

Wound Management for Severe Open Fractures: Use of Antibiotic Bead Pouches and Vacuum-Assisted Closure

Mark L. Prasarn, MD, Gregory Zych, DO, and Peter A. W. Ostermann, MD, PhD

Abstract

Open fractures complicated by infection, or those requiring extensive soft-tissue procedures, are disabling problems for patients and result in significant costs for the health care system. As an adjuvant to current protocols involving open fractures, antibiotic bead pouches (ABPs) provide high concentrations of local antibiotics and can help reduce infection rates. Vacuum-assisted closure (VAC) has been shown to decrease the need for, and enhance the success of, free-flap coverage for traumatic wounds that are significant enough to preclude primary closure, delayed primary closure, or healing by secondary intention. These 2 modalities may help decrease the complications and costs involved in the management of severe open fractures.

In this article, we review the theory, technique, and efficacy of ABPs and VAC in the management of severe open fractures.

Open fractures are injuries in which the skin and soft-tissue integument are disrupted and the underlying bone is exposed to the external environment. This communication results in contamination by microorganisms that can cause deep or superficial infection. Impaired vascularity, devitalized tissue, and loss of skeletal stability are all factors leading to increased susceptibility to infection after open fracture.¹ The goals in managing such injuries include infection prevention, fracture union, function enhancement, long-term skin and soft-tissue coverage, cosmesis, adjacent joint mobility, and cost and physiologic efficiency. Such injuries are typically classified using the system proposed by Gustilo and Anderson¹ and later modified by Gustilo and colleagues.² Despite reportedly poor

Dr. Prasarn is Orthopaedic Trauma Attending, University of Rochester, Rochester, New York.

Dr. Zych is Chief, Orthopaedic Trauma, University of Miami/Jackson Memorial Hospital, Miami, Florida.

Dr. Ostermann is Chief, Orthopaedic Trauma, St. Agnes Hospital, Bocholt, Germany.

Address correspondence to Mark L. Prasarn, MD, 59 Lac Kine Drive, Rochester, NY 14618 (tel, 786-514-0226; fax, 212-717-4340; e-mail, markprasarn@yahoo.com).

Am J Orthop. 2009;38(11):559-563. Copyright 2009, Quadrant HealthCom Inc. All rights reserved.

interobserver agreement in its use, this system is prognostic with respect to complications associated with open fractures. Mean rates of infection have ranged from 0% to 2% for type I open fractures, from 2% to 5% for type II, from 5% to 10% for type IIIA, from 10% to 50% for type IIIB, and from 25% to 50% for type IIIC.¹⁻³

Current protocols for treating open fractures include early administration of antibiotics, timely surgical débridement, skeletal stabilization, sterile dressing, systemic support, and establishment of soft-tissue coverage in a wound environment that is clean.^{3,4-8} According to a recent Cochrane review, infection rates can be reduced 59% with prompt administration of systemic antibiotics.⁴ In addition, thorough surgical débridement of these wounds is of utmost importance in preventing infection.^{1,5,7-9} Other adjunctive modalities, including pulsatile lavage, use of antibiotic bead pouches (ABPs), and vacuum-assisted closure (VAC) of wounds, remain controversial.

In several studies, investigators have promoted early coverage of open fractures by demonstrating decreased infection rates and improved flap survival.¹⁰ Even so, there is always concern about clostridial myonecrosis (gas gangrene), which can arise from premature closure of such wounds. Also, in many cases, treating physicians early on deem open fractures not closeable because of contamination and the need for repeat débridements. Another problem arising at many institutions is that the "fix and flap" protocol is not feasible, as microvascular surgery consultations cannot be obtained promptly, and polytrauma patients with high injury-severity scores are unstable. Free flaps also incur significant financial and physiologic costs. Such scenarios demonstrate a need for alternative measures for treating traumatic open wounds. In addition, as most organisms cultured from infected open fractures are nosocomial, it would be advantageous to provide an early barrier between the wound and the hospital environment. In a study by Carsenti-Etesse and colleagues,¹¹ 92% of infected open fractures were caused by bacteria acquired in the hospital.

