Negative Pressure Wound Therapy

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Introduction

“Creativity…consists largely of rearranging what we know in order to find out what we do not know. Hence, to think creatively, we must be able to look afresh at what we normally take for granted.” — George Kneller

Negative pressure wound therapy (NPWT) is the process by which negative pressure is distributed across a wound base via a dressing with the specific intent to promote wound healing. Over the centuries, popularity for using negative (subatmospheric) pressure to treat wounds has waxed and waned. In medical literature, negative pressure-based therapies used for wound healing have been referred to as cupping, pneumatic occlusive therapy, passive hyperemia therapy, active drainage, suction drainage therapy, active aspiration, vacuum drainage, vacuum sealing technique (VST), topical negative pressure (TNP), subatmospheric pressure dressings (SPD), NPWT, vacuum sealing dressing (VSD), irrigation drainage, and a patent filed in China in 2010 brought it full circle with reduced pressure wound cupping treatment. With each advancing generation, healthcare practitioners have observed the wound healing potential of negative pressure interpreted through the limitations of their existing knowledge of medical sciences. Spurred by innovative equipment, advances in healthcare technology, and the artistic ingenuity and technical competency of the practitioner caring for the wounded patient, NPWT has been constrained by the risk of complications, technical difficulties, inappropriate patient selection, and the need to develop a clear, defensible evidence base to support the safe and effica-

Objectives

The reader will be challenged to:

• Describe the use of negative pressure wound therapy (NPWT) as a standard in advanced wound care
• Review the appropriate most up-to-date information on the use of NPWT in chronic wound care
• Summarize the current understanding of proposed mechanisms of action for NPWT
• Recognize potential complications related to NPWT usage and determine interventions to reduce risks.

Additional Resources:

Cochrane Review: Negative pressure wound therapy for treating pressure ulcers

Cochrane Review: Negative pressure wound therapy for treating surgical wounds healing by secondary intention

Developing Evidence-Based Algorithms for Negative Pressure Wound Therapy in Adults with Acute and Chronic Wounds: Literature and Expert-based Face Validation Results
http://www.o-wm.com/content/developing-evidence-based-algorithms-negative-pressure-wound-therapy-adults-acute-and-chroni

cious use of the proposed technique. The advent of new, portable, computer-programmable negative pressure generators, novel treatment materials, newer understandings of “cellular” healing responses, and modern cause-effect validation coupled with the healthcare community’s burgeoning interest in tissue regeneration created the perfect storm for resurgence of a modern-day platform for NPWT. The utility of NPWT for managing complex wounds, ulcers, burns, post-operative wounds, and non-surgical tissue defects has emerged as a readily available, frequently employed, and internationally adopted therapeutic practice with applicability for acute and chronic wounds in a variety of care settings.1,2

The current NPWT platform was built with the full anticipation of eventually using modulations in the negative pressure profile to direct specific cellular responses to improve the healing rate, quantity, and quality of tissue generated. As with all wound care practices, the “evidential clarity and defensibility” for NPWT will be bounded by the capability of the scientific wound care community to understand and judge the merits of the process within the existing conceptual and technological constraints of the era in which they live.

Modern Perspectives of NPWT

“No single achievement in science is possible without the painstaking work of the many hundreds who have built the foundation on which all new work is based.”
— Nobel Laureate Polykarp Kusch

The current NPWT platform witnessed a surge in popularity when Dr. Louis Argenta and Dr. Michael Morykwas at Wake Forest University developed Vacuum Assisted Closure® (V.A.C.®) Therapy (KCI USA, Inc., San Antonio, Texas) to optimize the benefits of subatmospheric (negative) pressure for wound healing1,2 with special focus on perfusion and granulation tissue development.3 This integrated system uses a computerized therapy unit to intermittently or continuously deliver negative pressure through a resilient, open-cell foam surface dressing that is sealed with an adhesive drape. The original tubing design had a terminal pad, sealed in contact with the foam, which delivered wound space pressures and redirected wound exudate into a specially designed, disposable canister.

While the basic components of the NPWT systems remain the same, ongoing research has led to the development of added features and associated benefits for many devices. For example, the Therapeutic Regulated Accurate Care (T.R.A.C.™) Pad used with the V.A.C. Therapy system added pressure sensing ports along the collection tubing to improve monitoring and maintenance of the set target pressure at the wound site as an initial design improvement over the process of inserting the cut end of the collection tube directly into the foam. The SensaT.R.A.C.™ Technology design improvement facilitated increased exudate collection. Improved ability to accurately maintain pressure in a variety of environmental conditions and to alert caregivers through various alarms has contributed to acceptance of NPWT for certification as safe-to-fly on some military air transport vehicles.

Additional refinements have included Smart Alarms™ that alert caregivers when corrective action is needed and, in some conditions, interrupt therapy if critical programmed parameters are met. The therapy unit alarms in any of the following conditions:

- The canister is full, missing, or improperly placed
- The tubing is blocked
- The tubing or dressing has air leaks
- Therapy is inactive
- The battery is low.

V.A.C. Therapy is intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, removing exudate and infectious material, reducing edema, promoting granulation tissue formation, and promoting perfusion.2 V.A.C. Therapy is indicated for patients with chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic or pressure); flaps; and grafts.4

NPWT Systems

“Without continual growth and progress, such words as improvement, achievement, and success have no meaning.” — Benjamin Franklin

V.A.C. Therapy System, marketed in the United States since 1995, serves as a predicate device...

CHRONIC WOUND CARE: The Essentials e-Book
Negative Pressure Wound Therapy

for a series of products approved for NPWT. Characteristically described, the current NPWT platform has evolved to include several key components: 1) an electric-powered or non-powered negative pressure generating “pump” with continuous and/or intermittent negative pressure modality, 2) connective tubing to convey pressure changes to the wound space, provide a conduit to remove exudate, and, in some cases, monitor the pressure delivered to the wound space, 3) a water-impermeable, adhesive-sealed occlusive, oxygen- and water vapor-semipermeable drape to protect against pressure loss and wound contamination, 4) an interface dressing (with or without a nonadherent intervening contact layer) that interacts with the tissue at the wound base, helps wick exudate from the recesses of the wound, and through which the negative pressure is delivered to the wound space, and 5) an exudate collection process to contain exudate removed from the wound.

NPWT System Designs and Innovations

At present, 13 manufacturers of NPWT devices are recognized by the US Centers for Medicare & Medicaid Services (CMS) for reimbursement after undergoing 510K, substantial equivalency determination with the V.A.C. Therapy System as the predicate device. US Food and Drug Administration (FDA)-approved negative pressure pumps span from simple vacuum generators to fully computerized feedback systems, non-powered or electrically powered with and without battery backup, variably capable of generating and monitoring continuous and intermittent negative pressure. Device alarms strive to improve the therapeutic safety profile, especially related to identifying situations that may be related to serious and potentially fatal blood loss. NPWT has undergone a tremendous expansion attesting to the extensive applicability of subatmospheric (negative) therapy to multiple clinical situations and care settings. The following generalized, non-comprehensive review of key component modifications is designed to provide insight to the product variation available. Comparative impact of specific therapy and device variances on clinical wound healing outcomes has yet to be fully determined.

Pumps. Prior to the development of computer-regulated pumps, wall suction was used for evacuation of exudate from wounds. While effective for wound exudate management, wall suction techniques create an abrupt drawdown and do not allow for pulsed regulated pressure delivery. Initial modifications on the predicate device were focused on proof of concept and assuring delivery of programmed negative pressure through wound site feedback, monitoring for continuous and intermittent pressure, expanding ranges for negative pressure (–40 mmHg to 230 mmHg) to increase number of approved manufacturers, validating antimicrobial gauze dressing as an appropriate alternative “filler material,” decreasing noise, and improving portability. Presumably, modulating pressure cycle times, peak pressure, pressure wave patterns, and treatment regimes influences tissue cellular content, collagen and extracellular matrix deposition, and quantity and rate of generation. “Optimal” tissue healing would be achieved through response-adjusted negative pressure treatment profiles. Previously, lower pressure ranges and gauze were the focus of newer devices to distinguish themselves from the predicate device. Current device improvements seek further portability, ease of use, and universal applicability. Some newer devices are designed for use with both gauze and foam, without preferential styling, thereby securing their utilization independent of the physician’s choice of therapy. For instance, XLR8® (Gendyne Biotechnologies, Great Neck, New York) was designed for maximal suitability with low weight (600 g), full-range peak pressure profile capacity (50 mmHg–230 mmHg), continuous and intermittent modality, and 3-hour charge time with minimal noise levels.5

Power source. Previously, newer models remained electrically powered with a focus on extended battery life. Now attention has turned toward achieving non-powered, alternative energy-sourced devices and devices that are solely battery powered with imminent disposability for short-term, out-of-hospital therapy. Powered and non-powered device clinical safety considerations remain similar to those of the predicate device, even though in the United States non-powered NPWT devices are managed under a separate FDA classification guidance document.6
The SNaP® Wound Care System (Spiracur Inc., Sunnyvale, California) is an exceptionally lightweight, “ultraportable,” non-powered, mechanically generated negative pressure unit that showed special utility for ambulatory, out-of-hospital disaster-injured patients in Haiti where community electricity suffered prolonged disruption.7

**Portability.** Device evolution progressed from remarkably heavy, stationary units to exceptionally lightweight, ultraportable devices, applicable in all care settings from inpatient bedridden to outpatient fully ambulatory. The SNaP device spearheaded this body of devices by switching to a mechanically powered device that maintains a preset constant or intermittent pressure (-75, -100, or -150 mmHg) without electricity or batteries.8 A novel engineering approach to exceptional portability was achieved through innovative design exemplified by the pocket-sized NPD 1000™ Negative Pressure Wound Therapy device (Kalypco Medical, Mendota Heights, Minnesota) that runs on 3 AA batteries coupled with an antimicrobial combination collection system dressing pad.9 Other devices followed suit to join the roles of improved portability through “miniaturization,” improved economy of size for off-the-shelf availability, and improved “disposability” to optimize application for the post-operative, surgically closed, 7-day treatment, acute wound market (V.A.C.Via™ Negative Pressure Wound Therapy System, KCI USA, Inc.; XLR8 and A4–NWPT pump®, Genadyne Biotechnologies; PICO™ Single Use Negative Pressure Wound Therapy System, Smith & Nephew, Inc., St-Laurent, Quebec, Canada). Accessories also aid portability; for example, car chargers (Vario 18, Medela Inc., McHenry, Illinois) and various out-of-hospital bed connectors, hospital trolley carts, and personal carrying cases provide convenient mobility.5,10–13

**Device-related clinical safety.** Safety considerations for potential complications, such as bleeding, foreign body retention, pain, tissue ingrowth, infection, and exsanguination, exist for all NPWT systems, regardless of care setting, portability, and recommended pressure profiles. Caution should be taken to mitigate potential complications with appropriate patient selection and therapy adjustments, as needed. Alarm types are variable, but most devices have some ability to notify in the event of an air leak and non-delivery of the intended pressure.4

**Tubing and collection systems (drains).** Tube collection systems remove exudate from the wound and deliver negative pressure to the wound space. Across various systems, tubing differs in lumen length and diameter, which affects the rate of exudate removal and the potential for obstruction development. If blockage occurs without clearance, maceration, infection, and wound deterioration may ensue. Some systems use the collection tubing as a simple conduit; others add the benefit of wound space pressure monitoring through the terminal pad (Prevena™ Incision Management System, T.R.A.C. Pad and SensaT.R.A.C., KCI USA, Inc.).14,15 Another level of advanced negative pressure therapy delivery is achieved through software programming automatic response feedback loops. The Mobility Solutions Miller drains (Miller Digivac Toe and Finger Chambers, Miller Extremity Garments, Miller DermiVex Drain, and Miller Encompass Drain) are body location-specific silicone drains modified for use with gauze interfaces.16,17 Dressing techniques that assist with digits and unusual contours, even in pediatric populations, have been described.

