software (RevMan Ver. 5.3 2014; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The mean difference with 95% confidence intervals (CIs) was used to compare continuous variables, and risk difference was used to compare categorical. A probability of P-value <0.05 was considered to be statistically significant. An I^2 test was used to calculate the statistical heterogeneity, with a value exceeding 50% representing substantial heterogeneity.

RESULTS

Search Results

A total of 2398 articles were initially identified using the search strategy (Fig. 2). An additional 51 records were identified using reference lists and other sources. In total,

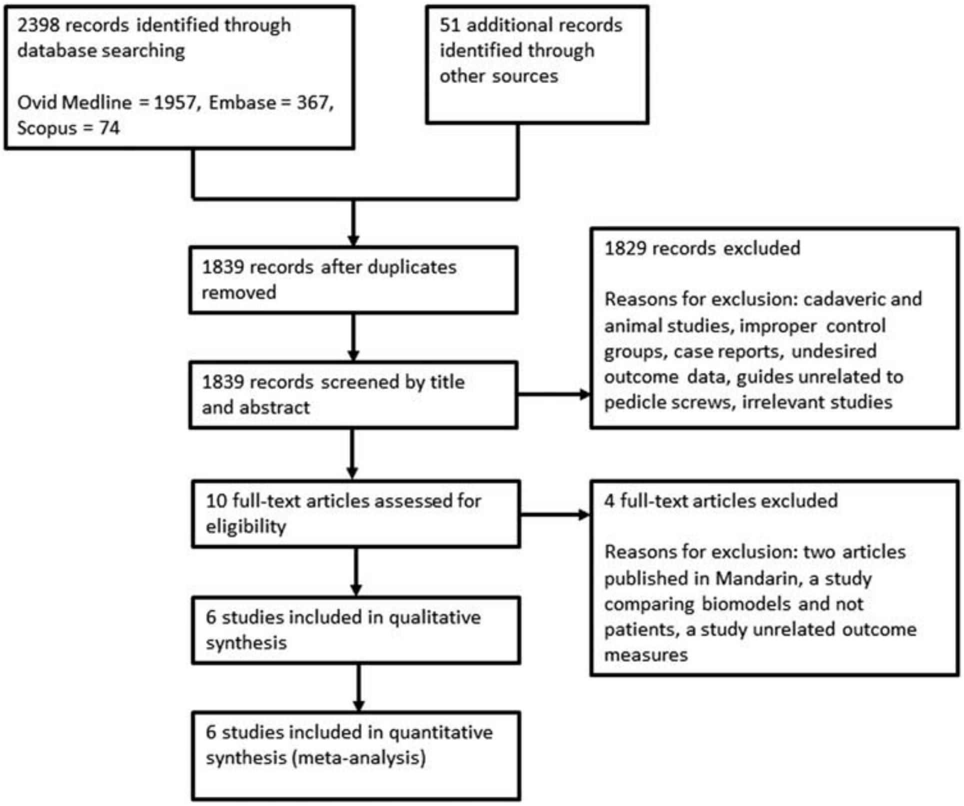


FIGURE 2. Flow diagram of the study selection process.

610 articles were excluded due to duplication. After screening the titles and abstracts, 1839 articles were excluded (Cohen κ value for interrater reliability = 0.888). The remaining 10 studies underwent a comprehensive full-text evaluation. Finally, 6 studies with a total of 205 patients met the inclusion criteria and were included in this meta-analysis.[14–19]

Study Characteristics and Quality Assessment

Among the 6 included studies, there was 1 randomized controlled trial, 2 prospective cohorts, 2 retrospective cohorts, and 1 cross-over trial (Table 1). Five studies were conducted in China, and a single study was performed in India. Three studies compared atlantoaxial pedicle and lateral mass screw fixation and 3 studies compared thoracolumbar (TL) pedicle screw placement. Spinal pathologies within the studies included: disk herniation, spondylolisthesis, canal stenosis, scoliosis, tubercular kyphosis, rheumatoid arthritis, congenital dysplasia, and trauma. For the 5 nonrandomized studies, Minor scores ranged from 17 to 20. Three studies were deficient in the blinded assessment of endpoints (Garg and colleagues, Liu and colleagues, Xiong and colleagues) and none of the studies included power analysis for prospective calculation of study size. Four studies did not include consecutive patients (Jiang and colleagues, Liu and colleagues, Pu and colleagues, Xiong and colleagues) and 1 study had poor control groups (Liu and colleagues). The single randomized controlled trial reported adequate sequencing, allocation, detection, and blinding, but did not address attrition during follow-up nor account for reporting bias (Chen and colleagues).

