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Introduction

Negative Pressure Wound Therapy (NPWT) has been utilized in wound care and limb salvage/limb function preservation for almost 30 years. This technology is considered an adjunctive standard of care treatment modality utilized in both the inpatient and outpatient settings. Imparting negative pressure onto the surface of wounds optimizes the wound bed by promoting the generation of granulation tissue, neovascularization, enhancing venous and lymphatic drainage, reduction of bacteria, and decreasing wound size. The

device consists of a porous interface (foam or gauze material), drape, tubing, canister, and a pump. Further, NPWT is used over closed incisions to decrease incision-related complications. There have been many innovations in the original device design that include improvements in the software, hardware interface, the addition of instillation, foam and drape construct. Other innovations include increasing portability through smaller devices as well as mechanically and not electrically powered pumps (Fig. 27.1) (Table 27.1).

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Fig. 27.1 There are a variety of innovations that have branched from the traditional NPWT device

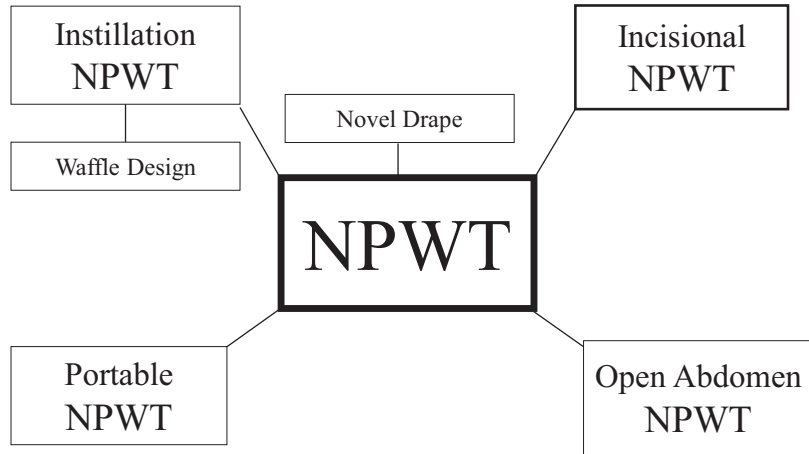


Table 27.1 Advantages and disadvantages to NPWT systems

| | Advantages | Disadvantages |
|------------------------------------|--|---|
| Standard NPWT | Promotes wound bed conversion to a healthier state | Has battery backup but still needs electricity for recharge |
| Mechanically powered portable NPWT | Mobility | Limited for the use of smaller, minimally exudative wounds |
| Incisional NPWT | Decrease in incisional complications | No direct visualization of the incision Higher cost than traditional incision dressings |
| NPWT with instillation | Clearance of bacteria | Potential for leaks and maceration Can only be utilized in the acute setting or some long-term acute care settings |

NPWT negative pressure wound therapy

Mechanism of Action

There are multiple proposed mechanisms of action for NPWT. The base device of NPWT provides multiple positive effects on the wound bed beyond that of decreasing overall wound dimensions and exudate removal (Fig. 27.2). Some believe that the primary clinical goal for the use of NPWT is to promote the growth of granulation tissue. Morykwas et al. in a porcine study exam-

ined the effect of different pressures on granulation tissue growth [1]. This study may have been erroneously extrapolated to suggest that granulation tissue growth is the goal of NPWT. However, it is important to understand that granulation tissue should be viewed simply as a sign of wound bed health and not necessarily the clinical end goal. The presence of granulation tissue indicates adequate perfusion and low bioburden (bacteria and nonviable tissue). Granulation tissue is essentially a bed of capillaries imbedded in a collagen matrix. This environment increases the likelihood of epithelization or provides a base to receive and incorporate a split-thickness skin graft, allograft, or xenograft.

