Negative-Pressure Wound Therapy I:
The Paradox of Negative-Pressure Wound Therapy

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Abstract

Background: Does negative-pressure wound therapy reduce or increase the pressure of wound tissues? This seemingly obvious question has never been addressed by a study on living tissues. The aim of this study was to evaluate the nature of tissue pressure changes in relation to negative-pressure wound therapy.

Methods: Three negative-pressure wound therapy dressing configurations were evaluated - circumferential, noncircumferential, and those within a cavity - on 15 human wounds, with five wounds in each category. Tissue pressure changes were recorded (using a strain gauge sensor) for each 75-mmHg increment in suction, up to 450 mmHg. In the circumferential and noncircumferential groups, tissue pressure was also measured over a 48-hour period at a set suction pressure of 125 mmHg ($n = 10$).

Results: In all three groups, mean tissue pressure increased proportionately to the amount of suction applied ($p < 0.0005$). Mean tissue pressure increments resulting from the circumferential dressings were significantly higher than those resulting from the noncircumferential ($p < 0.0005$) or cavity group ($p < 0.0005$); however, there was no significant difference between the latter two groups ($p = 0.269$). Over the 48-hour period, there was a significant mean reduction in the (increased) tissue pressure ($p < 0.04$ for circumferential and $p < 0.0005$ for noncircumferential), but in only three of 10 cases did this reduce to pressures less than those before dressing application.

Conclusions: Negative-pressure wound therapy increases tissue pressure proportionately to the amount of suction, although this becomes less pronounced over 48 hours. This suggests that negative-pressure wound therapy dressings should be used with caution on tissues with compromised perfusion, particularly when they are circumferential.

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Negative-pressure wound therapy has revolutionized wound care since it was popularized by Morykwas et al. and Argenta and Morykwas in 1997.[1,2] Its versatility has resulted in it being used in every surgical discipline. Despite many theories, however, the mechanism of action of negative-pressure wound therapy remains largely unknown. A common assumption is that the reduction of tissue pressure caused by the hypobaric environment within the dressing results in a reduction in edema and an increase in perfusion.[1-6] A recent study, however, has demonstrated that although the air pressure in the foam may be decreased, the pressure in the underlying substance on which the foam is placed is paradoxically increased.[7] This increased pressure occurred regardless of whether the negative-pressure wound therapy dressing is circumferential or not, and is directly proportional to the amount of suction applied. A limitation of that study was that it was carried out on inanimate material, which may not share the same pressure distribution characteristics as living tissue.

Understanding how the pressure within living tissues responds to negative-pressure wound therapy is fundamental to understanding its mechanism of action. The aim of this study was to assess whether human tissue pressures increase or decrease in response to varying degrees of negative-pressure wound therapy. Tissue pressure changes over the first 48 hours were also evaluated.

Patients and methods

As with the previous study on inanimate materials, three fundamentally different negative-pressure wound therapy configurations were assessed: circumferential, noncircumferential, and foam placed in a cavity. The term “circumferential negative-pressure wound therapy” implies there is foam in contact with the entire circumference of the limb. The foam used was reticulated, open- cell, polyurethane foam (Kinetic Concepts, Inc., San Antonio, Texas). When testing tissue pressure changes over 48 hours, a Kinetic Concepts pump (or KCI pump) set at -125 mmHg was used.

This pump does not generate pressures higher than -200 mmHg; therefore, to test the effects of suction pressures up to -500 mmHg, a medical suction pump (Schuco, Carle Place, N.Y.), with an accurate pressure gauge, was used.

"Tissue pressure" in this article refers to the mechanical pressure measured within the tissues (i.e., the interstitial hydrostatic pressure). It is this pressure that, if greater than capillary intravascular pressure, will result in capillary occlusion. This was measured using an intracranial tissue pressure microsensor (Codman/Johnson & Johnson, Raynham, Mass.). This strain-gauge transducer can accurately (within 1 mmHg) measure both positive and negative pressure in gas, liquid, and soft tissue inside the cranium. Its small size allows for pressure measurement, with minimal disruption of tissues (Fig. 1). Measuring exact intracranial pressure is possible because the cranial vault is essentially a rigid container. In tissues (e.g., a muscle) that are not encased in a rigid structure, pressure variations in response to an external force depend on where the measurement is taken. Therefore, for the purposes of this study, "specific pressures" were not considered as important as "pressure changes" at a given point. For this reason, the pressure transducer was zeroed after placement, allowing for recording of pressure changes above or below baseline pressures, rather than actual tissue pressures. To ensure correct functioning of the sensor in situ, the transducer was tested after placement by applying manual pressure to the tissues, which would result in increased tissue pressure measurements.

