Deep brain stimulation hardware–related infections: 10-year experience at a single institution

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OBJECTIVE Deep brain stimulation is an effective surgical treatment for managing some neurological and psychiatric disorders. Infection related to the deep brain stimulator (DBS) hardware causes significant morbidity: hardware explantation may be required; initial disease symptoms such as tremor, rigidity, and bradykinesia may recur; and the medication requirements for adequate disease management may increase. These morbidities are of particular concern given that published DBS-related infection rates have been as high as 23%. To date, however, the key risk factors for and the potential preventive measures against these infections remain largely uncharacterized. In this study, the authors endeavored to identify possible risk factors for DBS-related infection and analyze the efficacy of prophylactic intrawound vancomycin powder (VP).

METHODS The authors performed a retrospective cohort study of patients who had undergone primary DBS implantation at a single institution in the period from December 2005 through September 2015 to identify possible risk factors for surgical site infection (SSI) and to assess the impact of perioperative (before, during, and after surgery) prophylactic antibiotics on the SSI rate. They also evaluated the effect of a change in the National Healthcare Safety Network's definition of SSI on the number of infections detected. Statistical analyses were performed using the 2-sample t-test, the Wilcoxon rank-sum test, the chi-square test, Fisher's exact test, or logistic regression, as appropriate for the variables examined.

RESULTS Four hundred sixty-four electrodes were placed in 242 adults during 245 primary procedures over approximately 10.5 years; most patients underwent bilateral electrode implantation. Among the 245 procedures, 9 SSIs (3.7%) occurred within 90 days and 16 (6.5%) occurred within 1 year of DBS placement. Gram-positive bacteria were the most common etiological agents. Most patient- and procedure-related characteristics did not differ between those who had acquired an SSI and those who had not. The rate of SSIs among patients who had received intrawound VP was only 3.3% compared with 9.7% among those who had not received topical VP (OR 0.32, 95% CI 0.10–1.02, $p = 0.04$). After controlling for patient sex, the association between VP and decreased SSI risk did not reach the predetermined level of significance (adjusted OR 0.32, 95% CI 0.10–1.03, $p = 0.06$). The SSI rates were similar after staged and unstaged implantations.

CONCLUSIONS While most patient-related and procedure-related factors assessed in this study were not associated with the risk for an SSI, the data did suggest that intrawound VP may help to reduce the SSI risk after DBS implantation. Furthermore, given the implications of SSI after DBS surgery and the frequency of infections occurring more than 90 days after implantation, continued follow-up for at least 1 year after such a procedure is prudent to establish the true burden of these infections and to properly treat them when they do occur.

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KEY WORDS DBS complication; vancomycin powder; risk factors; prophylaxis; infection

ABBREVIATIONS ASA = American Society of Anesthesiologists; BMI = body mass index; DBS = deep brain stimulator; GPI = globus pallidus internus; IPG = implantable pulse generator; IV = intravenous; MSSA = methicillin-susceptible *Staphylococcus aureus*; NHSN = National Healthcare Safety Network; OCD = obsessive-compulsive disorder; SSI = surgical site infection; STN = subthalamic nucleus; VC = ventral capsule; VIM = ventralis intermedius; VP = vancomycin powder; VS = ventral striatum.

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BEKHTEREVA et al. were some of the first clinicians to employ deep brain stimulators (DBSs) in clinical practice in 1963.⁴ Since then, Benabid and colleagues' successful use of DBSs to treat Parkinson's disease in the 1980s^{5,32} made this therapeutic device a regular part of clinical practice in the 1990s and beyond.²³ Subsequently, the DBS proved to be an effective surgical device for some movement^{15,18,30,44,45,52} and psychiatric disorders,^{26,33,34,36,38,39,48,51} and DBS implantation has become increasingly common,³⁵ with estimates of more than 100,000 systems implanted world-wide. However, placement of these systems can be associated with significant complications, including stroke, death, and hardware-related infection.

Infections related to DBS systems are common, and patients may require additional hospitalizations and surgical procedures to eradicate such infections through complete or partial hardware removal and prolonged antibiotic therapy.^{7-10,16,19-21,25,28,41,42,46,50} Estimates of infection rates following DBS implantations differ but have been reported to be as high as 23%.^{7-10,16,20,21,25,28,41,42,46,50} Reported rates may vary in part because of discrepancies in the definition of surgical site infection (SSI), which can be affected by the duration of surveillance, whether reoperation is required, and whether superficial incisional infections are considered an SSI.^{7-10,16,20,21,25,28,41,42,46,50} The duration of surveillance is guided in part by the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN), which in January 2013 decreased the duration of surveillance for SSI following hardware placement from 1 year to 90 days.^{13,29}