NPWT can be programmed for continuous application of negative pressure or intermittent application of negative pressure. The evidence suggests that the intermittency (periods of lower or no negative pressure) is the preferred method in stimulating the wound bed. Morykwas et al. report that there is a 40% greater granulation tissue growth with intermittent negative pressure as compared with continuous negative pressure [2]. The intermittency appears to stimulate a greater response in cell proliferation and angiogenesis [3]. The engagement and disengagement of negative pressure provides the stimulus to the wound bed to react in response to tissue stress. The effect appears to be on small vessels in promoting a more organized, more dense vascular structure [4, 5]. Despite the evidence to suggest that intermittency is superior, many clinicians

Fig. 27.2 There is good alignment between the goals of wound healing and the mechanism of NPWT

Well Aligned

| Goals of Wound Healing | Mechanism of NPWT |
|---|---|
| <ul style="list-style-type: none"> • Remove exudate • Promote granulation tissue • Increase local perfusion • Decrease bacteria and contamination | <ul style="list-style-type: none"> • Remove exudate • Promote granulation tissue • Increase local perfusion • Decrease bacteria and contamination |

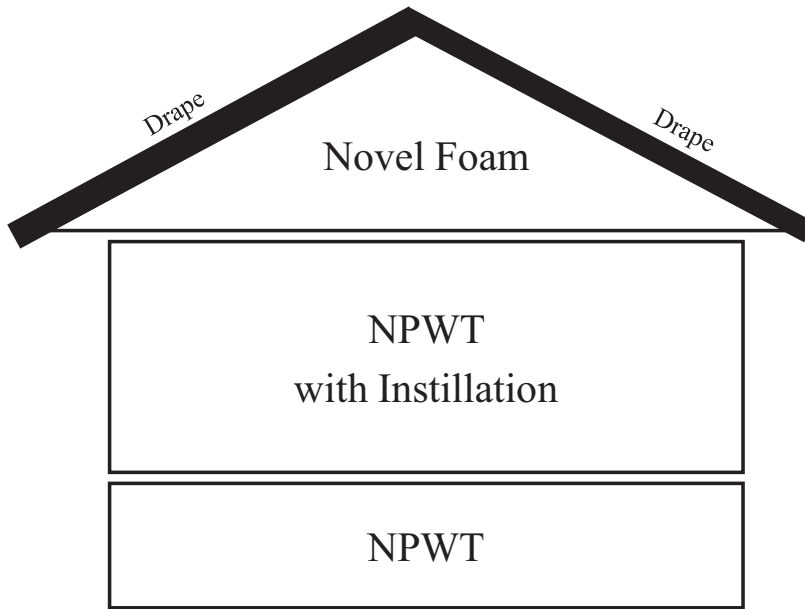


Fig. 27.3 This figure conceptualizes the combination of the innovations of NPWT. NPWT is the foundation of the house, while NPWT with instillation is its walls, the novel

foam is the roof, and the novel drape is the shingles. The innovations build on the fundamental benefits of standard NPWT

utilize the continuous setting for pragmatic reasons including the reduced likelihood of leaks and alarms, and for greater patient comfort. A more recent porcine study by Lessing et al. reports no difference in granulation tissue thickness between continuous and intermittent negative pressure [6]. Further, they report that the use of NPWT with instillation promotes greater granulation thickness than either continuous or intermittent negative pressure.

The mechanical forces imparted by negative pressure provides for both macrodeformation and microdeformation [7]. Macrodeformation is essentially the centripetal forces that shrink the overall wound dimensions when negative pressure is applied. The decrease in overall wound dimen-

sions decreases the strain across the wound bed and provides laxity in the tissue. Thus, the type of tissue or anatomical location of the wound dictates the degree of macrodeformation [8]. For example, indurated tissue will have less ability for macrodeformation. Microdeformation is imparted through the perforations in the porous foam. This type of force is responsible for protein activation and the cellular effects that promote cell migration and neovascularization [3]. The variants of NPWT including Negative Pressure Wound Therapy with Instillation (NPWTi) and incisional NPWT provide additional and different effects on tissue.

