Standard Review Article

OPEN

Consensus statement on the prevention, diagnosis, and management of infection following transcutaneous osseointegration for patients with limb loss: current state-of-the-art and proposed future studies

Jason S. Hoellwarth, MD[a], Colin Harrington, MD[b], S. Robert Rozbruch, MD[a], Benjamin K. Potter, MD, FACS[c,*], and Global Collaborative Congress on Osseointegration (GCCO)

Abstract The diagnosis, risk factors, treatment algorithms, and long-term sequelae of superficial and deep, implant-related infections in transdermal, bone-anchored osseointegration are not well-defined. In contrast to the robust experience diagnosing and managing periprosthetic joint infections in total joint arthroplasty, osseointegration surgery has only recently been adopted at a small number of osseointegration centers in the United States, contributing to the lack of long-term outcomes. Through the pooled experience from these osseointegration centers, we present a consensus statement on the perioperative management, incidence, treatment, and diagnostic workup for infectious complications following transdermal, bone-anchored osseointegration.

Keywords: ossoeintegration, bone-anchored limb, transdermal, amputation, infection

1. Introduction

The most frequent postoperative concern for osseointegration is that of infection. However, the assessment and management of patients who demonstrate possible infection remains difficult, primarily because it is often uncertain what actually defines an infection of the osseointegration device or skin penetration aperture. Accordingly, it is difficult to categorize and manage a situation that is not reasonably well defined and mutually agreed upon.

The goals of this consensus article are to provide a focused summary of the relevant literature, offer insights and opinions based on the experience of the authors, and propose strategies to advance the prevention, diagnosis, and management of patients with possible or overt infections of osseointegrated limbs.

2. Existing Literature

One of the most cited reviews of osseointegration was performed by Hebert et al in 2017.[1] They noted that among the 14 included articles, infection and soft tissue irritation at the skin penetration aperture (SPA) were the most common adverse situations, with

Robert Rozbruch reports consulting fees from Nuvasive and J&J. He also reports having stock with Osteosys. Kyle Potter has a CDMRP PRORP grant/contract with DoD-USUHS Restoral. He also has consulting fees with Integrum and Signature. Dr. Hsu reports consultancy for Globus Medical and personal fees from Smith & Nephew speakers' bureau. Danielle Melton has DoD contract OP220013 and CDMRP Grant OR210169. She also has consulting fees for Paradigm Medical Director and has received payment for lectures at the State of the Science Conference on Osseointegration. Danielle Melton has received payment for expert testimony while acting as a consultant and expert witness in multiple cases. She has received support from Amputee Coalition BOD to travel and attend meetings. She has participated in the Data Safety Monitoring Advisory Board for External Advisory Panel for Limb Loss Prevention Registry. Danielle Melton has a leadership or fiduciary role in METRC Executive Council, Amputee Coalition Board of Directors, and in Catapult Board of Directors. Leah Gitajn received consulting fees from Stryker and Paragon28. She also has a leadership or fiduciary role in the OTA program committee and AO research committee. Jason Stoneback reports royalties from AQ Solutions as well as consulting fees from AQ Solutions and Smith and Nephew. He reports payment for lectures from Smith and Nephew and AQ Solutions. Jason Stoneback states he has received payment for expert testimony in multiple cases. He notes he has received support to travel and attend meetings from Smith and Nephew and AQ Solutions. He reports planning a patent for a Rotational Intramedullary Nail. Jason Stoneback states he is the secretary for ISPO Special Interest Group for Bone-Anchored Limbs and is a board member for Justin Sports Medicine Team Annual Conference. He also reports stock with Validus Cellular Therapeutics. Jason Souza is a paid consultant for Balmoral Medical, LLC, Checkpoint, Inc, and Integrum, Inc. The remaining authors declare they do not have any conflicts of interest.

[a] Hospital for Special Surgery, New York, NY, [b] Division of Orthopaedics, Department of Surgery, Uniformed Services University, Walter Reed National Military Medical Center, Bethesda, MD, [c] University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

** Corresponding author. Address: University of Pennsylvania Perelman School of Medicine, 3737 Market St, Suite 600, Philadelphia, PA 19104. E-mail address: benjamin.potter@pennmedicine.upenn.edu (B. K. Potter).*

Source of funding: Nil.

Members of the Global Collaborative Congress on Osseointegration (GCCO) are included in an Appendix at the end of the article.