**Canisters.** Exudate collection canisters may be open or sealed with gel packs (isolyzers) for solidification of wound exudate. Out-of-hospital disposal of liquid blood-contaminated waste may be limited, depending upon local restrictions imposed by environmental protection regulations. Rules for collection, storage, and disposal of biohazardous materials, both liquid and solid, may apply. The isolyzer assists in converting restricted liquid waste to disposable solid waste to facilitate disposal. One-way valves between canisters and tubing systems prevent backflow of biohazardous materials onto the wound when negative pressure is discontinued. Similarly, some systems may utilize backflow prevention between the pump and the canister connection system to prevent contamination of the pump system and internal filters. Canister sizes vary depending upon the size of the associated pump, desired portability, and wound type being targeted. Canister capacities range from 25 cc to 1500 cc with and without the ability to be emptied and reused. Procedures and policies must be established for reusable products.
to reduce the likelihood of cross-contamination. Caution must be used with canisters greater than 500 cc as their use may increase the risk of severe fluid loss, dehydration, and exsanguination. Larger canister sizes are not recommended for neonates, infants, children, or adults with low-volume states or problems with coagulation where the removal of a large percent total body fluid volume or coagulation factors may pose a significant risk. Although evidence supports the safe use of NPWT in children, the therapy should be applied with caution to ensure safety.

**Adhesive drape.** Most adhesive drapes used with NPWT consist of water vapor-semipermeable polyurethane film coated with a hypoallergenic, pressure-sensitive acrylic adhesive. Drapes seal the environment, maintaining the negative pressure over the wound, create a barrier to outside contaminants, and provide a moist wound healing environment. This allows the underlying wound exudate to condense into a gelatinous coagulum, which supports re-epithelization at the wound margins. There are no distinctions between the drapes used in foam-based systems versus those used in gauze-based systems, and both systems typically require oxygen and water vapor semipermeability to allow for moisture balance and oxygenation of the peri-wound skin. Many NPWT providers will contract dressing manufacturers to produce a drape with their specific requirements for size, shape, peel tabs, adhesive content, and branding. Since these products are usually essentially equivalent to 3M™ Tegaderm™ Dressings (3M Health Care, St Paul, Minnesota), transparent films are frequently used to repair leaks when the brand-specific drape is not available. Some dressing systems distinguish themselves through attempts to innovate the dressing application process. The NPD 1000 Negative Pressure Wound Therapy device does not require a secondary occlusive drape because the interface dressing and exudate process are integrated within the pad. Additionally, hydrocolloid wafers and stoma paste are often helpful to achieve a seal in difficult-to-dress locations.

**Irrigation systems.** NPWT “instillation systems” also have undergone design changes for programmed wound irrigation treatments with prolonged, intermittent, or continuous profiles. Although these systems have been used predominately to treat osteomyelitis and soft tissue infections, they can be used to deliver agents other than antibiotics, such as antimicrobial agents, chemical debriders, anti-inflammatory agents, growth factors, oxygen and energy molecules, chemotherapeutics, “liquefied” cellular and tissue components, and tissue nutritional factors. Appropriate testing to prove the safety and clinical efficacy of expanded indications would be required. This is no small feat, since the medical scientific evidence bar has been set high for demonstrating both mechanisms of action and clinical outcomes. Even with a current, fairly robust clinical retrospective evidence base, achieving full reimbursement approval for NPWT for pediatric indications has been difficult to attain in all countries. The V.A.C. Instill® Therapy Unit (KCI USA, Inc.) and the irrigation systems, Svedman® and SVED® (Innovative Therapies Inc., Gaithersburg, Maryland), are the most commonly used devices.

**NPWT pressure treatment modalities.** Most manufacturers offer devices with both continuous and intermittent pressure modalities for inpatient and outpatient care settings. Two schools of thought surround the “optimal” negative pressure treatment target: low pressure at −80 mmHg or high pressure at −125 mmHg. Some devices are designed to provide only the lower negative pressure treatment range, while others are designed to treat both the lower and higher ranges. As care setting focus shifts toward alternative care settings/ambulatory out-of-hospital, the trend has shifted to develop NPWT devices specifically designed to target wound types amenable to the continuous pressure modality, simplified operation, and lowered out-of-hospital treatment costs.

**NPWT Wound Interface Materials**

An interface dressing, with or without a nonadherent intervening contact layer, directly influences 1) microstrain delivery to the tissue surface, 2) exudate removal by helping to wick fluid from the recesses of the wound, and 3) negative pressure modulation as it passes into the wound space and then out to the periwound tissues. The most commonly prescribed NPWT interface dressings are foams composed of either open-cell reticulated polyethylene (PU) foam or polyvinyl alcohol (PVA) foam and an absorbent cotton-blend antimicrobial gauze containing...
Polyhexamethylene biguanide hydrochloride (PHMB). Some devices have developed device-specific foams: KCI USA, Inc. with GranuFoam® and GranuFoam Silver®, Medela Inc. with Avance™ (green foam), Smith & Nephew with RENASYS®-F and Innovative Therapies Inc. with SVEF Svamp® Foam. Most gauze-based dressing kits offer antimicrobial gauze, eg, Kendall™ AMD Antimicrobial Dressings containing 0.2% PHMB (Covidien, Mansfield, Massachusetts). Silverlon® (Argentum Medical, LLC, Chicago, Illinois), a silver-impregnated woven nylon, has received special recognition for utility with NPWT. Dressings specifically designed for NPWT systems include the Bio-Dome™ dressing and Bio-Dome EasyRelease (Convatec, Inc., Skillman, New Jersey) and the Kalypso collection pad. Adapted for use with any NPWT system, Hydrofera Blue® (Hydrofera, LLC, Willimantic, Connecticut) is a PVA sponge with two broad-spectrum bacteriostatic agents, methylene blue and gentian violet. An intervening nonadherent contact dressing layer (eg, Mepitel® or Mepitel One, Mölnlycke Health Care, Norcross, Georgia) may be applied to any of the dressing systems in an effort to reduce potential complications related to dressing adherence and tissue in-growth.

NPWT foam dressings. PU and PVA are the two most common materials used to create open-cell, hydrophilic or hydrophobic, NPWT foams. Pore size and strut measurements determine the density, tensile strength, and porosity of the foam. Pore diameter, strut (cell or walls of the foam) thickness, and applied negative pressure define the microstrain delivered to the tissue surface.

V.A.C. GranuFoam. The black V.A.C. GranuFoam PU dressing has reticulated or open pores ranging in size from 400 µm to 600 µm and is considered effective at promoting granulation tissue formation while aiding in wound contraction. It is hydrophobic (or moisture repelling), which enhances exudate removal. Several specialized V.A.C. GranuFoam dressings have also been designed to accommodate the needs of specific wound sites (ie, abdominal cavity, heel, and hand). These facilitate the application of negative pressure to anatomical locations with contours that make it difficult to achieve an airtight seal (Plates 28–31, page 348).

V.A.C. GranuFoam Silver. The V.A.C. GranuFoam Silver Dressing combines the properties of V.A.C. GranuFoam with those of silver. The reticulated or open pores of this dressing have microbonded metallic silver uniformly distributed throughout the dressing, providing continuous delivery of silver. The V.A.C. GranuFoam Silver Dressing is an effective barrier to bacterial penetration and may help reduce infection (Plates 32–35, page 348). Topical silver has broad-spectrum antimicrobial activity. The only silver dressing specifically designed for use with V.A.C. Therapy is the V.A.C. GranuFoam Silver Dressing. This dressing provides continuous release of ionic silver for up to 72 hours and has been shown to be effective against 150 microbial species. A subset of 6 organisms considered clinically relevant was selected for quantitative antimicrobial testing. A sample of the V.A.C. GranuFoam Silver Dressing was added to 50 mL of the challenge organism at approximately 10² colony-forming units per milliliter (CFU/mL) and incubated over time. The dressing showed significant antimicrobial activity in as little as 30 minutes after exposure to the organisms. The open-celled, reticulated structure of this dressing allowed for microdeformational changes at the foam-tissue interface in the same manner as the V.A.C. GranuFoam Dressing. A study was conducted on porcine full-thickness wounds treated with either the V.A.C. GranuFoam Dressing or the V.A.C. GranuFoam Silver Dressing to determine if granulation rates would be comparable. There were no significant differences (P > .05) in wound granulation rates (as measured using wound volume measurements) between these 2 V.A.C. Therapy dressings. Together, these studies indicate that the properties of the V.A.C. GranuFoam dressing are retained by the V.A.C. GranuFoam Silver dressing, which assists with granulation tissue formation and serves as an effective barrier against microorganism invasion.

V.A.C.® WhiteFoam® Dressing. V.A.C. WhiteFoam PVA dressing is a dense foam with a higher tensile strength that requires higher negative pressures (125 mmHg–175 mmHg) in order to provide adequate distribution of negative pressure throughout the wound. V.A.C. WhiteFoam is hydrophilic (or moisture maintaining), is premoistened with sterile water, and possesses relatively nonadherent properties. It is generally recommended for use in tunnels and tracts and...
other situations where special attention is necessary to avoid the possibility of tissue in-growth into the foam.

