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ORIGINAL ARTICLE

Pedicle screw insertion with patient-specific 3D-printed guides based on low-dose CT scan is more accurate than free-hand technique in spine deformity patients: a prospective, randomized clinical trial

Riccardo Cecchinato[1] · Pedro Berjano[1] · Alberto Zerbi[1] · Marco Damilano[1] · Andrea Redaelli[1] · Claudio Lamartina[1]

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Abstract

Background Screw misplacement incidence can be as high as 15–30% in spine deformity surgery, with possible devastating consequences. Some technical solutions to prevent misplacement require expensive devices. MySpine^{TM} comprises a low-dose CT scan of the patient's spine to build a virtual model of the spine to plan the screw trajectories and a 3D-printed patient-specific guide system to prepare the screw trajectories and to implant the screws in the vertebrae in order to increase reproducibility and safety of the implants. The aim of this open-label, single-center, prospective randomized clinical trial with independent evaluation of outcomes was to compare the accuracy of free-hand insertion of pedicle screws to MySpine^{TM} 3D-printed patient-specific guides.

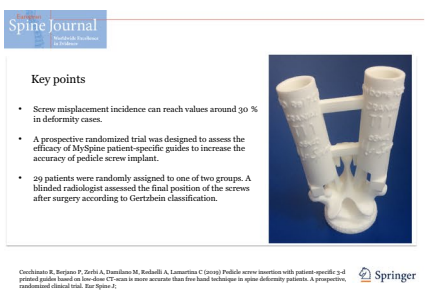
Methods Twenty-nine patients undergoing surgical correction for spinal deformity were randomized to Group A (pedicle screws implantation with MySpine^{TM}) or Group B (free-hand implantation). Group A received 297 pedicle screws, and Group B 243 screws. Forty-three screws in Group A crossed over to free-hand implantation. Screw position was graded according to Gertzbein in grades 0, A, B or C, with grades 0 or A considered as "safe area." Total fluoroscopy dose and time were compared in six patients of each group.

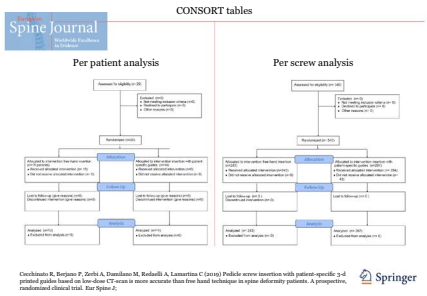
Results Comparing the two study groups, we observed a statistically significant difference between the two groups ($p < 0.05$), with 96.1% of screws in the "safe area" in Group A versus a 82.9% in Group B. Group-A patients had a mean effective dose of 0.23 mSv compared to 0.82 mSv in Group B. Patient-specific, 3D-printed pedicle screw guides increase safety in a wide spectrum of deformity conditions. In addition, the total radiation dose is reduced, even considering the need of a low-dose preoperative CT for surgical planning.

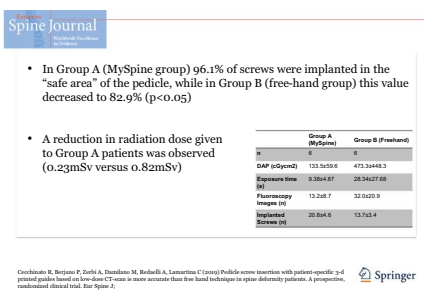
Level of evidence I.

Graphical abstract

These slides can be retrieved under Electronic Supplementary Material.







Keywords Scoliosis · Navigation · 3D printing · Accuracy · Spine deformity

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Extended author information available on the last page of the article

Introduction

Surgery for spinal deformity, either in adult or younger patients, is a well established procedure, whose complication rates are well described in the literature [1–4]. Among the different risks for patients and surgeons, pedicle screw malpositioning is one of the most common. The rate of inadequate pedicle screw placement can reach incidences up to 29.1% [5], and potential complications derived from severe misplacements can represent a life-threat for patients or cause permanent neurological impairment [6]. New technologies have been developed to reduce the incidence of malpositioned screws, such as CT navigation and robotics. However, they show specific limits as the amount of the radiation dose given to the patient [7] or the complexity of equipment with consequent increase in surgical time or costs [8, 9]. Radiation dose to patients has attracted substantial attention after an increase in incidence of tumor occurrence in spinal surgeons and in adolescent idiopathic scoliosis (AIS) patients was confirmed [10–12]. The development of patient-specific guides for pedicle screw implantation is a new option to contain the risk of instrumentation. A variety of systems have been recently proposed, and some of them have been tested on specimens or in case–control series [13, 14], with limited scientific validity or generalizability. The main goal of this study is to evaluate the effectiveness of a new patient-specific guide technology (MySpine Medacta) to improve the accuracy of pedicle screw placement in spinal deformity cases compared to free-hand insertion in a single-center prospective randomized trial (P-RCT). The secondary goal is to compare surgical time, complications, fluoroscopy usage and intraoperative radiation dose.

Materials and methods

Design

This was an open-label, parallel, single-center prospective randomized controlled trial with 1:1 allocation ratio. After commencement, no changes were introduced in the design of the study. Only one initial exclusion criterion was removed early after the commencement of the study, but it did not affect the design (see "Patients" section).

