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ORIGINAL ARTICLE

A CT-based study investigating the relationship between pedicle screw placement and stimulation threshold of compound muscle action potentials measured by intraoperative neurophysiological monitoring

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Abstract
Purpose Neurophysiological monitoring aims to improve the safety of pedicle screw placement, but few quantitative studies assess specificity and sensitivity. In this study, screw placement within the pedicle is measured (post-op CT scan, horizontal and vertical distance from the screw edge to the surface of the pedicle) and correlated with intraoperative neurophysiological stimulation thresholds.
Methods A single surgeon placed 68 thoracic and 136 lumbar screws in 30 consecutive patients during instrumented fusion under EMG control. The female to male ratio was 1.6 and the average age was 61.3 years (SD 17.7). Radiological measurements, blinded to stimulation threshold, were done on reformatted CT reconstructions using OsiriX software. A standard deviation of the screw position of 2.8 mm was determined from pilot measurements, and a 1 mm of screw—pedicle edge distance was considered as a difference of interest (standardised difference of 0.35) leading to a power of the study of 75 % (significance level 0.05).
Results Correct placement and stimulation thresholds above 10 mA were found in 71 % of screws. Twenty-two percent of screws caused cortical breach, 80 % of these had stimulation thresholds above 10 mA (sensitivity 20 %, specificity 90 %). True prediction of correct position of the screw was more frequent for lumbar than for thoracic screws.
Conclusion A screw stimulation threshold of >10 mA does not indicate correct pedicle screw placement. A hypothesised gradual decrease of screw stimulation thresholds was not observed as screw placement approaches the nerve root. Aside from a robust threshold of 2 mA indicating direct contact with nervous tissue, a secondary threshold appears to depend on patients' pathology and surgical conditions.

Keywords Pedicle screw · Neurophysiological monitoring · Computer tomography imaging · Spinal fusion · Compound muscle action potential · Study power

Introduction

Several studies have reported misplacement rates of up to 40 % during pedicle screw insertion [1, 2]. The complication rate secondary to spinal instrumentation can amount to 33 % [3–6], but only partially as a consequence of impingement of nervous tissue. A method that monitors the accuracy of pedicle screw placement during the surgery is highly desirable, helping to prevent neurological injury. Neurophysiological monitoring is aimed at improving the safety of screw insertion. It is assumed, that a low response threshold indicates close proximity of the screw to the nerve root [7]. A correctly placed screw entirely enveloped by electrically resistant bone is thought to be less likely to cause an electrical depolarisation of closely situated nerve roots when stimulated. If a low response threshold is signaled by neurophysiological values, the surgeon can provide intra-operative feedback on pedicle integrity based on palpation. Given the structural complexity of physiological

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electrical circuits in contact with the measurement device, there is no simple relationship between monitored values and screw position. Few studies have assessed the final position of pedicle screws on postoperative images and compared them to the intra-operative neurophysiological measurements [8–10]. In one study the authors developed a semi quantitative grading for the pedicle screw position [11], with a relatively small number of screws, concluding that a stimulation threshold in the range of 10–15 mA indicates an increased likelihood of a pedicle breach. The interest of the presented study is test the utility of measuring compound muscle action potentials (CMAP) to intra-operatively determine whether the placement of pedicle screws is acceptable. The current study compares the intra-operative stimulation threshold with the screw's final horizontal and vertical distance from the pedicle edge obtained from reconstructed postoperative CT's of a total of 204 screws. The hypothesis to be tested is that an envelope of at least 1 mm of bone around the screw should result in stimulation thresholds larger than 10 mA, with falling threshold values as the screw approaches the pedicle wall (minimum at important breach).

Table 1 Number of screws per vertebral level

Vertebral level	Number of inserted screws
Thoracic	
T01	6
T02	10
T03	4
T04	6
T05	2
T06	2
T07	4
T09	6
T10	8
T11	12
T12	8
Lumbar	
L01	6
L02	12
L03	20
L04	41
L05	40
Sacral	
S01	18

Materials and methods

A total of 204 screws were inserted in thoracic and lumbar spines of 30 patients during instrumented fusion under EMG control. The female to male ratio was 1.6 and the average age was 61.3 years (SD 17.7). Table 1 lists the instrumented levels. Diagnoses included: 4 degenerative disc disease, 14 spinal stenosis with spondylolisthesis, 7 degenerative scoliosis and 5 vertebral fractures. Cases were consecutive, unless the neurophysiologist or postoperative CT was not available. All cases were operated under general anesthesia (Diisopropylphenol) by the same surgeon.

