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An Ex Vivo Study Measuring the Effects of Circumferential and Near-Circumferential Closed Incisional Negative Pressure Wound Therapy Dressings on a Porcine Model

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Abstract

To investigate the effects of circumferential and near-circumferential closed incisional negative pressure wound therapy (ciNPWT) dressings on compartment pressures within varying tissue levels using an ex vivo porcine model. A deceased swine model was utilized, with bilateral hind legs disarticulated and prepared for experimentation. ciNPWT dressings were applied at 100%, 75%, 50%, and 25% circumferential coverage, with negative pressures set at -200 mmHg, -125 mmHg, and -25 mmHg. A STIC pressure monitor device measured pressures at tissue depths of 10 mm, 20 mm, and 40 mm. Measurements were repeated 3 times for each configuration, and the averages were calculated. Compartment pressures increased with greater magnitudes of negative pressure and were highest at superficial tissue layers. The pressure differences between superficial and deeper layers were most pronounced in 25%-75% circumferential configurations, suggesting that non-circumferential dressings create a pressure gradient. These findings align with a compressive rather than a "lift-off" force mechanism. This study highlights ciNPWT's compressive effects, particularly on superficial tissues, and suggests that pressure gradients in non-circumferential configurations may enhance fluid dynamics and wound healing. The findings also support the potential role of ciNPWT in inducing mechanotransduction and angiogenesis. Limitations include the use of an ex vivo model and variability in measurement accuracy. Especially in superficial layers, ciNPWT exerts a compressive force with non-circumferential dressings allowing greater pressure gradients. Future in vivo studies are needed to confirm these findings and further explore the therapeutic mechanisms and potential applications of ciNPWT.

Abrreviations

ciNPWT= closed incisional negative pressure wound therapy
ECM=extracellular matrix
NPWT=negative pressure wound therapy

Introduction

Efforts to investigate negative pressure wound therapies effects on wound healing have increased since the 1997 study by Morykwas et al, which showed improved wound perfusion in a swine model utilizing negative pressure wound therapy (NPWT).[1,2] Likewise, improvements in technology have also continued, as exemplified by the advent of closed incisional negative pressure wound therapy (ciNPWT), a variation of NPWT, thus continuing to expand indications and applicability of a NPWT system.[3] Yet, even with accumulating studies examining clinical and surgical use or indications, understanding of physiologic effects and mechanisms remain incompletely understood.[4] Prior authors have postulated that mechanotransduction signaling resultant of microdeformation and macrodeformation from the interaction of soft tissue and NPWT sponge may be responsible.[5-8] In earlier literature, macrodeformation through compression in a circumferential NPWT led some to theorize there may be diminished perfusion distal to NPWT dressings in an extremity.[5] Though, in a recent study by Livingstone et al, the effects of circumferential and near circumferential ciNPWT on an elastic ball model suggested near-circumferential or circumferential NPWT at certain negative pressures may decrease the pressure of the extremity exposed to a NPWT system. Livingstone et al's findings seem to suggest, particularly in a near circumferential configuration, a "lift-off" force occurring rather than compressive force, which could possibly facilitate improved venous and lymphatic drainage from an extremity.[4] Even so, literature concerning NPWT or ciNPWT has yet to reliably or wholly explained its physiologic effects or mechanisms. This study aimed to examine compartment pressures within varying tissue levels at differing degrees of circumferential compression, and magnitudes of negative pressures in an *ex vivo* porcine tissue model. The authors hypothesize there would be higher compartment pressures at more superficial tissue layers, and a linear increase in compartment pressures at larger magnitudes of negative pressure, suggesting a more compressive force being imparted. The authors additionally theorized compartment pressure differences, between superficial and deeper layers, would have the greatest difference at circumferential and near circumferential ciNPWT dressing configurations.

