Implantable Direct Current Spinal Fusion Stimulators Do Not Decrease Implant-Related Infections in a Rabbit Model

Ebrahim Paryavi, MD, MPH, Moshe Yanko, MD, David Jaffe, MD, Naren Nimmagadda, MD, Jenna Noveau, MD, Jason Schiavone, BA, Mohit Gilotra, MD, Daniel Gelb, MD, and Steven C. Ludwig, MD

Abstract

Electrical current detaches bacterial biofilm from implanted instrumentation. Hypothetically, this can decrease implant-related infection and allow retention of instrumentation in cases of postoperative wound infections.

We conducted a prospective animal study to investigate whether a 60-μAmp implantable direct current (DC) fusion stimulator decreases implant-related infection rates in a multilevel fixed-implant postoperative spinal wound infection model in rabbits. Three dorsal sites, T13, L3, and L6, were instrumented in each rabbit. A 60-μAmp DC fusion stimulator was implanted in a subcutaneous pouch lateral to the instrumented sites, and leads were connected to 2 of 3 sites in each rabbit. All sites were inoculated with methicillin-sensitive *Staphylococcus aureus* (MSSA). Rabbits were euthanized at 7 days, and cultures were obtained from the surgical sites, including wound swab, bone, and implants.

No significant reduction was observed in postoperative infection rates of bone or implant with 60-μAmp DC (95% and 77%, respectively) compared with no current (91% and 82%, respectively) ($P > .5$). No significant difference was observed in bacterial load (Ps = .25-.72) between sites receiving DC and control sites.

Currently used 60-μAmp DC implantable spinal fusion stimulators do not significantly reduce the rate of postoperative implant-related spinal wound infections in a rabbit model.

The incidence of surgical site infections (SSIs) in the United States is about 2 million cases annually. Aggregate economic costs associated with SSIs are estimated to be more than $1.8 billion annually in the United States.[1-3] Costs associated with treatment of spinal wound infections are estimated to increase total expenditure 4-fold per affected patient.[4] The incidence of postoperative wound infection associated with elective nonfusion spine surgery without implants or biologics is about 1%.[5] Despite widespread adoption of standard antibiotic prophylaxis, the advent of instrumented fusion has increased rates of infection associated with elective surgery to 2.8% to 6%.[6-11] In the trauma setting, the rate of infection associated with instrumented spine surgery increases to about 10%.[9,12] About half of all SSIs are associated with surgically implanted instrumentation and require an average of 2 surgical procedures for effective treatment.

Established implant-related infections are difficult to eradicate with antibiotics alone and require surgical intervention in up to 50% of cases.[13] The most common isolated organism has repeatedly been shown to be *Staphylococcus aureus*.[6,13-17] Formation of bacterial biofilm by *S aureus* on implant surfaces renders these organisms resistant to systemic antibiotics. Persistent infection and chronic osteomyelitis can impair bony fusion and compromise the structural integrity of a spinal implant construct.[18,19] It therefore is necessary to perform direct irrigation and debridement of the wound and implant surfaces or, in some cases, to remove the implants to adequately treat the infection.[20]

Use of electricity in treating infection—the "bioelectric effect"—has been well described.[21] Although electric current alone has not been shown to totally eliminate bacteria from biofilm on implanted surgical instrumentation, it has been

Authors' Disclosure Statement: Biomet provided partial funding for this research and donated the experimental devices. No other outside funding was received for this work. Our institution receives fellowship support from the Orthopaedic Research and Education Foundation and from Synthes Spine. Dr. Gelb wishes to report that he receives royalties from Synthes Spine and Globus Medical, has stock ownership in Advanced Spinal Intellectual Property, is a paid speaker for AO Spine North America, and serves on the scientific advisory board for Globus Medical. Dr. Ludwig wishes to report that he receives royalties from DePuy, Synthes Spine, and Globus Medical, has stock ownership in Globus Medical, has part ownership in Progressive Spinal Technologies and Advanced Spinal Intellectual Property, serves as a paid consultant for DePuy and Synthes Spine, and serves on the Board of Directors for Globus Medical. The other authors report no actual or potential conflict of interest in relation to this article.