Despite the significance of such infections and the availability of various preventive measures, few studies have examined either risk factors for DBS-related infections or measures to prevent them.^{6,37} One recent before-and-after study found that patients who used a preoperative 70% ethyl alcohol antiseptic skin wash had a lower SSI rate after DBS implantation than those who did not.²⁸ Prophylactic antibiotics are recommended for DBS implantation; however, few studies have assessed whether specific antimicrobial agents are more effective than others.⁶ While some investigators have found that intrawound topical vancomycin powder (VP) is associated with lower SSI rates following spine operations^{14,31,40,47,49,53} and craniotomy,¹ to our knowledge, only one study has assessed whether intrawound VP is associated with lower SSI rates after DBS placement procedures.⁴³

To address this knowledge gap, we conducted a retrospective single-center cohort study to identify possible risk factors for DBS infections. We investigated the effect of patient characteristics and operative factors, including the number of procedures used to implant the DBS system, the antibiotic used for perioperative (before, during, and after surgery) prophylaxis, and the placement of intrawound VP, on SSI rates following DBS implantation.

Methods

Study Design

We conducted a retrospective cohort study of all adult patients (≥ 18 years old) who had undergone primary

DBS implantation procedures performed by one surgeon (J.D.W.G.) between December 1, 2005, and September 30, 2015, at the University of Iowa Hospitals and Clinics (UIHC). Patients were identified using UIHC's electronic medical record. We reviewed each patient's record to obtain data on demographics, patient characteristics, procedural factors, and SSI. We included only those patients who had received DBS implants for the first time, regardless of whether the devices were implanted during a single "unstaged" procedure (concurrent implantation of lead[s], extension[s], and implantable pulse generator[s] [IPG]) or during staged procedures (lead[s] implanted during one procedure, and extension[s] and IPG[s] implanted during a subsequent procedure). We excluded patients who had undergone revision procedures or isolated IPG replacements. Data were collected to evaluate the incidence of SSI using both the current NHSN definition, which requires surveillance for only 90 days after implantation, and the prior NHSN definition, which required surveillance for 1 year after DBS implantation.^{13,29} One infection preventionist, who had more than 25 years' experience doing surveillance for SSI, independently identified the SSIs. Consistent with the NHSN definitions, we did not consider stitch abscesses or cellulitis to be an SSI. This study was approved by the University of Iowa Institutional Review Board.

Surgical Technique

The techniques for lead placement are the same for both staged and unstaged implantations. After a patient was deemed an appropriate candidate for DBS implantation, a movement disorder neurologist selected the appropriate target nucleus: typically the subthalamic nucleus (STN) or globus pallidus internus (GPI) for patients with Parkinson's disease, the ventralis intermedius (VIM) for patients with essential tremor, and the GPI for patients with dystonia. Indirect targeting was used for these patients, and intraoperative electrophysiology (microelectrode recording for GPI and STN targets and macrostimulation for VIM targets) was used to determine the final lead position. A small subset of patients, identified by psychiatric experts, underwent DBS implantation for medically refractory obsessive-compulsive disorder (OCD). For these patients, MRI-based direct targeting was used to place leads in the ventral capsule and ventral striatum (VC/Vs). Most lead implantations were performed under local and monitored anesthesia; however, 3 patients required general anesthesia because they were very anxious. Microelectrode recording was not used for VC/Vs placements.

Frame-based stereotaxy was used for all lead placements, and trajectories and entry points were chosen to avoid prominent sulci, the ventricles, and the caudate nucleus. Hair was clipped only around the areas to be incised, and 2-stage skin preps were done with either alcohol swabs or chlorhexidine/alcohol combination sponges (Chloraprep, BD Inc.) followed by povidone-iodine gel. Povidone-iodine adhesive skin drapes (Ioban, 3M) were applied.

All patients received prophylactic antibiotics intravenously 30–60 minutes before their incisions. Intracranial leads were placed under monitored anesthesia care. Standard stereotactic techniques were used for lead placement,

and plastic caps (Stimloc, Medtronic Inc.) were used to secure the leads. For bilateral lead placements, one lead was tunneled subgaleally to the contralateral side of the head to facilitate placement of a single dual-channel IPG (for example, Aactiva PC, Medtronic Inc.). The distal lead ends were capped and coiled in a subgaleal or subperiosteal pocket around the burr hole cap. The wounds were irrigated copiously with a bacitracin and saline solution. In a subset of patients, approximately 200–250 mg of VP was placed in their incisions before wound closure.