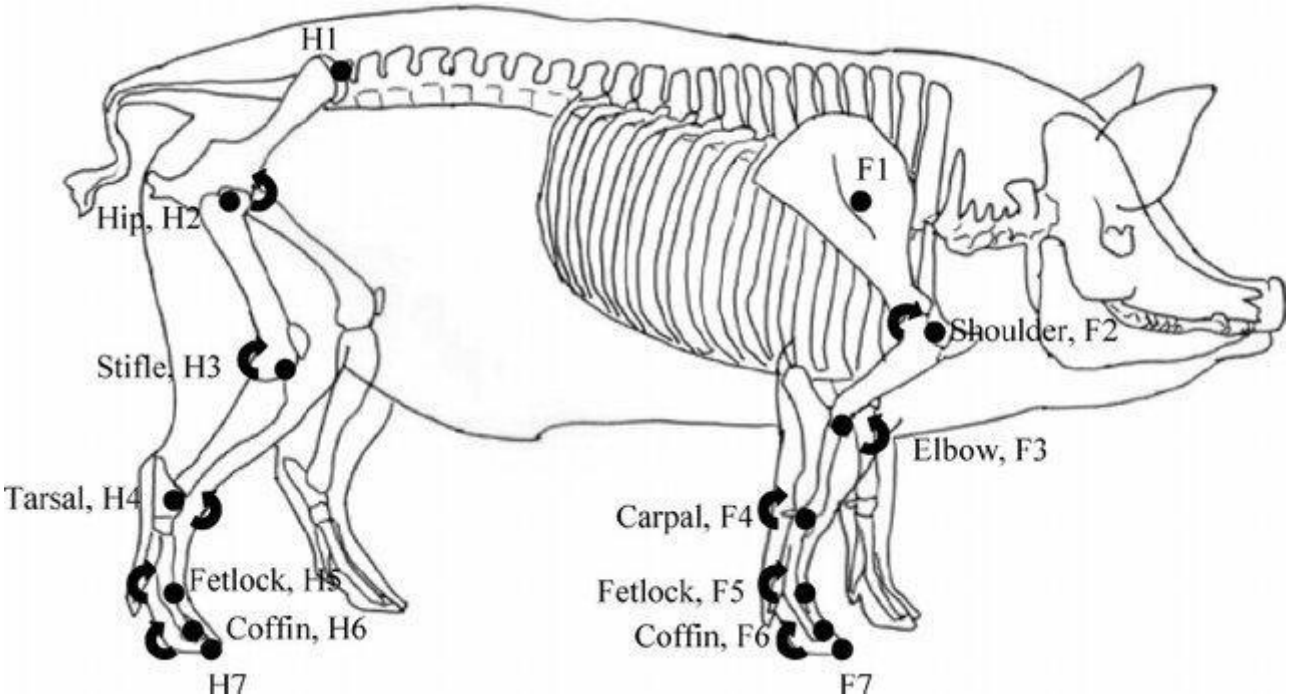

Figure 1. Labeled Joints of a Porcine Specimen[a]

[a]Used with permission from Thorup et al[9]

Methods

Preparation of specimen

A 27-pound deceased whole pig was purchased from a commercial retailer. Bilateral hind legs were disarticulated through the hip joints. Hind legs were then left to thaw until room temperature prior to further manipulation and to ensure compartments were not affected by frozen tissue conditions.

Measurement of tissue levels

One hind leg was chosen for determination of tissue level depth. An incision was made at a point approximately half the distance between the hip joint and stifle joint of the specimen (**Figure 1**). This incision was carried down to the porcine femur bone. There was negligible subcutaneous tissue, and the distance did not allow for adequate penetrance of the compartment measuring needle, therefore the distance from the skin to the most superficial muscular layer was measured and found to be 10 mm. The distance between skin and the intermediate muscular layer was then found to be 20 mm. And then the distance from skin to femur bone was then measured to be 40 mm.