Surgical technique: Non-depolarizing muscle relaxants were used for intubation only. Anesthesia was maintained using continuous propofol infusion. No wake up test was performed. Pedicle screws were inserted before canal decompression (if required) in an effort to diminish blood loss. The entry point was determined based on anatomical landmarks and verified with lateral fluoroscopy. A pedicle finder was used to cannulate the pedicle and its position verified again by lateral fluoroscopy. Five mm (in thoracic vertebrae) and 6 mm (in lumbar vertebrae) titanium polyaxial screws were inserted (Expedium, DePuy Spine, Raynham, MA). The integrity of the pedicle was verified with a fine ball tipped probe provided by the implant manufacturer.

EMG bipolar electrodes (Xomed™) were placed on muscles innervated by the correspondent myotomal root (surface electrodes on rectus abdominis muscle for thoracic screws, needle electrodes on quadriceps, tibialis anterior and gastrocnemius for lower limb roots) [12]. EMG signal was acquired ™using an Eclipse system (Axon™), band-passed filtered between 10 and 1,000 Hz and visualized usually at a 1 cm/mV scale. CMAP were induced by single stimulations in 25 patients and bursts of monopolar cathodic stimulations in five patients [13]. A burst consisted of three monopolar 0.2 ms duration stimulations. Intra-burst frequency was 500 Hz and inter-burst frequency was 1 Hz. The anode was placed close to the C7 spinous process. Stimulation current was increased gradually up to 50 mA or as soon as a CMAP was observed on the computer screen or as a clinical contraction of the corresponding muscle. Spontaneous EMG was recorded during pedicle screw insertion in order to detect signs of motor root mechanical stimulation (spikes, bursts or train).

Radiological measurements: an observer, blinded to the stimulation threshold, measured the horizontal and vertical 'screw edge to pedicle edge' distance perpendicular to the longitudinal axis of the screw on reformatted CT reconstructions using OsiriX software (Version 3.6. Antoine Rosset, Geneva, 2003–2010) (Fig. 1). These distances were analysed with their corresponding stimulation threshold, taking into account individual differences in bone conduction. This involved calculating the simplified triangular bone area situated medially and inferiorly to the screw center on coronal reconstructions perpendicular to the

Fig. 1 Measurement of horizontal and vertical distance from the screw edge to the surface of the pedicle. When the screw was out of pedicle, exact measurements were not possible

longitudinal screw axis and relating it to the ratio 'obtained stimulation threshold to 'mStimThresh' (where 'mStimThresh' equals the average of all stimulation thresholds of screws totally within pedicle). Data from 68 thoracic and 136 lumbar screws were processed separately. A second observer, who had to perform the whole reconstruction process, define the longitudinal axis of the screw and measure the aforementioned distances, measured the screw positions of 16 screws.

Study power and statistical analysis: A standard deviation of the screw position of 2.8 mm was determined from pilot measurements. 1 mm of screw—pedicle edge distance was considered as a difference of interest. These assumptions lead to a standardised difference of 0.35. Thus, 204 screws allow for a power of the study of 75 % (significance level 0.05). The interobserver reliability of distance measurements was calculated using paired *t* test. A diagnostic test was performed.

Results

Distance measurements were reliable (paired t test, $P = 0.13/0.98$ horizontal/vertical). No patient suffered from postoperative neurological complication. The least well placed screw found breached the pedicle wall by approximately 2 mm. The trajectory of two lumbar screws on the same patient were changed for a less convergent one following further inspection due to low stimulation thresholds (Final stimulation threshold: [1] 31 mA–before 4.2 mA; [2] 24 mA–before 9.8 mA; screw edge to pedicle edge distance: horizontal/vertical [1] 0.51 mm/0.5 mm and [2] 0 mm/0.46 mm, respectively).

