

Three-dimensional Printing in Spine Surgery: Protocol of a Systematic Review and Meta-analysis

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Protocol

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Abstract

Background

The complexity and diversity of spine pathology lead to the complexity and diversity of spinal surgery. The emergence and application of three-dimensional printing (3DP) technology has brought good news to surgeons and patients. However, the use of 3DP in spinal surgery remains controversial. Therefore, this study was designed to investigate whether 3D printing technology is beneficial for spinal surgery.

Methods

Three English online databases including EMBASE (via embase.com), Medline (via PubMed), and Cochrane Central Register of Controlled Trials (CENTRAL) will be searched from inception until August 31, 2020. Document records retrieved according to the pre-defined search strategy will be managed by EndNote X7. The MINORST (methodological index for non-randomized studies) item recommended for non-randomized controlled interventional studies in surgery will be used to assess the quality of non-randomized controlled studies. The "Risk of bias" (ROB) table will be used to assess the quality of randomized controlled studies. The data extraction will be completed by two authors independently, one of whom extracts and the other checks. If there is any missing data, original author will be contacted to obtain the data required. Any inconsistencies were agreed upon by discussion with a third investigator. If the collected data can be synthesized, Review Manager (RevMan5.3) will be used to estimate the overall effect of 3DP for Spinal surgery. Otherwise, only the qualitative analysis will be carried out. According to the results of clinical heterogeneity test, random effects model or fixed effects model will be used for data synthesis. The sources of clinical heterogeneity will be explored by meta-regression and subgroup analysis. If more than 10 studies are included, funnel plots will be used to assess the publication bias. This review will be carried out in strict accordance with Cochrane Handbook for Systematic Reviews of Interventions.

Conclusion

This study will can provide surgeons and patients with evidence-based evidence for the use of 3D printing technology in spinal surgery.

Systematic review registration

PROSPERO/ID = CRD42020204053.

Background

Description of Condition

The causes of spine pathology are varied including tumors, fractures, scoliosis, degeneration, and infections [1,2]. The purpose of spine surgery is to restore mechanical conduction and restore normal

structure [1-4]. All spinal surgeries have different complex aspects that require a variety of complex techniques to address. The operation method and detailed procedures of the operation are affected by the adjacent inherent anatomical structure, disease characteristics and the technical level of the surgeon [5]. Therefore, the above factors must be carefully considered in the preparation of preoperative planning. And, spinal surgeons must be able to deal with these complex issues. A solid knowledge of anatomy is the key to solving complex surgical problems, which involve a long and steep learning curve. Visualization techniques such as computerized tomography (CT)-based, X-ray based and navigating techniques are used to help analyze and make an operation plan. However, there are some drawbacks to using these techniques, such as high radiation exposure to patients and operators, prolonged operation time, and high cost [6,7].

Description of Intervention

Three-dimensional printing (3DP) technique, also known as additive manufacturing technique, was first used in industry for printing new products, and then introduced into medicine [8]. It is based on the three-dimensional (3D) digital model file, slices the 3D data according to the set layer thickness to form a series of two-dimensional (2D) contour layers. Under the control of the computer, the machine prints the materials layer by layer according to the requirements of the two-dimensional contour layer and glues them together to create three-dimensional objects [9]. Nowadays, 3DP technology has gained popularity in many aspects of spinal surgery.

How can 3DP benefit spinal surgery?

Although two-dimensional imaging has become the standard imaging method in spinal surgery, the spine is a three-dimensional object with complex anatomical structures and relationships, which cannot be fully understood in two-dimensional imaging[10]. Moreover, due to the poor accuracy and the lack of real-time monitoring of two-dimensional imaging technology, surgeons usually use long-term and repeated fluoroscopy to improve the accuracy and safety of the operation. While, the application of 3DP technology not only enables surgeons to have a more comprehensive understanding of the complex spinal anatomy and pathological changes, but also enables surgeons to experience the surgical process virtually, formulate more appropriate preoperative plans to ensure the safety and efficacy of surgery[11,12]. In addition to the advantages reported above, the application of 3DP technology in spinal surgery has the following advantages: 1) Facilitate communication between surgeons and patients or guardian; 2) Shortening operation time; 3) Reduce radiation doses for doctors and patients; 4) Reduce intraoperative blood loss[10].

