Negative pressure wound therapy: Unusual and Innovative Applications

James Cipolla, MD1, Daniel R. Baillie, MD2, Steven M. Steinberg, MD3, Niels D. Martin, MD4, Nikhil P. Jaik, MD5, John J. Lukaszczyk, MD2, S. Peter Stawicki, MD3

1 St Luke’s Regional Level I Resource Trauma Center, Bethlehem, PA, USA
2 Department of Surgery, St Luke’s Hospital and Health Network, Bethlehem, PA, USA
3 Department of Surgery, Division of Critical Care, Trauma, and Burn, The Ohio State University Medical Center, Columbus, OH, USA
4 Department of Surgery, Division of Acute Care Surgery, Thomas Jefferson University, Philadelphia, PA, USA
5 Opus 12 Foundation, Columbus, OH, USA

ABSTRACT
Negative pressure wound therapy (NPWT), based on application of subatmospheric pressure, has revolutionized the management of wounds. It has been successfully used in the setting of wounds complicated by the presence of burn, infection, poor circulation, exposed bone or artificial implants, or previous wound dehiscence. Negative pressure wound therapy facilitates healing by reportedly improving the rate of angiogenesis, endothelial proliferation, the integrity of the capillary basement membrane, capillary blood flow, capillary caliber, and by decreasing interstitial edema and bacterial burden within the wound. It is undisputable that the NPWT paradigm is here to stay. This review summarizes the unusual and innovative applications of NPWT, focusing on the practical aspects relevant to daily clinical practice. The authors present two illustrative cases, followed by a detailed discussion of novel applications of NPWT. Topics included in this manuscript encompass NPWT use in the settings of orthopedic and vascular implant infections, complex abdominal wounds, enterocutaneous and enterocutaneous fistulae, skin grafting, challenging anatomic locations (i.e., face, neck, and distal extremities), sternal wounds, and ascites. A section on special issues in NPWT then follows.

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Correspondence to: S. P. Stawicki, MD. OPUS 12 Foundation, 1011 Rutherford Glen Drive, Columbus, OH 43235 USA.

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INTRODUCTION
Negative pressure wound therapy (NPWT), based on application of subatmospheric pressure, has revolutionized the clinical management of wounds.1-3 It has been successfully used in the setting of wounds complicated by burn, infection, poor circulation, exposed bone or artificial implants, or dehiscence.4-5 Negative pressure wound therapy facilitates healing by reportedly improving the rate of angiogenesis, endothelial proliferation, the integrity of the capillary basement membrane, capillary blood flow, capillary caliber, and by decreasing interstitial edema and bacterial burden within the wound.6-9 It is undisputable that the NPWT paradigm is here to stay. This review summarizes the unusual and innovative applications of NPWT, focusing on the practical aspects relevant to daily clinical practice.

METHODS
A comprehensive review of unusual and innovative clinical applications of NPWT was conducted. A literature search was performed using Internet search engines/repositories, including Google™ Scholar, BioLine International, Medline/Pubmed, Public Knowledge Project Open Archives, and ScientificCommons. In addition, referenced articles not listed in the above medical search engines, as well as other Internet resources relevant to the current topic, were also included. Two illustrative clinical cases are also presented. Appropriate permissions were obtained prior to publication of photographs included in this manuscript.

ILLUSTRATIVE CASE #1
A 73-year-old woman presented with complaints of right lower extremity rest pain. The patient had a long-standing history of peripheral arterial occlusive disease, including right femoropopliteal arterial bypass with autologous vein graft seven years prior to the current admission, which failed after years of scheduled follow-up appointments and regular surveillance with arterial Duplex scans. The graft was revised three years prior to the current admission because of focal segment of distal stenosis. The patient’s past medical and surgical history were also remarkable for hypertension, hyperlipidemia, hypothyroidism, osteoarthritis, and bilateral cataracts. Her medications included amitriptyline, aspirin, atorvastatin, hydrochlorothiazide, irbesartan, metoprolol, and levOTHYroxine. The patient continued to use tobacco despite worsening claudication and continued educational efforts by her physicians.

Noninvasive arterial studies demonstrated ankle-brachial index of 0.7 on the left and 0.2 on the right. The patient’s symptoms were disabling, and she opted for right lower extremity arterial reconstructive procedure at this time. Arteriography demonstrated occluded right superficial femoral artery, occlusion of the femoropopliteal bypass graft, with reconstitution of the popliteal artery at the knee and two-vessel run-off. Venous ultrasonographic study demonstrated no conduit of quality suitable for the planned iliac to below-knee popliteal bypass.

The patient subsequently underwent right iliac to below-knee popliteal bypass using 6 millimeter ringed polytetrafluoroethylene (PTFE) graft (Distaflo®, Bard Peripheral Vascular, Inc., Tempe, Arizona, USA) with immediate restoration of distal extremity arterial flow and relief of symptoms. Postoperatively, the patient began to develop recurrent, spiking fevers, right groin erythema, and peri-incisional swelling. Because of continued symptoms and worsening leukocytosis (white blood cell count of 18,000/mL) on the fifth postoperative day, the patient was taken back to the
A 53-year-old man presented to the clinic with a history of a midline abdominal wound sinus chronically draining purulent material following a synthetic (PTFE) mesh placement for a ventral hernia repair two years earlier. His past medical history included severe coronary artery disease, insulin-dependent diabetes mellitus, and moderately severe chronic obstructive pulmonary disease secondary to long-term tobacco use. The patient was subsequently taken to the operating room, where the midline abdominal wound was opened and the sinus was found to be associated with an infected upper portion of the PTFE mesh.

The infection appeared to be contained to the upper portion of the mesh, and there was no evidence of any recurrent infection six months after the initial clinic presentation.

ILESSIVE CASE #2

A 53-year-old man presented to the clinic with a history of a midline abdominal wound sinus chronically draining purulent material following a synthetic (PTFE) mesh placement for a ventral hernia repair two years earlier. His past medical history included severe coronary artery disease, insulin-dependent diabetes mellitus, and moderately severe chronic obstructive pulmonary disease secondary to long-term tobacco use. The patient was subsequently taken to the operating room, where the midline abdominal wound was opened and the sinus was found to be associated with an infected upper portion of the PTFE mesh.