Screw Accuracy

All included studies evaluated pedicle screw accuracy with postoperative CT scans. A total of 555 screws were placed using 3DP drill guides and 588 screws placed under fluoroscopic, freehand technique. All screw accuracy data was condensed into the 3 categories: poor, good, excellent. The studies by Jiang and colleagues, Liu and colleagues, and Pu and colleagues recorded different grades for screws between 0–2 and 2–4 mm of pedicle violation. These screws were combined and included in the "good" category. After pooling all data, there was no significant difference in the risk of poor screw placement (4 + mm violation) between groups (WRD = −0.01, 95% CI = −0.02 to 0.01). However, there was a significantly higher rate of excellent screw placement (no violation) with the 3DP drill guide (WRD = −0.12, 95% CI = −0.17 to 0.07) (Fig. 3). No significant heterogeneity was found.

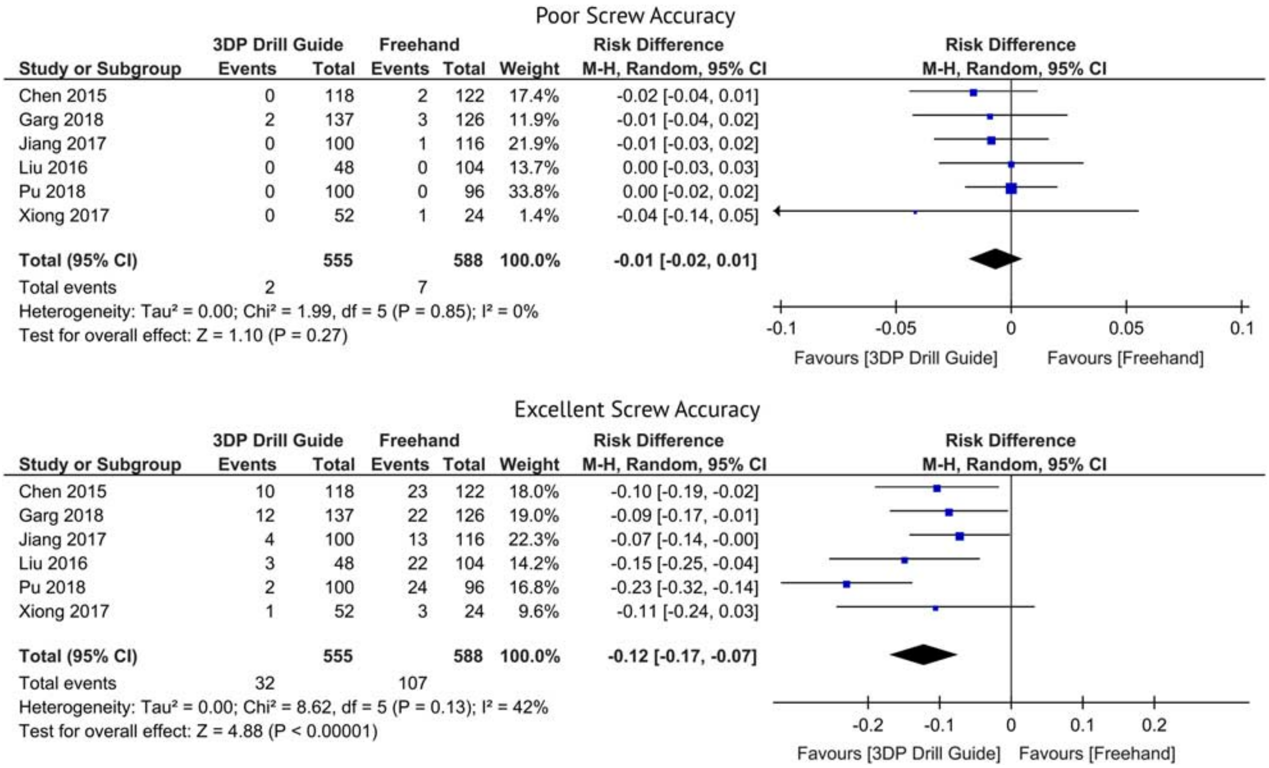
Operative Outcome Measures

All studies but Liu and colleagues included data for EBL in milliliters between groups. For EBL analysis, a total of 93 cases with 3DP drill guides and 92 with fluoroscopy guidance were pooled. There was a significant difference in EBL favoring 3DP guides [weighted mean difference (WMD) = −51.42 mL, 95% CI = −81.12 to −21.72]. Garg and colleagues, Jiang and colleagues, Pu and colleagues, and Xiong and colleagues recorded data on surgical time. Surgical time was defined by the time of

