BMJ Open

The European Robotic Spinal Instrumentation (EUROSPIN) study: protocol for a multicentre prospective observational study of pedicle screw revision surgery after robot-guided, navigated and freehand thoracolumbar spinal fusion

Victor E Staartjes,[1,2,3] Granit Molliqaj,[4] Paulien M van Kampen,[5] Hubert A J Eversdijk,[1] Aymeric Amelot,[6] Christoph Bettag,[7] Jasper F C Wolfs,[1,8] Sophie Urbanski,[9] Farman Hedayat,[9] Carsten G Schneekloth,[10] Mike Abu Saris,[11] Michel Lefranc,[12] Johann Peltier,[12] Duccio Boscherini,[13] Ingo Fiss,[7] Bawarjan Schatlo,[7] Veit Rohde,[7] Yu-Mi Ryang,[14,15] Sandro M Krieg,[14] Bernhard Meyer,[14] Nikolaus Kögl,[16] Pierre-Pascal Girod,[16] Claudius Thomé,[16] Jos W R Twisk,[17] Enrico Tessitore,[4] Marc L Schröder[1]

To cite: Staartjes VE, Molliqaj G, van Kampen PM, *et al*. The European Robotic Spinal Instrumentation (EUROSPIN) study: protocol for a multicentre prospective observational study of pedicle screw revision surgery after robot-guided, navigated and freehand thoracolumbar spinal fusion. *BMJ Open* 2019;**9**:e030389. doi:10.1136/bmjopen-2019-030389

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-030389).

VES and GM contributed equally.

VES and GM are joint first authors.
ET and MLS are joint senior authors.

Received 12 March 2019
Revised 15 August 2019
Accepted 21 August 2019

For numbered affiliations see end of article.

Correspondence to
Dr Victor E Staartjes;
victor.staartjes@gmail.com

ABSTRACT

Introduction Robotic guidance (RG) and computer-assisted navigation (NV) have seen increased adoption in instrumented spine surgery over the last decade. Although there exists some evidence that these techniques increase radiological pedicle screw accuracy compared with conventional freehand (FH) surgery, this may not directly translate to any tangible clinical benefits, especially considering the relatively high inherent costs. As a non-randomised, expertise-based study, the European Robotic Spinal Instrumentation Study aims to create prospective multicentre evidence on the potential comparative clinical benefits of RG, NV and FH in a real-world setting.

Methods and analysis Patients are allocated in a non-randomised, non-blinded fashion to the RG, NV or FH arms. Adult patients that are to undergo thoracolumbar pedicle screw instrumentation for degenerative pathologies, infections, vertebral tumours or fractures are considered for inclusion. Deformity correction and surgery at more than five levels represent exclusion criteria. Follow-up takes place at 6 weeks, as well as 12 and 24 months. The primary endpoint is defined as the time to revision surgery for a malpositioned or loosened pedicle screw within the first postoperative year. Secondary endpoints include patient-reported back and leg pain, as well as Oswestry Disability Index and EuroQOL 5-dimension questionnaires. Use of analgesic medication and work status are recorded. The primary analysis, conducted on the 12-month data, is carried out according to the intention-to-treat principle. The primary endpoint is analysed using crude and adjusted Cox proportional hazards models. Patient-reported outcomes are analysed using baseline-adjusted linear mixed models. The study is monitored according to a prespecified monitoring plan.

Ethics and dissemination The study protocol is approved by the appropriate national and local authorities. Written informed consent is obtained from all participants. The final results will be published in an international peer-reviewed journal.

Trial registration number Clinical Trials.gov registry NCT03398915; Pre-results, recruiting stage.

Strengths and limitations of this study

- Large, pragmatic, prospective observational controlled study carried out in 13 pan-European centres.
- Long-term, 2-year follow-up with standardised and validated patient-reported outcomes.
- Non-randomised 'expertise-based' study design.
- Even with adjusted analyses, lack of randomisation may introduce biases.
- Potential performance bias due to lack of blinding of surgeons and patients.

INTRODUCTION

In the USA alone, an estimated 3.6 million spinal instrumentations were performed between 2001 and 2010, with an associated US$287 billion in total healthcare charges.[1] Both numbers demonstrate a steadily increasing trend.[1] In 2013, only 11% of spine surgeons routinely used navigation systems.[2] Meanwhile, more and more surgeons are implementing computer assistance into their

clinical practice, one reason being the adoption of minimally invasive (MI) techniques, further increasing the need for navigation due to often inexistent line-of-sight.[2 3]