In short, the emergence and development of 3DP technology enables the surgical treatment team to improve preoperative planning, practice and explore various surgical methods, as well as custom surgical tools and the design of patient-specific implants.

Why this review is important?

Currently, a number of studies have shown that 3D printing technology can benefit spinal surgery. In the study of Wu and his colleagues [13], sixty-two patients with hemivertebra had undergone spinal surgery either by the 3DP technique or the conventional intraoperative fluoroscopy technique. Accuracy of pedicle screw placement was evaluated. The results showed that compared with the C-arm group, the 3D assisted surgery group had higher accuracy and shorter operation time. A recent study that objective is to compare the clinical effect of 3DP technology and X-ray assisted surgical placement of sacroiliac screws showed that compared with traditional surgery, 3D printing technology has the advantages of shortening the operation time and reducing the number of X-ray irradiations [7]. A retrospective study compared 3DP template-assisted screw placement and the C-arm based navigation-assisted screw placement group of C2 Pedicle or Pars Screw Placement shows that 3D printing assisted surgery and traditional surgery are similar in terms of safety and clinical superiority, but the accuracy of surgical screw implantation with the assistance of 3D printing is higher [14]. The similar result was also confirmed in other studies [15,16].

Meanwhile, there are some different voices. In many studies, the time required to plan and create a 3D model is seen as an obstacle. The 3DP process itself, including the creation of computer-aided design (CAD) models on the software, usually takes 10 to 12 hours. This makes 3DP technology unsuitable for emergency cases and hospitals with high output and high turnover [17]. The cost of purchasing 3D printing equipment is considerable for any hospital, not to mention those hospitals with few cases of complicated spinal surgery. These costs include the purchase of CAD software, cameras, purchase and maintenance of 3D printers, and other auxiliary costs. Usually, the time cost and economic cost of training professionals who can use CAD software are also factors that must be considered [18]. Due to the diversity of printer manufacturers and material manufacturers, the quality of the biological materials used to make 3D printing tools or implants is still questionable. Since 3D printed implants have only been used in the past ten years or so, data on their long-term safety are missing, which is also a problem in the application of 3DP technology [19].

Therefore, it is necessary to conduct a comprehensive and systematic evaluation of the pros and cons of 3DP technology in spinal surgery, in order to provide evidence-based basis for medical and health policy makers, hospital administrators, clinicians, patients and their families.

Methods

Design and registration

The design and implementation of this protocol were conducted in strict accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P) statement (checklist in Additional file 1) [20]. The protocol of this study was registered in the international prospective register of systematic reviews (PROSPERO). The unique registration ID is CRD42020204053.

Selection criteria

Type of participants

All patients undergoing spinal surgery will be included in this study. There is no limitation on age, gender, nature of disease, focus of disease, etc.

Type of intervention

All clinical studies that used 3DP for preoperative planning and spinal surgery procedures will be included in this study. The 3DP equipment, software and materials are not restricted. Control interventions in the control group was traditional spinal surgery without 3DP including CT-based computer-assisted guide system, X-ray fluoroscopy, and other methods. For the studies that comparison of two experimental interventions with no control intervention group will be excluded.

Type of Outcomes

The primary outcomes include the accuracy and precision, perioperative blood-loss volume, and X-ray fluoroscopy times. Other outcomes such as complications, the operation time, Visual analogue scale (VAS), Japanese Orthopedic Association (JOA), the Neck Disability Index (NDI), hospitalization length, and patient expenditures were defined as secondary outcomes.

