The SPINE JOURNAL

ELSEVIER

The Spine Journal 000 (2021) 1−8

Basic Science

The effect of hydroxyapatite on titanium pedicle screw resistance: an electrical model

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Received 24 March 2021; revised 10 November 2021; accepted 15 November 2021

Abstract

BACKGROUND CONTEXT: Intraoperative detection of a pedicle wall breach implicitly reduces surgical risk, but the reliability of intraoperative neuromonitoring has been contested. Hydroxyapatite (HA) has been promulgated to increase pedicle screw resistance and negatively influence the accuracy of electromyography.

PURPOSE: The primary purpose of this experiment is to evaluate the effect of HA on pedicle screw electrical resistance using a controlled laboratory model.

STUDY DESIGN: Controlled Laboratory Study.

METHODS: Stimulation of pedicle screws was performed in normal saline (0.9% NaCl). The experimental group included 8 HA coated (HAC) pedicle screws and matched manufacturer control pedicle screws without HAC (Ti6Al4V). All screws were stimulated at 5, 10-, 15-, 20-, and 25-mm submersion depths. Circuit current return was recorded, and pedicle screw electrical resistance was calculated according to Ohm's Law. Data were assessed for normality and variance. Mann-Whitney U and Kruskal-Wallis tests compared groups with Bonferroni correction for multiple testing. Effect size is reported with 95% confidence intervals (95CI). p values <.05 were considered significant.

RESULTS: Current return was detected for all screws (N=24) following subclinical 8.5 μA stimulation at 5, 10-, 15-, 20-, and 25-mm submersion depths (N=144). The effect estimate of HA on pedicle screw electrical resistance is -0.07 (-0.17 to 0.01 95CI). The estimated effect of HA on pedicle screw electrical resistance did not differ across manufacturers. Electrical resistance values were inversely related to submersion depth. Electrical resistance values were lower in the experimental group at 10 mm (p=.04), 15 mm (p=.04), and 25 mm (p=.02) submersion depths. The HA effect ranged from -0.03 to -0.08 as submersion depth varied.

CONCLUSIONS: We found no evidence that HA increased pedicle screw electrical resistance in a matched manufacturer control laboratory model. Electrical stimulation of pedicle screws may be reliable for pedicle breach detection in the presence of HA. Future research should investigate if laboratory findings translate to clinical practice and confirm that electrical stimulation of pedicle

Abbreviations: HA, hydroxyapatite; HAC, Hydroxyapatite coated; UC, Uncoated; IONM, intraoperative electrophysiological monitoring; EMG, electromyography; tEMG, triggered electromyography; 95CI, 95% confidence interval

FDA device/drug status: Approved (Zimmer-Biomet Pedicle Screw, Medtronic Pedicle Screw, Precision Spine Pedicle Screw, NeuroStructures Pedicle Screw).

Author disclosures: ***SD***: Nothing to disclose. ***JPW***: Nothing to disclose. ***SC***: Nothing to disclose. ***MK***: Disclosures unrelated to submitted work-Level A (Royalties, Orthofix), Level B (Royalties, Precision Spine). ***TW***: Nothing to disclose. ***DL***: Disclosures unrelated to submitted work-Level B (Consulting, Zimmer-Biomet).

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https://doi.org/10.1016/j.spinee.2021.11.009
1529-9430/

screws is a reliable method to detect pedicle breach in the presence of HA.

Keywords: Electromyography; Hydroxyapatite; Intraoperative neuromonitoring (IONM); Material science; Pedicle screw; Titanium; Triggered electromyography

Introduction

Thoracolumbar spine surgery incorporates pedicle screws into posterior spinal fixation constructs [1−4]. Commonly performed under fluoroscopic guidance [5,6] and intraoperative electrophysiological monitoring [7−9] including electromyography (EMG), somatosensory, and motor evoked potentials. To assess the positioning of the screw within the pedicle, triggered EMG (tEMG) is a tool used to assess specific myotomes' activity upon activation of corresponding spinal nerves [10,11]. The minimum current necessary to evoke a tEMG response is defined as the stimulation threshold, [12,13] and the stimulation thresholds that should inform the surgeon of likely mispositioned screw is debated [14−17].