Single-Stage (Unstaged) Implantation

For single-stage procedures, the stereotactic frame was removed after both frontal incisions had been closed. The patient was subsequently placed under general endotracheal anesthesia for implantation of the lead extensions and the IPG. The scalp, neck, and chest were prepared and draped. Incisions were made in the infraclavicular and retroauricular regions, and the frontal burr hole incision ipsilateral to the planned generator site was reopened. The DBS hardware was placed. In a subset of patients, approximately 400 mg of VP was distributed among the frontal, retroauricular, and infraclavicular incisions before closure. All patients were admitted to the hospital after lead placements, and intravenous (IV) prophylactic antibiotics were continued for 24 hours postoperatively.

Staged Implantation

Most patients underwent 2-stage implantation procedures. The first procedure involved the placement of intracranial leads under monitored anesthesia care as described above. Postoperatively, patients were admitted to the hospital overnight and received IV prophylactic antibiotics for 24 hours. The second procedure typically occurred 7–10 days after lead implantation and was performed under general endotracheal anesthesia in an outpatient surgery setting. Each patient received prophylactic IV antibiotics prior to incision. In a subset of patients, VP was placed in the 3 incisions before wound closure during the second-stage procedure; thus, some patients received VP in their incisions during both procedures. Patients also received oral antibiotics for 24 hours after the second-stage procedure.

Perioperative Antibiotics

During the study period, we implemented several changes in perioperative antibiotic administration. From January 1, 2005, to May 31, 2011, all patients without penicillin allergies received perioperative IV nafcillin. On June 1, 2011, we began administering cefazolin perioperatively based on data from a study of neurosurgical spine procedures at our hospital²⁷ and an update in clinical practice guidelines.¹² Patients who were allergic to penicillin received either vancomycin or clindamycin, according to surgeon preference. Recent work in the surgical and neurosurgical literature has demonstrated the efficacy of topical vancomycin in preventing SSI.^{14,31,40,47,49,53} Starting March 1, 2012, all patients who were not allergic to vancomycin received VP in their surgical incisions; therefore, VP was not administered in a randomized fashion.

Management of SSI

Patients with SSI were managed using a lead-sparing algorithm initially described by Sillay et al.⁴⁶ and modified based on experience at our institution.¹⁹ Briefly, localized infection at the site of the IPG or lead extensions was managed with explantation of the IPG and extensions. The distal ends of the preserved cranial leads were secured in antibiotic-impregnated ventricular catheter segments (approximately 4 cm long) containing clindamycin and rifampin (Bactiseal, Codman, Johnson & Johnson). This was followed by a 6- to 8-week course of directed IV antibiotics based on intraoperative culture and antimicrobial sensitivities results; extensions and the IPG were reimplanted after resolution of the SSI and patients had been off all antibiotics for at least 6 weeks. Initial management of localized SSI involving a burr hole incision included incision and drainage followed by targeted IV antibiotics for 6–8 weeks. Our current practice is to treat any patients with gram-negative SSI, signs of meningitis, or widespread infection (that is, multiple scalp wounds involved) via complete hardware removal. All patients with SSI and preserved leads were followed up in the neurosurgery clinic for at least 6 months to ensure sustained resolution of infection.

Statistical Analysis

Statistical analysis was performed using SAS version 9.3 (SAS Institute Inc.). We used the 2-sample t-test for normally distributed continuous variables (for example, age, body mass index [BMI], blood glucose) or the Wilcoxon rank-sum test for continuous variables that were not normally distributed. For categorical variables (for example, sex, side of surgery, use of VP), we used the chi-square test or Fisher's exact test to compare proportions between non-SSI and SSI groups. The odds ratio and p value for each comparison were computed when appropriate. The 95% confidence intervals for the odds ratios, reflecting the range of possible odds ratios given the inherent variance of the data, were also determined. Given the independent association of patient sex with the SSI rate (see *Results*), we performed logistic regression to control for sex when determining the associations between VP use and SSI. All statistical tests were 2-tailed. A $p < 0.05$ was considered significant.

Results

During the 10.5-year study period, we identified 242 patients who had received 464 new electrode placements during 245 primary DBS implantation procedures. Nine SSIs (3.7%) were detected within 90 days of DBS placement, and 16 (6.5%) were detected within 1 year. The median time to the onset of all 16 SSIs was 79 days (range 30–244 days; Table 1); for the 9 SSIs that occurred fewer than 90 days after the procedure, the median time to onset was 50 days. Eleven infections (68.8%) affected scalp wounds; 9 of these occurred at or near burr holes and 2 were associated with lead extensions. Five infections (31.2%) affected chest wounds.