TABLE 1. Characteristics of Included Studies

		Demographics		
References	**Design**	**3DP**	**Freehand**	**Printing Characteristics**
Chen et al[14]	Randomized controlled trial	N = 20 (9M, 11F) Mean age: 52.3 Level of fixation: L	N = 23 (12M, 11F) Mean age: 55.4 Level of fixation: L	Printer: 100-3D (German EOS) Material: polyamide PA220 Printer type: NA Software: NA
Garg et al[15]	Retrospective cohort	N = 10 (6M, 4F) Mean age: 16.6 Level of fixation: TL	N = 10 (3M, 7F) Mean age: 15.5 Level of fixation: TL	Printer: Stratasys Mojo Material: ABS P430 Printer type: STL Software: MIMICS Base v18.0, 3-matic
Jiang et al[16]	Prospective cohort	N = 25 (16M, 9F) Mean age: 43.5 Level of fixation: C1–C2	N = 29 (18M, 11F) Mean age: 46.9 Level of fixation: C1–C2	Printer: Formlabs Form 1+ Material: acrylate resin Printer type: STL Software: MIMICS Base v17.0, 3-matic 9.0
Liu et al[17]	Cross-over trial	N = 10 (4M, 6F) Mean age: 17.7 Level of fixation: TL	N = 10 (4M, 6F) Mean age: 17 Level of fixation: TL	Printer: SLA600 Material: unknown resin Printer type: STL Software: MIMICS 10.01, Geomagic Studio 7
Pu et al[18]	Prospective cohort	N = 25 (11M, 14F) Age range: 25–56 Level of fixation: C1–C2	N = 24 (14M, 10F) Age range: 22–51 Level of fixation: C1–C2	Printer: Formlabs Material: NA Printer type: NA Software: MIMICS 17.0 Creo 2.0
Xiong et al[19]	Retrospective cohort	N = 13 (7M, 6F) Mean age: 46.1 Level of fixation: C1–C2	N = 6 (3M, 3F) Mean age: 48.7 Level of fixation: C1–C2	Printer: Meditool 3D Material: Pangu 4.0 resin Printer type: NA Software: MIMICS 17.0

C indicates cervical; 3DP, 3-dimensional printing; F, female; L, lumbar; M, male; NA, Not available; STL, stereolithography; TL, thoracolumbar.



Poor Screw Accuracy

Study or Subgroup	3DP Drill Guide Events	3DP Drill Guide Total	Freehand Events	Freehand Total	Weight	Risk Difference M-H, Random, 95% CI
Chen 2015	0	118	2	122	17.4%	-0.02 [-0.04, 0.01]
Garg 2018	2	137	3	126	11.9%	-0.01 [-0.04, 0.02]
Jiang 2017	0	100	1	116	21.9%	-0.01 [-0.03, 0.02]
Liu 2016	0	48	0	104	13.7%	0.00 [-0.03, 0.03]
Pu 2018	0	100	0	96	33.8%	0.00 [-0.02, 0.02]
Xiong 2017	0	52	1	24	1.4%	-0.04 [-0.14, 0.05]
Total (95% CI)		**555**		**588**	**100.0%**	**-0.01 [-0.02, 0.01]**
Total events	2		7			

Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 5 (P = 0.85); I² = 0%

Test for overall effect: Z = 1.10 (P = 0.27)

Excellent Screw Accuracy

Study or Subgroup	3DP Drill Guide Events	3DP Drill Guide Total	Freehand Events	Freehand Total	Weight	Risk Difference M-H, Random, 95% CI
Chen 2015	10	118	23	122	18.0%	-0.10 [-0.19, -0.02]
Garg 2018	12	137	22	126	19.0%	-0.09 [-0.17, -0.01]
Jiang 2017	4	100	13	116	22.3%	-0.07 [-0.14, -0.00]
Liu 2016	3	48	22	104	14.2%	-0.15 [-0.25, -0.04]
Pu 2018	2	100	24	96	16.8%	-0.23 [-0.32, -0.14]
Xiong 2017	1	52	3	24	9.6%	-0.11 [-0.24, 0.03]
Total (95% CI)		**555**		**588**	**100.0%**	**-0.12 [-0.17, -0.07]**
Total events	32		107			

Heterogeneity: Tau² = 0.00; Chi² = 8.62, df = 5 (P = 0.13); I² = 42%

Test for overall effect: Z = 4.88 (P < 0.00001)

FIGURE 3. Forest plots for screw accuracy comparing excellent and poor screw placement between 3DP and freehand groups. CI indicates confidence interval; 3DP, 3-dimensional printing; M-H, Mantel-Haenszel method. full color online

incision to skin closure. Chen and colleagues also recorded surgical time but only reported minutes required per screw. This time data was not included. 73 cases with 3DP guides and 69 with fluoroscopy were pooled. 3DP drill guides showed a significantly shorter surgical time (WMD = −32.32 min, 95% CI = −53.19 to −11.45). In both analyses, there was substantial heterogeneity (Fig. 4).