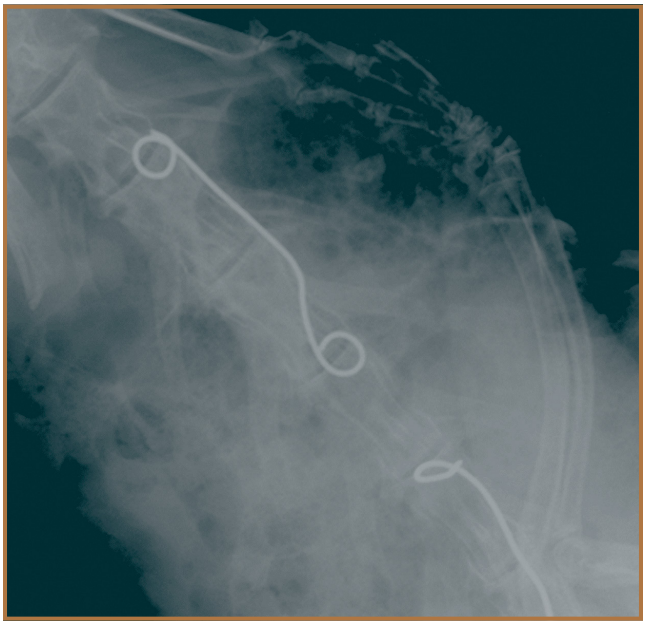

Figure 1. Postoperative radiograph shows fixed implant instrumentation.

shown to work synergistically with antimicrobial agents. Electrophoretic forces allow antimicrobial agents to overcome diffusion barriers that would otherwise limit access of these agents to targets within bacterial cells. Electric current has been shown to disrupt cell membrane electrical equilibrium, generate free radicals, oxidize enzymes, and alter alpha helix content and orientation of membrane proteins, all of which lead to leakage of essential cytoplasmic constituents.[22,23] In addition, low-amperage direct current (DC) repels microorganisms from electro-conducting devices, disrupting initial colonization of instrumentation and reducing formation of bacterial colonies and biofilm.[22]

Our goals were to describe and validate a technique modification to the previously established postoperative spinal wound infection model in rabbits and to subsequently investigate our hypothesis that an implanted DC fusion stimulator device decreases implant-related infection rates and bacterial loads in the same rabbit model.

Materials and Methods

Animals, Pathogen, and Device Selection

This study was approved by our institutional animal care and use committee. Based on an a priori sample size calculation, we determined that 4 animals (12 total surgical sites) would be required to demonstrate a 70% SSI rate, similar to previously established models. We calculated that 12 rabbits (36 surgical sites) would be required to show a 75% decrease in infection rates between control and experimental sites. Sample size calculations assumed 80% power at $\alpha = 0.05$.

Seventeen female New Zealand White rabbits weighing 7 lb to 9 lb each were used. One nonsurvival rabbit was used to determine the technical feasibility of our proposed fixed-implant procedure. Methicillin-sensitive *S aureus* (MSSA) (ATCC 25923) was the causative infectious agent for postoperative SSI. The SpF PLUS-Mini Spinal Fusion Stimulator (Biomet, Warsaw, Indiana) was used to deliver electric current. The device delivers 60 μAmp of continuous DC.

Bacterial Preparation

One day before surgery, a suspension of 5 mL of Trypticase Soy Broth (Becton, Dickinson, Franklin Lakes, New Jersey) and 3 *S aureus* colonies were placed into a 10-mL test tube and incubated at 37°C, 150 rpm, for 16 hours. The next morning, the supernatant was decanted, and 5 mL of sterile saline was added. The mixture was centrifuged at 4000 rpm for 10 minutes. Washing was repeated in the same fashion. The final concentration of bacteria was estimated with a densimetric apparatus and assay (LaMotte 2020e; LaMotte, Chestertown, Maryland). A concentration of 10^6 colony-forming units (CFUs) consistently produced a 70% infection rate (infective dose 70 [ID70] = dose of bacteria producing infection in 70% of sites), confirmed by plating a 100-μL aliquot of this concentration onto 5% sheep blood agar plates (Fisher Scientific, Boston, Massachusetts).