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OVERVIEW OF UNUSUAL AND INNOVATIVE APPLICATIONS OF NPWT

This review will begin with a discussion of NPWT use in the setting of exposed and/or infected vascular and orthopedic implants. A discussion of negative pressure therapy application over exposed bone, wounds of variable depth and/or shapes, wounds in ‘difficult’ anatomic locations, and burn wounds will then follow. The discussion will also touch upon the use of NPWT with skin grafts and open abdomens. Finally, we will discuss the use of negative pressure wound therapy in the setting of ascitic fluid leaks, where NPWT can be highly successful in controlling ascitic fluid drainage and helping to quantify fluid losses and guiding fluid replacement therapy.

NPWT USE IN THE SETTING OF VASCULAR AND ORTHOPEDIC GRAFT INFECTIONS: GENERAL COMMENTS

Graft infections are seen all-too-commonly following placement of vascular and orthopedic grafts. These complications can be devastating for several reasons, including patient population characteristics (older age, co-morbidities including diabetes and heart disease, immunosuppression), patterns of escalating antibiotic resistance, and increasing bacterial virulence. Hospitals are plagued by infections with polyresistant bacteria. Methicillin-resistant staphylococcus aureus (MRSA), vancomycin-resistant enterococcus (VRE), and multi-drug resistant non-lactose fermenting gram-negative bacilli are now commonplace. More recently, even the traditionally antibiotic-susceptible gram-negative organisms (i.e., Escherichia coli, Morganella, Proteus, Salmonella, Serratia) began displaying patterns of high antibiotic resistance associated with the emergence of the so-called extended-spectrum beta-lactamas (ESBL).

Antibiotic resistant wound infections become even more problematic when there is an implanted graft or an anastomosis in proximity to the open wound. Traditional teaching calls for the removal of all infected grafts. However, this may not always be a feasible option because surgical removal of infected vascular or orthopedic grafts can be associated with high morbidity and mortality. Therefore, new methods of treating the infection with the goal of graft preservation are being actively developed. Application of NPWT-based systems in wounds complicated by infected and/or exposed prosthetic materials has been shown to be effective in isolated case reports and small case series.

NPWT: VASCULAR GRAFT INFECTIONS

Wound infections have been reported in up to 40% of vascular surgical cases involving groin incisions. In addition, infections involving vascular grafts occur in 1% to 5% of all vascular bypass cases. Traditionally, these infections required complete excision of the graft and an extra-anatomic bypass. However, these frequently extensive surgical procedures can be associated with an amputation rate of between 10% and 70% and an overall mortality rate of 10% to 20%.

Based on the high morbidity and mortality associated with vascular graft infections and/or their operative treatment, the

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search for alternative therapies has been ongoing for decades. Such alternative therapies are focused on graft preservation, aggressive debridement of any infected tissue, muscle flap coverage of the exposed graft, and administration of broad-spectrum antibiotics. This nonoperative approach can produce good results. However, it is still associated with a re-infection in more than one third of cases. In very high-risk surgical patients, this may be acceptable because such therapy offers a good chance of wound healing and prevention of amputation as long as certain criteria with regards to the condition of the patient and the wound are met. Calligaro et al demonstrated that graft preservation is indicated when the graft is patent and is not involved in the infectious process in its entirety, there are no systemic signs of sepsis, and the infection does not contain *Pseudomonas aeruginosa*. The question arises, “what about the patient who does not meet clinical requirements for graft preservation strategies but continues to be at high risk due to the required remedial procedures?” One option that is slowly gaining acceptance is the use of NPWT in such situations. In addition to the illustrative case presented in this report, there are several other literature reports describing the use of this promising modality to treat wounds complicated by vascular graft infections.

Demaria et al presented a case report in which they described successful use of NPWT in an infected groin wound after vascular bypass with a reversed saphenous vein graft. The wound was characterized by high bacterial burden and the anastomosis was exposed at the base of the wound. Their patient had multiple medical co-morbidities and was a poor candidate for re-operation. The authors placed the polyurethane sponge directly over the exposed anastomosis without any complications. The patient did well and at one year follow-up the wound had healed completely, with preserved graft patency and no evidence of aneurysmal or other complications.

In a case series of NPWT use following vascular surgical procedures, Dosluoglu et al report on four patients with severe groin wound infections requiring extensive debridement, resulting in polytetrafluoroethylene (PTFE) graft exposure. The authors applied NPWT to these wounds, with a layer of non-adherent dressing or Silvason® (Medline Industries, Inc., Mundelein, Illinois, USA) between the graft and the NPWT sponge. Muscle flap closure was not attempted in that study because of poor overall medical condition of patients and/or severe groin scarring secondary to multiple previous groin operations. The authors reported no re-infections, and the time to wound closure was between 30 and 63 days, with a mean of 41 days with NPWT as the primary therapeutic modality.

**NPWT: ORTHOPEDIC WOUNDS WITH INFECTED OR EXPOSED IMPLANTS**

Exposed orthopedic implants are traditionally considered infected simply because of their exposure to the environment and bacteria. However, exposed hardware does not necessarily need to be surgically removed. In fact, it is possible to form granulation tissue over exposed implants. In this setting, one may use NPWT as an intermediate step before performing definitive wound closure or until the wounds heal via secondary intention. It is important to remember that NPWT in the setting of exposed orthopedic implants should only be considered if the hardware is still required for skeletal stabilization and if any associated infectious process can be controlled with the combination of antibiotics, surgical washouts, and/or NPTW (with or without adjunctive topical antimicrobial dressings).

In the orthopedic patient population, infected wounds and/or implants can lead to potentially disabling and severe chronic complications. Orthopedic wound infections can be especially devastating because they often occur in areas with limited skin coverage, tend to involve bone, frequently require elaborate muscle-coverage schemes, may lead to limited joint or extremity mobility, and have predilection to involve artificial implants. Chronic osteomyelitis can result in persistent pain, recurrent sinus drainage, bone destruction, sepsis, disfigurement, and sarcomatos transformation. With exposed implants, the traditional management involves removal of the hardware with serial debridement(s) and staged closure of the wound. However, gross structural instability, non-union, and further progression of infection can also be associated with removal of orthopedic implants. Much like in the setting of vascular surgery, the high morbidity and mortality associated with complete removal of orthopedic hardware prompted the search for alternative methods of treating these infections. Implantation of antibiotic beads in and around the areas of infection has offered some success. The use of topical NPWT has also been shown in small series to be potentially beneficial in such clinical situations.