The sensitivity and specificity of tEMG may be influenced by internal circuit factors and the environment in which the pedicle screw is stimulated [18]. The pedicle screw malposition measurement may be influenced by factors such as screw trajectory and placement, bone quality/density, and spinal level [19−23]. Further, advances in spinal instrumentation resulted in new materials and coatings for pedicle screws, such as hydroxyapatite (HA), which is reported to increase the electrical resistance of the screw, increasing stimulation thresholds and decreasing the probability of detecting screw misplacement [16,24]. Conversely, HA coating (HAC) conferred favorable properties to pedicle screws like increased bony purchase [25,26] and increased pullout strength [27−29]. To our knowledge, there has been only 1 published study concluding that HAC increased the resistive value of pedicle screws when stimulated and therefore could not be reliably used with current established parameters [30].

Anecdotal, scientifically unconfirmed clinical observations on behalf of the authors (DL, MK) may suggest otherwise. Therefore, further scientific study is warranted. Understanding the electrical behavior and quantifying the effect of HAC on electrical resistance will enable data-driven ascertainment of its clinical importance. The primary purpose was to estimate the effect size of HA on pedicle screw electrical resistance relative to a match-control in a controlled laboratory model. Secondarily, we explored the effect of increased submersion depth in normal saline (0.9% NaCl) on pedicle screw electrical resistance and the manufacture HA effect on pedicle screw electrical resistance. Our primary hypothesis was that HA would increase pedicle screw electrical resistance compared to matched controls. Secondary hypotheses included (1) no change in HA effect with increased pedicle screw submersion depth and (2) no manufacture HA effect on pedicle screw electrical resistance compared to matched controls.

Methods

This experiment was conducted in the Department of Anesthesiology department at LSU School of Medicine in New Orleans, LA. All data were sequentially collected in the laboratory on 1 day using the same microamp meter with resolution of 0.2 μA (Model 7045 Absolute Process Instruments, Inc., Libertyville, IL, USA). Data were collected on 8 HAC pedicles screws (experimental group), including 2 from each manufacturer: (1) Zimmer-Biomet (ZB) (Zimmer-Biomet, Warsaw, IN, USA), (2) Medtronic (MT) (Medtronic, Dublin, Ireland), (3) Precision Spine (PS) (Precision Spine, Inc., Parsippany, NJ, USA) and (4) NeuroStructures (NS) (NeuroStructures, Inc., Irvine, CA, USA). Three manufacturers used a plasma-spray coating process (ZM, MT, NS) for HAC, and 1 used a thermal-spray (PS) coating process. The manufacturer control group included uncoated Ti6Al4V pedicle screws (UC). The experimental group was matched in a 1:2 ratio (1 HAC: 2 UC) to the manufacturer control group. All screws (N=24) measured 45 mm in length and 6.5 mm in diameter. This study did not require IRB approval.

Pedicle screws were held on a stereotaxic apparatus, and the screw shaft was lowered into a beaker containing 0.9% NaCl solution. Pedicle screws were stimulated on the head of the screw using an alligator clip connected to a Grass S88 stimulator with a square wave constant voltage output of 20 V and a duration of 4 seconds. A 1 megohm (MΩ) resistor was put in series to bring the current down into the subclinical microamp (μA) range. Without a screw in the circuit, a stainless-steel bus wire submerged in the saline solution was connected to the circuit, and an 8.5 μA current return was recorded. The stimulation was repeated with a second 1 MΩ resistor placed in series. A 4.0 μA current return was recorded, confirming an ability to record an accurate measurement in the presence of a voltage divider to reduce recording bias and establish internal validity. Stimulation of each screw was performed, and the current return was measured with an alligator clip clamped to a bus wire in the saline bath and hooked to a microamp meter. Resistive values were calculated using Ohm's Law. Stimulation was performed, and values were recorded with the screw tip at 5, 10, 15, 20, and 25-mm submersion depths. At no time was the head or tulip of the screw submerged.

