Mode of action and clinical benefits of closed incision negative pressure: A literature review

Brian Andrews

Whether defined as incisional negative pressure wound therapy iNPWT, closed incision negative pressure wound therapy ciNPWT, or closed incision negative pressure therapy ciNPT, there is no escaping the fact that there is a growing body of evidence attesting to the benefits of applying vacuum dressings to closed surgical incisions in many surgical disciplines[1-5]. Accordingly, in the interest of furthering the understanding as to how the application of negative pressure in closed incisions may improve clinical outcomes. In this paper we discuss the attributable benefits and how they may be manifest.

Brian Andrews is a Global Marketing Manager with Molnlycke Healthcare, responsible for the company's negative pressure wound therapy devices developments. A nursing, biological sciences and business graduate, Brian has worked in the field of advanced wound care for more than 20 years. He has worked for leading global medical device manufacturers ConvaTec, KCI Inc., and Molnlycke, and has been fortune live and work in a number of international markets including Australia, UK, USA, Singapore, Japan, he presently resides in Sweden. Passionate about the medical devices industry and wound care, Brian is motivated by the need to provide adequate healthcare to all members of society, regardless of social or economic status. And in order to do this, he believes the industry need to move beyond the supply of products, and to partner with healthcare providers in the provision of sustainable solutions. Clinically appropriate, yet economically response solutions.

Originally developed to aid in the healing of acute and chronic open wounds, negative pressure wound therapy, NPWT, has been used to great effect for more than 20 years. In contrast, the application to closed surgical incisions is far more recent, first reported in 2006[6], and there are many open questions with respect of mode of action. How does the application of negative pressure aid in the healing of an incision where there is no open tissue defect? In this paper, through a review of the literature, we attempt to shed some light on possible cause and effect relationships.

The most often cited beneficial actions attributed to ciNPT include; reduction in tension at the incision union, clearance of oedema, the reduced occurrence of fluid accumulation, and improved perfusion. With subsequent clinical benefits being reported as a lower incidence of SSI [7-11] and haematoma seroma formation[6,15,16], and the reduction in occurrence of events such as dehiscence[9,12-14].

In regard to reduced stresses on the incision, some of the most relevant observations can be drawn from animal studies paired computer finite element analysis (FEA) with the later providing a window on activity that cannot be observed in the biological model. The earliest of these complimentary modelling studies sponsored by KCI Inc., manufacturer of the Prevena Closed Incision Management System, included three separate animal, and two FEA models.

The first of the animal studies, a porcine model was designed to quantify effect in the reduction in haematoma/seroma formation[17]. In this model a subcutaneous void was created to emulate dead-space under an incision and isotope-labelled nanospheres were introduced prior to closure. A total of eight incisions were randomised to negative pressure or a control semipermeable film dressing. Following therapy remaining defects were weighed, and where negative pressure was applied, canisters were measured and biopsy were taken from five key organs in all subjects.

The results showed a 63% decrease in defect mass favouring the negative pressure group, having a mean mass of 15 ± 3g vs 41 ± 8g for the control. Further, in biopsied lymph nodes, there were ~60 µg (~50%) more 30- and 50-nm nanospheres from Prevena Therapy-treated incisions compared to control sites ($P=0.04$ and 0.05, respectively). The authors concluded that the difference between the two groups may be explained by increased lymph clearance perpetuated by the application of negative pressure.

In the second animal model, again porcine with a standard dressing control, investigators sort to assess the biomechanical properties

>>

of healed spinal incisions, specifically, the strength of the tissue union and the cosmetic appearance[18]. Post closure incisions were assessed at three or five days using scar scale and histological evaluation. Incisions treated with negative pressure were reported as having a significantly improved scar scale height grade ($P<0.026$) compared to those treated with standard dressings, which showed inflammation, oedema and swelling around the incision whereas the incision line treated with negative pressure was barely visible. With respect to tissue union, control group scores were lower for failure load (4.9 ± 4.0 vs. negative pressure, 16.5 ± 14.6N), energy absorbed (8.0 ± 9.0 vs. 26.9 ± 23.0 mJ), and ultimate stress (62 ± 53 vs. 204 ± 118 N/mm²). Histological analysis demonstrated no differences in incision scar width between the two groups but the authors noted “a trend toward improved early healing strength, and improved incision appearance” for incisions treated with negative pressure.