The most widely used NPWTi device utilizes a solution that is programmed to intermittently bathe the surface of the wound (Fig. 27.3). There

are other NPWTi devices that provide continuous flow of solution across the wound bed. Essentially, NPWTi combines the benefits of negative pressure and wound irrigation. The proposed mechanism of action of NPWTi is to provide a medium, through the instillate, to hydrate, solubilize, and evacuate the nonviable tissue as well as provide a medium for the bacteria to be removed and perhaps decrease the likelihood of reattachment. NPWTi has been demonstrated to not only reduce planktonic bacteria amounts but also destroy mature biofilm in *in vivo* and *ex vivo* porcine models [9, 10]. Yang et al. report in chronic human wounds a 48% reduction of bacterial amount utilizing NPWTi as compared with a 14% increase in bacterial amount with the use of standard NPWT [11]. Some have postulated that the reduction of bacteria may simply be the effect of an antimicrobial solution on the wound bed and has little to do with the NPWTi device itself. Kim et al. report in a randomized controlled trial of NPWTi in infected wounds; no difference in various surrogate clinical outcomes (e.g., length of hospitalization, number of surgeries) utilizing normal saline as compared with polyhexanide with betaine [12]. Kim et al. reported in a retrospective study on infected wounds a significant decrease in the number of operations, length of hospitalization, and shorter time to final surgical procedure utilizing NPWTi with normal saline as compared with standard NPWT [13]. This study suggests that there is an additive positive effect for the use of NPWTi beyond that of solely utilizing an antiseptic solution or standard NPWT.

A variety of solutions have been utilized with NPWTi. To date there is no robust data to suggest one type of solution is clearly superior to another. Antiseptics may have a role in highly infected or contaminated wounds. However, there may be cytotoxic effects on healthy tissue that prohibit its prolonged use. Normal saline is a viable alternative in many cases due to its wide availability and its tolerability. The instillate can also serve to moisturize the wound surface, thereby hydrating the underlying tissue and reduce desiccation. This is especially important for tissues such as ligament, tendon, and joint capsule. Another potential advantage is that NPWTi requires inter-

mittency of negative pressure which the evidence suggests is superior to that of a continuous negative pressure setting as discussed above.

Incisional NPWT decreases the initial tensile forces experienced along the incision line by 50% by distributing the forces over a wider surface area [14]. Further, incisional NPWT has been reported to decrease edema through relieving venous congestion and enhancing lymphatic drainage [15–17]. This may have 2 consequences: (1) the decrease in edema decreases the tension along the incision, (2) expedite healing by more rapidly removing inflammatory factors. Incisional negative pressure is not designed to directly remove the underlying fluid in the incisional area. It is recommended that drains be used to serve this purpose. These drains should be placed at a distance from the foam/drape or gauze/drape construct to prevent interference with the device. Some have proposed that there are long-term benefits that include an increase in tensile strength across the incisional area and more organized scarring [17].

Indications

NPWT is utilized for soft tissue defects in all areas of the body. It is not indicated in areas such as inside the abdominal or thoracic cavities, spinal cord or brain, directly over identifiable vessels or nerves. NPWT can promote granulation tissue over less vascular structures such as bone, capsule, ligament, or tendon. However, the area must have adequate perfusion in order for this to occur. Thus, noninvasive or invasive vascular studies and/or intervention should be conducted prior to treatment onset. NPWT should be reserved for wounds that are not progressing, for complex wounds, or in compromised patients. Historically, NPWT was utilized to promote wound healing over time in a relatively clean wound bed. Armstrong et al. in the pivotal study in post-amputation foot wounds report a faster time to granulation with the use of NPWT compared with standard gauze dressing (42 vs. 84 days) [18]. The technology has evolved as an adjunctive therapy in wounds that are infected/

contaminated, and for closed surgical incisions in high-risk populations. Each NPWT platform has unique properties and characteristics that require proper application in order to maximize its benefits (Table 27.2).

Chronic Wounds

NPWT should be considered for wounds that are not healing as demonstrated by wound volume or surface area reduction. Further, the quality of the tissue in the wound bed may also benefit from NPWT by promoting the growth of granulation

tissue over deeper exposed structures. In the lower extremity the fundamental principles of optimized perfusion, medical management and optimization of comorbidities, nutritional enhancement, serial sharp excisional debridement, and offloading/immobilization should be adhered to along with NPWT. There should be an ultimate treatment goal when utilizing NPWT. This includes: (1) terminal epithelialization, (2) creation of a wound bed that will support a split-thickness skin graft or other grafts, (3) as part of staged approach for a local flap or free tissue transfer. NPWT should not be used for a lengthy period without regular wound evaluation to assess that NPWT has had positive effects on the wound. If NPWT has demonstrated little or no change to the wound bed, other treatment options should be considered.

