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RESEARCH

Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery

A REVIEW OF EVIDENCE AND MECHANISMS FOR AN EMERGING INDICATION

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Objectives

The period of post-operative treatment before surgical wounds are completely closed remains a key window, during which one can apply new technologies that can minimise complications. One such technology is the use of negative pressure wound therapy to manage and accelerate healing of the closed incisional wound (incisional NPWT).

Methods

We undertook a literature review of this emerging indication to identify evidence within orthopaedic surgery and other surgical disciplines. Literature that supports our current understanding of the mechanisms of action was also reviewed in detail.

Results

A total of 33 publications were identified, including nine clinical study reports from orthopaedic surgery; four from cardiothoracic surgery and 12 from studies in abdominal, plastic and vascular disciplines. Most papers (26 of 33) had been published within the past three years. Thus far two randomised controlled trials – one in orthopaedic and one in cardiothoracic surgery – show evidence of reduced incidence of wound healing complications after between three and five days of post-operative NPWT of two- and four-fold, respectively. Investigations show that reduction in haematoma and seroma, accelerated wound healing and increased clearance of oedema are significant mechanisms of action.

Conclusions

There is a rapidly emerging literature on the effect of NPWT on the closed incision. Initiated and confirmed first with a randomised controlled trial in orthopaedic trauma surgery, studies in abdominal, plastic and vascular surgery with high rates of complications have been reported recently. The evidence from single-use NPWT devices is accumulating. There are no large randomised studies yet in reconstructive joint replacement.

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Article focus

- This article reviews the evidence for the prophylactic use of negative pressure wound therapy (NPWT) on closed incisions as a means of reducing the incidence of surgical site complications in orthopaedic surgery
- The evidence for understanding the mechanism of action of NPWT on closed incisions is critically reviewed
- The development of lower cost single-use NPWT devices will stimulate further studies

Key messages

- Randomised studies have been performed that argue for the use of NPWT on high-risk closed incisions

Strengths and limitations

- This is a fast-moving field so reviews quickly move out of date
- There is insufficient evidence yet within single indications to enable meta-analysis from multiple studies

Introduction

The concept of negative pressure wound therapy (NPWT) or vacuum-assisted closure (VAC) will be familiar to most orthopaedic

surgeons. Since its commercial introduction more than 20 years ago,[1,2] NPWT has transformed the management of complex open wounds such that it is now the standard approach in many institutions. There is a growing evidence base of randomised and comparative cohort studies of its use in the management of open fractures,[3,4] open complex wounds following failures of arthroplasty,[5,6] or spinal surgery.[7] There is also an extensive literature on the use of NPWT in chronic wound healing and in reconstructive surgery.[8-11] What may be less familiar is the emerging evidence base for the use of NPWT on the closed incision.

Although at first sight it may appear counterintuitive, NPWT is beginning to be used as a preventative tool in reducing the incidence of surgical site infection (SSI) and dehiscence of the closed incision. The purpose of this article is to review the current status of the literature on the use of NPWT on closed incisions in orthopaedic surgery and evaluate the status of 'incisional NPWT' in other surgical disciplines. Additionally we appraise the understanding about possible mechanisms of action. In a future article we plan to assess the evidence for identifying those patients at greatest risk of SSI in orthopaedic procedures and review the status of guidelines to target certain patient groups with NPWT as a preventative technology, and discuss the economic implications for such an approach.

Materials and Methods

Review of existing evidence on incisional NPWT. The concept of applying negative pressure to a closed incision began to be explored in the early years following commercial availability of NPWT. Webb[12] alluded to studies of weeping surgical wounds treated with -50 mmHg negative pressure as early as 2002, but the first peer-reviewed reports did not appear until 2006.[13,14] Negative pressure was applied through standard open-cell polyurethane foam to incisions that were intrinsically at high risk of complication. Unusually for an emerging indication, the first published report of the use of negative pressure on closed incisions was a randomised controlled study. Stannard et al[13] studied patients after high-energy orthopaedic trauma and enrolled 88 patients in two studies between 2001 and 2003, with results published in June 2006. The authors used a traditional NPWT device (VAC; KCI Inc., San Antonio, Texas) set at -125 mmHg. Their paper reported the interim results from two randomised controlled trials (RCTs) on the use of NPWT on draining haematomas and calcaneus, pilon, and tibial plateau fractures.[13] In both studies wound drainage ceased statistically significantly earlier in the wounds treated with NPWT, but there were no statistically significant differences in the incidence of dehiscence or infection. Gomoll et al[14] also described this technique for high-risk incisions in December of the same year. They also used a traditional NPWT device set at -75 mmHg in high-risk obese patients operated on for fracture fixation and total hip reconstruction.[14] Using "Incisional VAC" for a mean of three days, they experienced no cases of wound breakdown in 35 high-risk patients.