Surgical Preparation

Rabbits were anesthetized with a ketamine-xylazine combination (ketamine 20 to 40 mg/kg, xylazine 2 to 5 mg/kg) and received a preoperative dose of buprenorphine at time of anesthetic induction. Maintenance anesthesia was administered with isoflurane 1.5% to 3% inhalation by nose cone. Appropriate intraoperative monitoring was performed by trained veterinary personnel. Ceftriaxone 20 mg/kg of body weight was intravenously administered before surgery to mimic preoperative prophylaxis in humans. Rabbit backs were shaved along the entire length of the spine and were prepared with povidone-iodine (Betadine; Purdue Pharma, Stamford, Connecticut) and 70% ethanol in typical fashion. Rabbits were placed prone on a disinfected operating room table in a dedicated veterinary operating room facility and were draped with sterile towels.

Surgical Procedure

Surgery was performed on 3 noncontiguous sites, the T12, L3, and L6 vertebrae. Newly sterilized instruments were used for each animal and each site. A dorsal skin incision extending from L7 to L5 was made. Overlying fascia was incised over the spinous process of the vertebral element involved. This spinous process, along with surrounding musculature and ligaments, was removed with a small rongeur, leaving a characteristic "dead-space defect." The ligamentum flavum was not excised; the dura was not exposed. A small towel clamp was used to pierce holes at the spinolaminar junction of the vertebrae above and below the defect site (eg, L6 removed, wire cerclage placed L5-L7). Sterile 1.25-mm stainless steel cerclage wire was hooked through the created holes and tightly twisted to be secured. **Figure 1** shows a postoperative radiograph of the implanted wires.