ANTIBIOTIC BEAD POUCHES

Antibiotic beads were initially used in treating total joint infections and chronic infections, but gradually their use as a prophylactic measure was implemented in open fractures.¹² Results from multiple studies have shown that ABPs can help reduce infection rates in such traumatic

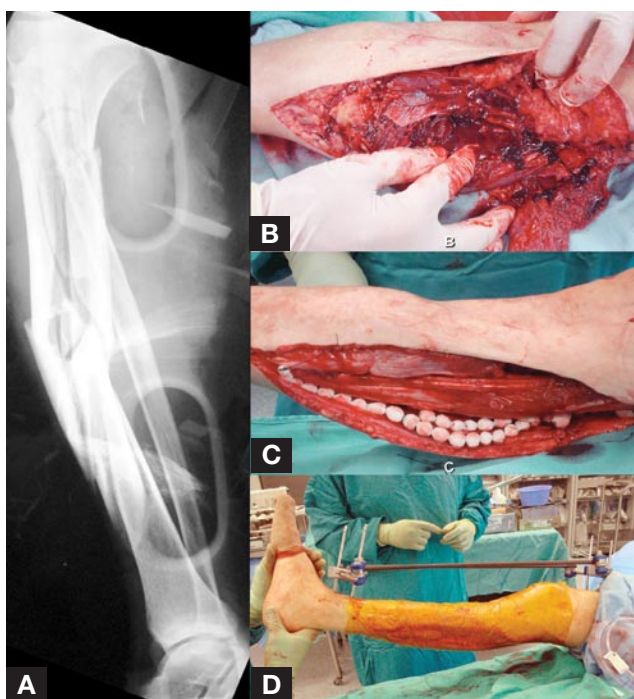


Figure 1. (A) Lateral radiograph of type IIIC open tibia fracture in 77-year-old man. (B) Clinical photograph of open wound before débridement. (C) Clinical photograph of wound after débridement and placement of string of antibiotic beads. (D) Clinical photograph after external fixation and placement of impermeable dressing around wound.

wounds.^{2,5,13-16} ABPs provide both a high concentration of locally delivered antibiotics¹⁷⁻¹⁸ and a barrier to the hospital-dwelling pathogenic bacteria that cause many of the infections resulting from open fractures.¹¹ The most commonly used delivery vehicle is polymethylmethacrylate (PMMA) cement, but research has been focused on alternative materials that do not require later removal.^{17,19-21} Besides helping prevent infection, ABPs provide a moist environment that prevents desiccation of exposed tendons, bone, and neurovascular structures.

PMMA, which is inexpensive and widely available, elutes significant amounts of antibiotic into the surrounding wound, providing significant local concentrations without causing systemic toxicity.²²⁻²⁷ The downside of PMMA is that its removal requires reoperation. There is much focus on developing bioabsorbable delivery vehicles, which would obviate the need for removal. Materials being investigated include plaster of Paris, calcium sulfate, polyglycolic acid, polylactide-polyglycolide copolymers, and fibrin clots.^{8,17,20,28} The elution rate is higher for plaster of Paris than for PMMA.²⁹ Studies have also shown elution differences between brands of PMMA cement and between commercially and noncommercially made beads.^{19,30}

Many factors govern elution of antibiotic beads. Already mentioned is delivery vehicle type. Bead size and shape are also important. Beads that are elliptical and approximately 7 mm in diameter maximize the surface-area-to-volume ratio.^{31,32} A surrounding fluid environment is necessary for

elution, and an impermeable dressing is used to maintain a fluid medium in the wound. Obviously, the turnover rate for this fluid environment determines the antibiotic concentration maintained within the implanted area. Therefore, suction drains are not used for open fractures being treated with ABPs. Some authors advocate using a sump drain in such systems.^{13,32-35} Antibiotic leaching is highest during the first day, declines gradually over the next few days, and stabilizes after about 5 days.¹⁹