Wound vac application

The negative pressure wound vacuum sponge was placed 100% circumferentially at a point corresponding to the center of the incision made on the contralateral leg. Wound sponge was then placed circumferentially, in a transverse orientation. Adhesive tape was placed over the sponge creating a seal, and the dressing was connected to negative pressure wound vacuum machine. Appropriate seal was confirmed on manufacturer's negative pressure wound vacuum machine (3M science, St. Paul, MN). This process of confirming appropriate seal was repeated for 75% circumferentially wrapped wound vac, 50% or 25%, with dressings in same place and orientation as placed in the 100% circumferentially wrapped configuration. An example of specimen preparation can be seen in **Figure 2**.

Measurement of pressures

A STIC pressure monitor device (C2Dx INC., Schoolcraft, MI), which included a pressure monitor console and accompanying needle, was used to obtain pressures at selected levels. Calibration was accomplished based on manufacturers recommendation. The needle was then introduced at a distance of 50 mm directly adjacent to sponge, at a point corresponding to the center of the incision on the contralateral leg, and directly adjacent to the lily pad suction tubing used to achieve negative pressure. At each tissue level, the compartment measuring needle was equilibrated to ensure accurate measurements according to manufacturer's recommendations. Prior to measurement, the pressures were recorded without any NPWT and found to 0 mmHg. The needle was then inserted at depths of 10 mm, 20 mm, and 40 mm. This process was repeated for all percentages of circumferential wound vacuum compression, and magnitude of negative pressures, including -200 mm Hg, -125 mm Hg, and -25 mm Hg. Compartment pressures were repeated a total of 3 times for each magnitude of negative pressure, tissue level, and degree of circumferential wrapping configurations, and the averages were calculated.

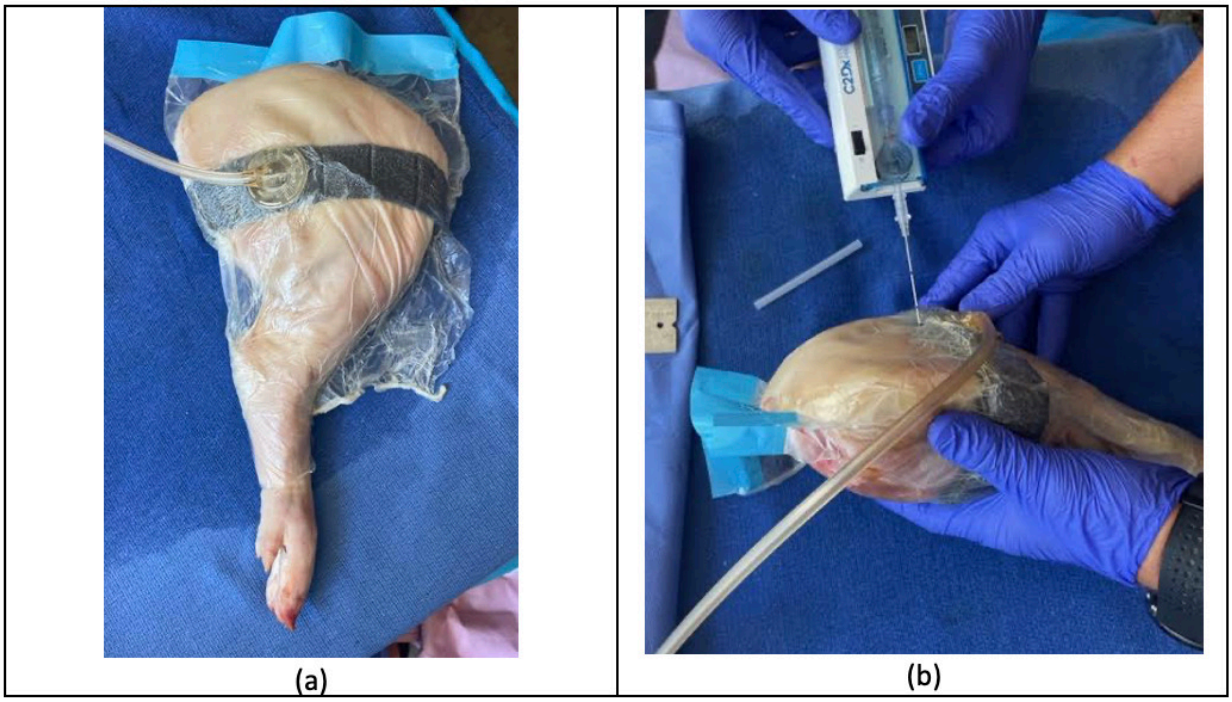

Figure 2. Specimen Preparation and Illustration of Compartment Pressure Measurement