The decision to use a subclinical microamp (μA) versus milliamp (mA) stimulus was both practical and purposeful.

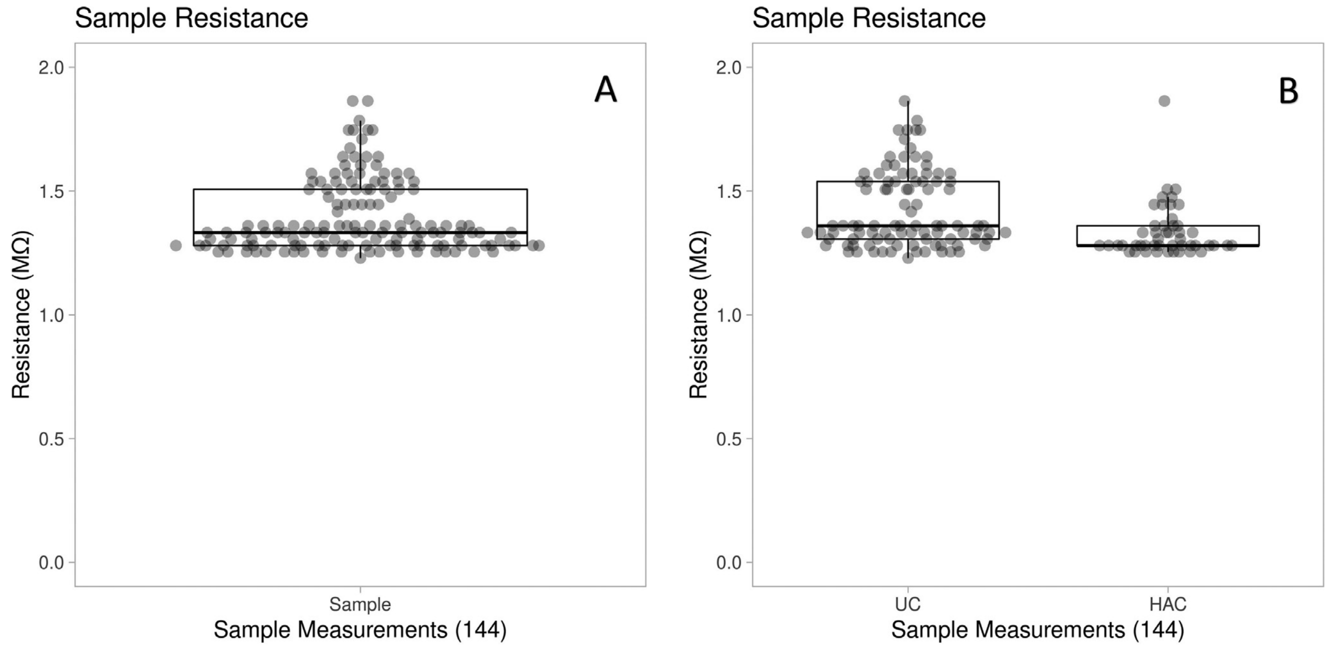

Fig. 1. (A-B) The summary of the data is shown as a boxplot, with the box indicating the interquartile range (IQR), the whiskers showing the range of values within 1.5*IQR, and a horizontal line indicating the median. (A) Sample electrical resistance measurements (N=144). (B) Sample electrical resistance measurements stratified by screw coating (N=144). HAC, Hydroxyapatite-coated; IQR, Interquartile range; UC, Uncoated.

One criticism of the use of HAC screws and tEMG is that the coating increased thresholds to supratherapeutic levels, rendering synchronous use of tEMG and HAC screws ineffective [30]. Stimulus intensity in this experiment was a constant voltage set at 20 V, equivalent to 8.5 μA (0.0085 mA) compared to 2000 μA (2 mA) [31] direct stimulation intensity to trigger nerve roots and reported trigger thresholds between 200 and 50,000 μA (0.2−50 mA) stimulation intensities [8,12,14,21,32−34]. Therefore, clinical significance was defined as subclinical stimulation (8.5 μA) for this study.