Fascia of the dorsal spinal incisions was closed with 3-0

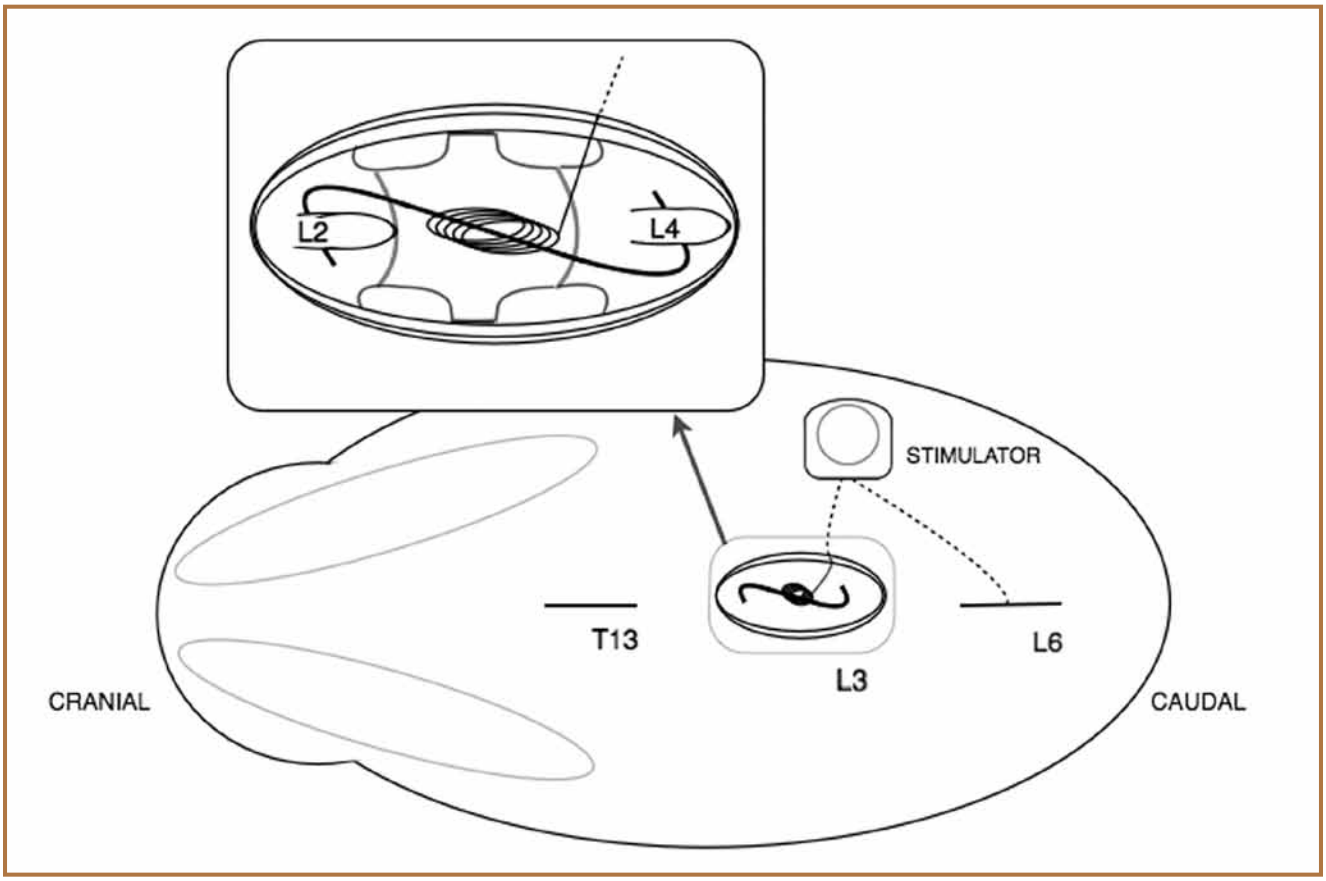

Figure 2. Schematic illustration of instrumented rabbit with implanted fusion stimulator. (Illustration by John Sarandria, MD, MS.)

Vicryl sutures (Ethicon, Somerville, New Jersey), and skin was closed with 2-0 nylon sutures. The identical process was performed at the other 2 sites (L3, T13) with newly sterilized instruments. Skin and fascia overlying 1 spinal segment were left intact between incision sites to minimize cross-contamination. At the end of the procedure, each defect was inoculated percutaneously with 100 μL of 10^6 CFUs per 100 μL MSSA.

During the intervention phase of the study, this identical procedure was performed with the addition of spinal fusion stimulator implantation. The output of the sterile device (SpF PLUS-Mini Spinal Fusion Stimulator) was verified by connecting it to a voltmeter with disposable sterile wires. After ensuring the device was functional and producing 60-μAmp current, a small subcutaneous pocket was created on the right dorsal thoracic area. With blunt dissection, leads from the device were tunneled subcutaneously to L6 and L3. Each output wire contained positive and negative leads and was tightly wrapped around L6 and L3 cerclage wires, creating 2 parallel circuits; T13 served as the internal control site (**Figure 2**). The device pocket was closed in a manner similar to that used for closing the dorsal spinal incisions.

Postoperative Period and Euthanasia

All animals were monitored twice daily for the first 48 hours and subsequently once daily until euthanasia on postoperative day 7. Guidelines presented by Morton and Griffiths[24] were used in evaluating animal well-being. Euthanasia was performed after ketamine–xylazine sedation with intravenously administered pentobarbital 100 mg/kg, cardiac puncture, and exsanguination.

Data Collection

The veterinary technician recorded operative times per rabbit. After euthanasia, a wound culture was obtained by sterile swab, and bone was rongeured from the remaining defect plus adjacent spinous processes at each site. A venous blood sample was drawn from each rabbit at time of euthanasia. Operation of the fusion stimulator was verified at time of sample collection with a voltmeter. The implanted cerclage wire was retrieved and placed into 20 mL of sterile saline, and bone was placed into 10 mL of sterile saline. Collection tubes with saline were weighed before and after samples were collected.

After weighing, bone was homogenized for 3 minutes, and cerclage wire was sonicated (Pulsating Ultrasonic Wave Cleaner; World Precision Instruments, Sarasota, Florida) and vortexed to detach biofilm, adhering to the implant, into solution. Serial 1/10 dilutions of biofilm solution and homogenized bone from each site were then plated onto 5% sheep blood agar. Wound swabs and 0.1 mL of venous blood from each rabbit were directly plated. Agar plates were incubated at 37°C

for 24 hours. Colonies were subsequently counted. Dilutions were taken into account, and counts per dilution factor were averaged. Final CFU value was determined per gram of tissue sample.

Data Analysis

Infected sites were categorically defined as growing at least 10 CFUs on a blood agar plate without any sample dilution. Number of infected sites and percentage of total sites were determined. Mean and standard deviations of CFUs per gram of tissue sample were calculated for each type of sample (wound swab, bone, implant) by site and as an average of all sites. Differences in infection severity, as measured by CFUs per gram of tissue sample, were determined by a nonparametric Wilcoxon rank-sum test. Differences in infection rates were determined by Fisher exact test. All P values were 2-tailed, and α was set at .05. Statistical analysis was performed with Stata Statistical Software release 11 (StataCorp, College Station, Texas).