Literature search on incisional NPWT. In order to establish the extent of the subsequent literature on the use of NPWT for closed incisions, a systematic search was conducted within the PubMed database using the terms: "Negative Pressure Wound Therapy OR Topical Negative Pressure OR Vacuum Assisted Closure" (n = 2238) AND either "closed wound" (n = 172), "incision" (n = 44), "incisional" (n = 33), "well wound therapy" (n = 240) OR "prevent" (n = 86). The database was last searched on 3 June 2013. No exclusions were placed on language or publication date. Abstracts were reviewed by an author (RM) and any relevant articles were obtained. Additional articles cited in these papers were also retrieved. A total of 33 unique papers were recovered specifically discussing the application of NPWT to closed incisions. The retrieved articles were grouped according to the main indication and subject. There were nine papers from orthopaedic surgery (Table I),[13-21] four dealing with cardiothoracic surgery (Table II)[22-25] and 12 studies from abdominal, plastic and vascular indications (Table III).[26-37] There were also four reviews reporting on mixed cases (Table IV)[38-41] and four *in vitro* or animal studies investigating mechanisms of action (Table V).[42-45] The rate of publications is increasing, with the majority of articles published in the last three years.

NPWT on closed orthopaedic incisions. Table I summarises the nine papers in the literature on the use of incisional NPWT in orthopaedic surgery. Further to the original 2006 reports from Stannard et al[13] and Gomoll et al,[14] Reddix et al[15,16] published two evaluations in high-BMI patients undergoing repair of acetabular fracture using traditional NPWT devices set at -75 mmHg for up to three days on the closed incision. In the later series[16] the incidence of infection and dehiscence reduced approximately six-fold from 6% to 1% and from 3% to 0.5%, respectively, when compared against historical cases before the introduction of incisional NPWT.

In primary arthroplasty a randomised study in knee replacement using traditional NPWT on closed incisions *versus* a dry gauze dressing did not show any significant reduction in infection (2.8% *vs* 4.8% for NPWT patients) or time to achieve a dry wound (4.1 days *vs* 4.3 days for NPWT patients), but the investigation was terminated early due to excessive skin blisters and the full number of patients were not recruited.[17] The formation of skin blisters is a familiar occurrence in orthopaedic surgery when adhesive dressings are used on tissue that will undergo swelling due to oedema.[46] Blisters are significant as they may provide a nidus for infection. A number of articles describing incisional NPWT report the use of non-adherent dressings to prevent the excoriating action of polyurethane foam on unprotected tissue.[14,15] Purpose-designed single-use NPWT devices such as PICO™ (Smith & Nephew, Hull, United Kingdom) or Prevena™ (KCI,

Table I. Literature on the use of negative pressure wound therapy (NPWT) on closed incisions in orthopaedic surgery