Clinical Outcomes Measures

Xiong and colleagues, Jiang and colleagues, and Pu and colleagues reported pain values on a 10-point scale at the time of presentation and 1 year following treatment. (Fig. 5). At both baseline and 1 year, the WMD between patients treated with 3DP drill guides and fluoroscopy did not show a statistical difference (WMD baseline = −0.03, 95% CI = −0.41 to 0.35; WMD 1 year = −0.13, 95% CI = −0.45 to 0.19). Jiang and colleagues and Pu and colleagues recorded Japanese Orthopedic Association scores at baseline and 1-year follow-up. Neither baseline nor 1-year follow-up showed significant difference between 3DP and fluoroscopy (WMD baseline = −0.15, 95% CI = −0.41 to 0.35; WMD 1 year = −0.14, 95% CI = −0.47 to 0.75) (Fig. 6). No significant heterogeneity was seen in the analysis of clinical outcomes.

Surgical Complications

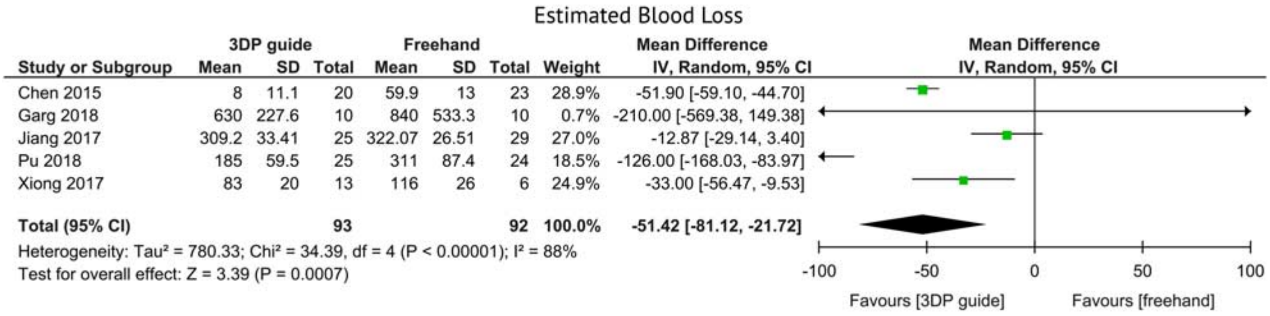
Two complications were reported during pedicle placement with 3DP navigation, 1 venous plexus bleed, and 1 superficial surgical site infection. Nine complications were reported with the conventional method, 5 venous plexus bleeds, 1 superficial surgical site infection, 2 occipital neuralgias, 1 occipital hyperpselaphesia. When pooled, there was no significant difference in risk between treatment groups (WRD = −0.04, 95% CI = −0.12 to 0.03) (Fig. 7). No significant heterogeneity was present.

Publication Bias and Subgroup Analysis

Due to the limited number of included studies, no formal assessment of publication bias was performed. Subgroup analysis was performed for the high heterogeneity found within the EBL and surgical time comparisons. In both analyses, the data was divided into subgroups based on the level of the spine. Cervical approaches will differ tremendously from TL approaches in an operative time of exposure and anticipated blood loss. For EBL comparison, both TL and cervical studies still showed significant differences when pooled separately though, cervical studies retained significant heterogeneity (TL: 95% CI = −51.96 to −44.76 mL; cervical: 95% CI = −103.91 to −2.76 mL). For a surgical time, the cervical studies again retained significant differences when pooled, although no separate analysis was performed for the single TL study (cervical: 95% CI = −49.54 to −6.06 min).

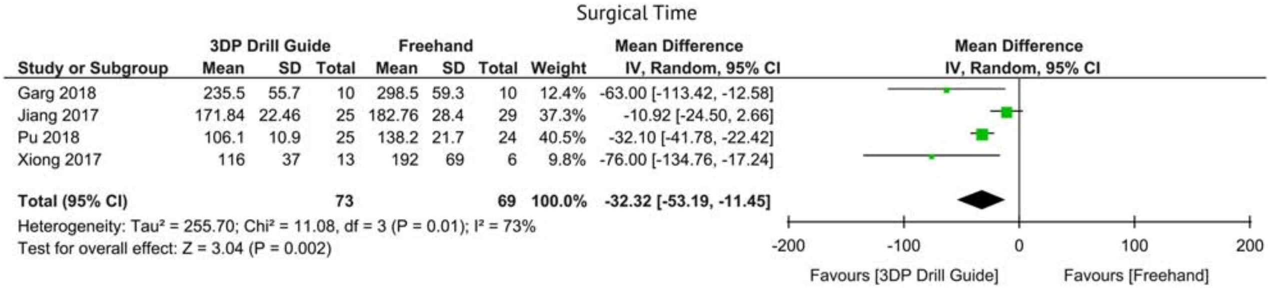
DISCUSSION

Given the proximity of nerves, blood vessels, spinal cord, and visceral organs, pedicle screw placement poses significant risks to several vital anatomic structures.