Given the change in our practice of using VP, we examined the SSI-causative pathogens since VP covers gram-

TABLE 1. Infection occurrence and treatment

SSI Organism	No. (%)	Days to SSI	Op Outcome	VP
MSSA	6 (37.5)			
MSSA alone	4 (25.0)	51	LP; +	N
		56	NHR; +	N
		97	LP; +	N
		119	NHR; +	Y
MSSA, <i>Propionibacterium acnes</i>	1 (6.3)	156	LP; –	N
MSSA, GPR suggestive of diphtheroids	1 (6.3)	76	NHR; +	N
<i>P. acnes</i>	7 (43.8)*			
<i>P. acnes</i> alone	1 (6.3)	32	NHR; +	Y
<i>P. acnes</i> , GPR suggestive of diphtheroids	1 (6.3)	207	NHR; +	N
<i>P. acnes</i> , <i>Pseudomonas aeruginosa</i>	1 (6.3)	30	LP; –	N
<i>P. acnes</i> , methicillin-resistant CoNS, <i>Staphylococcus epidermidis</i>	1 (6.3)	195	NHR; –	N
<i>P. acnes</i> , <i>Enterobacter cloacae</i>	1 (6.3)	114	LP; –	N
<i>P. acnes</i> , <i>S. lugdunensis</i>	1 (6.3)	244	NHR; +	N
Gram-positive cocci	1 (6.3)	36	LP; +	N
Methicillin-resistant <i>S. epidermidis</i>	1 (6.3)	82	NHR; +	Y
<i>Serratia marcescens</i>	1 (6.3)	38	T; +	Y
Mixed skin flora	1 (6.3)	50	NHR; +	N
All infections	16 (100)	30–244		4 (25)

CoNS = coagulase-negative staphylococci; GPR = gram-positive rods; LP = lead preservation technique (see also Dlouhy et al., 2012); N = no; NHR = no hardware removed; T = total hardware removal; Y = yes; + = hardware preserved; – = hardware ultimately removed.

* Includes 1 infection also reported with the MSSA SSI.

positive organisms. Gram-positive bacteria, including *Propionibacterium acnes* (7 cases [43.8%]) and *Staphylococcus aureus* (6 cases [37.5%]) alone or in combination with other organisms, were still the most common etiological agents (Table 1). Gram-negative organisms alone or in combination with *P. acnes* caused 3 SSIs (18.8%). Five (71.4%) of 7 patients with SSIs occurring after 90 days had polymicrobial infections, all of which included *P. acnes*. Among the 9 patients with SSIs occurring before 90 days, only 3 (33.3%) had polymicrobial infections; this difference did not reach statistical significance. Any SSI from which *P. acnes* was isolated had a median onset of 156 days, compared with 56 days for SSIs caused by other organisms. However, the median time to SSIs caused by more-virulent organisms (*S. aureus*, *S. lugdunensis*, and gram-negative organisms; 86.5 days) was longer than SSIs caused by less-virulent organisms (*P. acnes*, coagulase-negative staphylococci, and mixed skin flora; 66 days).

All 16 patients with SSI were readmitted, compared with only 8 patients (3.5%) without SSI ($p < 0.0001$). Fifteen of the 16 patients with SSI were initially treated with hardware-preservation strategies, whereas 1 patient had upfront total hardware removal due to suspected SSI at multiple incision sites. Nine of the 16 patients had focal scalp SSI at or near the site of the burr hole. These SSIs were managed with incision and drainage without hardware explantation, followed by an extended course of antibiotics (“NHR” in Table 1); only 1 of these 9 patients later developed SSI relapse necessitating hardware removal. Six (37.5%) of the 16 patients with SSI had infection at the site of the IPG or lead/extension junction, and this

hardware was removed without cranial lead explantation per our lead-sparing algorithm (“LP” in Table 1).¹⁹ While all 6 of these patients underwent re-implantation of the IPG and extensions, 3 of the 6 had delayed SSI recurrence and ultimately required total hardware removal. All SSI patients were closely followed up to ensure resolution of infection.

Patients with SSI and those without were similar with respect to age, BMI, preoperative glucose level, American Society of Anesthesiologists (ASA) score, preoperative diagnosis, procedure laterality, procedure duration, and antibiotic used for perioperative IV antimicrobial prophylaxis (Table 2). Male patients were less likely than female patients to acquire an SSI (OR 0.28, 95% CI 0.10–0.80, $p = 0.01$) after DBS implantation procedures. Although the IV antibiotic used for prophylaxis was not significantly associated with the incidence of infection, none of the 17 patients who had received vancomycin developed an SSI. Twelve (9.7%) of the 124 patients who had not received intrawound VP had an SSI, whereas only 4 (3.3%) of the 121 patients who had received topical VP had an SSI. Approximately half of the patients without SSI and 25.0% of those with SSI had received intraoperative topical VP (OR 0.32, 95% CI 0.10–1.02, $p = 0.04$). After controlling for patient sex via logistic regression, the association between VP and decreased SSI risk did not quite reach the predefined level of significance (adjusted OR 0.32, 95% CI 0.10–1.03, $p = 0.06$). Wound dehiscence was observed in more patients with SSI than in those without (25.0% vs 2.2%, OR 14.9, 95% CI 3.5–62.9, $p < 0.01$). Wound dehiscence rates were similar for the VP and non-VP groups.