Authors	Study type*	Indication	Results†	Negative pressure delivery and use‡
Stannard et al[13]	RCT	Draining haematomas: n = 22 *vs* n = 22 NPWT	Mean time to dry wound: 3.1 *vs* 1.6 days (p = 0.03)	tNPWT PU foam -125 mmHg; until no drainage
	RCT	High-risk lower extremity fracture: n = 22 *vs* 22 NPWT	Mean time to dry wound: 4.8 *vs* 1.8 days (p = 0.02)	tNPWT PU foam -125 mmHg; until no drainage
Gomoll et al[14]	NC	High-risk orthopaedic: n = 35 NPWT	No infections or dehiscence	tNPWT PU foam -75 mmHg; 3 days
Reddix et al[15]	NC	High-risk orthopaedic: n = 19 NPWT	No infections or dehiscence	tNPWT PU foam -75 mmHg; 24 to 72 hrs
Reddix et al[16]	CC	High-risk acetabular fractures n = 66 *vs* 235 NPWT	Deep infection: 6.06% *vs* 1.27% (p = 0.04). Dehiscence: 3.03% *vs* 0.426%	tNPWT PU foam -75 mmHg; 24 to 72 hrs
DeCarbo and Hyer[19]	Description of method	Foot and ankle surgery		tNPWT PU foam -125 mmHg; 24 to 48 hrs
Pachowsky et al[18]	RCT	Primary hip arthroplasty: n = 10 *vs* n = 9 NPWT	Mean reduction in seroma volume: 5.08 ml *vs* 1.97 ml (p = 0.021)	suNPWT PU foam -125 mmHg; 10 days
Howell et al[17§]	RCT	High-risk primary knee arthroplasty: n = 36 *vs* n = 24 NPWT	Mean time to dry wound: 4.1 *vs* 4.3 days (NS). Deep infection: 2.8% *vs* 4.8% (NS)	tNPWT PU foam -125 mmHg; 48 hrs
Stannard et al[20]	RCT	High-risk lower extremity fracture: n = 122 *vs* n = 141 NPWT	Deep infection: 19.0% *vs* 10.0% (p = 0.049). Dehiscence: 16.5% *vs* 8.6% (p = 0.044)	tNPWT PU foam -125 mmHg; 2.5 days
Hansen et al[21]	NC	Primary/revision hip arthroplasty with prolonged post-operative drainage: n = 109 of 5627 (2%)	76% required no further surgery; 24% required surgery	tNPWT PU foam -125 mmHg; post-op day 3 or 4 for 48 hrs

* RCT, randomised controlled trial; NC, non-comparative case series; CC, comparative cohort† NS, not significant
‡ tNPWT, traditional NPWT (durable NPWT pump); suNPWT, single-use NPWT; PU, polyurethane
§ study terminated prematurely due to adverse events skin blister in NPWT group[47]

Table II. Literature on the use of negative pressure wound therapy (NPWT) on closed cardiothoracic incisions

Authors	Study type*	Indication	Results	Negative pressure delivery and use†
Atkins et al[22]	NC	High-risk sternotomy incisions: n = 57 NPWT	No infections or dehiscence	tNPWT silver PU foam; -125 mmHg; 4 days
Atkins et al[23]	CC	High-risk sternotomy incisions: n = 10 *vs* n = 10 NPWT	Difference in skin perfusion (p = 0.004)	tNPWT silver PU foam; -125 mmHg; 4 days
Colli and Camara[24]	NC	High-risk sternotomy incisions: n = 10 NPWT	No infections or dehiscence	suNPWT PU foam -125 mmHg; 5 days
Grauhan et al[25]	RCT	High-risk sternotomy incisions: n = 75 *vs* n = 75 NPWT	Infection: 16% *vs* 4% infection (p = 0.027)	suNPWT PU foam -125 mmHg; 6 to 7 days

* NC, non-comparative case series; CC, comparative cohort; RCT, randomised controlled trial
† tNPWT, traditional NPWT (durable NPWT pump); suNPWT, single-use NPWT; PU, polyurethane

San Antonio, Texas) incorporate features to address these issues through the use of different wound contact materials, but there are as yet no published reports that verify such success in substantial numbers of arthroplasty patients.[38,47] However, effects of NPWT are detectable in primary arthroplasty incisions. A statistically significant lower volume of seroma was found using ultrasound imaging in hip replacement patients treated with a single-use incisional NPWT device set at -125 mmHg (Prevena; KCI Inc.) for five days *versus* a conventional dry dressing.[18] The mean size of seroma was 1.97 mL with NPWT compared with 5.08 mL (p = 0.021). The randomised study only consisted of 19 normal-risk patients, so it is unsurprising that there was no difference in the incidence of infection or dehiscence. Prolonged post-operative drainage is already known to be a risk factor for SSI and a recent paper from Hansen et al[21] reports their institutional use of NPWT applied at post-operative day 3 or 4 in cases where there is prolonged drainage in closed wounds (2% of total). Overall 76% of 109 patients treated in this way healed with no further problems. This is a variant of a strategy to select high-risk patients pre-operatively and thereby limit those patients needing NPWT.