Estimated Blood Loss

Study or Subgroup	3DP guide Mean	SD	Total	Freehand Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2015	8	11.1	20	59.9	13	23	28.9%	-51.90 [-59.10, -44.70]
Garg 2018	630	227.6	10	840	533.3	10	0.7%	-210.00 [-569.38, 149.38]
Jiang 2017	309.2	33.41	25	322.07	26.51	29	27.0%	-12.87 [-29.14, 3.40]
Pu 2018	185	59.5	25	311	87.4	24	18.5%	-126.00 [-168.03, -83.97]
Xiong 2017	83	20	13	116	26	6	24.9%	-33.00 [-56.47, -9.53]
Total (95% CI)			**93**			**92**	**100.0%**	**-51.42 [-81.12, -21.72]**

Heterogeneity: Tau² = 780.33; Chi² = 34.39, df = 4 (P < 0.00001); I² = 88%
Test for overall effect: Z = 3.39 (P = 0.0007)


Surgical Time

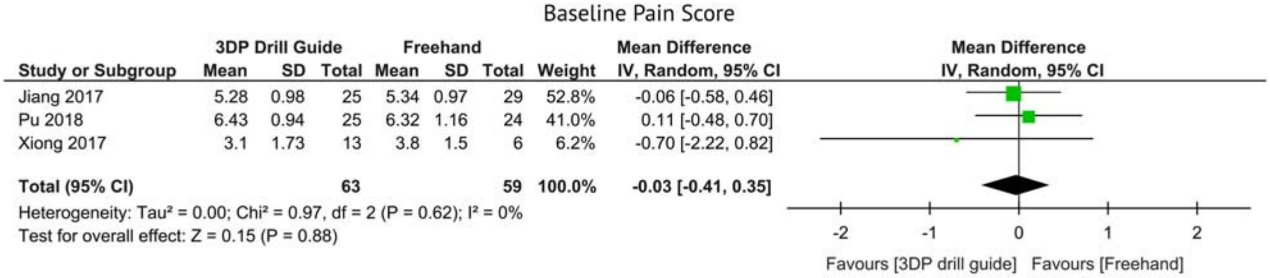
Study or Subgroup	3DP Drill Guide Mean	SD	Total	Freehand Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Garg 2018	235.5	55.7	10	298.5	59.3	10	12.4%	-63.00 [-113.42, -12.58]
Jiang 2017	171.84	22.46	25	182.76	28.4	29	37.3%	-10.92 [-24.50, 2.66]
Pu 2018	106.1	10.9	25	138.2	21.7	24	40.5%	-32.10 [-41.78, -22.42]
Xiong 2017	116	37	13	192	69	6	9.8%	-76.00 [-134.76, -17.24]
Total (95% CI)			**73**			**69**	**100.0%**	**-32.32 [-53.19, -11.45]**

Heterogeneity: Tau² = 255.70; Chi² = 11.08, df = 3 (P = 0.01); I² = 73%
Test for overall effect: Z = 3.04 (P = 0.002)

FIGURE 4. Forest plots comparing estimated blood loss and surgical time between 3DP and freehand groups. CI indicates confidence interval; 3DP, 3-dimensional printing; IV, inverse variance. full color online

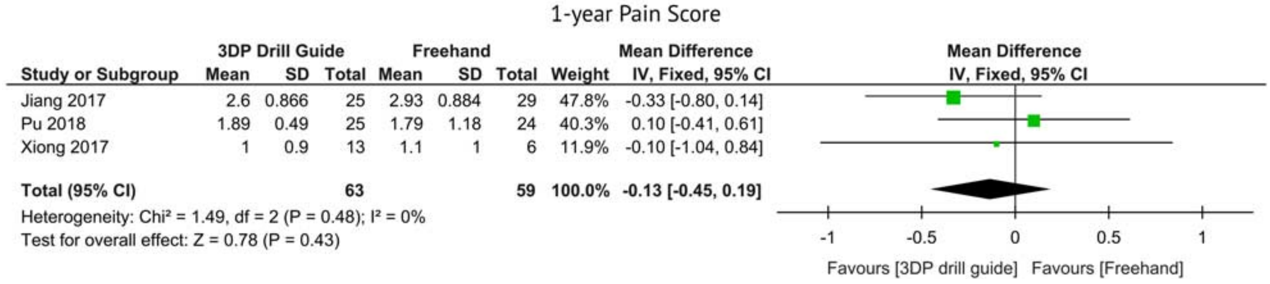
Freehand, fluoroscopic techniques have high reported pedicle violation rates (3%–54.7%),[25,26] and complications from misplaced screws are reported to occur in 0%–7% of patients.[26] Malpositioned screws can cause pedicle fractures, dural lacerations, neurological, and vascular injuries and can weaken overall fixation of the construct.[27,28] These errors may lead to instrument failure, pseudoarthrosis formation, persistent pain, and need for revision surgery.