Patients

Eligible patients were adolescents or adults scheduled for primary surgical treatment of spinal deformity.

Inclusion criteria were:

- Coronal or sagittal spinal deformity that received indication for surgical treatment with pedicle screw instrumentation and posterior-only or combined approaches in the same session
- suitable to undergo spinal stabilization (according to the label indication/contraindications)
- patients affected by idiopathic, congenital or degenerative spinal deformity
- willingness to participate, to undergo pre- and postoperative evaluations and to provide written informed consent for participation in the study.

Exclusion criteria included patients who:

- had previous vertebral fractures of one or more of the vertebrae planned for instrumentation
- had previous spinal surgery at the target levels
- were allergic to implant components
- had concurrent diagnosis of tumor, infection, chronic inflammatory disease
- had syndromic deformity of the spine
- were unable or unwilling to provide a written informed consent for participation in the study
- were unable to will or intend

Though the original criteria excluded congenital deformities, since we observed from the first data of this trial and from the previous published studies a high precision in pedicle screw implantation, indications were extended to include patients with congenital deformities.

Patients were recruited by the principle and sub-investigators. Screening for eligibility was made at the outpatients facilities of the investigators, who provided information for consent to patients and (if under 18 years of age) to their parents. Patients' preoperative data collection was made by one of the investigators at the institution during the preoperative evaluation. Intraoperative and postoperative data were collected at the authors' institution at the appropriate time intervals. Postoperative CT scans were evaluated by one senior radiologist who was blinded to patients' allocation. The evaluation of screw positioning was made using Gertzbein's classification [15].

Interventions

Patients were blindly allocated to one of the two groups.

Group A included subjects undergoing surgery using 3D-printed patient-specific guides for pedicle screw implantation (MySpine^{TM}, Medacta, CH, Fig. 1a, b).

Group B was composed of subjects undergoing surgery using the free-hand screw implantation technique which is the standard at the authors' institution.

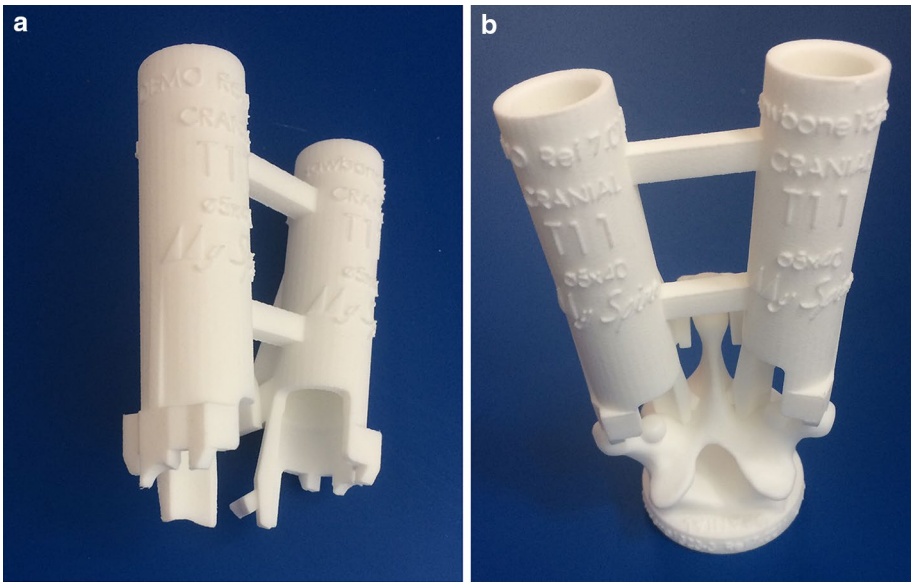

Fig. 1 Image of the MySpine guide (**a**) and its application on a 3D reconstruction of the target vertebra (**b**) before its application on the spine

Outcomes

The main outcome of the study was comparison between groups of the incidence of malpositioned screws (pedicle screw placement inaccuracy).

Secondary outcomes were the evaluation of the incidence of malpositioning on the medial or lateral side, the incidence of hardware-related adverse events (AE), comparison of surgical time and comparison of intraoperative fluoroscopy use between groups.

No variations of these endpoints were adopted during the study period.

Pedicle screw accuracy was classified according to Gertzbein [15] in four categories: grade 0: screw completely in the pedicle; grade A: violation of the wall of the pedicle of less than 2 mm; grade B: violation of 2 to 4 mm; grade C: violation of more than 4 mm. Screws classified as grade 0 or A were considered in the "safe zone" and thus correctly positioned, while grade B or C screws were considered malpositioned, for both the main and secondary outcomes. Furthermore, the number of grade-C screws was compared between groups, as grade-C misplacements carry the highest risk of complications.

For secondary endpoints, medial and lateral malpositioning were computed for those pedicles that fulfilled the criteria for grade-B or grade-C violations, respectively, of the medial and lateral walls of the pedicle. Intraoperative use of fluoroscopy was computed as the total number of C-arm shots needed during the operation. Surgical time was normalized to seconds per implanted screw calculated as the total time from the beginning of implantation of the first screw to the end of implantation of the last one times the number of implanted screws. Duration of surgery was recorded from the moment of incision to the moment of the last suture. Any adverse event was recorded on adequate study forms.