> “The most often cited beneficial actions attributed to ciNPT include; reduction in tension at the incision union, clearance of oedema, the reduced occurrence of fluid accumulation, and improved perfusion. With subsequent clinical benefits being reported as a lower incidence of SSI and haematoma seroma formation, and the reduction in occurrence of events such as dehiscence.”

In a third pilot study, investigators described contralateral incisions of swine sutured and treated with negative pressure or gauze pads for five days after which they were left untreated for a further 35 days[19]. At 40 days, post-surgery histological sample testing demonstrated a substantial difference in the tensile strength of the tissue union. Authors reported 65% increase in force required to separate the tissue union.

Subsequent to these animal studies and the encouraging observations, investigators have sort to further qualify and quantify causal relationships through the use of FEA technology, and models designed to mimic human tissue and an incision. Published in 2012 the investigators describe the use of two separate FEA models and a bench test validation model[17].

The first of the two FEA models was focused on the evaluation of lateral force across an incision overlaying a subcutaneous void (Figure 1). The mechanical properties of the incision were those of adipose tissue and the negative pressure dressing is described as being an open cell foam, similar to that used for filling cavities in the application of negative pressure to cavity wounds. The foam is bonded to a frictionless incision contact layer with an adhesive border, all of which is covered by a pleated polyurethane film that provides the vacuum seal. The dressing is coupled to a battery powered pump that generates a vacuum of -125mmHg. And, under vacuum pressure the dressing is described as both contracting laterally as well as compressing. In this FEA model two simulations were run, one with negative pressure and one without.

The model was first run to simulate closure of the incision with sutures only, and lateral tension in the range (2.2 to 2.5 kPa at the skin surface) was recorded as the baseline.