Results

Four rabbits were successfully instrumented during the model validation phase of our study and were subsequently monitored for 7 days. Mean operating time was 58 minutes (range, 38 to 76 minutes). The surgical procedure was straightforward, with adequate surgical field of view and nominal bleeding. Minimal force was needed to pierce the holes in the spinous processes so that the implant could be secured. Survival to postoperative day 7 was 100%. The rabbits suffered no surgical complications and exhibited no signs of distress based on characteristics noted in the protocol. No rabbits were bacteremic, as evidenced by a lack of growth in the cultures of blood samples obtained at the time the animals were euthanized.

Varying propensity for infection by anatomical level was not noted in our model. Infection incidences among the T13, L3, and L6 sites by bone and implant biofilm cultures were similar, with comparable severity of infection as measured by CFUs per gram of tissue sample (**Table I**). All bone cultures (12/12 inoculated sites) had osteomyelitis by bacterial colony growth. Implant-related infection occurred in 9 (75%) of the 12 total inoculated sites (**Table II**). Wound swab cultures grew bacteria in 83% of sites, and CFUs were too numerous to count.

Eleven of 13 rabbits had successful surgery and were instrumented during the experimental phase involving the DC fusion stimulator. Two rabbits died during anesthesia induction and were excluded from study; in both cases, veterinary staff attributed cause of death to pneumonia. The remaining 11 rabbits survived until euthanasia without any complications. All DC fusion stimulators demonstrated amperage output of about 60 μAmp at time of implantation and at end of 7-day observation. Culture of blood samples obtained from rabbits during the experimental phase of the study demonstrated no cases of systemic infection.

DC stimulation did not have a statistically significant treatment effect on infection incidence in wound swab, bone, or implant biofilm cultures ($P > .5$) (**Table III**). Rates of bacterial growth in these samples from sites stimulated by DC (L3, L6) versus internal control sites (T13) are listed in **Table III**. Differences in severity of infection, as measured by mean CFUs per gram per sample type, were also not statistically significant between DC-stimulated and internal control sites ($Ps = .25$-$.72$) (**Table IV**).

Table I. Incidence of Infection Based on Vertebral Site With Measured Severity of Infection

	Infection					
	Wound Swab		Bone		Implant	
Site	No. of Sites Infected	Mean (SD) CFUs/g	No. of Sites Infected	Mean (SD) CFUs/g	No. of Sites Infected	Mean (SD) CFUs/g
T13	3	TNTC	4	1060 (327)	3	528 (210)
L3	4	TNTC	4	1585 (809)	3	578 (216)
L6	3	TNTC	4	1627 (815)	3	596 (213)

Abbreviations: CFUs/g, colony-forming units per gram of tissue sample; SD, standard deviation; TNTC, too numerous to count.

Table II. Total Incidence of Infection Across All 12 Sites With Measured Severity of Infection

	Infection		
	Wound Swab	Bone	Implant
No. of sites (%)	10 (83)	12 (100)	9 (75)
Mean (SD) CFUs/g	333 (45)	1424 (368)	567 (111)

Abbreviations: CFUs/g, colony-forming units per gram of tissue sample; SD, standard deviation.

Discussion

Animal models have been used to study treatment and preventive interventions for implant-related SSIs.[25-27] However, few models were specifically designed to study spine infections. A rabbit model recently proposed by Poelstra and colleagues[28] described single-level spinal instrumentation through posterior exposure as simulating human posterior spinal procedures. That model has been used to study the efficacy of a local antibiotic delivery device[29] and use of noninvasive capacitive coupling current in reducing postoperative infection rates.[30] Limitations of this model and its permutations include single-level design, which does not accurately represent multilevel instrumented procedures performed in patients, and, in some cases, lack of a fixed implant (a rod freely floats in the iatrogenic dead-space defect). Our study, which used an enhanced design of the previous model, with 2-level fixed-implant instrumentation at 3 noncontiguous sites within a single rabbit, showed consistent localized *S aureus* infection. This allowed 1 or 2 of these instrumented sites to be internal controls for intervention. Total operative times were short, about 1 hour per rabbit, and consistent.