In 1995, the concept of computer-assisted navigation was introduced to spine surgery.[4] Modern navigation systems (NV) assist in pedicle screw insertion by projecting screw trajectories onto preoperatively or intraoperatively obtained and coregistered CT or 3D-fluoroscopic (3DFL) images.[5] Robotic guidance (RG), introduced in 2006, takes one further step by providing mechanical guidance according to preplanned screw trajectories, eliminating the need of on-the-spot establishment of trajectories by the surgeon.[6–8] These systems can be considered cooperative robots ('cobots'), since they do not insert screws autonomously, rather exclusively providing stable guidance.[9] To achieve mechanical guidance, the robot's working channel moves into the preplanned trajectory based on coregistration of preoperative and intraoperative imaging while accounting for any potential differences in real-time spinal anatomy such as those caused by distraction, cage insertion or changes between the supine positioning on preoperative CT and prone positioning during surgery.[6–8 10 11] By restricting the surgeon's natural full motion range of 6 degrees of freedom (DOF) to 2 DOFs—motion up and down as well as yaw in the cannula—the robot guides the surgeon's tool according to the predefined trajectories while simultaneously providing stability for drilling, which is assumed to result in greater radiological screw accuracy.[6] When comparing the published literature on FG, NV and RG, rates of radiologically well-placed screws of 69%–94% for freehand (FH), 81%–100% for NV and 85% to 98% for RG are found,[6 10–15] with significant differences among subgroups of various NV devices.[16]

While there is some evidence that RG and NV lead to higher radiological accuracy than FH instrumentation,[12 16–21] this may not translate directly to real-world clinical benefits, especially in light of the high acquisition and maintenance costs inherent to these systems.[22] A recent systematic review on the cost-effectiveness of RG concluded that, although the technology is often claimed to be cost-effective, there appears to be a lack of published data to warrant this statement.[22] Possible benefits could include shorter operating times, and decreased incidences of radiculopathy and costly revision surgery for screw malposition, although the current level of evidence is very low, and there are no large prospective controlled studies comparing clinically relevant outcome such as pedicle screw-related revision surgery, as opposed to radiological surrogate measures alone.[5 6 14 21–30]

Currently, few published studies compare these techniques in a prospective setting, although they often suffer from insufficient power to demonstrate any potential clinical benefits, or report major conflicts of interests. Furthermore, while many studies compare RG to FH, there are no powerful studies comparing RG and NV.[5] We aim to conduct a prospective observational controlled study comparing RG, NV and FH to create real-world evidence on these instrumentation techniques.[31]

METHODS AND ANALYSIS

Study design

The European Robotic Spinal Instrumentation (EUROSPIN) study is a prospective, international, multicentre, pragmatic, open-label, non-randomised, observational controlled study comparing the effectiveness of three techniques for pedicle screw instrumentation, namely RG, NV (CT-, O-Arm, or 3DFL-based) and FH.[31–33] Following the baseline evaluation, patients receive pedicle screw fixation by the senior surgeons on the author's list, and are subsequently followed up for 24 months. The primary analysis is conducted using the 12-month data. The study is designed to evaluate the superiority of RG and NV over FH in terms of the time to revision surgery for a malpositioned or loosened pedicle screw within the first postoperative year. This study protocol is compiled according to the Standard Protocol Items: Recommendations for Interventional Trials Statement.[34] Thirteen European centres from the Netherlands, Switzerland, Germany, Austria and France participate in recruitment. Most centres contribute to at least two of the three study arms.

Study population

Inclusion criteria

Patients with the following indications for thoracolumbar pedicle screw placement are considered for inclusion: degenerative pathologies (spinal stenosis, spondylolisthesis, degenerative disc disease, recurrent disc herniation), infections, vertebral tumours, as well as traumatic and osteoporotic fractures. Patients are required to give informed consent. Only patients aged 18 years or older are considered for inclusion.

Exclusion criteria

Patients undergoing deformity surgery for scoliosis or kyphosis are not eligible. Patients undergoing surgery at more than five vertebral levels are also not eligible.

Patient and public involvement

Patients were not involved in the development of the research question or study design, and will not be involved in recruitment or conduct of the study.

Study procedures

Participating surgeons screen all patients with an indication for thoracolumbar pedicle screw placement for eligibility during the first consultation. If eligible, the patient receives an informative letter containing details on the EUROSPIN study after surgical consent has been given, including risks and benefits of participation. If written informed consent for study participation is given, the clinician or study nurse records baseline data. At this first visit, group allocation is determined.

Group allocation

This is a non-randomised study. In this study, patients are not randomly allocated to treatment and control groups. Instead, patients undergo pedicle screw placement with the technique that the treating surgeon is most experienced with, and for which equipment is available at the centre.[31] One reason concerns the surgeons' level of experience with a particular technique.[14 27 35 36] Because it has been demonstrated that the learning curve for some instrumentation techniques is steep, we did not deem it rational to have surgeons carry out procedures with a technique that they are not experienced with.[37] Instead, surgeons carry out the procedures with the technique that they are highly experienced with. This allows us to compare true effectiveness, similar to a prospective registry, as opposed to efficacy.[33] We have not implemented a prestudy 'learning curve' phase, accordingly. A second reason is recruitment. Although some randomised controlled trials on RG in spinal instrumentation have been successful,[14 38 39] they have suffered from rather slow recruitment and consequently relatively low power to demonstrate differences in an infrequently occurring endpoint, such as our primary endpoint. Multiple initialised randomised studies even had to be closed prematurely due to slow recruitment.[29]

Blinding

This is an open-label study. Both patients and treating physicians are aware of group allocation. However, the primary analysis is carried out by an epidemiologist blinded to group allocation, according to the prespecified statistical protocol. Rating of CT images is carried out by independent radiologists blinded to group allocation.

