NEGATIVE PRESSURE WOUND THERAPY:
A CLINICAL REVIEW
The Nature of Chronic Wounds

Many factors, including the presence of foreign bodies, tissue maceration, ischemia, and infection, can impair healing. Systemic factors as diverse as advanced age, malnutrition, diabetes, and renal disease may complicate the clinical picture. Other factors include the following:

- **Reduced levels of active growth factors.** Chronic wounds have reduced levels of a number of growth factors compared with acute wounds. Growth factors may be degraded by proteases to an excessive degree, resulting in nonhealing.

- **Imbalance between proteinases and their inhibitors.** Excessive activity of proteinase in chronic wounds results in abnormal degradation of the extracellular matrix. Many new treatment strategies are directed at modifying the imbalance, such as the topical application of proteinase inhibitors, inducing the expression of endogenous inhibitors, or combining proteinase inhibitors with growth factors.

- **Senescent cells.** Fibroblasts have an age-related decrease in proliferation potential, called senescence. Fibroblasts in chronic wounds have impaired responsiveness to growth hormone, which may be due to an increased number of senescent cells.

Morbidity associated with difficult-to-heal chronic wounds negatively impacts the patient’s quality of life and may result in exorbitant healthcare costs. The common treatments for wounds are debridement of necrotic or infected tissue, maintenance of a moist wound environment, control of infection, and provision of nutritional support. Despite these treatments, some wounds continue to resist healing. Therefore, emerging treatments are being assessed to improve the prognosis of patients with complicated wound profiles.

One such treatment, negative pressure wound therapy (NPWT), is a topical treatment used to promote healing in acute and chronic wounds by applying negative pressure to the wound bed. These NPWT devices work through application of a disposable, open-cell antimicrobial gauze dressing with a nonadherent contact layer or foam dressing to the wound base, which is covered with a semipermeable film drape or transparent adhesive film dressing. An evacuation tube embedded in the dressing is connected through an adjustable vacuum pump to remove effluent to a remote col-
lection container. Microprocessor controls can be programmed for varying pressures and cycles of constant and intermittent suction. The application of subatmospheric pressure to the dressing results in multiple benefits including:5
• Increased local blood flow via enhancement of capillary blood flow
• Increased angiogenesis with profuse granulation formation
• Increased number of active fibroblasts and macrophages
• Enhanced epithelial cell migration
• Decreased bioburden, bacterial toxins, and subsequent cessation/delay of healing and decreased tensile strength of the wound
• Decreased harmful, chronic wound fluid and by-products and subsequent senescent cells and tissue damage
• Decompressed excess interstitial fluid with subsequent decreased periwound induration, inelasticity, and microvascular occlusion
• Reduced number of dressing changes and subsequent decreased damage to delicate new tissue, pain, desiccation, and exposure to nosocomial infection
• Provision of a moist, normothermic wound environment that allows more efficient epithelization, growth factor synthesis and availability, and overall wound healing potential
• Provision of mechanical approximation of wound edges
• Promotion of viscoelastic flow and distraction histogenesis due to tissue stretch and stimulation of the cytoskeleton with subsequent enhanced mitosis
• Decreased shear forces to the graft during inosculation via uniform wound bed immobilization
• Decreased seroma/hematoma of grafts and flaps
• Limitation of zone of injury after acute orthopedic trauma
• Splinting effect (sternal, abdominal).

Clinical Evidence of NPWT Efficacy

The evidence supporting the use of NPWT in the treatment of chronic nonhealing wounds exists primarily in the form of nonrandomized, controlled trials; prospective and retrospective large and small case series; single-center studies; and single case studies, with few randomized, controlled trials (RCTs).

Diabetes-associated wounds. A multicenter RCT of 162 patients was conducted to investigate the effect of NPWT compared to standard care in complex wounds secondary to partial foot amputation in patients with diabetes.6 Patients were randomly assigned to NPWT (n = 77; 48%) and received dressing changes every 48 hours. The control group (n = 85; 52%) received standard moist wound care. Wounds were treated until healing or completion of the 112-day period of active treatment. Fifty-six percent of the patients healed in the NPWT group compared with 39% of the control group (P = .04). The rate of wound healing and granulation was faster in the NPWT group (P = .002). The frequency and severity of adverse events were similar in both groups. The investigators concluded that NPWT appeared to be a safe and effective treatment for complex diabetic foot wounds and could lead to a higher proportion of healed wounds, faster healing rates, and potentially fewer re-amputations than standard care.

