Variable topical negative pressure for wound care

The role of topical negative pressure (TNP) in the closure of acute wounds has become a new and dynamic area of research in medicine. Clinicians have to date been using continuous or intermittently applied therapy, with little scientific evidence to demonstrate the difference between them. Variable TNP combines the positive effects of continuous and intermittent to produce an optimal environment of sub-atmospheric pressure to a wound bed. Through experience with a new device, the Atmos pump, this paper demonstrates the advantages of this new technique.

Robert Staruch, Steven Jeffery

KEY WORDS
Topical negative pressure (TNP)
Continuous TNP
Intermittent TNP
Variable TNP
Wound care

Topical negative pressure (TNP) dressings are indicated in acute and chronic wounds before wound closure (Morykwas et al, 1997, 2001; Stadelmann et al, 1998). Intermittent TNP, where the pressure cycles between therapeutic negative pressure and zero, has become popularised recently, as reports of its more favourable effects on wound healing and tissue growth have been published (Scherer et al, 2008; Wilkes et al, 2009). However, there have been reports of loss of seal and efficacy when the pump reduces the pressure to zero (Suresh and Terrazas, 2004). Furthermore, when TNP is used to splint a wound, such as over a skin graft, the authors would be reluctant to use 'standard' intermittent therapy, as the desired splinting effect of the dressing is only intermittent.

Robert Staruch is a Military Foundation Year 2 Doctor, The Queen Elizabeth Hospital, Birmingham; Steven Jeffery is a Consultant Burns and Plastic Surgeon, Royal Centre for Defence Medicine, The Queen Elizabeth Hospital, Birmingham. This paper was originally submitted in October, 2010

Types of topical negative pressure

Continuous

With continuous TNP, the sub-atmospheric pressure setting remains constant. Literature reports (Morykwas et al, 1997) the optimal pressure setting as 125mmHg, although many people now use lower pressures such as 80mmHg. Continuous TNP creates a moist wound bed, promotes infiltration of cytokines, angiogenesis and the blood supply to wound edges and reduces bacterial load. It also prevents loss of seal and ultimately accelerates wound healing (Mullner et al, 1997; Page et al, 2004; Scherer et al, 2008; Wackenfors et al, 2004).

Intermittent

In intermittent TNP, the sub-atmospheric pressure drops to zero for a preset period of time before returning to set atmospheric pressure. This reduction in pressure can be 'passive', i.e. the pump stops sucking and the reduction in pressure is facilitated by leak, or 'active', i.e. air is actively pumped into the dressing to reduce the pressure. Intermittent TNP has been shown to accelerate angiogenesis and reduce microvascular forces that can decelerate the formation of granulation tissue (Deva et al, 1997; Morykwas et al, 1997; Mendes-Eastman 1998; Stadelmann et al, 1998; Tang et al, 2000; Lu et al, 2003; Banwell and Musgrave, 2004; Jeffery, 2009; Borgquist et al, 2010).

Variable

Variable TNP allows control over the maximum and minimum sub-atmospheric pressures. If required, the machine can be set to maintain a sub-atmospheric pressure during 'low' periods. Furthermore, users can alter the time that the machine spends on 'high' and 'low' periods. In the authors' opinion, variable TNP combines the advantages of continuous and intermittent therapies.

Figures 1–3 show the difference between continuous, intermittent and variable TNP.

Atmos pump

The Atmos pump (Atmos Med) is a TNP device that allows users to control both the duration of pressure as well as the level of sub-atmospheric pressure during the 'on' and 'off' period.

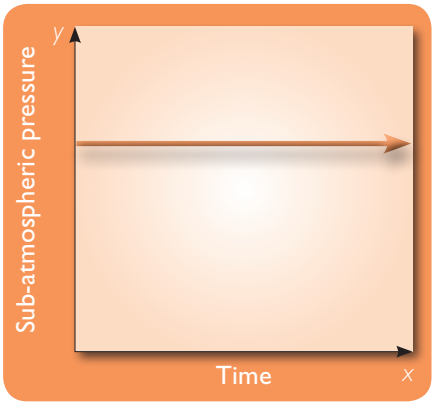

Figure 1. Continuous TNP. Sub-atmospheric pressure constant over time.