Table III. Literature on the use of negative pressure wound therapy (NPWT) on closed abdominal, plastic and vascular incisions

Authors	Study type*	Indication	Results†	Negative pressure delivery and use‡
López-Cano and Armengol-Carrasco[26]	NC	Incisional hernia repair: n = 3 NPWT	No infections or seroma	tNPWT wide-field PU foam -125 mmHg; 5 days
Condé-Green et al[27]	CC	Incisional hernia repair: n = 33 *vs* n = 23 NPWT	Wound complication: 63.6% *vs* 22% (p = 0.02). Skin dehiscence: 39% *vs* 9% (p = 0.014)	tNPWT PU foam -125 mmHg; 5 days
Dutton and Curtis[28]	Single case	High-risk abdominal incision: n = 1 NPWT	-	tNPWT PU foam, -75/-100 mmHg; 7 to 10 days
Schmedes et al[32]	CC	Skin flap donor site closures: n = 42 *vs* n = 52 NPWT	Major complication: 12% *vs* 5.8% (NS)	tNPWT PU foam, -175 mmHg; 14 to 16 days
Masden et al[37]	RCT	High-risk primary or delayed primary lower extremity closures: n = 37 *vs* n = 44 NPWT	Infection: 13.5% *vs* 6.8% (NS). Dehiscence: 29.7% *vs* 36.4% (NS)	tNPWT PU foam -125 mmHg; 3 days
Haghshenasskashani and Varcoe[33]	Single case	High-risk incision following vascular graft: n = 1	-	suNPWT PU foam -125 mmHg; 5 days
Vargo[29]	NC	High-risk abdominal closure: n = 30	No infections	tNPWT PU foam -75 mmHg; mean 5.6 days
Blackham et al[30]	CC	High-risk abdominal oncology: n = 87 *vs* n = 104 NPWT	Infection: 35.5% *vs* 16.0% (p = 0.011)	tNPWT PU foam -125 mmHg; 4 days
Bollero et al[35]	NC	Scar excision and closure: n = 8	No complications	suNPWT foam -125 mmHg; 8 days
Pauli et al[31]	CC	High-risk ventral hernia repair: n = 70 *vs* n = 49 NPWT	Infection: 25.8% *vs* 20.4% (p = 0.50)	tNPWT PU foam -75 mmHg; 7 days
Matatov et al[34]	CC	Femoral vascular procedures: n = 63 *vs* n = 52 NPWT	Infection: 30% *vs* 6% (p = 0.001)	suNPWT foam -125 mmHg; 5 to 7 days
Tauber et al[36]	CC	Inguinal lymph node dissection closures: n = 30 *vs* n = 15 NPWT	Intervention for complications: 23% *vs* 7% (p = 0.63)	tNPWT PVA foam; -100 mmHg; up to 7 days

* NC, non-comparative case series; CC, comparative cohort; RCT, randomised controlled trial
† NS, not significant
‡ tNPWT, traditional NPWT (durable NPWT pump); suNPWT, single-use NPWT; PU, polyurethane; PVA, polyvinyl alcohol

NPWT for closed incisions continues to expand its use in traumatic injury, particularly in the lower extremity where the incidence of post-operative infection is much greater than in primary arthroplasty.[19,20] Following on the interim report on 44 patients that appeared in 2006,[13] Stannard et al[20] went on to published the results of the full randomised study of incisional NPWT applied to high-energy fractures. A total of 263 lower extremity fractures were evaluated, with 122 managed with standard care and 141 with incisional NPWT (mean duration 2.5 days). The authors found a statistically significant reduction in the rate of deep infection (19.0% *vs* 10.0%; p = 0.049) and dehiscence (16.5% *vs* 8.6%; p = 0.044).[20]

In summary, good evidence exists for incisional NPWT in orthopaedic surgery where comorbidities and incidences of infection are known to be significant. The evidence is less persuasive for reduction in infections and dehiscence in uncomplicated primary joint replacement and further studies are needed.

NPWT on closed cardiothoracic incisions. The risk of post-operative sternal wound infection in open cardiothoracic surgery has been widely studied as the mortality associated with deep sternal wound infections (DSWI) is substantial. In a typical survey as many as 33% of patients died within a year of the occurrence of a DSWI.[48] The possibility of using incisional NPWT to reduce the incidence of DSWI was first proposed by Atkins et al[22] (Table II), who also investigated perfusion in order to elucidate potential mechanisms.[23] Using traditional devices with thin strips of silver-impregnated polyurethane foam at -125 mmHg, a series of 57 high-risk cases were recorded without incidence of infection.[22] A small case series of ten high-risk patients was reported using a single-use NPWT device, again with no incidences of infection.[24]

The calculation of risk for post-operative wound infection has been the subject of extensive publication in cardiothoracic surgery. The scoring system devised by Fowler et al,[49] who used the results from 300 000 patients in the Society for Thoracic Surgeons database who underwent coronary artery bypass graft, is widely used. Pre-operative factors include age, obesity and diabetes, but risks based on the intra-operative events are also considered, such as the use of internal thoracic arteries for the grafts.[49] In a recent randomised clinical study of standard care *versus* single-use NPWT device (Prevena; KCI) in 150 evaluable high-risk patients (mean age 68 years, mean BMI 37 kg/m^2, diabetes in 54%), the overall rate of sternal wound infection was reduced from 16% to 4% (p = 0.027) after five to six days of prophylactic NPWT.[25]

NPWT on closed abdominal, plastic and vascular incisions. Interest in incisional NPWT has also been evident among general, plastic and vascular surgeons (Table III). In abdominal surgery such as incisional hernia repair, the use of traditional NPWT devices has shown some promise in difficult abdominal closures under tension using polyurethane foam at either -75 mmHg or -125 mmHg,[26-29] including difficult high-risk abdominal oncology patients.[30] However, one comparative

Table IV. Literature on the use of negative pressure wound therapy (NPWT) on closed incisions: reviews and mixed cases

Authors	Study type*	Indication	Results	Negative pressure delivery and use†
Stannard et al[39]	NC	High-risk closed incision: n = 4	Case examples	tNPWT PU foam -125 mmHg; 4 to 5 days
Stannard et al[40]	NC	High-risk closed incision: n = 5	Case examples	tNPWT & suNPWT PU foam -125 mmHg; 4 to 7 days
Canonico et al[41]	NC	High-risk closed incision: n = 9	6 abdominal, 3 orthopaedic case examples	suNPWT multi-layer silicone -80 mmHg; up to 7 days
Hudson et al[38]	NC	High-risk closed incision: n = 16	6 abdominal and plastics, 10 orthopaedic case examples	suNPWT multi-layer silicone -80 mmHg; up to 7 days

* NC, non-comparative case series
† tNPWT, traditional NPWT (durable NPWT pump); suNPWT, single-use NPWT; PU, polyurethane

Table V. Literature on the mechanisms of action in the use of negative pressure wound therapy (NPWT) on closed incisions

Authors	Study type*	Indication†	Results‡	Negative pressure delivery and use§
Meeker et al[43]	RC	Standardised incisions: n = 28 *vs* n = 28 NPWT in 6 pigs	Mean tensile strength (load to fail): 0.35 N/mm *vs* 0.47 N/mm (p = 0.001). Mean haematoma size: 1.31 cm^2 *vs* 0.94 cm^2 (p = 0.024). Wound appearance (10-point VAS): 3.4 *vs* 6.2 (p < 0.001)	tNPWT gauze dressing -125 mmHg; 3 days
Kilpadi and Cunningham[45]	RC	Undermined incisions: n = 16 *vs* n = 16 NPWT in 8 pigs	Mean reduction in haematoma/seroma mass: 48 g *vs* 15 g (p = 0.002). Increase in clearance to lymph nodes of 52% (p = 0.004)	suNPWT PU foam -125 mmHg; 4 days
Wilkes et al[42]	C	Laboratory models and FEA	Normalisation of lateral forces	suNPWT PU foam -125 mmHg
Glaser et al[44]	RC	Spinal incisions: n = 8 *vs* n = 8 NPWT in 8 pigs	Scar height of 0 in 3/8 *vs* 8/8 NPWT (p = 0.026). Wound breaking strength (NS)	suNPWT PU foam -125 mmHg; 3 and 5 days

* RC, randomised controlled, C comparative laboratory study
† FEA, finite element analysis
‡ NS, not significant
§ tNPWT, traditional NPWT (durable NPWT pump); suNPWT, single-use NPWT; PU, polyurethane

cohort study saw no effects in ventral hernia closures.[31] Donor sites for large free flaps often present issues with infection and dehiscence, and a recent comparative cohort analysis (42 standard treatment *vs* 52 NPWT) suggested that traditional NPWT with foam at -175 mmHg over ten to 14 days may be helpful in reducing failure of the closed donor site incision (12% *vs* 5.8%), but the effect not did not reach significance.[32] A randomised controlled trial of lower extremity ulcers treated with surgery and closed primarily (37 standard treatment *vs* 44 traditional NPWT over three days) reported a lower rate of infection (13.5% *vs* 6.8%) and a slightly higher rate of dehiscence with NPWT (29.7% *vs* 36.4%), but neither difference was statistically significant.[37] The population was high-risk, including many patients with diabetes and peripheral vascular disease, but there was no clear effect of NPWT. It is perhaps instructive to reflect on the fact that the first study in the field of incisional NPWT was the interim report of the randomised trial by Stannard et al[13] in just 44 subjects, which also found no statistically significant effect on infection and dehiscence. It was not until the full study on 249 subjects was published that statistically significant effects were shown.[20]

Closed incisions following open vascular surgery for the lower extremity also have a high incidence of complications.[50] Incisional NPWT is being explored to see if the rate of infections or dehiscence can be reduced by preventative application of NPWT.[34] In a comparative cohort analysis one group reported a good effect of single-use NPWT (Prevena; KCI) on closures for femoral vascular procedures.[34] Other procedures receiving exploration for incisional NPWT include scar revision[35] and inguinal lymph node dissection.[36]

Other publications – mixed cases and reviews. The remaining publications at present showing clinical cases of incisional NPWT are all non-comparative in nature (Table IV), covering traditional NPWT[39] (VAC; KCI Inc.), single-use NPWT with foam[40] (Prevena; KCI Inc.) and single-use canister-less NPWT (PICO; Smith & Nephew).[38,41]

Mechanisms of action. The scientific understanding of the mechanisms of action of NPWT on open wounds has grown steadily since the first descriptions of work in pigs.[1,51] Initial focus was on the stimulation of blood flow, increased growth of granulation tissue and reduction in bioburden. With respect to any effects on closed incisions it is perhaps only the action of NPWT on perfusion that is of immediate relevance.

Tissue perfusion effects. Following the initial animal studies showing a stimulation of relative perfusion as assessed by laser Doppler needle probes in the tissue surrounding a full-thickness excision,[1] subsequent research showed a pattern whereby NPWT caused a relative hypoperfusion close to the wound edge (0.5 cm), whereas an increase in perfusion was only observed when the laser Doppler probes were inserted about 2.5 cm away from the wound edge.[52-54] Independent evidence for effects on tissue perfusion in the (stretched) zone surrounding an open wound were obtained using direct video microscopy.[55] It is possible that the establishment of adjacent hypo- and hyper-perfused tissue zones may enhance angiogenesis and evidence for such effects was recently described in a diabetic mouse model in open wounds, in which the highest concentrations of VEGF were detected in areas of relative hypoxia at the foam-wound edge interface.[56] Using alternative surface-probe Laser Doppler techniques, others have demonstrated significant increases in relative perfusion in intact skin in healthy volunteers.[57] The level of stimulation continued to increase up to -500 mmHg; a pressure at which all effects on the stimulation of granulation tissue in open wounds on pigs have vanished.[51] Such perfusion effects might be relevant to healing of incisional wounds but the differences in techniques, the location and type of probes leaves some room for doubt as to whether one or the other is relevant. Indeed it has been claimed that the stimulation of perfusion as measured by Laser Doppler needle probes is an artefact due to compression of capillary beds.[58] However, in a recent study changes in relative perfusion around full-thickness wounds in pigs were compared with three different methods.[59] Both Laser Doppler filament probes and thermo-dilution probes gave similar patterns: hypoperfusion at the edge of the wound and hyper-perfusion further away, validating the earlier findings.[52-54] In contrast, a surface-mounted perfusion sensor (O2C Device; LEA Medizintechnik, Giessen, Germany) showed small increases close to and away from the wound edge confirming the principle, if not the magnitude, of the earlier studies in volunteers.[57,59] An abstract of a preliminary study with the O2C device, again on healthy volunteers, also showed some increase in perfusion upon application of a single-use NPWT device.[60]

Notwithstanding the above discussion, it has been known for some time that perfusion stimulation on application of NPWT is a temporary phenomenon.[1] In these animal studies the perfusion stimulation decays after 20 minutes, although it reappears if there is at least a two-minute return to atmospheric pressure[1] – hence so-called intermittent NPWT. In open wounds intermittent NPWT stimulates more granulation tissue than continuous NPWT, although it is less frequently used in clinical practice as the intermittent feature can be painful.[61] More recent NPWT devices have variable settings so that negative pressure cycles from high to low but not to atmospheric levels, which may avoid issues with pain. At present all publications describing incisional NPWT have used continuous negative pressure and no studies have appeared using intermittent or variable intermittent NPWT on closed incisions. Four articles that deal specifically with investigations into the mechanisms of action of incisional NPWT are summarised in Table V. At present there have been no publications that have reported what happens to perfusion adjacent to closed incisions treated with NPWT.

Lateral tension and wound strength. The function of sutures or other surgical closures is to bring the wound edges together and to reduce lateral tension that causes the wound to gape. Granulation tissue forms where the wound gapes and this will form scarring in the healed incision. Reductions in lateral tension across a closed incision have been demonstrated under constant NPWT with computer modelling and *in vitro* measurements.[42] There is similar data that non-NPWT mechanical forces can stress-shield closed incisions and reduces scarring.[62] There is also evidence from animal studies that the breaking strength of wounds is increased through the application of continuous NPWT to closed incisions.[43,44]

Effects on oedema. Although it was not investigated in the early animal studies there is wide agreement, based in a large measure on clinical experience, that elimination of tissue oedema is a critical mechanism of NPWT action on open wounds.[1,2,12] Surprisingly there are only a handful of studies that have directly measured this effect. Reduction in oedema was inferred from a study in patients with bilateral hand burns, in which increased perfusion was observed in hands subjected to NPWT.[63] In a porcine model of a septic open abdomen, wet/dry weight comparisons showed that NPWT-treated pigs had less tissue oedema than those treated by passive drainage.[64] High-frequency ultrasound has been used to quantify reduction of oedema in the peri-wound tissue in a small group of pressure ulcer patients on commencement of NPWT.[65] While no direct quantification of oedema reduction has been reported for closed incisions, a recent study has reported data that argue strongly for an effect of incisional NPWT in increasing the activity of lymphatic drainage in the deep tissue treated with NPWT.[45] Radiolabel microspheres were cleared to lymph nodes more rapidly from tissue beneath incisions treated with NPWT than from control incisions dressed conventionally.

Reduction in haematoma and seroma. Collections of blood and serum in sub-incisional tissues create dead spaces that may predispose towards infection. Two animal studies have independently shown reductions in haematoma volume under incisional NPWT[20,43] and this has also been demonstrated clinically for seroma in a small randomised controlled trial.[18]

In summary, the evidence supports the hypothesis that reduction of lateral tension and haematoma or seroma, coupled with an acceleration of the elimination of tissue oedema, are the main mechanisms of action of incisional