**Hydrofera Blue Bacteriostatic Dressing.** Hydrofera Blue Bacteriostatic Dressing (“Blue Foam”) is a PVA sponge with two broad-spectrum bacteriostatic agents, methylene blue and gentian violet. These agents are effective against the drug-resistant organisms, methicillin/oxacillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE). The foam’s open cell structure naturally provides capillary vacuum action to draw excess fluid and exudate from the wound bed. Hydrofera Blue must be moistened with sterile saline or sterile water and squeezed out before application to the wound bed. Color change from blue to white indicates complete release of antimicrobial agents. Case studies support the use of this foam at negative pressure ranges, both low (-80 mmHg) and high (-125 mmHg), to improve chronic wounds without any significant complications.35,36

**Avance (“Green Foam”) Dressings.** Avance Foam is open-cell, hydrophobic polyurethane specifically designed for use with the Avance NPWT device at negative pressure (-120 mmHg) to provide the desired 5%–20% microstrain for enhanced cellular proliferation. Preclinical studies conducted by Malmsjö et al compared Avance Foam’s biological effects to the predicate V.A.C. GranuFoam (-125 mmHg) and to AMD gauze (-80 mmHg), with and without intervening contact layers, Mepitel and Mepitel One. Specific investigations related to wound bed granulation tissue quantity, tissue in-growth into the filler material, delivery of negative pressure to the wound bed, and blood flow in the wound bed. Malmsjö and colleagues noted a more pronounced granulation tissue formation with foam (green and black) than with gauze. When a wound contact layer was applied, granulation tissue formation was slightly greater under foam than under gauze, with the degree of granulation tissue development being similar for both Avance Foam and V.A.C. GranuFoam. Both foams showed a slightly greater amount of wound contraction as compared with AMD gauze. The two intervening contact layers supported equal degrees of contraction. The wound bed tissue grew into foam but not into gauze, and the degree of tissue in-growth was similar for both Avance Foam and V.A.C. GranuFoam. The investigators’ results confirmed observations that gauze was easier to remove and antimicrobial AMD gauze does not disrupt the wound bed. Moreover, the presence of an intervening contact layer, such as Mepitel and Mepitel One, hinders in-growth and lessens the force needed for removal of foam in NPWT.37,38

**RENASYS-F foam.** The RENASYS-F foam is open-cell, hydrophobic, black, polyurethane foam developed for specific use with the Smith & Nephew RENASYS EZ and RENASYS GO NPWT systems. Smith & Nephew’s EZCARE and VISTA systems (formerly BlueSky Medical devices) utilize AMD gauze dressings at negative pressure ranges from 40 mmHg to 80 mmHg, while the RENASYS system platform uses gauze or foam at negative pressure ranges from 40 mmHg to 200 mmHg. Bondojki et al used the RENASYS-F system to treat 18 patients in a prospective, multicenter study with a variety of wound types, including pressure ulcers, diabetic foot ulcers, and traumatic and surgical wounds. Results showed that at the end of the 14.6 day mean treatment duration, 83% of wounds (15/18) had progressed sufficiently to discontinue NPWT. Reductions in wound dimension, exudate level, odor, and nonviable tissue during the therapy with a significant increase in “beefy red” granulation tissue suggested the viability of utilizing the new RENASYS-F foam.39

**Svamp Foam.** Innovative Therapies Inc. (ITI) combines continuous irrigation with negative pressure therapy in its AC electric-powered NPWT systems: the original larger, 5.5 lb, 18-hour battery Svedman device intended for hospital use and the smaller, more portable, 1.9 lb, 14-hour battery SVED device. The proprietary open-celled, hydrophobic black and hydrophilic white PU Svamp Foams may be used with both devices that provide negative pressure therapy prior to, during, or after irrigation. The dry white foam is denser with a higher tensile strength. Irrigation and negative pressure application are achieved by two different pathways within the tubing system, which allows flexibility in the timing of irrigation in relation to the institution of negative pressure. As with other NPWT devices, the ITI systems are intended for use on patients with chronic, acute, traumatic, subacute, and de-
hisced wounds; diabetic ulcers; pressure ulcers; flaps; and grafts. Antimicrobial and amino acid preparation may be used with the system and all preparations should be used in accordance with the manufacturer’s product instructions for use (IFU). Dressings are changed every 48–72 hours and if the irrigation has been discontinued for more than 2 hours, and nonadherent intervening contact layers may be used to reduce patient discomfort with dressing changes. Both continuous (−70 mmHg, −120 mmHg, and −150 mmHg) and intermittent modalities are available with a negative pressure (−25 mmHg) maintained during the off phase of the on-off cycle (5 min/2 min). Visual and audible alarms alert to notify instances of low pressure, air leaks, and full canister as the volume approaches maximum capacity (SVED 300 cc; Svedman 1,200 cc). Teder, Sandén, and Svedman conducted swine model, infected full-thickness wound healing studies to validate their proof of concept to demonstrate that the passage of fluid cleanses both the NPWT pad and the wound. The irrigation systems assisted with avoiding the collection of blood, exudate, or infectious materials, and the negative pressure treatment facilitated granulation tissue development. Antimicrobial gauze dressings (cotton blends). NPWT systems using moistened gauze typically recommend the Chariker-Jeter Technique where a nonadherent intervening contact layer covers the wound bed; moistened gauze is lightly layered to fill the wound space surrounding a flat, fenestrated drain and enclosed by a transparent polyethylene adhesive drape. The most frequently recommended gauze has a cotton-nylon blend containing 0.2% PHMB, antimicrobial dressing AMD. PHMB is a polymeric, broad-spectrum, cationic antimicrobial agent that impairs the outer membrane of gram-positive and gram-negative bacteria, showing sustained killing activity against MRSA, VRE, Escherichia coli, Pseudomonas aeruginosa, Bacteroides fragilis, Clostridium perfringens, and yeasts, such as Candida albicans.28 Studies show antimicrobial gauze dressings with PHMB may expand options for extended occlusive dressing duration without significantly increasing wound bacterial load or human cellular cytotoxicity profiles. If the negative pressure therapy becomes inactive, dressings do not need to be removed immediately but may be left intact for 24 hours or more depending upon the manufacturer’s IFU. Other attributes of PHMB include the reduction of wound pain, odor, and fibrin slough and the prevention of necrotic tissue build-up in chronic wounds.31,43 Antimicrobial dressings are more commonly used for infection prevention. Dressings may be used clinically to augment treatment of active infections but are not considered stand-alone therapies.

NPWT devices recommending preferential use of AMD Gauze with pressure ranges 60 mmHg–80 mmHg include Prospera® PRO-I™, PRO-II™, and PRO-III™ (Prospera, Fort Worth, Texas), Verseatile™ (BlueSky Medical, Carlsbad, California), EZCARE and V1STA (Smith & Nephew), Excudex™ (RecoverCare, Louisville, Kentucky), Invia® Liberty™ and Vario (Medela Inc.), Moblvac® (Ohio Medical Corporation, Gurnee, Illinois), A4-NWPT pump (Genadyne Biotechnologies), VENTURI AVANTI and VENTURI COMPACT (Tally Medical USA, Lansing, Michigan), and SnAP (Spiracur Inc.).5,8,13,43–47 Silverlon Negative Pressure Dressing (nylon). Silverlon NPD (Argentum Medical, LLC), awarded the Frost & Sullivan 2006 Product Innovation Award for the US antimicrobial dressings market, is an absorbent, nonadherent silver nylon product that releases silver for 7 days. The autocatalytic silver-plating process uniformly and permanently coats the entire polymeric substrate surface circumferentially with silver that is readily released in ionic form when contacted by wound exudate. In the presence of moisture, this unique product continuously emits a very high level of ionic silver into the wound bed. The tight nylon weave resists in-growth and adherence while its porous quality permits negative pressure delivery to the tissue without obstructing exudate evacuation. This product serves as the wound contact layer for the Kalypto collection pad. The use of silver as an antimicrobial agent extends back many centuries. Silver has broad antimicrobial activity against both gram-negative and gram-positive bacteria and has demonstrated minimal development of bacterial resistance. Bio-Dome and Bio-Dome EasyRelease (ConvaTec). This innovative wound dressing, designed for use with the Engenex® NPWT System (licensed from Boehringer Technologies), is comprised of non-woven polyester layers joined
by a silicone elastomer, which effectively fills the wound while permitting exudate fluid transport. The Bio-Dome dressing has specifically engineered open pore spaces that resist collapse under negative pressures 30 mmHg–75 mmHg, presenting an unobstructed area for tissue growth influenced by a 5%–20% cellular microstrain tissue-interface pressure. The product’s pore structure was designed to lower risks for in-growth and adherence-related pain, bleeding, and foreign body retention with a higher material tensile strength and a lower bioadhesion profile. The silicone elastomer reduces adherence but the Bio-Dome EasyRelease was specifically designed with a flat profile to further reduce tissue adherence and potential in-growth. Studies conducted by Girolami et al demonstrated the ability of the system to reduce aggressive adherence in the wound bed, eliminate risk of foreign body deposits, and reduce pain during removal and re-application while optimizing granulation tissue proliferation. This is the only non-foam-based dressing system purposely designed to further the application of the new NPWT platform focusing on microstrain to specifically direct cellular proliferative responses. The Engenex has unique software programming to provide patient compliance tracking.

Kalypto Negative Pressure Device Collection Pad. The Kalypto NPD pad is an innovative combination “all-in-one” styled negative pressure dressing designed for specific use with the Kalypto Medical NPD 1000 lightweight (8 oz) pump. The design allows for maximum portability. The dressing pad has a Silverlon contact nonadherent layer for minimal adherence and antimicrobial activity. The intermediate layer is composed of a two-fiber, non-woven, exudate collection system where absorbent hydrophilic fibers wick fluids into a super absorbent, bonding inner pad. The inner pad is surrounded by a non-woven, semi-occlusive polyurethane film. The indicated negative pressure is delivered to the tissue even though the pad swells as exudate accumulates in the inner core. The periwound margin is protected by a hydrophobic Gore® membrane, which protects against maceration as long as the system fluid limits are not exceeded (25 cc, 50 cc, 75 cc, 140 cc). The hydrogel adhesive gasket allows for easy application. The pump runs on 3 AA alkaline batteries, provides negative pressures of 40 mmHg–125 mmHg, and offers both continuous and intermittent pressure modes. The Silverlon-generated antimicrobial activity is present with and without active therapy as established by Davis et al measuring bacterial clearance in full-thickness wounds inoculated with Pseudomonas aeruginosa ATCC 37312 using a porcine model.