Traditional NPWT should not be used if there is an active infection or necrotic tissue in the wound bed. The infection should be treated and the necrotic tissue removed prior to application of NPWT. If the patient is not a surgical candidate or the patient refuses surgical intervention, NPWTi with the novel foam with the large perforation may be an option for wounds that have areas of necrotic and fibrotic tissue. This foam will be discussed in further detail below.

NPWT has also been utilized as a bolster for grafts [19, 20]. The foam or gauze is applied over an autologous graft, allograft, or xenograft and negative pressure is applied. The proposed benefit for this approach is to reduce seroma or hematoma formation that could otherwise lift the graft off the wound bed surface by evacuating fluid. The other proposed benefit is to affix the wound bed and the graft together to prevent graft drift or floating of the graft. There have been multiple reports of this technique in the literature; however these have been relegated to case studies/case series and underpowered comparative studies, thus the ultimate benefit remains unclear [21–25].

Table 27.2 Tips and pearls for the use of NPWT systems

| | Tips and pearls |
|------------------------------------|---|
| Standard NPWT | <ul style="list-style-type: none"> • Establish a definitive treatment goal (terminal epithelialization, wound bed preparation for a graft) • Use bridging techniques away from weightbearing or bony prominences |
| Mechanically powered portable NPWT | <ul style="list-style-type: none"> • Use only on small, minimally exudative wounds • Should be reserved for outpatient to maximize its portability |
| Incisional NPWT | <ul style="list-style-type: none"> • Utilize drains as necessary away from the incision line • If utilizing the traditional black foam (not the prefabricated construct), cut the width that expands at least 2 cm on both sides of the incision line |
| NPWT with instillation | <ul style="list-style-type: none"> • Do not use large volumes of solution per dwell cycle • The volume of instillate may need to be adjusted at each dressing change with changing dimensions of the wound • Use of ostomy rings or paste may be helpful to maintain a seal utilizing the traditional polyvinyl drape, but do not use these products with the silicone composite drape • The novel foam should only be used with NPWT with instillation and not with traditional NPWT |

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Closed Incisions

NPWT has been demonstrated to decrease complication in high-risk populations across all sur-



Fig. 27.4 (a) A photo of the posterior aspect of the heel after a partial calcaneotomy and primary closure was performed to treat a chronic plantar heel ulcer with underlying osteomyelitis. This is a patient with type 2 diabetes and peripheral vascular disease. (b) An intraoperative

photograph of an incisional negative pressure device applied over the incision. This device was applied for 10 days. (c) A clinical photograph 4 weeks after closure. Note the well-healed incision

gical specialties over closed incisions (Fig. 27.4). The device is placed over an incision at the time of surgical closure in the operating room. Surgical dehiscence can occur for a variety of reasons including host factors including age, comorbidities, and anatomical location. Incisional NPWT provides for local management of the incision. The literature is replete with publications supporting the use of incisional NPWT to decrease complications (dehiscence and infection) related to surgical incisions in a variety of anatomical locations. Stannard et al. were one of the first to report a significant decrease (1/5th less likely) in surgical site infections for open fracture management [26]. De Vries et al. report in a metaanalysis of randomized controlled trials that there is a decrease in surgical site infections with the use of incisional NPWT as compared with customary dressings [27]. The potential cost saving in complication prevention is difficult to estimate. Karlakki et al. report in a randomized controlled trial a significant reduction of length of hospitalization for primary hip and knee arthroplasties but do not report a significant reduction in surgical wound complications although there was a

strong trend ($p = 0.06$) with a fourfold reduction [28].

Prior to the introduction of the prefabricated dressings for incisional NPWT, traditional dressing kits were utilized. It is important that if utilizing the traditional dressing kits, the width of the contact foam/gauze span the incision with the material applied at least 2 cm on each side of the incision line. This allows for negative pressure to affect the tissue surrounding the incision line. The prefabricated dressing kits are specifically constructed for closed incisions and are constructed with these specific dimensions. There has been some speculation that lower negative pressure settings should be utilized over closed incisions. There is no robust evidence in either direction whether this should be conducted.