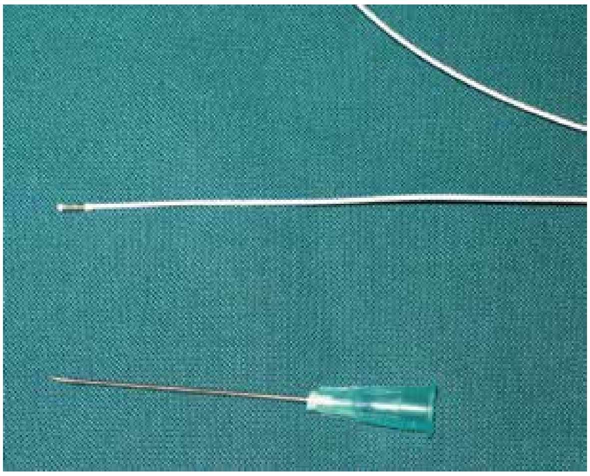

Figure 1. Codman's intracranial pressure sensor, with a 21-gauge needle for comparison.

A total of 14 patients were recruited into the study, with one patient being used twice with the sensor in different areas (15 tests). Four patients had wounds requiring a circumferential negative-pressure wound therapy dressing, five had wounds requiring a noncircumferential negative-pressure wound therapy dressing, and the other five required a negative-pressure wound therapy dressing to be inserted into a cavity. All patients gave informed consent to having the sensor placed, and the study was approved by the institutional review board. The only exclusion criteria were wounds in children, nonconsenting adults, and wounds in which negative-pressure wound therapy was contraindicated according to current guidelines.[8,9]

Circumferential Negative-Pressure Wound

Therapy Dressings

The wounds that required circumferential negative-pressure wound therapy were all hand injuries, most of which had relatively contaminated wounds that precluded immediate reconstructive surgery (Fig. 2). After initial debridement of the wounds, the microsensor was placed through the existing wound into the surrounding tissues, at different anatomical locations in each hand. The first patient had undergone flap surgery 1 week earlier to resurface a wound but was complicated by partial necrosis of the flap. The necrotic portion was débrided and the sensor was placed beneath the remaining viable flap and a circumferential negative-pressure wound therapy dressing (V.A.C. Granufoam Hand Dressing; Kinetic Concepts) was applied. One week later, this patient was taken to operating room again to cover the remaining palmar wound with a full-thickness skin graft. Circumferential negative-pressure wound therapy was again used, this time to secure the graft. On this occasion, the sensor was tunneled and placed beneath the dorsal skin of the proximal phalanx of the index finger. The second patient had the sensor placed beneath the skin overlying the dorsum of the middle phalanx of the middle finger. The third case had the sensor placed over the third metacarpophalangeal joint, and the fourth case had the sensor placed in the second web space.

Figure 2. Photograph demonstrating deep abrasion on the dorsum of the hand. Application of a circumferential negative-pressure wound therapy dressing is not only beneficial to the wound but reduces edema in the entire hand.

Care was taken to not allow the sensor to be in communication with the air pressure over the wound, as this would be a measurement of the suction pressure rather than the tissue pressure. With the dressing in place, the transducer was zeroed. Suction pressure was then increased gradually from 0 through -450 mmHg at -75-mmHg increments. Tissue pressure changes were recorded for each increment of suction pressure. Suction was then switched off and tubing disconnected, allowing the foam to reexpand. After 1 minute, the sequence was repeated, for a total of five times. The means of the five values for each increment were calculated.

After this, the negative-pressure wound therapy dressing was then connected to the quieter Kinetic Concepts pump with a preselected suction pressure of -125 mmHg. Tissue pressure readings were recorded every hour for 48 hours. On completion of the experiment, the negative-pressure wound therapy dressing was removed, the transducer was withdrawn from the tissues, and wounds were managed on their own merits.

Noncircumferential Negative-Pressure Wound

Therapy Dressings

Any wounds that required a negative-pressure wound therapy dressing that was neither circumferential nor placed in a cavity were included in this arm of the study (Fig. 3). After intraoperative débridement, the transducer was inserted approximately 5 mm deep to the surface of the wound bed. The negative-pressure wound therapy dressing was placed over the wound, the transducer was zeroed, and the same experimental sequence was then followed as for the circumferential negative-pressure wound therapy group. The following cases were enrolled in this part of the study: a forearm wound, a scalp abrasion, a heel wound, and two thigh degloving wounds.

Figure 3. Photograph showing a thigh wound on an obese woman before placement of a noncircumferential negative-pressure wound therapy dressing.

Cavity Negative-Pressure Wound Therapy

Dressings

The wounds that were selected for this part of the study were those that formed a deep cavity (Fig. 4). Unlike the previous two categories, where most of the foam lies *on top* of the wound, these wounds result in the foam lying *inside* the wounds, with the outer surface of the foam being essentially flush with the skin before suction is applied (Fig.5). The reason for cavity wounds being placed in a category of their own was because, in this scenario, it can be envisaged that the foam will attempt to suck the walls of the cavity inward, thereby reducing the surrounding tissue pressure. This is in contrast to the previous two categories, where the foam merely collapses down onto the underlying wound.

