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# Clinical significance of positive cranial bone flap cultures and associated risk of surgical site infection after craniotomies or craniectomies

## Clinical article

**Hsiu-yin Chiang, M.S.,[1,2] Victoria M. Steelman, Ph.D.,[5] Jean M. Pottinger, M.A.,[6] Annette J. Schlueter, M.D., Ph.D.,[3] Daniel J. Diekema, M.D., M.S.,[2,3,6] Jeremy D.W. Greenlee, M.D.,[4] Matthew A. Howard III, M.D.,[4] and Loreen A. Herwaldt, M.D.[1,2,6]**

*[1]Department of Epidemiology, University of Iowa College of Public Health; [2]Departments of Internal Medicine, [3]Pathology, and [4]Neurosurgery, University of Iowa Carver College of Medicine; [5]University of Iowa College of Nursing; and [6]Clinical Quality, Safety and Performance Improvement, University of Iowa Hospitals and Clinics, Iowa City, Iowa*

*Object*. The risk of surgical site infection (SSI) after craniotomies or craniectomies in patients in whom contaminated bone flaps have been reimplanted has not been determined. The objectives of this study were to identify the prevalence of bone flaps with positive cultures—especially those contaminated with *Propionibacterium acnes*—to assess the risk of SSI after reimplanting (either during the initial operation or subsequently) bone flaps with positive cultures, and to identify risk factors for SSI following the initial craniotomies or craniectomies.

*Methods*. The authors conducted a retrospective review of cases in which patients underwent craniotomy/craniectomy procedures between January and October 2007 in the neurosurgery department at the University of Iowa Hospitals and Clinics. They also reviewed processes and procedures and did pulsed field gel electrophoresis of *P. acnes* isolates to look for a common source of contamination. They then conducted a prospective cohort study that included all patients who underwent craniotomy/craniectomy procedures between November 2007 and November 2008 and met the study criteria. For the cohort study, the authors obtained cultures from each patient's bone flap during the craniotomy/craniectomy procedures. Data about potential risk factors were collected by circulating nurses during the procedures or by a research assistant who reviewed medical records after the procedures. An infection preventionist independently identified SSIs through routine surveillance using the Centers for Disease Control and Prevention's definitions. Univariate and bivariate analyses were performed to determine the association between SSI and potential risk factors.

*Results*. The retrospective review did not identify specific breaks in aseptic technique or a common source of *P. acnes*. Three hundred seventy-three patients underwent 393 craniotomy/craniectomy procedures during the cohort study period, of which 377 procedures met the study criteria. Fifty percent of the bone flaps were contaminated by microorganisms, primarily skin flora such as *P. acnes*, coagulase-negative staphylococci, and *Staphylococcus aureus*. Reimplanting bone flaps that had positive culture results did not increase the risk of infection after the initial craniotomy/craniectomy procedures and the subsequent cranioplasty procedures ($p = 0.80$). Allowing the skin antiseptic to dry before the procedures ($p = 0.04$, OR 0.26) was associated with lower risk of SSIs. Female sex ($p = 0.02$, OR = 3.49) was associated with an increased risk of SSIs; Gliadel wafer implants ($p = 0.001$, OR = 8.38) were associated with an increased risk of SSIs after procedures to treat tumors.

*Conclusions*. Operative factors such as the way the skin is prepared before the incision rather than the skin flora contaminants on the bone flaps may play an important role in the pathogenesis of SSIs after craniotomy/craniectomy. Gliadel wafers significantly increased the risk of SSI after procedures to treat tumors.
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**Key Words • infection • surgical site infection • craniotomy • positive culture • cranial bone flap • skin antiseptics • Gliadel wafer**

Neurosurgeons frequently have cranial bone flaps cryopreserved after craniectomies when significant cerebral edema is present or anticipated. After the edema has resolved, patients undergo a second operation for cranioplasty. Allograft bone is not commercially available to match the thickness and contour of the skull. If necessary, a synthetic prosthesis can be manufactured. However, these patient-specific prostheses are very expensive. The patient's cranial bone flap matches the surgical defect, and, thus, surgeons often prefer this autograft for the cranioplasty.

Currently, there is no standard method for processing patients' autografts. At some institutions, including the

*Abbreviations used in this paper:* CHG = chlorhexidine gluconate; CoNS = coagulase-negative staphylococci; SSI = surgical site infection; UIHC = University of Iowa Hospitals and Clinics.

This article contains some figures that are displayed in color online but in black and white in the print edition.

UIHC, cranial flaps are routinely cultured for bacterial contamination after they are removed and before they are packaged and cryopreserved. However, we did not identify any published studies that assessed the risk associated with reimplanting cranial flaps with positive cultures.

The DeGowin Blood Center at the UIHC acquired the Tissue Bank from Perioperative Nursing in 2006. Until that time, staff of the Tissue Bank discarded all cranial flaps with positive cultures. Staff of the DeGowin Blood Center reconsidered this practice on the basis of studies assessing patients who received hematopoietic stem cell products that had positive cultures. Stem cells are unique, life-saving products, and patients who received infusions of stem cells with positive cultures rarely had complications.[9,10,15,17,18,20,24] Accrediting agencies also accept infusions of such products given their unique nature. Following a similar line of logic, staff of the DeGowin Tissue Bank decided that a neurosurgeon could reimplant cranial flaps with positive cultures if the surgeon deemed the risk-benefit ratio favorable.