Computer-aided surgical navigation devices were developed to address these inaccuracies encountered with freehand methods. These systems have been well received in many institutions and have significantly improved pedicle screw accuracy.[29–31] However, these navigation systems rely on intraoperative CT, need substantial up-front investments, and require a team of technically trained staff to operate. Stereotactic navigation systems are not without error as they depend on proper sensor


Baseline Pain Score

Study or Subgroup	3DP Drill Guide Mean	SD	Total	Freehand Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Jiang 2017	5.28	0.98	25	5.34	0.97	29	52.8%	-0.06 [-0.58, 0.46]
Pu 2018	6.43	0.94	25	6.32	1.16	24	41.0%	0.11 [-0.48, 0.70]
Xiong 2017	3.1	1.73	13	3.8	1.5	6	6.2%	-0.70 [-2.22, 0.82]
Total (95% CI)			**63**			**59**	**100.0%**	**-0.03 [-0.41, 0.35]**

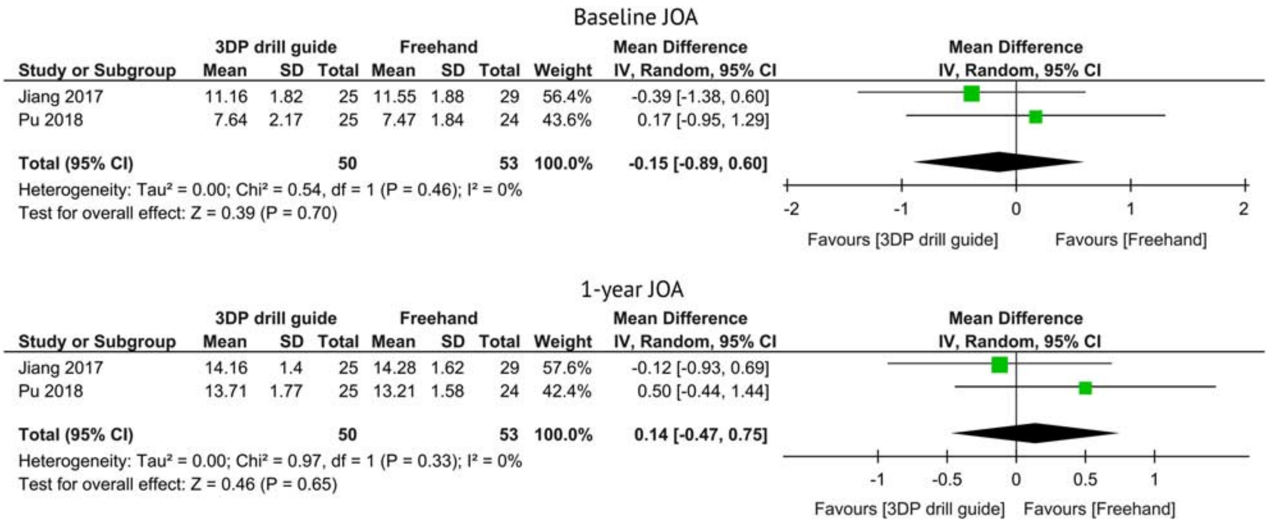
Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.15 (P = 0.88)


1-year Pain Score

Study or Subgroup	3DP Drill Guide Mean	SD	Total	Freehand Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Jiang 2017	2.6	0.866	25	2.93	0.884	29	47.8%	-0.33 [-0.80, 0.14]
Pu 2018	1.89	0.49	25	1.79	1.18	24	40.3%	0.10 [-0.41, 0.61]
Xiong 2017	1	0.9	13	1.1	1	6	11.9%	-0.10 [-1.04, 0.84]
Total (95% CI)			**63**			**59**	**100.0%**	**-0.13 [-0.45, 0.19]**

Heterogeneity: Chi² = 1.49, df = 2 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.43)

FIGURE 5. Forest plots for the mean difference of baseline pain score at the time of surgery and 1-year follow-up between 3DP and freehand groups. CI indicates confidence interval; 3DP, 3-dimensional printing; IV, inverse variance. full color online