Beads are made by first mixing antibiotic powder and packets of PMMA polymer to obtain uniform distribution of the antibiotic. Then the liquid monomer is added and the components mixed until the cement begins to set. The antibiotics that can be used must be in powder form and must be heat-stable enough to withstand the exothermic reaction produced during cement mixing. Vancomycin and aminoglycosides are most widely used secondary to their broad spectrum of activity, high bioavailability, and low allergenicity. Antibiotics should be selected according to the suspected microorganisms involved, and there should always be concern about creating resistant bacteria.^{17,22,25,31,36} A typical dose of antibiotic added to 40 g of PMMA cement is 4.0 g vancomycin or 3.6 g tobramycin or gentamycin.^{29,31,36} Beads are either rolled by hand or made with molds. Then they are strung on wire or on heavy, nonabsorbable suture for ease of removal from the wound. After all avascular, necrotic, and contaminated tissue is removed surgically, and the wound copiously irrigated, the beads are placed in any dead space, and a film dressing (OpSite; Smith & Nephew, Memphis, Tenn) is applied (Figure 1).

In one of the first reported series on the clinical efficacy of ABPs, Henry and colleagues¹³ reviewed 404 open fractures treated with either systemic antibiotic therapy plus an ABP or systemic antibiotic therapy alone. Decisions to use an ABP as adjuvant therapy were a matter of attending surgeon preference or bead availability. Acute wound infection rates were 2.7% for patients who received the combination therapy and 11.4% for patients who received systemic therapy alone. There were significantly more type IIIC fractures in patients who received systemic therapy alone. There was a statistically significant decrease in combination-therapy patients' infection rate for all types of open fractures, except type I. Again, this study was retrospective, and treatment groups were not randomized.

In the largest series on ABP efficacy, Ostermann and colleagues³⁵ retrospectively reviewed 1,085 open fractures and found that the infection rate was statistically significantly ($P < .001$) lower for patients treated with combination therapy (3.7%) than for patients treated with systemic antibiotics alone (12.1%). When Gustilo-Anderson types were compared, the lower infection rate was statistically significant only for type III fractures. Decisions to include antibiotic beads were once again not randomized and were a matter of attending surgeon preference or bead availability. In addition, soft-tissue management differed between the groups; wounds that were treated more frequently with local antibiotic therapy closed sooner.



Figure 2. (A) Vacuum-assisted closure (VAC) device and necessary components. (B) Clinical photograph of VAC placed in traumatic open wound after both-bone forearm fracture.

Keating and colleagues³⁷ examined open tibial fractures and found local antibiotic therapy in addition to systemic antibiotics to be associated with lower risk for infection (4% vs 16%) compared with systemic antibiotics alone. These results were not statistically significant. After patients who were lost to follow-up or required amputation were excluded, only 58 patients remained for the study group. It is therefore possible that, with a larger sample, results may have shown a significant difference. Moehring and colleagues¹⁸ conducted a randomized prospective study on management of type II, IIIA, and IIIB open fractures. Even though the authors' intent was to compare local versus systemic antibiotics, all patients received an initial dose of systemic antibiotics before being taken to the operating suite. Because of inadequate powering (small sample size, large attrition rate), a statistical difference in infection rates could not be shown. In addition, 13 fractures were inadvertently randomized to receive local and systemic antibiotics.

VACUUM-ASSISTED CLOSURE

VAC is being used to obviate the need for, or enhance the success of, free-flap coverage in open fractures that are significant enough to preclude primary closure, delayed primary closure, or healing by secondary intention.^{9,14,38-40} The idea of wound VAC was introduced by Morykwas and colleagues.⁴¹ With VAC devices, a reticulated polyurethane foam dressing is placed into the wound and connected to a suction tube. Figure 2A shows a VAC device and its components, which in a closed system expose the open wound bed to negative pressure. This pressure removes edema or hemorrhage, mechanically pulls on the wound edges, improves circulation, and enhances proliferation of granulation tissue. VAC devices have been used in many surgical disciplines but only recently have become popular in orthopedics.^{7,9,14,15,38-44}