Type of studies

Randomized controlled trials (RCTs), case-control studies, and cohort studies concerning the use of 3D printing in spinal surgery will be included in this review. The reviews, abstracts, case reports, case series, editorials and opinion pieces, letters to the editor will be excluded in this review. This review will exclude non-clinical research such as laboratory research, animal research, and cadaver research, etc. The studies that 3D printing technology was not used for spine surgery planning or surgery procedures such as education, surgical, and simulation purposes, etc. will be excluded. The studies that 3D printing technology was used to develop patient-specific instrumentation (PSI) (e.g. cutting jigs etc.) also will be excluded. Only the studies that published using English will be included.

Search methods

Online databases

Three English online databases will be searched from inception until August 31, 2020. They are EMBASE (via embase.com), Medline (via PubMed), and Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library. The English terms were used individually or combined “three-dimensional printing (3DP),” “additive manufacturing technique,” “rapid prototyping (RP),” “spine,” “spinal fusion,” “spinal surgery”.

Additional resources

Other literature materials will be obtained by searching the reference list of qualified studies.

Data management and processing

Document collection and management

Document records retrieved according to the pre-defined search strategy will be imported into the document manager, EndNote X7. Duplicate document records will be identified and deleted based on related information such as title, publication date, author, and periodical, etc. The titles and abstracts of the remaining literature will be reviewed and studies that might meet the inclusion criteria will be identified by two independent authors. After two authors read the full text of the literature independently, qualified literature will be included according to the inclusion criteria established in this study. The final decision will be made via through group discussion with a third reviewer if there is uncertainty at this stage. The process of study inclusion will be carried out and reported in accordance with the PRISMA flow diagram (Fig. 1).

Data extraction (selection and coding)

The data extraction process will be completed by two authors. A reviewer will use a tabular summary to guide extraction and record the data and the other author will check it. The following information for each report will be extracted: 1) General information such as country, region, author, title, journal, publication date, etc., 2) Information about the research object such as the source of patients, the nature of the disease, the severity of the disease, and the location of the disease, etc., 3) Information related to the operation, such as the location of the operation, the method of the operation, the level of the surgeon, the biological materials that may be used in the operation, etc., 4) Information related to outcome evaluation, such as outcome evaluation indicators, outcome evaluation tools, outcome evaluation time, follow-up information, etc., 5) Information related to study design, such as randomized controlled studies, case-control studies, cohort studies, etc.

Conversion to the desired format of the data will be performed before data analysis, for example, standard error will be converted into standard deviation. For the studies that are not pair-wise comparisons of interventions, the data of two groups that best meet the inclusion criteria will be extracted. The Cochrane review writing soft (RevMan5.3) will be used to manage and synthesize data. The final decision will be made via through group discussion with a third reviewer if there is uncertainty at this stage.

Risk of bias (quality) assessment

The MINORST (methodological index for non-randomized studies) item recommended for non-randomized controlled interventional studies in surgery will be used to assess the quality of non-randomized controlled studies. The "Risk of bias" (ROB) table will be used to assess the quality of randomized controlled studies [21]. This stage will be completed independently by two authors. The final decision will be made via through group discussion with a third reviewer if there is uncertainty at this stage.

Handling of missing data

When encountering missing data at any stage, we will do our best to obtain the required data, including but not limited to contacting the original author via email. If data acquisition fails, only the available data will be analyzed. The potential impact of missing data on the final composite result will be discussed in the discussion section.

Identifying and addressing heterogeneity

The chi-squared test will be used to identify whether observed differences in results are compatible with chance alone. The inconsistency across studies will be quantified using I^2 statistic to assess its impact on the meta-analysis. When I^2 value is less than 75%, which means that the included studies have good homogeneity, the overall effect will be synthesized in a meta-analysis. Otherwise, a series of measures will be performed to deal with heterogeneity such as check the data, perform subgroup analysis, carry out meta-regression, perform a random-effects meta-analysis, change the effect measure and exclude the studies, etc.

Detecting reporting biases

Funnel plots asymmetry will be used to distinguish the reporting biases only when there are at least 10 studies included in the meta-analysis for each outcome respectively, because when the number of studies is too small, the test power is too low to identify true asymmetry³². Potential source of funnel plot asymmetry will be mainly considered from the following aspects: differences in methodological, intervention effects, language biases, location biases, delayed publication, etc. The different possible reason for funnel plots asymmetry will be interpreted and discussed in part of discussion for this study.