Baseline JOA

Study or Subgroup	3DP drill guide			Freehand			Weight	Mean Difference
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI
Jiang 2017	11.16	1.82	25	11.55	1.88	29	56.4%	-0.39 [-1.38, 0.60]
Pu 2018	7.64	2.17	25	7.47	1.84	24	43.6%	0.17 [-0.95, 1.29]
Total (95% CI)			**50**			**53**	**100.0%**	**-0.15 [-0.89, 0.60]**

Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 1 (P = 0.46); I² = 0%

Test for overall effect: Z = 0.39 (P = 0.70)

1-year JOA

Study or Subgroup	3DP drill guide			Freehand			Weight	Mean Difference
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI
Jiang 2017	14.16	1.4	25	14.28	1.62	29	57.6%	-0.12 [-0.93, 0.69]
Pu 2018	13.71	1.77	25	13.21	1.58	24	42.4%	0.50 [-0.44, 1.44]
Total (95% CI)			**50**			**53**	**100.0%**	**0.14 [-0.47, 0.75]**

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.33); I² = 0%

Test for overall effect: Z = 0.46 (P = 0.65)

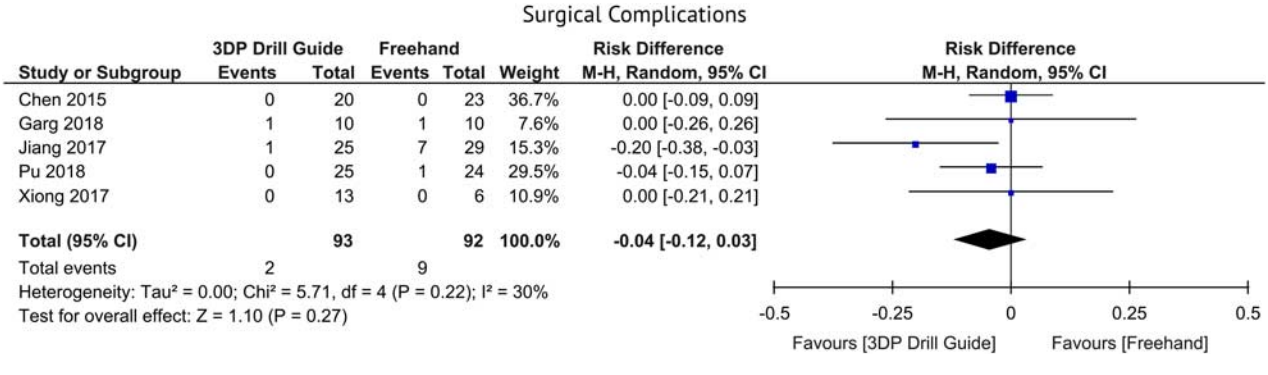
FIGURE 6. Forest plots for the mean difference of baseline JOA score at the time of surgery and 1-year follow-up between 3DP and freehand groups. CI indicates confidence interval; 3DP, 3-dimensional printing; IV, inverse variance; JOA, Japanese Orthopedic Association. full color online

placement and registration. Inaccuracies can arise with increased distances from reference frames, alterations in patient position, or movement of the reference array. If not noticed and corrected, these errors will degrade navigation accuracy.[28,32]

3DP navigation systems may offer a solution to the challenges faced by freehand and computer-aided navigation systems by providing proper screw trajectories via geometric congruence between the patient anatomy and drill guide. This meta-analysis included 205 patients and compared the accuracy and clinical outcomes of 1143 total pedicle screws placed either with 3DP drill guides or fluoroscopic guidance. Pooling the data of the 6 included studies showed a statistically higher probability of excellent screw placement by the 3DP drill guide. In addition, there was a significant reduction in operative time and blood loss when compared with screws placed under fluoroscopic, freehand technique. Moreover, there was no difference in clinical outcomes at 1 year. However, the overall complication rates between the 2 groups showed no difference. This is consistent with published literature comparing other methods of navigation to conventional techniques. To date, no form of computer-aided navigation has shown to decrease surgical complication rates despite increases in screw accuracy.[26,29,30]

The 3DP guides significantly improved the rate of excellent screw placement compared with the freehand, fluoroscopic-guided screws, but this improvement has unknown clinical relevance. Perforations > 4 mm outside of the pedicle are presumed to endanger the neural and vascular elements of the spine and are shown to correlate more frequently with neurological deficits.[25] Pedicle breech <2 mm is generally considered within the safe zone.[8,29] The largest differences seen between accuracy rates of 3DP drill guides and conventional technique was noted in the "excellent screw" placement category.