Infected/Contaminated Wounds

There is a growing acceptance for the use of NPWT with instillation (NPWTi) as an adjunct treatment for infected/contaminated wounds [29–34]. Typically, these wounds are excisionally

debrided and antibiotic therapy initiated prior to application of NPWTi. Kim et al. report in a prospective, multicenter, randomized trial a 3-log difference in the reduction of bacteria in favor of NPWTi as compared with conventional NPWT [35]. All wounds in this study were surgically debrided and managed in the acute care setting. It is important to explore all tunnels to prevent instillate fluid from being trapped in deeper tissue pockets. NPWTi can be used in the interval between staged excisional debridement. NPWTi is discontinued once the wound bed is ready for closure or coverage. However, NPWTi can also be utilized to prepare the wound bed prior to the single-staged closure or coverage or utilized after the initial excisional debridement with no immediate plan for coverage or closure [36].

A recent metanalysis suggests that NPWTi, as compared to NPWT and other wound therapies, has positive clinical and economic benefits by facilitating efficiency in wound bed conversion. Gabriel et al. report that NPWTi: (1) requires a fewer number of surgical debridements, (2) a

quicker conversion of the wound bed for closure or coverage with a graft, (3) reduces bacteria amounts, (4) has a lower number of postoperative wound-related complications [37]. In the acute care setting, NPWTi may be the preferred negative pressure platform.

Innovation

Foam

A novel foam with larger perforations have more recently been introduced (Fig. 27.5). This construct involves the use of at least 2 stiffer foam pieces stacked on top of each other. The perforated foam dressing is placed in contact with the wound bed, then another foam dressing is placed on top of the perforated foam dressing. This foam construct is used in conjunction with NPWTi and not with standard NPWT. The probable mechanism of action is as follows: (1) the solution emulsifies the nonviable tissue (necrotic

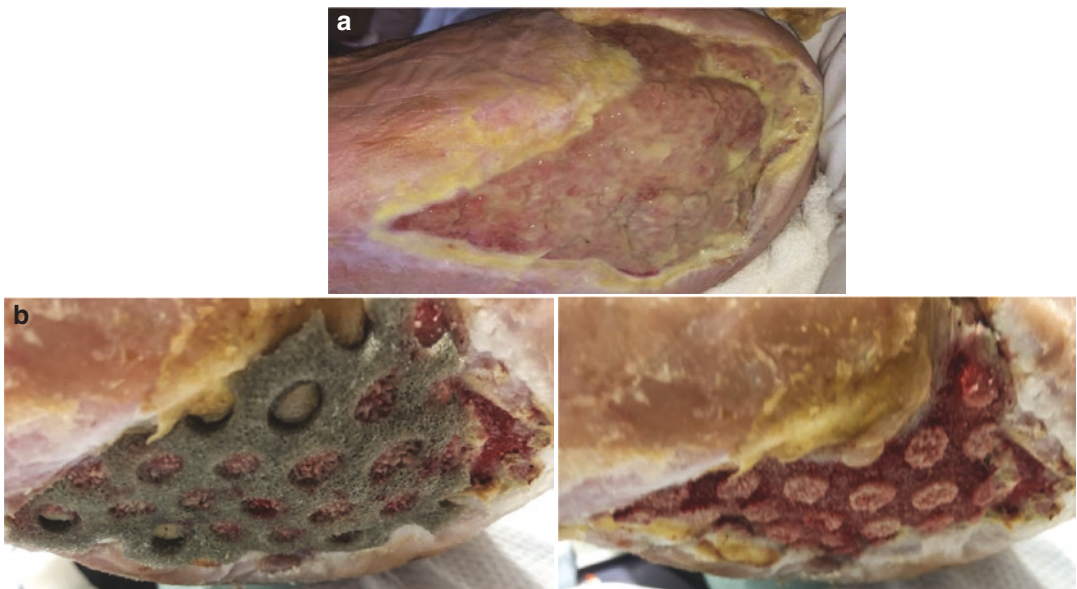


Fig. 27.5 (a) This photograph of a chronic plantar foot wound with significant amount of liquified, nonviable tissue. The patient had a prior surgical intervention that dehiscid creating a chronic ulcer. This is a patient who refused surgical intervention for excisional debridement. (b) This photograph is at the first dressing change after

application of NPWT with instillation (normal saline) and the novel foam. This was applied for 3 days. Note the conversion of the wound to a healthier state with a decrease in the amount of nonviable tissue as well as the growth of granulation tissue