Overall, 17 procedures (6.9%) were unstaged implanta-

TABLE 2. Characteristics of patients and procedures stratified by the presence or absence of SSI

Variable	All Patients	No SSI	SSI	OR for SSI (95% CI)	p Value
No. of patients	245	229	16		
Patient-related factors					
Mean age at surgery in yrs	62.9 ± 11.3	62.7 ± 11.5	65.6 ± 6.7		0.13
Male sex	162 (66.1)	156 (68.1)	6 (37.5)	0.28 (0.10–0.80)	0.01
Mean BMI in kg/m ²	29.2 ± 6.3	29.2 ± 6.4	30.3 ± 4.6		0.49
Mean blood glucose in mg/dl*†	104.9 ± 34.1	105 ± 33.6	104.1 ± 40.9		0.92
ASA score ≥3†	125 (51.2)	119 (52.2)	6 (37.5)	0.55 (0.19–1.56)	0.26
Preop diagnosis					
Dystonia	13 (5.3)	12 (5.2)	1 (6.3)	1.21 (0.15–9.90)	0.59
Essential tremor	94 (38.4)	86 (37.6)	8 (50.0)	1.66 (0.60–4.59)	0.32
OCD	6 (2.4)	6 (2.6)	0 (0)		1.00
Parkinson's disease	131 (53.5)	124 (54.1)	7 (43.8)	0.66 (0.24–1.83)	0.42
Post-stroke thalamic pain syndrome	1 (0.4)	1 (0.4)	0 (0)		1.00
Procedure-related factors					
Side of surgery					
Bilat	219 (89.4)	204 (89.1)	15 (93.8)	1.84 (0.23–14.5)	1.00
Lt	12 (4.9)	12 (5.2)	0 (0)		1.00
Rt	14 (5.7)	13 (5.7)	1 (6.3)	1.11 (0.14–9.09)	1.00
Anatomical target					
GPI	48 (19.6)	45 (19.7)	3 (18.8)	0.94 (0.26–3.45)	1.00
STN	98 (40.0)	93 (40.6)	5 (31.3)	0.66 (0.22–1.98)	0.46
VC/VS	6 (2.4)	6 (2.6)	0 (0)		1.00
VIM	93 (38.0)	85 (37.1)	8 (50.0)	1.69 (0.61–4.68)	0.30
Staged procedure	228 (93.1)	213 (93.0)	15 (93.8)	1.13 (0.14–9.08)	1.00
Median time to 2nd stage in days (range)‡	10 (0–346)	10 (0–84)	9 (7–346)		0.61
Mean op duration in min†§	168.3 ± 46.9	167.6 ± 47.0	178.3 ± 44.5		0.38
Other factors					
Antimicrobial prophylaxis					
Cefazolin	151 (61.6)	140 (61.1)	11 (68.8)	1.40 (0.47–4.16)	0.54
Nafcillin	52 (21.2)	48 (21.0)	3 (18.8)	0.87 (0.24–3.18)	1.00
Vancomycin	17 (6.9)	17 (7.4)	0 (0)		0.61
Other	26 (10.6)	24 (10.5)	2 (12.5)	1.22 (0.26–5.70)	0.68
Topical VP	121 (49.4)	117 (51.1)	4 (25.0)	0.32 (0.10–1.02)	0.04
Postop seroma	1 (0.4)	0 (0)	1 (6.3)		0.07
Wound dehiscence	9 (3.7)	5 (2.2)	4 (25.0)	14.9 (3.5–62.9)	<0.01

Values expressed as the mean ± standard deviation or as number (%), unless indicated otherwise. Boldface type indicates statistical significance.

* Blood glucose was recorded during a preoperative assessment within the month preceding the procedure.

† Available data: All Patients, 244; No SSI, 228.

‡ Available data: All Patients, 228; No SSI, 213; SSI, 15.