Statistical analysis

Data were assessed for normality and variance to inform statistical tests. Descriptive statistics are reported as the median and interquartile range (IQR). The primary outcome was pedicle screw electrical resistance. The HA effect size estimate on pedicle screw electrical resistance was calculated to convey the clinical significance and a 95% confidence (95CI) for a precision estimate. Exploratory analyses considered submersion depth and manufacture as independent variables. Mann-Whitney U and Kruskal-Wallis tests were used to determine group differences for primary and secondary hypotheses, both adjusted for multiple testing by Bonferroni correction. p values <.05 were considered statistically significant and 95% confidence intervals (95CI) are reported. SPSS statistical software (SPSS Statistics for Windows, IMB Corp., New York City, USA) and MedCalc (MedCalc Software, Ostend, Belgium) were used for statistical analysis. Figures were made with the PlotsofData web app [35].

Results

The current return when there was no pedicle screw in the circuit was 8.50 μA. All screws (N=24) conducted electricity during all trial measurements (N=144, 100%) with subclinical 8.5 μA stimulation to facilitate electrical resistance calculations (Fig. 1). Our total sample had a 1.33 (1.33−1.36 95CI) median electrical resistance (MΩ) and ranged 1.23 to 1.86 MΩ (1.28−1.51 IQR). The HAC sample (N=48) median was 1.28 MΩ (1.28−1.33) and ranged 1.25 to 1.86 MΩ (1.28−1.36 IQR), whereas the UC sample

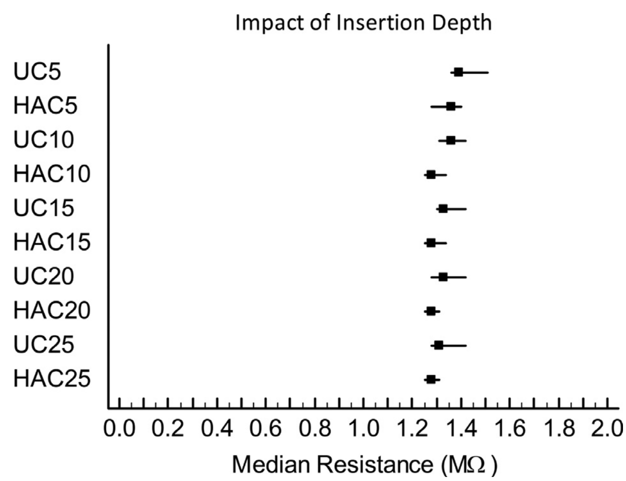

Fig. 2. Sample Screw Electrical resistance as a function of insertion depth. The sample was stratified by pedicle screw coating, and the point estimate at each depth is presented with a 95% confidence interval. HAC, Hydroxyapatite-coated; UC, Uncoated.

Table 1
Median resistance values in megaohms (MΩ) for uncoated (UC) and hydroxyapatite coated (HAC) pedicle screws at varied depths and the median difference in resistance values

Depth	UC (MΩ)	HAC (MΩ)	HA effect estimate (MΩ)
5 mm	1.39 (1.25−1.64)	1.36 (1.28−1.45)	-0.03
10 mm*	1.36 (1.25−1.64)	1.28 (1.25−1.36)	-0.08
15 mm*	1.33 (1.25−1.64)	1.28 (1.25−1.33)	-0.05
20 mm	1.33 (1.23−1.60)	1.28 (1.25−1.33)	-0.05
25 mm*	1.31 (1.25−1.60)	1.28 (1.25−1.31)	-0.03

HAC, hydroxyapatite coated; MΩ, megaohm; UC, uncoated.
* Indicative of statistical significance: 10 mm (p=.04), 15 mm (p=.04), 25 mm (p=.02).