a) Specimen with dressing and negative pressure wound vacuum sponge b) Using compartment pressure device to collect data

The data was recorded in a Microsoft Excel Spreadsheet (Microsoft Corp, Redmond, WA)

Results

The results can be observed in **Table 1** and **Figure 3**. Compartment pressures remained low regardless of negative pressure setting, thus increasing negative pressure value did not translate into meaningful deep tissue compression. Compartment pressures tended to be lower with 100% circumferential dressing configuration. Pressures were at the highest between 25% and 75% circumferential configurations.

Discussion

While NPWT and ciNPWT have become increasingly utilized augments for wound management, the mechanisms of action by which they appear to affect wound healing are not fully elucidated.[1-3] Very few studies in the literature have examined the measurable compartment pressures within tissues subjected to NPWT or ciNPWT.[10] This study, is the first to the authors' knowledge, examining pressures within various tissue levels at varying absolute values of negative pressure and varying percentage of circumferential dressing configurations. The findings in this study seem to suggest a more compressive force, particularly at more superficial layers of tissue, imparted by the ciNPWT and NPWT, rather than a "lift off" phenomenon.[4] There were greater increases in pressures at more superficial layers at greater absolute magnitudes of negative pressures, suggesting greater magnitudes of negative pressure increase the compressive force on underlying tissues. Prior literature has examined the effects of a compressive force's effects on affected tissues, and specifically angiogenesis, though not in a NPWT setting. Ruehle et al found immediate load initiation on nascent microvascular vascular sprout tips inhibited angiogenesis, while delayed compression of extracellular matrix (ECM) increased microvascular formation, and additionally upregulated upstream signaling pathways. Their research suggested not only timing, but mode, and magnitude of a compressive force may affect angiogenesis.[11] This could explain why negative pressure wound therapy has been associated with improved wound healing and increased angiogenesis.[7,12] The mechanism by which a compressive force induces angiogenesis was evaluated by Vaeyens et al, who described a tractional force between ECM and vasculature at the microscopic level facilitated by cytoskeletal components linking the nascent vasculature to the surrounding ECM, inducing budding angiogenesis.[12] A pressure gradient created by ciNPWT or NPWT, as seen in this study, in theory could provoke an angiogenic response by inducing mechanical stimuli facilitated by the ECM and its cytoskeletal connections to nascent vasculature, as understood by works from Vaeyens et al and Ruehle et al.[11, 12] This concept of a pressure gradient was also discussed in a study by Murphey et al examining penetrance of negative pressure in a NPWT model, in which the authors also postulated a potential pressure gradient created under the dressings, and subsequent fluid movement due to these pressure differences.[10] The resultant fluid dynamics and pressure gradient could additionally be enhancing edema clearance, which has been linked with improved wound healing.[13-15] Based on these findings, it is theoretical that NPWT, in part, may be inducing mechanical stimuli both directly to nascent or budding vasculature and indirectly by inducing a

Table 1. Compartment Pressures Measured at 10 mm, 20 mm, and 40 mm Depth Using Varying Negative Pressures and Dressing Configurations