§ For staged procedures, overall duration was defined as the sum of time from incision to wound closure for each stage.

tions, only 1 (5.9%) of which was bilateral; 228 procedures (93.1%) were staged, and 218 (95.6%) of these were bilateral (Table 3). Patients with Parkinson's disease (OR 3.54, 95% CI 1.43–8.77, $p = 0.004$) and those with ASA scores ≥ 3 (OR 3.77, 95% CI 1.45–9.80, $p = 0.004$) were more likely to undergo bilateral procedures rather than unilateral procedures. In addition, these patients were more likely to undergo staged rather than unstaged procedures. Given their underlying diseases, patients who underwent staged procedures were probably sicker than those who underwent unstaged DBS implantation. Nonetheless, the

SSI rate was similar between patients who underwent staged (6.6%) and those who underwent unstaged (5.6%) procedures. Rates of other complications, such as wound dehiscence and postoperative seroma, did not differ between the staged and unstaged groups.

Discussion

Our retrospective cohort study is the first to compare the SSI rate after DBS implantation between patients who received VP and those who did not. We found that intra-

TABLE 3. Characteristics of patients and procedures stratified by staged and unstaged implantation

Variable	Staged Procedure	Unstaged Procedure	OR for Staged Procedure (95% CI)	p Value
No. of procedures	228	17		
Patient-related factors				
Mean age at surgery in yrs	63.0 ± 11.0	60.8 ± 14.2		0.43
Male sex	150 (65.8)	12 (70.6)	0.80 (0.27–2.36)	0.69
Mean BMI in kg/m ²	29.3 ± 6.4	28.6 ± 4.8		0.70
Mean blood glucose in mg/dl*	105.6 ± 34.9	95.6 ± 18.0		0.05
ASA score ≥3†	121 (53.1)	4 (25.0)	3.39 (1.06–10.83)	0.03
Diagnosis				
Dystonia	13 (5.7)	0 (0)		0.61
Essential tremor	83 (36.4)	11 (64.7)	0.31 (0.11–0.88)	0.02
OCD	5 (2.2)	1 (5.9)	0.36 (0.04–3.26)	0.35
Parkinson's disease	127 (55.7)	4 (23.5)	4.09 (1.29–12.92)	0.01
Post-stroke thalamic pain syndrome	0 (0)	1 (5.9)		0.07
Procedure-related factors				
Side of surgery				
Bilat	218 (95.6)	1 (5.9)	348.8 (42.0–2898.3)	<0.01
Lt	5 (2.2)	7 (41.2)	0.03 (0.01–0.12)	<0.01
Rt	5 (2.2)	9 (52.9)	0.02 (0.01–0.07)	<0.01
Mean op duration in mins‡	168.4 ± 47.6	167.0 ± 35.9		0.91
Other factors				
Antimicrobial prophylaxis				
Cefazolin	141 (61.8)	10 (58.8)	1.13 (0.42–3.09)	0.81
Nafcillin	47 (20.6)	4 (23.5)	0.84 (0.26–2.71)	0.76
Vancomycin	15 (6.6)	2 (11.8)	0.53 (0.11–2.53)	0.33
Other	25 (11.0)	1 (5.9)	1.97 (0.25–15.50)	1.00
Topical VP	113 (49.6)	8 (47.1)	1.11 (0.41–2.97)	0.84
Postop seroma	1 (0.4)	0 (0)		1.00
Wound dehiscence	9 (4.0)	0 (0)		1.00
SSI	15 (6.6)	1 (5.9)	1.13 (0.14–9.08)	1.00

Values expressed as the mean ± standard deviation or as number (%), unless indicated otherwise. Boldface type indicates statistical significance.

* Blood glucose was recorded during a preoperative assessment within the month preceding the procedure. Available data: Staged Procedure, 227.

† Available data: Unstaged Procedure, 16.

‡ For staged procedures, overall duration was defined as the sum of the time from incision to wound closure for each stage.

wound topical VP was associated with a lower SSI rate following DBS implantation than the rate observed after our standard practice, suggesting that topical VP may be an important preventive measure for patients undergoing this procedure. In addition, we found that men were less likely than women to acquire an SSI and that 43.8% of the infections occurred more than 90 days after the procedures.

Intrawound VP provides supratherapeutic antibiotic concentrations locally³ while reducing the risk of toxicities seen with systemic delivery.²² Numerous groups have found that intrawound VP is associated with decreased SSI rates after spinal procedures,^{1,3,14,24,31,40,47,49,53} and neurosurgeons are now using topical VP to prevent SSI after other procedures, including craniotomy and cranioplasty.^{1,2} To date, only one other group has described the use of VP among patients undergoing DBS implantation.⁴³ Rasouli and Kopell reported a case series of 297 patients who had undergone DBS or IPG placement or replacement. All DBS placements were staged. Fifty percent of the patients