Treatment groups

Experimental intervention I: robot-guided pedicle screw placement

RG in the form of the following systems is applied: Mazor X, Renaissance or SpineAssist (Mazor Robotics, Ltd., Ceasarea, Israel) or ROSA Spine (Zimmer Biomet, Warsaw, IN, USA).[5 6 14 25 26 28] Fluoroscopic control is available.

Experimental intervention II: navigated pedicle screw placement

Navigated procedures are carried out under image guidance connected to a computer-assisted navigation system.[4 5 23] Preoperative or intraoperative image acquisition by spiral CT, cone-beam CT (O-Arm), or three-dimensional isocentric flurosocopy (3DFL) is applied for navigation.[4 5 23 40–42] Fluoroscopic control is available.

Control intervention: FH pedicle screw placement

Conventional FH surgery was chosen as the comparator because it is currently the most widely used and accepted standard technique around the world.[2] FH procedures are carried out according to surgeon preference, under fluoroscopic control.[5 14 19 23 25 26 28 40] Computer assistance is not available.

Cointerventions

Analgesic medication is available to the patients, if necessary. In addition, patients are able to undergo any further desired cointerventions such as elastic corsets or rigid casts, physiotherapy or others.

Prognostic factors

At the baseline assessment, patient age, height, weight, BMI, history of back or leg pain in months, prior surgery at any of the index levels, as well as highest level of education (elementary/high school/higher education/(post-) doctoral) and type of work (employed/self-employed/housework/student/retired/unemployed) are recorded. We also assess the use of analgesic medication (daily/at least once a week/not regularly) including over-the-counter drugs, patient satisfaction with current symptoms on a 3-step Likert scale (satisfied/neutral/dissatisfied), smoking status (active smoker/ceased/never smoked) and working status (able to work/unable to work/not applicable). Documented osteoporosis with or without treatment is recorded, as well as any procedures for osteoporotic fractures.

Outcome measures

Primary endpoint

We defined the primary endpoint as time to revision surgery for a malpositioned or loosened pedicle screw within the first postoperative year. In patients who experience the primary endpoint, CT imaging is carried out before revision surgery, and the degree of malposition is graded according to the classification described by Gertzbein and Robbins.[43]

Secondary endpoints

A range of secondary endpoints is assessed. The following patient-reported outcome measures (PROMs) are captured at baseline and follow-up: Numeric Rating Scales (NRS) for back pain severity (NRS-BP) and leg pain severity (NRS-LP), as well as validated translations of version 2.1 of the Oswestry Disability Index (ODI) for subjective functional impairment, and the three-level version the EuroQOL 5-dimensions (EQ-5D-3L) questionnaire (EQ-5D index and thermometer) for health-related quality of life.[44] The EQ-5D index is evaluated according to the respective national tariffs.[45] The proportion of patients in which revision or redirection of a pedicle screw was required intraoperatively (*intraoperative revision*) is recorded, as well as the number of instrumented index levels per patient. We record whether the procedure was carried out in a MI or open approach, and capture duration of the procedure in minutes, total intraoperative fluoroscopic radiation dose as dose area product in mGy×cm^2, estimated blood loss in mL, need for blood transfusion, as well as any intraoperative or postoperative adverse events. We also record the level of experience of the surgeon placing the pedicle screws (resident/fellow/board-certified ≤10 years/board-certified >10 years). Conversions from one study arm to another, as well as from MI to open surgery are tracked. All serious adverse events are reported to the principal investigators' site.

Table 1 Chart demonstrating items collected at baseline and follow-up

Item	Baseline	Surgery	Discharge	1 to 3 months postop.	12 months postop.	24 months postop.
Informed consent	X					
Group allocation	X					
Demographics	X					
Surgeon experience		X				
Surgery		X				
Intraoperative parameters		X				
Perioperative parameters		X	X			
Blood transfusion		X	X			
Length of stay			X			
ODI	X			X	X	X
NRS-BP + NRS-LP	X			X	X	X
EQ-5D-3L	X			X	X	X
Satisfaction (Likert)	X			X	X	X
Work status	X			X	X	X
Smoking status	X			X	X	X
Use of analgesia	X			X	X	X
Intraoperative screw revision		X				
Revision surgery for screw malposition or loosening	With occurrence					
CT	With occurrence of revision surgery					
Adverse events	With occurrence					
Reoperations	With occurrence					
Other treatments	With occurrence					

EQ-5D-3L, 3-level version of the EuroQOL five-dimensions questionnaire; NRS-BP, Numeric Rating Scale for back pain severity; NRS-LP, Numeric Rating Scale for leg pain severity; ODI, Oswestry Disability Index.

