

Smith+Nephew

Unlocking the Mode of Action of PICO sNPWT


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PICO sNPWT – PICO single use negative pressure wound therapy
tNPWT – traditional negative pressure wound therapy

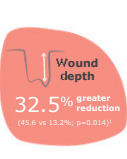
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Improved clinical outcomes with PICO^o sNPWT versus tNPWT in lower extremity wounds


In a phase 4, randomised, controlled study, use of PICO sNPWT helped to significantly reduce wound area, depth and volume compared with tNPWT in patients with lower extremity wounds (venous leg ulcers and diabetic foot ulcers) over 12 weeks¹



Wound area
39.1% greater reduction
(90.2 vs 51.0%, p<0.001)¹



Wound depth
32.5% greater reduction
(45.6 vs 13.2%, p=0.014)¹



Wound closure
51.0% relative increase
in patients achieving wound closure
(45.6 vs 22.2%, OR: 0.294, p=0.002)¹

Intention-to-treat population (ITT; n=161)

To help understand the reasons for superior clinical outcomes with PICO sNPWT versus tNPWT, mechanism of action (MoA) studies were conducted

PICO^o sNPWT mechanism of action

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Can MoA explain differences in clinical outcomes with PICO^o sNPWT versus tNPWT?

Wider Zone of therapy

Delivery of NPWT across an area beyond the wound:

- ABRILOCK^o Technology delivers NPWT across the entire dressing^{1,4}
- Consistent delivery of NPWT for the duration of therapy^{1,4}
- Consistent compressive forces and tissue displacement¹
- Uncompromised skin surrounding the wound (periwound skin)²

Improved clinical outcomes

Portability and simplicity

A user-friendly device may offer benefits to patients and carers

- Reductions in application time and dressing change frequency¹
- Increased wear time¹
- Healthcare professional and patient satisfaction^{4,5,7}
- Positive impact on daily living (eg, mobility, sleep, ability to work)^{4,7}

Undisturbed healing

An improved healing environment that may deliver:

- Greater reduction in wound area¹
- Faster re-epithelialisation¹
- Increased quality of granulation tissue⁸
- A mature wound bed with dampened inflammation⁹
- Reduced tissue damage upon dressing removal¹⁰

PICO^o sNPWT mechanism of action



PICO^o sNPWT MoA
Study outline

Porcine model of wound healing used to assess:²

- Wound healing outcomes (macroscopic measures)
- Histology (microscopic measures)
- Skin health measures around the wound
- Transcriptional profiling of surrounding skin and wound (gene activation outcomes)

Full-thickness excisional wounds (3cm diameter) were created, treated and monitored (2 per flank)
A total of 12 pigs utilised in the study²

PICO sNPWT
changed every
6 days
(vs. tNPWT)

Traditional NPWT
changed every
3 days
(vs. tNPWT)

Wound and skin assessments: days 0, 6, 12²

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PICO^o sNPWT mechanism of action

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Greater reductions in wound area: PICO^o sNPWT versus tNPWT
Due to re-epithelialisation, not contraction

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At days 6 and 12 post wounding, compared with tNPWT, PICO sNPWT showed significantly greater:²

- Wound closure ($p < 0.001$)²
- Wound re-epithelialisation ($p < 0.01$)²

Effects on wound contraction were similar for PICO sNPWT and tNPWT up to day 12²

Full-thickness excisional wounds (3cm diameter) in pigs²

Wound area remaining open²

Day	tNPWT (%)	PICO sNPWT (%)
Day 0	100	100
Day 6	~85	~65
Day 12	~65	~45

Re-epithelialisation²

Day	tNPWT (%)	PICO sNPWT (%)
Day 0	0	0
Day 6	~10	~25
Day 12	~25	~55

PICO^o sNPWT mechanism of action

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Increased epithelial migration and reduced wound edge hyperproliferation with PICO^o sNPWT versus tNPWT

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Increased epithelial migration with PICO sNPWT²

Epithelial migration was increased with PICO sNPWT treatment compared to tNPWT as shown by length of crawling neopepithelium (arrows; histology images)²

Reduced wound edge hyperproliferation with PICO sNPWT²

Epithelial hyperproliferation with tNPWT compared to PICO sNPWT, where arrows indicate thickened wound edge (line separates epidermal and dermal regions; histology images)²

PICO^o sNPWT mechanism of action

Increased wound maturity and improved quality of granulation tissue with PICO^o sNPWT versus tNPWT