The study was deemed exempt from institutional review board and animal use committee review.

OTAI (2025) e369

Received: 30 October 2024 / Received in final form: 12 December 2024 / Accepted: 16 December 2024
Published online 7 March 2025

http://dx.doi.org/10.1097/OI9.0000000000000369

rates ranging from 34% to 66%. The review further expressed that iterative improvements to implants and, potentially, surgical technique would likely lead to reduction in the infection incidence. Given our evolving experience with and understanding of skin–implant homeostasis at the aperture site, it is also possible that this apparent decrease in infections could be attributed to improved definitions. Branemark et al[2] presented the first study of a substantial number of patients describing infectious events for transfemoral osseointegrated patients as part of a broad description of 51 patients. They stated that superficial infection was far more common than deep infection, and all superficial infections resolved with antibiotic treatment, mostly 10 days of oral antibiotics. They also wrote that of 4 patients whose implants were removed, 1 was determined to be infected. In this early and otherwise comprehensive article, the authors did not state what criteria defined infection nor how superficial versus deep infection was differentiated. Another early article that discussed infection was by Al Muderis et al,[3] who presented outcomes of 86 patients. More attention was given to the determination of infection, as the authors reported the clinical and radiographic findings that were considered (with patient photographs provided for reference), and a grading system was proposed (Table 1) centered around extent of management required. A similar grading system was proposed by others.[4] Numerous other studies[5–7] confirm the theme of infection being the most common adverse event, with decreasing frequency compared to earlier studies, with superficial infections managed by oral antibiotics being much more common than infection prompting surgery or implant removal. One interesting study noted that although *S. aureus* is a common colonizer of the skin-implant interface, the organism is rarely associated with subsequent infection.[8] Alam et al[9] performed the first investigation regarding algorithmic prediction of infection (defined as positive cultures from deep surgical exposure) based on the combination of clinical, laboratory, and culture data. The most important finding of the study was that peri-implant limb pain (highly correlated with infection), erythrocyte sedimentation rate (ESR) $>$ 30 (highly correlated against infection), positive preoperative culture swab (moderately correlated with infection), gross implant motion (moderately correlated against infection), and erythema or cellulitis of the transcutaneous region (mildly correlated with infection) were variables included in the best area under the curve model, which achieved an 85% positive predictive value; C-reactive protein (CRP) was not informative. Various gram-negative species were the most commonly involved organisms in this study. Furthermore, external swabs yielded false negatives for 26% of patients with a deep infection, and antibiotics directed against bacteria cultured from periportal swabs would have been incorrect for 58% of patients.

2.1. Opinions regarding Osseointegration-Related Infection

During the 2022 and 2023 breakout sessions of the Global Collaborative Conference on Osseointegration (GCCO), the authors sought and recorded consensus on 4 key areas of focus related to osseointegration-related infection: (1) managing inflammation and hygiene; (2) studies to characterize infection in this unique population and guide treatment are needed; (3) indications for explanation of the implant; and (4) recommendations for the diagnostic workup for infection in osseointegration patients.

3. Consensus Opinions Regarding Osseointegration-Related Infection

3.1. Consensus Statement 1: Managing Inflammation and the Importance of Skin Penetration Aperture Hygiene

Our most important consensus opinion related to infection prevention and management is avoiding increased inflammation, and possibly subsequent or related infection, by performing daily hygiene care (and not generally otherwise touching) the apertures. The aperture is an unnatural body orifice, whereas our bodies have many natural orifices. Relatively familiar examples are our ears, eyes, nose, digestive, and genito-urinary orifices. These all produce various types of discharge that must be provided a route of egress and generally result in semisolid material such as eye rheum or earwax. While not quite the same size of orifice, hair follicles also produce discharge that requires cleaning and skin, in general, will exfoliate into crevasses. One historic study noted these discharges can build up between the implant and the bone or living skin and cause obstruction leading problems such as infection or implant loosening, which those authors called the "wedge effect."[10] Cleaning the debris mitigated this problem. Most people routinely clear these discharges from their orifices casually and naturally throughout the day or in specific bathing episodes. In effect, using a fluid such as water to aid mechanical removal of the material is an informal irrigation and debridement.

Table 1

Infection grading.