Follow-up

Patients undergo an 'early' follow-up at 1–3 months. Subsequently, patients are followed-up at 12 and 24 months postoperatively (table 1). At follow-up, PROMs, use of analgesic medication, satisfaction with symptoms, smoking status, time to return to work in weeks, as well as any reoperations are captured.

Data collection

Data are collected using a validated, secure web-based electronic data capturing system (CASTOR EDC, Amsterdam, The Netherlands). Each centre is able to enter anonymised data into an electronic research form (eCRF). Investigators from each centre assign identifiers to patients, and store demasking lists. For follow-up of PROMs, centres also have the option of dispatching standardised, scheduled surveys directly to the patients.[46] All data handling (data entry, storage and analysis) is confidential and complies with data protection regulations of participating countries and the European Union. Deidentified data are stored for 15 years.

Sample size calculation

It was determined that, to detect an absolute intergroup difference of 5% in the primary endpoint, 205 patients are required per group to achieve a power of 1 - β=0.8 at α=0.05.[47] Recruitment for a specific arm is stopped once the 205 patients have been included. The incidence rates are based on the published literature, with an approximated incidence rate of the primary endpoint of ~0% for the intervention and 5% for the control group.[5 6] Because the study protocol is in line with the normal clinical follow-up protocol of most centres, a low dropout rate is expected. This leads to a minimum total sample size of 615 patients.

Statistical analysis

Overview

All analyses are carried out in R (The R Foundation for Statistical Computing).[48] A p≤0.05 on two-tailed tests is considered statistically significant. The primary analysis, conducted on the 12-month data, is carried out according to the intention-to-treat principle, with

the intention-to-treat definition applying to the index surgery.[49] Results are reported as effect size estimates and their 95% CIs.

Analysis of primary endpoint

The effect on the primary endpoint is reported as HRs and their 95% CIs, calculated from crude and adjusted Cox proportional hazards models. The crude model is considered the primary analysis. The primary endpoint is specified as the dependent variable, and group assignment as the independent variable, with the FH group as the reference category. Our null hypothesis is that neither RG nor NV lead to a significant decrease in the primary endpoint incidence compared with FH. Patients who do not experience a primary endpoint are censored at the 12-month follow-up, with respect to the primary endpoint only.

Analysis of secondary endpoints

PROMs (NRS-BP, NRS-LP, ODI, EQ-5D) are analysed using baseline-adjusted linear mixed models. The mean overall effect over time, as well as effects at the specific follow-up timepoints, are estimated. The proportions of patients achieving MCID for each PROM, as well as proportions of patients reporting satisfaction, return to work, reoperations and using analgesic medication are reported. MCIDs for the ODI, NRS-BP and NRS-LP are defined as a reduction of ≥30% according to Ostelo *et al*.[50] The MCID threshold for the EQ-5D is set to 0.2 points according to Asher *et al*.[51] Return to work and overall reoperations are statistically analysed using crude and adjusted Cox proportional hazards models. In addition, intergroup comparison is performed for patient satisfaction and use of analgesic medication by logistic regression.

Subgroup analysis

Prespecified subgroup analyses of the primary outcome are performed in the intention to-treat population to test for an interaction between study group and the subgroup variable. Stratified analyses are performed by indication for surgery, specific device used,[16] type of exposure, as well as single-level or multilevel fusion.

Monitoring

Monitoring is performed according to the prespecified monitor plan. An epidemiologist from the sponsor institution organises an initiation monitor visit at every participating centre before starting recruitment. This monitor visit checks whether all study staff are properly trained and the delegation of tasks are well documented (complete Investigator Site File, training and delegation logs). An additional audit is carried out at 6 months after initiation of recruitment to check whether source documentation and eCRF documentation is similar. Throughout the entire study, additional queries by the monitor are sent to the investigator in the data capturing system to ensure proper data capturing.

Expected completion

Recruitment is expected to be completed by January 2021, with the 2-year follow-up period extending to January 2023 for the final results.

ETHICS AND DISSEMINATION

Ethical approval and study registration

The study protocol is approved by the appropriate national and local authorities. Written informed consent is obtained from all participants. This study is registered at ClinicalTrials.gov under the identifier NCT03398915.

Dissemination

The final results will be published in an international peer-reviewed scientific journal, and communicated to study participants. No interim analyses have been specifically planned. To avoid any bias, the results of any interim analyses are neither shared with the investigators nor published until recruitment has been completed. There are no further restrictions to publication.