Many of these cavity wounds had bone or very little soft tissue in the base of the wound, making placement of the sensor in the base of the wound difficult. The sensor was therefore inserted (through a puncture wound through intact skin) into one of the walls of the cavity, 1 cm away from the cavity and 1 cm deep to the surface of the normal tissues (Fig. 5, *below*). As with the aforementioned experiments, tissue pressures were measured for different suction pressures. Most patients in this category were paraplegics who were frequently rotated to prevent further pressure sores. As this would interfere with readings, no monitoring over 48 hours was performed in this group.

One ischial and three trochanteric bedsore cavities were included in this category. The fifth patient had a septic spinal wound dehiscence following excision of a meningioma.

Figure 4. Deep ischial pressure sore cavity before a negative-pressure wound therapy dressing being inserted, with the pressure sensor in place in the wall (1 cm deep to skin and 1 cm from the cavity).

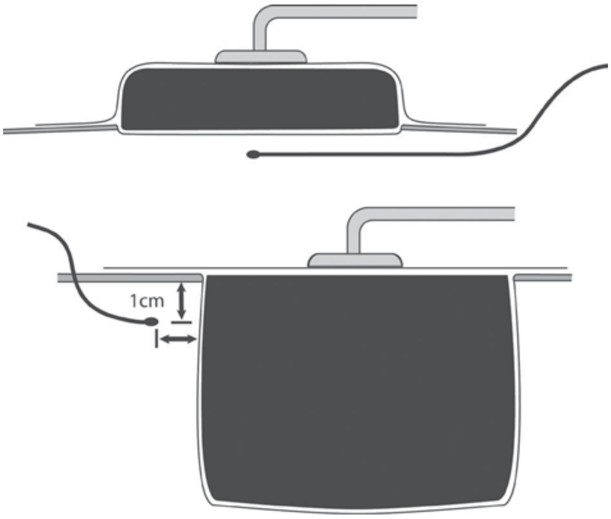

Figure 5. Cross-sectional diagrams illustrating a negative-pressure wound therapy dressing on a conventional wound (*above*) and inside a cavity (*below*), where the foam is essentially flush with the skin. Note that the sensor is within the wound tissue.

Statistical Analyses

The change in tissue pressures are presented as mean values with standard deviations. Data for suction pressure increments were analyzed using the repeated measures analysis of variance with pressure as a factor (with values of $p < 0.05$ regarded as significant) using SPSS version 14 (SPSS, Inc., Chicago, Ill.). Change in pressure with time was assessed by estimating the mean gradients (ß, the standardized regression coefficient) using regression analysis. To determine whether circumferential and noncircumferential dressings had a differential effect, this variable was added to the regression analysis.

Results

The sensor recorded increased tissue pressures when manual pressure was applied to the foam over the wound in all wound groups, before starting the experiment. This demonstrated that the sensor was detecting the appropriate pressure changes in the tissues. None of the patients developed complications as a result of the indwelling pressure sensor.

Circumferential Negative-Pressure Wound

Therapy Dressings

In this dressing group, there was a significant increase in tissue pressure on application of suction ($p < 0.005$), with increasing suction pressures generating increased tissue pressures (Fig. 6). There were no negative pressures recorded.

Over the 48-hour period, the increased tissue pressure decreased significantly (ß = -0.21, $p = 0.04$) for this group. When evaluated individually, there was a significant reduction of the (increased) pressure in three of the five cases (Figs. 7 and 8, with *p* values in Figure 7). In one case (with the sensor over the third metacarpophalangeal joint), the pressure increased gradually, although this was not statistically significant. One case (the hand that had the palmar full-thickness skin graft) was excluded from all statistical analyses because the suction pressure was altered during the experiment. This was because the increased tissue pressure caused progressive pain in the patient's fingertips, resulting in the surgeon reducing the suction pressure to -75 mmHg. This was performed after 28 hours and tissue pressures were seen to reduce accordingly, as did the patient's pain. The resultant trendline of the pressures in this particular case should therefore not be taken into account. Despite reducing the suction pressures in this case, however, tissue pressures gradually continued to rise.

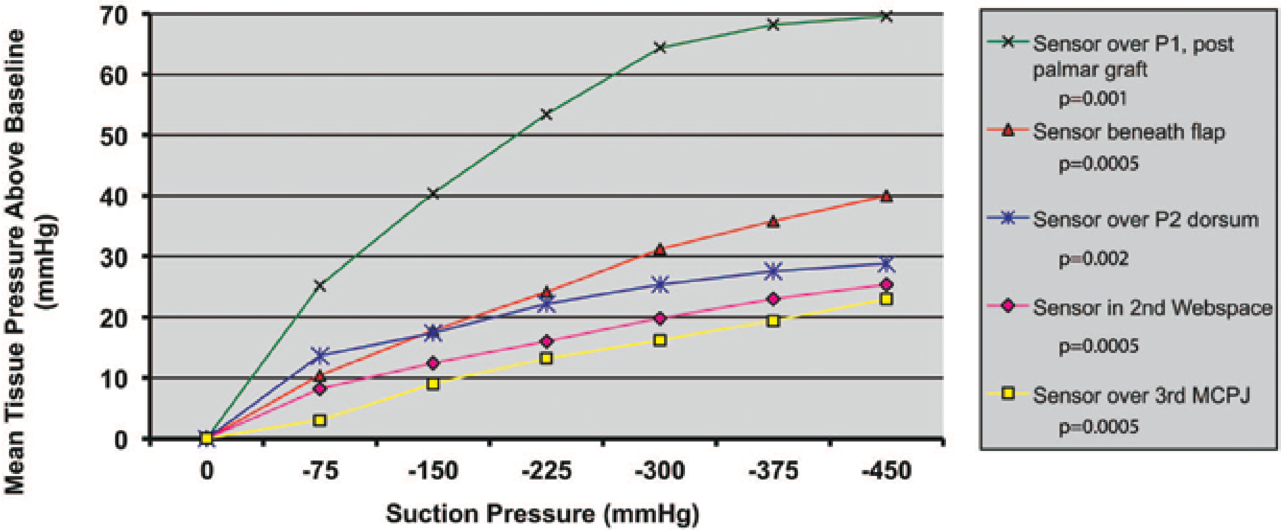

Figure 6. Graph showing increasing tissue pressures beneath circumferential negative-pressure wound therapy dressings in response to increasing suction pressure. The *p* values refer to significance of the gradients of the curves. *P1*, proximal phalanx; *P2*, middle phalanx; *MCPJ,* metacarpophalangeal joint.

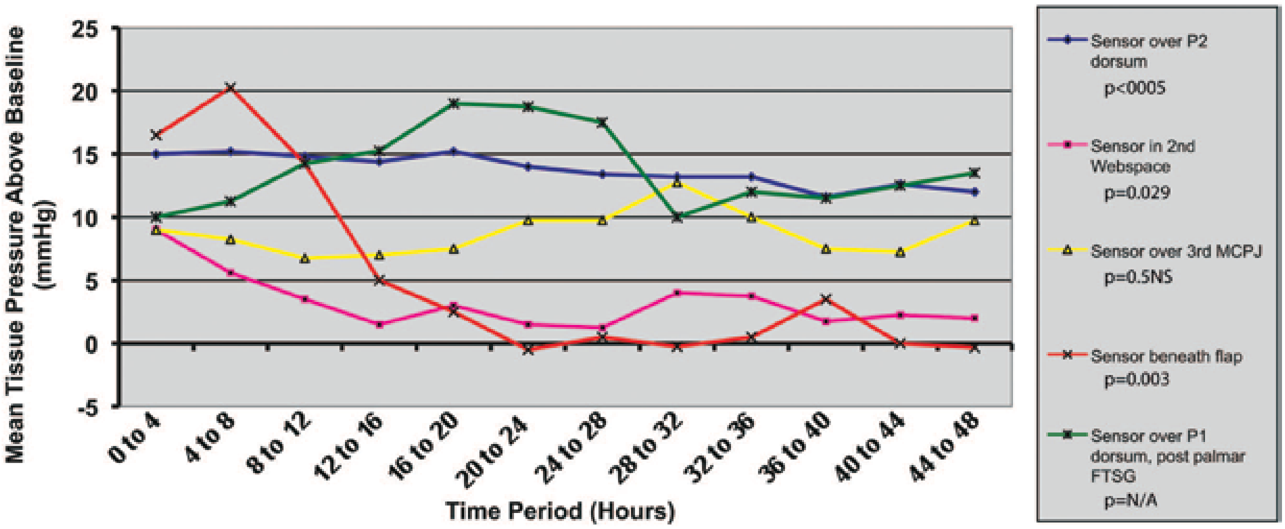

Figure 7. Graph showing a gradual decline of increased tissue pressure (above baseline) for wounds undergoing circumferential negative-pressure wound therapy over a 48-hour period. The *p* values refer to significance of the gradients of the curves. *P1*, proximal phalanx; *P2*, middle phalanx; *MCPJ*, metacarpophalangeal joint; *FTSG,* full-thickness skin graft.

By the end of the 48-hour period, only one case (sensor beneath flap) demonstrated pressures less than the baseline pressure. In this patient, the return to baseline was reached after 24 hours.

Noncircumferential Negative-Pressure Wound

Therapy Dressings

In this group, too, tissue pressures increased significantly ($p < 0.005$) in proportion to suction (Fig. 9). There were no negative pressures recorded.

For the group as a whole, there was a significant reduction of the (increased) pressure over the 48-hour period (ß = -0.494, $p < 0.0005$). Individual analyses revealed that three of the five wounds had a significant reduction (Figs. 10 and 11). The reduction in the two thigh wounds was not significant. In two of the wounds (forearm and scalp), the (increased) pressure decreased to a level below the initial baseline pressure at the conclusion of the experiment. This was accomplished after 38 and 43 hours for the forearm and scalp wounds, respectively.

Negative-Pressure Wound Therapy Dressings in Cavities

There was a significant increase in tissue pressure in relation to suction pressure in four of the five wounds in this group (Fig. 12, with relevant *p* values). The tissue pressure in the dehisced spinal wound did not increase significantly with suction ($p = 0.51$).

The mean increase in tissue pressures in the circumferential dressing group was significantly greater than that of the noncircumferential group ($p < 0.0005$) or the cavity group ($p < 0.0005$), although the difference between the latter two groups was not statistically significant ($p = 0.269$).

The mean reduction in increased tissue pressure over the 48-hour period was significantly more in the noncircumferential group than in the circumferential group ($p < 0.0005$), although both groups demonstrated a significant reduction.

Discussion

In all categories, the sensor demonstrated a mean increase in tissue pressure in relation to the amount of suction applied. The increase in tissue pressure was most pronounced in the wounds in the

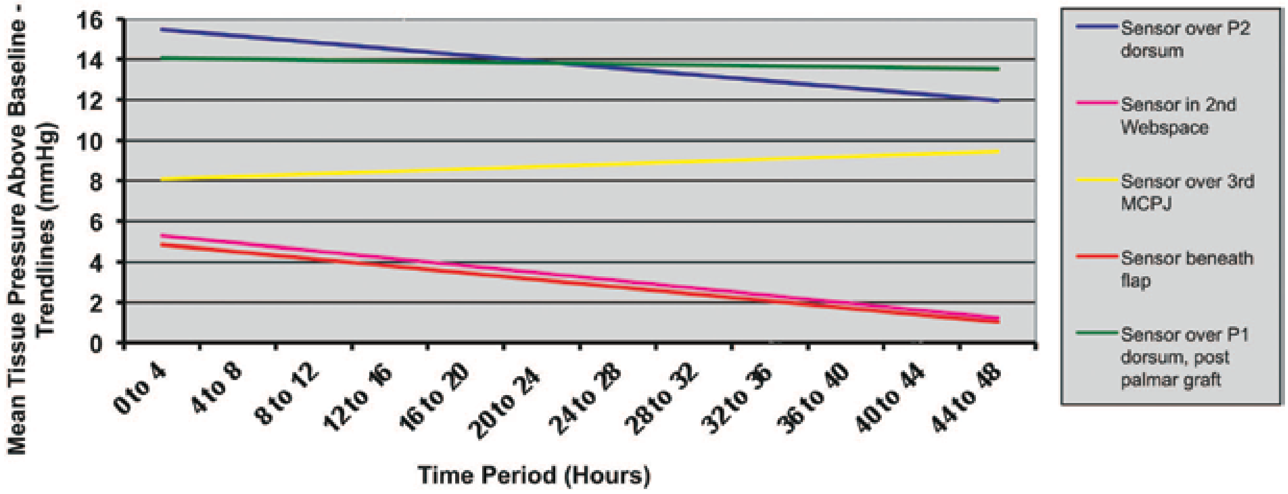

Figure 8. Graph illustrating a trend for the increased tissue pressure (above baseline) to reduce over 48 hours during circumferential negative-pressure wound therapy. *P1*, proximal phalanx; *P2*, middle phalanx; *MCPJ*, metacarpophalangeal joint.