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- Increased granulation tissue deposition with tNPWT than with PICO sNPWT² at day 12 ($p < 0.001$) but.....
- PICO sNPWT-treated wound granulation tissue reached a more advanced stage of healing
 - More collagen (with maturity) and fewer proliferating cells in PICO granulation tissue than with tNPWT²

Granulation tissue (%)

Region of wound: Outer, Inner, Central

More collagen with increased maturity with PICO sNPWT than with tNPWT (** $p < 0.001$; outer and inner wound regions)²

Proliferation of granulation tissue (cells/mm)

Region of wound: Outer, Inner, Central

Significantly fewer proliferating cells (mature wounds) with PICO sNPWT versus tNPWT (** $p < 0.001$; all wound regions)²

PICO^o sNPWT mechanism of action

Transcriptional profiling shows a mature wound bed with PICO^o sNPWT versus tNPWT

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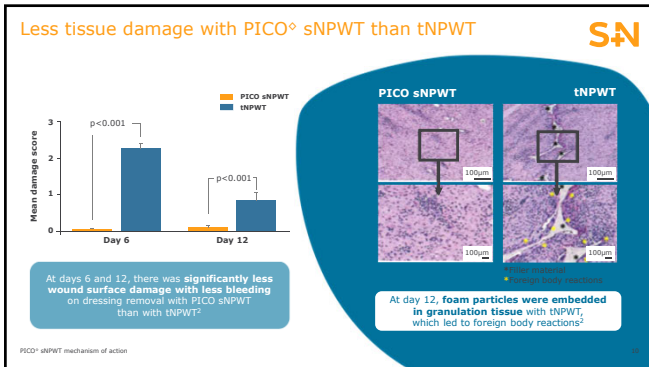
Wound bed gene expression data²

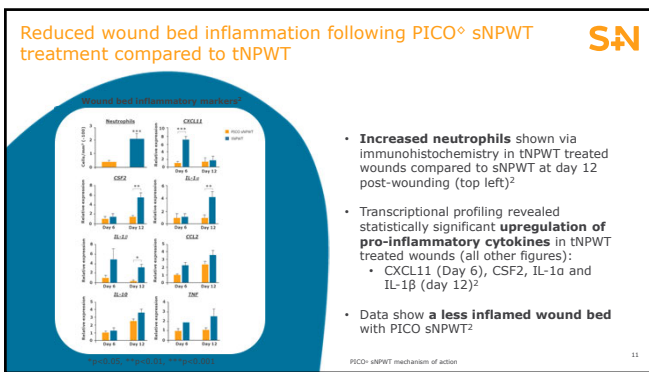
Relative expression

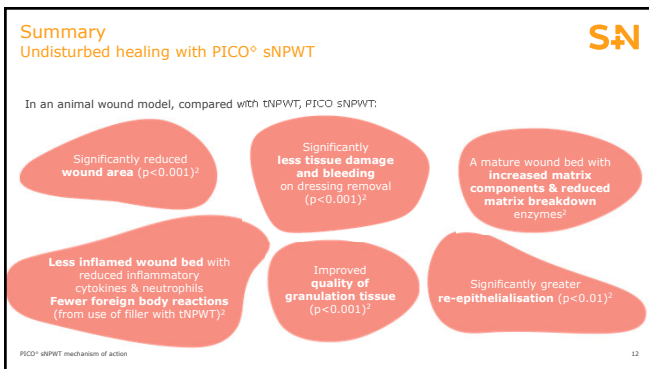
Legend: Normal skin (black), PICO sNPWT (orange), tNPWT (blue)

- With PICO sNPWT versus tNPWT, there was increased expression of:²
 - Wound matrix components** (COL1A2 and COL3A1)
 - Granulation-promoting factors** (CTGF)
 - Proteoglycans** (DCN)
- Levels of **tissue breakdown matrix metalloproteinases** (MMP3 and MMP9) were substantially elevated in tNPWT-treated wounds²

PICO^o sNPWT mechanism of action









PICO® sNPWT delivers NPWT consistently across the dressing for the duration of therapy S+N

In laboratory wound model plate tests*, conducted over 72 hours:²

Exudate flow (number of tests)	Mean (range) negative pressure delivered	Time within -40 to -100mmHg ³
Low (n=8)	-82mmHg (-90 to -82mmHg)	100%
Moderate (n=8)	-81mmHg (-79 to -83mmHg)	100%