Webb et al described the use of NPWT in the setting of infected orthopedic wounds. They emphasized the use of NPWT as a bridge to skin grafting and then as a bolster used with skin grafting that facilitated reduced healing time. They also described the use of NPWT in wounds complicated by significant contamination and exposed osseous tissue. The authors provided an example of a severe circumferential traumatic wound involving the lower leg, with bone and tendon exposure, for which NPWT was used in conjunction with Integra (Integra LifeSciences Corp., Plainsboro, New Jersey, USA) to temporize the wound surface until a skin graft could be applied. Pelham et al described the ability of NPWT to promote the formation of granulation tissue in a variety of clinical situations involving exposed orthopedic implants (various screws, plates, total knee arthroplasty implants, intramedullary nails, and wires) in ten patients who went on to definitive closure with free or local tissue flaps. The authors placed NPWT over various implants following surgical debridement, with the NPWT foam being strategically placed under the edges of raised flaps. Once the wound bed developed adequate granulation tissue, the NPWT was discontinued and wounds were closed with local random pattern flaps, regional muscle flaps, or free flaps. Of the ten patients, only one required eventual removal of the implant with placement of a temporary spacer and eventual re-implantation. Another patient experienced a minor wound complication requiring local wound care only. The time from the initial application of NPWT to definitive coverage ranged between 4 and 14 days, with a mean time of 9 days. The authors concluded that NPWT is a valuable adjunctive technique that can be used to help facilitate the closure of complicated orthopedic wounds. In fact, NPWT appears to be cost-effective in this clinical setting and provides a clear advantage from the standpoint of risk-benefit ratio in the absence of other nonoperative treatment alternatives.

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NPWT IN THE SETTING OF COMPLEX ABDOMINAL WOUNDS

Complex abdominal wounds represent a formidable surgical therapeutic challenge. Negative pressure wound therapy has been used in the setting of abdominal damage control in both trauma and non-trauma populations for quite some time (Figures 1-3). The use of NPWT for chronic abdominal wounds has also been well described. Such wounds are notoriously difficult to treat, and can be associated with infection, poor tissue healing, chronic inflammation, edema, bacterial colonization and the loss of abdominal domain. In addition, complex open abdominal wounds may be associated with an increased risk of anastomotic leak, enterocutaneous, and enteroatmospheric fistula formation during the wound healing process. In one report, a group of patients with skin and fascial dehiscence following laparotomy underwent wound therapy with saline-soaked gauze for one to six weeks before the application of NPWT to the open wound. In another study, protocolized approach to open abdominal wound management resulted in better-than-predicted patient survival and acceptable complication rates.

Heller et al described a series of 21 patients with severe systemic co-morbidities known to adversely affect wound healing. The authors treated complex abdominal wounds with serial debridements, NPWT dressings, and subsequent wound closure with local skin flaps, STSG, or via secondary intention. Nine of the patients had exposed bowel and underwent either the application of polyvinyl alcohol sponge directly over the bowel or had specialized non-adherent dressings placed beneath the regular NPWT sponge and the bowel. The duration of treatment was between 2 and 21 weeks with a mean of 5 weeks. Stable cutaneous coverage was eventually obtained in all patients. The authors reported three complications – partial skin loss in one patient and enterocutaneous fistula formation in two cases. All patients had stable, well-healed wounds on six-month follow-up. The rate of enterocutaneous fistula (22%) reported by Heller et al, although lower than that reported by Fansler et al, is somewhat higher than that reported by Stawicki et al.

Interestingly, NPWT has also been used as a dedicated therapeutic modality in the treatment of enterocutaneous fistulae. Goverman et al presented a series of five cases of NPWT use to help control wounds complicated by enterocutaneous fistulae. They describe a method wherein the enterocutaneous fistula is excluded from the NPWT dressing and sealed using ostomy paste to allow drainage of enteric contents into an ostomy bag and preventing drainage under the NPWT sponge. This so-called ‘floating ostomy’ prevents pooling of enteric contents behind the sponge and thereby prevents or reduces continued contamination of the wound, allowing NPWT to promote healing. After exclusion of the enterocutaneous fistulae, abdominal wounds were noted to heal well, with eventual split thickness skin graft placement over the granulated tissue.

Allen et al also describe successful application of NPWT in the setting of complex enterocutaneous fistulae. They emphasize that the use of NPWT in wounds with complex fistulae often requires negative pressure titration, starting with 75 mmHg and increasing the pressure to as high as 150 mmHg when indicated. A more detailed discussion dedicated to management of enterocutaneous and enteroatmospheric fistulae will now follow.

NPWT: ENTEROCUTANEOUS AND ENTEROATMOSPHERIC FISTULAE

Patients who are undergoing damage control or open abdominal management often have severe systemic co-morbidities and their wounds may be complicated by exposed bowel and enterocutaneous fistulae. Negative pressure wound therapy offers the potential to promote wound healing in this setting and can be used safely even in the presence of large areas of exposed bowel and/or concurrent enterocutaneous/enteroatmospheric fistulae.

NPWT: ENTEROCUTANEOUS FISTULAE

Enterocutaneous fistulae represent an abnormal communication between hollow viscera and the abdominal wall, and present a difficult problem for both patients and clinicians. Enterocutaneous fistulae are multifactorial in origin, often resulting from a combination of surgical technical errors, post-traumatic injury sequelae, poor nutritional status, co-morbid conditions, and the overall degree of metabolic derangement due to the initial injurious stimulus. Enterocutaneous fistulae may lead to a multitude of untoward consequences, including nutritional deficiencies, volume depletion, septic complications, and long term wound management problems. They are most often characterized as high output (>500 mL/24 hours) or low output (<200 mL/24 hours) with the remainder being classified as having intermediate output. Most patients with high or intermediate output enterocutaneous fistulae require hospital-
based treatment for the associated physiologic derangements. Low output fistulae may be treated on an outpatient basis with frequent skilled nursing and wound care visits.