The VAC device is applied to an open traumatic wound only after thorough surgical débridement and wound cleaning. Before application, meticulous hemostasis should be obtained, and vital structures should be covered by mobilizing muscle or other soft tissue in the surrounding area. (There have been case reports of VAC devices eroding into vascular structures and causing significant hemorrhage.⁴⁵) The wound is then measured, and the sponge is cut to conform to it. The sponge is then laid into the wound, with care taken to ensure that the edges of the sponge do not overlie the surrounding skin. An adhesive drape is then applied over the sponge and on the adjacent skin to obtain an airtight seal (Figure 2B). The tubing is connected to the collection canister, which in turn is connected to the vacuum pump. Negative pressure can then be adjusted from 50 to 200 mm Hg, and suction set to be either continuous or intermittent. The dressings are placed after the wound is deemed clean and typically are changed at bedside every 48 to 72 hours thereafter. Dressings are typically applied in a clean fashion and provide a barrier to hospital-acquired pathogenic bacteria. VAC use allows for definitive reconstruction with delayed primary closure, flap coverage, or skin grafting several weeks later, on an elective basis.⁴²

There has been much investigation into the basic science by which application of subatmospheric pressure to wounds increases the healing rate. Several animal studies have demonstrated increased local perfusion to wounds subject to negative pressure as measured by laser Doppler.^{32,41} Studies have shown that this increased blood flow results from decreased capillary afterload leading to improved inflow.^{15,38,41} Increased local blood flow then leads to proliferation of granulation tissue. DeFranzo and colleagues⁴² demonstrated an 80% increase in formation of granulation tissue with VAC use versus traditional wet-to-dry dressings. Evacuation of wound fluid removes factors that suppress fibroblasts, vascular endothelial cells, and keratinocytes, all of which are known to promote wound healing.^{14,15,38} The postulation is that continuous removal of this fluid also removes any accumulating purulence or slime.³⁸ However, VAC-treated wounds have not demonstrated lower bacterial loads.¹⁶ Finally, VAC applies a mechanical force to surrounding soft tissues and causes the wound to contract.^{15,16,40,41} In a randomized, prospective trial, Mouës and colleagues¹⁶ showed a positive effect on wound healing because of a significant decrease in wound surface area compared with controls.

Only a handful of studies have specifically examined the clinical efficacy of wound VAC in the acute setting of open traumatic wounds, and they all had the primary focus of attempting to avoid a local or free-tissue transfer. Parrett and colleagues⁹ retrospectively reviewed 290 open tibia fractures, specifically examining the number of free-tissue transfers required over a 12-year period. Since VAC was introduced in 1997, those authors have used it in most type III open fractures and in 50% of all open fractures. They have demonstrated that there has been a significant decrease in use of free-flap procedures since 1997. They

were unable to demonstrate any differences in infection, amputation, or malunion/nonunion rates.

Dedmond and colleagues³⁹ reported on 50 type III open tibia fractures, all treated with wound VAC before definitive closure or coverage. Of these 50 fractures, 24 were classified IIIB, indicating need for major soft-tissue reconstruction. Ultimately, only 14 of these 24 wounds required flap or free-tissue coverage. In addition, 7 of 24 type IIIA fractures required flap or free-tissue coverage. The authors demonstrated, in total, a 29% reduction in flap coverage required as per Gustilo–Anderson fracture grading. In terms of infection rates and union, results were equivalent to those reported for other modalities, including ABPs and early flap coverage. In another retrospective review, of 15 pediatric patients with open tibia fractures treated with wound VAC, Dedmond and colleagues⁴⁶ reported an estimated 50% reduction in need for free-tissue transfer but a 33% infection rate.