Classification of Infection			
Level of severity	**Symptoms and signs**	**Treatment**	**Grade**
Low-grade soft tissue infection	Cellulitis with signs of inflammation (redness, swelling, warmth, stinging pain, pain that increases on loading, tense)	Oral antibiotics Parenteral antibiotics Surgical intervention	1 1A 1B 1C
High-grade soft tissue infection	Pus collection, purulent discharge, raised level of C-reactive protein	Oral antibiotics Parenteral antibiotics Surgical intervention	2 2A 2B 2C
Bone infection	Radiographic evidence of osteitis (periosteal bone reaction), radiographic evidence of osteomyelitis (sequestrum and involucrum)	Oral antibiotics Parenteral antibiotics Surgical intervention	3 3A 3B 3C
Implant failure	Radiographic evidence of loosening	Parenteral antibiotics, explantation	4

Reprinted with permission from Wolters Kluwer Health, Inc. Journal of Bone & Joint Surgery. Safety of osseointegrated implants for transfemoral amputees: a two-center prospective cohort study. Munjed Al Muderis, Aditya Khemka, Sara J. Lord, et al. 2016;98(11).

The SPA is a new, non-native orifice that our body did not evolve to self-manage the way our mouth, ears, or other orifices generally do successfully. In the experience of the authors, simple hygiene principles seem to be highly associated with avoiding infection, in particular frequent low-grade infections. Patients must be very strongly counseled to not touch the aperture, especially with their fingers. Our hands contact more of our external environment than perhaps any other part of our body, from everyday objects to more heavily colonized parts of our own body such as our mouth, nose, and genital regions. Understandably, many patients may have the impulse to fidget with their external abutment, which is likely to transmit colonized organisms and potential pathogens[11] to the aperture which is recently reconstructed and does not have a natural barrier to resist microbial ingress. This transmission is likely even when hand hygiene has been specifically attempted because the fingertips are often missed.[12] We therefore repeatedly and directly counsel our patients to avoid touching the 2–3 cm surrounding their implant. The singular exception is when performing SPA hygiene care, which is the other portion of this consensus point.

Hygiene routines for the SPA should be performed once each day as a routine, or more frequently when there is potentially excess contamination such as when performing heavy labor, swimming, or other similar high-exposure activities. Our recommendation is to have patients take a regular shower (with municipal water which is generally rather clean, not with well or cistern water). They should perform a full regular shower such as washing their hair and full body, all the while their hands and fingers are exposed to shampoo and soap. At the conclusion of their shower, with their hands in the cleanest state, they should perform specific skin portal hygiene care. This comprises opening a fresh, sterile gauze pad (not an open gauze pad from a stack or a wash rag), lathering the sterile gauze pad with the shower water and some gentle cleanser (ie, baby shampoo or soft soap), then gently but thoroughly wiping the implant starting from the base at the skin, circumferentially, and moving distal to the end of the implant. We advise the patient to "wipe the implant as you wipe your eyes" meaning you wipe all the eye rheum (eye crust), but avoid digging into the eye itself. The patient should wipe the crust from the osseointegration portal, but not dig under the skin which is prone to excessively irritate the skin or internal granulation tissue. The patient should then rinse the region and let it air dry (rather than wiping with the towel that has wiped the entire body). Patients may benefit from wrapping the implant with a fresh sterile gauze roll to absorb drainage depending on their regular amount of drainage and the anticipated near-term activities. We explicitly caution against using more caustic cleansers such as tea tree oil (Fig. 1), castile soap, carbonic soap, or similar agents. It may be appropriate to use chlorhexidine or even Dakin type solutions on rare occasions or during periods of atypical exposure or irritation, but frequent use of these seems to irritate the aperture and induce worsening inflammation or infection, which often abates upon cessation of such products.

These 2 behaviors—daily hygiene care and not touching the portal—are strongly recommended to help prevent infected-appearing apertures.