DISCUSSION

The EUROSPIN study is a large, multicentre, pragmatic study that is aimed at resolving the discussion on whether computer assistance in thoracolumbar instrumentation leads to measurable and clinically relevant improvements in patient-reported clinical outcome or complication rate.

Previous studies have created some evidence that both RG and navigation lead to a somewhat higher radiological accuracy than FH pedicle screw insertion, with inconsistent results at a rather low level of evidence.[12 14 16–21 23] It is still unclear whether this increased radiological accuracy, usually measured as the degree of deviation from the desired transpedicular trajectory, translates to a clinical benefit to patients. It is hypothesised that, when using computer assistance, the lower rate of pedicular cortical encroachment leads to a lower incidence of radiculopathy,[24 52] thus preventing revision surgery,[6] decreasing overall treatment costs[53] and improving overall patient-oriented outcomes.[38] A meta-analysis has demonstrated that both RG and navigation lower the incidence of revision surgery for malpositioned pedicle screws.[5] However, the rate of intraoperative screw revisions was markedly but not statistically significantly increased, the quality of the included individual studies was low, and it was determined that prospective studies assessing this research question with larger sample sizes are necessary to draw conclusions.[5] In addition, there are only very few, small studies comparing RG to navigation directly.[29 54] For these reasons, we designed our study to address these biases, and to provide higher-level evidence on clinical questions, comparing all three concepts of pedicle screw placement.

A specific goal of the EUROSPIN trial is to avoid potential conflicts of interest.[55] Therefore, we decline any sort of direct involvement and study-related financial support by the industry, and aim to minimise personal conflict of interests with device manufacturers. This may enable execution and critical appraisal of the study results with less bias.[55 56]

The study has some limitations. First, for logistical and practical reasons, not all sites are able to contribute to all three study arms. This may create centre bias. However, the rationale for this design is to prospectively collect data obtained from surgeons experienced with the three techniques, resulting in a design similar to a prospective multicentre registry. Furthermore, we are unable to conduct a detailed evaluation of cost-effectiveness. The cost–value relationship of robotic and intraoperative imaging systems remains controversial, and it is as of yet unclear if there are any demonstrable clinical benefits that warrant the high acquisition and maintenance costs inherent to these systems.[22] In addition, preoperative radiation that may be required for surgical planning may differ among the groups, and is not captured. In this light, it is important to consider that, even if the navigated and robotic techniques would result in decreased intraoperative radiation, this benefit to the patient may be levelled out by the additional radiation dose necessary for planning.

Furthermore, although all participating surgeons are experienced with the respective techniques applied, as we do not specify a minimum case number for participating surgeons, surgeon experience may constitute a potential bias. We aim to correct for this potential bias by collecting data on the degree of experience of the surgeons placing the pedicle screws, which allows for statistical adjustment if necessary. Another potential limitation exists in the fact that thresholds for revision of a malpositioned or loosened screw may vary among centres and surgeons. Moreover, our study is likely underpowered for subgroup analyses analysing treatment effects among the single devices and the different indications for surgery. Lastly, some potential confounders such as comorbidities and symptom duration are not collected.

Patients are not randomly assigned to treatment groups in the EUROSPIN study. As detailed above, there are two main reasons that randomisation was deemed disadvantageous in this specific study. First, most centres do not have both a robotic system and conventional neuronavigation available, making it impossible to randomise to all three groups at every centre. Furthermore, we aim to have the surgeons perform the procedures with the technique they are most experienced with.[27 31 36] This enables us to compare the treatment modalities in a more clinically applicable scenario, assessing effectiveness instead of study-specific efficacy, similar to a prospective registry.[33] Accordingly, no learning curve phase was implemented. Even for randomised studies, Devereaux *et al* suggest that surgeon-based or 'expertise-based' group assignment, in which patients are not randomised to treatments but rather to clinicians experienced with a certain treatment, may lead to greater real-world applicability of study results.[31] In addition, some commenced randomised trials comparing robotic surgery with conventional techniques have had to be declared futile due to slow recruitment, usually because of a patient preference towards newer techniques. A split design, similar to the Spine Patient Outcomes Research Trial, with a randomised and non-randomised subgroup was available as an alternative.[57] However, due to the aforementioned logistic difficulties and possible bias in experience, we have decided on a simple, registry-like design for the EUROSPIN study.