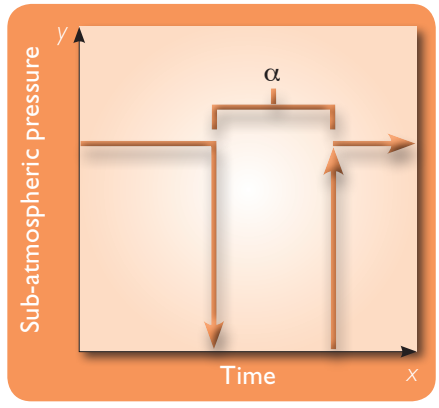

Figure 2. Intermittent TNP. Duration of normal pressure (α) can be controlled. Device alternates between sub-atmospheric and normal pressure.

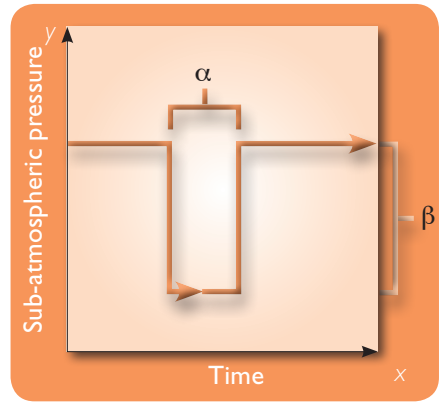

Figure 3. Variable TNP. Duration of alternative pressure (α) and level of alternative pressure (β) can be controlled. Device can be programmed to fluctuate between these two variables.

When the authors need the advantages of intermittent therapy, such as for enhanced angiogenesis (Banwell and Musgrave, 2004), reduced local vessel permeability (Lu et al, 2003) and accelerated granulation tissue formation (Morykwas et al, 1997; Borgquist et al, 2010), without the disadvantages of loss of seal as a result of exudate, or loss of the splinting action of the dressing, they routinely use the Atmos pump which allows for intermittently variable TNP to be applied. The authors routinely use the settings of 40mmHg and 80mmHg, as they have found this offers a good combination of negative pressure, without loss of seal.

The following three case reports illustrate this technique. All patients had wounds dressed using the Chariker-Jeter system of application for TNP (Jeffery, 2009).

Case report one

This case involved a soldier who sustained a rocket-propelled grenade (RPG) injury to his left foot, with open fractures. The wounds were debrided initially in Afghanistan and then on return to Birmingham, when intermittent variable TNP was applied for one week before primary closure was achieved (*Figure 4*).

Case report two

In this case, a soldier was left with a sacral defect following an improvised explosive device (IED) attack. He required multiple debridements with TNP application in between. His rotational flap was planned when a suitable period of time had elapsed and no further dead tissue was found on exposure. Variable TNP was applied between theatre sessions (*Figure 5*).

Case report three

A civilian presented with contractures to the right hand and elbow following flame burns and had contracture releases. Intermittent variable TNP was applied over the skin grafts, with the dressings being left in place for one week. On removal of the dressings, there was 100% graft take (*Figure 6*).

Discussion

The current widespread use of TNP therapy for accelerated wound healing has positively reshaped the management of the exuding wound (Ubbink et al, 2009). A literature search of MEDLINE, EMBASE, MoM, CKS, Cochrane library, NHS Evidence and Specialist collections and PUBMED using the keywords 'topical negative pressure wound therapy' 'intermittent' and 'continuous' provided 39 results which focused on the use of this modality with reference to skin grafting, abdominal wound closure, hernia repair and diabetic ulcers.

Despite the varied scope that the potential application of TNP offers, few authors have focused on the underlying principles with regard to the different physiological and biomechanical processes involved (Morykwas et al, 1997, 2001). In addition, a Cochrane collaboration review of randomised controlled trial (RCT) evidence (Ubbink et al, 2009), concluded that there was no significant evidence to suggest that TNP increased healing rates of chronic wounds.