*Recommended therapeutic range is -40 to -150mmHg²

AIRLOCK® Technology in the PICO sNPWT dressing enables NPWT to be applied consistently across the entire dressing for the duration of therapy³

≥99,9%
within pressure limits (not less than -60mmHg)⁴

*A benchtop wound model incorporating an air bleed of 3ml/min to allow for an incomplete dressing seal. Tests used simulated wound fluid at two exudate flow rates: low (0.6g/cm²/24hr) and moderate (1.1g/cm²/24hr). Eight PICO sNPWT systems were tested from four product batches with a pressure sensor at each end of the dressing.¹

PICO® sNPWT mechanism of action

PICO® sNPWT delivers NPWT across the dressing to surrounding tissue (biomechanics*) S+N

PICO sNPWT

24h post application

PICO sNPWT delivers compressive forces across and beyond the wound spanning the entire dressing (within 60mm of wound centre line)^{5,6}

tNPWT


24h post application

tNPWT delivers localised therapy to the wound itself (within 35mm of wound centre line)^{5,6}

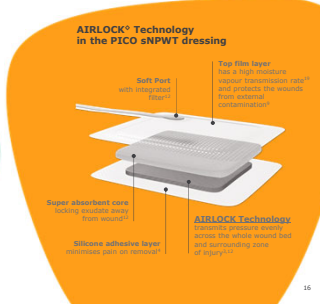
*A benchtop model using metallic markers inserted into porcine tissue at 50mm intervals (total 150mm). Tissue displacement was analysed at the wound bed, edge of dressing, and inside the dressing using computed tomography.^{1,4}

PICO® sNPWT mechanism of action

Delivery of negative pressure beyond the wound with PICO^o sNPWT in clinical practice



Visible effects of PICO sNPWT on tissue surrounding the wound in patients who underwent spinal surgery (dressing boundary clearly visible on patient after removal) ¹⁵



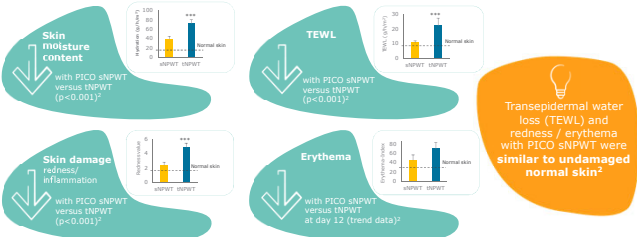
AIRLOCK^o Technology in the PICO sNPWT dressing

- Top film layer: Top a PICO^o Medical Vapor Transmission Cap^o and protects the wounds from bacterial contamination?
- Soft Peril: with integrated foam?
- Super absorbent core: which maintains a moist wound?
- Silicone adhesive layer: minimizes pain on removal?
- AIRLOCK^o Technology**: creating pressure evenly across the whole wound bed and surrounding area of injury?

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Effects of PICO^o sNPWT on skin health and barrier function

In a porcine wound healing model, PICO sNPWT causes far less disruption to the skin surrounding the wound with **periwound remaining uncompromised?**

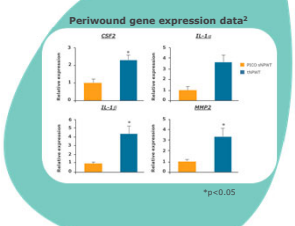


- Skin moisture content**: with PICO sNPWT versus tNPWT (p<0.001)²
- TEWL**: with PICO sNPWT versus tNPWT (p<0.001)²
- Skin damage (redness/ inflammation)**: with PICO sNPWT versus tNPWT (p<0.001)²
- Erythema**: with PICO sNPWT versus tNPWT at day 12 (trend data)²

Trans-epidermal water loss (TEWL) and redness / erythema with PICO sNPWT were similar to undamaged normal skin²

PICO^o sNPWT mechanism of action, Day 12 data, ***p<0.001 17

Transcriptional profiling shows that PICO^o sNPWT supports a pro-healing periwound environment



Periwound gene expression data²

- In a porcine wound healing model, **inflammatory markers were elevated** in tNPWT-treated periwound skin compared to PICO sNPWT:²
 - CSF2
 - IL-1 α
 - IL-1 β
- MMP2 levels were also elevated²
- Data indicate that PICO sNPWT **reduced inflammatory damage to periwound skin** compared to tNPWT²

*p<0.05

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Summary:
Extended zone of therapy with PICO^o sNPWT

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Possible explanations for improved clinical outcomes with PICO sNPWT include:

- Consistent delivery of negative pressure for the duration of therapy^{1,4}
- Delivery of negative pressure across the dressing to surrounding tissue^{7,5,18}
- Reduced periwound inflammation yielding a pro-healing environment²
- Fewer changes to skin health and barrier function than with tNPWT³

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Portability and simplicity

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PICO^o sNPWT can offer significantly higher patient satisfaction than tNPWT

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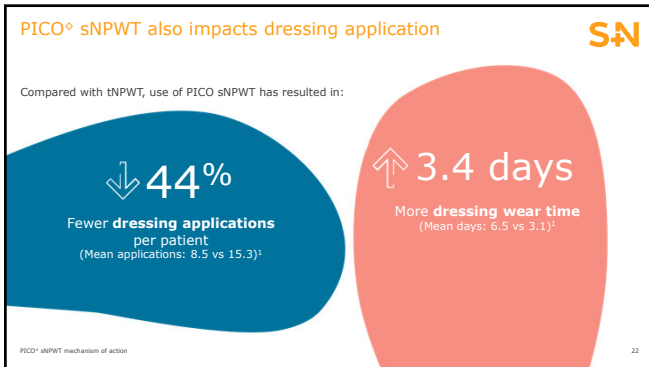
Patient satisfaction with PICO sNPWT versus tNPWT was evaluated in a study of 161 patients with lower extremity wounds (venous leg ulcers and diabetic foot ulcers)^{1,5}

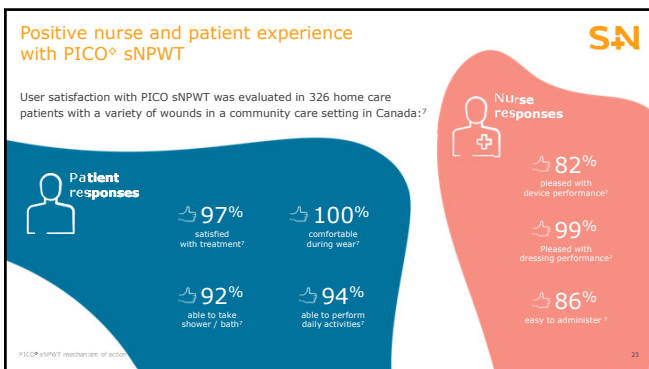
Category	PICO sNPWT (%)	tNPWT (%)
Overall satisfaction	87.2%	68.9%
Use again	89.1%	67.0%
Comfort	65.2%	35.1%
Interferes with mobility	9.7%	44.2%
Reduced activity	8.8%	15.3%
Disrupts sleep	4.2%	25.9%

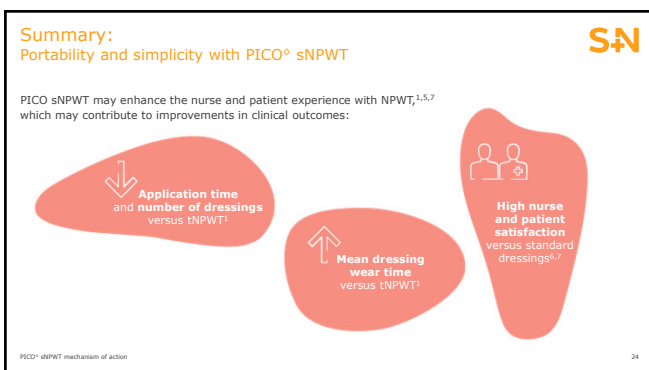
Patients reported significantly greater satisfaction with PICO sNPWT than tNPWT (p<0.05 for all)^{1,5}

“...patients clearly prefer the advantages of a quieter and less intrusive system.”¹¹

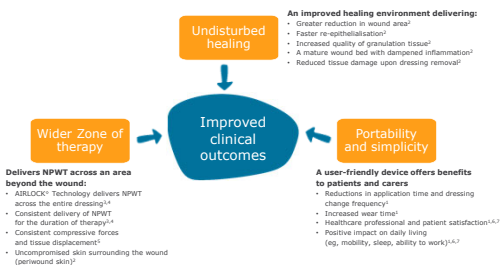
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The MOA of PICO is down to three key attributes which leads to improved clinical outcomes



PICO® NPWT mechanism of action

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PICO® NPWT mechanism of action