underwent primary procedures, and all patients received 1000 mg of intrawound VP. Patients who had undergone DBS placement received 1000 mg of vancomycin every 12 hours and 1500 mg of cefuroxime every 8 hours intravenously for the first 24 hours in the postoperative period. Patients who had undergone IPG placements received 100 mg of doxycycline by mouth every 12 hours during the first 24 hours of the postoperative period. Four (1.3%) of the 297 patients, all of whom had Parkinson's disease, acquired SSIs. That SSI rate was lower than the 3.3% rate in our patients who had received intrawound VP. Given that 50% of their patients underwent reoperations and 72% underwent procedures for the treatment of Parkinson's disease, one would expect their SSI rate to be higher than that in our patients, who all underwent primary procedures and only 53.5% of whom had Parkinson's disease. However, Rasouli and Kopell used a higher dose of intrawound VP (1000 mg) than we did (approximately 200–400 mg), and they used both vancomycin and cefuroxime as systemic

perioperative prophylaxis. Of note, none of the 17 patients in our study who had received IV vancomycin for perioperative prophylaxis acquired an SSI. The results of the case series by Rasouli and Kopell and our retrospective cohort study suggest that a large prospective study should investigate the role of intrawound VP and perioperative vancomycin prophylaxis for the prevention of SSI after DBS placement. In addition, future studies should assess the dose of intrawound VP needed to prevent SSI.

The association between VP and decreased SSI risk did not quite achieve statistical significance (adjusted OR 0.32, 95% CI 0.10–1.03, $p = 0.06$) when we controlled for patient sex. This result may suggest that the “protective” effect of male sex is driving the differences in SSI seen with the use of VP; however, males were not significantly overrepresented among the patients receiving VP (approximately 67% male) as compared with the patients not receiving VP (approximately 65% male). Instead, the lack of statistical significance after calculating an adjusted OR may be related to a lack of power in our study. Given that the incidence of SSI is relatively low, the ability to detect a further reduction in the incidence with VP would require a larger number of patients than is reported on here.

We found that the duration of surveillance substantially affected the number of SSIs identified and, thus, the SSI rate. When we applied the new NHSN surveillance duration of 90 days for procedures involving implants, our SSI rate following DBS implantation was 3.7% compared with 6.5% when we applied the prior surveillance duration of 1 year. Published SSI rates after DBS procedures have ranged from 0% to 23%.^{7,9–11,16,20,21,25,28,41,42,46,50} Differences in the duration of surveillance probably account for some of this variation in published SSI rates. Our findings suggest that truncating SSI surveillance at 90 days after DBS procedures may result in an underestimation of the true burden of SSI.

Consistent with the published literature,^{16,21,25} gram-positive bacteria were the most common microorganisms isolated from SSIs in our study population. In fact, 75% of the infections were caused by methicillin-susceptible *S. aureus* (MSSA), *P. acnes*, or both. Recent observational studies have found that *P. acnes* SSI tends to have an indolent course and presents late.^{27,41} We found similar results; however, we also found that SSIs caused by more virulent organisms occurred later, on average, than those caused by less virulent organisms. Thus, one cannot predict which organism is causing an infection based on the time to infection.

Our findings have clinical implications as well. Given that approximately 44% of the SSIs occurred more than 90 days after the procedures and that approximately 38% were caused by skin commensals alone, clinicians must be aware that infectious complications of DBS implantation can occur well outside the immediate postoperative period and that relatively avirulent organisms can cause SSI in this patient population. Longer-term infectious monitoring is warranted for these patients. Our data do not particularly inform causative differences between early and late SSI. More specifically and as seen in Table 1, virulent pathogens (for example, *Pseudomonas* sp., *Serratia* sp., MSSA, *Enterobacter* sp.) did manifest SSIs both early and late (> 90 days). Additional studies with larger numbers of both

SSIs and patients are needed to identify initial procedure-related factors (that is, contamination) versus potential seeding of DBS implants from unrelated sites (that is, urinary tract infection, pneumonia, bacteremia).

Several studies have not found a relationship between SSI risk and patient demographics^{7,11,45} or between SSI and the reason for placing the DBS.^{45,49} In contrast, Bhatia et al. found that comorbidities were more frequent among patients with SSI than among those without SSI.⁷ Thus, we were surprised that the ASA score, a proxy measure for patient comorbidities, was not associated with SSI risk in our study. Of the patient-related and procedure-related factors we analyzed, only female sex was associated with SSI. Other groups have found procedure-specific differences in SSI rates between men and women.^{15,35} For example, a very large German study found that men had a higher SSI rate after abdominal operations than did women, although men had a lower SSI rate after cardiac operations.³⁵ These investigators also found that the microorganisms isolated from the SSI varied by patient sex, with coagulase-negative staphylococci being isolated more commonly from SSIs in men, and MSSA and *Pseudomonas aeruginosa* being isolated more frequently from SSIs in women. Sex steroids modulate epidermal and dermal thickness and, thus, could affect wound healing.¹⁷ Moreover, results of a recent study of the skin microbiota indicate that skin flora varies by sex, which may help to explain the sex difference we found.⁵⁴

We did not find associations between SSI risk and procedure-related factors such as procedure duration. This observation is consistent with the results of previously published studies^{11,25,45,49} and suggests that interventions targeting specific aspects of the procedure itself may not decrease the SSI rate significantly.