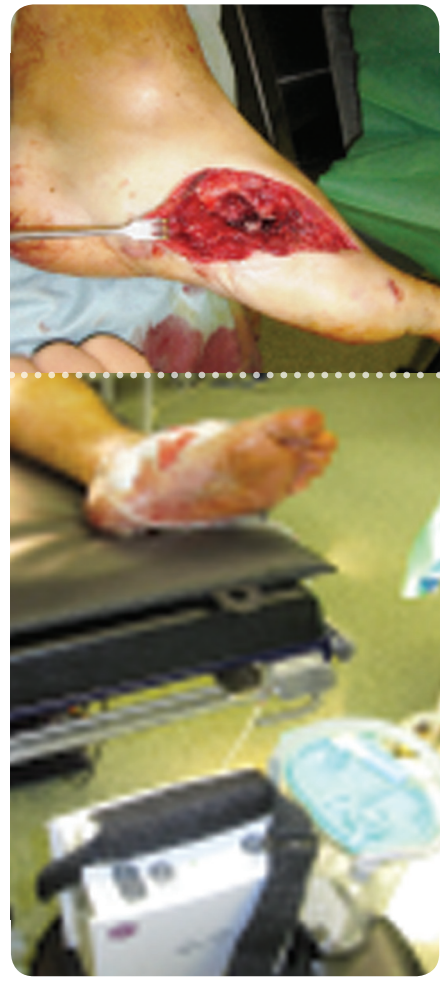

Figure 4. Case report one.

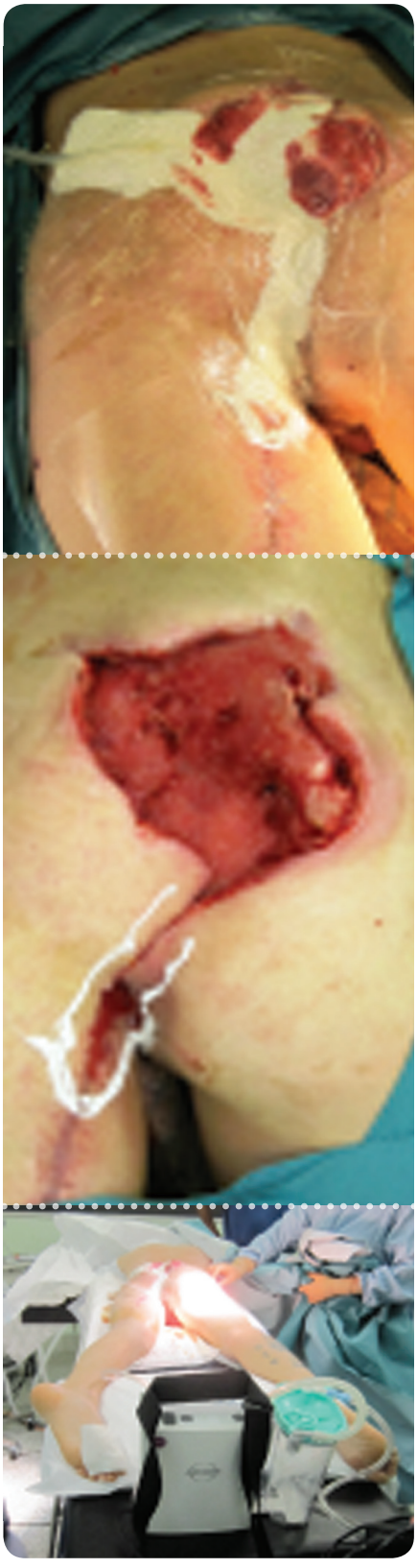

Figure 5. Case report two.

The widespread use of TNP therapy and developments of this modality have allowed modifications to the level of pressure and the duration of application. There are now three methods of TNP application — continuous, intermittent and, more recently, variable. This discussion explores these mechanisms to give users a greater understanding of their appropriate application.