Author affiliations
[1]Department of Neurosurgery, Bergman Clinics Amsterdam, Amsterdam, The Netherlands
[2]Department of Neurosurgery, Clinical Neuroscience Center, University Hospital Zurich, University of Zurich, Zurich, Switzerland
[3]Amsterdam UMC, Vrije Universiteit Amsterdam, Neurosurgery, Amsterdam Movement Sciences, Amsterdam, The Netherlands
[4]Department of Neurosurgery, Geneva University Hospitals, Geneva, Switzerland
[5]Department of Epidemiology, Bergman Clinics Amsterdam, Amsterdam, The Netherlands
[6]Department of Neurosurgery, La Pitié Salpétrière Hospital, Paris, France
[7]Department of Neurosurgery, Medical Center, Georg August University of Göttingen, Göttingen, Germany, Göttingen, Germany
[8]Department of Neurosurgery, Haaglanden Medical Center, Den Haag, The Netherlands
[9]Center for Spinal Surgery and Pain Therapy, Ortho-Klinik Dortmund, Dortmund, Germany
[10]Department of Spinal Surgery, St. Josef Brothers Hospital, Paderborn, Germany
[11]Department of Neurosurgery, Martini Hospital, Groningen, , Netherlands
[12]Department of Neurosurgery, Amiens University Hospital, Amiens, , France
[13]Department of Neurosurgery, Clinique de la Source, Lausanne, Switzerland
[14]Department of Neurosurgery, Klinikum rechts der Isar, Technical University Munich, Munich, Germany
[15]Department of Neurosurgery, HELIOS Klinikum Berlin-Buch, Berlin, Germany
[16]Department of Neurosurgery, Medical University of Innsbruck, Innsbruck, Austria
[17]Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Epidemiology and Biostatistics, Amsterdam, The Netherlands

Twitter @staartjesneuro

Contributors VES, GM, PMvK, ET and MLS conceived and designed the study. VES, PMvK and JWRT conceived the statistical analysis plan. VES, GM, PMvK, ET and MLS prepared the first draft of the study protocol. VES, GM, PMvK, HAJE, AA, CB, JFCW, SU, FH, CGS, MAS, ML, JP, DB, IF, BS, VR, Y-MR, SMK, BM, NK, P-PG, CT, JWRT, ET and MLS contributed to the final design of this study protocol, assisted with drafting the manuscript and carried out a critical revision of the manuscript. VES, GM, PMvK, HAJE, AA, CB, JFCW, SU, FH, CGS, MAS, ML, JP, DB, IF, BS, VR, Y-MR, SMK, BM, NK, P-PG, CT, JWRT, ET and MLS approved the final version of the manuscript and agree to be accountable for the accuracy of the work. MLS supervised the work and is the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests VES, GM, PMvK, ET and MLS conceived and designed the study. VES, PMvK and JT conceived the statistical analysis plan. VES, GM, PMvK, ET and MLS prepared the first draft of the study protocol. VES, GM, PMvK, HAJE, AA, CB, JFCW, SU, FH, CGS, MAS, ML, JP, DB, IF, BS, VR, Y-MR, SMK, BM, NK, P-PG, CT, JT, ET and MLS contributed to the final design of this study protocol, assisted with drafting the manuscript and carried out a critical revision of the manuscript. VES, GM, PMvK, HAJE, AA, CB, JFCW, SU, FH, CGS, MAS, ML, JP, DB, IF, BS, VR, Y-MR, SMK, BM, NK, P-PG, CT, JT, ET and MLS approved the final version of the manuscript and agree to be accountable for the accuracy of the work. MLS supervised the work and is the guarantor.