Planning the analysis

An overall statistic will be performed using Cochrane Review Manager (Revman5.3) if quantitative synthesis is appropriate. One preferred method for each outcome, the fixed-effect method or the random-effect, will be performed based on whether there is heterogeneity between studies. Otherwise, only the qualitative analysis will be performed.

Subgroup analysis

Subgroup analysis will be undertaken base on the results of heterogeneity test and the number of included studies for each outcome. Subgroup analyses will be done for subsets of interventions (such as different surgical approaches), subsets of patients (such as children, adolescent, adult, and elderly), subsets of surgical sites (cervical spine, lumbar spine, thoracic spine).

Sensitivity analysis

Sensitivity analysis will be done to identify whether the overall results and conclusion are affected by the different decisions that could be made during the review process. It will be undertaken completed in two steps: first, including all included studies in the meta-analysis, and second, deleting the poor quality

studies (such as small size, low methodological design, ultra-wide confidence interval, etc.) to identify the influence of special studies on the overall results and the conclusions.

Grading the quality of evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system will be used to evaluate the quality of evidence for outcomes which rate the quality as very low, low, moderate, or high levels.

Discussion

The diversity of pathological changes in the spine leads to the complexity of spinal surgery. The method of spinal surgery is affected by many factors, among which the anatomical structure of adjacent tissues is the most critical factor. Although 2D visualization techniques such as CT scan and X-ray scan have been used to help surgeons better understand the anatomical knowledge involved in spinal surgery and formulate appropriate surgical plans, the application of these technologies has many drawbacks, such as excessive radiation exposure dose for patients and doctors, longer operation time. The application of 3D printing technology in spinal surgery has brought good news to doctors and patients. It can not only help doctors make more suitable surgical plans and virtual preoperative exercises, but also improve the accuracy of the operation, shorten the operation time, reduce the amount of intraoperative blood loss, and reduce the intraoperative radiation exposure dose. However, there are still some controversies about the application of 3DP technology in spinal surgery, such as its high cost, personnel training cost, material diversity and safety. Therefore, it is very necessary to conduct a comprehensive and systematic assessment of the pros and cons of 3DP technology in spinal surgery.

This study can comprehensively and systematically evaluate the advantages and disadvantages of 3DP technology in spinal surgery. The results of this study can provide evidence-based evidence for medical and health policy makers, hospital administrators, surgeons, patients and their families, with a view to providing help in considering the application of 3DP technology in spinal surgery.

Strict program design and implementation ensure the reliability of the research results. However, there are some issues that we have to pay attention to. First of all, although we will identify and analyze clinical heterogeneity, even if the included subjects have the same pathological changes of the spine, the complexity and location of the disease will still bring about clinical heterogeneity that cannot be dealt with. Secondly, different surgical methods can also lead to clinical heterogeneity between studies. Furthermore, the level of diagnosis and treatment of surgeons and their medical institutions is also one of the sources of clinical heterogeneity. Finally, different 3DP equipment and materials may cause instability in research results.

Abbreviations

3DP, three-dimensional printing; CT, computerized tomography; 2D, two-dimensional; CAD, computer-aided design; VAS, Visual analogue scale; JOA, Japanese Orthopedic Association; NDI, the Neck Disability Index; RCTs, randomized controlled trials; ROB, Risk of bias.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: Not applicable.

Competing interests: All authors declare that they have no conflict of interest.

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Authors' contributions: J.L.L. and L.Y.L. conceived and designed the study; G.L.X. and T.W. wrote the draft manuscript; B.J. and C.Y.Y. developed the search strategy; X.P. X., H.M. S., and J. L., made the manuscript preparation; D.G. L. and Y. S. performed preliminary literature search. All authors contributed to draft the manuscript and have read and approved the final manuscript.