Sternal wounds following cardiac surgery. A prospective study was conducted on the impact of NPWT on healing of sternal wounds.7 The study consisted of 27 patients with acquired postoperative mediastinal infection who were managed with either NPWT as a sole treatment or NPWT followed by myocutaneous flap or primary wound closure. Group A (n = 14) received NPWT for a median duration of 13.5 days. Group B (n = 13) received NPWT for a median duration of 8 days, followed by myocutaneous flap (n = 8) or primary wound closure (n = 5). The choice of additional treatment was based on wound size (i.e., larger wounds required ultimate surgical closure). In Group A, a satisfactorily healed scar was achieved in 64% of cases. Median durations of NPWT and hospital stay in Group A were 13.5 days and 20 days, respectively. The treatment failure rate in Group B was 15%. Median duration of NPWT in Group B was 8 days, and median hospital stay was 29 days. During the year before institution of NPWT, post-sternotomy infection (n = 13) was managed with rewiring and a closed irrigation system. Treatment during this year failed in 31% of cases (n = 4/13). The total cost—hospitalization and treatment—per patient for NPWT was $16,400 compared with $20,000 for the closed irrigation system treatment. The researchers reported that using NPWT as the sole treatment produced an overall success rate of 70% healed wounds in patients with infected sternal wounds secondary to cardiac surgery.

Sternal wounds and dressing changes. A retrospective review of a 2-year period examined records of 35 patients
with sternal wound complications to evaluate the efficacy of the NPWT device as a bridge between debridement and definitive closure. Eighteen patients (51%) were treated with traditional twice-daily dressing changes and 17 patients (49%) were treated with NPWT alone. The NPWT group had a trend toward a shorter interval between debridement and closure, with a mean of 6.2 days; the dressing change group had a mean of 8.5 days. The NPWT group had a significantly lower number of dressing changes (mean = 3 changes); the twice daily dressing change group had a mean of 17 changes (P < .05). Reconstruction required an average of 1.5 soft-tissue flaps per patient treated with traditional dressing changes versus 0.9 soft-tissue flaps per patient for those treated with NPWT (P < .05). The researchers concluded that NPWT led to faster wound healing and lower usage of resources in the management of patients with sternal wound complications than did traditional treatment.

**Wet-to-moist dressings versus NPWT.** A single-blind RCT was performed to evaluate the efficacy of NPWT for chronic wound healing. Twenty-four patients with several different wound types were randomized to 6 weeks of either standard moist dressings or NPWT. A total of 36 wounds were treated. The researchers reported that 64% of the NPWT group demonstrated granulation tissue formation, whereas 81% of the wet-to-moist group had inflammation and fibrosis. The researchers concluded that NPWT promoted faster healing than standard wet-to-moist dressings and increased the rate of granulation tissue formation.

**Home health pressure ulcers.** A retrospective study was conducted to determine the prevalence of severe pressure ulcers in the home health population. This study also sought to quantify the impact of NPWT in reducing acute care hospitalizations and emergent care, in general, and wound infection or deteriorating wound status, in particular. Data from 1.94 million federally mandated Outcome Assessment Information Set (OASIS) at-of-care assessments over a 2-year period were evaluated to estimate pressure ulcer prevalence and a retrospective matched group analysis compared patients using (n = 60) and not using (n = 2,288) NPWT. Approximately 7% of patients had pressure ulcers at start of care. Of these, 23% were Stage III or Stage IV and 31% were “not healing.” Those receiving NPWT experienced lower rates of hospitalization (35% versus 48%; P < .05), hospitalization due to wound problems (5% versus 14%; P < .01), and emergent care for wound problems (0% versus 8%; P = .01). The authors specified that additional research is needed with a larger, nationally representative sample to compare other quality outcomes as well as the cost of providing NPWT to other specific wound care modalities.