Ethics approval The study protocol is approved by the appropriate national and local authorities.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. Goz V, Weinreb JH, McCarthy I, *et al*. Perioperative complications and mortality after spinal fusions: analysis of trends and risk factors. *Spine* 2013;38:1970–6.
2. Härtl R, Lam KS, Wang J, *et al*. Worldwide survey on the use of navigation in spine surgery. *World Neurosurg* 2013;79:162–72.
3. Goldstein CL, Phillips FM, Rampersaud YR. Comparative effectiveness and economic evaluations of open versus minimally invasive posterior or Transforaminal lumbar interbody fusion. *Spine* 2016;41(Suppl 8):1–89.
4. Nolte L-P, Zamorano L, Visarius H, *et al*. Clinical evaluation of a system for precision enhancement in spine surgery. *Clin Biomech* 1995;10:293–303.
5. Staartjes VE, Klukowska AM, Schröder ML. Pedicle screw revision in Robot-Guided, Navigated, and Freehand thoracolumbar instrumentation: a systematic review and meta-analysis. *World Neurosurg* 2018;116:433–43.
6. Schröder ML, Staartjes VE. Revisions for screw malposition and clinical outcomes after robot-guided lumbar fusion for spondylolisthesis. *Neurosurg Focus* 2017;42:E12.
7. Togawa D, Kayanja MM, Reinhardt MK, *et al*. Bone-mounted miniature robotic guidance for pedicle screw and translaminar facet screw placement: part 2--Evaluation of system accuracy. *Neurosurgery* 2007;60(2 Suppl 1):ONS129–39. Discussion ONS139.
8. Lieberman IH, Togawa D, Kayanja MM, *et al*. Bone-mounted miniature robotic guidance for pedicle screw and translaminar facet screw placement: Part I--Technical development and a test case result. *Neurosurgery* 2006;59:641–50. Discussion 641-650.
9. Wang MY, Goto T, Tessitore E, *et al*. Introduction. robotics in neurosurgery. *Neurosurg Focus* 2017;42:E1.
10. Fujishiro T, Nakaya Y, Fukumoto S, *et al*. Accuracy of pedicle screw placement with robotic guidance system. *Spine* 2015;40:1882–9.
11. Pechlivanis I, Kiriyanthan G, Engelhardt M, *et al*. Percutaneous placement of pedicle screws in the lumbar spine using a bone mounted miniature robotic system: first experiences and accuracy of screw placement. *Spine* 2009;34:392–8.
12. Gelalis ID, Paschos NK, Pakos EE, *et al*. Accuracy of pedicle screw placement: a systematic review of prospective in vivo studies comparing free hand, fluoroscopy guidance and navigation techniques. *Eur Spine J* 2012;21:247–55.
13. Devito DP, Kaplan L, Dietl R, *et al*. Clinical acceptance and accuracy assessment of spinal implants guided with SpineAssist surgical robot. *Spine* 2010;35:2109–15.
14. Ringel F, Stüer C, Reinke A, *et al*. Accuracy of robot-assisted placement of lumbar and sacral pedicle screws: a prospective randomized comparison to conventional freehand screw implantation. *Spine* 2012;37:E496–501.
15. van Dijk JD, van den Ende RPJ, Stramigioli S, *et al*. Clinical pedicle screw accuracy and deviation from planning in robot-guided spine surgery: robot-guided pedicle screw accuracy. *Spine* 2015;40:E986–91.
16. Du JP, Fan Y, Wu QN, *et al*. Accuracy of pedicle screw insertion among 3 image-guided navigation systems: systematic review and meta-analysis. *World Neurosurg* 2018;109:24–30.
17. Marcus HJ, Cundy TP, Nandi D, *et al*. Robot-Assisted and fluoroscopy-guided pedicle screw placement: a systematic review. *Eur Spine J* 2014;23:291–7.
18. Kosmopoulos V, Schizas C. Pedicle screw placement accuracy: a meta-analysis. *Spine* 2007;32:E111–20.
19. Shin BJ, James AR, Njoku IU, *et al*. Pedicle screw navigation: a systematic review and meta-analysis of perforation risk for computer-navigated versus freehand insertion. *J Neurosurg* 2012;17:113–22.
20. Tian N-F, Huang Q-S, Zhou P, *et al*. Pedicle screw insertion accuracy with different assisted methods: a systematic review and meta-analysis of comparative studies. *Eur Spine J* 2011;20:846–59.
21. Gao S, Lv Z, Fang H. Robot-assisted and conventional freehand pedicle screw placement: a systematic review and meta-analysis of randomized controlled trials. [Review]. *Eur Spine J* 2017;1.
22. Fiani B, Quadri SA, Farooqui M, *et al*. Impact of robot-assisted spine surgery on health care quality and neurosurgical economics: a systemic review. *Neurosurg Rev* 2018;39.
23. Fichtner J, Hofmann N, Rienmüller A, *et al*. Revision rate of misplaced pedicle screws of the thoracolumbar -comparison of three-dimensional fluoroscopy navigation with Freehand placement: a systematic analysis and review of the literature. *World Neurosurg* 2018;109:e24–32.
24. Gautschi OP, Schatlo B, Schaller K, *et al*. Clinically relevant complications related to pedicle screw placement in thoracolumbar surgery and their management: a literature review of 35,630 pedicle screws. *Neurosurg Focus* 2011;31:E8.
25. Molliqaj G, Schatlo B, Alaid A, *et al*. Accuracy of robot-guided versus freehand fluoroscopy-assisted pedicle screw insertion in thoracolumbar spinal surgery. *Neurosurg Focus* 2017;42:E14.
26. Schatlo B, Molliqaj G, Cuvinciuc V, *et al*. Safety and accuracy of robot-assisted versus fluoroscopy-guided pedicle screw insertion for degenerative diseases of the lumbar spine: a matched cohort comparison. *J Neurosurg* 2014;20:636–43.
27. Schatlo B, Martinez R, Alaid A, *et al*. Unskilled unawareness and the learning curve in robotic spine surgery. *Acta Neurochir* 2015;157:1819–23. Discussion 1823.
28. Solomiichuk V, Fleischhammer J, Molliqaj G, *et al*. Robotic versus fluoroscopy-guided pedicle screw insertion for metastatic spinal disease: a matched-cohort comparison. *Neurosurg Focus* 2017;42:E13.
29. Roser F, Tatagiba M, Maier G. Spinal robotics: current applications and future perspectives. *Neurosurgery* 2013;72(Suppl 1):12–18.
30. Siccoli A, Klukowska AM, Schröder ML, *et al*. A systematic review and meta-analysis of perioperative parameters in Robot-Guided, Navigated, and Freehand thoracolumbar pedicle screw instrumentation. *World Neurosurg* 2019;127:576–87.
31. Devereaux PJ, Bhandari M, Clarke M, *et al*. Need for expertise based randomised controlled trials. *BMJ* 2005;330.
32. Ford I, Norrie J, Trials P. Pragmatic trials. *N Engl J Med* 2016;375:454–63.
33. Haynes B. Can it work? does it work? is it worth it? *BMJ* 1999;319:652–3.
34. Chan A-W, Tetzlaff JM, Gøtzsche PC, *et al*. Spirit 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
35. Hu X, Lieberman IH. What is the learning curve for robotic-assisted pedicle screw placement in spine surgery? *Clin Orthop Relat Res* 2014;472:1839–44.
36. Ryang Y-M, Villard J, Obermüller T, *et al*. Learning curve of 3D fluoroscopy image-guided pedicle screw placement in the thoracolumbar spine. *Spine J* 2015;15:467–76.
37. Härtl R. Comment to the article: "Tubular diskectomy vs conventional microdiskectomy for sciatica: a randomized controlled trial". *Minim Invasive Neurosurg* 2010;53:95–6.
38. Hyun S-J, Kim K-J, Jahng T-A, *et al*. Minimally invasive robotic versus open fluoroscopic-guided spinal instrumented fusions. *Spine* 2017;42:353–8.
39. Kim H-J, Jung W-I, Chang B-S, *et al*. A prospective, randomized, controlled trial of robot-assisted vs freehand pedicle screw fixation in spine surgery. *Int J Med Robotics Comput Assist Surg* 2017;13.
40. Villard J, Ryang Y, Demetriades A, *et al*. Radiation exposure to the surgeon and the patient during posterior lumbar spinal instrumentation: a prospective randomized comparison of navigated versus non-navigated freehand techniques. *Spine* 2014;39:1004–9.
41. Houten JK, Nasser R, Baxi N. Clinical assessment of percutaneous lumbar pedicle screw placement using the O-arm multidimensional surgical imaging system. *Neurosurgery* 2012;70:990–5.
42. Shin M-H, Hur J-W, Ryu K-S, *et al*. Prospective comparison study between the Fluoroscopy-guided and navigation coupled with O-arm-guided pedicle screw placement in the thoracic and lumbosacral spines. *J Spinal Disord Tech* 2015;28:E347–51.
43. Gertzbein SD, Robbins SE. Accuracy of pedicular screw placement in vivo. *Spine* 1990;15:11–14.
44. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol group. *Ann Med* 2001;33:337–43.
45. Lamers LM, Stalmeier PFM, McDonnell J, *et al*. [Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff]. *Ned Tijdschr Geneeskd* 2005;149:1574–8.
46. Schröder ML deWMP, Staartjes VE. Are patient-reported outcome measures biased by method of follow-up? evaluating paper-based and digital follow-up after lumbar fusion surgery. *Spine J Off J North Am Spine Soc* 2019;19:65–70.