Sample size

Based on the study by Amiot in 2000 [16], we set the study power to detect a meaningful difference between groups in the incidence of misplacement of pedicle screws of 10% between study arms. Type-1 two-tailed error (a) was set at 0.05, and type 2 error (b) at 0.10, with a test power ($1-b=0.90$) of 90%, the application of correction for continuity and the use of two different groups. Considering that the implant of a single screw does not influence the positioning of adjacent or far screws, 207 screws were needed for each study group to obtain an adequate statistical power.

Randomization

Patients were randomly assigned to one of the two groups at the time of informed consent, using a computer block randomization list generated by four size blocks. Allocation ratio was 1:1.

Allocation was occult to the investigators before randomization. After the investigators screened and enrolled the patients, the random allocation was provided by the study coordination office to the investigator. The same investigator allocated the patient to one of the groups. Surgery was scheduled at least 4 to 6 weeks after the preoperative visit in order to provide time for making available the surgical planning and/or the patient-matched guides (for Group A).

Based on the protocol definition, the study was open label for surgeons. Patients could not be blinded as subjects in Group A underwent one low-dose preoperative CT scan that was not deemed necessary in Group B. The radiologist

evaluating the postoperative CT scans was blinded to patients' group allocation.

Procedures

Preoperatively, all the patients were diagnosed with full spine front and lateral standing films plus, in cases of idiopathic scoliosis, supine side bending films. Patients in Group A received an additional preoperative CT of the spinal segments planned to be instrumented, using a low-dose protocol that reduces by 80% the radiation dose per pedicle (unpublished data). This low-dose protocol allowed for accurate reconstruction of bony anatomy though lacked the gray depth needed to process the images for formal radiological diagnosis, exception made of bony profile and the anatomical relationships of bone to implants (Fig. 2a, b). The dose released by this study protocol was in the range of one full spine radiograph. The preoperative low-dose CT scan was acquired in a proprietary CAD–CAM computer program in order to perform the preoperative planning of the pedicle screw trajectories and to custom-manufacture the patient-specific guides. Patients in both groups received a postoperative low-dose CT scan of the instrumented spinal segments to evaluate the final position of screws.

During surgery, all the patients received a posterior instrumentation with pedicle screws and rods and fusion, with part of them receiving in the same anesthesia a first anterior interbody fusion procedure through a transpsoas approach. The phases of dissection, screw implantation, rod positioning and deformity correction were not performed by senior authors, who performed eventual pedicle subtraction osteotomies (PSO). All the osteotomies were performed after screws implantation. In Group A, during the approach the dissection was carefully carried on to avoid any disruption of bony elements, in order to reduce the risk of instability of the corresponding guide and to obtain a perfect matching. Once vertebral levels were checked, screw implantation started with the positioning of the more cranial guide. Entry points were flattened to expose soft cancellous bone (Fig. 3). A meticulous check of the correct positioning of the guide was performed, to avoid any defect of matching with bone anatomy that could reduce the accuracy of the system. Once the guide was in proper position, one awl was completely inserted into bone in one side in the direction given by the guide, followed by the insertion of the contralateral awl. Always keeping one instrument into bone on one side to improve the stability of the guide, the awl was substituted by a graduated pedicle probe that allowed the preparation of the pedicle for a pre-set length. Once the probe was in its final position, the contralateral awl was removed and the second probe inserted. After this phase, a feeler could be used at one side to check the integrity of the pedicle walls and the planned screw was implanted (Fig. 4a, b). The same procedure was repeated on the other side and, once the screws were completely implanted, the screwdrivers were unlocked and the guide removed. When one level was