Between January 2006 and December 2006, 9 (12.9%) of 70 autograft cranial bone flaps sent to the Tissue Bank for storage and later reimplantation had positive cultures when they were removed; 6 bone flaps (66.7%) grew small numbers of *Propionibacterium acnes*. Between January and October 2007, 23 (38%) of 60 of the cranial bone flap cultures were positive; 15 bone flaps (25%) grew *P. acnes* (3 cultures also grew an additional organism), and 8 (13%) grew other organisms. Bone flaps that grew *P. acnes* were reimplanted in 2 patients, both of whom subsequently acquired *P. acnes* SSIs that necessitated further operations. One patient acquired a *P. acnes* SSI after a culture-negative bone flap was reimplanted. Thus, staff questioned the safety of reimplanting cranial flaps contaminated with small numbers of *P. acnes* or other organisms and placed a moratorium on reimplanting these cranial flaps.

A multidisciplinary team of neurosurgeons, perioperative nurses, Tissue Bank staff members, and staff of the Program of Hospital Epidemiology conducted an initial investigation of cases occurring between January and October 2007 to investigate potential sources of endogenous or exogenous contamination. Furthermore, we conducted a prospective cohort study that included all patients who underwent craniotomy/craniectomy procedures in UIHC between November 2007 and November 2008 to: 1) determine the frequency of positive cranial flap cultures; 2) assess the relationship between positive bone flap cultures obtained during the original craniotomy/craniectomy and SSI after reimplantation during either the initial operation or a subsequent cranioplasty; and 3) identify risk factors for SSI following the initial craniotomies or craniectomies.

## Methods

### *Retrospective Investigation of Patients Undergoing Craniotomy/Craniectomy Between January and October 2007*

The multidisciplinary team investigated potential sources of endogenous contamination and of exogenous contamination, including surgeons, nursing personnel, anesthesia providers, operating rooms, equipment, instruments, and supplies. As part of this investigation, a subset of the *P. acnes* isolates identified before November 2, 2007 was typed using pulsed field gel electrophoresis as previously described.[19] Whole-chromosomal DNA in agarose was digested with *Spe*I (Sigma-Aldrich) and the restriction fragments were separated on a CHEF DRII apparatus (Bio-Rad Labs). After electrophoresis, the gels were stained with ethidium bromide, illuminated under ultraviolet light, and photographed. Pulsed field gel electrophoresis patterns were analyzed visually. Isolates with no band differences were considered indistinguishable, those with 1–3 band differences were considered possibly related, and those with more than 3 band differences were considered unrelated. A Fisher exact test was used to assess whether contaminated bone flaps were more likely to be associated with emergency procedures than with scheduled procedures.

### *Prospective Cohort Study*

All neurosurgery patients undergoing craniotomy/craniectomy procedures at the UIHC between November 1, 2007 and November 30, 2008 whose cranial flaps were reimplanted during the initial craniotomy/craniectomy or were sent to the Tissue Bank were evaluated for inclusion in the cohort study. Patients with cranial infections (for example, scalp infections, meningitis, or abscesses) at the time of their initial procedures and patients undergoing craniectomy during otolaryngological procedures were excluded from the study. If a patient had more than one craniotomy/craniectomy within 30 days, only the first surgical procedure was included. If a patient had more than one craniotomy/craniectomy separated by more than 30 days, both surgical procedures were included in the study and the procedures were considered to be independent.

### *Processing Bone Flaps During the Prospective Cohort Study*

Nursing personnel swabbed all surfaces of the cranial flaps for aerobic and anaerobic cultures before soaking the tissue in Bacitracin (50,000 U in 500 ml of saline) for 10 minutes. The cranial flaps were then either reimplanted during the same procedure or packaged for storage. Cranial flaps that were going to be banked were wrapped in a sterile towel, secured, labeled with the patients' identifiers, and placed into a sterile freezer bag. The autograft was then sent to the Tissue Bank and cryopreserved at –70°C or colder until cerebral edema had resolved.

Clinical microbiology laboratory personnel performed aerobic and anaerobic cultures using a standard semiquantitative method. Technologists streaked the sample to 4 quadrants of each agar plate and incubated the plates for 3 days (aerobic) or 5 days (anaerobic) at 35°C. Growth on the semiquantitative cultures was described as "rare" if colonies were found only in the first (primary) quadrant, "few" if they also grew in the second quadrant, "moderate" if they grew in the third quadrant,

and "many" if they grew in the fourth quadrant of the streaked agar plate.