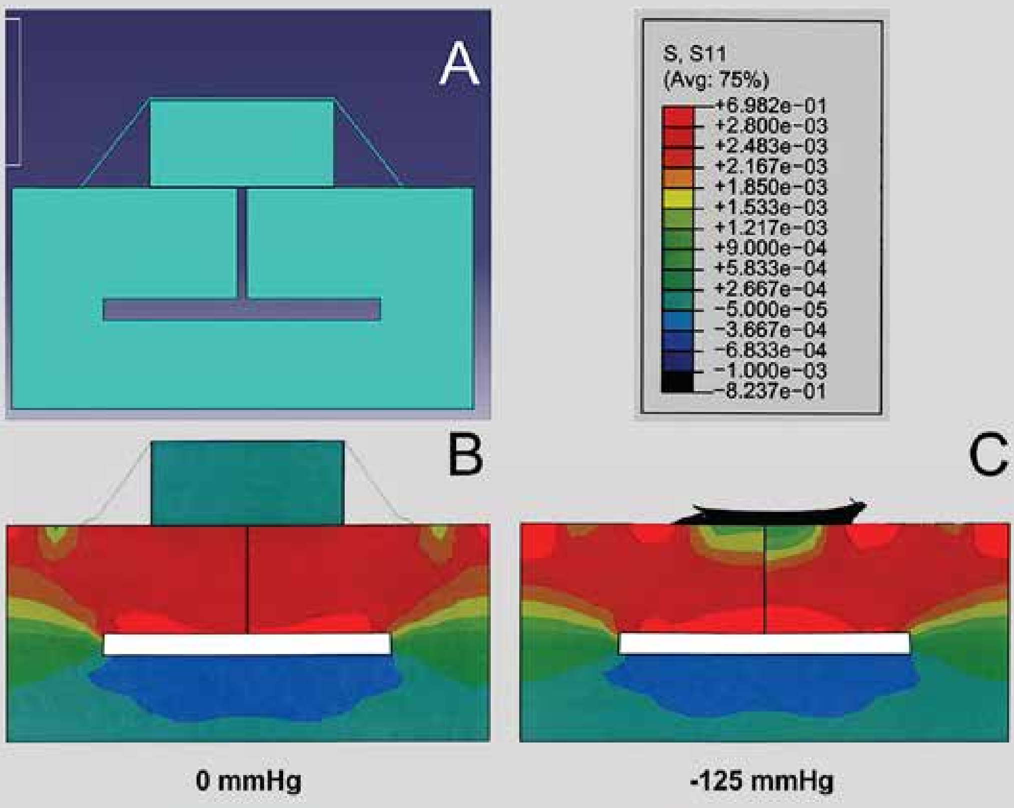

Figure 1: Finite element analysis-1: a 2mm wide incision cuts from the skin surface to the void (A). The incision is joined by sutures (B) and lateral stress develops (colour contours, MPa). Negative pressure (-125mmHg) is applied to the dressing (C), and lateral stresses become more compressive.

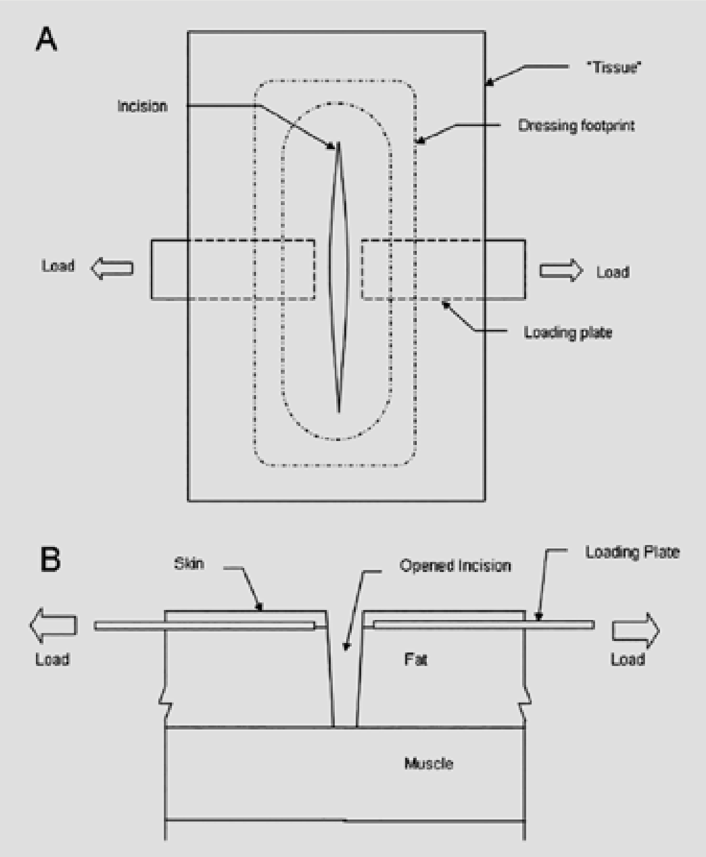

Figure 2: Schematic of bench test setup: overhead view (A) and cross-section (B).

> "In regard to reduced stresses on the incision, some of the most relevant observations can be drawn from animal studies paired computer finite element analysis (FEA) with the later providing a window on activity that cannot be observed in the biological model."

When run again, the model included the application of the negative pressure using the dressing previously described, and a vacuum of -125mmHg. In the computer model, this combination of a contractile dressing and a vacuum of -125mmHg reduced lateral tension at the skin level to 0.9 to 1.2 kPa (a reduction of about 50%).

In the second, and more complex FEA model, authors described a tissue model that included the nonlinear mechanical behaviour of epidermal, dermal, and subdermal tissue layers. The thickness of each layer was modelled to anatomic proportions[21] and a vertical incision was cut through the epidermis, dermis, and upper fat layers. A fascial separation between the fat layers was included and following suturing a tension condition was induced by applying pressure (–150 kPa) to the dermis and epidermis exposures at the model sides. The application of the pressure produced a 2mm incision gap prior to suturing. When measured prior to the application of negative pressure, the average lateral stress on the sutured incision was measured at; 28.05kPa in the epidermis, 14.5kPa in the dermis and 3.31kp in fat.

In this second FEA model when negative pressure was applied investigators described a sequence where the dressing contracts and collapses, eliminating vertical stress and making horizontal stress more uniform. As compared to baseline tensile stress at the sutures was reduced by 45% while stress at deeper sutures reduced by as much as 50%.

The final test in this evaluation series, the benchtop model made from vulcanised liquid silicone[17], was designed to enable the measurement of closing forces or resistance to opening when put in tensions (Figure 2,3). At the baseline, using sutures only to maintain tissue approximation, a force of 61.7N was required to stretch the model 10mm. When negative pressure at -125mmHg was applied the force required to produce the same separation increased to 92.9N, an increase of 51%. Authors concluded that this simple physical test corroborates FEA modelling observations.

Some four years on, 2016, a new group investigators have taken a similar approach to evaluating the performance of their system, again using a combination of benchtop Biomechanical and FEA models[22]. As with the earlier research the FEA modelling is built around a human tissue model comprising of three layers, skin, fat and muscle (Figure 4). The incision takes the form of a vertical cut into the skin and 10mm into the fat. At the base of the incision there was a 50mm fascial separation. Of note, while the models are similar there are differences in the thickness of the different tissue layers however these variations and how they might influence the results are not discussed.

The dressing applied to incision is described as a two layer structure the lower of which is a silicone adhesive wound contact layer. The upper layer is comprised of a spacer to manifold the vacuum, a super absorber layer to manage fluid and moisture vapour transmission layer to form the seal.

To determine effect at different pressure settings negative pressure was applied to the incision model in increments, specifically -40 and then -80mmHg. The resultant outcome was recorded as a reduction of 43% in tensile stress at the incision from no negative pressure at 1.31 to 0.56 N with the application of -40mmHg. Repeated at the higher vacuum pressure of -80mmHg produced a reduction of 31% in tensile stress at the incision from no negative pressure at 1.31 to 0.40 N. Authors concluded that this simple FEA model demonstrates that this system with a mulitlayer dressing and an applied vacuum pressure of -80mmHg can can apply lateral forces to a closed incision, reducing the tension on the sutures in a way similar to that demonstrated for a system with a contractile foam dressing and an applied vacuum pressure of -125mmHg. >>

Figure 3: Incision bench model configured for horizontal extension-force testing with negative pressure wound therapy dressing applied.

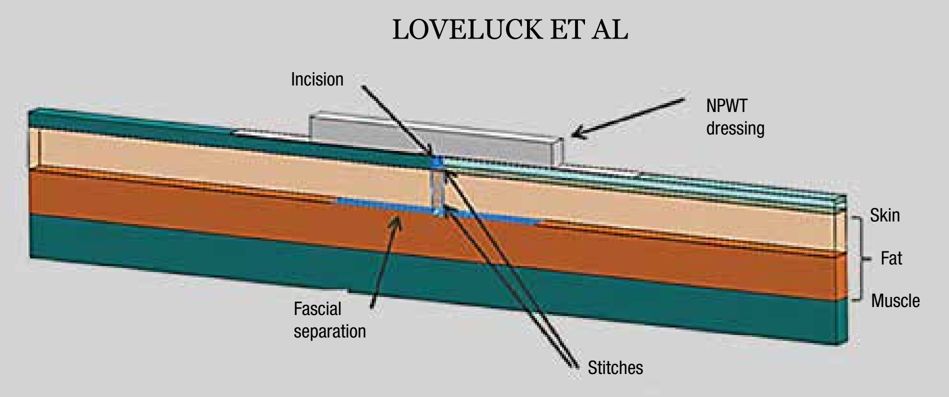

Figure 4: Three dimensional finite element analysis computer model of skin incision. The model comprises three layers: skin, fat, muscle. The incision consisted of a vertical cut through the skin and 10mm into the fat. A 50mm wide horizontal fascial separation was created at the bottom of the incision.