**Costs and times of healing versus conventional therapies.** A retrospective review sought to determine if pressure ulcers and other chronic wounds treated at home with NPWT close faster and result in reduced treatment costs compared to conventional therapies (eg, low-air-loss surface and saline-soaked gauze). Records for 1,032 Medicare home healthcare patients with 1,170 wounds (Stage III and Stage IV trochanteric and trunk wounds) that failed to respond to previous interventions—and were subsequently treated with NPWT—were reviewed. In this study, wounds averaged 22.2 cm² in area and closed at an average of 0.23 cm² per day. The average 22.2 cm² wound in this study would take 247 days to heal and cost $23,465 using conventional therapies. Using NPWT, the wound would heal in 97 days and cost $14,546. The study concluded that NPWT is an efficacious and economical treatment modality for a variety of chronic wounds.

**Battlefield wounds.** Negative pressure wound therapy has been used with surprising success on the battlefields of Iraq. Wartime missile injuries are frequently high energy wounds that devitalize and contaminate tissue, with high risk for infection and wound complications. Debridement, irrigation, and closure by secondary intention are fundamental principles for the management of these injuries. However, closure by secondary intention was impractical in Iraqi patients amid a war setting. Therefore, wounds were closed definitively before discharge in all Iraqi patients treated for such injuries. High energy injuries were treated with rapid aggressive debridement and pulsatile lavage, then covered with negative pressure dressings. Patients underwent serial operative irrigation and debridement until wounds appeared clean to gross inspection, at which time they were closed surgically. Treatment and outcomes data from September 2004 through May 2005 were analyzed retrospectively. There were 88 high-energy soft tissue wounds identified in 77 patients. Amazingly, the wound infection rate was 0% and the overall wound complication rate was 0% in this subset of patients. This series of cases is the first report of the use of NPWT as part of the definitive management of high-energy soft tissue wounds in a deployed wartime environment. The experience gained from these patients suggests that conventional wound management
doctrine may be improved with NPWT, resulting in earlier, more reliable primary closure of wartime injuries.

The Evolving Issue of Defining the Appropriate Negative Pressure

The effect of exposing wounds to subatmospheric pressure has been studied in a variety of settings for at least half a century. However, practice parameters that define pressure intensity, duration of treatment, and interval between treatments to provide the most efficient therapy are still lacking. In 1997, Morykwas et al showed that microvascular blood flow increases 4 times the baseline values with negative pressures of 125 mmHg, while blood flow was inhibited at negative pressures greater than or equal to 400 mmHg. Based on this result, negative pressure of 125 mmHg became the most common setting when using this technique. However, previous to that research, Russian physicians were refining NPWT. In 1987, Usupov and Yefipanov used a rabbit model and concluded that to avoid tissue damage, pressures in active drainage systems should not exceed –80 mmHg and that lower pressures were less likely to demonstrate postoperative hemorrhage. The same study also demonstrated new tissue hemorrhage of previously coagulated vessels with pressures below –120 mmHg to –125 mmHg. Aside from inconsistencies in pressure levels, differences in pressure intervals were also evident between the studies of Morykwas et al and the Russian studies. Morykwas et al stated that optimal results were obtained when NPWT was applied continuously for the first 48 hours and then applied in an intermittent manner (5 minutes on and 2 minutes off) after the initial 48-hour treatment. In 1986, the Russian researchers published a study that revealed that NPWT could be successfully applied twice daily for 2.5–3 hours. The disparity in findings underscored the need to better define pressure intensity parameters, duration of treatment, interval between treatments, mode of application, and timing of application to provide the most efficient and cost-effective therapy. In 2004, a Swedish study by Wackenfors et al was published in which the microvascular blood flow to inguinal wounds in pigs was observed during negative pressures ranging from 50 mmHg to 200 mmHg. The investigators used laser Doppler to measure blood flow in which the sum of all erythrocytic motion was quantified in a volume of 1 mm³, thereby making it feasible to reliably perform measurements in small, closely spaced skin areas. The study was then properly designed to examine how NPWT affects microvascular blood flow, with consideration of tissue type and the distance of blood flow from the wound edge—parameters that were not factored into the work done by Morykwas et al. The results of the later study found that NPWT induced an increase in microvascular blood flow a few centimeters from the wound edge, which may accelerate granulation tissue formation and the healing process. Conversely, closer to the wound edge, the negative pressure resulted in hypoperfusion that increases along with increasing subatmospheric pressure with the possible outcome of ischemic tissue damage.