and fibrotic tissue) during the dwell cycle, (2) as the negative pressure is applied, the larger perforations draws tissue through these holes, (3) the cycling of dwell and negative pressure against this novel foam construct mechanically breaks up the tissue, (4) the instillate provides an avenue for the nonviable tissue to be evacuated into the egress canister. This novel foam may be a good option for wounds that contain nonviable, necrotic, or sloughy tissue in patients who are not surgical candidates, refuse surgical intervention, there is no surgeon available for excisional debridement, or have had inadequate sharp debridement performed [38]. Although this innovation is promising, there is currently no robust studies with only a limited number of case studies/series reporting positive outcomes [39, 40].

Drape

Since the introduction of NPWT, the drape used to affix the foam dressing has been a polyurethane film coated with an acrylic adhesive on the contact side. The newest construct utilizes a polyurethane/acrylic/silicone composite. It has been suggested that the stiffness of the original polyurethane material can lead to leaks by breaking the contact with the surrounding skin with movement of the patient. This can result in maceration of the surrounding skin and the loss of suction. Therefore, ostomy rings and paste have been used to secure the drape onto the skin. Further, once the polyurethane drape is applied, the same drape cannot be removed and reapplied. Additional drapes are applied or bolster strips of the drape in order to create a better seal. This results in wasted material and time. Further, skin damage can occur with removal due to the tacky nature of the acrylic adhesive. The polyurethane/acrylic/silicone blend is more tolerant to stretch and can be applied and reapplied without the need for additional supplies. For this novel drape to be utilized effectively, the surrounding skin must be dry and if the skin is cold, it may take some time for the acrylic/silicone to

activate to adhere to the skin surface. The silicone contact layer is also safe on fragile skin. This drape can be used for traditional NPWT or with NPWTi. This novel drape is yet to be widely available or adopted but it is a significant step forward.

Portability

Portability has allowed for NPWT to be more easily transferred from the acute setting to home or rehabilitation facility. Rechargeable battery powered NPWT devices allow for the patient to be more mobile. Other portable NPWT devices do not require electrically powered pumps but rather rely on potential energy stored in a coiled spring. These mechanically powered devices are small and extremely portable. However, this construct has no exudate container, thus is reserved for small, low exudative wounds. Armstrong et al. in a multicenter, randomized trial report no inferiority in wound size reduction or wound closure between a mechanically and an electrically powered NPWT devices [41]. The next leap in innovation for portability of NPWT should include the ability to provide instillation.

Remote Monitoring

As delivery of healthcare has evolved with a movement towards shorter hospital stays while maintaining quality of care provided to patients, monitoring of a NPWT device in the acute care setting is simpler than in an outpatient setting. Currently some NPWT devices have embedded sensors that provide information of NPWT use (device turned off) and malfunction (blockage, leaks, alarms) information. This information can be relayed to the patient, facility, visiting nurses, or wound center in real time. This allows for a quicker response to problems associated with the device. Newer software updates on some devices provide step-by-step troubleshooting animations to assist in NPWT management.

Conclusion

NPWT has emerged as an adjunctive frontline approach to complex/chronic wounds. NPWT is used globally in the continuum of care of a wound from the acute care setting to outpatient facility to home. The innovations have accelerated in the past decade and NPWT indications have expanded significantly. Data continues to be generated that report the effectiveness of this therapy as well as its impact on overall healthcare costs. Further, technological advances have improved its utility, reliability, and efficacy. It is important to maintain and practice fundamental principles of wound care and limb function preservation along with the use of NPWT and its derivatives.