High output fistulae are more likely to require surgical intervention whereas low and moderate output fistulae have greater chances of spontaneous closure. Conventional treatment of enterocutaneous fistulae revolves around adequate nutritional support, electrolyte replacement and volume repletion. The decision for total “bowel rest” with TPN versus some type of enteral feeding is the clinician’s choice, as both are supported in the literature. Along with normalization of metabolic derangements, the mechanical aspects associated with control of fistula drainage and wound management must be addressed. This is classically accomplished with some type of ostomy appliance and non-desiccating dressing. More recently, the use of NPWT for wounds complicated by fistulae has been described (Figure 3). Finally, if the enterocutaneous fistula does not spontaneously close with conservative therapy, a surgical resection of the fistula may be considered. The decision to proceed with surgery is often delayed due to the overall poor medical condition of these patients. Patients who develop protein-calorie malnutrition, sepsis or organ failure during nonoperative therapy may have poor operative fistula closure rates.

Figure 2. Proposed algorithm for management of open abdomens. Clinical application of this algorithm resulted in good overall abdominal closure rates with acceptable morbidity. Modified from Cipolla et al.42

Figure 3. An example of a complex open abdominal wound in a patient who underwent trauma damage control surgery. Here, NPWT sponges are first secured with the use specialized adhesive dressings, followed by a creation of a tract that will allow drainage of enterocutamospheric fistula contents into an ostomy appliance bag (both top pictures and left bottom picture). The resulting ‘floating ostomy’ provided good control of the drainage and hastened the wound healing process. This particular wound was also complicated by an enterocutaneous fistula, for which a separate ostomy appliance was used lateral to the main NPWT dressing (right bottom picture).

In 2001, the use of NPWT in the treatment of enterocutaneous fistulae was reported by Erdmann et al.37 The authors theorized that negative pressure therapy could provide better control of fistula output and potentially provide an avenue for spontaneous closure of the fistula. In 2006, the same group published a series of 15 patients with enterocutaneous fistulae treated using NPWT. In that study, wound care included negative pressure wound therapy with dressing changes performed three times per week. The authors reported an impressive 73% rate of spontaneous closure of the fistulae. Three of the closures were in patients with high output fistulae, and another was achieved in a patient who received neoadjuvant radiation therapy. Mean time to closure was 14 days, with no reported mortalities or other adverse clinical events. The common clinical feature in the four failures was the presence of visible bowel mucosa in the abdominal wound.

In addition to these reports, there have been three other reports with similar success rates, including a case of gastro-cutaneous fistula. Overall, combined literature studies describe over 100 patients with enterocutaneous fistulae treated with NPWT. Again, the benefits noted include improved spontaneous closure rates, a good patient safety profile, economic viability of this therapy, relative simplicity of the treatment, and decreased hospital length of stay.

NPWT: ENTEROATMOSPHERIC FISTULAE

Damage control laparotomy is the accepted standard method of care for patients at risk of developing intra-abdominal hypertension and abdominal compartment syndrome. The
open abdomen that results from this therapeutic maneuver can predispose to the development of enteroatmospheric fistulae. These fistulae are characterized by the lack of an immediately adjacent epithelialized surface and thus the inability to form a fistula tract. There is an associated free leakage of bowel contents onto the surrounding exposed viscera and abdominal wall/fascial components. Due to the deficient abdominal wall and/or skin coverage in this group of patients, fashioning an ostomy appliance is considerably more difficult. This results in increased spillage of bowel contents into the wound, further excoriation of the surrounding skin and visceral surfaces, and creates a potential nidus for sepsis. The use of NPWT has been shown to decrease the resource intensive, and often ineffective in the setting of high regimen, treatment tends to be time-consuming, costly and fistulae only. Despite the overall success of the conventional care support, bowel rest, control of sepsis and a standard ostomy derangements. Conventional care, consisting of nutritional and mortality associated with physiologic and mechanical complications. The primary goal in managing enteroatmospheric fistulae is not spontaneous closure. Instead, one hopes to control contamination, prevent further visceral compromise and prepare the wound for a more stable ostomy appliance. Multiple methods have been employed to address these problems, including multi-layered dressings, vacuum-assisted closure, fibrin sealants, multiple drainage catheters, local repair and reinforcement, bioprosthetic patching and custom ostomy appliances. Complete success is rare, and various combinations of the aforementioned methods are usually attempted. The ultimate goal of therapy here is skin closure or split-thickness skin grafting over the exposed bowel, providing a more stable wound environment that is conducive to the application and subsequent use of a simple ostomy appliance. The use of NPWT for management of enteroatmospheric fistulae is still in its preliminary stages. The largest reported experience comes from Goverman et al, and consists of five patients with large, complex open abdomens that developed enteroatmospheric fistulae. The primary endpoint of therapy was not closure of the fistula, but rather control of the wound environment around the fistula. Using NPWT, the authors were able to successfully divert and control the stream of enteric contents in these challenging wounds. By accomplishing this diversion, NPWT not only provided a more controlled wound environment, but also contributed to enhanced wound granulation. This allowed for earlier split thickness skin grafting and a resultant stable base for ostomy application. In terms of the ostomy appliance placement in these challenging open abdominal wounds, the ostomy was placed at the periphery of the NPWT sponge whenever possible, allowing for some native abdominal wall to be used as an anchor for the appliance. In other cases, the floating ostomy was created through the NPWT sponge using the polyurethane drape as the appliance anchor (see example in Figure 3). Goverman et al reported that patients can be successfully ‘bridged’ with this technique and can safely undergo surgery at a later date for primary resection of their enteroatmospheric-converted-to-enterocutaneous fistulae. In conclusion, enteroatmospheric and enterocutaneous fistulae constitute complex surgical problems with significant morbidity and mortality associated with physiologic and mechanical derangements. Conventional care, consisting of nutritional support, bowel rest, control of sepsis and a standard ostomy appliance are effective mostly in low output enterocutaneous fistulae only. Despite the overall success of the conventional care regimen, treatment tends to be time-consuming, costly and resource intensive, and often ineffective in the setting of high output fistulae. The use of NPWT has been shown to decrease the time to closure of low-output fistulae and may increase the likelihood of controlling the ostomy output and ultimately spontaneous closure of high-output fistulae. These results can be achieved with lower resource utilization and in a cost-effective manner using NPWT. In addition, NPWT can be successfully utilized to control contamination in complex enteroatmospheric fistulae and provide a safe and effective bridge to a more manageable wound.