For a minimum of 6 months, Herscovici and colleagues¹⁴ followed 21 patients with high-energy open wounds. Twelve of these patients did not need treatment beyond VAC sponge changes every 72 hours. Five of the other 9 patients required only a split-thickness skin graft, and all 9 required free-tissue transfer. There were no VAC-related complications in the series. Mean cost was \$103 per day for VAC therapy versus \$100 per day for wet-to-dry dressing changes. The cost of having nursing personnel perform dressing changes was factored into the total cost of each modality. The cost of surgical fee alone (Medicare rates) for free-tissue transfer was estimated to be \$6,000. The authors therefore concluded that VAC use can reduce the need for expensive traditional soft-tissue reconstructions and that the overall cost of this modality is only slightly higher than the cost of traditional wound care.

Kanakis and colleagues⁴⁷ performed a comprehensive review of the clinical evidence in the English-language literature regarding use of negative pressure wound therapy in the setting of acute trauma and burns to the lower extremity. They evaluated 11 papers on acute blunt and penetrating trauma but did not conduct a meta-analysis. Only 3 of the 11 papers specifically examined wound VAC in the setting of acute open fractures. All 3 of these papers^{9,39,46} are discussed in the present article. The conclusion drawn by Kanakis and colleagues was that “existing clinical evidence does support the use of [negative pressure wound therapy] in the acute phase of blunt, penetrating and thermal trauma of the extremities.”

SUMMARY

The morbidity and costs associated with open fractures that secondarily become infected are devastating to patients and to the health care system. Clearly, all trauma patients who sustain open fractures require prompt application of prophylactic antibiotics, skeletal stabilization, and meticulous débridement in the operating suite. The adjuvant therapies of pulse lavage, local antibiotic therapy, and wound VAC have less substantial support in the literature. Although minimal cost, lack of systemic effects, and ease of use lend much credibility to use of

ABPs in treating open fractures, randomized clinical trials that more clearly demonstrate the effectiveness of ABPs in preventing infection would be helpful. Wound VAC has proved its efficacy in treating open wounds by reducing the need for costly free-flap transfers, which also cause significant donor-site morbidity. Because of the difficulty in obtaining early flap coverage, we place VAC devices over open fractures that are clean but that will later require flap coverage or skin grafting. We still advocate performing soft-tissue reconstruction (when necessary) at the earliest opportunity. The ability of VAC devices to help prevent infection is questionable, and we believe that using them for extended periods while delaying definitive coverage may expose patients to a higher risk for infection. Better designed clinical studies are once again necessary to improve the level of evidence for using these devices. Although both local antibiotic therapy and wound VAC are in widespread use,⁴⁰ these modern advances are merely adjuvants to thorough surgical débridement.

AUTHORS' DISCLOSURE STATEMENT

The authors report no actual or potential conflict of interest in relation to this article.