Our multilevel postoperative spine infection rabbit model demonstrated a control implant-related infection rate of 70% to 80%, consistent with the ID70 previously established.[28-30] We used a validated technique for quantifying implant biofilm formation by sonicating and vortexing retrieved instrumentation.[31-33]

The experimental phase, which investigated efficacy of the 60-µAmp implantable DC fusion stimulator, failed to demonstrate any additional antibacterial effect of electrical current compared with simple systemic antibiotic prophylaxis. It is important to note, however, that 60 µAmp is the total output of our device to the L3 and L6 sites combined; in actuality, each site received 30 µAmp of current. Nonetheless, DC as low as 20 µAmp applied to *S aureus* biofilm in vitro was shown to have a statistically significant decrease of about 4 $\log_{10}$ CFUs per cm^2 by day 7 of current application in a study conducted by Del Pozo and colleagues.[34] The comparison of in vivo and in vitro biofilm susceptibility seems to indicate that the efficacy of minimal in vitro doses of current does not apply to in vivo models.

Despite these findings, DC in the range of magnitude used in our study has had positive treatment effects in other in vivo models of biofilm growth. The use of 100-µAmp DC on external fixator frames infected with *Staphylococcus epidermidis* on a goat tibia model decreased infection incidence from 89% to 11%.[35] In another study, in which a foreign body was implanted in the medullary cavity of a rabbit tibia, a 200-µAmp DC against *S epidermidis* biofilm proved to be statistically significantly better than doxycycline treatment.[36] Ultimately, although 60 µAmp was not efficacious in our experiment, the dose of current seemed to be well tolerated. Perhaps the spine presents an environment different from those of other investigated anatomical regions, or DC is more effective against *S epidermidis*. Perhaps unknown factors in the dorsal spine decrease the conduction and efficacy of DC. Our model used stainless steel instrumentation, which is less often used in modern spine surgery and has lower conductivity than that of titanium, the most commonly used metal. We were limited in the dose of current we could apply to the rabbit spine because the safety of higher current devices in humans has not been established, and our results would not have been as readily translatable to patients if higher doses of current had been used. Furthermore, a single dose of

Table III. Incidence of Infection in Wound Swab, Bone, and Implant-Related Biofilm Cultures: Internal Control Versus Direct Current Sites

	Total No. of Sites	Infection		
		Wound Swab	Bone	Implant
Internal control	11	9 (82%)	10 (91%)	9 (82%)
30-µAmp direct current per site	22	17 (77%)	21 (95%)	17 (77%)
P	—	.571	.562	.571

Table IV. Severity of Infection in Wound Swab, Bone, and Implant-Related Biofilm Cultures: Internal Control Versus Direct Current Sites

	Infection: Mean (SD) CFUs/g		
	Wound Swab	Bone	Implant
Internal control	327 (49)	1142 (160)	516 (116)
30-µAmp direct current per site	301 (36)	1411 (207)	511 (64)
P	.72	.65	.25

Abbreviations: CFUs/g, colony-forming units per gram of tissue sample; SD, standard deviation.

perioperative antibiotic was used, consistent with the standard in clinical practice. This might not result in a substantial reduction in infection in our model from a mechanistic standpoint. In the future, we would test the effect of sustained antibiotic administration in addition to DC. It is possible that the effect could be increased efficacy by the synergistic detachment of biofilm and the bactericidal activity of systemic antibiotics.

Our study had limitations. Internal control sites were not used to confirm that cross-contamination among surgical sites in the same rabbit did not occur with our modification of the model. The original description of this model[28] reported no cases of cross-contamination despite deliberately operating on and inoculating the midlevel site first, before proceeding to the suprajacent and subjacent sites. We are confident that the risk for cross-contamination was further minimized in our study by applying instrumentation to all 3 sites while maintaining the same skin and fascial bridge between sites, as in the original description of the model, and by inoculating all sites simultaneously, at the end of the procedure. Our control site infection rates were consistent with those of the previous model, which supports our supposition. Our treatment allocation was not randomized and outcome assessment not blinded because we thought our objective outcomes would unlikely be affected by measurement bias. We found this to be the case, as our results were not biased in favor of the treatment group.

Considering the notable public health burden of SSIs and the current push toward performance-based reimbursements, it is prudent to continually strive to decrease the incidence of SSIs through new interventions and policies. Accurate animal representation of the human milieu after spinal instrumentation procedures permits experimental application of potentially efficacious interventions and preventive strategies.