References

- Morykwas MJ, Faler BJ, Pearce DJ, Argenta LC. Effects of varying levels of subatmospheric pressure on the rate of granulation tissue formation in experimental wounds in swine. *Ann Plast Surg.* 2001;47(5):547–51.
- 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):553–62.
- Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. *Plast Reconstr Surg.* 2004;114(5):1086–96; discussion 97–8.
- Erba P, Ogawa R, Ackermann M, Adini A, Miele LF, Dastouri P, et al. Angiogenesis in wounds treated by microdeformational wound therapy. *Ann Surg.* 2011;253(2):402–9.
- Greene AK, Puder M, Roy R, Arsenault D, Kwei S, Moses MA, et al. Microdeformational wound therapy: effects on angiogenesis and matrix metalloproteinases in chronic wounds of 3 debilitated patients. *Ann Plast Surg.* 2006;56(4):418–22.
- Lessing MC, James RB, Ingram SC. Comparison of the effects of different negative pressure wound therapy modes—continuous, noncontinuous, and with instillation—on porcine excisional wounds. *Eplasty.* 2013;13:e51.
- Orgill DP, Manders EK, Sumpio BE, Lee RC, Attinger CE, Gurtner GC, et al. The mechanisms of action of vacuum assisted closure: more to learn. *Surgery.* 2009;146(1):40–51.
- Huang C, Leavitt T, Bayer LR, Orgill DP. Effect of negative pressure wound therapy on wound healing. *Curr Probl Surg.* 2014;51(7):301–31.
- Phillips PL, Yang Q, Schultz GS. The effect of negative pressure wound therapy with periodic instillation using antimicrobial solutions on pseudomonas aeruginosa biofilm on porcine skin explants. *Int Wound J.* 2013;10(Suppl 1):48–55.
- Davis K, Bills J, Barker J, Kim P, Lavery L. Simultaneous irrigation and negative pressure wound therapy enhances wound healing and reduces wound bioburden in a porcine model. *Wound Repair Regen.* 2013;21(6):869–75.
- Yang C, Goss SG, Alcantara S, Schultz G, Lantis II JC. Effect of negative pressure wound therapy with instillation on bioburden in chronically infected wounds. *Wounds.* 2017;29(8):240–6.
- Kim PJ, Attinger CE, Oliver N, Garwood C, Evans KK, Steinberg JS, et al. Comparison of outcomes for normal saline and an antiseptic solution for negative-pressure wound therapy with instillation. *Plast Reconstr Surg.* 2015;136(5):657e–64e.
- Kim PJ, Silverman R, Attinger CE, Griffin L. Comparison of negative pressure wound therapy with and without instillation of saline in the management of infected wounds. *Cureus.* 2020;12(7):e9047.
- Wilkes RP, Kilpad DV, Zhao Y, Kazala R, McNulty A. Closed incision management with negative pressure wound therapy (CIM): biomechanics. *Surg Innov.* 2012;19(1):67–75.
- Kamolz LP, Andel H, Haslik W, Winter W, Meissl G, Frey M. Use of subatmospheric pressure therapy to prevent burn wound progression in human: first experiences. *Burns.* 2004;30(3):253–8.
- Kilpadi DV, Cunningham MR. Evaluation of closed incision management with negative pressure wound therapy (CIM): hematoma/seroma and involvement of the lymphatic system. *Wound Repair Regen.* 2011;19(5):588–96.
- Kilpadi DV, Lessing C, Derrick K. Healed porcine incisions previously treated with a surgical incision management system: mechanical, histomorphometric, and gene expression properties. *Aesthetic Plast Surg.* 2014;38(4):767–78.
- Armstrong DG, Lavery LA, Diabetic Foot Study C. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet.* 2005;366(9498):1704–10.
- Blackburn JH 2nd, Boemi L, Hall WW, Jeffords K, Hauck RM, Banducci DR, et al. Negative-pressure dressings as a bolster for skin grafts. *Ann Plast Surg.* 1998;40(5):453–7.
- Gabriel A, Thimmappa B, Rubano C, Storm-Dickerson T. Evaluation of an ultra-lightweight, single-patient-use negative pressure wound therapy system over dermal regeneration template and skin grafts. *Int Wound J.* 2013;10(4):418–24.
- Webster J, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention. *Cochrane Database Syst Rev.* 2014;10:CD009261.
- Gkotsoulas E. Split thickness skin graft of the foot and ankle bolstered with negative pressure wound