3.2. Consensus Statement 2: Studies to Characterize Infection and to Develop Appropriate Treatments are Needed

The second consensus perspective the authors wish to express is that the true rate of low-grade infection around the skin portal is difficult to determine and is likely both over-reported and overtreated with oral antibiotics. Indeed, the diagnosis of early infection for osseointegrated patients remains exceptionally uncertain. This is because the redness, warmth, swelling, pain, and drainage of inflammation (which is a bodily response to irritation such as a foreign body pulling on the skin) is also the cardinal sign of cellulitis,[13] which remains difficult to determine—even in patients without an implant through their skin.[14] Indeed, the skin adjacent to the SPA remains in a higher inflammatory state at baseline versus normal skin,[15] but may tip from inflammation to infection, similar to other skin piercings.[16] Antibiotics will usually improve the appearance of the skin portal because, in addition to antimicrobial action, many antibiotics also have an anti-inflammatory function.[17] Furthermore, the presence of purulent drainage is often considered as proof of microbial infection, but, in reality, pus is a heterogeneous composition of immune-related cells and factors, which respond both to infection and also noninfectious insults, such as mechanical irritation.[18] The presence of purulent drainage at an osseointegration aperture may often not be an infection in the absence of other signs and symptoms, and many patients have some amount of this drainage at baseline. Based on the specific osseointegration studies by Tillander[8] and Alam,[9] obtaining a swab of the SPA or implant is as likely to yield a bacteria as any surface of skin[19] and is unlikely to help guide whether the patient has an infection, let alone the actual dominant pathogen.[9,19] This does not mean that providing antibiotics to a patient that is experiencing pain or drainage that is interfering with quality of life is inappropriate.

The consensus statements are that there is not a recognized reliable technique to correctly identify the inciting bacteria possibly responsible for drainage, erythema, or even deep infection. Obtaining external swabs of the skin, SPA, or implant is recommended against. Providing antibiotics may indeed reduce the signs and symptoms of cellulitis or inflammation, but be mindful that their improvement following antibiotic therapy does not prove an infection had been present. Recognize that any antibiotic coverage is empirically based, as there is no strategy to obtain reliable culture data.

3.3. Consensus Statement 3: Explantation of the Implant

The third consensus opinion the authors offer is that removing an implant because of concern for infection should be considered only after thorough efforts to address the infectious-type symptoms have been thoroughly attempted. As repeatedly expressed in the literature, the overwhelming majority of implants that are considered to have infectious concerns do not need to be removed. This is true even of implants that have had surgical debridement, provided that the implant remains well-fixed. Furthermore, removal of a well-fixed osseointegrated implant is very difficult.[20] The experience of the authors is that the infection is usually successfully treated by antibiotics with or without surgery and implant retention; if the infection persists but the implant is neither compromised nor is the infection compromising patient function or quality of life, antibiotic suppression, and continued implant retention is reasonable and often successful. However, if a patient strongly expresses the desire for the implant to be removed, their right to autonomy should be considered; likewise, we do not retain compromised implants or well-fixed implants in the face of relentless, progressive infection. Instead, it is our recommendation to provide counseling that infection-related events are rarely catastrophic and can usually be managed with various interventions short of formal device removal. Unlike

Figure 1. This patient used tea tree oil for several weeks without informing the surgeon, in an effort to prevent infection. He complained of worsening pain and presented with skin that was cracking, red, and tender. Upon recommendation, he returned to routine hygiene of baby shampoo, and his portal skin returned to a more natural skin appearance within 2 weeks. The patient has remained fully active in a labor career and has not had any infectious concerns in over a year since.

arthroplasty implants which are sealed within the body, osseointegration implants provide a route of egress and patients rarely develop systemic symptoms even in the presence of deep infections. Indeed, infection has not been found to be related to patient mortality.[21]

The recommendation for managing apparent persistent infection is to first reinforce hygiene principles, then consider a course of oral or parenteral antibiotics. Consider an infectious workup (described subsequently) and if there is a surgical target such as an abscess or necrotic tissue then consider surgical debridement. Implant removal should be contemplated only when these measures fail and/or when the implant has been mechanically compromised.

3.4. Consensus Statement 4: Recommendations for the Diagnostic Workup for Infection

The fourth consensus recommendation regards the diagnostic workup for potential infection. Beyond routine history, physical, radiographs, and laboratory studies—consider advanced imaging. We again emphasize that the external appearance of the SPA is often not a reliable guide for care. We have seen deep infections in the presence of healthy-appearing apertures, and some patients with chronically irritated apertures never require antibiotics or develop worsening symptoms, let alone deep infection. A patient's skin aperture may be leaking, even with pus, but this is often not associated with apparent bacterial infection and typically improves with improved SPA hygiene. Although typical infectious laboratory test results may be reasonable, the limited current literature suggests they may not be informative[9]; there is insufficient evidence to recommend against familiar laboratory work such as ESR, CRP, and white blood cell count or other potential markers for infection.