Figure 4. An example of NPWT use in the setting of split thickness skin grafting. In this example, and extremity wound underwent skin grafting (top) with subsequent application of NPWT sponge over the skin graft (bottom). Note the irregular topography of the wound – a perfect setting for the use of NPWT over a skin graft.

NPWT: SKIN GRAFTING
Split thickness skin grafting (STSG) for definitive wound closure has been utilized in various clinical scenarios. Wounds secondary to trauma, burns, various surgical procedures and chronic medical conditions such as venous stasis and diabetes mellitus have all been traditionally closed with skin grafting techniques. The most feared complication associated with STSG is graft failure. The most common reasons for graft failure are hematoma/seroma formation, infection and unwanted post-placement lateral skin graft movement. Less common reasons for STSG failure include inadequate graft bed, technical error and grafting over complex/irregular or contoured surfaces. Attempts at minimizing these complications resulted in the development of various bolster dressings that usually feature a combination of topical pressure application and an absorptive sponge secured with and adhesive tape or suture material. In addition, the use of adjunctive antibacterial silver-containing dressings combined with NPWT has also been reported to increase STSG success rates.
In 1998, the first attempts at using NPWT to prevent skin graft failure were reported.54-49 These early clinical investigations reported STSG take rates greater than 95% and attributed the success of this approach to total immobilization of the graft, limited shear stress, elimination of fluid collections and decreasing bacterial contamination.46-49 Following these initial publications, Scherer reported on 61 patients who had STSG.51 In that study, 27 patients were managed with standard bolster dressings and 34 were managed with NPWT. There were eight graft failures in the entire study, with seven out of eight being in the non-NPWT group. There were no significant differences between the groups with respect to patient age or length of hospital stay. The authors concluded that NPWT was an excellent alternative for securing STSG but that the major drawback of the study was its retrospective nature.51

In 2004, Moisidis et al conducted a prospective randomized trial of bolster dressings versus vacuum assisted therapy in 22 patients.52 All of the wounds had areas greater than 25 cm² and were judged clinically ready for skin grafting. The authors found no significant differences regarding epithelialization or graft take rates, but a statistically significant difference in graft quality as determined by blinded clinician bedside analysis.52 In another randomized, double-blinded, controlled trial done by Llanos et al, 66 patients were assigned to either a bolster dressing or vacuum assisted therapy.53 In that study, dressings were constructed so that the evaluating physician could not determine in which arm of the study the patient was enrolled. Two statistically significant findings were noted: (a) the median loss of STSG in the group treated with NPWT was 0.0 cm² versus 4.5 cm² in the group treated with bolster dressing; and (b) the length of hospital stay in the NPWT group was shorter than that in the bolster group (median 13.5 days versus 17 days).53 There were no NPWT-related complications in that study.53

Roka et al reported on 29 burn patients who underwent STSG coverage of their wounds.46 In their experience, 28 out of 29 patients with deep dermal and full thickness burn wounds who underwent NPWT-facilitated postoperative STSG fixation, had excellent clinical outcomes and were discharged from the hospital with complete wound closure.46 The authors strongly advocated the use of NPWT for postoperative STSG immobilization, especially for moist and irregular wound surfaces, and for areas exposed to significant amount of movement.46 In addition, Roka et al advocate the use of NPWT in elderly burn victims with multiple medical co-morbid conditions.46 Others report significant reduction of burn-associated tissue edema when using NPWT, with the resultant shortening of the wound healing process.54

There are several theories that support the use of NPWT in the setting of STSG. First, hematoma or seroma formation can be minimized secondary to continuous removal of fluid, thus promoting graft-to-wound apposition.51 Second, good wound-graft approximation, which can be difficult to achieve on irregularly contoured surfaces, can be easily accomplished using NPWT due to the uniform distribution of negative pressure by the NPWT apparatus.55 Third, by ensuring moist wound environment, graft desiccation is minimized and imbibition is enhanced, lessening the chance of graft loss. Finally, it has been previously demonstrated that the use of NPWT may contribute to decreased bacterial counts and improved oxygenation within the wound.56 Since skin graft infection is a major factor in graft loss, the decrease in local bacterial burden may improve graft survival.

There is good evidence to support the use of NPWT for STSG-related applications. Graft survival, overall clinical results, and hospital length of stay can all be improved when employing this technique. Improving graft survival can also result in decreased need for re-grafting. This can be vitally important in patients who lack adequate donor sites such as burn patients and children. Future studies should examine the cost effectiveness of NPWT, its application in the outpatient setting and the feasibility of early mobilization in patients with large STSG’s or grafts covering complex anatomical areas.

**NPWT IN “DIFFICULT” ANATOMIC LOCATIONS: FOOT AND HAND**

Diabetic foot infections are very common, and their frequency is likely to increase as the overall patient population ages.55 In order to appropriately treat these infections, surgical debridements are often necessary. Once the infected or necrotic tissue is removed, there are frequently large remaining soft tissue defects. Traditional methods of treatment of open wounds on feet and hands include topical dressing changes, such as normal saline wet-to-moist dressing changes performed two or three times per day. Negative pressure wound therapy devices have been proposed as a way to help close these wounds with less frequent dressing changes and less patient discomfort.50 Most often, NPWT foam can be used to allow granulation tissue to gradually fill the post-debridement soft tissue defect and assist eventual wound closure. Skin grafts or tissue transfers can then be utilized once the wound bed has reached the granulation stage.