47. Fleiss JL, Tytun A, Ury HK. A simple approximation for calculating sample sizes for comparing independent proportions. *Biometrics* 1980;36:343–6.
48. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R foundation for statistical computing, 2018. Available: https://www.R-project.org/
49. Staartjes VE, Siccoli A, de Wispelaere MP, *et al*. Patient-Reported outcomes unbiased by length of follow-up after lumbar degenerative spine surgery: do we need 2 years of follow-up? *Spine J* 2019;19:637–44.
50. Ostelo RWJG, Deyo RA, Stratford P, *et al*. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine* 2008;33:90–4.
51. Asher AL, Kerezoudis P, Mummaneni PV, *et al*. Defining the minimum clinically important difference for grade I degenerative lumbar spondylolisthesis: insights from the quality outcomes database. *Neurosurg Focus* 2018;44:E2.
52. Woo EJ, DiCuccio MN. Clinically significant pedicle screw malposition is an underestimated cause of radiculopathy. *Spine J* 2017;0.
53. Watkins RG, Gupta A, Watkins RG. Cost-Effectiveness of image-guided spine surgery. *Open Orthop J* 2010;4:228–33.
54. Laudato PA, Pierzchala K, Schizas C. Pedicle screw insertion accuracy using O-Arm, robotic guidance, or Freehand technique: a comparative study. *Spine* 2018;43:E373–8.
55. Staartjes VE, Klukowska AM, Sorba EL, *et al*. Conflicts of interest in randomized controlled trials reported in neurosurgical journals. *J Neurosurg* 2019;11.
56. Azad TD, Veeravagu A, Mittal V, *et al*. Neurosurgical randomized controlled Trials-Distance travelled. *Neurosurgery* 2018;82:604–12.
57. Birkmeyer NJO, Weinstein JN, Tosteson ANA, *et al*. Design of the spine patient outcomes research trial (sport). *Spine* 2002;27:1361–72.