NPWT. Together these mechanisms are able to improve the speed, strength and quality of incisional wound healing, thus minimising the failures of healing that lead to infection and/or dehiscence. It remains possible that some redistribution of blood flow around closed incisions could supplement these mechanisms. In fact these attributes are reminiscent of the fourth set of experiments in the work by Morykwas et al,[1] in which survival of random pattern flaps was improved through application of NPWT to the intact skin. If the skin around a closed incision, particularly where undermining is involved, can be compared to a random pattern flap, then these early experiments provide support for the emerging field of incisional NPWT. Recently, a significant clinical study on the effect of NPWT on skin grafted free muscle flaps has been published.[66] In this investigation 15 patients were randomised to receive NPWT at -125 mmHg as a post-operative dressing and 15 control patients received paraffin gauze in the absence of NPWT. Taking biopsies before ischaemia (when the flap was detached) and at five days after implantation, it was demonstrated that NPWT reduced the ischaemia-reperfusion inflammatory and oedema response.[66] It seems reasonable that much of the same biology will be relevant to closed incisions. What is not yet clear is how individual patient risk factors such as age or obesity are influenced by the mechanisms of incisional NPWT.

Level of negative pressure and other variables. Despite the relatively good understanding of the mechanisms through which incisional NPWT might have an effect, there is surprisingly little information on the optimum negative pressure for clinical use. Tables I to V show that a range of pressure levels have been used with traditional NPWT devices (with -75 mmHg[14-16] and -125 mmHg[13,40] being the most frequently used) without any obvious benefits in clinical efficacy one way or the other. There have been no published studies that have investigated levels of pressure on desirable endpoints such as reduction of haematoma or seroma, reduction of oedema, increase in wound strength or reduction in complications. The emergence of single-use devices with one fixed pressure setting perhaps reduces the likelihood that such studies might be performed.[25,41] In the study of NPWT on free flaps discussed above, tissue pressure was monitored at two locations: at the interface between the flap and the device (white PVA foam) and deeper at the level of the vascular anastomosis.[66] Positive, not negative, pressure at the surface of the flap was detected, with little difference seen in the deeper tissue: +8 mmHg to +12 mmHg when NPWT was varied from -50 mmHg to -150 mmHg, respectively. This is similar to the situation with NPWT for open wounds where the accumulation of evidence suggests the efficacy of negative pressure has a broad range between -50 mmHg and -150 mmHg.[9] In open wounds only the extremes of NPWT have been explored with -25 mmHg and -500 mmHg having been shown not to stimulate granulation tissue formation in animals.[51] No similar studies have been reported in closed incisions.

Additional variables concern the construction of the incisional NPWT device. There is a general consensus that intact skin should not be exposed to polyurethane foam, but there is no consensus on the optimum area of tissue that should be subjected to NPWT, with traditional devices using either thin strips[14,22] or treatment of wider zones.[26,43] With evidence that the reduction of tissue oedema has significance, treatment of a wider area than just the immediate incision may be desirable. The material for delivery of NPWT is also variable: the predominant use has been of polyurethane foam, although a perforated adhesive silicone tissue contact device is now commercially available.[38,41] The studies on free flaps discussed above that show similarity in their physiology to closed incisions were conducted with PVA "White foam".[66,67] A study in pigs used gauze pads at -125 mmHg and showed reduction in haematoma, improved wound strength and improved visual appearance.[43] It seems reasonable to conclude that negative pressure between -50 mmHg to -150 mmHg applied to the zone of tissue surrounding the incision is the principle component of the effect, although much scope remains for investigation.

Conclusions

In its ten-year gestation, incisional NPWT has developed so that there are now reasonable grounds for confidence that this approach is widely applicable to a range of indications. There is RCT evidence for reduction in dehiscence and infection in orthopaedic trauma[20] and sternal incisions.[25] The rate of publication within the field is growing rapidly. There are gaps in our understanding of the mechanisms of action. It seems likely that there are effects on resolving post-operative oedema through effects on lymph drainage[45]; it seems likely that wound breaking strength is regained more rapidly[43] and that haematoma and seroma are reduced[18,43,45] but we have little idea of precise mechanisms. Effects on perfusion outside of reduced oedema are still in the balance.[57,59] There are insufficient data yet to identify optimum levels of negative pressure. Nevertheless, the availability of single-use NPWT devices[24,25,38,41] means that costs of therapy are now such that exciting opportunities for building clinical evidence in large randomised studies are a prospect over the coming years.

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- S. Karlakki: Reviewing of the literature, Revision of the article
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- S. Giannini: Reviewing of the literature, Revision of the article
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- J. Stannard: Reviewing of the literature, Revision of the article
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