(N=96) median was 1.36 MΩ (1.33−1.45) and ranged 1.25 to 1.86 MΩ (1.31−1.54 IQR). The primary outcome was an effect estimate of HA on our pedicle screw sample resistance and was found to be -0.07 MΩ (-0.17 to 0.01 95CI).

Secondarily, the pedicle screw resistance was inversely related to insertion depth (Fig. 2) and decreased in the experimental and control group as depth increased. The HA effect estimate ranged -0.08 to 0.03 MΩ across depth changes (Table 1). The UC ZB pedicle screw electrical resistance was the highest in our sample, whereas HAC PS and HAC NS were the lowest (Table 2). UC ZB pedicle screw resistance (Fig. 3) was significantly elevated compared to NS (p<.001) and PS (p=.001). The HA effect estimate was largest for ZB (-0.25) and lowest for MT (0.02).

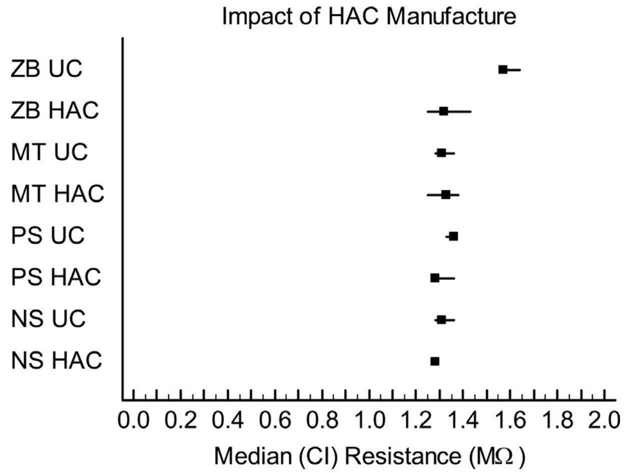

Fig. 3. Impact of HAC Manufacturer on Screw Resistance with UC Control Comparison. The sample was stratified by pedicle screw coating and the point estimate is presented with a 95% confidence interval. HAC, Hydroxyapatite-coated; MT, Medtronic; NS, Neurostructures; PS, Precision Spine; UC, Uncoated; ZB, Zimmer-Biomet.

Discussion

We found no evidence of increased electrical resistance in HAC screws compared to UC manufacturer control screws. Our primary hypothesis was supported by our results in that all screws (N=24, 100%) conducted electricity with subclinical 8.5 μA stimulation and facilitated the calculation of the HA effect. Our secondary null hypotheses failed to be rejected. There was no evidence of higher resistive values using HAC screws; on the contrary, HAC screws demonstrated lower electrical resistance values relative to UC screws (p<.001). Screw depth within the saline solution influenced the mean electrical resistance (Table 1), albeit the observed trend is unlike to be of any clinical significance. Electrical resistance was highest at 5 mm of insertion (1.39 for UC and 1.36 for HAC). Electrical resistance was lowest at 25 mm (1.31 for UC and 1.28 for HAC). Lastly, electrical resistance values varied significantly across manufacturers, with screws (UC and HAC) Zimmer-Biomet demonstrating significantly higher electrical resistance.

The primary purpose of this experiment was to observe any differences in the mean resistive values between UC and HAC screws and quantify the absolute difference if present. Our results do not provide evidence to suggest increased electrical resistance of HAC screws, which would render HAC screws incompatible with tEMG. This study controlled for the possible effects of current shunting through adjacent tissues as posed by Davis et al. [30]. Conversely, subclinical stimulation of HAC screws refuted the published conclusion that *any* response from stimulation is conditional on shunting through adjacent tissue [30] because shunting was controlled by stimulating the unsubmerged head of the screw. We believe stimulation at subclinical intensity removed uncertainty related to intraoperative electrophysiological monitoring utility.