Dressing Type	Pressure Setting (mmHg)	Pressure (mmHg) at 10 mm	Pressure (mmHg) at 20 mm	Pressure (mmHg) at 40 mm
100% Circumferential NPWT	-200	4.2	3.5	0.5
	-125	3.3	4.2	2.2
	-25	3.2	3.8	1.2
75% Circumferential NPWT	-200	7.0	7.0	7.0
	-125	10.0	5.0	1.0
	-25	7.0	2.0	1.0
50% Circumferential NPWT	-200	5.0	4.0	3.0
	-125	4.0	3.0	3.0
	-25	6.0	5.0	3.0
25% Circumferential NPWT	-200	8.0	3.0	0
	-125	4.0	1.0	1.0
	-25	4.0	1.0	0

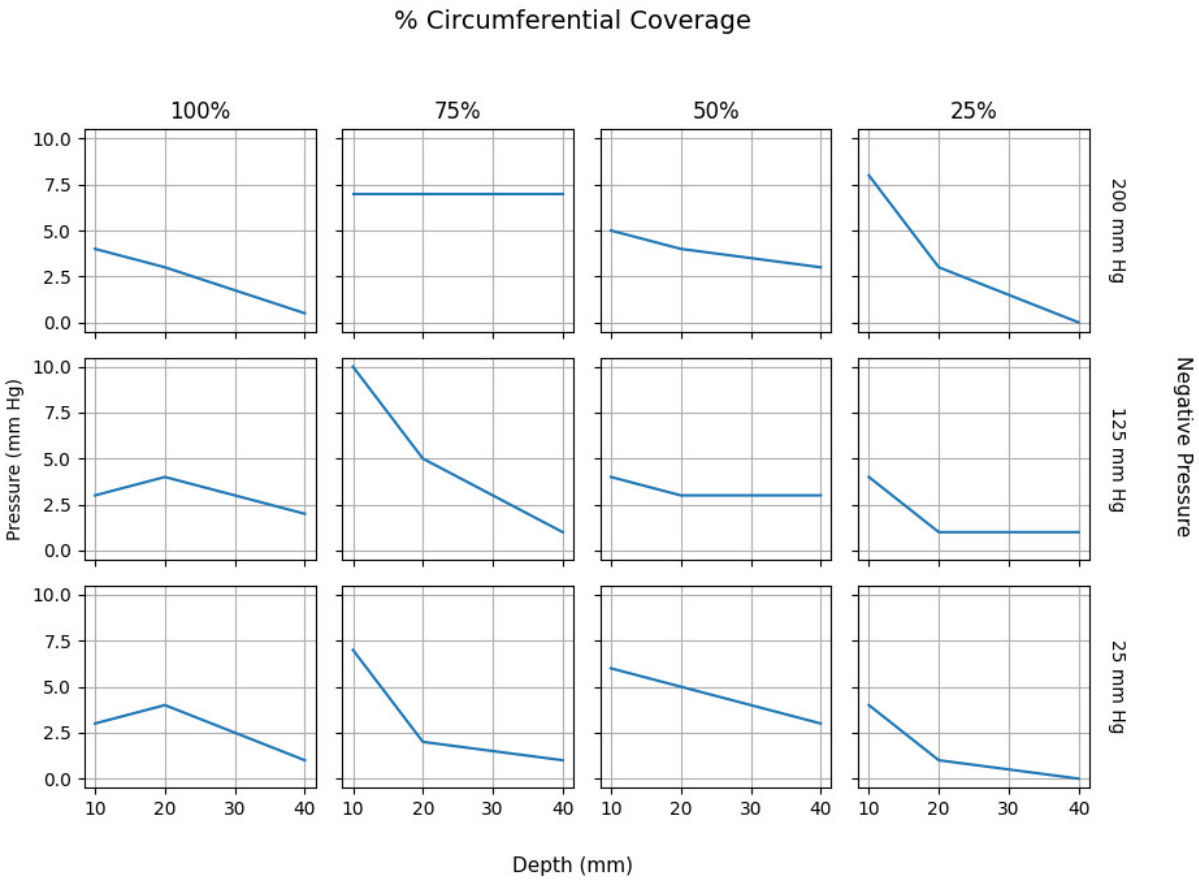

Figure 3. Compartment Pressure Measurements on Circumferential and Near-Circumferential Closed Incisional Negative Pressure Wound Therapy Dressings

mechanical stimuli within interstitial fluid and extracellular matrix, as well as augmenting fluid dynamics to enhance angiogenesis and wound healing. Based on the findings of this study, whatever downstream effects NPWT or ciNPWT may be inducing appear to be via a compressive force imparted from the NPWT or ciNPWT dressings, rather than an externally produced negative pressure in the underlying tissues.