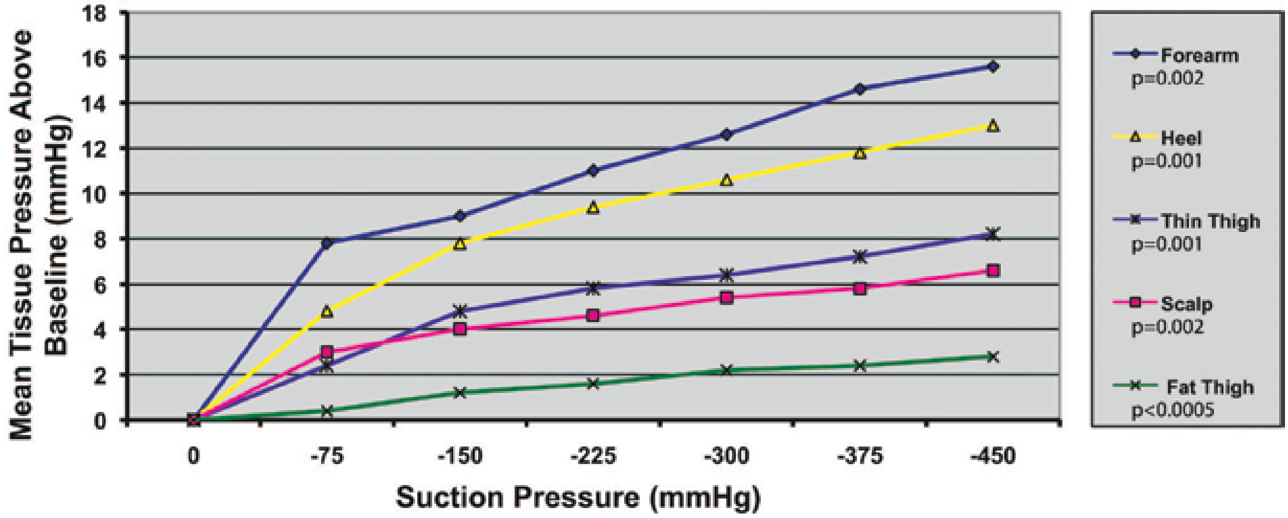

Figure 9. Increasing tissue pressure beneath a noncircumferential negative-pressure wound therapy dressing in response to increasing suction pressure. The *p* values refer to significance of the gradients of the curves.

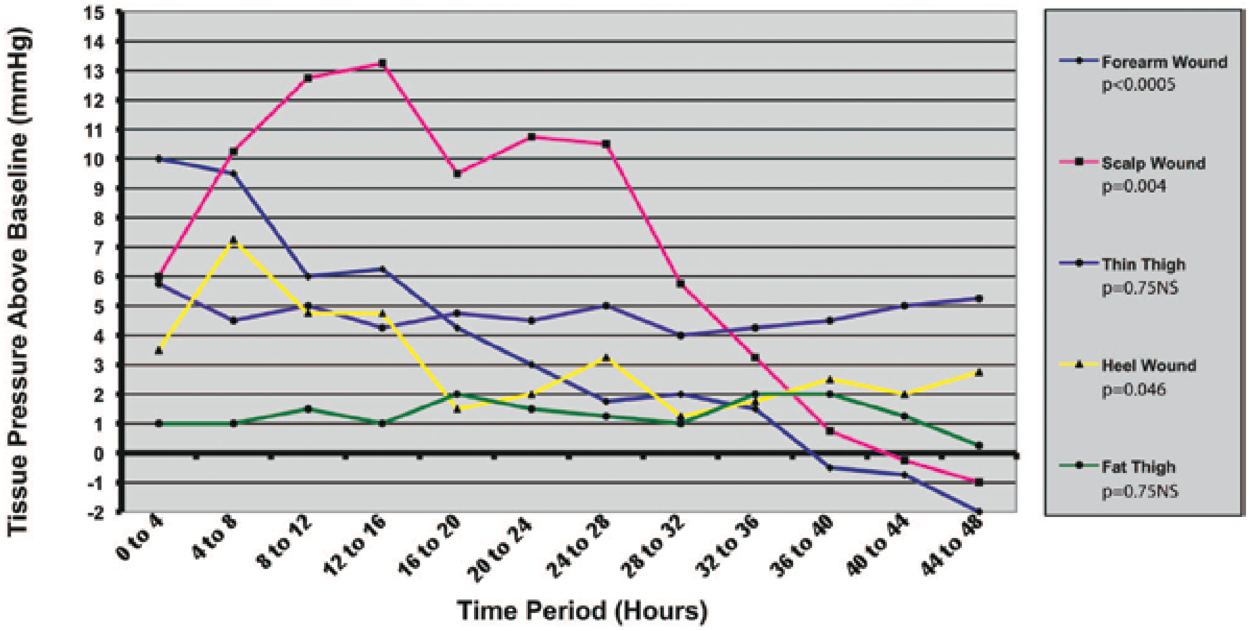

Figure 10. Graph demonstrating the gradual decline of increased tissue pressure (above baseline) for wounds undergoing noncircumferential negative-pressure wound therapy over the 48-hour period. The *p* values refer to significance of the gradients of the curves.