There is no standardized methodology to measure screw electrical resistance. Only 1 study to date has evaluated the resistive values of HAC pedicle screws. The prior study

Table 2
Median resistance values in microohms (MΩ) for uncoated (UC) and hydroxyapatite coated (HAC) pedicle screws for each manufacturer along with the median difference in electrical values

Manufacturer	UC (MΩ): median (range)	HAC (MΩ): median (range)	HA effect estimate (MΩ)
Zimmer-Biomet*	1.57 (1.51−1.86)	1.32 (1.25−1.86)	-0.25
Medtronic	1.31 (1.25−1.75)	1.33 (1.25−1.48)	0.02
Precision Spine	1.36 (1.31−1.75)	1.28 (1.28−1.45)	-0.08
NeuroStructures	1.31 (1.25−1.54)	1.28 (1.25−1.51)	-0.03

HAC, hydroxyapatite coated; MΩ, megaohm; UC, uncoated.
The UC screw sample included 16 measurements, whereas the HAC sample included 8 measurements.
* Zimmer-Biomet screws tested with significantly elevated resistance values compared to Neurostructures (p<.001) and Precision Spine (p=.001)

measured screw electrical resistance in air. We designed our model to assess electrical resistance in normal saline (0.9% NaCl), which more accurately reflects the animal model [36,37] triggered EMG was validated in and clinical practice. Consequently, our reported electrical resistance is valid for relative internal model comparison and requires external validation. We wish to highlight the limitations of electrical testing of pedicle screws using a model [18]. As such, the surgeon must be conscious of the model limitations to inform decision-making. Davis et al. published data showing that HAC screws had an axial electrical resistance that averaged 3.97×10^{-3}Ohms than UC screws, which had an average axial electrical resistance of 1.75×10^{11} Ohms [30]. There appeared to be an error in either the figures or the text of the Davis et al. paper as they conclude that the HAC screws have a higher electrical resistance than the UC screws, but the text and table conflict. The study's key conclusions were that HA insulated the screw, increasing its electrical resistance beyond a useful stimulation threshold. The authors used an independent lab to perform the experiments and lack sufficient detail in the published methods to reproduce their work. We present evidence that HAC screws have a significantly lower stimulation threshold than UC screws. Notably, we believe the difference to be statistical [38] and not clinically significant [39]. Considering the absolute difference is almost undetectable at a precision several magnitudes below clinical instrumentation, the effect size is not clinically relevant if present. Thus, we believe this represents a random error rather than a systematic error. Nevertheless, nonparametric tests and Bonferroni correction were included to strengthen statistical methodology and reduce spurious findings [40−42]. However, we observed inter-manufacture differences in electrical resistance. Subsequently, the differences may be a function of the titanium alloy or the coating process.

In a prior investigation of titanium and stainless-steel pedicle screws, [24] the authors concluded the electrical resistance values were similar and not clinically significant. They opined that constant-current stimulators provided clinically accurate values up to an electrical circuit resistance of at least 1000 Ohms, and their detected electrical resistance value range (0−36 Ohms) would not be clinically significant. The report included an observation that electrical resistance values trend toward infinite electrical resistance (open circuit) as a byproduct of poor circuit component contacts. The screws were stimulated at the head and avoided possible stimulation at a site coated in HA. Further, the laboratory design incorporated a baseline assessment of the circuit that incorporated a standardized resistor to confirm accurate measurements. Our results were consistent across our HAC and UC screw pool, whereas their data was reported for 1 manufacturer.