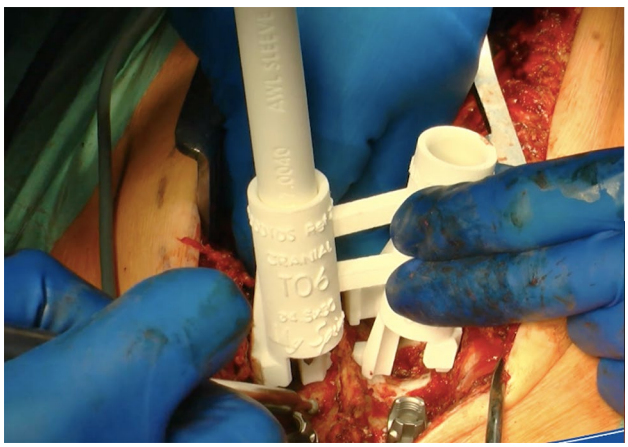

Fig. 3 Preparation of the entry point of the screw after guide application

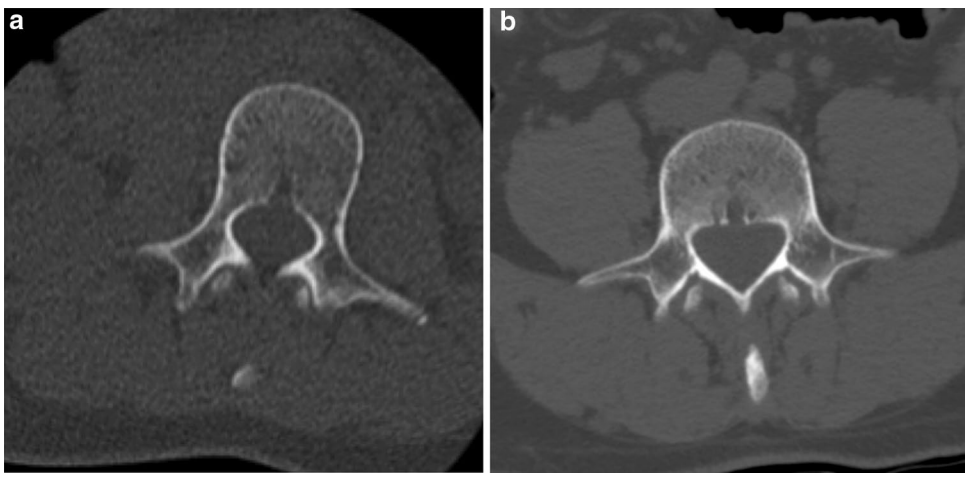

Fig. 2 Low-dose (**a**) and standard-dose (**b**) axial CT scans of the lumbar spine. Notice how the details of the inner vertebral bony pattern and of the surrounding structures (muscles and abdominal content) are unrecognizable in the low-dose CT

completely instrumented, it was possible to move caudally and instrument the next vertebra repeating the same steps. In Group A, all the planned levels were instrumented using the guides with a 100% hardware density, apart from those cases in which the use of the guides was impossible. At the end of screw implantation, and after eventual osteotomies, two appropriately contoured rods were used to correct the deformity (Fig. 5a, b).