Forty of 68 thoracic screws (59 %) and 114 of 136 lumbar screws (84 %) had a stimulation threshold above 10 mA and were correctly placed. The average distance from the pedicle edge was 1.9 mm (SD 1.5 mm) horizontally and 3.3 mm (SD 2.4 mm) vertically for thoracic screws and 3.9 mm (SD 2.3 mm) horizontally and 4.2 mm (SD 3.1 mm) vertically for lumbar screws. Additionally 24 % (16 screws) of thoracic and 15 % (21 screws) of lumbar screws caused cortical breach in either horizontal, vertical or both directions, but had stimulation thresholds above 10 mA (false negatives, Table 2). Split into three regions (10–20, 20–30 and >30 mA, Fig. 2) the stimulation threshold range of 10–20 mA hosts both, the majority of correctly placed and the majority (67 %) of misplaced thoracic screws. False positives amounted to 10 % (7 screws) of thoracic screws and 2 % (3 screws) of lumbar screws. A poor correlation between stimulation thresholds and screw position was found for thoracic and lumbar screws (as example see Fig. 3). Also no correlation was found between the ratio of obtained stimulation threshold to 'mStimThresh' and bone area (horizontal distance*vertical distance/2). The minimum and maximum values found for thoracic screws totally within bony boundaries were 6 and 31.8 mA, respectively (average of all patients mixed 20.7 mA with SD 14.9). For lumbar screws those values were of 11 and 42.5 mA respectively with an overall average of 26.9 mA (SD 8.7).

Table 2 Relationship between pedicle screw stimulation threshold and screw placement for 68 thoracic screws (a) and 136 lumbar screws (b)

Stimulation threshold	Screw placement				Total
	Pedicle breach (+)		Totally within pedicle (−)		
	Horizontal	Vertical	Horizontal	Vertical	
(a)					
<10 mA (+)	5	3	8	10	13
>10 mA (−)	15	4	40	51	55
Total	20	7	48	61	68
(b)					
<10 mA (+)	3	1	3	5	6
>10 mA (−)	16	10	114	120	130
Total	19	11	117	125	136

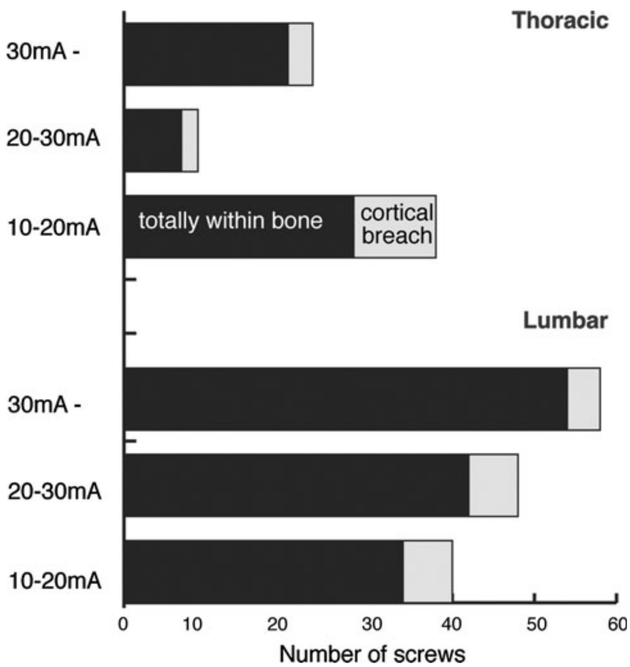

Fig. 2 Fraction of false negatives (misplaced screws) per range of stimulation threshold for thoracic and lumbar screws

There was no relation between the diagnosis, the patient age and the obtained stimulation thresholds.

Discussion

The vast majority of thoracic and lumbar screws were placed within the pedicle, which was also indicated by their corresponding stimulation thresholds above the threshold (10 mA), in accordance with results found by others [14]. A non-negligible number of screws breaching the pedicle edge were not detected. None of the misplaced screws led to a neurological deficit. Unnoticed cortical breach was more frequent in thoracic screws. Thoracic screws were more often subject to false alerts than lumbar screws.