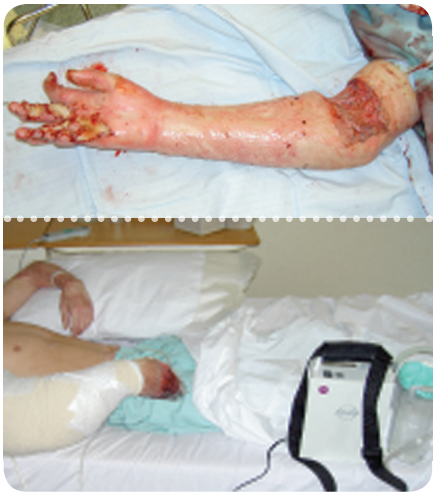

Figure 6. Case report three.

Wound healing is a complex mechanism of acute inflammatory changes, cell proliferation, deposition of a structurally sound extracellular matrix, and a maturation phase which includes long-term remodelling of the extracellular matrix (Stadelmann et al, 1988). Different tissue types have specific remodelling and healing phases, therefore the greater variety of tissue involved in a wound, the more complex the chronological course of its healing process (Stadelmann et al, 1988).

Acute inflammatory phase

Tissue injury results in activation of three mechanisms:

- Platelet aggregation with resultant clot formation activates the clotting cascade
- Tissue injury sensitises the humoral arm of the immune system, initiating the complement cascade and resulting in local tissue inflammation
- The acute inflammatory process that follows sees local capillary vasodilation and increased vascular permeability, as a result of local cytokine and biochemical release from immune cells. This large influx of inflammatory cells and release of growth factors and cytokines prepares the area for further cell proliferation and phagocytosis of necrosed tissue and bacteria.

Proliferation phase

Proliferation and migration of local epithelial cells allow production of a firm extracellular matrix within the first 48 hours. In addition, migration of key fibroblasts allows synthesis of extracellular matrix components, including collagen and ground substance. Endothelial cell migration allows simultaneous angiogenesis and fibroblast proliferation. This is dependent on the effectiveness of key metalloproteinases which have a strong proteolytic activity. Such components are heavily reliant on essential co-factors such as zinc. Thus, an important factor for effective wound healing is to ensure that patients are not malnourished or vitamin-deficient (Gray and Cooper, 2001).

Maturation phase

The maturation phase allows remodelling of the initial matrix. This essentially allows a change in scar colour due to devascularisation, and an increase in tensile strength due to modifications in the collagen fibril bonding. This stage may take months, unlike the previous two phases which are more immediate.

Underlying mechanisms

In the authors' clinical experience, the mechanism for TNP is not clearly understood. However, several compounding mechanisms are thought to produce the resultant effect.

Application of pressure allows exudate to be drawn away from the wound (Bucalo et al, 1993), preventing bacterial colonisation (Weed et al, 2004) and allowing for the acceleration of keratinocyte and epithelial growth factors (Borgquist et al, 2010). TNP has also been shown to heighten angiogenesis (Ichioka et al, 2008; Labler et al, 2009). Immunohistochemistry anaylsis of blood vessel density using CD31 and

cell proliferation with ki67 has shown a statistically significant increase seven days after wounding with use of TNP (Labler et al, 2009).

Furthermore, analysis of cytokines in a swine model has shown the ability of TNP to reduce cytokine proliferation (Kilpadi et al, 2006). Research has identified that negative pressure results in an increase in IL10 levels and a maintainence of IL6 levels (Kilpadi et al, 2006). One study has identified that negative pressure switches endothelial cells to a migratory and proliferative phenotype. In addition, the same study identified that TNP promotes a pro-angiogenic state (Baldwin et al, 2009).

Sub-atmospheric pressure imposes micro and macro stress forces on wound tissue. The macro strain forces can be seen in the visible stretch that occurs when the negative pressure contracts the foam used for TNP. One study showed that wounds treated with TNP demonstrated significant levels of microdeformation (Scherer et al, 2008). This draws the wound edges together, providing direct and complete wound bed contraction, allowing even distribution of pressure and removal of oedema and local exudative fluid. At a microcellular level, microstrain forces are responsible for reducing oedema which, in turn, promotes capillary perfusion, cell migration and proliferation. Microcellular pressure has been shown to produce mechanical deformation that results in protein and matrix molecular synthesis (Baldwin et al, 2009; Wilkes et al, 2009: Borgquist et al, 2010).