Furthermore, tissue type was a factor: the increase in blood flow occurred closer to the wound edge in muscular as compared to subcutaneous tissue (1.5 cm and 3 cm at negative pressures of 75 mmHg). Wackenfors and her team proposed that a balance is necessary when selecting the amount of negative pressure for NPWT treatments. The vacuum should be adequately robust to drain the wounds and arrest superficial bleeding. Yet, simultaneously, the vacuum should not create a significant ischemic zone. Based on their findings, the investigators concluded that when treating stiff tissue, such as muscle, a negative pressure of 100 mmHg may be reasonable, thereby limiting the extent of the hypoperfused zone to 1 cm from the wound edge. When treating softer tissue, such as fat and subcutaneous tissue, which is more vulnerable to hypoperfusion, the application of a lower negative pressure, such as 75 mmHg, may be more beneficial. Although such pressure recommendations are not common NPWT practices, the Russian literature supports the use of these pressures during treatment.

Guidelines for Using NPWT

During the European Tissue Repair Society (ETRS) Open Focus Meeting in 2000, Teot presented the following general guidelines for NPWT.

When and with which wounds to apply NPWT. Large trauma wounds with exposed bones, tendons, vessels, and closed joints. Large trauma wounds with exposed bones, tendons, vessels, and closed joints can be treated effectively using NPWT. The pathogen-free environment will favor the formation of granulation tissue over these structures. Mean duration of treatment is ~2 weeks.

Large sacral ulcers. For large sacral ulcers, the contraction obtained with NPWT can enhance healing. To prevent infection of any undrained area, the dressing must fill the cavity entirely. Mean duration of treatment is ~3 weeks.

Post-sternotomy wounds. For post-sternotomy wounds.
wounds, NPWT is indicated when the sternal bone is exposed and generally infected and a large open cavity exposes the anterior mediastinal area. Mean duration of treatment is long enough to obtain a uniform granulation tissue base.

**Post-surgical debridement.** After a surgical debridement, NPWT can be an effective means of treating these poorly vascularized wounds. For post-operative wounds of the abdominal wall, Teot suggests that 2 different situations can be encountered: 1) the existence of a parietal muscular defect and 2) the need to close the peritoneal cavity using a mesh. In the latter case, NPWT must be left in place a period of time long enough to obtain a uniform granulation tissue entirely covering the mesh. A skin graft will be proposed as soon as this result is obtained.

**When to stop NPWT.** Negative pressure wound therapy should be discontinued for the following reasons:
- A uniformly granulating tissue is achieved
- Psychological intolerance
- No progression of the wound is observed on 2 successive dressing changes.

**When not to use NPWT.** Relative and absolute contraindications and precautions include malignancy in the wound margins, untreated osteomyelitis or necrotic wound eschar, fistulas to organs or cavities, exposed blood vessels and nerve, exposed organs, exposed bone, severe peripheral vascular disease, dry wounds, active bleeding, anticoagulants and difficult hemostasis, and proximity to sutured or irradiated vessels or organs. Complications are rare but can include infection, desiccation, pain, erosions, odor, tissue ingrowth, maceration, and bullae.

**Conclusion**
The first step in wound healing is to remove or correct factors that impair healing. Many wounds will heal with good wound care that removes necrotic tissue, maintains a moist wound environment, controls infection, and provides nutritional support. Once these primary factors are addressed, some wounds will benefit further from adjunctive therapies, such as NPWT. As evident in the literature, NPWT has proven a successful adjunctive therapy in healing a variety of wounds. However, more RCTs are needed to support which wound type is most appropriate for this treatment, the duration of therapy, and the negative pressure settings.

**References**