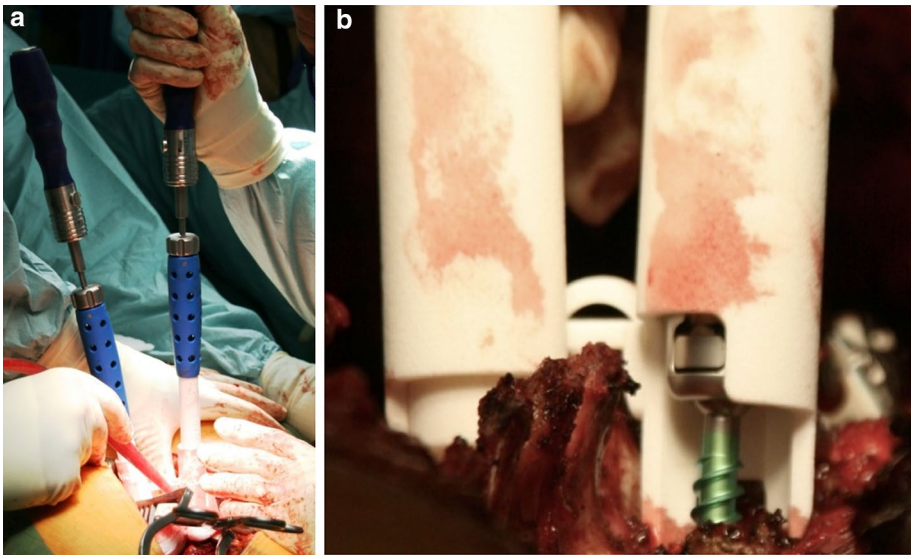

Fig. 4 **a**, **b** Screwing after pedicle preparation

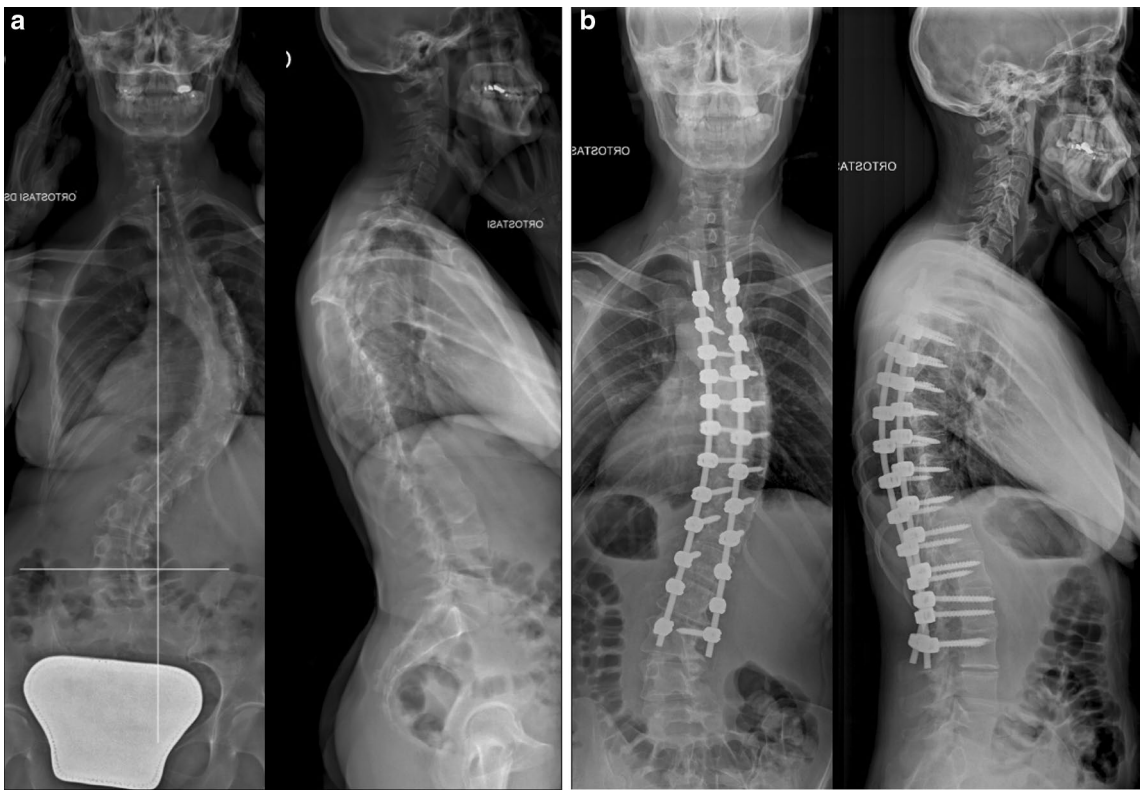

Fig. 5 **a**, **b** Preoperative and postoperative X-rays of a patient enrolled in the study

Statistical methods and reporting

Statistical analysis was performed with Minitab Statistical Software (Minitab Inc.).

Normal variables were compared with the Student's *T*-test for independent or dependent samples as appropriate. Categorical variables were compared with the use of the Chi-squared test. Threshold for statistical significance was set at $p < 0.05$. Reporting followed the CONSORT 2010 guidelines for RCTs.

Ethics

Each patient or patient's parents signed an informed consent. The study was approved by the local ethics committee, protocol number: P05.005.01. An insurance against unintentional harm derived from the study for all the participants was provided (insurance number 14.077.396—AXA Winterthur). Monitoring of the study was provided by Medacta International. The study was carried out following the recommendations of the World Medical Association declaration of Helsinki. The study was registered on clinicaltrials.gov code NCT03369158.

Results

Participants

A total of 540 screws were implanted in 29 patients (3 males, 26 females), who were enrolled from January 2015 to October 2016. Fourteen patients (2 males, 12 females) were randomly assigned to Group A (MySpine® technology) and presented with adolescent idiopathic scoliosis (AIS, six cases), adult degenerative scoliosis (ADS, six cases) and with congenital deformities (CD, two cases). The mean preoperative angle of the major coronal curve was 76 ± 29 Cobb degrees, with a minimum of 36° and a maximum of 140°. One of the two congenital deformities was a hyperkyphosis of 126°.

Of the 15 patients ($M = 1$, $F = 14$) randomly assigned to Group B (free-hand technique), ten presented with AIS, four with ADS and one with CD. The mean preoperative angle of the major coronal curve was of 74° ± 24°, with a minimum of 42° and a maximum of 134°. The congenital hyperkyphosis was of 121°. No statistical differences were observed between the baseline characteristics of the two groups (Table 1).

Primary endpoint: screw accuracy

Table 2 summarizes the distribution of the total sample regarding allocation group and final modality of pedicle screw implantation. To stress the system, all the screws of Group A were implanted by the junior surgeons of our division (RC, MD, AR). All the patients in Group A received a 100% implant density, while in the free-hand group the implant density was lower.

Intention-to-treat analysis

A total 297 screws were implanted in Group A. In the intention-to-treat analysis, 224 (75.4%) were classified as grade 0, 44 (14.8%) as grade A, 16 (5.4%) as grade B and 13 (4.4%) as grade C, resulting in 268 (90.2%) screws in the "safe zone" and 29 (9.8%) malpositioned screws.

A total of 243 screws were implanted in Group B. Of these 160, (65.8%) were classified as grade 0, 42 (17.3%) as grade A, 19 (7.8%) as grade B and 22 (9.1%) as grade C, having a total of 202 (83.1%) screws in the "safe zone" and 41 (16.9%) malpositioned screws.

Results of the intention-to-treat analysis are reported in (Tables 3, 4).

Table 1 Baseline characteristics of the sample

	Group A	Group B
Number	14	15
Age	34 ± 15.3	26 ± 17.2
Male/female	2/12	1/14
Diagnosis	AIS = 6	AIS = 10
	ADS = 6	ADS = 4
	CD = 2	CD = 1
Average coronal deformity (main curve Cobb angle)	76° ± 29°	74° ± 24°
Average sagittal deformity (main curve Cobb angle)	53° ± 24°	42° ± 33°
Planned instrumented levels	10.86 ± 3.74	9.87 ± 2.67
Final number of instrumented levels	11.47 ± 3.01	9.80 ± 2.57
Number of PCOs	1	1
Number of PSOs	4	2
Number of VCRs	0	0

Table 2 Summary of the distribution of the whole sample with initial allocation and final modality of implantation for screws

	Group A			Group B	
Patient planned	Guide	Guide	Guide	Free-hand	Free-hand
Pedicle planned	Guide	Guide	Uninstrumented	Free-hand	Free-hand
Pedicle inserted	Guide	Free-hand	Free-hand	Free-hand	Guide
Screw group	A	B	C	D	E
Grade 0	194	21	9	160	0
Grade A	39	4	1	42	0
Grade B	14	2	0	19	0
Grade C	7	5	1	22	0
Totals (per subgroup)	254	32	11	243	0
Totals (per group)	297			243	

Table 3 Intention-to-treat analysis

	Group A (MySpine)	Group B (Free-hand)	Marginal row totals
Grade B–C	29 (9.76%) (CI 6.39–13.14%)	41 (16.87%) (CI 12.16–21.58%)	70
Grade 0–A	268 (90.24%) (CI 86.86–93.61%)	202 (83.13%) (CI 78.42–87.84%)	470
Marginal column totals	297	243	540 (grand total)