Advantages of NPWT dressings over conventional dressings on the foot are similar to those for NPWT being used in other anatomic locations – better management of wound drainage and less frequent dressing changes. In addition, application of adjunctive silver-containing dressings may provide better control of localized infection.50 More recently, wound perfusion assessment studies suggested that the use of NPWT in the setting of diabetic foot was associated with improved wound perfusion.58
In the anatomic area of the hand, NPWT has been used successfully in the setting of burns, degloving injuries, and staged reconstructive procedures. In the area of soft tissue reconstruction, NPWT has been used as a part of a staged procedure following surgical excision of various hand lesions, especially when awaiting the final pathology report prior to definitive soft tissue reconstruction. This approach also allows the wound-associated edema to decrease before placement of definitive flap or skin coverage. In addition, specialized NPWT dressings have been developed to facilitate post-injury care of degloving wounds and burn wounds of the hand. These specialized foam dressings are designed specifically to fit contours of the hand, with finger contours providing excellent healing environment, especially for partial-thickness burns and degloving hand injuries.

Figure 6. An example of NPWT use in a complex soft tissue wound of the chest, shoulder and neck area. Of note, the central part of the wound contains exposed clavicle. Early granulation tissue can be seen on the exposed bone tissue following the application of adjunctive silver therapy (center box).

In the case of acute necrotizing soft tissue infections and fasciitis, NPWT closure techniques have been used for wound management in both the upper and lower extremities (Figures 5-7). The use of NPWT in the setting of necrotizing soft tissue infections was found to be effective in managing the post-excisional open wound and was found to have lower morbidity when compared to conventional wet-to-moist gauze dressings. Of note, negative pressure wound therapy should only be used on wounds resulting from necrotizing soft tissue infections after the acute infectious process has been definitively controlled and is no longer clinically extending into the adjacent areas of healthy tissue.

NPWT IN “DIFFICULT” ANATOMIC LOCATIONS: HEAD, NECK, AND FACE

Negative pressure wound therapy, as mentioned in other sections of this manuscript, has been used in the treatment of infected sternal wounds, non-healing extremity wounds, and pressure ulcers. In addition to these more traditional indications, new applications for NPWT have emerged, including the use of this therapy on the head (scalp) and face. In fact, NPWT has been used successfully to treat complex, large infected wounds of the face (Figure 7).

When dealing with significant loss of tissue to the head and/or face, NPWT can be utilized to enhance wound healing by the way of promoting granulation tissue formation and new blood vessel in-growth. Skin grafting or vascularized flap placement can then be used in delayed fashion to definitively close the wound. Andrews et al have successfully used NPWT for closure of complicated head and neck wounds. Nine of their patients had exposed calvarium, and were able to be ‘bridged’ to wound closure despite several of the wounds having failed previous placement of pedicle flaps. An example of NPWT use in the setting of a complex scalp wound can be seen in Figure 8.

NPWT USE IN WOUNDS INVOLVING GENITAL AREAS AND PERINEUM

Complex wounds of the penis are rarely encountered. In the pediatric population, NPWT has been successfully used to help close large soft tissue defects of the penis. In this setting, the NPWT has been used to supplement wound debridements and speed up the rate of granulation tissue formation. Local flaps were then used to close the residual tissue defects.

Negative pressure wound therapy has also been used successfully following the application of skin grafts over complex penile wounds. Here, NPWT is used primarily to more effectively hold skin grafts in place in the early postoperative period, thus facilitating prompt fixation of the skin graft to the underlying tissues of the penis. Other variations of NPWT application over
penile areas have also been described, some involving the use of adjunctive therapies, such as silver-containing dressings.50

Figure 8. Application of NPWT to a complex wound of the scalp. After two weeks of NPWT, the patient’s full-thickness wound was closed with a combination of partial approximation of wound edges and application of full thickness skin grafting. Placement of the NPWT dressing in this case required regular hair removal in order to promote adherence between the dressing and the scalp.

Vulvovaginal reconstructions often require split thickness skin grafting or full thickness skin grafting. In this anatomic area, often exposed to radiation therapy, skin grafts are especially prone to infection and sloughing.67 In fact, the incidence of skin graft-related complications may be as high as 22% in this setting.67 The use of NPWT in conjunction with fibrin tissue adhesives has reportedly decreased the rate of skin graft-related complications by providing better graft adherence and maximizing graft viability.67 Shvartsman et al presented a case of NPWT use in a patient with recurrent Paget’s disease of the vulva.68 Due to the fact that recurrence of Paget’s disease is usually related to inadequate surgical margins, the authors utilized NPWT to safely and effectively temporize wound closure until the final histopathologic results were available.68 In addition, negative pressure wound therapy allowed the authors to secure the skin graft to the large and irregular surface of the soft tissue defect when the wound was deemed to be safe to close.68

In an example of a different but equally innovative treatment, neovagina reconstruction performed for Mayer-Rokitansky-Kuster-Hauser Syndrome has been described using the combination of NPWT and skin grafting. Plagued by the high rate of late strictures, the effectiveness of this complex operative reconstruction has been reportedly improved with the use of skin grafting and NPWT application. Here, NPWT has been used in several cases of split thickness and full thickness skin grafting with successful results and minimal patient discomfort at the point of coitus within a month of the surgical reconstruction.69

Figure 9. An example of NPWT use in the setting of a simultaneous damage control abdomen and complex groin wounds following an airplane crash. These wounds were especially challenging because of their multiple, irregular, and discontinuous nature.

Over the last several years, there has been an increased use of NPWT in the clinical setting of difficult perineal wounds – a testament to the versatility of the NPWT technology. In one case, a 67-year-old woman with a previous history of rectal cancer presented with necrotizing fasciitis extending from her perineal region down into her posterior thigh to just above the knee, requiring massive surgical excision (Figure 5). Initially the wound was packed with gauze, then starting on the second day and every 2-4 days thereafter for approximately three weeks, the patient was taken back to the operating room for further debridements and NPWT dressing placements. Regular NPWT foam was used to treat the areas of the rectum, vagina, and the entire posterior thigh (Figure 5). Eventually, split thickness skin grafts were placed over the left thigh and NPWT was used to maintain the skin graft in place (Figure 5). The wound went on to heal very well, ultimately resulting in a small area that required only a small absorbent pad for control of wound drainage.

Fournier’s gangrene in the perineal region can lead to extensive tissue loss. Traditional wound management techniques included wet-to-moist dressing changes. Such traditional dressing changes are often untidy, difficult to perform, and need to be replaced two to three times per day. Negative pressure wound therapy has been used successfully to help control wound drainage after extensive debridements, promote granulation tissue formation, and decrease the overall number of dressing changes, making the entire process much more comfortable for the patient.70 An example of such complex perineal wounds treated with NPWT can be seen in Figures 9 and 10.

NPWT IN THE SETTING OF COMPLEX STERNAL WOUNDS

Median sternotomy is the preferred incision for approaching the heart and great vessels. One of the most devastating complications of procedures performed via median sternotomy is sternal wound
infection and dehiscence. The incidence of wound infections after sternotomy ranges between 0.15% and 5%.[71] The optimal treatment of this complication has yet to be determined. Basic surgical principles, which include aggressive surgical debridement of non-viable or infected tissues, accompanied by some type of vascularized tissue coverage constitute the mainstay of therapy. It is not uncommon for the wound care process to continue for days or even weeks before adequate, definitive coverage can be accomplished. Oftentimes, multiple dressing changes and wound treatments are required.

Various adjunctive therapies have been reported to facilitate wound closure and decrease the time and need for inpatient therapy. These therapies include hyperbaric oxygen, CO₂ laser treatment, continuous antibiotic irrigation, sternal “zippers”, bone grafts, and various retention suture techniques.[72-73] All of these procedures have their benefits and pitfalls. One of the more recent advances in the treatment of sternal wound dehiscence and/or infection is the use of NPWT.

The first use of NPWT for sternal wounds was reported by Obdeijn et al in 1999.[74] The authors reported on three patients who developed mediastinitis and sternal wound infection after coronary bypass surgery. Due to their poor overall physiologic status, these patients were deemed to be at prohibitive risk to undergo operative closure of their sternal wounds. Negative pressure wound therapy was chosen as an alternative to surgical closure. Following opening of the sternum, wound debridement and irrigation, the NPWT device was contoured to fit the size of the tissue defect. The NPWT sponge was changed at the bedside every 48 hours. All three wounds were eventually closed without complications and without the need for subsequent operative procedures. The authors also noted that the NPWT apparatus was able to provide sternal stabilization, which allowed for more aggressive cardiac rehabilitation. Since this report, over 400 more cases have been reported in the literature with similar results.[74]

Figure 10. Complex perineal wound secondary to a severe episode of Fournier’s gangrene. Upper windows show the extent of this complex wound after control of the infectious process was established. Tension-free skin approximation was performed wherever possible. The perianal wound required creation of diverting colostomy and intubation of the anus for control of rectal mucus drainage (lower windows). The penile tissue is protected from the effects of NPWT using non-adherent dressing for coverage (right upper window).

Figure 11. Top – a depiction of abdominal NPWT system used to control ascitic fluid leaks. A bottom layer of biohesive was placed over patient’s skin overlying the incision, and a slit was created over the incision site to allow for drainage. A sponge was placed over the biohesive and incision. Finally, a top layer of biohesive was placed over the sponge and attached to the bottom biohesive layer. A small cruciate incision was made in the top biohesive, to which the NPWT was attached. Bottom – cross-sectional view of the abdominal wall and the NPWT dressing. The presumed vectors of negative pressure forces are indicated by arrows. Hersh et al used NPWT for sternal wound management as a “bridge” to surgical closure on 16 patients.[75] Although all of these patients were candidates for surgical closure of the sternum, heavy wound contamination prevented a one-stage procedure. Upon completion of NPWT, absence of clinical signs of infection and quantitative cultures were used to determine surgical candidacy. Ultimately 94% of the wounds were successfully closed.[75] The authors of this study also reaffirmed previously published
observations that stabilization of the sternum by the NPWT apparatus helps to facilitate earlier extubation and mobilization of the patient. Patients with greater number of co-morbidities and more severely contaminated wounds were noted to require longer durations of therapy. In a similar study, Cowan et al noted that the overall number of wound treatments was reduced when NPWT was utilized. This was due to the fact that NPWT sponges were changed, on average, every 48 hours versus twice a day for standard gauze dressings. In some cases, NPWT allowed for earlier patient discharge, with home nursing arrangements made to change NPWT sponges regularly. The overall duration of NPWT ranged from 3-80 days in all of the above studies.

There are many potential complications associated with managing a sternal wound infection. Morbidity and mortality remain high despite aggressive therapy. Negative pressure wound therapy in this setting is also not without complications. One of the most devastating complications of chronic sternal wound infections managed with NPWT is right ventricular rupture. There have been seven reported right ventricular ruptures associated with NPWT use in the setting of sternal wound infections. Due to this potential complication, the NPWT technique was modified by placing paraffin gauze over exposed viscera prior to instituting therapy. Using this modified technique, NPWT was used to treat over 80 patients without any further ventricular ruptures. Other reported complications of using NPWT for the management of sternal wounds include minor bleeding, subcutaneous fistulization, and air leaks. In two other series, totaling 38 patients, there were no reported complications of NPWT.

Definitive conclusions about the safety and efficacy of NPWT are difficult to make due to the lack of randomized, prospective evidence. The cumulative data suggest that with standard surgical principles applied, NPWT for sternal wound infections may improve wound closure rates and decrease the need for regional flap usage. In patients unable to undergo primary debridement and closure, NPWT can be utilized as an alternative to primary closure or, more frequently, as a safe bridge to primary closure while the patient recovers form cardiac surgery and sepsis. Not only does NPWT provide a wound environment that promotes granulation formation and limits tissue edema, but it offers the secondary advantage of sternal stabilization. This allows for aggressive and safe mobilization of the patient, which can decrease intensive care needs and facilitate discharge to home with ancillary nursing care. The advantages of NPWT allow it to be considered a primary mode of treatment, especially when dealing with a heavily contaminated sternal wound or a physiologically unstable patient.

NPWT IN THE SETTING OF ASCITES AND RELATED APPLICATIONS

One unusual, and quite counter-intuitive, use of NPWT has been described in the setting of postoperative incisional ascitic leaks. This unconventional use of NPWT appears to be effective in managing the flow of ascitic fluid and facilitating sealing of large-volume ascitic fluid leaks. One published series describes four cases of successful management of intractable postoperative ascitic fluid leaks utilizing NPWT. In one case, closure of a profusely draining perineal wound resulting from an abdominoperineal resection was accomplished within five days of specialized NPWT dressing application (Figure 12). In the other three cases, refractory drainage from midline laparotomy incision was successfully managed with the use of NPWT (Figures 11 and 13). In all four cases, the negative pressure-based system was effective in controlling drainage of ascites and subsequently sealing the wounds. Postoperative use of NPWT in conjunction with optimization of medical therapy and judicious tapping of ascites appears to provide a safe and effective method of controlling ascitic fluid leaks and promoting definitive tissue sealing in patients with hepatic cirrhosis.

In a related clinical application, NPWT was utilized in the setting of persistent leakage around left ventricular assist device (LVAD) driveline. Here, NPWT effectively assisted in tissue ingrowth and tissue closure around the driveline. The use of negative pressure therapy also appeared to promote enhanced granulation tissue formation, decreased the amount of wound drainage, and reduced bacterial burden in the area of therapy application. This limited experience with three patients suggested that NPWT can be used effectively for sealing LVAD driveline-related fluid leaks. Similar to the previously discussed article on the use of NPWT in the setting of ascites, the authors also noted that NPWT was particularly useful for patients with abdominal fluid leakage.

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**Figure 12.** Top – Diagram of NPWT dressing used in the setting of ascitic leakage from a perineal wound. A small sponge is placed in the anterior portion of the incision. This sponge is then covered with bioclusive, with a cruciate incision in the region overlaying the sponge. The NPWT suction device was then attached over this incision in the Bioclusive material. Bottom – cross-sectional view of the NPWT dressing. The proposed vectors of force are indicated by arrows.

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NPWT: SPECIAL ISSUES AND TOPICS
Despite the evolving number of indications for NPWT, some controversial points persist regarding this treatment modality. Specifically, it has not been definitively determined whether the currently recommended 24-72 hour NPWT dressing change regimen is optimal. While it is appropriate to change NPWT dressings frequently (i.e., every 12 to 24 hours) in the setting of severe and moderate wound contamination, it seems that dressing change regimens in the setting of minimally contaminated and clean wounds may be spaced further apart than the currently recommended 24 to 72 hours interval.\(^{21}\)

Factors at the center of the debate between more frequent (every 24-72 hours) and less frequent (every 72-144 hours) NPWT dressing change regimens for minimally contaminated and clean wounds include: (a) significant costs associated with NPWT dressing supplies; (b) unpleasant and potentially painful experience for the patient; and (c) significant amount of healthcare resources required to change dressing (personnel and/or operating room time).\(^{21}\)

Previously published data from patients with open abdomens indicates that patients treated with NPWT regimen of dressing changes performed every four days apart demonstrated similar mortality, morbidity, time to abdominal closure, and length of stay figures when compared to patients who underwent NPWT dressing changes approximately every 2.5 days.\(^{21,29}\) Due to the retrospective nature of the data and differences in patient populations studied, it is difficult to ascribe the above observations to specific clinical parameters or patterns of practice. What was clear, however, is that some patients were treated successfully utilizing dressing changes, on average, nearly 2 times less frequent than the usual 48 hours. In addition, NPWT dressings placed over skin grafts were kept in place between 4 and 5 days.\(^{21}\)

Considering other published reports and series, it appears that there is some support for less frequent NPWT dressing changes.\(^{66,80-83}\) It is well established that NPWT therapy applied over skin grafts can be safely left in place for a period of 5 days.\(^{66,80}\) A seven-day regimen of NPWT changes was used successfully in the setting of extensive soft tissue defects following resection of deep infiltrating leiomyosarcoma, with no observed infectious complications.\(^{81}\) There are also reports of the use of adjunctive silver-based dressings combined with NPWT, with significant labor- and cost-related savings secondary to a less frequent 5-day and 7-day dressing change regimens.\(^{82,83}\)

Among other developments in negative pressure wound therapy, dual-modality therapies featuring both the benefits of negative pressure wound therapy and irrigation/instillation wound therapy have been introduced.\(^{84}\) In this new system, instillation therapy is automated to control the delivery of topical solutions such as anesthetics, antibiotics, antifungals, antiseptics, and various cleansers to the wound site.\(^{84}\) This combination of NPWT and irrigation/instillation therapy could help enhance the benefits of single-modality NPWT by providing the ability to cleanse, irrigate, and remove infectious material/debris from the wound.\(^{84}\) It has been postulated that this combined wound care modality could benefit a variety of traumatic and chronic wounds, help maximize patient comfort, and minimize the time-consuming caregiver intervention of manual wound irrigation.\(^{84}\) This may be especially true when NPWT is used as a ‘bridge’ therapy before definitive closure of complex and odd-shaped wounds.\(^{85}\)

CONCLUSIONS
Negative pressure wound therapy is being used in an increasing number of clinical indications. Over the years, it has become the modality of choice in the setting of skin grafting, burns, complex extremity and perineal wounds, and open abdomens. New, emerging applications of NPWT include management of sternal wound infections, various types of fistulae, and ascitic fluid leaks. More elaborate dressings, new types of NPWT devices, and the

Figure 13. An example of application of the NPWT ‘ascites’ system to a midline abdominal wound. Note the protective layer of bioclusive film and the non-adherent dressing applied to protect the underlying skin from direct effects of the NPWT sponge.
emergence of combination therapies involving simultaneous suction-irrigation schemes, provide wound care specialists with an increasing array of treatment options. It is undisputable that the NPWT paradigm is here to stay. Some controversial points persist regarding this treatment modality. Specifically, the optimal timing of NPWT dressing changes based on the type of wound, has not been fully determined. The use of NPWT in the setting of infected implants and exposed oseous tissue constitute another promising but still controversial area of clinical application of this therapy. In addition, significant portion of evidence supporting the use of NPWT in clinical practice is based on case reports and retrospective case series. Prospective evaluation of specific NPWT-related complications is warranted.

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