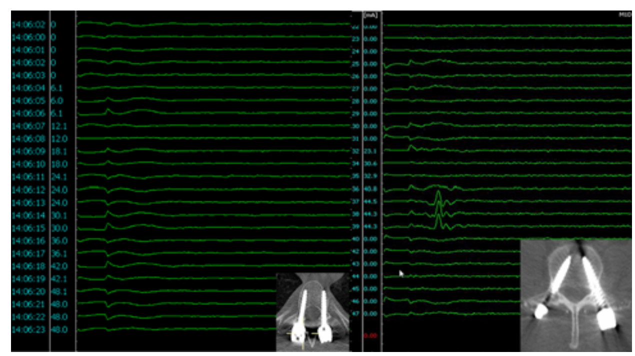

Fig. 3 Example of a high stimulation response and corresponding screw placement as seen on axial CT image for a thoracic (*left*) and a lumbar (*right*) screw with medial breach. The time window shown and the amplitude scale of stimulation response are 100 ms and 20 μV/div, respectively

The diagnostic test (Table 3) shows a rather low sensitivity [14] but high specificity, with more correct predictions for lumbar screws. Numbers are expressed with respect to screws, not to patients (sensitivity of 0.25 with respect to thoracic screws turns into 0.5 with respect to patients). From our set of measurements we cannot state that surface electrodes are less accurate due to secondary influences like obesity, since we observed non-detected medial breaches for patient with body mass index above and below 25. Displacement of surface electrodes or innervation variability might play a role.

There was no evident correlation between the screw edge to pedicle edge distance and the corresponding stimulation threshold, neither for lumbar nor for thoracic screws. A decrease of the stimulation threshold with the screw approaching and breaching the pedicle edge failed to emerge despite a considerable difference of bone and soft tissue electrical conductivity. Bone conductivity is <0.1 S/m while muscle conductivity is >0.15 S/m [15]. The screw stimulation threshold might be individual to each patient according to their particular condition. A screw

Table 3 Results of the diagnostic test

	Thoracic	Lumbar
Sensitivity	0.25	0.16
Specificity	0.83	0.97
Positive predictive value	0.38	0.43
Negative predictive value	0.73	0.88
Prevalence	0.29	0.14
Total correct prediction	0.66	0.85

stimulation threshold of 15 mA in a patient suffering chronic nerve root compression might correspond to a value inferior to 10 mA in a patient without nerve tissue damage (assuming good electrical contacts in both patients). Possibly, nerve root compression, osteoporosis, depth of anaesthesia, patient temperature, length of surgical procedure, screw position, diabetes, re-innervations of tissue by adjacent nerve roots, medication, resistance of screw head might be more influential than imagined. Some of these factors however lack systematic measurements, some are already under investigation. Measurements taken on top of the screw head bear the danger of current fluctuations caused by mobile polyaxial screws heads. Anderson [16] found that the electrical resistance of polyaxial screws can considerably vary, between 0.1Ω and an open circuit. An open circuit was measured in 28 of 75 screws and high resistance (above 1,000Ω) in another five screws. This is an inherent source of abnormally high stimulation thresholds and difficult to assess during surgery. Holland [17] showed that chronically compressed nerve roots do need higher threshold for a reaction. Pre-operative neurophysiological measurements become important to eliminate bias introduced on individual basis. In our study 14 patients were diagnosed with spinal stenosis with nerve root compression, but we could not observe a particularly different stimulation threshold as compared to other patients.

Fehlings [18] searched the literature for evidence for intraoperative neurophysiological monitoring in spine surgery. Diagnostic test values were judged based on the existence of a new or worsened neurological postoperative deficit. In their conclusion, mainly due to lack of well-designed studies, there was weak evidence that intraoperative monitoring helps to avoid iatrogenic neurological damage. We noted 22 % of total thoracic and 12 % of total lumbar screws caused undiscovered breaches of the pedicle cortex, however no patient suffered from nerve damage. Therefore, it is difficult to compare our study to other studies, in which 0.8 % of undiscovered postoperative neurological deficit [19, 20] are given. Donohue [13] collected pulse trained EMG using a ball probe inside the pedicle canal, EMG obtained directly through screw stimulation and the screw position on postoperative CTs. Of 116 screws, 51 screws were clinically acceptably placed, 19 screws were medially misplaced and 46 screws laterally. All medially misplaced screws had thresholds above 11.8 mA and laterally misplaced screws above 18 mA. Eight of 19 misplaced screws failed to elicit a lower limb EMG below thresholds of 25 or 30 mA. Palpation alone often did not reliably detect pedicle breach. The ball probe pedicle canal measurements reliably detected medially misplaced screws but thresholds could reach 15 mA. We performed few measurements directly inside the drilled pedicle hole (28 screws) finding stimulation thresholds up to 20 mA for misplaced lumbar screws and up to 40 mA for misplaced thoracic screws.

Rodriguez-Olaverri [21] presents 311 high thoracic screws that were all verified on post-operative CTs. Eleven screws with stimulation thresholds between 6 and 20 mA were not within the pedicle. Four screws breaching the cortical pedicle wall had stimulation thresholds above 20 mA, without any postoperative neurological deficit in any patient. We looked more closely at the screws breaching the pedicle in any direction (not only towards the nerve tissue) however they did not show systematically lower stimulation thresholds.

Also, Bose [14] reported 14 significant neurophysiological events in 3 of 61 patients, out of which, only 6 were identified as cortical breaches through an EMG event below 7 mA (without radiological confirmation). One patient developed a postoperative deficit.

The reports about false alarms occupy many authors, and different factors are outlined, as shown in the following. Kim [22] describes a correlation of false positive results of transcranial motor evoked potential with higher obesity and longer surgical procedure. Beatty [23] reports spontaneous firing at baseline recording that was clinically related to weakness. Firing continued up to a maximum of 24 h after decompression of corresponding nerve root. The false negative rate was 23 % in lumbar surgery and 20 % in cervical surgery. All 150 patients were operated for radiculopathy due to disc herniation or spondylosis. When a nerve root was retracted, there was a prominent positive–negative wave deflection, which was more frequent and increased with greater retraction. They found that pre-surgery skin marking with surface electrodes reduced the false negative rate. False negatives are explained by electrodes that are too far from the electrical discharge or that they were due to technical difficulties during needle insertion.

According to Lehmann the surgeon's level of training determined the ability to accurately detect the presence or absence of pedicle tract violation [24]. Raynor [25] analysed 21 false positives (total 677 screws) including radiological inspection. All screws with stimulation thresholds above 6 mA were considered intraosseous and not further analysed. Thus, potentially existing false negatives failed to appear.

Another way to improve safety of pedicle screw insertion is to measure impedance while cannulating the pedicle with a specific device commercially available under the name of PediGuard. Bolger et al. [26] reported on 28 spinal operations with this particular device and noted a 16 % rate of pedicle perforations which were nearly all (96 %) detected by the system. A more recent study [27] showed no difference in screw accuracy with or without the PediGuard but found that fluoroscopy usage could be decreased significantly. The authors nevertheless admit that the PediGuard can give rise to false positives for breach in particular when the surgeon relaxes pressure from the probe and allows blood to reach the tip of the instrument.

In conclusion we note that the prevalence of false negatives might be generally underestimated. The results of the diagnostic test of the current study are shown in Table 3. Technical improvements like pedicle canal neurophysiological measurements, preoperative assessment of neurophysiological status and multimode measurements can be helpful.

Thoracic pedicle breach detection remains problematic, partially because surface electrodes are used within the rectus abdominis muscle making individual dermatome analysis impossible.

In summary this elaborate study shows that a screw stimulation threshold of >10 mA does not indicate a well placed pedicular screw surrounded by bone, as often is believed. A gradual decrease of the screw stimulation thresholds was not discovered as the screw position approaches the nerve root. There appear to be two thresholds: One robust threshold of 2 mA that signals direct contact with nervous tissue, and another threshold that is not generalised but considering patient's case and surgical conditions. Neurophysiological monitoring remains useful and might be regarded as a minimal acceptable standard of care for all spinal procedures except perhaps simple lumbar disc surgery.

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Conflict of interest None.

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