Although no formal cost analyses were performed by the studies, 3DP drill guides may offer an alternative option for navigation with less upfront investment cost than existing methods. Watkins et al[33] compared the



Surgical Complications

Study or Subgroup	3DP Drill Guide		Freehand		Weight	Risk Difference
	Events	Total	Events	Total		M-H, Random, 95% CI
Chen 2015	0	20	0	23	36.7%	0.00 [-0.09, 0.09]
Garg 2018	1	10	1	10	7.6%	0.00 [-0.26, 0.26]
Jiang 2017	1	25	7	29	15.3%	-0.20 [-0.38, -0.03]
Pu 2018	0	25	1	24	29.5%	-0.04 [-0.15, 0.07]
Xiong 2017	0	13	0	6	10.9%	0.00 [-0.21, 0.21]
Total (95% CI)		**93**		**92**	**100.0%**	**-0.04 [-0.12, 0.03]**
Total events	2		9			

Heterogeneity: Tau² = 0.00; Chi² = 5.71, df = 4 (P = 0.22); I² = 30%

Test for overall effect: Z = 1.10 (P = 0.27)

FIGURE 7. Forest plot for surgical complications between 3DP drill guide and freehand groups. CI indicates confidence interval; 3DP, 3-dimensional printing; M-H, Mantel-Haenszel method. full color online

cost-effectiveness of 3D image-guidance compared with freehand, fluoroscopic techniques. Their study found a decrease in revision rates of 3% using navigation over a 100-case comparison. This equated to a reduction in surgical revision costs of $71,286. They did not find a significant difference in operative times between navigation and freehand groups but noted an average cost of 1 hour of operating room (OR) usage was $5580 ($93/min). This is more than other published rates of average OR usage costs (ranging from $30 to $60/min), but well within the expected costs given the level of complexity, these cases create.[34,35] The study also reported on 4 occasions the navigation systems failed (1 system error, 3 user errors) which increased operative times by 7–25 minutes per case. This meta-analysis found that the use of 3DP drill guides decreased operative times by 32.3 minutes on average, which would roughly translate to $3000 in OR usage costs. A single-level drill guide typically ranges from $20 to $500 to manufacture.[32] The cost depends on a number of factors including material, resolution, and printer used. The FIREFLY system (Mighty Oak Medical, Englewood, CO), which uses an epoxy-resin on an SLA printer, on average will cost $450 per vertebral level (depending on the levels manufactured). It also has the option to include a separate, autoclavable bone model for intraoperative reference. Comparatively, Watkins and colleagues reported the upfront cost for the navigation and imaging systems they used were $475,000 [$225,000 for NaviVision (Vector Vision-BrainLAB) and $250,000 for Arcadis Orbic (Siemens)], which does not include costs of disposable equipment, such as reflective navigation balls, required for each case.

To produce the 3D printed guides, the manufacturing company will require volumetric DICOM images of the patient to be uploaded to an online uploader. High-resolution CT images improve patient-device congruence and accuracy, so 1.25 mm, contiguous spiral CT scans of the desired levels are typically recommended. At our institution, the cost of scanning can range from $383 to $1158 for a simple lumbar scan or for the entire spine, respectively. The images are then used for 3D reconstruction modeling of the spine to determine optimal screw size and orientation using CAD software. The presurgical plan is then sent to the surgeon to review and approve or request any changes. Once approved, the reverse-engineered drill guide and corresponding vertebrae biomodel is fabricated and shipped back to the ordering surgeon. The process to design, approve, manufacture, and ship the navigation guides will typically range from 6 to 10 days, so a surgeon must factor in these time requirements to appropriately schedule a procedure.

This meta-analysis has several limitations to consider. First, the number of high-quality randomized controlled studies was sparse, and many of the included papers were prospective and retrospective cohorts. Nearly all of these systems were designed, printed, and tested by a single institution and none of the included papers addressed the inherent biases that exist when trialing one's own navigation system. Second, there was considerable heterogeneity between treatment arms of included studies, as all levels of spine instrumentation and all spine pathologies were included. We attempted to eliminate some of this heterogeneity by performing subgroup analyses. But given the limited number of studies, there were only a few meaningful ways to subdivide the manuscripts. Third, the small sample size of included patients limited the power to detect a true difference in screw accuracy, complications rates, and subtle clinical outcomes. Last, nearly all included studies were performed in China and India, limiting external validity. The biases from local patient populations, regional surgical training, treatment tendencies, etc. weaken the conclusions.

CONCLUSIONS

This meta-analysis suggests that 3DP pedicle screw drill guides may shorten the operative time, lessen blood loss, and improve the probability of excellent screw placement compared with conventional techniques. We conclude that 3DP drill guides have the potential to develop into a safe, efficient, and cost-effective navigation system for pedicle screw placement. Additional randomized controlled trials with larger numbers of patients are needed to detect the more subtle differences in screw accuracy and complications. Moreover, a comparison with computer-aided navigation with cost analysis would help establish the benefits and drawbacks between the 2 navigation systems.

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