Not dissimilar to the model described earlier, the benchtop biomechanical model was designed to enable the measurement of the force required to separate the incision as a function of the negative pressure (Figure 5). Using a tensile test machine investigators measured the force required to separate the incision by 10mm. As with the FEA model investigators assessed tissue displacement at both -40 and -80mmHg noting that the majority of the resistance effect was realised at -40mmHg. The example given was for an 8.0mm displacement wherein the force required to produce an 8.0mm separation at -40mmHg was a mean of 30.5 N (n=5) as compared to a mean of 33.0 (n=5) with the vacuum at -80mmHg. Authors noted further that the multilayer dressing was able to resist the lateral tension to an unspecified degree even without the application of negative pressure.

In summary, in respect of mechanical forces generated by the application of negative pressures dressings over closed surgical incisions, the FEA and benchtop models provide useful insights as to cause an effect and how the enhancement of a dressing with negative pressure may aide in reducing tension at the tissue union and to reduce the potential for dead-space and fluid accumulation.

On the final, and perhaps the most difficult benefit to illuminate, improved perfusion, there is very little commentary associated with blood flow and the application of negative pressure to closed incisions, however some useful references may be drawn from studies undertaken in open wounds. Specifically, in early research conducted by Argenta LC and Morykwas MJ[23,27] where Laser Doppler probes were inserted into tissue adjacent to open wounds in a porcine model. It was observed that the application of negative pressure resulted in increased blood flow to the area under the defect. At their peak, the application of -125mmHg resulted in blood flows four times that of baseline. Subsequently, it was postulated that a possible mechanism of action of increased blood flow was that the application of negative pressure reduced local oedema and thus pressure on blood vessels, allowing the restoration of flow.

An alternative but not altogether contradictory view of the mechanism of action proposed by Karinos et. al[25], is that the application of negative pressure results in the compression of vessels that is observed by Laser Doppler as increased flow, but this does not translate to increased perfusion. To put this theory to test in the clinical setting, a study was undertaken where pressure transducers were situated under the skin in shallow wounds located on the forearm, a scalp, a heel and two thigh degloving wounds. The wounds were covered with open cell foam sealed under a film with vacuum applied in increasing increments with interstitial pressures being recorded at each increase.

Although the effect reduced to near baseline by 48 hours, it was observed that there was a progressive increase in tissue pressure proportionate with the amount of suction applied. And, although no direct comparison was made, it may be suggested that this increase in tissue pressure, would likely result in the compression of capillaries resulting in the increased flow rate observed with Laser Doppler in early research. Further, it may be suggested that the increase in flow, but not volume, may in fact result in low grade tissue hypoxia that are recognised stimuli for angiogenesis [25-28]. In their conclusions, the authors did postulate that the increase in tissue pressure could explain the reduction in oedema associated with the application of negative pressure, along with advancing the theory that the accelerated blood flow arising from vessel compression may through the Venturi principal draw fluid into the vessels thus reducing oedema.

Figure 5: Experimental setup with Syndaver tissue model. The incision was closed with running stitch using 2-0 non-dissovable suture 5mm apart. Dressing was applied on top of the incision model.

Discussion

Undoubtedly the application of different evaluation models, biological and computer, provide useful insights as to mode of action of negative pressure in closed incision indications. However, differences in modelling techniques and basic parameters such as tissue thicknesses, make it difficult to draw absolute conclusions leading these reviewers to conclude that the advancement of this therapy would benefit from standardised tissue models and test protocol. Further, with one of the primary indications for use being obesity, it would be useful, perhaps mandatory, to understand how tissue load and incision lines stresses change with the increase in fat and the lassitude of muscle common in obesity. Improved knowledge in this manner will enable clinicians to discriminate based on system attributes and differences in mode of action that may vary between system solutions, ultimately benefitting patients, clinicians and solution developers. ■

References

References can be found online at www.boa.ac.uk/publications/JTO.