Comparison of main outcome (grade-B or grade-C misplaced screws) between groups

Chi squared = 5.9851 $p = 0.014$. This result is significant at $p < 0.02$

CI is the 95% confidence interval for the proportion (Binomial exact calculation)

Table 4 Intention-to-treat analysis

	Group A (MySpine)	Group B (Free-hand)	Row totals
Grade C	7 (2.36%) (CI 1%–4.8%)	22 (9.05%) (CI 5.8–13.4%)	29
Grade 0–A–B	290 (97.64%) (CI 95.2–99.0%)	221 (90.95%) (CI 86.6–94.2%)	511
Column totals	297	243	540 (grand total)

Comparison of main outcome (grade-C misplaced screws) between groups

Chi squared = 11.7936. $p = 0.000594$. This result is significant at $p < 0.0001$

CI is the 95% confidence interval for the proportion (Binomial exact calculation)

It is of note that of 29 misplaced screws (grades B or C) in Group A, 11 screws (7 B-grade and 4 C-grade screws) were preoperatively planned with an in–out–in technique, being the pedicle too small for a screw to be implanted completely into the bone. In these cases, the postoperative position of the screws matched the preoperative planning even if the radiologist (who was blinded to the group allocation) graded them as B or C.

Per protocol analysis

Of the 254 pedicle screws in Group A, 32 screws were planned with guides but implanted free-hand and 11 screws were implanted free-hand at previously unplanned levels. Destruction of the bony contact points during dissection that caused guide instability, interference with ribs or previously implanted screws, apparent inadequate position at the final C-arm control or pull-out during the correction maneuvers were the reasons for implantation with a free-hand technique.

All the screws implanted in patients allocated to Group B were implanted free-hand. The per protocol analysis analyzed each pedicle screw in the group corresponding to the final insertion technique (guide vs free-hand). Per protocol analysis is summarized in Table 5.

Table 5 Per protocol analysis

	Group A (MySpine)	Group B (Free-hand)	Marginal row totals
Grade B–C	21 (8.2%) (CI 5.2–12.4%)	49 (17.1%) (CI 13.0–22.0%)	70
Grade 0–A	233 (91.8%) (CI 87.6–94.8%)	237 (82.9%) (CI 78.0–87.0%)	470
Marginal column totals	254	286	540 (grand total)

Comparison of main outcome (grade-B or grade-C misplaced screws) between groups

Chi squared = 9.3707 $p = 0.0022$. This result is significant at $p < 0.01$

CI is the 95% confidence interval for the proportion (Binomial exact calculation)

Table 6 Average surgical time per implanted screw (from start to end of implantation)

	Group A (MySpine)	Group B (Free-hand)	Difference
n	14	15	
Mean time per screw (min and s)	6′10″	9′11″	1′01″ ($p = 0.002$)
SD	2′32″	2′28″	

Table 7 Number of intraoperative C-arm fluoroscopy shots per case

	Group A (MySpine)	Group B (Free-hand)	Difference (sig)
	14	15	
Number of C-arm fluoroscopy shots	11.0	47.5	36.5 ($p = 0.001$)
SD	9.87	15.3	

Secondary endpoints

Adverse events

One dural lesion was observed in each group. Both the dural lacerations were unrelated to the hardware, as they happened during vertebral osteotomies. No clinical complications were observed due to misplaced screws in both groups.

Duration of surgery

The mean duration of surgeries in the two groups was, respectively, of 7 h, 2 min and 26 s versus 7 h, 3 min and 51 s ($p > 0.05$).

To normalize the timing between the two groups, we considered the ratio of time/screw, considering the time from the beginning of implantation of the first screw to end of implantation of the last one and dividing it for the number of implanted screws. Based on this, we observed a mean ratio of 6 min and 10 s per screw in Group A, versus 9 min and 11 s in Group B (Table 6, $p = 0.002$).

Intraoperative fluoroscopy

Number of fluoroscopy shots was available for all the patients included in the study. In Group A, the C-arm was used intraoperatively for an average of 11 shots, while in Group B this value was 47.5 (Table 7, $p = 0.001$).

Intraoperative dose data from the C-arm fluoroscopy device were available for 12 patients, six in Group A and six in Group B. We observed a mean dose reduction during the surgery of 72% in Group A with respect to Group B. The mean effective dose in Group A was 0.23 mSv, and 0.82 mSv in Group B. The delivered dose is strictly linked to the number of intraoperative imaging. In fact, we registered a mean number of images per screw of 0.7 ± 0.6 in Group A, 2.6 ± 2.0 for the control group. The time per image was independent of the group of patients, since it is a parameter operator and device dependent. Table 8 summarizes data available regarding dose. Due to small numbers, no statistical analysis was performed.