There is evidence to show that the presence of exudate compresses local capillaries preventing oxygentation of underlying microcellular tissue (Urschel et al, 1988; Katz et al, 1991). In addition, exudate contains inhibitory factors that suppress cell proliferation and tissue formation (Morykwas et al, 1997; Herscovici et al, 2003). It is believed that these microforces which are exerted on cells cause migration of intracellular signalling mechanisms, so as to produce tissue growth and granulation (Katz et al, 1991; Wilkes et al, 2009).

Several papers (Morykwas et al, 1997; Morykwas et al, 2001) have identified the ability of TNP to reduce wound volume. The use of 125mmHg of sub-atmospheric pressure has been shown to significantly ($p<0.0001$) reduce wound volume by day 8, when compared to wounds treated with any other form of treatment (Morykwas et al, 1997, 2001).

Finally, it has been postulated (Weed et al, 2004) that TNP decreases the colonisation of bacterial flora and enhances bacterial clearance in the wound. Studies that took punch biopsies in wounds with a large microorganism count found a decrease in count numbers after four days of TNP. In addition, the increase in blood flow and oxygenation to the damaged tissue will improve the resistance to infection (Morykwas et al, 1997; 2001; Weed et al, 2004).

Continuous

Continuous TNP applies a constant degree of sub-atmospheric pressure to the wound surface. This promotes the above mechanisms and accelerates wound healing.

Initial research performed in animal studies showed that continuous TNP increased wound blood inflow by 400% at 125mmHg (Morykwas et al, 2001). This pressure level also produced the fastest time to 100% granulation tissue production and reduction in wound volume. This pressure value was originally adopted as the gold standard until recent experience of the Royal Centre for Defence Medicine (RCDM) under the military plastic surgery nurses, has shown 80mmHg to be of adequate pressure to achieve optimal wound outcomes.

A disadvantage of continuous therapy is its ability to cause low intensity protein and vitamin loss in long-term usage, which are essential for intracellular signalling, cytokine production and wound healing (Mullner et al, 1997; Morykwas et al, 1997; 2001).

The appropriate length of usage in continuous therapy is debatable, and no specific regimen is currently established. It is often tailored to the complexity and nature of the wound. However, it has been demonstrated that continuous therapy for the first 48 hours of application allows accelerated wound closing (Suresh and Terrazas, 2004). Conversely, continuous pressure provides excessive stimulation of the cell during mitosis, thus inhibiting the stimulation for the rest phase during the cell cycle and, in turn, cell growth becomes ineffective (Baldwin et al, 2009).

Intermittent

Intermittent therapy does not alter the level of sub-atmospheric pressure applied, but allows a fluctuation in pressure over defined time periods, with a period of normal pressure intervening between periods of sub-atmospheric pressure (Borgquist et al, 2010).

This method allows relaxation of the tissues (Kairinos et al, 2010), which theoretically provides an enhanced wound healing process as the tensile forces enforced on tissues are periodically relieved. Such an approach produces an elastic-like motion for tissue re-growth (Morykwas et al, 1997; Lu et al, 2003; Banwell and Musgrave, 2004; Borgquist et al, 2010). Cyclic mechanical stretch induces vascular endothelial growth factor (VEGF) and fibroblast growth factor-2 (FGF-2) expression in pulmonary vascular smooth muscle cells (Labler et al, 2009). Furthermore, intermittent therapy decreases the overall volume of multivitamins and exudate removal from the wound (Wackenfors et al, 2004; Borgquist et al, 2010).

Intermittent therapy is believed to increase granulation tissue production

by 103% (Borgquist et al, 2010). The cyclical pressure is also thought to deactivate capillary autoregulation allowing rhythmic perfusion of tissues (Venturi et al, 2005; Urschel et al, 1988). Intermittent therapy allows cellular rest, which further permits successful tissue regeneration (Borgquist et al, 2010). It has also been shown that it increases wound edge microvascular blood flow by 40–50% during periods of normal pressure (Wackenfors et al, 2004). Furthermore, the extension of negative pressure periods results in a longer reactive hyperaemia during times of normal pressure.