Our study is one of the few to compare SSI rates after staged and unstaged DBS implantation. Some groups have reported higher SSI rates after staged procedures,¹⁶ whereas others have found no difference.⁴⁹ We found that the SSI risk did not differ between patients who underwent staged procedures and those who underwent unstaged procedures. But because very few patients in our study had unstaged DBS implantations, our finding could have resulted from a type II error.

All patients who acquired SSIs after DBS implantation were readmitted to the hospital, and all required additional surgery, some even requiring multiple surgeries. Thus, these infections increase patient suffering, morbidity, and costs. In particular, patients whose DBS systems are removed are likely to have their motor or psychiatric symptoms recur,¹⁹ which is particularly debilitating for patients who depend on their DBS for symptom control. For example, the wife of a patient whose DBS system was infected recently told one of the authors (L.A.H.), “without the DBS there is no life.”

To reduce the burden caused by SSI after DBS implantation, we must identify and implement effective preventive measures. Our data did not reveal any modifiable patient- or procedure-related factors associated with a lower SSI rate, though we and others have yet to examine other factors that may impact the SSI rate, such as preoperative warming and intraoperative body temperature or the

number of individuals participating in the surgery. Given that we did not identify either patient-related or procedure-related factors that could be addressed to decrease the risk of SSI, our observation that intrawound VP was associated with a lower risk of SSI than that in our standard practice may be very important.

This study has several strengths. Although retrospective cohort studies can be subject to selection bias and recall bias, we attempted to minimize these potential biases by collecting objective data from the medical records of all patients who had primary DBS implantations performed by one surgeon during the study period. We also attempted to minimize undocumented inconsistencies in procedural technique by restricting the study population to those patients whose procedures were performed by a single neurosurgeon at a single institution. In addition, an experienced infection preventionist independently conducted SSI surveillance.

This study also has some limitations. First, we were limited to the information included in the patient medical records. Second, a small proportion of patients underwent unstaged DBS placement, and these patients may not be representative of those undergoing unstaged DBS placement. Therefore, data about patient- and procedure-related factors associated with unstaged procedures must be interpreted with caution. Third, although our study period was longer than 10 years, the number of patients with SSIs was relatively low. Thus, the confidence intervals for the association between intrawound VP and SSI crossed 1. Fourth, the effect of VP use could be confounded by other variables such as surgeon experience or by additive or synergistic effects with preoperative antibiotics. The impact of surgeon experience is likely to be minimal as the use of VP was initiated 7 years into the senior surgeon's practice. Additive or synergistic effects with topical VP would probably have manifested as covariance in the data; however, no relationship was identified between perioperative antibiotics and SSI incidence. Finally, as this study was based on procedures performed by a single surgeon at a single institution, the results may not be generalizable to all patients undergoing DBS implantation.

Conclusions

This retrospective cohort study is, to our knowledge, the first to compare SSI rates after DBS procedures between patients who did and those who did not receive VP. We found that the risk of SSI was 68% lower in the group that received intrawound VP and that intrawound VP was the factor most strongly associated with the risk of DBS hardware-related infections, although a sex difference weakened the statistical strength. This observation of potential VP efficacy is particularly important given the morbidity and costs associated with DBS-related infections and the paucity of other remediable patient-related and procedure-related risk factors. Given the low baseline incidence of SSI after DBS implantation, a large prospective study is required to confirm our findings.

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Disclosures

The authors report no conflict of interest concerning the materi-

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Author Contributions

Conception and design: Greenlee, Herwaldt. Acquisition of data: Greenlee, Abode-Iyamah, Woodroffe, Park, Nagahama, Winslow. Analysis and interpretation of data: all authors. Drafting the article: Greenlee, Abode-Iyamah, Chiang, Jareczek, Nagahama, Herwaldt. Critically revising the article: Greenlee, Abode-Iyamah, Chiang, Jareczek, Nagahama, Herwaldt. Reviewed submitted version of manuscript: Abode-Iyamah, Chiang, Jareczek, Herwaldt. Approved the final version of the manuscript on behalf of all authors: Greenlee. Statistical analysis: Chiang, Herwaldt. Study supervision: Greenlee.

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