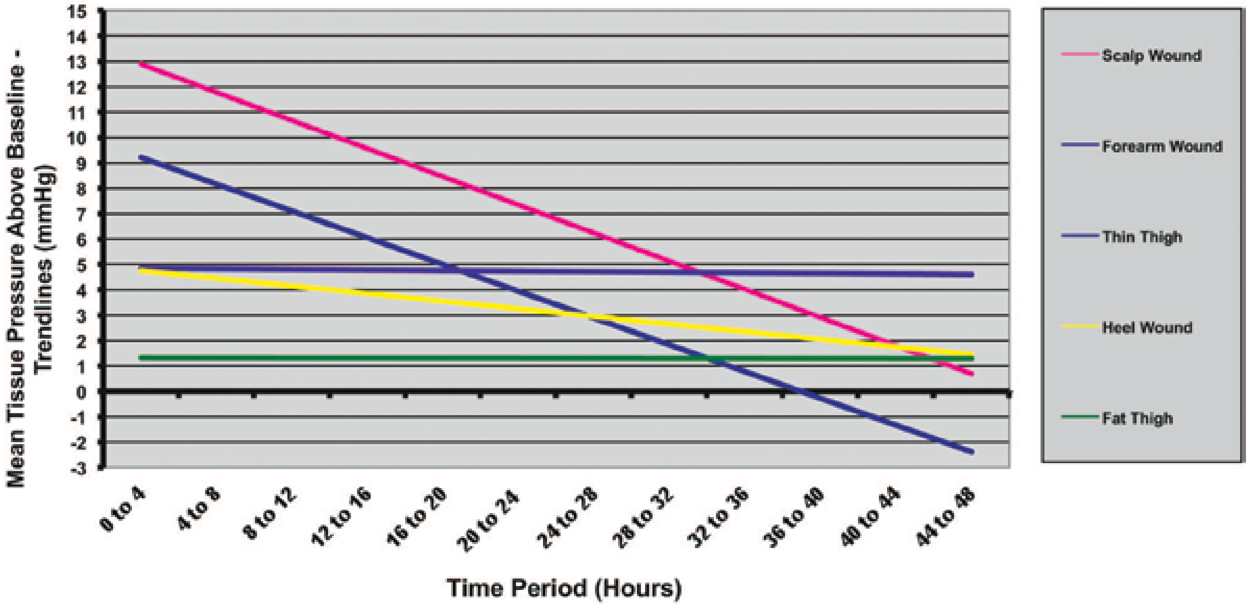

Figure 11. Graph illustrating a trend for the increased tissue pressure (above baseline) to reduce over 48 hours during noncircumferential negative-pressure wound therapy.

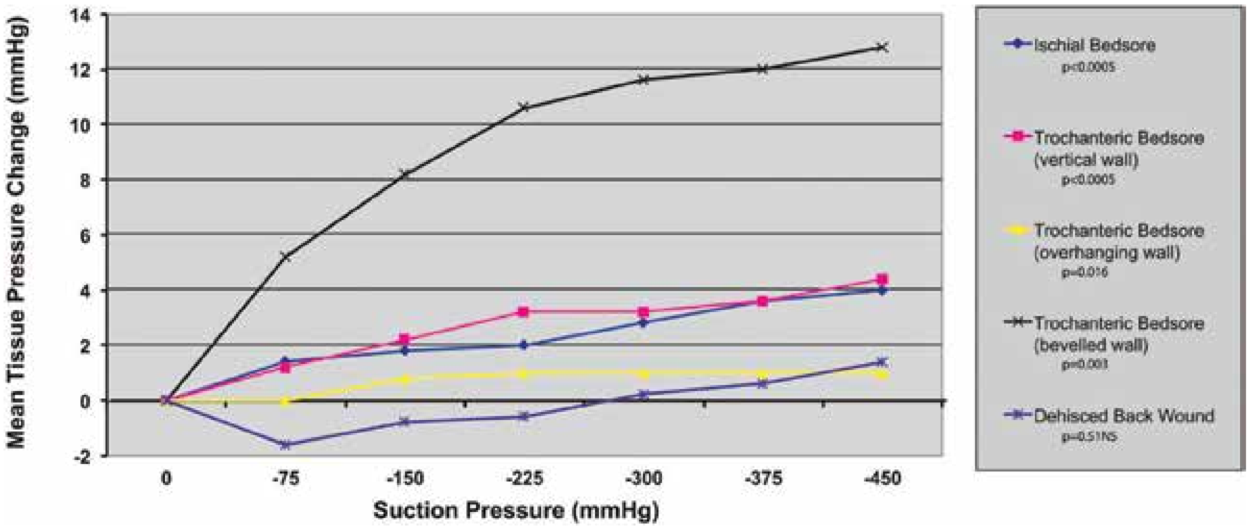

Figure 12. Tissue pressures in the walls of a cavity undergoing negative-pressure wound therapy increase proportionately to increasing suction pressure. The *p* values refer to significance of the gradients of the curves.

circumferential negative-pressure wound therapy category and least pronounced in the cavity wounds.

The increased pressure in six of the 10 wounds monitored over 48 hours reduced substantially with time, but only three of the 10 decreased to levels below the pre–negative-pressure wound therapy baseline pressures. The soonest this occurred was after 24 hours. In two of the 10 cases, tissue pressure increased even further with time. Both of these cases belonged to the circumferential negative-pressure wound therapy category. In three of the 10 cases, tissue pressure remained 10 mmHg or more above recorded baseline pressures after 48 hours. In normal tissue, which has a capillary perfusion pressure ranging from 10 to 35 mmHg,[10] negative-pressure wound therapy is unlikely to cause capillary occlusion. However, in tissue with severely compromised perfusion, the capillary perfusion pressures may be so low that an increment in tissue pressure of 10 mmHg (or even less) may be sufficient to cause capillary occlusion and tissue necrosis, particularly if this is continued for longer than 24 hours.