Conclusion

We have presented an improved and readily translatable animal model for investigation of implant-related postoperative spinal wound infection. Although we were unable to show the effect of DC from a commercially available and US Food and Drug Administration–approved spinal fusion stimulator, we demonstrated technically feasible instrumentation and implantation of the device, which was well tolerated in rabbits. Future studies will investigate safety and efficacy of a higher current output device and the effects of using different microbial pathogens and instrumentation metals.

Dr. Paryavi is Chief Resident Physician, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, Maryland. Dr. Yanko is Attending Orthopaedic Spine Surgeon, Hillel Yaffe Medical Center, Hadera, Israel. Dr. Jaffe is Resident Physician, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, Maryland. Dr. Nimmagadda is Resident Physician, Department of Urology, Massachusetts General Hospital, Boston, Massachusetts. Dr. Noveau is Resident Physician, Department of Obstetrics and Gynecology, Rutgers Medical School, New Brunswick, New Jersey. Mr. Schiavone is Researcher, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, Maryland. Dr. Gilotra is Fellow, Department of Orthopaedics, University of Pennsylvania, Philadelphia, Pennsylvania. Dr. Gelb is Associate Professor of Orthopaedics, and Dr. Ludwig is Professor of Orthopaedics, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, Maryland.

Acknowledgment: The authors thank Dori Kelly, MA, for professional manuscript editing.

Address correspondence to: Steven C. Ludwig, MD, Department of Orthopaedics, University of Maryland School of Medicine, 110 S. Paca Street, 6th Floor, Suite 300, Baltimore, MD 21201 (tel, 410-328-6040; fax, 410-328-0534; e-mail, sludwig@umoa.umm.edu)

Am J Orthop. 2014;43(5):E98-E104.

References

1. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol*. 1999;20(11):725-730.
2. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis*. 2003;9(2):196-203.
3. Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med*. 2004;350(14):1422-1429.
4. Calderone RR, Garland DE, Capen DA, Oster H. Cost of medical care for postoperative spinal infections. *Orthop Clin North Am*. 1996;27(1):171-182.
5. Weinstein MA, McCabe JP, Cammisa FP Jr. Postoperative spinal wound infection: a review of 2,391 consecutive index procedures. *J Spinal Disord*. 2000;13(5):422-426.
6. Massie JB, Heller JG, Abitbol JJ, McPherson D, Garfin SR. Postoperative posterior spinal wound infections. *Clin Orthop*. 1992;(284):99-108.
7. Rechtine GR, Bono PL, Cahill D, Bolesta MJ, Chrin AM. Postoperative wound infection after instrumentation of thoracic and lumbar fractures. *J Orthop Trauma*. 2001;15(8):566-569.
8. Hodges SD, Humphreys SC, Eck JC, Covington LA, Kurzynske NG. Low postoperative infection rates with instrumented lumbar fusion. *South Med J*. 1998;91(12):1132-1136.
9. Sasso RC, Garrido BJ. Postoperative spinal wound infections. *J Am Acad Orthop Surg*. 2008;16(6):330-337.
10. Sheridan RL, Tompkins RG, Burke JF. Prophylactic antibiotics and their role in the prevention of surgical wound infection. *Adv Surg*. 1994;27:43-65.
11. Bratzler DW, Houck PM, Richards C, et al. Use of antimicrobial prophylaxis for major surgery: baseline results from the National Surgical Infection Prevention Project. *Arch Surg*. 2005;140(2):174-182.
12. Lim MR, Lee JY, Vaccaro AR. Surgical infections in the traumatized spine. *Clin Orthop*. 2006;(444):114-119.
13. Levi AD, Dickman CA, Sonntag VK. Management of postoperative infections after spinal instrumentation. *J Neurosurg*. 1997;86(6):975-980.
14. François P, Vaudaux P, Foster TJ, Lew DP. Host–bacteria interactions in foreign body infections. *Infect Control Hosp Epidemiol*. 1996;17(8):514-520.
15. Glassman SD, Dimar JR, Puno RM, Johnson JR. Salvage of instrumental lumbar fusions complicated by surgical wound infection. *Spine*. 1996;21(18):2163-2169.
16. Lonstein J, Winter R, Moe J, Gaines D. Wound infection with Harrington instrumentation and spine fusion for scoliosis. *Clin Orthop*. 1973;(96):222-233.
17. Theiss SM, Lonstein JE, Winter RB. Wound infections in reconstructive spine surgery. *Orthop Clin North Am*. 1996;27(1):105-110.
18. Vinh DC, Embil JM. Device-related infections: a review. *J Long Term Eff Med Implants*. 2005;15(5):467-488.
19. Young PM, Berquist TH, Bancroft LW, Peterson JJ. Complications of spinal instrumentation. *Radiographics*. 2007;27(3):775-789.
20. Kim JI, Suh KT, Kim SJ, Lee JS. Implant removal for the management of infection after instrumented spinal fusion. *J Spinal Disord Tech*. 2010;23(4):258-265.
21. Del Pozo JL, Rouse MS, Patel R. Bioelectric effect and bacterial biofilms: a systematic review. *Int J Artif Organs*. 2008;31(9):786-795.
22. Liu WK, Brown MR, Elliott TS. Mechanisms of the bactericidal activity of low amperage electric current (DC). *J Antimicrob Chemother*. 1997;39(6):687-695.
23. Costerton JW, Ellis B, Lam K, Johnson F, Khoury AE. Mechanism of electrical enhancement of efficacy of antibiotics in killing biofilm bacteria. *Antimicrob Agents Chemother*. 1994;38(12):2803-2809.
24. Morton DB, Griffiths PH. Guidelines on the recognition of pain, distress