Table 8 Fluoroscopy dose for patients with available data

	Group A (MySpine)	Group B (Free-hand)
n	6	6
DAP (cGycm2)	133.5 ± 59.6	473.3 ± 448.3
Exposure time (s)	9.38 ± 4.87	28.34 ± 27.68
Fluoroscopy images (*n*)	13.2 ± 8.7	32.0 ± 20.9
Implanted screws (*n*)	20.8 ± 4.6	13.7 ± 3.4

CT scan radiation doses

The mean DLP for the low-dose CT scan was 139.3 ± 20.7 mGycm, considering both MySpine and control patients. As for the fluoroscopic exam, the mean effective dose evaluated from the DLP values of the low-dose CT scan was rated on the number of implanted screws to consider the complexity of the procedure. The effective dose of the low-dose CT scan protocol evaluated in this way was

2.15 mSv. The same evaluation was performed considering the parameters of the scanner for a standard diagnostic spine protocol with the scan length of the real acquisitions. In this case (standard CT scan evaluation), the mean effective dose weighted on the number of implanted screws resulted 17.90 mSv. Therefore, the optimized low-dose CT scan protocol allowed a dose reduction of 88%.

Medial/lateral side violation (intention-to-treat analysis)

In Group A, of the total of 29 misplaced screws, 21 screws were implanted using the guides, while eight were implanted free-hand. Of the 21 screws implanted using MySpine technology, ten grade-B and four grade-C screws were laterally misplaced (total 14 screws), while three grade-B and four grade-C screws (total seven screws) were medially misplaced (Table 9).

Discussion

Generalizability

Custom-made instruments in orthopedic surgery have been investigated since the early 1990s by Radermacher et al. [17], and their use has spread in the different specialities. In this study, a substantially representative sample of spinal deformity patients has been evaluated after undergoing pedicle screw instrumentation with free-hand technique versus patient-specific guides. Groups were comparable, and the grade of deformity varied from moderate to very severe. All the pedicle screws have been inserted by spine surgeons in the first 7 years of practice. Their misplacement rate was low with free-hand technique, much in line with what is reported in the literature, and it was significantly reduced by the use of patient-specific guides. This suggests that average spine surgeons can provide their patients further safety by the use of this technology, and that this may apply to a wide range of spinal conditions. Compared to fluoroscopy-guided or 3D-image-guided navigation, the proposed technique does not need special equipment or hospital investments. The cost of this patient-specific disposable navigation is a portion of the cost of the spinal implant and can be used in most surgical settings, from high volume-to-low volume hospitals and from developed to developing countries, thus making possible more universal access to this additional degree of safety. The relative reduction in risk depends on the specific misplacement rate of the individual surgeon and case: A more experienced surgeon in an easier case would be expected to have a lower misplacement rate, and vice versa for a less experienced surgeon in a more difficult case. In our study, the intention-to-treat analysis showed an NNT of 14.1 (every 14.1 pedicle screws instrumented with this technology avoided one grade-B or grade-C misplacement). In this study, the average number of screws implanted per patient was 17.37. Under these conditions, the patient-specific guide system would avoid in each patient more than one (1.23) grade-B or grade-C malpositioned screws.

Table 9 Details on direction of displacement of misplaced grade-B and grade-C screws in Group A

Group A	Grade B	Grade C
Lateral misplacement	10	4
Medial misplacement	3	4

Interpretation

MySpine® guide system is a patient-matched technology intended to drive the insertion of pedicle screws, reducing the rate of hardware malpositioning. The design of the guides is based on a preoperative low-dose CT scan that allows a 3D reconstruction of patient's spine. The primary endpoint of this P-RCT was the evaluation of the accuracy of this system, comparing it with the accuracy of free-hand technique in two homogeneous groups of patients. The system showed a good versatility in both coronal and sagittal deformities, even if 21 screws in Group A were implanted free-hand because of problems related to the use of the guides (mainly because of the unplanned breakage of the bony landmarks during spinal dissection, that made the guide unstable. In one severe case, an encroachment of the ribs heads in the convexity of the curve created a mechanical instability of the guide). In two patients, the guide was not applicable to the target level: in one case, because of the excessive kyphotic deformity, creating a conflict between the guide and the head of the patient and in a second case because of a combination of extreme rotation of a thoracic curve and adjacent rib hump with consequent conflict between the guide and the ribs. In both cases, the screws were inserted free-hand.

Screw accuracy

Screw accuracy in deformity spine surgery is a main issue, having in some retrospective series rates up to 29% of misplaced screws [6]. MySpine® aims to be a patient-matched technology designed to improve pedicle screw accuracy in deformity cases. The comparison between the two Groups showed a statistically significant difference in pedicle screw accuracy, demonstrating how MySpine® allows a better positioning of the hardware looking both the intention-to-treat (90.2% vs 83.1%, $p < 0.02$) and the per protocol analysis (91.8% vs 82.9%, $p < 0.01$). The difference

is evident also in the type of misplacement, having only seven (2.36%) grade-C screws in MySpine group versus 22 (9.05%) using free-hand technique ($p < 0.0001$). Analyzing the misplaced screws in Group A, we observed that 7 B-grade and 4 C-grade screws were preoperatively planned with an in–out–in technique, being the pedicle too small for a screw to be implanted. The postoperative position of the screws corresponded perfectly to the preoperative planning, but the radiologist graded them as B or C because of the blind fashion of the analysis. For this reason, we considered these screws as well implanted, raising the number of "safe" screws up to 244 (96.4%). Both the study groups showed no adverse events related to screw positioning. Forty-three screws crossed over from Group A to Group B. Thirty-two screws were implanted with a free-hand technique even if they were planned with MySpine, either for impossibility to use the guides (bony contact points breakage during dissection with consequent guide instability, interference with pre-implanted screws, interference with the head or ribs) or for unsatisfactory position at C-arm control, while 11 screws in MySpine group were implanted with a free-hand technique because their levels were not planned preoperatively for instrumentation (change in instrumented levels). Thus, it should be kept in mind that the technique had in this cohort a 12.6% chance of having a screw-implanted free-hand even in a pedicle for which a guide had been crafted.