The second step after obtaining a history and performing a physical exam, however, is to obtain orthogonal radiographs. This can show receding bone or perhaps areas where bone may be undermined and lifted from the implant. Although this can represent stress shielding, in the setting of persistent drainage, it may be indicative of progressive inflammatory lysis of the bone due to bacteria. The consensus of these authors, however, is that the most informative diagnostic evaluation for infection is magnetic resonance imaging (MRI). The authors typically perform such studies without intravenous contrast, but it is reasonable to consider contrast to improve visibility and differentiation of potentially infected or necrotic tissue.[22,23] All osseointegration implants currently available for commercial or custom use are made of titanium alloy, which is safe for MRI; however, certain external sleeves and connectors are not MRI safe and may need to be removed prior to MRI. A cobalt-chrome implant that is no longer manufactured and of relatively low circulation has not, to our knowledge, formally tested for MRI safety (although this device may be MRI-compatible at the expense of greater artifact). Although several other cobalt implants have not caused problems,[24] this implant has not been directly studied in MRIs and we do not have experience with it. If there is a target identified on MRI, such as an abscess or necrotic region of bone or sinus tract, directed surgical intervention can be performed (Fig. 2). Positron emission tomography (PET) has demonstrated utility, as well, particularly for cases where MRI information is inconclusive or patients cannot undergo MRI scanning for other reasons.

Our consensus opinion is that the diagnostic process for potential osseointegration-related infection is to solicit history, perform a physical examination, and obtain orthogonal radiography followed by laboratory evaluation of inflammatory parameters. MRI or PET are often the most useful subsequent diagnostic step(s).

4. Future State Consensus Targets

Our consensus opinion is that the most important topic related to infection is the establishment of objective and quantitative criteria to define active infection and the grading of said infections specific to the osseointegration patient population. Toward that end, our first proposal is to explicitly characterize infection among osseointegration (OI) patients through a prospective observational study to capture and report on the variations in presentation, treatment, and outcomes. History and symptoms, inflammatory markers, aperture swabs, and imaging captured from all patients presenting with concern for infection would provide valuable data that can guide the definition of infection in OI and, importantly, also guide optimal prevention and treatment. Explicitly studying the range of presentations in OI, from study of the percentage of portal sites that appear potentially infected but which resolve with only hygiene care (and not antibiotic coverage), to those requiring operative treatment, will

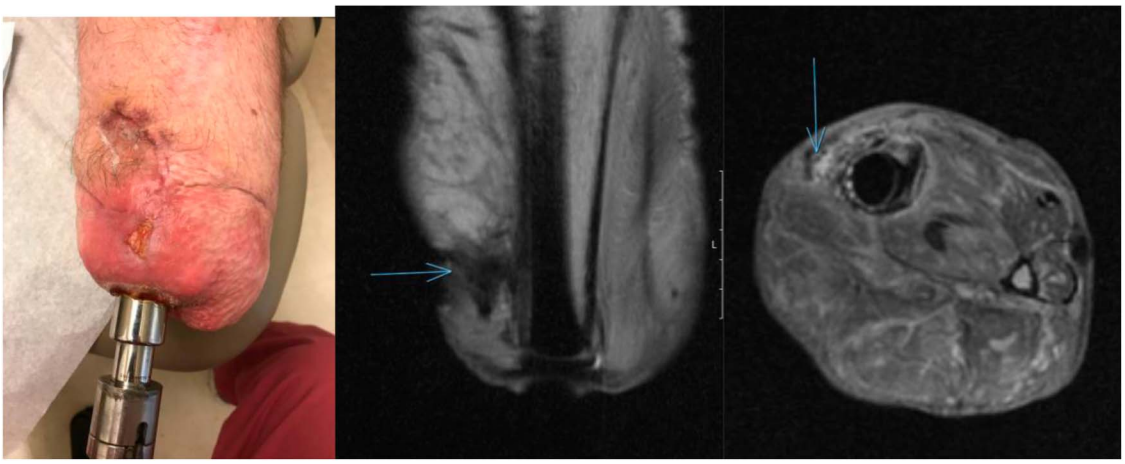

Figure 2. Clinical photograph and MRI left tibia of a patient with sinus tract that was identified as a periosteal abscess, not an implant-threatening infection. This was managed with debridement with implant retention and a course of parenteral antibiotics. The patient remains highly ambulatory and has not had another infectious episode in over 3 years since.

be an important step in developing care pathways and to develop consensus regarding superficial and deep infection criteria.

Since this scenario of uncertain inflammation versus infection is the most common adverse situation, with a very low risk of leading to patient harm, this seems to be the most immediate option to begin to study how to more confidently diagnose superficial infection. Admittedly, some infections may resolve without antibiotics via natural body processes, but an important question, particularly for novice OI surgeons, would be answered.

A next level of diagnostic exploration should be to compare photographs of the skin penetration apertures with orthogonal radiography and MRI without contrast or PET as a diagnostic tool, before empiric antibiotics. The intent of this is to help determine which scenarios may represent localized inflammation versus cellulitis versus abscess or osteomyelitis. Other than an apparent or overt sinus tract, clinical examination often provides little evidence of what is occurring within the depths of the residuum. Further complicating matters, the skin portal itself may become or already serve as a sinus tract. As radiographic changes are important, they are also late, so consideration of early MRI or PET scanning may be indicated for suspicious cases.

Currently, few articles describe the criteria for superficial infection, much less differentiating the apparent value of symptoms such as loading pain, unloading (leg lifting) pain, tenderness to palpation, change in presence of drainage odor, or aperture features (such as size and morphology). In their research to establish an algorithm to diagnose infection, Alam et al[9] differentiated peri-implant limb pain from other history and examination features such as gross implant motion, drainage, and erythema. At least in that study, gross implant motion was more associated with noninfectious implant loosening—a separate and theoretical conundrum in the field of transcutaneous osseointegration. A broader differential for either loading or unloading pain is includes aperture pain or inflammation, infection, noninfectious inflammatory loosening, infectious loosening, stress fractures, implant fracture, and enthesopathy, in addition to potential neurogenic and less frequent causes. As patient volume and overall experience with osseointegration increases, we hope that specific attention to, and documentation, of signs and symptoms may improve our clinical acumen in determining the root cause(s) of each patient's symptoms.

The final consensus recommendation regarding infection is to better understand the hygiene routines of patients. This article has placed a very high emphasis on SPA hygiene care, as it is the opinion of the authors that this is the most important post-operative and patient-controllable factor to prevent infection (although we believe that surgically achieving a stable SPA may be more important), but this issue remains controversial even for patients with short-term external fixators. We acknowledge that we do not have explicit data to support this opinion. For that matter, we have little evidence that superficial infections are directly correlated and linked to, or represent risk factors for, deep infections; it is merely intuitively inferred to be so. Like any habit, deviations occur either intentionally or unintentionally, such as patients forgetting to perform their hygiene care or performing the care with different cleansers or frequency. It is difficult to assess compliance, but it is nonetheless important to directly challenge even seemingly intuitive assumptions. We are aware that some of our patients who have done very well have not strictly followed our hygiene recommendations. On the other hand, some patients who report high compliance nonetheless struggle with recurrent drainage. Therefore, we encourage clinicians to attempt to explicitly study the hygiene habits of their patients to determine general best practices. Some ways this may be done include asking at office visits, scheduled phone calls, or perhaps by providing supplies and requesting patients contact the clinician when a supply refill is needed. Just as important as diagnosing and managing infection might be determining strategies to prevent its possible development in the first place.

Appendix 1. Collaborators

Global Collaborative Congress on Osseointegration (GCCO): Joseph R. Hsu[1], Rachel B. Seymour[1], Danielle Melton[2], Bailey Fearing[1], Leah Gitajn[3], Jason Souza[4], Jason Stoneback[5], Amber Stanley[1], Meghan K. Wally[1], Josh Wenke[6]. [1]Department of Orthopaedic Surgery, Atrium Health Musculoskeletal Institute, Charlotte, NC; [2]University of Colorado School of Medicine, Aurora, CO; [3]Dartmouth Health, Lebanon, NH; [4]Departments of Plastic and Reconstructive Surgery & Orthopedic Surgery, The

Ohio State University Wexner Medical Center, Columbus, OH; [5]Department of Orthopedics, University of Colorado Anschutz Medical Campus, Aurora, CO; [6]University of Texas Medical Branch, Shriners Hospitals for Children, Galveston, TX.