Variable

Literature regarding the use of variable TNP therapy is limited. In general, the lack of randomised controlled data means that new models, such as variable pressure, are often used with limited available evidence.

In vivo research (Borgquist et al, 2010) has shown some findings that support the physiological theory behind TNP. Cycling of pressure between five (high) and two minutes (low), with baseline pressures of -10, -45, -75 and -125mmHg were used. Previous evidence demonstrated that these settings produced a positive correlation to maximal blood flow change (Borgquist et al, 2010).

Application of five cycles of variable pressure on porcine models has shown that microvascular blood flow at 0.5cm from the wound edge is decreased with fluctuating pressures, but that in both intermittent and variable pressure models blood flow at 2.5cm from the wound edge revealed a reciprocal increase (Borgquist et al, 2010). Large differences between pressures (-10mmHg to -125/-75mmHg) show the greatest effects on blood flow to tissue edge (Borgquist et al, 2010).

The importance of the reduction of microvascular blood flow proximal to the tissue is its stimulation of angiogenesis and granulation at the tissue site. Increases in distal microvascular blood flow prevent tissue ischaemia (Borgquist et al, 2010), allow removal of waste products, and permit good penetration of antibiotics. Continuous TNP exerts pressure and microstatic forces against the wound edge, causing hypoperfusion and tissue injury. Furthermore, cyclical negative pressure causes arterioles to dilate, increasing blood flow to the area, reducing capillary afterload and causing resultant increased inflow (Herscovici et al, 2003; Borgquist et al, 2010). Cycling of pressures prevents this, reducing the risk of long-term tissue ischaemia and promoting the influx of growth factors (Labler et al, 2009).

A longstanding limitation of intermittent TNP has been the loss of splinting and seal during cycling to atmospheric pressure. Variable TNP prevents this by never letting the pressure applied to the wound go to '0' or normal pressure. It also possibly reduces the number of dressing changes required, which, in turn, lessens patient discomfort.

Conclusion

The successful biophysiological principles of TNP on wound healing can be summarised into three principles:

- Firstly, negative pressure removes exudate from inflammation, colonised bacteria and tissue oedema. This promotes tissue perfusion and granulation
- Secondly, it draws the wound together by distributing the force of contraction evenly, resulting in better functional and aesthetic outcomes
- Lastly, microstress and microstrain forces applied to the tissues promote intracellular signalling and migration that increases cell growth, division and mobilisation of keratinocytes to the wound edge for healing.

The achievement of an environment to allow the optimal effects of these priniciples has required a significant amount of trial and error, reflected in the lack of significant controlled studies in the literature.

Application of continuous pressure is useful in the first 48 hours of treatment. However, it has been shown to produce over-aggressive forces on microvascular wound edge flow and suboptimal wound healing.

Intermittent therapy provides a much more stable environment for tissue growth. The cycling of atmospheric and sub-atmospheric pressures stimulate two separate mechanisms required for tissue growth: intermittent ischaemia to promote angiogenesis, followed by adequate tissue oxygenation to promote growth factors. However, the use of atmospheric pressure in the cycling process often causes the loss of the splinting effect required, and loss of the seal, causing the need for further dressing changes.

The authors' experience of the variable pressures provided by the Atmos pump has shown it to be more effective at dealing with complex traumatic wounds. The Atmos pump allows clinicians to utilise the advantages of intermittent TNP, as well as those of continuous. Previous complications, such as loss of seal, are reduced by this method. The authors have found variable TNP to give greater flexibility and better patient outcome for patients with complex wounds. WUK

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Key points

- Variable TNP prevents loss of seal by never going to zero.
- Variable TNP is safe over skin grafts as the splintage effect is maintained.
- Variable TNP allows for the benefits of cycling pressure changes without some of the disadvantages of intermittent TNP.
- Reduction of pressure to zero can be active (i.e. pumping air into the system), or passive (relying on leak).