Radiation dose and timing

According to the recent literature, patients affected from adolescent idiopathic scoliosis suffer from cancer 4.8 times more than common population due to radiation exposure during diagnostic process, surgery and follow-up [10]. Moreover, orthopedic surgeons show an increased risk of contracting cancer for the repeated X-ray exposition during surgeries [11, 12]. Modern navigation systems usually increase the radiation dose to patients, being based on preoperative or intraoperative CT scan and 3D reconstruction [7–9]. Moreover, in free-hand technique, intraoperative C-arm is frequently utilized to check the positioning of the screws, especially in severe deformities, increasing the radiation dose given to the patient.

In our study, the guides were crafted on a preoperative low-dose CT scan. This is a particular CT radiation protocol that allows a good representation of the cortical bone of the vertebrae with an X-ray dose up to 80 times lower than reported with the use of O-arm [19]. Moreover, intraoperative C-arm use was significantly decreased in MySpine Group in respect to free-hand group. This resulted in lower radiation dose given to the patient and likely to surgeons and OR staff as well.

Considering surgical time, for each patient we recorded the time from the preparation of the pedicle of the first screw to the implant of the last one, and divided this period for the number of implanted screws. In this way, we obtained a ratio of time/screw that allowed us to normalize the surgical time in the two different groups. Based on this, we observed that screw insertion with MySpine system required less time than free-hand technique. Furthermore, a part of the Group-A screws was implanted free-hand, and this could have introduced a change in the time/screw ratio that increased the average time per screw in the MySpine Group.

Limitations

This is the first P-RCT on the use of patient-specific implantation guides for pedicle screw fixation in patients with spinal deformity. Preliminary testing gave a proof on feasibility [18–20] and safety. The study has some limitations. First, sample size was calculated for the number of pedicle screws, as far as one single error in placement of a pedicle screw can have devastating consequences for the patient. Still, the number of patients included is small. Studies with greater numbers would be desirable for confirmation of our findings. Second, the study was open label, as patients and surgeons could not be blinded to the arm of the study they were allocated to. To reduce the potential for bias, we blinded the rater (radiologist) of the main outcome, but we cannot completely exclude bias due to lack of triple blinding. Third, the evaluation of the pedicle screw accuracy was based on low-dose CT scan. We do not have information that provides certainty that this modality of CT scan could not introduce bias in the evaluation of the position of pedicle screw. Essentially, the low-dose protocol cannot change the direction of the screws and the global shape of screws and bone but might have introduced a change in the exact position of the limits. In the preliminary discussion of the project and in the cadaveric study, we accumulated experience on the use of this CT scan protocol, and the involved radiologist interpreted that low dose could be safely used in patients for this purpose. Moreover, the preoperative CT scans that were used to craft the guides for screw implantation in Group A were preoperatively available on the informatics system of the hospital. It could be thought that these images could have been used to preoperatively improve the anatomical knowledge of the surgeons (and thus increase the accuracy of the screws), but in Group A pedicle screws were inserted using the guides. We thus think that the availability of the CT scans did not influence the accuracy of pedicle screw implantation. The monocentric design of the study could be considered a limit, even if multiple spinal surgeons participated in surgeries. The shortness of the follow-up on hospitalized patients allowed the reduction in attrition bias, with no loss of patients at the final follow-up. Crossover was observed during the study only. Due to the characteristics of

the design, crossover happened only for screws from Group A to Group B. Forty-three screws passed from Group A to Group B. Of these, 11 screws were unplanned, so guides were not available for implantation. Regarding the other 32 screws, the causes of free-hand implantation were the following: pull-out during correction maneuvers ($n = 11$), insufficient stability of the guide/inability to fit the guide to the anatomical landmarks ($n = 17$), apparent unsatisfactory position at C-arm control ($n = 4$). The intention-to-treat analysis provides a better understanding of the actual advantage of the patient-specific guides in real conditions (where pull-out, inability to use the guides or unsatisfactory position can all contribute to reduction in the performance of the new technology).

Conclusions

Patient-specific guides reduced significantly the incidence of pedicle screw malpositioning compared to the standard free-hand technique in a patients' sample representative of the spectrum of difficulty of standard and highly complex spine deformity surgery. The difference was statistically significative. Secondarily, the patient-specific guided technology reduced the intraoperative exposure to radiation and the surgical time of the implantation phase. No differences were observed in the total time of surgery. No increase in adverse effects was observed.

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Compliance with ethical standards

Conflict of interest Authors RC, PB, AZ, MD and CL are consultants for Medacta SA.

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Affiliations

Riccardo Cecchinato[1] · Pedro Berjano[1] · Alberto Zerbi[1] · Marco Damilano[1] · Andrea Redaelli[1] · Claudio Lamartina[1]

✉ Riccardo Cecchinato
dott.cecchinato@gmail.com

[1] GSpine4, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy