The Effects of Normal Saline Instillation in Conjunction With Negative Pressure Wound Therapy on Wound Healing in a Porcine Model

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Abstract: Acute and chronic wounds impact the lives of millions of patients. Since its introduction, negative pressure wound therapy using reticulated open cell foam (NPWT/ROCF) has significantly improved the healing outcome for many of these wounds. Methods. The effects of intermittent instillation of normal saline in conjunction with NPWT were investigated to determine if instillation therapy provides additional benefits in wound healing. Conventional NPWT/ROCF as delivered by V.A.C.® Therapy was compared to V.A.C. Instill® Therapy with normal saline in the treatment of porcine full-thickness excisional wounds. Wounds were treated with NPWT/ROCF or NPWT/ROCF with instillation therapy at approximately 4 cycles of normal saline instillation per day and dwell times of either 5 or 60 minutes for the instilled saline on the wound bed. Results. Instillation therapy with normal saline at either dwell time elicited a faster rate of wound filling with granulation tissue that contained an increase in total collagen content compared to continuous NPWT/ROCF alone. Analyses of wound contraction and the hydration state of the treated tissue exhibited no apparent differences between the experimental instillation therapy groups and the control NPWT/ROCF group. Conclusion. Collectively, these data suggest that instillation therapy with normal saline may lead to wound fill with higher quality granulation tissue composed of increased collagen following wounding of cutaneous tissue compared to the use of NPWT/ROCF alone.

Negative pressure wound therapy using reticulated open cell foam (NPWT/ROCF) has proven to be effective in healing wounds faster than traditional moist wound healing approaches. More than 500 publications, including at least 20 randomized controlled trials (RCTs), have shown the benefits of NPWT/ROCF in wound healing. This enhancement in wound healing may occur through multiple mechanisms including, but not limited to, uniform drawing of the wound edges together, stimulation of per-
fusion, and removal of fluids and infectious materials that may be present within the wound.54 These outcomes of NPWT, among many others, promote the ability to fill a wound defect with granulation tissue,7,8 which is a key requirement for proper wound closure. The rate at which a wound heals is highly dependent on the granulation process.

Traditional wound care routinely involves cleansing the wound with aqueous solutions such as water or normal saline. Typically, wounds are cleansed at least at every dressing change, if not more frequently. Keeping the wound properly cleansed is believed to mitigate factors that impair wound healing.7 Wound cleansing with a non-toxic fluid (e.g., water or normal saline) has been shown to remove debris, wound exudates, and detrimental cellular products that may be present in the wound bed while also removing any nidus for bacterial infection.10 This, in turn, may aid in creating an optimal wound bed environment for wound healing. Instillation therapy combines NPWT/ROCF with the ability to instill fluids into the wound during breaks in the application of NPWT. Based on its potential wound cleansing attributes, the goal of this strategy would be to combine these two therapies (i.e., wound cleansing and NPWT/ROCF) to determine if there is a synergistic effect, leading to further acceleration of the wound healing process and the development of granulation tissue beyond that seen with the use of NPWT alone.

Various types of solutions have been recommended for use in the cleansing of wounds. For example, fluids with antiseptic properties have been traditionally used for the treatment of infected wounds; however, published preclinical research has suggested that antiseptic solutions may hinder the healing process.11 As such, normal saline (0.9% NaCl) is currently the favored wound cleansing solution for non-infected wounds because it is isotonic, and as such, does not interfere with the normal healing process, induce tissue damage, cause sensitization/allergies, or alter the normal bacterial flora of the skin.12

As a means to combine NPWT/ROCF with a wound cleansing lavage or the ability to introduce antiseptic fluids to reduce bioburden, the V.A.C. Instill® Therapy System (instillation therapy) was introduced. It combines NPWT/ROCF with the ability to intermittently instill a solution in a controlled fashion.13,14 Specifically, instillation therapy allows for the controlled instillation of fluid onto the wound bed, whereby the fluid dwells at the interface between a ROCF dressing and the wound surface for a predetermined amount of time. At the end of the specified dwell time, vacuum is once again applied, thereby removing the irrigation fluid and wound exudate. Current indications for use of instillation therapy include patients who would benefit from NPWT/ROCF in conjunction with the controlled delivery and drainage of topical wound solutions to and from the wound bed, respectively. Specifically, this system has proven to be effective for the removal of infectious material and for decreasing the bacterial burden in infected wounds.15,16 However, to date, the effects of combining saline instillation with NPWT/ROCF on the rate and quality of granulation tissue formation as part of the wound healing continuum are unknown.

A combinatorial therapy approach with both NPWT/ROCF and normal saline instillation was hypothesized to result in improved wound bed preparation, enhance the rate of wound filling, and potentially enhance the quality of granulation tissue present in a wound bed due to intermittent cleansing of the wound during NPWT/ROCF Therapy. Since published RCTs have shown the benefits of NPWT/ROCF over moist wound healing,14,17 the current study was designed to examine whether or not combining instillation therapy with normal saline to NPWT/ROCF would offer additional benefits. This study examined the rate of wound filling in full-thickness excisional dermal wounds in swine over a 9-day period. During this time, NPWT/ROCF was applied either alone or in conjunction with the instillation of normal saline at defined time points each day. Tissue biopsies were isolated at the end of the in-life phase and processed to determine the wet: dry tissue weight ratio and for HPLC analysis of total collagen content. The results of the present study suggest that instillation of saline in conjunction with NPWT/ROCF increases the rate of wound fill and leads to better quality of granulation tissue as determined by the total content of collagen when compared to use of continuous NPWT/ROCF alone.

Methods

The Institutional Animal Care and Use Committee (IACUC) at the University of Texas Health Science Center at San Antonio (UTHSCSA) approved the experimental protocol for this study. Eight domestic castrated male Yorkshire pigs (Sus scrofa), with a mean body weight of 135.0 lb ± 17.2 lb, were quarantined for 14 days prior to the surgical procedures. During this acclimation period, the swine were housed individually and

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had access to food and water ad libitum. All of the animals received care in compliance with the Guide for the Care and Use of Laboratory Animals from the National Academy Press, 1996.

Anesthesia and surgical procedures. The swine were fasted for a minimum of 12 hours prior to administration of the anesthetic. The animals were then anesthetized with Telazol® (4.5 mg/kg–5.5 mg/kg, Wyeth, Fort Dodge, IA) or a combination cocktail of ketamine/xylazine (5:1 v/v) dosed at 3 cc per 50 lb, intra-muscularly. Following intubation, a surgical plane of anesthesia was maintained using 1.5% to 3.0% isoflurane. Eight paraspinal wound sites were outlined by tattoo using a round, 5-cm diameter template and an electric tattoo device (Spaulding & Rogers Mfg., Inc., Voorheesville, NY). Four wound sites were demarcated on each side of the spine with the two columns located between the crest of the shoulders and the coccygeal tuberosity.

Eight full-thickness, round, excisional wounds (5 cm in diameter) were created on each animal by vertically excising the skin immediately interior to the tattooed margins down to the level of the subcutaneous fascial layer above the muscle (approximately 1 cm deep). The excised tissues were removed and snap frozen in dry ice for subsequent biochemical analysis. Hemostasis at the wound sites was obtained through the application of direct pressure. The dressings were applied following wound creation and hemostasis.

Experimental design. This study was designed to assess the effects of two different treatment regimes of instillation therapy with varying dwell times of normal saline (5 or 60 minutes) compared to a control continuous NPWT (V.A.C.® Therapy, KCI, San Antonio, TX)/ROCF group alone. Each wound site on a given animal was assigned to an experimental or control group with the three treatment groups shown in Table 1. All of the wound sites were treated with NPWT, consisting of a ROCF dressing, T.R.A.C.* pad connector with tubing (KCI), and when necessary, an Instill* pad connector with tubing (KCI), all connected to a V.A.C. Instill (KCI) set to deliver 125 mmHg of negative pressure to the wound. Each pair of wounds was bridged with strips of the ROCF dressing to evenly distribute the negative pressure and instill saline to each pair of adjacent wound sites. Each pair was then sealed with transparent adhesive drape (V.A.C.* Drape, KCI), which overlapped the periwound margins. A flexible, protective layer was placed over the wound dressings and secured in place with the adhesive drape. Each pair of wounds was connected to a single V.A.C. Instill, and with the exception of the control continuous NPWT/ROCF group, a corresponding peristaltic pump (Variable-Speed Pump; Cat. No. 13-876-2; Fisher Scientific; Waltham, MA). The peristaltic pumps were used with instillation therapy to automatically deliver saline to each pair of wounds at specified intervals without supervision. Animals were maintained on treatment by securing the V.A.C. Instill units and peristaltic pumps to a customized aluminum turntable placed above the animal cages. This setup allowed the animals to move freely within their cages without restriction.

Therapy settings. Control group wounds were treated with continuous NPWT/ROCF at a negative pressure of 125 mmHg. For the other two treatment groups, therapy was applied at a negative pressure of 125 mmHg for 5 consecutive hours followed by instillation of 100 mL of normal saline to each pair of wound sites, with a dwell time of either 5 or 60 minutes prior to resumption of negative pressure therapy for another 5-hour cycle.

### Table 1. Negative pressure settings, therapy time per cycle, number of instillation cycles, and hold times for the treatment groups.

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Type of NPWT</th>
<th>Negative pressure applied (mmHg)</th>
<th>NPWT time applied (hr/cycle)</th>
<th>No. cycles/day</th>
<th>Instillation of saline (Y/N)</th>
<th>Saline hold time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous NPWT/ROCF (control)</td>
<td>Continuous</td>
<td>125</td>
<td>~24</td>
<td>1</td>
<td>N</td>
<td>N/A</td>
</tr>
<tr>
<td>Saline instillation therapy (5-min dwell)</td>
<td>Intermittent</td>
<td>125</td>
<td>5</td>
<td>~4.7</td>
<td>Y</td>
<td>5</td>
</tr>
<tr>
<td>Saline instillation therapy (60-min dwell)</td>
<td>Intermittent</td>
<td>125</td>
<td>5</td>
<td>4</td>
<td>Y</td>
<td>60</td>
</tr>
</tbody>
</table>
The ROCF dressings were changed every 2 days during the first 4 days following wound creation and every day thereafter until the end of the in-life phase, which was 9 days following surgery. As such, the dressings were changed at 2, 4, 5, 6, 7, and 8 days following wound creation with euthanization of the animal on day 9. At each dressing change, photographs of the wound bed were taken and wound contraction and wound volumes were measured. On day 9, two 8-mm diameter punch biopsies were taken from the medial and lateral sides of the wound site, and two corresponding punch biopsies were also taken from the adjacent periwound areas in the same orientations. A punch biopsy from the wound and adjacent periwound biopsy were analyzed for wound hydration measurements. A similar pair of biopsies was analyzed biochemically for total collagen content. In each case, the periwound biopsy was considered control tissue and wound biopsy values were compared to periwound (control) values.

Wound volume and area measurements. In order to determine wound volumes, the wound sites were covered with adhesive drape, which was not stretched excessively in order to prevent wrinkling. The drape was maintained level to the surrounding tissue in the periwound margins and sterile saline was introduced into the wound cavity with a syringe. The volume of saline required to fill the defect was recorded.

Digital planimetry was used to determine wound area and the degree of contraction of the wound. The margins of each tattooed wound site were traced onto a clear plastic grid (Visitrak®, Smith & Nephew, Hull, UK). Defect contraction and wound area were then calculated using imaging software (SigmaScan® Pro 5.0, Systat, Inc., Chicago, IL).

Tissue hydration determination. Punch biopsies (8-mm) were set aside from tissue removed during surgery as well as at necropsy. These biopsies were placed into 2-mL tubes and subsequently weighed to obtain their wet weights. The samples were lyophilized under pressure for at least 72 hours. The lyophilized samples were then weighed to obtain their dry weight. The wet:dry tissue weight ratio was then calculated based on these two readings.

Biochemical analysis of total collagen content. The total collagen content of the tissue biopsies was analyzed using a protocol adapted from a method described previously.¹⁸ Punch biopsies (8-mm) collected during surgery as well as at necropsy were placed into 2-mL cryovials and frozen at -80°C until time of biochemical processing. For processing, approximately 100 mg of the frozen tissue biopsies were pulverized and lyophilized overnight. The lyophilized tissues were defatted by treatment with 70% ethyl alcohol, sonicating for 5 minutes, and incubating at room temperature for 15 minutes. Samples were pelleted using centrifugation at 13,000 rpm for 15 minutes. The pellet was treated sequentially as described above with the following exceptions: 100% ethyl alcohol and acetonitrile were used, followed by two acetone washes. The washed samples were dried and hydrolyzed using 5 mg/mL 6N-HCl and overnight heating at 110°C followed by overnight drying in a vacuum oven at 60°C. The samples were reconstituted in water and buffered to pH 9.0 with 50 mM sodium bicarbonate. Amino acids in hydrolyzed tissue were derivatized using a 1.3 mg/mL solution of dabsyl chloride in acetonitrile. Following dabsylation, the samples were lyophilized and reconstituted with 70% ethyl alcohol. Samples were then filtered with polysulfone (PSU) syringe filters and injected into the Waters Alliance 2695 HPLC system equipped with a Waters 2996 photodiode array detector (Waters Corp., Milford, MA). Dabsylated amino acids were detected and quantified by measuring the absorption at 436 nm. The reverse phase HPLC method utilized a Phenomenex Gemini™ C18, 15 cm x 4.6 mm, 3 µm analytical column with a Phenomenex Gemini C18, 4 mm x 3.0 mm, Security Guard Cartridge. The mobile phase was 70:30 potassium phosphate buffer (pH 11.0):acetonitrile and the amino acids were eluted from the column isocratically at a flow rate of 0.5 mL/minute with a total run time of 45 minutes. Data were acquired using Waters Empower Software. Analyte concentrations were calculated for hydroxyproline, glycine, and proline using calibration curves for each analyte and percent total collagen determined by summation of the concentrations of the three amino acids.

Statistical Analysis

The wound volumes, wound areas, and total collagen content were analyzed using one-factor repeated measures analysis of variance (ANOVA). The Dunnett’s test was performed to compare each treatment group with the control group (ie, continuous NPWT/ROCF). This test was implemented at different days and was not adjusted for multiplicity. The wet:dry tissue weight ratios between the wound and periwound areas for each treatment group were analyzed using a paired t-test. P values < 0.05 were considered to be significant, while P values
Instillation therapy values at 5 minutes dwell time that * and # represent instillation therapy values at 5- or 60-minute dwell time, respectively, that are significantly higher than control NPWT/ROCF values (P < 0.05).

^ Instillation therapy values at 5 minutes dwell time that exhibit highly suggestive trends toward an increase compared to control NPWT/ROCF values (0.05 < P < 0.10).

Figure 1. Percentage reduction of the initial wound volume over the 9-day, in-life period. The wound volume was measured at defined time points by measuring the volume of saline required to fill the wound. Data are presented as the mean ± SEM at each time point (n = 8).

* Significant difference compared to control NPWT/ROCF values (0.05 < P < 0.10).

^ Highly suggestive trend compared to control NPWT/ROCF values at P < 0.05.

Figure 2. Percentage of the initial wound area over the 9-day, in-life period. The wound area was assessed by performing digital planimetry on tracings of the tattooed wound margins taken at each time point. Data are presented as the mean ± SEM (n = 8).

Figure 3. Percentage of moisture in tissue biopsies taken from the wound and periwound areas 9 days following wound creation. Punch biopsies (8 mm) were taken from the granulation tissue as well as the adjacent periwound area and weighed to determine the wet weight. Following lyophilization of the tissue samples, the biopsies were weighed to determine the dry weight. The difference in wet to dry weights of the biopsies divided by the wet weight provided a ratio of moisture present in the tissue. Data are presented as the mean ± SEM (n = 8).

# Significant differences compared to the wet:dry weight of the wound biopsies at P < 0.0001.

Figure 4. Total collagen content normalized to the mean content of the uninjured tissue at Day 0. Punch biopsies (8-mm) were taken from the granulation tissue and processed via HPLC to determine the total content of hydroxyproline, proline, and glycine. Data are presented as the mean ± SEM (n = 5).

* Significant difference compared to control NPWT/ROCF values at P < 0.05.

^ Highly suggestive trend compared to control NPWT/ROCF values at 0.05 < P < 0.10.
between 0.05 and 0.10 were considered as exhibiting a trend toward significance.

Results

The experimental instillation therapy and control NPWT/ROCF groups were compared to examine the effects of saline instillation. Any differences due to the introduction of normal saline to the wound bed were noted. The two primary endpoints for the study included measurement of wound volume fill over time and quantification of total collagen content in punch biopsies taken from the granulation wound bed at necropsy. The two secondary endpoints were the degree of wound contraction, as determined from wound area measurements/tracings, and the wet: dry tissue weight ratio as a measure of tissue hydration.

Wound volume reduction and area measurements. Figure 1 shows the percentage change in wound volume over time. Instillation therapy with normal saline and dwell times of both 5 and 60 minutes exhibited either a trend or a significantly higher percentage of wound volume filled with granulation tissue on days 6 and 7. Specifically, there were significant differences in the percentage of wound filling observed between continuous NPWT/ROCF and instillation therapy at dwell times of 5 minutes \( P = 0.025 \) and 60 minutes \( P = 0.002 \) on day 6 and at a dwell time of 60 minutes on days 7 \( P = 0.023 \) and 8 \( P = 0.038 \). A highly suggestive trend toward differences in the percentage of wound filling was observed between continuous NPWT/ROCF and instillation therapy at a dwell time of 5 minutes on day 7 \( P = 0.077 \), [Figure 1].

Wound area was evaluated over time to ascertain the degree of wound contraction over the course of the granulation phase. These data were plotted as the mean area inside the tattoo lines as a function of time (Figure 2). Statistical analysis of the area values for each time point indicated that there were no differences between the experimental and control groups, which suggests that the differences in volume observed at days 6 and 7 between the instillation therapy and control NPWT/ROCF groups are not due to wound contraction, but rather due to granulation tissue filling the defect.

Tissue hydration. The wet: dry tissue weight ratio from punch biopsies taken from the wound sites on day 9 was evaluated to determine if the instillation of normal saline affected the hydration levels of the underlying granulation tissue. The amount of moisture in the tissue biopsies was determined by subtracting the lyophilized (dry) biopsy weight from the wet weight and dividing this value by the wet weight. These data were plotted as the mean percentage of moisture in the tissue for each instillation therapy and control NPWT/ROCF group (Figure 3). Differences in hydration observed across treatment groups for the wound biopsies were not found. Therefore, instillation therapy with normal saline did not alter the hydration levels of the underlying granulation tissue in pig wounds.

Total collagen content. Impaired wound healing can often be attributed to the synthesis of poor quality collagen or due to increased collagen degradation. Therefore, the total collagen content in the wound biopsies was evaluated as an indirect measure of the quality of the newly formed granulation tissue. A distinctive hallmark of collagen is the regular arrangement of amino acids in each of the three chains that comprise collagen microfibrils. The sequence often follows the pattern Glycine-Proline-X or Glycine-Y-Hydroxyproline. Thus, the total content of the amino acids hydroxyproline, glycine, and proline were used to determine the total collagen content in punch biopsies taken from both the wound and periwound areas. The total collagen content from the wound biopsies were then normalized to the periwound values and plotted for each experimental and control group (Figure 4). A significant increase in total collagen content was observed in the instillation therapy group with a dwell time of 60 minutes compared to the NPWT/ROCF group \( P = 0.015 \). A highly suggestive difference was also observed in total collagen content between the NPWT/ROCF-treated wounds and wounds instilled with normal saline with a 5-minute dwell time \( P = 0.072 \).

Discussion

Alterations in the integrity of the skin lead to an ordered healing process consisting of four main phases. These phases are, in sequential order, hemostasis, inflammation, proliferation, and maturation or remodeling. While the hemostatic and inflammatory phases are critical for restoring tissue homeostasis, much of the wound fill process occurs during the proliferative phase. In this phase, the migration and proliferation of fibroblasts and the subsequent production of collagen and other extracellular matrix proteins are crucial for the formation of granulation tissue and resultant wound closure.

NPWT/ROCF has proven to be effective in healing a wide range of wounds including acute, chronic, traumatic, and dehisced wounds, as well as partial-thickness burns, diabetic ulcers, pressure ulcers, flaps, and grafts.
NPWT/ROCF facilitates and promotes wound healing via secondary or tertiary intention through multiple mechanisms including increasing perfusion, reducing edema, reducing inflammation, and creating an environment that promotes granulation tissue formation. The effects of NPWT/ROCF on wounds are mediated, presumably, through the microstrain that is manifolded to the tissue through the ROCF dressing during NPWT. The V.A.C. Instill capitalizes on the advantages of NPWT/ROCF combined with the added benefits of controlled instillation of topical wound solutions to the wound bed. Much of the previously reported research with instillation therapy has focused on the effects of instilling normal saline, antibiotics, or antiseptics as it pertains to bioburden reduction and/or treatment of infection. While the effects of using fluid instillation in conjunction with NPWT/ROCF on infection clearance and wound healing have been investigated, its effects on the rate of granulation tissue formation and quality have not specifically been determined. The present study investigated how instillation therapy with approximately four cycles per day of normal saline instillation and hold times of 5 or 60 minutes affect wound healing compared to NPWT/ROCF alone. This study utilized a full-thickness acute wound-healing model in normal healthy swine.

The primary measure of wound healing was wound volume reduction over time. The data showed the use of NPWT/ROCF in conjunction with instillation therapy elicited an increased rate in wound filling compared to wounds treated with NPWT/ROCF alone. For example, at 6 days following wound creation, the wound was filled with 15% to 20% more granulation tissue in the instillation therapy groups compared to the NPWT/ROCF control group. The instillation of normal saline also led to trends towards a significant increase in wound filling on day 7. Additionally, comparison of the percentage of the wound that was filled in the instillation therapy groups compared with the control NPWT/ROCF group for any given day from day 5 onward indicated a shift of nearly a day in the percentage of wound volume that was filled. In other words, instillation therapy appeared to lead to filling of the wound defect 1 day faster than when continuous NPWT/ROCF was applied. Evaluation of the wound area was done using digital planimetry to ascertain how much wound closure was occurring due to contraction. The results indicated that there were no differences in the area within the tattooed margins of the wound sites between the instillation therapy and control NPWT/ROCF groups for any of the time points evaluated. This suggests that there were no differences in wound contraction between groups. Since a fairly large volume (100 mL) of normal saline was instilled into each pair of wound sites, there was also a possibility that local tissue edema may have occurred. Evaluation of the tissue hydration in punch biopsies taken from the granulation tissue showed that there were no differences in the ratio of the wet: dry tissue weight between the instillation therapy groups and the control NPWT/ROCF group. This suggests that the increased fill observed in the instillation therapy groups was due to increased granulation tissue formation rather than due to increased tissue edema.

The effects of saline instillation on constituents of the dermal extracellular matrix, and collagen in particular, were also evaluated. Fibroblasts, which are the predominant cells in the dermis, produce structural extracellular matrix proteins in the proliferative phase of wound healing to help restore tissue integrity following dermal injury. As part of this proliferative response, collagen types I and III are the major constituents of the extracellular matrix (ECM) in cutaneous tissue. Type I collagen and, to a lesser extent, type III collagen combine with newly formed vasculature elements to form granulation tissue. The presence of collagen provides tensile strength, integrity, and structure to the regenerating dermal tissue. In order to ascertain the degree of collagen present in the granulation tissue, a technique was adapted based on a published method to quantify the amount of hydroxyproline, proline, and glycine (ie, the main amino acids in collagen) using high performance liquid chromatography (HPLC). The data indicated a significant increase in total collagen content in granulation tissue that was treated with NPWT/ROCF in conjunction with saline instillation and a dwell time of 60 minutes. In addition, the collagen data was highly suggestive of an increase in total collagen content in wounds treated with instillation therapy and a dwell time of 5 minutes. Since collagen is the predominant structural ECM molecule in cutaneous tissue and is crucially important for providing tensile strength and integrity to the regenerated skin, an increase in total collagen content in the granulation tissue is suggestive of an increase in the quality of the regenerated granulation tissue. A key limitation to this assessment was that wound biopsies were only taken at day 9. This was done to avoid affecting the wound volume measurements that were obtained during the study. Future experiments will look at the effects...
of instillation therapy on the extracellular matrix at various time points to correlate these results with the wound volume measurements.

Conclusion

The data presented herein indicate that in a preclinical wound model, instillation therapy with saline provides an additional benefit to NPWT/ROCF. The instillation of saline 4 times per day led to significantly increased wound fill at days 6 and 7. Not only was the wound fill increased but the quality of granulation tissue was also increased as evidenced by increased collagen content. Together, these data indicated an improved healing response in this model during treatment with saline instillation therapy. An additional consideration is that NPWT/ROCF was shut down for either 5 or 60 minutes around 4 times per day during instillation therapy. As such, this could be considered a form of intermittent NPWT, which may have a role in the results that were observed in this study since intermittent NPWT/ROCF has previously been shown to increase granulation tissue formation compared to continuous NPWT/ROCF. However, unpublished data from our group showed an added benefit with the instillation of normal saline versus intermittent NPWT alone. Future studies will define the role of intermittency as part of instillation therapy as well as how to optimize these conditions. This will allow us to determine if additional benefit may be achieved by varying the dwell time and/or the number of instillations per day.

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References