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Figures

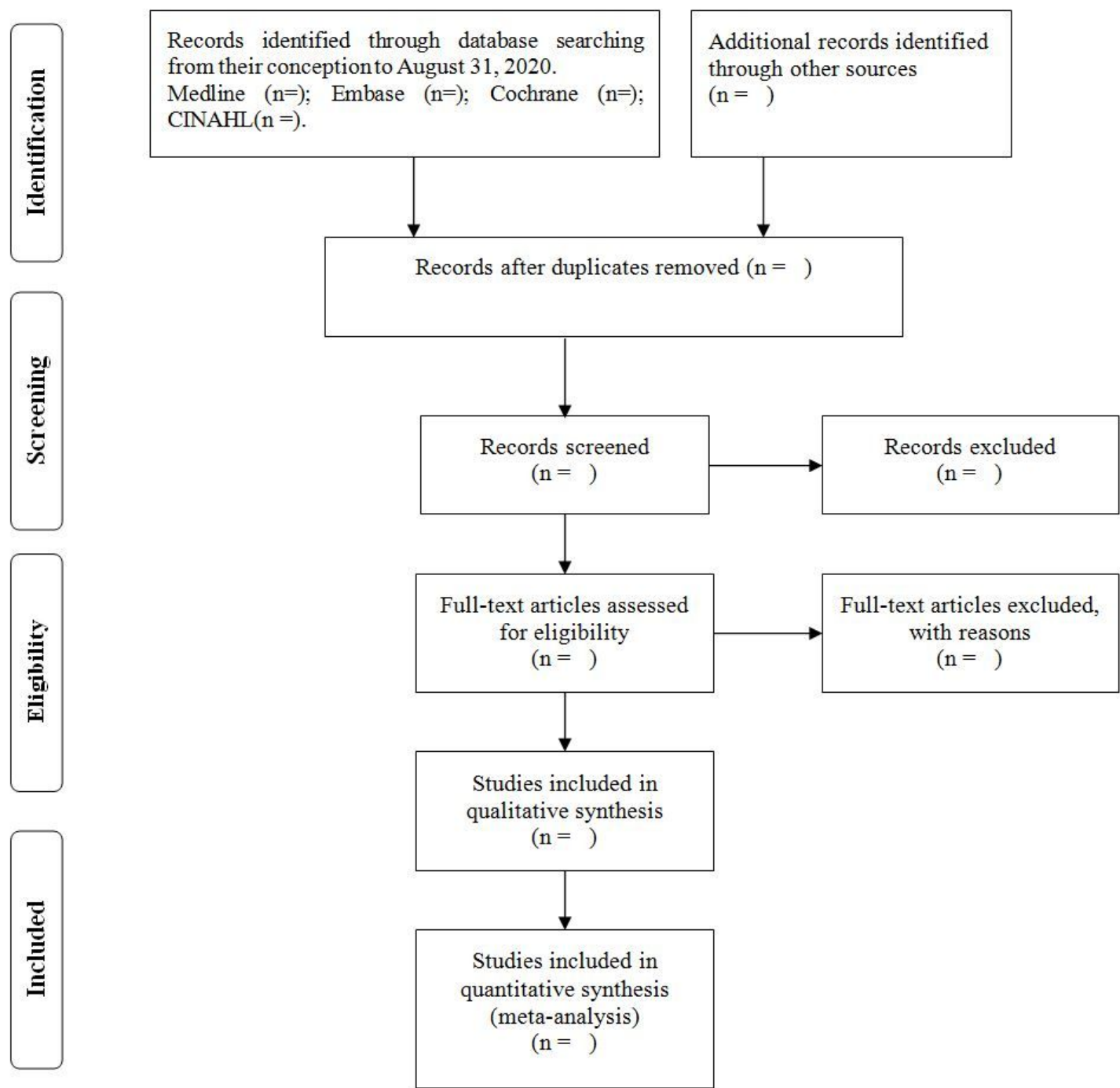


Figure 1
Flow diagram of the study selection process

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