and discomfort in experimental animals and an hypothesis for assessment. *Vet Rec*. 1985;116(16):431-436.
25. Belmatoug N, Crémieux AC, Bleton R, et al. A new model of experimental prosthetic joint infection due to methicillin-resistant *Staphylococcus aureus:* a microbiologic, histopathologic, and magnetic resonance imaging characterization. *J Infect Dis*. 1996;174(2):414-417.
26. Eerenberg JP, Patka P, Haarman HJ, Dwars BJ. A new model for post-traumatic osteomyelitis in rabbits. *J Invest Surg*. 1994;7(5):453-465.
27. Petty W, Spanier S, Shuster JJ, Silverthorne C. The influence of skeletal implants on incidence of infection: experiments in a canine model. *J Bone Joint Surg Am*. 1985;67(8):1236-1244.
28. Poelstra KA, Barekzi NA, Grainger DW, Gristina AG, Schuler TC. A novel spinal implant infection model in rabbits. *Spine*. 2000;25(4):406-410.
29. Stall AC, Becker E, Ludwig SC, Gelb D, Poelstra KA. Reduction of post-operative spinal implant infection using gentamicin microspheres. *Spine*. 2009;34(5):479-483.
30. Gilotra M, Griffith C, Schiavone J, Nimmagadda N, Ludwig SC. Capacitive coupling reduces instrumentation-related infection in rabbit spines: a pilot study. *Clin Orthop*. 2012;470(6):1646-1651.
31. Kobayashi H, Oethinger M, Tuohy MJ, Procop GW, Bauer TW. Improved detection of biofilm-formative bacteria by vortexing and sonication: a pilot study. *Clin Orthop*. 2009;467(5):1360-1364.
32. Trampuz A, Piper KE, Jacobson MJ, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. *N Engl J Med*. 2007;357(7):654-663.
33. Piper KE, Jacobson MJ, Cofield RH, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. *J Clin Microbiol*. 2009;47(6):1878-1884.
34. Del Pozo JL, Rouse MS, Mandrekar JN, Steckelberg JM, Patel R. The electricidal effect: reduction of *Staphylococcus* and *Pseudomonas* biofilms by prolonged exposure to low-intensity electrical current. *Antimicrob Agents Chemother*. 2009;53(1):41-45.
35. van der Borden AJ, Maathuis PG, Engels E, et al. Prevention of pin tract infection in external stainless steel fixator frames using electric current in a goat model. *Biomaterials*. 2007;28(12):2122-2126.
36. Del Pozo JL, Rouse MS, Euba G, et al. The electricidal effect is active in an experimental model of *Staphylococcus epidermidis* chronic foreign body osteomyelitis. *Antimicrob Agents Chemother*. 2009;53(10):4064-4068.

This paper will be judged for the Resident Writer's Award.