- therapy in a diabetic population: the results of a retrospective review and review of the literature. *Foot Ankle Spec.* 2020;13(5):383–91.
23. Petkar KS, Dhanraj P, Kingsly PM, Sreekar H, Lakshmanarao A, Lamba S, et al. A prospective randomized controlled trial comparing negative pressure dressing and conventional dressing methods on split-thickness skin grafts in burned patients. *Burns.* 2011;37(6):925–9.
 24. Moisisidis E, Heath T, Boorer C, Ho K, Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg.* 2004;114(4):917–22.
 25. Nguyen TQ, Franczyk M, Lee JC, Greives MR, O'Connor A, Gottlieb LJ. Prospective randomized controlled trial comparing two methods of securing skin grafts using negative pressure wound therapy: vacuum-assisted closure and gauze suction. *J Burn Care Res.* 2015;36(2):324–8.
 26. Stannard JP, Volgas DA, Stewart R, McGwin G Jr, Alonso JE. Negative pressure wound therapy after severe open fractures: a prospective randomized study. *J Orthop Trauma.* 2009;23(8):552–7.
 27. De Vries FEE, Wallert ED, Solomkin JS, Allegranzi B, Egger M, Dellinger EP, et al. A systematic review and meta-analysis including GRADE qualification of the risk of surgical site infections after prophylactic negative pressure wound therapy compared with conventional dressings in clean and contaminated surgery. *Medicine (Baltimore).* 2016;95(36):e4673.
 28. Karlakki SL, Hamad AK, Whittall C, Graham NM, Banerjee RD, Kuiper JH. Incisional negative pressure wound therapy dressings (iNPWTd) in routine primary hip and knee arthroplasties: a randomised controlled trial. *Bone Joint Res.* 2016;5(8):328–37.
 29. Kim PJ, Attinger CE, Constantine T, Crist BD, Faust E, Hirche CR, et al. Negative pressure wound therapy with instillation: international consensus guidelines update. *Int Wound J.* 2020;17(1):174–86.
 30. Brinkert D, Ali M, Naud M, Maire N, Trial C, Teot L. Negative pressure wound therapy with saline instillation: 131 patient case series. *Int Wound J.* 2013;10(Suppl 1):56–60.
 31. Lehner B, Fleischmann W, Becker R, Jukema GN. First experiences with negative pressure wound therapy and instillation in the treatment of infected orthopaedic implants: a clinical observational study. *Int Orthop.* 2011;35(9):1415–20.
 32. Kim PJ, Attinger CE, Steinberg JS, Evans KK, Powers KA, Hung RW, et al. The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study. *Plast Reconstr Surg.* 2014;133(3):709–16.
 33. Gabriel A, Kahn K, Karmy-Jones R. Use of negative pressure wound therapy with automated, volumetric instillation for the treatment of extremity and trunk wounds: clinical outcomes and potential cost-effectiveness. *Eplasty.* 2014;14:e41.
 34. Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis. *Wound Repair Regen.* 2009;17(2):278–86.
 35. Kim PJ, Lavery LA, Galiano RD, Salgado CJ, Orgill DP, Kovach SJ, et al. The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: pilot randomised, controlled trial. *Int Wound J.* 2020;17(5):1194–208.
 36. Kim PJ, Attinger CE. Negative-pressure wound therapy with instillation: a tool in the multidisciplinary approach to limb function preservation. *Plast Reconstr Surg.* 2021;147(1S-1):27S–33S.
 37. Gabriel A, Camardo M, O'Rorke E, Gold R, Kim PJ. Effects of negative-pressure wound therapy with instillation versus standard of care in multiple wound types: systematic literature review and meta-analysis. *Plast Reconstr Surg.* 2021;147(1S-1):68S–76S.
 38. Kim PJ, Applewhite A, Dardano AN, Fernandez L, Hall K, McElroy E, et al. Use of a novel foam dressing with negative pressure wound therapy and instillation: recommendations and clinical experience. *Wounds.* 2018;30(3 suppl):S1–S17.
 39. Teot L, Boissiere F, Fluieraru S. Novel foam dressing using negative pressure wound therapy with instillation to remove thick exudate. *Int Wound J.* 2017;14(5):842–8.
 40. Blalock L. Use of negative pressure wound therapy with instillation and a novel reticulated open-cell foam dressing with through holes at a level 2 trauma center. *Wounds.* 2019;31(2):55–8.
 41. Armstrong DG, Marston WA, Reyzelman AM, Kirsner RS. Comparative effectiveness of mechanically and electrically powered negative pressure wound therapy devices: a multicenter randomized controlled trial. *Wound Repair Regen.* 2012;20(3):332–41.