Statistically significant differences in electrical behavior across manufacturers were identified. There was a statistically significant increased mean resistive value for Zimmer-Biomet UC screws relative to Medtronic ($p<.001$), Neurostructures ($p<.001$), and Precision Spine ($p=.001$). Our data indicated discrepancies in the electrical behavior in UC screws that were not appreciated in HAC screws. Prior reports documented that not all HA coatings are the same [25,26,43,44]. There are no standardized manufacturing guidelines for depositing HA on implants, which may influence integrity and bias findings to explain differential findings in published data partially [45]. These reports demonstrate that coating methods alter the base material properties and compromise the structure. As such, the authors called for vendor comparison studies to reduce controversial and confounding results, which may be residuals of HA-induced substrate alteration [46]. Three manufacturers in our study use a plasma-sprayed coating process (ZM, MT, NS) and 1 used a thermal-spray coating process (PS). Three manufacturers demonstrated a negative HA effect estimate on resistance (ZM, PS, NS), whereas 1 demonstrated an increase (MT). If the coating or coating process contributed to the divergence, it would only partially explain the electrical behavior. The manufacturer effect on tested differences may be more important than the coating effect, unintentionally introduced earlier in the production of the screw. The potential impact on our results is unclear and necessitates further investigation. In any case, the absolute difference in electrical resistance is believed to be below clinically relevant thresholds [24]. We postulate the intraoperative electric field that pedicle screw resistance is tested may be impacted to a greater degree by patient factors than technical factors like HAC. Several reports have suggested bone resistivity is a function of bone density and patient factors related to bone density (osteopenia vs. osteoporosis) may warrant future investigation [47−49]. Our data does not enable meaningful conclusions about the magnitude of change or alternative variables but does refute the implication that HAC increases electrical resistance, thus diminishing the clinical utility of tEMG. The authors believed the increased conduction of the HAC screws as identified with subclinical stimulation is likely insignificant in the clinical setting. Further clinical testing is warranted to support or refute such contentions.

To the authors' knowledge, this is the first study to investigate the properties of HAC screws with a manufacturer control and investigate the potential influence of screw insertion depth. Manufacturer control is critical considering the impact that subtle processing differences may have on screw behavior and topography, possibly influencing electrical properties [50,51]. Second, this study provided clinically relevant data: no evidence of tEMG and HAC incompatibility. Our data suggests the use of tEMG, a powerful modality to detect malpositioned screws, and HAC screws are compatible [8,19,52,53]. These findings are particularly relevant for surgeons considering the increased awareness of misplaced screws [16,17]. Per-patient analysis illuminated that over 40% of patients had concerning screws that had been previously misrepresented by a screw-oriented [15] surrogate analysis of misplacement rate [17].

Third, research on implant design, materials, and techniques critically focuses on biological and mechanical properties rather than electrical [54]. This contribution addresses a relative void in the literature and hopefully encourages further electrical investigations applied to spinal surgery.

One limitation is that this study is a small sample size. The cost of pedicle screws was an impeding barrier to the investigation, subsequently imposing the possibility of type II error. Nevertheless, the importance of our study is not dependent on statistical significance. Instead, the significance is derived from an internally valid model revealing an HA effect estimate magnitude with narrow precision estimates consistently below clinically detectable resistance measurements. Second, a similar study's methods were not available, and a reproducibility assessment was not possible [30]. Though, our model aligns more closely with clinical practice, and our results benefited from multiple manufacturers for increased generalizability. Third, the results revealed an inexplicable difference in UC screw properties between manufacturers. Considering the sensitivity of our instrument and the magnitude of the difference, we feel the difference is likely a clinically significant and spurious finding. The finding would not be clinically detectable and a consequence of our small sample. Smaller samples tend to adopt more extreme values, whereas larger samples better approximate the population's true value [55]. This study was not designed to determine the rationale for the differences identified between screws and between differences between manufacturers. We emphasize that statistical significance does not imply clinical significance. When stimulated, the observational data of screw behavior is critical, demonstrating an absolute difference that would be undetectable with clinical instrumentation. Nevertheless, the exploratory basic science investigation incorporated a Bonferroni correction to minimize spurious results and justify future clinical research. Lastly, limitations to basic science study designs: findings do not always translate into meaningful applications within one's clinical practice [56].

Conclusions

Electrical stimulation of pedicle screws may be reliable for pedicle breach detection in the presence of HA. We found no evidence that HA increased pedicle screw electrical resistance in a matched manufacturer control laboratory model. Future research should investigate if laboratory findings translate to clinical practice and confirm that electrical stimulation of pedicle screws is a reliable method to detect pedicle breach in the presence of HA.

Acknowledgment

The authors received no specific funding for this work.

Declarations of Competing Interests

The authors declare no conflict of interest.

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