At a given suction pressure, there was a wide variation of increased tissue pressures for different wounds. This questions the recommended use of a standard suction pressure of -125 mmHg on all wounds. Adapting the suction pressure to the consistency and type of tissues, and the status of perfusion, may be a more scientific approach and is currently the subject of ongoing research at this center.

These findings represent a paradigm shift in our understanding of the physics of negative-pressure wound therapy and conflict with the popular perception that negative-pressure wound therapy reduces tissue pressure. A clear understanding of the physics relating to negative-pressure wound therapy dressings should be the first step toward understanding their mechanism of action, and this alternative perspective allows for new research avenues to be explored. The following novel theories can now be put forward regarding the mechanism of action of negative-pressure wound therapy:

1. The compression of tissue by negative-pressure wound therapy will decrease perfusion beneath the foam, as recently demonstrated in research at this center.[11] These shear forces and concurrent hypoxia are recognized stimuli for angioneogenesis, a key component of granulation tissue formation.[12,13]
2. Tissue hypoxia results in release of nitric oxide and local vasodilatation. This aspect, however, would only be beneficial once the suction is removed or during the “suction-off” periods of intermittent negative-pressure wound therapy. The perfusion during this “off” period is increased because of the reactive hyperemia,[3,5] which is likely to follow. This may explain why intermittent negative-pressure wound therapy has been found to be more advantageous than continuous.[1]
3. Physiologic interstitial fluid hydrostatic pressure is usually hypobaric (approximately -1 mmHg).[14] It has been demonstrated that with injury, this hypobaric pressure can decrease rapidly even further (up to -30 mmHg).[14] This, together with increased permeability of vessels caused by inflammation, greatly contributes to the formation of edema. The increased tissue pressure generated by negative-pressure wound therapy is likely to reduce, if not reverse, this process.
4. Compression of a vessel through which fluid is flowing results in increased velocity of the fluid (known in physics as the principle of continuity). When fluid velocity is increased in a vessel, this fluid’s hydrostatic pressure decreases (Bernoulli’s principle). This reduced intravascular pressure, in combination with the increased tissue pressure, would result in less efflux of plasma from the vessel, resulting in decreased edema.
5. The increased blood velocity is more likely to draw extracellular fluid into the vessel, on the basis of the Venturi principle (Fig. 13).
6. In addition to the edema reduction of the last two mechanisms, the compressive forces of negative-pressure wound therapy may physically force edema away from the injured tissues in a manner similar to an anti-edema garment. This will ultimately result in less interstitial hydrostatic pressure, less compression of the vessels, and also improved oxygen and nutrient diffusion to the cells. It is the authors’ impression that this is likely to be the most important contribution of negative-pressure wound therapy.
7. Splinting of the wound, which is achieved by this positive pressure, also aids in wound healing.[15,16]

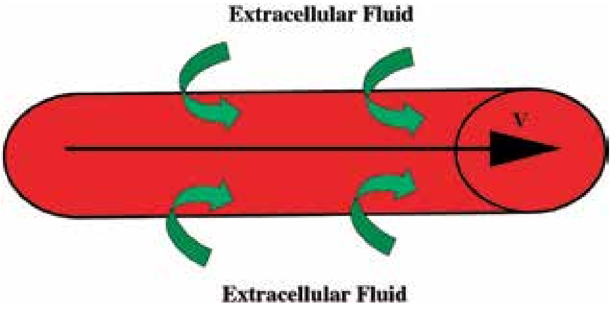

Figure 13. As blood velocity (v) increases, an increasing amount of extracellular fluid is drawn into the vessel, based on the Venturi principle.

The above theories predominantly consider perfusion and edema reduction, but other factors also contribute. The theory on microdeformation/microstrain at the wound interface[17] causing effects similar to tissue expansion, with release of growth factors, offers another mechanism. Although the net pressure inside the tissue is positive, the pressure on the portion of tissue cells directly beneath a pore of the foam may in fact still be negative, resulting in microexpansion on those particular cells. This could explain why granulation tissue occurs much faster beneath the black polyurethane foam, which has larger pores than the white polyvinyl alcohol foam. This theory has found support in recent studies.[18,19]

Similar effects also occur at a macroscopic level (macrostrain), when wound edges are pulled closer to one another when the foam volume reduces in size.

Conclusions

Negative-pressure wound therapy dressings appear to increase tissue pressures in all types of wounds. This increase is directly proportional to the amount of suction applied and is most pronounced in circumferential negative-pressure wound therapy dressings. In most wounds, the increased pressure gradually reduces over 48 hours and may decrease to levels lower than recorded baseline pressures.

Although these findings give rise to a multitude of novel theories regarding the mechanism of action of negative-pressure wound therapy, concerns regarding the safety of negative-pressure wound therapy on tissues with compromised perfusion are also raised, particularly when circumferential negative-pressure wound therapy dressings are used or higher suction pressures are used.

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