REFERENCES

- Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and analyses. *J Bone Joint Surg Am.* 1976;58(4):453-458.
- Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma.* 1984;24(8):742-746.
- Patzakis MJ, Wilkins J. Factors influencing infection rate in open fracture wounds. *Clin Orthop.* 1989;(243):36-40.
- Gosselin RA, Roberts I, Gillespie WJ. Antibiotics for preventing infection in open limb fractures. *Cochrane Database Syst Rev.* 2004;(1):CD003764
- Gustilo RB, Merkow RL, Templeman D. Current concepts review. The management of open fractures. *J Bone Joint Surg Am.* 1990;72(2):299-304.
- Holtom PD. Antibiotic prophylaxis: current recommendations. *J Am Acad Orthop Surg.* 2006;14(10 Spec No):S98-S100.
- Okike K, Bhattacharyya T. Trends in the management of open fractures. A critical analysis. *J Bone Joint Surg Am.* 2006;88(12):2739-2748.
- Wenke JC, Owens BD, Svoboda SJ, Brooks DE. Effectiveness of commercially-available antibiotic impregnated implants. *J Bone Joint Surg Br.* 2006;88(8):1102-1104.
- Parrett BM, Matros E, Pribaz JJ, Orgill DP. Lower extremity trauma: trends in the management of soft-tissue reconstruction of open tibia-fibula fractures. *Plast Reconstr Surg.* 2006;117(4):1315-1322.
- Gopal S, Majumder S, Batchelor AG, Knight SL, De Boer P, Smith RM. Fix and flap: the radical orthopaedic and plastic treatment of severe open fractures of the tibia. *J Bone Joint Surg Br.* 2000;82(7):959-966.
- Carsenti-Etesse H, Doyon F, Desplaces N, et al. Epidemiology of bacterial infection during management of open leg fractures. *Eur J Clin Microbiol Infect Dis.* 1999;18(5):315-323.
- Henry SL, Ostermann PA, Seligson D. Prophylactic management of open fractures with the antibiotic bead pouch technique. *Orthop Trans.* 1989;13:748.
- Henry SL, Ostermann PA, Seligson D. The prophylactic use of antibiotic impregnated beads in open fractures. *J Trauma.* 1990;30(10):1231-1238.
- Herscovici D, Sanders RW, Scaduto JM, Infante A, DiPasquale T. Vacuum-assisted wound closure therapy (VAC therapy) for the management of patients with high-energy soft tissue injuries. *J Orthop Trauma.* 2003;17(10):683-687.
- Morykwas MJ, Simpson J, Pungler K, Argenta A, Kremers L, Argenta J. Vacuum-assisted closure: state of basic research and physiologic foundation. *Plast Reconstr Surg.* 2006;117(7 Suppl):121S-126S.
- Mouës CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: a prospective randomized trial. *Wound Repair Regen.* 2004;12(1):11-17.