References

1. Hebert JS, Rehani M, Stiegelmar R. Osseointegration for lower-limb amputation: a systematic review of clinical outcomes. *JBJS Rev*. 2017;5: e10.
2. Brånemark R, Berlin O, Hagberg K, et al. A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: a prospective study of 51 patients. *Bone Joint J*. 2014;96-B:106–113.
3. Al Muderis M, Khemka A, Lord SJ, et al. Safety of osseointegrated implants for transfemoral Amputees: a two-center prospective cohort study. *J Bone Joint Surg Am*. 2016;98:900–909.
4. Hoellwarth JS, Reif TJ, Henry MW, et al. Unexpected positive intraoperative cultures (UPIC) at index osseointegration do not lead to increased postoperative infectious events. *J Bone Joint Infect*. 2022;7: 155–162.
5. Juhnke D-L, Beck JP, Jeyapalina S, et al. Fifteen years of experience with integral-leg-prosthesis: cohort study of artificial limb attachment system. *J Rehabil Res Dev*. 2015;52:407–420.
6. Atallah R, van de Meent H, Verhamme L, et al. Safety, prosthesis wearing time and health-related quality of life of lower extremity bone-anchored prostheses using a press-fit titanium osseointegration implant: a prospective one-year follow-up cohort study. *PLoS One*. 2020;15: e0230027.
7. Reif TJ, Khabyeh-Hasbani N, Jaime KM, et al. Early experience with femoral and tibial bone-anchored osseointegration prostheses. *JB JS Open Access*. 2021;6:e21.00072.
8. Tillander J, Hagberg K, Hagberg L, et al. Osseointegrated titanium implants for limb prostheses attachments: infectious complications. *Clin Orthop Relat Res*. 2010;468:2781–2788.
9. Alam SH, Hoellwarth JS, Tetsworth K, et al. Development of an evidence-based diagnostic algorithm for infection in patients with transcutaneous osseointegration following amputation. *J Bone Joint Infect*. 2024;9: 49–57.
10. Hall CW, Cox PA, McFarland SR, et al. Some factors that influence prolonged interfacial continuity. *J Biomed Mater Res*. 1984;18:383–393.
11. *Transmission of Pathogens by Hands*. Geneva, Switzerland: World Health Organization Press; 2009.
12. Gniadek A, Ogórek-Tęcza B, Inglot A, et al. Hand areas which are commonly missed during hand disinfection by nursing students who completed a basic educational course in hand hygiene. *Int J Environ Res Public Health*. 2021;18:2590.
13. Raff AB, Kroshinsky D. Cellulitis: a review. *JAMA*. 2016;316:325–337.
14. Patel M, Lee SI, Akyea RK, et al. A systematic review showing the lack of diagnostic criteria and tools developed for lower-limb cellulitis. *Br J Dermatol*. 2019;181:1156–1165.
15. Holgers K-M, Thomsen P, Tjellström A, et al. Morphologic evaluation of clinical long-term percutaneous titanium implants. *Int J Oral Maxillofac Implants*. 1994;9:689–697.
16. Meltzer DI. Complications of body piercing. *Am Fam Physician*. 2005;72: 2029–2034.
17. Al-Banna NA, Pavlovic D, Gründling M, et al. Impact of antibiotics on the microcirculation in local and systemic inflammation. *Clin Hemorheol Microcirc*. 2013;53:155–169.
18. Serhan CN. Novel ω−3-derived local mediators in anti-inflammation and resolution. *Pharmacol Ther*. 2005;105:7–21.
19. Ogai K, Nagase S, Mukai K, et al. A comparison of techniques for collecting skin microbiome samples: swabbing versus tape-stripping. *Front Microbiol*. 2018;9:2362.
20. Ong G, Hoellwarth JS, Testworth K, et al. Techniques to remove press-fit osseointegration implants. *JBJS Essent Surg Tech*. 2024;14:e23.00017.
21. Hoellwarth JS, Tetsworth K, Oomatia A, et al. Association between osseointegration of lower extremity amputation and mortality among adults. *JAMA Netw Open*. 2022;5:e2235074.
22. Towers JD. The use of intravenous contrast in MRI of extremity infection. *Semin Ultrasound CT MRI*. 1997;18:269–275.
23. Kan JH, Young RS, Yu C, et al. Clinical impact of gadolinium in the MRI diagnosis of musculoskeletal infection in children. *Pediatr Radiol*. 2010; 40:1197–1205.
24. Mosher ZA, Sawyer JR, Kelly DM. MRI safety with orthopedic implants. *Orthop Clin North Am*. 2018;49:455–463.