The largest reduction in bacterial concentration was seen at 48 hours after inoculation. Case studies in diabetic foot wounds, venous insufficiency, and chronic leg wounds demonstrated the product’s ability to support chronic wound healing with minimal complications as long as the fluid handling capacity of the dressing is observed.

Intervening nonadherent contact layers. Early nonadherent contact layers (primary contact dressings) were designed to address the issues of adherence, tissue trauma, and pain. Subsequent evolution added the qualities of avoiding the deposition of fibers, cytotoxic agents, or irritating extractable additives. Both gauze and foam applied directly to the wound surface have been associated with bio-adherence and tissue in-growth. Additives to the materials, such as soft paraffin, oils, or silicone, may alter the adherence of the product. The application of intervening contact layers reduces negative pressure transduction to the tissue. The degree of reduction depends upon the product and number of layers applied. Over the years, the development of potential complications and required corrective surgical intervention has prompted a variety of suggested remedies that still influence clinical practice today: careful patient selection, more frequent dressing changes, institution of intervening nonadherent contact dressings, selection of alternative interface materials, lowered treatment pressures, and, in some situations, postponing the use of negative pressure therapy. These remedies should be considered to reduce complications regardless of the interface being applied (gauze, foam, fabricated construct).

Paraffin-coated dressings. Some of the earliest modern-day nonadherent dressings are cotton blends coated with soft paraffin (eg, Vaseline Petrolatum Gauze, Covidien, and Adaptic™ with knotted viscose, Systagenix Wound Management, Gargrave, United Kingdom). These are manufac-
tured with and without antimicrobials, such as povidone-iodine (eg, Betadine™ gauze, Purdue Frederick, Norwalk, Connecticut) or 3% bismuth tribromophenate (eg, Xeroform™ gauze, Covidien). Available since the 1900s, tulle gras is absorbent cotton coated with balsam of Peru, paraffin, and oils. Plain cotton has been substituted with nylon-blended cotton to improve strength, and balsam of Peru has been replaced with newer, less sensitizing antimicrobials, such as chlorhexidine acetate 0.5% (eg, Bactigras®, Smith & Nephew) and 0.2% PHMB hydrochloride (eg, AMD). The combination of nonadherence and antimicrobial properties increases application duration for some gauze dressings.

Hydrocolloid pectins. Dressings made with hydrocolloid pectins have been used with NPWT (eg, GranuFlux®, Convatec) for their increased absorption and ability to “dissolve” into spaces when contacted by exudate yet still be easily removed with rinsing. Generally recommended for open wounds, hydrocolloid wafers used with NPWT-treated wounds help obliterate air spaces between the tissue and the sealing dressing to facilitate the retention of a seal. This is very important for anatomically difficult-to-dress locations. Some products have the added advantage of paraffin and hydrocolloid pectins for increased nonadherence (eg, Urgotul®, Urgo Medical, Chenove, France).

Silicone preparations and other nonadherent materials. Silicone-coated dressings demonstrate improved nonadherent qualities while minimizing irritation or potential allergic reactions. Paraffin has long been an additive to coat materials to decrease adherence. Meshed and woven characteristics of properties of materials may still allow “in-growth,” which also affects adherence, ease of removal, and discomfort with extractions. Nonadherent products, such as Mepitel (Mölnlycke Health Care), Jelonet®, Biobrane® (Smith & Nephew), 3M™ Tegapore™, and Adaptive Touch® (Systagenix Wound Management), have become a product staple used under gauze or foam to reduce in-growth and pain during NPWT treatments. While soft silicone is not intrinsically absorbent, it is usually applied to cotton and cotton-blend gauzes to improve the absorptive capacity of the resultant product while still maintaining the nonadherent quality.

Inappropriate interface materials. Some products are deemed to be inappropriate for use with NPWT systems. Those materials that impede delivery of negative pressure to the wound surface or obstruct full evacuation of wound exudate should be avoided.

Natural sponges. Initially, sponge-based dressings were considered as potential alternative wound dressings because of their ability to conform to a space, fluid capacitance, tensile strength, and availability. However, natural sponges have limited application as NPWT dressings due to their “semi-open cell” communication pattern where some pores do not communicate with others. In a sponge and some “closed cell foams,” the fluid channeling may flow into a space that does not allow for complete fluid extraction. Variable pore size and communication make pressure transmission and fluid extraction unpredictable. Consequently, exudate fluids and small particulate infectious materials could become trapped within the body of the sponge and the distribution of negative pressures across portions of a sponge could be compromised.

Perforated plastic film and bordered products. Perforated plastic film composed of polyethylene terephthalate (PET), a thermoplastic polymer resin that does not contain polyethylene, can be used as an NPWT dressing cover; however, the ability of the dressing to function properly will depend upon size and number of perforations.53 The dressing must allow full exudate extraction while delivering negative pressure. Frenestrated film dressings with absorption layers (eg, TELFA™, Covidien) are available but may not be well suited for NPWT because of impermeable linings. Similarly, composite dressings made from absorbable cotton and polyester blends and water impermeable outer borders were created for “low-adherent” treatments (eg, Melolin® with borders, Smith & Nephew), but the impermeable borders make these dressings unsuitable for NPWT.

NPWT Application: Indications and Complications

“Healthcare providers will compete to offer the best record of patient safety at the lowest prices. Hospitals and patients will benefit from having accurate information about areas of excellence and areas that must be
Negative Pressure Wound Therapy

Table 1. Indications and contraindications for NPWT Therapy

**Indications**

- NPWT is intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing edema, promoting granulation tissue formation and perfusion, and removing exudate and infectious material.
- It is indicated for patients with chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic or pressure); flaps; and grafts.
- NPWT combined with antimicrobial dressings (silver, PHMB, etc) is an effective barrier to bacterial penetration and may help reduce infection in the above wound types.

**Contraindications**

- Exposed blood vessels, organs, or nerves
- Malignancy in the wound
- Untreated osteomyelitis
- Non-enteric and unexplored fistulas
- Necrotic tissue with eschar present
- Sensitivity to additive materials (eg, silver or antimicrobial agents)

Table 2. Safety precautions for NPWT (as stated in the V.A.C. Therapy IFU Safety Information Sheet)

<table>
<thead>
<tr>
<th>Category</th>
<th>Suggested NPWT Treatment</th>
</tr>
</thead>
</table>
| Exposed vessels and organs | • Cover with muscle flaps or other natural tissue or fine-meshed, nonadherent porous material prior to NPWT  
| | • Administer NPWT only in inpatient setting with skilled nursing and close monitoring, when vessels or organs are not completely covered and protected with a thick layer of natural tissue or fine-meshed, nonadherent porous material  
| | • Stop NPWT and seek immediate medical intervention if sudden, increased, or hemorrhagic bleeding is observed for any reason or if frank blood is seen in the tubing or in the canister  
| Inadequate hemostasis | • If wound hemostasis is tenuous, administer NPWT in inpatient setting with skilled nursing and close monitoring  
| Anticoagulants |  
| Platelet aggregation inhibitors |  
| Non-sutured hemostatic agents | • Protect against dislodging of agents  
| Bone wax | • Start with lowest negative pressure setting then monitor closely while progressing to target treatment pressure, as tolerated  
| Absorbable gelatin sponge | • Administer therapy only in inpatient setting with skilled nursing and close monitoring  
| Spray wound sealant |  
| Sharp edges or bone fragments | • Eliminate sharp edges or bone fragments from wound  
| | • Smooth or cover residual edges to decrease the risk of serious or fatal injury, should shifting of structures occur  
| | • Use caution when removing dressing components from wound  
| Blood vessel erosion due to infection | • Protect with thick layer of natural tissue, such as muscle flap, or nonadherent porous material  
| (Note: the depth of infection and degree of weakening are not always readily apparent through direct visual inspection of the exposed vessel) | • Administer therapy in inpatient setting with skilled nursing and close monitoring because there is increased risk of vascular rupture when blood vessel is infected  

CHRONIC WOUND CARE: The Essentials e-Book
### Table 2. Safety precautions for NPWT (as stated in the V.A.C. Therapy IFU Safety Information Sheet²⁴)

<table>
<thead>
<tr>
<th>Category</th>
<th>Suggested NPWT Treatment</th>
</tr>
</thead>
</table>
| Infected wounds                     | • Change NPWT dressings at least every 12–24 hours if wound is infected  
• Monitor patient closely if there are any signs of possible infection or related complications  
• Contact physician for immediate treatment if there are any signs of the onset of systemic infection or advancing infection at the wound site; discontinue NPWT until the infection or complication has been diagnosed and proper treatment has been initiated |
| Tendons, ligaments, and nerves       | • Protect with natural tissues or moist, fine-meshed, nonadherent material                                                                                   |
| Osteomyelitis (Note: V.A.C. Therapy should not be initiated on a wound with untreated osteomyelitis) | • Debride necrotic, nonviable tissue and infected bone (if necessary)  
• Initiate antibiotic therapy  
• Apply when osteomyelitis has been addressed |
| Foam placement                       | • Always use NPWT dressings from sterile packages that have not been opened or damaged  
• Do not place any foam dressing into blind/unexplored tunnels; the V.A.C. WhiteFoam dressing may be more appropriate for use with explored tunnels  
• Do not force foam dressings into any area of the wound, as this may damage tissue, alter the delivery of negative pressure, or hinder exudate removal  
• Always count the total number of pieces of foam used in the dressing and document that number on the drape and in the patient's chart; also document the dressing change date on the drape |
| Foam removal                         | • Ensure that all foam pieces have been removed from the wound with each dressing change, because NPWT foam dressings are not bio-absorbable  
• Follow manufacturer’s recommended time schedule for dressing changes; foam left in the wound for greater than the recommended time period may foster in-growth of tissue into the foam, create difficulty in removing foam from the wound, or lead to infection or other adverse events |
| Reaction to acrylic adhesive        | • Be aware that patients who are allergic or hypersensitive to acrylic adhesives may have an adverse reaction to the acrylic adhesive coating on the V.A.C. Drape  
• If a patient has a known allergy or hypersensitivity to such adhesives, or if any signs of allergic reaction or hypersensitivity develop, such as redness, swelling, rash, urticaria, significant pruritus, or bronchospasm, discontinue use and consult a physician immediately |
| Defibrillation                       | • Remove the NPWT dressing if defibrillation is required in the area of dressing placement                                                                 |
Negative Pressure Wound Therapy

All medical devices approved as substantially equivalent to provide NPWT share similar indications and complications as those reported in Table 1 for the V.A.C. Therapy predicate device. As with any medical therapy, potential risks have been reported. The volume of use may skew the number of reports toward the most frequently used device. Understanding the etiology of potential complications assists with mitigating the root cause regardless of the specific product being used. Table 1 lists indications and contraindications for NPWT, and Table 2 presents safety precautions. Although it rarely occurs, bleeding may result from exposed vessels and organs, inadequate hemostasis, inadequate protection of vital structures from sharp edges, or erosion of infected blood vessels. Other reported risks that may or may not be related to NPWT include wound infection, dressing material retention, irritation, and maceration of periwound skin. Pain also has been noted secondary to mechanical stress applied to the wound, chemical contact irritation, and in-growth of tissue into the dressing material. The use of an intervening nonadherent contact layer or natural tissue should lessen the likelihood of adherence or in-growth to the interface dressing. Decreasing treatment pressure, increasing frequency of dressing changes, and careful patient selection may also lessen the risk of complications.

**NPWT Guidelines**

**General guidelines for NPWT.** Several articles describe in detail the general wound care steps associated with the application of NPWT. The general process involves the following steps:

- Complete general wound assessment and care
- Debride wound if necessary
- Assess and treat infection
- Assess and protect periwound tissue
- Maintain moist wound environment
- Apply NPWT in accordance with the guidelines and IFU specific for that product and indication (eg, V.A.C. Therapy Clinical Guidelines and V.A.C. Therapy IFU)
- Continue therapy until a base of granulation tissue is robust enough to be maintained after

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**Table 2. Safety precautions for NPWT (as stated in the V.A.C. Therapy IFU Safety Information Sheet)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Suggested NPWT Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic resonance imaging (MRI)</td>
<td>• Do not take the V.A.C. Therapy unit into the MR environment because the unit is MR unsafe</td>
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<tr>
<td></td>
<td>• Leave V.A.C. GranuFoam dressing in place if therapy will not be interrupted for more than 2 hours</td>
</tr>
<tr>
<td></td>
<td>• Leave V.A.C. GranuFoam Silver Dressing in place only under certain conditions and if therapy will not be interrupted for more than 2 hours (Note: MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the V.A.C. GranuFoam Silver dressing)</td>
</tr>
<tr>
<td>Hyperbaric oxygen therapy (HBO)</td>
<td>• Remove V.A.C. Therapy unit prior to HBO; the unit is not designed for this environment and should be considered a fire hazard in this environment</td>
</tr>
<tr>
<td></td>
<td>• Replace dressing with compatible HBO dressing or cover V.A.C. Therapy dressing and tubing with moist cotton, gauze, or towel prior to HBO treatment</td>
</tr>
<tr>
<td>Maceration of periwound skin</td>
<td>• Do not allow foam to overlap intact skin</td>
</tr>
<tr>
<td></td>
<td>• Protect fragile/friable periwound skin with a skin preparation product, additional V.A.C. Drape, hydrocolloid, or other transparent film</td>
</tr>
<tr>
<td></td>
<td>• Realize that multiple layers of the V.A.C. Drape will decrease the moisture vapor transmission rate, which may increase the risk of maceration</td>
</tr>
</tbody>
</table>
discontinuation of the therapy or epithelization of the wound base.

**Guidelines for foam-based NPWT.** Articles provide consensus guidelines and/or algorithms that demonstrate how best to incorporate NPWT into the treatment of specific wound types. For example, Andros and members of a multidisciplinary expert panel\(^{58}\) updated guidelines for the application of V.A.C. Therapy to diabetic foot wounds. This report summarizes clinical evidence, provides practical guidance through a treatment algorithm, offers best practices to clinicians treating diabetic foot wounds, and addresses the appropriate use of V.A.C. Therapy in treating these complex wounds. In 2004, Gupta et al\(^{59}\) provided guidelines for the treatment of pressure ulcers, including the appropriate use of V.A.C. Therapy. Niezgoda and Mendez-Eastman\(^{60}\) published an update of these guidelines, including an algorithm to assist in clinical management decisions related to patients with Stage III and Stage IV pressure ulcers and guidelines for incorporating V.A.C. Therapy into a complete clinical program that should include targeted patient education, pressure ulcer prevention, nutrition, aggressive incontinence management, offloading, periwound care, and routine skin surveillance. Other guidelines and algorithms for the use of V.A.C. Therapy also have been published for traumatic wounds, such as the open abdomen,\(^{61}\) chest wounds,\(^{62}\) and lower leg trauma.\(^{63}\) In an international global expert panel, Runkel et al developed recommendations for traumatic wounds and reconstructive procedures and completed a formal consultative consensus involving 422 independent healthcare workers in 2011.\(^{64}\)

**Guidelines for gauze-based NPWT.** In 2011, Birke-Sorensen et al reported the determinations of an international consensus panel convened to initiate the steps necessary to determine best practices for treatment variables including treatment pressures, contact layers, and interface dressing selection.\(^{65}\) Additional information is being published by these and other authors to show the relative risks and benefits of gauze and foam-based dressings for NPWT. In most instances, AMD gauze appears to be similarly beneficial as an NPWT dressing.

**Treating Chronic Wounds with V.A.C. Therapy**

**Diabetic foot wounds.** V.A.C. Therapy has been used to treat diabetic foot wounds in randomized and nonrandomized studies (Table 3). Results from small RCTs by McCallon et al\(^{66}\) and Eginton et al\(^{67}\) demonstrated the ability of V.A.C. Therapy to reduce wound surface area and volume. Armstrong and Lavery\(^{68}\) validated these findings in a large RCT in patients with diabetes and partial foot amputation wounds. Of the 77 patients who were randomized to V.A.C. Therapy, 43 (56%) achieved complete wound closure in a median time of 56 days. In a retrospective study, Page et al\(^{69}\) reviewed the charts of 47 patients with open foot wounds with significant soft tissue defects. Of these patients, 22 (47%) were treated with V.A.C. Therapy. The authors found that V.A.C. Therapy was associated with a reduction in risk of one or more surgical procedures, complications, and admissions related to the treatment of the index wound during the first year after treatment. In another study using administrative claims data from both Medicare and commercial payors in patients with diabetic foot ulcers, the incidence of subsequent amputation was lower in V.A.C.-treated wounds than those treated without NPWT. Of note, while traditionally treated wounds of greater severity/depth had increasing rates of amputation, this trend was not evident for those treated with V.A.C. Therapy.\(^{70}\) Blume et al conducted a multicenter, randomized, controlled trial, enrolling 342 patients assigned to either NPWT or advanced moist wound therapy (AMWT) that consisted predominantly of hydrogels and alginates, with both treatment groups receiving standard offloading interventions and followed either 112 days or until 100% wound closure by any means. In this study, a greater proportion of diabetic foot ulcers achieved complete closure in the NPWT treatment group (73 of 169, 43.2%) than with the AMWT control (48 of 166, 28.9%) \((P = .007)\), without any significant difference in safety profile, including those subjects followed at 6 and 9 months for all wounds achieving 100% closure.\(^{71}\)

**Pressure ulcers.** V.A.C. Therapy also has been used to treat Stage III and Stage IV pressure ulcers (Table 4). The findings of 3 RCTs\(^{72-74}\) demonstrate that V.A.C. Therapy successfully reduced pressure ulcer size and may have positively affect-
ed wound histology. Philbeck et al. conducted a retrospective study of Medicare Part B home care patients who had chronic, nonhealing wounds treated with V.A.C. Therapy. The analyzed subset of pressure ulcer patients had an average wound area of 22.2 cm². Their finding that V.A.C. Therapy healed these ulcers at a rate of 0.23 cm² per day supports the findings of the 3 RCTs, which show V.A.C. Therapy to be a successful treatment for these chronic wounds. Wounds healed faster

<table>
<thead>
<tr>
<th>Table 3. V.A.C. Therapy findings from selected diabetic foot wound articles</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Author (Year)</strong></td>
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<td>--------------------------</td>
</tr>
</tbody>
</table>
| McCallon66 (2000) | Randomized, controlled trial | 5 patients | • Four patients achieved delayed primary healing in an average of 22.8 days  
• Wound surface area decreased by an average of 28.4% |
| Eginton67 (2003) | Randomized, controlled trial | 6 patients with 7 wounds | • Treatment lasted 2 weeks in this crossover design trial  
• Decreased wound volume 59% and depth 49% |
| Armstrong68 (2005) | Randomized, controlled trial | 77 patients | • 43 (56%) patients achieved complete wound closure  
• Median time to wound closure was 56 days  
• Median time to achieve 76%–100% granulation tissue formation was 42 days |
| Page69 (2004) | Comparative, retrospective study | 22 patients | • Median time for wound filling was 38 days  
• Associated with a reduction in risk of one or more surgical procedures, complications, and readmissions related to the treatment of the index wound during the first year after treatment |

<table>
<thead>
<tr>
<th>Table 4. V.A.C. Therapy findings from selected pressure ulcer articles</th>
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<tbody>
<tr>
<td><strong>First Author (Year)</strong></td>
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<tr>
<td>--------------------------</td>
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</tbody>
</table>
| Ford72 (2002) | Randomized, controlled trial | 20 wounds | • Two ulcers healed completely during controlled trial the 6-week treatment phase  
• Six ulcers underwent flap surgery  
• 51.8% mean reduction in ulcer volume |
| Joseph73 (2000) | Randomized, controlled trial | 18 wounds | • 66% reduction in wound depth  
• 78% final percent reduction in wound volume over time |
| Wanner74 (2003) | Randomized, controlled trial | 11 patients | • 50% reduction in initial wound volume in a mean (SD) of 27 (10) days  
• Reduced costs and improved comfort cited by authors as advantages of V.A.C. Therapy |
| Philbeck75 (1999) | Retrospective study | 43 wounds | • Ulcers averaged 22.2 cm² in area  
• Average rate of wound closure was 0.23 cm² per day |
than standard of care with a higher incidence of closure.

**Other V.A.C. Therapy chronic wound studies.** In addition to the previously discussed diabetic foot wound and pressure ulcer studies, several RCTs evaluated V.A.C. Therapy in chronic leg ulcers or in study populations that combined chronic and acute wounds (Table 5). Vuerstaek et al.\(^76\) conducted an RCT in 60 hospitalized patients with chronic leg ulcers. For the 30 V.A.C. Therapy patients, the median total healing time was 29 days and the median wound bed preparation time was 7 days. Two other V.A.C. Therapy RCTs included chronic and acute wounds in each of the randomized groups. In the Braakenburg et al. study,\(^77\) 32 of the 65 patients were treated with V.A.C. Therapy. Twenty-three patients in the V.A.C. Therapy group had chronic wounds, while the remaining 9 patients had acute or subacute wounds. The median time to healing for the overall V.A.C. Therapy group was 16 days. The median time to healing was 14 days for the subset of 18 diabetic or cardiovascular patients, median wound healing time was 14 days. The Moues et al RCT\(^78\) evaluated 54 patients with full-thickness wounds that “could not be closed immediately because of infection, contamination, or chronic character.” For the 29 patients randomized to V.A.C. Therapy, the median time needed to reach “ready for surgical therapy” was 6.00 ± 0.52 days (median ± SEM). The mean time was 5.00 ± 0.85 days for wounds existing < 4 weeks and 6.00 ± 0.99 days for wounds > 4 weeks. The mean rate of wound surface area reduction was 3.8 ± 0.5%/day.

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Study Type</th>
<th># of V.A.C. Therapy Patients/Wounds Analyzed</th>
<th>V.A.C. Therapy Findings</th>
</tr>
</thead>
</table>
| Vuerstaek\(^76\) (2006) | Randomized, controlled trial | 30 patients with chronic leg ulcers | • Median total healing time was 29 days  
• Median wound bed preparation time was 7 days  
• 90% of ulcers healed within 43 days  
• Demonstrated cost effectiveness |
| Braakenburg\(^77\) (2006) | Randomized, controlled trial | 32 patients with any type of acute or chronic wound | • V.A.C. Therapy group: 23 (74%) chronic (1 missing value), 2 (7%) acute, and 6 (19%) subacute wounds  
• An endpoint was a completely granulated wound or a wound ready for skin grafting or healing by secondary intention  
• Overall median time to healing was 16 days  
• In subset of 18 diabetic or cardiovascular patients, median wound healing time was 14 days |
| Moues\(^78\) (2004) | Randomized, controlled trial | 29 patients with full-thickness wounds that could not be closed immediately because of infection, contamination, or chronic character | • Wounds stratified by duration: early treated wounds (existing < 4 weeks before hospitalization) and late treated wounds (> 4 weeks)  
• Overall median time needed to reach “ready for surgical therapy” was 6.00 ± 0.52 days (median ± SEM)  
• Median time was 5.00 ± 0.85 days for wounds existing < 4 weeks and 6.00 ± 0.99 days for wounds > 4 weeks  
• The mean rate of wound surface area reduction was 3.8 ± 0.5%/day |
Close wounds, V.A.C. Therapy can assist in preparing the wound bed and bolstering the graft (Table 6). Moisidis et al. RCT study79 examined quantitative graft take and qualitative graft appearance (as determined by an independent evaluator who was blinded to treatment assignment). V.A.C. Therapy grafts achieved positive results quantitatively and qualitatively. In another RCT, Jeschke et al.80 evaluated 12 patients with large defects who underwent Integra™ Bilayer Matrix Wound Dressing (Integra LifeSciences, Plainsboro, New Jersey) grafting for reconstruction. For the 5 patients treated with fibrin glue and V.A.C. Therapy, the Integra take rate was 98 ± 2% and the mean period from Integra coverage to skin transplantation was 10 ± 1 days. Genecov et al.81 conducted a prospective, controlled study with 10 patients, where 7 of 10 donor sites re-epithelialized by Day 7. Carson et al.82 in a retrospective study of 70 patients, reported an 86% overall healing rate (60 out of 70 patients), with all 50 skin grafts healed in 11–24 days and remained stable at 6 months. NPWT appears to support improved graft take in selected large defect wounds.

Incision management of acute post-operative wounds. The use of NPWT over closed incisional wounds in patients who have a high likelihood of developing infection or mechanical stress–related dehiscence is increasingly being evaluated. Stannard et al.83 studied this application in the prophylactic use of NPWT in high-risk lower extremity fractures. Kilpadi and Cunningham described their experiences with using NPWT to assist with managing closed incisions, noting reduction of hematoma and seroma formation in a porcine model.84 Clearly, there may be a role for assisting patients in a prophylactic fashion.

Cost effectiveness of V.A.C. Therapy. Various studies have shown that V.A.C. Therapy is cost effective in a variety of care settings. Philbeck et al.75 considered cost in their retrospective study of Medicare home healthcare patients. In a subset analysis of pressure ulcers, the authors used wound closure rates reported by Ferrell et al.85 in 1993 for patients with trochanteric and trunk pressure ulcers averaging 4.3 cm² who were treated with a low-air-loss surface and saline-soaked gauze. Ferrell et al.85 reported that the wounds closed at an average of 0.090 cm² per day. Philbeck et al.75 analyzed patients who were treated with a low-air-loss surface and V.A.C. Therapy and who had Stage III and Stage IV trochanteric and trunk

### Table 6. V.A.C. Therapy findings from selected skin graft articles

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Study Type</th>
<th># of V.A.C. Therapy Patients/Wounds Analyzed</th>
<th>V.A.C. Therapy Findings</th>
</tr>
</thead>
</table>
| Moisidis79 (2004)   | Randomized, controlled trial | 20 wound halves | • Positive results in both qualitative and controlled trial quantitative measures  
• All wound halves healed without need for further debridement or regrafting  
• Dressings were well tolerated by the patients |
| Jeschke80 (2004)    | Randomized, controlled trial | 5 patients | • 5 were treated with fibrin glue-anchored Integra and postoperative V.A.C. Therapy  
• Integra take rate was 98 ± 2%  
• Mean period from Integra coverage to skin transplantation was 10 ± 1 days |
| Genecov81 (1998)    | Prospective, controlled trial | 10 patients | • 7 of 10 donor sites re-epithelialized by Day 7 |
| Carson82 (2004)     | Retrospective study | 70 patients | • 86% overall healing rate (60 out of 70 patients)  
• All 50 skin grafts healed in 11–24 days and remained stable at 6 months |
wounds that averaged 22.2 cm² in area. These wounds closed at an average of 0.23 cm² per day. The average 22.2 cm² wound in this study, treated as described by Ferrell et al, would take 247 days to heal, whereas the same wound would heal in 97 days with V.A.C. Therapy. While acknowledging the fact that larger pressure ulcers typically heal faster than smaller pressure ulcers, the V.A.C. Therapy healing rate described by Philbeck et al could potentially provide financial benefit associated with a reduced treatment course and patient benefit related to improved quality of life. In another large retrospective study of patients with chronic Stage III and Stage IV pressure ulcers in the home health environment, Schwien et al found that V.A.C. Therapy reduced the number of visits to hospitals and emergent care facilities secondary to wound complications. These studies demonstrate that V.A.C. Therapy is an economical, useful treatment modality for a variety of wound conditions.

Table 7. V.A.C. Therapy findings from selected acute wound articles

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Study Type</th>
<th># of V.A.C. Therapy Patients/Wounds Analyzed</th>
<th>V.A.C. Therapy Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burns</td>
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<tr>
<td>Kamolz²³ (2004)</td>
<td>Case series</td>
<td>7 patients with bilateral hand burns</td>
<td>• Enhanced perfusion reported in the V.A.C. Therapy-treated hand</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Reduction in edema was observed</td>
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<td>• 5 hands healed without skin grafts</td>
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<td></td>
<td></td>
<td></td>
<td>• V.A.C. Therapy hand dressing did not need additional splinting</td>
</tr>
<tr>
<td>Surgical wounds — dehisced/open abdominal</td>
<td></td>
<td>I4 trauma patients with open abdomens</td>
<td>• Early definitive fascial closure achieved in 13 patients (92%) in a mean of 9.9 ± 1.9 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• A mean of 2.8 ± 0.6 dressing changes were performed</td>
</tr>
<tr>
<td>Surgical wounds — sternal wound infections/mediastinitis</td>
<td></td>
<td>103 patients treated after median sternotomy</td>
<td>• 64% had a diagnosis of mediastinitis, while 36% had either superficial infections or a sterile wound</td>
</tr>
<tr>
<td></td>
<td>Retrospective study</td>
<td>103 patients treated after median sternotomy</td>
<td>• Patients were treated for an average of 11 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 70 patients (68%) achieved definitive chest closure with open reduction internal fixation and/or flap closure</td>
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<tr>
<td>Subacute wounds</td>
<td></td>
<td>94 subacute wounds (overall study evaluated 300 wounds)</td>
<td>• 94 subacute wounds included dehisced wounds, open wounds with exposed orthopedic hardware and/or bone, and other miscellaneous wounds open &lt; 7 days</td>
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<td></td>
<td>Case series</td>
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<td>• 26 healed completely</td>
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<td>• 68 reduced in size and were closed with split-thickness skin grafts, secondary closure, or minor flaps</td>
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<td>• 37 patients with exposed orthopedic hardware or bone were treated successfully with closure of adjacent muscle and granulation tissue over the bone and hardware</td>
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of chronic wounds, rendered in a variety of care settings. Additional negative pressure therapy options have been offered for developed and underdeveloped countries.

**Treating Acute Wounds with V.A.C. Therapy**

More than 125 articles report clinical and scientific results related to V.A.C. Therapy treatment of acute wounds, including burns, dehisced wounds, and subacute wounds. Table 7 briefly summarizes the findings of selected V.A.C. Therapy RCTs, case series, and retrospective studies in each of the aforementioned acute wound categories. Kamolz et al evaluated 7 patients with bilateral hand burns. One hand of each patient was treated with V.A.C. Therapy. The authors reported that V.A.C. Therapy helped to promote perfusion and reduced edema. Garner et al concluded that V.A.C. Therapy can “safely achieve early fascial closure,” based on their experiences using V.A.C. Therapy to treat 14 patients with open abdominal wounds. V.A.C. Therapy also has been used to treat sternal wound infections/mediastinitis. In a retrospective review of 103 patients who were treated with V.A.C. Therapy after median sternotomy, Agarwal et al reported that V.A.C. Therapy was administered for an average period of 11 days per patient. The authors also stated that definitive chest closure with open reduction and internal fixation and/or flap closure was achieved for 70 of 103 patients (68%).

In a large case series of 300 wounds, Argenta and Morykwas reported that 26 of 94 subacute wounds healed completely after treatment with V.A.C. Therapy. The remaining 68 subacute wounds reduced in size and were closed using split-thickness skin grafts, secondary closure, or minor flaps. The authors noted that in 37 patients with exposed orthopedic hardware or bone, V.A.C. Therapy successfully achieved closure of adjacent muscle and the formation of granulation tissue over the bone and hardware. Thus, the mechanisms of action that make V.A.C. Therapy a successful treatment for chronic wounds also enable this integrated wound care system to achieve positive results in the treatment of a variety of acute wounds. Additional trials are necessary to determine the economic benefit of adding NPWT to a surgical treatment regime. Certainly, high-risk patients or procedures with increased likelihood of failing would be optimal candidates.

**Treating Wounds with Gauze-Based NPWT**

Campbell et al performed a retrospective review of 30 patients treated with NPWT using the gauze-based Chariker-Jeter technique at negative pressure (−80 mmHg) to demonstrate the safety and efficacy of NPWT in a long-term care setting with VISTA, Versatile1, and EZCARE devices (Smith & Nephew). Chronic wounds (n = 11), surgical dehiscence (n = 11), and surgical incisions (n = 8) showed significant reduction in wound volume and area to be able to support discontinuation of NPWT after a median 41 days, with an overall median 88% reduction in wound volume, 68% reduction in area, and a 15.1% weekly overall rate of volume reduction, comparing comparably with foam-based systems. Hurd et al reported 80% pain-free dressing changes and 96% lack of tissue damage with dressing changes in a long-term care facility. Dunn et al validated factors associated with positive and negative outcomes in patients treated with gauze-based NPWT; these outcomes were similar to those noted with foam dressings. Gauze- and foam-based NPWT products appear to produce similar proportions of closed split-thickness skin graft (STSG) wounds according to Fraccalvieri et al; however, the wounds closed with a foam-based (~125 mmHg) system applied on average at 25.9 days as compared to a gauze-based (~80 mmHg) system applied on average at 24.7 days were less pliable with a thicker scar beneath the graft. Dunn et al noted a 96% overall STSG take, increase in granulation tissue to 90% median wound area, and a decrease in non-viable tissue (20%–0%) for wounds treated with gauze-based NPWT (~80 mmHg) for 12 days pre-treatment and 5 days post-treatment. Landsman et al demonstrated the effectiveness of a mechanically powered gauze-based dressing system used to treat diabetic lower extremity wounds. Non-inferiority clinical studies performed by Dorfshar et al demonstrated that gauze-based dressings show similar changes in wound volume and surface area as those observed with foam-based therapies in a clinical inpatient setting. Availability of dressing materials, familiarity with product use,
required dressing change intervals, and cost may influence a given practitioner’s selection.

**Mechanisms of Action for NPWT**

A clear understanding of how a therapy works is crucial for making the best use of that treatment. Ongoing research into the mechanisms of action for NPWT continues to clarify the effects that produce the overall wound healing outcome. The combined effects of direct mechanical stress on the cell and alterations in the cell’s environment unite to promote a positive wound healing response.

**Granulation tissue formation.** For healing to occur, the wound defect must fill with granulation tissue. Granulation tissue is composed of new blood vessels, fibroblasts, inflammatory cells, myofibroblasts, endothelial cells, and extracellular matrix. In experiments where V.A.C. Therapy was used to treat porcine surgical wounds, it appeared that V.A.C. Therapy assisted in the formation of granulation tissue. Armstrong and Lavery conducted a large RCT of 162 patients with complex diabetic foot amputation wounds. Their study assessed the time to achieve 76%–100% granulation in patients initially presenting with 0%–10% granulation at baseline. Results from the study indicated that V.A.C. Therapy patients achieved this level of granulation in a mean of 42 days. It is believed that mechanical forces resulting from V.A.C. Therapy and their effect on biochemical processes promote granulation tissue formation.

**Mechanical forces.** Virtually all aspects of cell physiology may be affected by mechanical stimulation. The cellular response to strain has long been known to result in increased tissue formation. Classic examples are the use of the Ilizarov or distraction osteogenesis technique in hard tissue and tissue expanders in soft tissue. With V.A.C. Therapy, externally applied forces may be subdivided into 1) macrostrain and 2) microstrain and microdeformations. Saxena et al. reported that V.A.C. Therapy and open-celled polyurethane foam produced tissue strains in the average range of 5%–20%. These values are consistent with those shown to result in increased cellular proliferation in bench studies. Furthermore, the theoretical models developed by Saxena et al. correlated well to actual deformations seen in clinical wounds that had been treated for 4–7 days with V.A.C. Therapy. Greene et al. investigated the effect of V.A.C. Therapy-induced microdeformations on capillary formation in chronic wounds. The authors performed an intra-wound comparison of tissue samples with and without exposure to the V.A.C. Therapy. The level of cellular microstrain is believed to be directly related to pore diameter of the interface of the dressing structure, strut thickness, and applied pressure. Wound tissue samples in contact with the GranuFoam Dressing (causing microdeformations) showed increased
microvessel density, suggesting improved cellular proliferation and angiogenesis. These changes were attributed to the properties of foam in these early trials specifically designed to investigate foam as an interface material.

**Collagen deposition.** Provisional matrix models have been generated to evaluate the impact of NPWT on cellular division and migration, extracellular matrix deposition, apoptosis, and angiogenesis. Parameters, such as pressure profile and interface material, show a marked influence on the development of key tissue components, such as collagen deposition, cellular composition, and vascularity **in vitro**. The full clinical impact of these findings has yet to be validated **in vivo**, where many other factors influence clinical outcomes and high pressures, or the influence of interface materials may potentially adversely influence tissue quality.

**Extracellular matrix deposition (hyaluronic acid).** Hyaluronic acid makes up approximately 80% of the extracellular matrix (ECM). Increased levels of hyaluronic acid may be a factor in the increased levels of granulation tissue formation shown in studies using V.A.C. Therapy. Hyaluronic acid is an important non-sulfonated glycosaminoglycan in the ECM. It is an extremely hygroscopic molecule that provides the tissue with resilience to compressive forces. Hyaluronic acid also may have a protective effect on tissues due to its ability to scavenge free radicals. In tissues biopsied from human mucosal wounds, Oksala et al demonstrated that hyaluronic acid levels rose early before decreasing at Day 7 post wounding. In a porcine full-thickness wound model, granulation tissue was biopsied at Day 9 post wounding and analyzed for hyaluronic acid. High levels of hyaluronic acid were measured in the tissue biopsied after 9 days of V.A.C. Therapy.

**Infection management.** Bacteria colonize all wounds. Infection occurs when the presence of replicating organisms increases to a high titer level, which then leads to the production and accumulation of bacterial toxins and proteases that impair wound healing. Chronic wound infection is associated with reduced fibroblast presence and improper collagen deposition. It is therefore important to control wound infection to ensure optimal wound healing.

**Exudate management.** A goal in proper wound bed preparation is to provide exudate management. Extensive evidence exists in the wound healing literature to indicate that the presence of edema in the wound bed can negatively impact wound healing. Removal of excess interstitial fluid by NPWT results in decreased tissue turgor, decreased intercapillary distance, increased lymphatic flow, and improved inflow of nutrients to and removal of waste by-products and proteases from the tissue. The ability of V.A.C. Therapy to favorably impact edema removal has been reported experimentally and clinically in diverse wound types, such as chronic wounds, burns, and acute traumatic wounds. Caution should be taken to avoid dehydration, coagulopathies, and protein nutritional deficits with excessive exudate removal.

**Enhanced perfusion.** Adequate perfusion is extremely important to the healing process. Nutrients (including oxygen) that are essential for wound healing are transported to the wound via the blood. Improved perfusion also allows for the removal of cellular waste products, such as carbon dioxide. Initial preclinical studies by Morykwas et al showed that compared to baseline levels, intermittent application of V.A.C. Therapy with the GranuFoam Dressing resulted in more than a 4-fold increase in perfusion. Subsequent studies have confirmed the increase in perfusion associated with V.A.C. Therapy.

While the aforementioned studies show the immediate effect of V.A.C. Therapy on perfusion, Kamolz et al showed that increased perfusion also may continue later into the wound healing continuum. It is commonly known that certain burn injuries can progress from partial-thickness to full-thickness burns within a few days of injury and that compromised microcirculation is a contributing factor. In a study of 7 patients with bilateral hand burns, Kamolz et al used video angiography to measure perfusion in the burns. They found that use of V.A.C. Therapy was associated with hyperperfusion and that this may have been a contributing factor to the prevention of burn progression. Five of the 7 V.A.C. Therapy-treated hand wounds healed without skin grafts.

**NPWT “filler material” debate.** Wound dressing materials are the topic of considerable debate. Yet, one of the most important scientific questions needs to be better addressed: the relevant physics of negative pressure on filler sub-
stance and its affect to either augment or diminish pressure distribution throughout the entire tissue plane. In an interdependent fashion, the negative pressure profile and the interface material alter exudate evacuation and tissue microstrain and thereby influence the rate, quantity, and quality of tissue generated. Interface material is not simply “filler material;” it impacts distribution of negative pressure within the wound space, modulates pressure waveforms, and dampens peak pressures delivered to tissue surfaces and extending into surrounding periwound tissue planes. The amount and viscosity of the fluid being evacuated also affects negative pressure delivery, and for some materials, this “fluid effect” is further amplified by variability introduced by the dressing material. Gauze, as compared to open-cell foam, is thought to be more likely to alter the programmed pressure based upon the amount of material used, packing density, method of packing, and interaction between the applied layers. The unique open-cell PU and PVA foams created for the modern NPWT platform were designed to transduce negative pressure to the wound surface with minimal pressure alteration regardless of the exudate quantity or quality, amount of filler material used, layers applied, or orientation of insertion. Foam facilitates delivery of negative pressure profiles in a very “exacting” fashion. The specially designed foams can be easily sized for most wounds and are readily available at a relatively low cost.

On the other hand, gauze is an abundant, inexpensive, and familiar wound dressing material. It can be easily molded around irregular contours and packed into wounds and tunnels and is now readily available in economical, antimicrobial, low-bioadherent, noninflammatory product lines utilized for some NPWT wound types, especially where lower peak pressure and the use of a nonadherent contact layer is required to reduce adherence, in-growth, bleeding, and pain. Many believe gauze has a tendency to “mat and wad” during application and under negative pressure, which may affect fluid evacuation and pressure transduction, especially in larger wounds. In confirmation, Anesäter et al performed a series of studies to examine the effect of material type (foam or gauze) and size (small or large) on wound contraction and tissue pressure in a porcine full-thickness peripheral wound model under exposure to negative pressure ranges (-20 mmHg to -160 mmHg). NPWT application caused a decrease in tissue pressure at 0.1 cm from the wound margin and an increase at 0.5 cm from the wound margin. Tissue pressure at 0.5 cm was higher with smaller amounts of foam, and smaller amounts of foam also caused significantly more wound contraction. In contrast, gauze created intermediate contraction unrelated to the amount of “filler” material used.

In summary, foam is more likely to deliver programmed pressure profiles, but not all clinical situations require that level of “exactness.” Gauze or large amounts of foam generate less contraction, which could be less painful and less likely to cause strain-related bleeding, while small amounts of foam would be most beneficial when maximal wound contraction and granulation tissue development are needed. Researchers are still trying to ferret out the interplay between mechanical pressure modulations and tissue responses.

High versus low NPWT peak pressure debate. Recent studies highlight the existence of 3 zones of perfusion established by NPWT: 1) the wound bed, 2) the wound margin, and 3) the periwound tissue. The current NPWT platform dictates a specific range of microstrain at the wound base and derived its justification based upon measurements of increased blood flow in the periwound tissue and the resulting amount of granulation tissue developed. Higher peak negative pressure (-125 mmHg) optimized flow in the periwound tissue and supported a significant increase in granulation tissue development. Lower peak negative pressures (-80 mmHg) generated lower levels of periwound tissue perfusion. Studies showed marginal tissue perfusion increased with increasing negative pressure to a plateau then decreased as additional negative pressure was instituted. Hypoxia (low oxygen content) and ischemia (low perfusion pressure) develop at different levels of pressure for different types of tissue. High levels of negative pressures can lead to hypoxia at the wound margin, and excessive pressures cause ischemic tissue breakdown, apoptosis, and necrosis. Certainly, prolonged hypoxia and ischemia have been associated with tissue necrosis; however, intermittent hypoxia and “mild ischemia” are both recognized stimuli for hypoxia-inducing
factor (HIF) and other biomolecules that signal wound healing cascades. It is interesting to note that the “hypoxia and potential ischemia” may be associated with at lower overall pressure at that 0.1 cm tissue plane because the applied energy source is a negative (suction) pressure. At present, there is insufficient information to fully interpret the relative importance of wound base, marginal, and distal blood flow in tissue under the influence of negative pressure forces.

**Negative pressure profiles and tissue quality.** Studies show that higher levels of peak pressure (-125 mmHg) and intermittent modality have been associated with more granulation tissue developed at a faster rate in full-thickness wounds with adequate vasculature for perfusion and a source for fibroblast cells needed for fibroplasias.1–3 Multiple factors influence the choice of negative pressure therapy parameters. These may relate to the health of the patient, quality of the tissue being treated, amount of exudate, tissue oxygen and perfusion, and other treatment modalities being used. A practitioner may prefer to use higher negative pressure in a large, well vascularized, highly exudative, post-operative, dehisced hip wound but choose a lower pressure level (-80 mmHg) for a dehisced, infected, abdominal wound with substantial amounts of poorly perfused fat tissue in an elderly patient with diabetes. Hypoxic, ischemic fat tissue may develop necrosis at higher pressure settings. Optimal negative pressure should be high enough to draw the wound margins toward each other without creating adverse tension, deliver sufficient tissue microstrain (5%–20%) to activate cellular division to create the desired amount and quality of collagen-ECM mix deposited, and effectively evacuate inflammatory exudate from the wound space to “perfect” the wound environment.

In an effort to adopt evidence-influenced practice models, some practitioners have utilized bedside diagnostics for perfusion (hand-held Doppler) and oxygenation (transcutaneous oxygen, TCPO2) along with patient comfort levels to guide treatment pressure profiles. While Doppler and TCPO2 assessments are not practical for commonplace application today, newer technology may assist with bedside perfusion and oxygenation verification to inform treatment choices in the future. Additional diagnostics are being developed and marketed to test wound environment matrix metalloproteinases and other inflammatory mediators. Nonetheless, up to this point, there has been a well established medical practice of reducing the peak negative pressure and slowing the rate of draw down to reduce pain, bleeding, and other potential complications. Those choices are made at the presumed potential loss of comparative granulation tissue generated. More information is needed to establish how those choices impact the actual rate and quality of tissue generated.

More scientific-focused research is required. Clearly, wound surface microstrain directly influences cellular proliferation, apoptosis, extracellular matrix deposition, and inflammatory mediator profiles; however, the relative importance of that influence to impact final clinical outcomes has yet to be fully delineated. Negative pressure profile may be manipulated to deliver different levels of strain by modulating peak pressure, pressure waveforms, pressure modality (continuous or intermittent), duration and frequency of application, and selection of different interfaces for transduction. Additionally, a host of non-pressure-related factors influences final clinical wound healing outcomes125 (Table 8). Several key areas need further investigation and definition: 1) interplay between mechanical stress and inflammatory mediator reduction alters the cell’s biomechanical profile either directly (microstrain) or indirectly through environmental changes (exudate evacuation) and their effects are interdependent; 2) pressure profile alterations related to dressing materials in the wound space; 3) tissue growth response (fibroplasias, angiogenesis, and collagen-ECM deposition) resulting from varied pressure profiles applied at different times throughout the human wound healing cycle; 4) tissue growth response in relation to varied pressure profiles depending upon initial tissue type (fat, muscle, tendon/ligament, bone); and 5) tissue growth response where various soluble additives are provided (ie, antimicrobials, nutrients, oxygen, nitric oxide, growth factors, cytokines, collagen, ECM, and cells). A great amount of additional research is warranted. In lieu of the current insufficient level of “evidential clarity” and minimal number of comparative clinical trials, it would be premature to designate a “best” dressing or “best” pressure. In all likelihood, it will not be one “best”
NPWT has widespread clinical acceptance. A substantial body of evidence reports its clinical utility in the treatment of chronic and acute wounds. NPWT is intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing edema, promoting granulation tissue formation and perfusion, and removing exudate and infectious material. It is indicated for patients with chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic or pressure); flaps; and grafts. NPWT design innovations have accelerated provider adoption and improved patient compliance, care setting appropriateness, and realized healthcare system cost reductions. Ease of use coupled with positive clini-

**Conclusion**

NPWT is a widely accepted treatment method for chronic and acute wounds. It promotes wound healing by preparing the wound bed for closure, reducing edema, and promoting granulation tissue formation and perfusion. NPWT is suitable for various wound types, including chronic, acute, traumatic, subacute, and dehisced wounds, as well as diabetic or pressure ulcers, flaps, and grafts. Design innovations have enhanced provider adoption and patient compliance, leading to cost reductions in healthcare systems.

<table>
<thead>
<tr>
<th>Table 8. Factors impacting wound healing</th>
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<tr>
<td><strong>NPWT Device-Related Factors</strong></td>
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<tr>
<td>• Interface materials to distribute pressure and interact with the underlying tissues</td>
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<td>• Presence or absence of an intervening nonadherent layer</td>
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<td>• Pressure profile</td>
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<tr>
<td>° Peak negative pressure (maximum)</td>
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<tr>
<td>° Pressure modality — continuous versus intermittent</td>
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<td>° Pressure wave forms — rapidity of pressure onset (“draw down”)</td>
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<tr>
<td>° Treatment regimes — application frequency and overall duration</td>
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<td><strong>Wound-Specific Factors</strong></td>
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<tr>
<td>• Etiology of tissue injury (eg, incision, contusion, blast, thermal, pressure, moisture)</td>
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<td>• Location, size, shape, depth</td>
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<td>• Exposed vital structures (eg, bone, blood vessels, tendons)</td>
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<td>• Tissue nutritional state</td>
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<td>• Local vascular status and perfusion</td>
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<td>• Local tissue inflammatory status</td>
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<tr>
<td>• Infectious status (local, systemic, biofilm, abscess, suppuration)</td>
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<tr>
<td>• Existing cells, extracellular matrix (ECM), and structural support tissues</td>
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<td>• Local oxygenation and tissue energy</td>
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<td>• Tissue fluid — edema, drainage, exudate</td>
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<td>• Temperature, moisture, and pH</td>
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<td><strong>General Health-Related Factors</strong></td>
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<tr>
<td>• Overall physical health and emotional status</td>
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<tr>
<td>° Medical diseases and disorders</td>
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<td>° Medications, prescribed, over-the-counter, herdals, homeopathic</td>
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<tr>
<td>° Psychiatric and emotional health</td>
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<td>• Socio-economic status and ability to access appropriate care</td>
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<tr>
<td><strong>Recommended Treatments and Interventions</strong></td>
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<tr>
<td>• Debridement — selective and non-selective</td>
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<td>• Antibiotic, antimicrobial, anti-inflammatory agents</td>
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<td>• Offloading therapy and the ability to mitigate future recurrent trauma</td>
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<tr>
<td>• Compression and manual massage therapy — continuous and intermittent pneumatic</td>
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<td>• Oxygenation and perfusion support</td>
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<td>• Nutritional supplementation</td>
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<tr>
<td>• Temperature and moisture management</td>
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<tr>
<td>• Case management</td>
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<tr>
<td>• Physical therapeutics</td>
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<tr>
<td>• Tissue-based therapy components (eg, growth factors, cytokines, collagen, hyaluronic acid, cells)</td>
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<tr>
<td>• Exogenous energy provision — electric, electromagnetic, infrared, ultrasound, or vibratory</td>
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Negative Pressure Wound Therapy

Take-Home Messages for Practice

- NPWT is a proven, clinically effective, and safe process that promotes healing for acute and chronic wounds.
- NPWT provides a mechanical strain that alters cellular proliferation, extracellular matrix deposition, and local perfusion; additionally, the removal of exudate facilitates the reduction of inhibitory mediators.
- Mechanical strain and inflammatory exudate removal act interdependently to positively impact wound tissue healing response.
- The type of material at the interface is not as important as the modification of NPWT pressure profiles and tissue growth responses.
- Adding nonadherent intervening contact dressings at the tissue-material interface helps mitigate complications.

Self-Assessment Questions

1. Which of the following is not an indication for use of NPWT?
   A. Chronic wounds and ulcers (such as diabetic or pressure)
   B. Acute, traumatic, subacute, and dehisced wounds
   C. Full-thickness burns
   D. Flaps and grafts

2. Peak pressure may alter which of the following?
   A. Cellular proliferation
   B. Collagen deposition
   C. Local arterial blood flow
   D. All of the above

3. Which of the following mechanisms of action relate to NPWT?
   A. Promoting edema
   B. Inhibiting granulation tissue formation and perfusion
   C. Wound space expansion
   D. Decreasing exudate and infectious material

4. What dressing has the best likelihood of reducing NPWT-related pain?
   A. Gauze
   B. Foam
   C. Bio-Dome
   D. Intervening nonadherent contact layer

Answers: 1-C, 2-D, 3-D, 4-D

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