17. Burd TA, Anglen JO, Lowry KJ, Kendricks KJ, Day D. In vitro elution of tobramycin from bioabsorbable polycaprolactone beads. *J Orthop Trauma*. 2001;15(6):424-428.
18. Moehring HD, Gravel C, Chapman MW, Olson SA. Comparison of antibiotic beads and intravenous antibiotics in open fractures. *Clin Orthop*. 2000;(372):254-261.
19. Nelson CL, Griffin FM, Harrison BH, Cooper RE. In vitro elution characteristics of commercially and noncommercially prepared antibiotic PMMA beads. *Clin Orthop*. 1992;(284):303-309.
20. Sanicola SM, Albert SF. The in vitro elution characteristics of vancomycin and tobramycin from calcium sulfate beads. *J Foot Ankle Surg*. 2004;44(2):121-124.
21. Winingar DA, Fass RJ. Antibiotic-impregnated cement and beads for orthopedic infections. *Antimicrob Agents Chemother*. 1996;40(12):2675-2679.
22. Adams K, Couch L, Cierny G, Calhoun J, Mader JR. In vitro and in vivo evaluation of antibiotic diffusion from antibiotic-impregnated polymethylmethacrylate beads. *Clin Orthop*. 1992;(278):244-252.
23. Bayston R, Milner RD. The sustained release of antimicrobial drugs from bone cement. An appraisal of laboratory investigations and their significance. *J Bone Joint Surg Br*. 1982;64(4):460-464.
24. Eckman JB Jr, Henry SL, Mangino PD, Seligson D. Wound and serum levels of tobramycin with the prophylactic use of tobramycin-impregnated polymethylmethacrylate beads in compound fractures. *Clin Orthop*. 1988;(237):213-215.
25. Seligson D, Pophan GJ, Voos K, Henry SL, Faghri M. Antibiotic-leaching from polymethylmethacrylate beads. *J Bone Joint Surg Am*. 1993;75(5):714-719.
26. Wahlig H, Dingeldein E, Bergmann R, Reuss K. The release of gentamycin from polymethylmethacrylate beads. An experimental and pharmacokinetic study. *J Bone Joint Surg Br*. 1978;60(2):270-275.
27. Walenkamp G. Small PMMA beads improve gentamicin release. *Acta Orthop Scand*. 1989;60(6):660-668.
28. McKee MD, Wild LM, Schemitsch EH, Waddell JP. The use of antibiotic-impregnated, osteoconductive, bioabsorbable bone-substitute in the treatment of infected long bone defects: early results of a prospective trial. *J Orthop Trauma*. 2002;16(9):622-627.
29. Bowyer GW, Cumberland N. Antibiotic release from impregnated pellets and beads. *J Trauma*. 1994;36(3):331-335.
30. Greene N, Holtom PD, Warren CA, et al. In vitro elution of tobramycin and vancomycin polymethylmethacrylate beads and spacers from Simplex and Palacos. *Am J Orthop*. 1998;27(3):201-205.
31. Seeley SK, Seeley JV, Telehowski P, et al. Volume and surface area study of tobramycin-polymethylmethacrylate beads. *Clin Orthop*. 2004;(420):298-303.
32. Xu L, Chen SZ, Qiao C. Effects of negative pressure on wound blood flow. *J Fourth Milit Med Univ*. 2000;21:967.
33. Henry SL, Ostermann PA, Seligson D. The antibiotic bead pouch technique. The management of severe compound fractures. *Clin Orthop*. 1993;(295):54-62.
34. Ostermann PA, Henry SL, Seligson D. The role of local antibiotic therapy in the management of compound fractures. *Clin Orthop*. 1993;(296):102-111.
35. Ostermann PA, Seligson D, Henry SL. Local antibiotic therapy for severe open fractures. *J Bone Joint Surg Br*. 1995;77(1):93-97.
36. Goodell JA, Flick AB, Hebert JC, Howe JG. Preparation and release characteristics of tobramycin-impregnated polymethylmethacrylate beads. *Am J Hosp Pharm*. 1986;43(6):1454-1461.
37. Keating JF, Blachut PA, O'Brien PJ, Meek RN, Broekhuysen H. Reamed nailing of open tibia fractures: does the antibiotic bead pouch reduce the deep infection rate? *J Orthop Trauma*. 1996;10(5):298-303.
38. Argenta LC, Morykwas MJ, Marks MW, DeFranzo AJ, Molnar JA, David LR. Vacuum-assisted closure: state of clinic art. *Plast Reconstr Surg*. 2006;117(7 Suppl):127S-142S.
39. Dedmond BT, Kortesis B, Punger K, et al. The use of negative-pressure wound therapy in the temporary treatment of soft-tissue injuries associated with high-energy open tibial shaft fractures. *J Orthop Trauma*. 2007;21(1):11-17.
40. Smith JM, Volgas D. Logistics of coverage of open tibia fractures: OTA survey. Paper presented at: 19th Annual Meeting of the Orthopaedic Trauma Association; October 2003; Salt Lake City, UT.
41. Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment. Animal studies and basic foundation. *Ann Plast Surg*. 1997;38(6):553-561.
42. DeFranzo AJ, Argenta LC, Marks MW, et al. The use of vacuum-assisted closure therapy for the treatment of lower-extremity wounds with exposed bone. *Plast Reconstr Surg*. 2001;108(5):1184-1191.
43. Webb LX. New techniques in wound management: vacuum-assisted wound closure. *J Am Acad Orthop Surg*. 2002;10(5):303-311.
44. Webb LX, Laver D, DeFranzo A. Negative pressure wound therapy in the management of orthopedic wounds. *Ostomy Wound Manage*. 2004;50(4A Suppl):26-27.
45. White RA, Miki RA, Kazmier P, Anglen JO. Vacuum-assisted closure complicated by erosion and hemorrhage of the anterior tibial artery. *J Orthop Trauma*. 2005;19(1):56-59.
46. Dedmond BT, Kortesis B, Punger K, et al. Subatmospheric pressure dressings in the temporary treatment of soft tissue injuries associated with type III open tibial shaft fractures in children. *J Pediatr Orthop*. 2006;26(6):728-732.
47. Kanakaris NK, Thanasis C, Keramaris N, Kontakis G, Granick MS, Giannoudis PV. The efficacy of negative pressure wound therapy in the management of lower extremity trauma: review of clinical evidence. *Injury*. 2007;38(Suppl 5):S9-S18.