*Collection of Epidemiological Data During the Prospective Cohort Study*

Circulating nurses collected data about the surgical team, hair removal, skin preparation, and use of a sealant or an incise drape and recorded these data on a data collection tool developed for the study. Tissue Bank staff recorded banking information for cranial bone flaps sent to the bank as well as the date of bone flap reimplantation. A research assistant collected data on demographics, the procedure (for example, operation date, wound classification, reason for the operation, the urgency of the operation, and duration of the operation), whether a Gliadel wafer (Carmustine, Guilford Pharmaceuticals) was implanted in the tumor bed (only patients with tumors), and microbiology results from the patients' medical records. The research assistant also determined the indication for the procedure by reviewing the procedure notes and then categorized the indications as tumor, bleed, trauma, or other. An infection preventionist independently identified SSIs occurring after the initial craniotomies/craniectomies or after delayed cranioplasties through routine surveillance using the Centers for Disease Control and Prevention's definitions.[3] The research assistant entered all data into Excel (Microsoft Corp).

This study was approved by the University of Iowa's institutional review board.

*Statistical Analysis*

Patients in whom bone flaps were replaced during their initial craniotomy/craniectomy procedures and those in whom the flaps were replaced during delayed cranioplasties were evaluated to assess the effect of reimplanting contaminated bone flaps. Only the initial craniotomy/craniectomy procedures were included in analyses assessing SSI risk factors. The analyses for risk factors were based on the number of procedures, not on the number of patients.

Univariate analysis was performed using Fisher exact test or logistic regression analysis for categorical variables and the 2-sample t-test for continuous variables. Exact logistic regression was used for the bivariate stratified analyses. Significance was set at $p = 0.05$, and 95% CIs were calculated. Statistical analysis was performed using the SAS software program (SAS Institute, Inc.).

## Results

*Retrospective Investigation*

Between January and October 2007, patients with positive bone flap cultures and those with sterile bone flap cultures were equally likely to be exposed to specific surgeons, nursing personnel, anesthesia providers, operating rooms, equipment, instruments, and supplies. None of the surgical instruments used had been affected by sterilization failures or sterilized improperly. New, disposable, presterilized perforating craniotome burs had been used for all patients. The surgical teams used povidone-iodine gel and solution dispensed in single-unit doses, not in multidose vials that could be contaminated, to prepare a patient's skin. Some surgical staff felt that the incisions were made too soon after the skin prep (that is, the contact time was too short) in some patients, but this observation could not be validated retrospectively. Positive bone flap cultures were equally likely to occur after emergency procedures (in 22 [95.7%] of 23) and scheduled procedures (in 33 [89.2%] of 37) ($p = 0.64$). Environmental cultures were negative for *P. acnes*, and 6 different pulsed field gel electrophoresis types were identified among 10 *P. acnes* isolates (8 from bone flap cultures and 2 from cultures of SSIs), indicating that the infections were not from a common source.

*Prospective Cohort Study*

*Demographic Data*. Between November 2007 and November 2008, 373 patients underwent 393 craniotomy/craniectomy procedures at the UIHC's neurosurgery department, of which 377 procedures met the study criteria (with 4 patients having undergone 2 procedures) (Fig. 1). Thus, the denominator for the following analyses, if it is not specified, is the 377 procedures. The mean age of the study population was 48 years (range 0–95 years), and 195 patients (52.3%) were male. The mean procedure duration was 215 minutes, which approximates the National Nosocomial Infections Surveillance risk index cut point of 219 minutes.[7] Hair was removed from the operative site in 334 (91.3%) of 366 procedures, and clippers were used to remove hair in 332 (99.4%) of these procedures. The operative site was prepared before the incision in 373 (98.9%) of the procedures, and circulating nurses answered the question on the data collection tool about whether the prep dried in 330 (88.5%) of the 373 procedures.

*Bone Flap Contamination and SSIs*. After these 377 initial procedures, 21 patients acquired 22 SSIs (5.8%) (1 patient acquired an SSI after each of 2 procedures). Twenty patients (5.4% of all 373 patients and 95.2% of those 21 with SSI) acquired SSIs after their index procedures. Two patients acquired SSIs after delayed cranioplasties, 1 of whom had an infection after the initial craniotomy/craniectomy as well. This patient's bone flap was contaminated with *P. acnes*, but the first SSI was caused by *Enterobacter cloacae* and *Acinetobacter baumannii*, and the second SSI was caused by *S. aureus* (Case 20 in Table 1). Most SSIs were deep (9 [40.9%]) or organ space (9 [40.9%]) infections.[3] The median time to onset of the infections was 20.5 days (range 2–117 days). Eighteen (85.7%) of 21 patients with SSIs (or 19 [86.4%] of 22 SSIs) required a second surgical procedure to treat their infections.

One hundred eighty-six (50%) of the 372 bone flaps for which culture results were known had positive cultures, of which 147 (79%) grew *P. acnes* alone or in combination with other flora (Table 2). Most (184) of the positive cultures had rare (range 1–18) colonies, and only 2 cultures had few colonies (neither culture report specified the number of colonies); no cultures had moderate or many colonies. In contrast to contamination, only 3 (13.6%) of 22 SSIs were caused by *P. acnes* (Table 1).

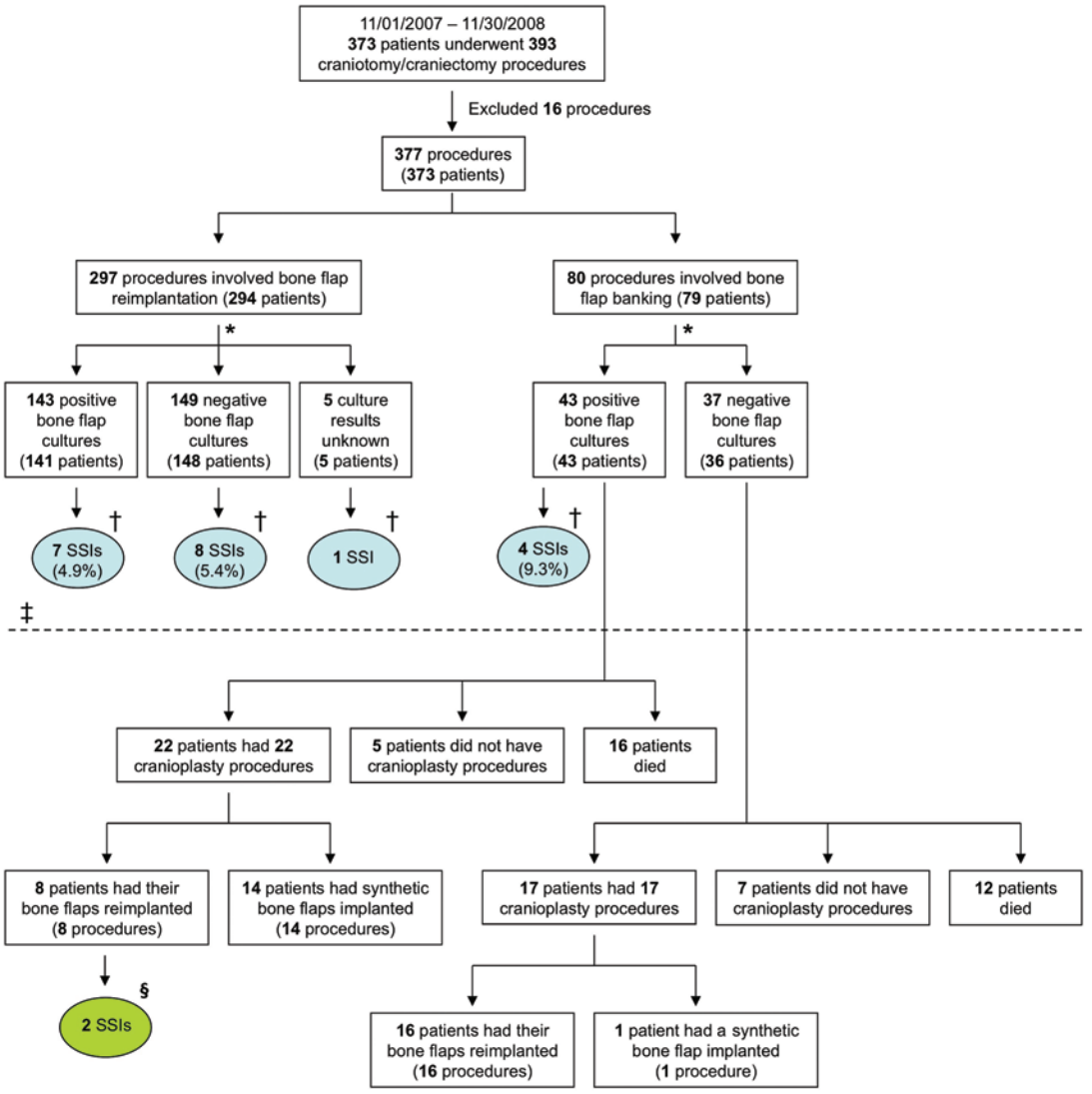


**Fig. 1.** Flow chart describing information obtained in the study population. *The risk of SSI after the initial craniotomies/craniectomies when bone flaps were reimplanted immediately (16 [5.4%] of 297) was not significantly different from the risk of SSI when bone flaps were banked (4 [5.0%] of 80) (p = 1.00, Fisher exact test). †Twenty SSIs occurred in 20 patients after the initial craniotomy/craniectomy procedures. ‡Follow-up information through 11/30/2009 is provided for the 80 procedures (79 patients) for which bone flaps were banked (beneath the *broken line*). However, risk factors for SSIs were assessed only for the initial craniotomy/craniectomy procedures (above the *broken line*), not for delayed cranioplasty procedures. §These 2 SSIs were not included in the study of risk factors for SSIs. One of the 2 patients also acquired an SSI after the initial craniotomy/craniectomy; this initial SSI was included in the risk factor study.

*Staphylococcus aureus* (including 4 cases that were resistant to methicillin) and CoNS were common etiological agents (Table 1). Only 2 patients (Cases 13 and 15) acquired SSIs with the organism or organisms contaminating their bone flaps. One patient's bone flap (Case 12) was contaminated with *S. aureus*, and the SSI was caused by methicillin-resistant *S. aureus*. Because the contaminating organism was not tested for antimicrobial susceptibility, we could not determine whether it caused the infection (Table 1).

Three hundred thirty-three patients underwent 336 procedures to reimplant bone flaps. Reimplantation was performed either during the initial procedure or during a separate cranioplasty. Nine (6.0%) of 151 procedures associated with positive bone flap cultures and 8 (4.8%) of 165 procedures associated with negative cultures were complicated by SSIs. Reimplantation, during either the initial procedure or a subsequent cranioplasty, of bone flaps with positive cultures was not significantly associated with SSI (p = 0.80).

*Risk Factors for SSIs After Craniotomy/Craniectomy.* Positive bone flap cultures (p = 0.64, OR = 1.39), having *P. acnes* in bone flap cultures, age, duration of the procedure, hair removal, emergency procedures, and the indication for the procedure (for example, tumor, bleeding, or trauma) were not risk factors for SSIs after the initial procedures (Table 3). It should be noted that the results of bone flap cultures were missing for 5 procedures. How-

**TABLE 1: Bacteria causing SSIs after the initial craniotomy/craniectomy and delayed cranioplasty procedures***

| Case No. | Organism(s) Contaminating Bone Flaps | Bone Flap Banked | Organism(s) Causing SSIs After Craniotomy/Craniectomy | Organism(s) Causing SSIs After Delayed Cranioplasty | SSI Depth |
|---|---|---|---|---|---|
| 1 | culture negative | no | *S. lugdunensis* & CoNS | not applicable | deep |
| 2 | culture negative | no | *P. aeruginosa* & *Enterococcus* sp. | not applicable | superficial |
| 3 | culture negative | no | *S. aureus* | not applicable | organ space |
| 4 | culture negative | no | CoNS | not applicable | superficial |
| 5 | culture negative | no | MRSA & *P. aeruginosa* | not applicable | organ space |
| 6 | culture negative | no | *P. acnes* & CoNS | not applicable | deep |
| 7 | culture negative | no | MRSA, *E. coli*, *Enterococcus* sp., & *Peptostreptococcus* sp. | not applicable | deep |
| 8 | culture negative | no | CoNS | not applicable | deep |
| 9 | *P. acnes* | no | *K. pneumoniae* | not applicable | organ space (brain abscess) |
| 10 | *P. acnes* | no | Not cultured | not applicable | superficial |
| 11 | *P. acnes* | no | MRSA | not applicable | deep |
| 12 | *S. aureus* | no | MRSA | not applicable | organ space (meningitis) |
| 13 | *P. acnes*, CoNS | no | *P. acnes* & CoNS | not applicable | organ space |
| 14 | *P. acnes*, CoNS | no | not cultured | not applicable | organ space (meningitis) |
| 15 | CoNS & probable *Peptostreptococcus* sp. | no | CoNS | not applicable | organ space |
| 16 | not cultured | no | *P. acnes*, CoNS, & *S. aureus* | not applicable | deep |
| 17 | *P. acnes* & CoNS | yes | No infection | CoNS | deep |
| 18 | *P. acnes* | yes | *S. aureus* | no infection | deep |
| 19 | *P. acnes* | yes | *E. cloacae* | no infection | organ space |
| 20 | *P. acnes* | yes | *E. cloacae* & *A. baumannii* | *S. aureus* | deep (initial), superficial (delayed) |
| 21 | *P. acnes*, CoNS, & *Propionibacterium* sp. | yes | *E. coli* | no infection | organ space |

* MRSA = methicillin-resistant *Staphylococcus aureus*; sp. = species.

ever, if all 5 of these procedures were associated with positive cultures, positive-culture results still would not be significantly associated with SSIs ($p = 0.49$).

Use of 10% povidone-iodine gel followed by povidone-iodine gel solution to prepare the skin (OR 0.21) and allowing the skin antiseptic to dry before the procedures (OR 0.26) were significantly associated with decreased risk of SSIs (Table 3). The difference between povidone iodine gel and solution and other prep solutions remained significant when the data were stratified by the scheduling of the case (emergency vs nonemergency; $p = 0.015$, OR = 0.29), indication for the procedure (trauma vs other; $p = 0.013$, OR = 0.28), and duration of the procedure (≥ 219 minutes vs < 219 minutes [the duration cut point for the National Nosocomial Infections Surveillance risk index];[7] $p = 0.016$, OR = 0.29). The difference between allowing the skin antiseptic to dry and not allowing it to dry also remained significant when the data were stratified by the scheduling of the case ($p = 0.026$, OR = 0.25), indication for the procedure ($p = 0.026$, OR = 0.26), and duration of the procedure ($p = 0.029$, OR = 0.26). Female sex ($p = 0.02$, OR = 3.49) was associated with an increased risk of SSIs; Gliadel wafers were significantly associated with an increased risk of SSIs after procedures to treat tumors (OR = 8.38) (Table 3).

Information about skin preparation was missing for 4 procedures. If the skin preparations for these 4 procedures were all done with povidone-iodine gel and solution, the relationship of skin preparation and SSI would no longer be significant ($p = 0.10$). Data about whether the skin preparation was allowed to dry or not was missing for 47 procedures. If the skin prep for all 47 procedures had been allowed to dry before the procedures were started, the protective effect of allowing the prep to dry would no longer quite reach statistical significance at the $p = 0.05$ level ($p = 0.057$).

## Discussion

### *Bone Flap Cultures*

This study assessed risk factors for SSIs in patients who underwent craniotomies or craniectomies. We were particularly interested in assessing whether positive flap cultures were associated with an increased risk of SSI. Despite the fact that 98.9% of procedures had skin preps documented before they were undertaken, 50% of bone

**TABLE 2: Bacteriological results of positive bone flap cultures obtained during the initial procedures**

| Organism(s) | No. of Cultures |
|---|---|
| overall no. of cultures | 186 |
| *P. acnes* | 106 |
| *P. acnes* & CoNS | 28 |
| CoNS | 24 |
| *Propionibacterium* sp. alone (2) or in combination w/ *P. acnes* (2) or CoNS (1) or both (3) | 8 |
| *Peptostreptococcus* sp. alone (2) or in combination w/ *P. acnes* (1) or CoNS (2) | 5 |
| gram-positive rods in combination w/ *P. acnes* (2) or *P. acnes* & CoNS (2) | 4 |
| diphtheroids alone (1) or in combination w/ *P. acnes* (1) or CoNS (1) | 3 |
| *Clostridium* sp. alone (1) or in combination w/ *P. acnes* & CoNS (1) | 2 |
| *S. aureus* | 2 |
| *P. granulosum*, *P. acnes*, & CoNS | 1 |
| alpha streptococci | 1 |
| *Bacillus* sp. | 1 |
| *Micrococcus* sp. | 1 |

flaps were contaminated by microorganisms, primarily skin flora. Only 2 or 3 (9.5% or 14.3%, respectively) of 21 patients with SSIs were infected with bacterial species found in their bone flap cultures; positive bone flap cultures, including those that grew *P. acnes*, were not associated with an increased risk of SSI after the initial craniotomy or craniectomy. If we assumed that all 5 procedures with missing culture results had positive bone flap cultures, positive bone flap cultures still were not associated with an increased risk of infections. Furthermore, among patients in whom bone flaps were reimplanted during the initial procedures or during subsequent cranioplasties, bone flaps with positive cultures did not increase the risk of SSI after reimplantation during either the initial procedures or during subsequent cranioplasties.

The results of molecular typing of *P. acnes* isolates from the retrospective study suggested that these isolates did not come from a common source and that they were probably from the patients' own normal flora. Surgical site infections following neurosurgical procedures are frequently caused by endogenous organisms that are part of normal skin flora, such as *S. aureus*, CoNS, and *P. acnes*.[11,16] The general dogma has been that skin flora around the surgical site can be inoculated into the incision during the procedure and subsequently cause infection, particularly if there are foreign bodies or devitalized tissue in the wounds. Whyte et al.[25] found that bacterial counts on the skin at the operative site were correlated with SSIs after general surgical procedures. However, Cronquist and colleagues[4] prospectively studied 609 neurosurgical patients with clean wounds and found that high microbial counts on the skin both before (RR 1.19) and after skin preparation (RR 1.79) were not associated with SSIs. Their study had 80% power to detect a 3-fold increase in risk for SSI in patients with high bacterial counts compared with patients with lower bacterial counts. However, these investigators did not assess whether positive bone flap cultures were associated with SSIs.

Most neurosurgical teams do not culture bone flaps unless they are sent to a tissue bank for storage and subsequent reimplantation. If cultures are obtained, many neurosurgical teams and tissue banks discard bone flaps that have positive cultures, regardless of the nature or degree of contamination. On the basis of our data, our neurosurgeons and the staff at our Tissue Bank decided that autografts contaminated with low numbers of skin flora could be reimplanted. This approach allowed patients to have their cranial defects repaired with bone implants—not titanium or polymethylmethacrylate—that are the exact size, shape, and thicknesses needed to repair their cranial defects, which our staff believed was preferable to using commercially available titanium or acrylic plates.

*Preoperative Skin Antiseptics*

The risk of SSIs increased when the skin antiseptics were not allowed to dry. The protective effect of allowing the povidone-iodine skin prep to dry was not profound ($p = 0.04$) and because data were missing for 47 procedures, we may have underestimated the effect because the missing data might have biased the result. For example, nurses may have been more likely to answer the question about whether the prep dried if they had allowed the prep to dry before the procedure began. If this supposition is correct, then the missing data would more likely be from patients whose skin preps were not allowed to dry. Because these data were missing, the protective effect associated with allowing the skin prep to dry would have been diminished. To determine whether the missing data might have affected our results, we evaluated the worst-case scenario in which all 47 procedures with missing data were in the group of procedures for which the skin prep was allowed to dry and 4 of these procedures were complicated by infections. In this case, the p value was slightly greater than 0.05. However, we think it is unlikely that all 47 procedures were in one category.

To our knowledge, other investigators have not assessed whether allowing the prep to dry affects the risk for SSIs, but this factor is biologically plausible because antiseptics need time to kill the bacteria on the skin. In particular, iodophors require about 2 minutes of contact time to release free iodine, the bactericidal component.[12] Furthermore, skin preps that contain alcohol can be ignited by electrosurgical equipment if they are not allowed to dry completely. Thus, allowing the skin prep to dry is a simple, yet important, patient safety practice. This observation is particularly pertinent because surgical personnel are under pressure to speed up their processes so that more procedures can be done in shorter periods of time, thereby, increasing revenue. However, if staff members respond by cutting corners in ways that increase the incidence of SSIs, the financial benefits gained through speed may be nullified by revenue lost related to SSIs or to nosocomial burns.

**TABLE 3: Potential risk factors and their associations with SSIs after craniotomy/craniectomy***

| Variable | Overall No. of Ops | SSI | Non-SSI | p Value | OR (95% CI) |
|---|---|---|---|---|---|
| no. of ops | 377 | 20 | 357 | | |
| mean age in yrs (range) | 47.8 (0–95) | 51.2 (8–71) | 47.6 (0–95) | 0.49 | NA |
| sex† | | | | 0.02 | |
| female | 180 | 15 (75.0%) | 165 (46.2%) | | 3.49 (1.24–9.81) |
| male | 197 | 5 (25.0%) | 192 (53.8%) | | 1.00 |
| mean op duration | 215 mins | 223 mins | 214 mins | 0.74 | NA |
| case classification | | | | 0.63 | |
| emergency | 115 | 7 (35.0%) | 108 (30.2%) | | 1.24 (0.48–3.20) |
| nonemergency‡ | 262 | 13 (65.0%) | 249 (69.8%) | | 1.00 |
| indication for procedure | | | | 0.14 | |
| tumor | 207 | 13 (65.0%) | 194 (54.3%) | | NA |
| bleed | 54 | 5 (25.0%) | 49 (13.7%) | | |
| trauma | 74 | 2 (10.0%) | 72 (20.2%) | | |
| other | 42 | 0 | 42 (11.8%) | | |
| organism contaminating bone flap¶ | | | | 0.70 | |
| none | 186 | 8 (42.1%) | 178 (50.4%) | | NA |
| *P. acnes* & other flora | 147 | 9 (47.4%) | 138 (39.1%) | | |
| others | 39 | 2 (10.5%) | 37 (10.5%) | | |
| hair removal§ | | | | 0.66 | |
| no | 32 | 2 (11.1%) | 30 (8.6%) | | 0.75 (0.17–3.44) |
| yes | 334 | 16 (88.9%) | 318 (91.4%) | | 1.00 |
| skin prep**†† | | | | 0.04 | |
| 10% PVP gel & solution | 230 | 6 (33.3%) | 224 (63.1%) | | 0.21 (0.05–0.91) |
| 10% PVP gel | 116 | 9 (50.0%) | 107 (30.1%) | | 0.67 (0.17–2.67) |
| CHG | 27 | 3 (16.7%) | 24 (6.8%) | | 1.00 |
| prep dried‡‡ | | | | 0.04 | |
| yes | 301 | 12 (75.0%) | 289 (92.0%) | | 0.26 (0.08–0.86) |
| no | 29 | 4 (25.0%) | 25 (8.0%) | | 1.00 |
| Gliadel wafer in tumor cases§§ | | | | 0.001 | |
| yes | 24 | 6 (46.2%) | 18 (9.3%) | | 8.38 (2.54–27.6) |
| no | 183 | 7 (53.8%) | 176 (90.7%) | | 1.00 |

* NA = not applicable; PVP = povidone-iodine.
† One hundred seventy-eight female patients underwent 180 procedures (2 female patients each had 2 procedures); 195 male patients underwent 197 procedures (2 male patients each had 2 procedures).
‡ Nonemergency cases included urgent and elective cases.
¶ Data obtained in 372 operations.
§ Data obtained in 366 operations.
** Calculated using logistic regression analysis.
†† Data obtained in 373 operations.
‡‡ Data obtained in 330 operations.
§§ Data obtained in 207 operations.

Surgeons use the preoperative skin preparation to reduce the number of bacteria at the site of the incision.[6] Skin antisepsis can be a 1- or a 2-step process. For the 2-step process, the skin is first washed ("scrubbed") with diluted antiseptic and then treated with full-strength antiseptic. To date, a standard procedure and a standard antimicrobial agent have not been established for neurosurgical procedures.[8] However, Darouiche et al.[5] recently found that chlorhexidine-alcohol skin preps were associated with significantly lower rates of superficial and deep incisional SSIs than were povidone-iodine preps in patients undergoing clean-contaminated surgical procedures.

Nearly all procedures in our study were preceded by a skin preparation, and 92.8% of these preps were done with povidone-iodine gel followed by povidone-iodine solution or with povidone-iodine solution alone. We found that SSIs were more likely to occur when the skin preparation was done with either povidone-iodine solution alone or with CHG. However, there are 2 reasons why our data should not be interpreted as suggesting that povidone-iodine is superior to CHG or that povidone-iodine gel combined with povidone-iodine solution is the most effective preoperative skin preparation. First, during the study period, some surgeons requested that the skin prep be changed from povidone-iodine to CHG. We

subsequently learned that staff members were not trained to use CHG; they used it as a "scrub" after diluting it with saline and did not do a second step with full-strength CHG. This process did not meet the manufacturer's requirements for cleaning the skin first and then treating the skin with full-strength CHG. Thus, the preps done with povidone-iodine gel and povidone-iodine solution may have been more thorough than those done with either povidone-iodine solution alone or with the diluted CHG scrub. Second, if all 4 procedures for which skin prep data were missing actually had the skin prepared with povidone-iodine gel and solution, the protective effect of gel plus solution would not be significant. Thus, our data should be interpreted as supporting the importance of following manufacturer's instructions when preparing the skin. A prospective trial comparing the effectiveness of different skin antiseptics for preventing infections after craniotomies and craniectomies would be useful. In addition, our experience underscores the importance of educating personnel about the products used for preoperative skin antisepsis and the optimal methods for using these products.

*Gliadel Wafer Implants*

Gliadel wafers are biodegradable, Carmustine-impregnated polymers implanted in tumor beds after the tumors have been resected. These wafers release the chemotherapeutic agent locally for about 3 weeks,[2] thereby treating brain tumors with a high concentration of Carmustine at the tumor site and minimizing adverse effects of systemic chemotherapy. Attenello et al.[1] retrospectively evaluated 1013 craniotomies done over 10 years for the treatment of malignant gliomas to characterize Gliadel wafer–associated morbidity. These investigators found that Gliadel wafers did not increase the risk of SSI ($p = 0.33$) or meningitis ($p = 1.00$). Their study had 80% power to detect a 2.8-fold increase in risk for SSIs in patients with Gliadel wafer implants compared with patients who did not have these implants. In contrast, McGovern et al.[14] followed 32 patients in whom Gliadel wafers were implanted and found that 28% acquired infections, which represented a higher incidence of infection compared with the average SSI rate for craniotomy (< 5%). Similarly, we found that Gliadel wafer implants were associated with a significantly increased risk of SSI. Unlike Attenello et al., we included all procedures that were done to treat tumors. Thus, our study may underestimate the risk because Gliadel wafers are used primarily to treat malignant glioma.

Patients receiving Gliadel wafer implants often have recurrent tumors and, thus, may have had previous operations or radiation therapy. In addition, they may be immunosuppressed from chemotherapy or from chronic steroid therapy. These factors increase postoperative infection rates and, thus, may have confounded our results.[13,22] We did not collect data on these possible confounders and, thus, could not control for them in the analyses.

*Female Sex*

Female patients had a higher risk of SSI after craniotomy/craniectomy procedures in the present study. Two prior studies identified sex as a risk factor for SSI after craniotomy. However, they found that male patients, not female patients, had a significantly higher risk of SSI. The authors did not explain the male predominance.[11,21,23] Of note, more men than women in our study population received Gliadel wafers. Thus, this factor did not confound the association of female sex with SSIs. Our observation should be studied in other populations to assess whether it is generalizable.

*Limitations*

Our study has several imitations. First, the small sample size limited our ability to detect risk factors that had small odds ratios or that increased the risk of SSI slightly at the significance level of 0.05. For example, given that 30% of the procedures were emergency, the study had a power of 80% to detect an OR of 3.75 in the risk of SSIs for emergency cases compared with nonemergency cases, but it had only a 33% power to detect an OR of 2.0. Moreover, the difference in the SSI rates between procedures associated with contaminated cranial flaps (11 [5.9%] of 186) and those associated with non-contaminated cranial flaps (8 [4.3%] of 186) was only 1.6%. Given our sample size and a 4.3% SSI rate among patients whose cranial flap cultures were negative, the smallest difference in SSI rates that we could detect as significant would be 8.7%. Thus, we may have missed some important risk factors that had smaller odds ratios or had less pronounced effects on the risk of SSI. Moreover, the lack of association between positive bone flap cultures and SSIs could be due to a Type II statistical error.

Second, very few cultures either grew even moderate numbers of bacteria or grew highly virulent organisms. Thus, we could not evaluate the effect of these factors on the risk of SSIs. Routine cultures of banked cranial flaps would allow staff to identify heavily contaminated flaps and flaps contaminated with particularly virulent organisms, which might be more likely to cause infections if they are reimplanted than were the bone flaps we evaluated. Further investigation is needed to determine whether particular organisms or levels of contamination are associated with SSIs and, thus, whether the additional costs of the cultures are justified.

Third, unmeasured patient factors (for example, comorbidities and smoking history) or operative factors (for example, antibiotic prophylaxis) may have confounded our results. We do not think that most of these factors would have been associated with whether the skin prep was allowed to dry or with the choice to use Gliadel wafers. However, factors such as prior operations, radiation therapy, and immunosuppression may have been correlated with recurrent tumors and, thus, with the choice to use Gliadel wafers.

## Conclusions

This pilot study evaluated the effect of contaminated bone flaps and identified other operative factors that may be associated with SSIs after craniotomy/craniectomy procedures. A high proportion of bone flaps were contaminated, but contaminated bone flaps were not associ-

ated with the risk of SSI. However, the way the skin was prepared preoperatively and the use of Gliadel wafers were associated with SSIs. Thus, operative factors may be more important than low numbers of skin flora contaminating the bone flap in the pathogenesis of SSIs after craniotomy/craniectomy.

### Disclosure

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*Address correspondence to:* Jeremy D. W. Greenlee, M.D., Department of Neurosurgery, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, Iowa 52242. email: jeremy-greenlee@uiowa.edu.