Another novel aspect of this study was examining the effects of different dressing configurations. Prior work by Livingstone et al also examined differing degrees of circumferential dressing coverage. In their elastic ball model, they

noted the greatest effects on pressure were seen in configurations between 20%-90% of circumferential coverage, with the greatest effect at a 66% of circumferential coverage.[4] In this study, the greatest differences in pressures were observed in the 25%-75% of circumferential configurations. The authors believe this may due to non-circumferential configurations allowing tissue and fluid shifts into the portion of the body not in contact with wound vacuum dressings. These "far side" of the models were not subject to a compressive force in a circumferentially dressed configurations, thus allowing for a greater gradient to occur with consistently higher tissue pressures seen at tissue levels closer to the sponge dressing in the non-circumferential configurations. In a full circumferential dressing configuration, any point along the sponge would have the effect of its compressive force mitigated by a corresponding opposing vector from a point directly 180 degrees from it along the sponge dressing. This could explain why higher pressure gradients were observed in non-circumferential dressing configurations, as there was a "far side" portion of the model without sponge dressing which could deform or change shape.

There are limitations to this study. First, a deceased swine model does not have the same compartment pressures of an in vivo model. An in vivo model, when subjected to compressive forces, would likely exhibit different changes due to increased compartment pressures at baseline within tissue compartments. Additionally, the swine model used was a disarticulated hind leg. The disarticulation theoretically could affect the intracompartmental pressures being measured. As such, to isolate the effects of NPWT with as much clinical approximation possible, in vivo whole intact models should be utilized. Another possible limitation is the method of measuring compartment pressures. Though the CD2x STIC instrument was used as recommended by manufacturer instructional guide, equilibration is achieved by introducing "less than 3/10 cc of saline " into a compartment. It is unknown how introducing 1/10 cc versus 2/10 cc may have affected any measurable difference in pressure with the chosen deceased swine model. It must also be noted the degree of accuracy for the CD2x STIC device is +/- 3.4 mmHg, which with the reported compartment pressure levels could affect the observed differences between varying tissue levels, magnitudes of negative pressure and degrees of circumferential dressing configurations. It is also unknown if there may be a greater effect at other varying negative pressure values than the -200 mmHg, -125 mmHg, -25 mmHg used in this study. These values were chosen to approximate values at a higher magnitude of negative pressure, a middle value, and a lower magnitude of negative pressure. And while prior studies have commented on the effects of NPWT dressing material and shape altering its effects on force transmission, this study was not designed to isolate or examine effects of differing sponge material designs or patterns.[7,16]

In conclusion, this study found compartment pressures measured at varying tissue levels and magnitudes of negative pressure showed a positive increase in compartment pressure which appeared to be inversely correlated with distance from the skin. This study also suggested non-circumferential dressing configurations allowed for a pressure gradient to form along the tissue layers. Future studies should include an in vivo model to further elucidate if these findings are replicated in an in vivo model. Likewise, additional studies further elucidating if the forces transmitted during NPWT reach a critical level to induce mechanotransduction and subsequent angiogenesis via mechanisms reported in prior literature. The implications of such a finding may suggest NPWT, and ciNPWT, could have a role in tissue healing beyond just wounds or incisions, if it is able to impart mechanical changes at tissue levels around deeper structures. While the findings in this study are novel, further work is needed to continue establishing NPWT and ciNPWT's mechanism of action, and elucidate their full therapeutic possibilities.

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